EDITORIAL
Scabies Then and Now
Lavery, Parish, and Wolf

ORIGINAL CONTRIBUTIONS
Erlotinib-Induced Scalp Perifolliculitis
Rallis, Petronic-Rosic, and Korfitis

New Findings in Delusions of Parasitosis
Fellner

REVIEW
Wound Care in Short-Term Rehabilitation Facilities and Long-Term Care: Special Needs for a Special Population
White-Chu and Reddy

CORE CURRICULUM
Cutaneous Tuberculosis: A Diagnostic Dilemma—Laboratory Inputs
Sehgal, Verma, Bhattacharya, Sharma, Singh, and Verma

DEPARTMENTS
PERILS OF DERMATOPATHOLOGY
Sometimes It Takes Darkness to See the Light: Pitfalls in the Interpretation of Cell Proliferation Markers (Ki-67 and PCNA)
Castilla, McDonough, Tumer, Lambert, and Lambert

INFECTIOUS DISEASE CAPSULES
The Lion Is NOT Sleeping Tonight
Carr, Bernstein, and Trevino

PHOTO CAPSULES
Actinomyctoma
Dlova and Mosam

CASE STUDIES
Malignant Melanoma Arising Within Nevus Spilus
Karam and Jackson

Pseudocyst of the Auricle: An Uncommon Entity of the Ear
Sheaffer, Sahu, and Lee

Necrotic Ulcer: A Manifestation of Leukemia Cutis
Aksu, Saracoglu, Sebuncu, Ciftci, Gulbas, and Isikoy

Inflammatory Linear Verrucous Epidermal Nevus With Genital Involvement
Balci, Yenin, Çelik, Sarikaya, and Atik

Oral Frictional Hyperkeratosis (Morsicatio Buccarum): An Entity to Be Considered in the Differential Diagnosis of White Oral Mucosal Lesions
Cam, Santoro, and Lee

Vesicular Palmoplantar Pityriasis Rosea
Singh, Sharma, Nanang, and Madan

BOOK REVIEW
Hall's Manual of Skin as a Marker of Underlying Disease
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Michael Joseph Lavery, MB BCh BAO; Laurence Charles Parish, MD, MD (Hon); Ronni Wolf, MD

ORIGINAL CONTRIBUTIONS

Erlotinib-Induced Scalp Perifolliculitis
Efstathios Rallis, MD, PhD; Vesna Petronic-Rosic, MD, MSc; Chrysovalantis Korfitis, MD

New Findings in Delusions of Parasitosis
Michael J. Fellner, MD

REVIEW

Wound Care in Short-Term Rehabilitation Facilities and Long-Term Care: Special Needs for a Special Population
E. Foy White-Chu, MD; Madhuri Ruddy, MD, MSc

CORE CURRICULUM

Virendra N. Sehgal, MD, Section Editor

Cutaneous Tuberculosis: A Diagnostic Dilemma—Laboratory Inputs
Virendra N. Sehgal, MD; Prashant Verma, MD; Sambit N. Bhattacharya, MD; Sonal Sharma, MD; Narjees Singh, MD; Nishant Verma, MD

DEPARTMENTS

PERILS OF DERMATOPATHOLOGY
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Sometimes It Takes Darkness to See the Light: Pitfalls in the Interpretation of Cell Proliferation Markers (Ki-67 and PCNA)
Carmen Castilla, BS; Patrick McDonough, BA; Gizem Tumer, MD; Peter C. Lambert, BA, MS; W. Clark Lambert, MD, PhD

INFECTIOUS DISEASE CAPSULES
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CASE STUDIES
Veena Petronic-Rosic, MD, MSc, Section Editor

Malignant Melanoma Arising Within Nevus Spilus
Susan L. Karam, BS; Scott M. Jackson, MD

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Alexis Shaffer, BS; Joya Sabu, MD; Jason B. Lee, MD

Necrotic Ulcer: A Manifestation of Leukemia Cutis
Ayse Ezra Koku Akeu, MD; Zeyneb Nurhan Saracoglu, MD; Ilham Sabuncu, MD; Evrim Cifci, MD; Zafer Gulbas, MD; Serap Isiksoy, MD

Inflammatory Linear Verrucous Epidermal Nevus With Genital Involvement
Didem Didar Balci, MD; Jülide Zehra Yenin, MD; Ebru Çelik, MD; Gökhan Sarıkaya, MD; Ersin Atik, MD
Oral Frictional Hyperkeratosis (Morsicatio Buccarum): An Entity to Be Considered in the Differential Diagnosis of White Oral Mucosal Lesions .......................................................... 114
Kristin Cam, MD; Anthony Santoro, MD; Jason B. Lee, MD

Vesicular Palmoplantar Pityriasis Rosea ........................................................................... 116
Varinder Singh, MD; Meghna Sharma, MD; Tarun Narang, MD; Manas Madan, MD

BOOK REVIEW
Noah S. Schieinfeld, MD, JD, Section Editor

Hall’s Manual of Skin as a Marker of Underlying Disease ................................................ 120
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There’s a squeak of pure delight from a matey little mite,
As it tortuously tunnels in the skin,
Singing furrow, folly furrow, come and join me in my burrow,
And we’ll view the epidermis from within.

Why should scabies remain a problem after centuries of knowing about its existence? Even Aristotle recognized this ectoparasitic disease. By the time of the scandal in Albert’s clinic in the early 19th century, with the cheese mite being substituted for the scabies mite, some laypeople often knew something of the ins and outs of the disease, but physicians were reluctant to make the correlation of the mite with the affliction.

People have been repelled and yet fascinated by this “matey little mite,” as confirmed by the audience laughing, but being equally disgusted by the cheese mite in a film documentary in 1903.

The cheese-mites asked how the cheese got there,
And warmly debated the matter;
The Orthodox said that it came from the air,
And the Heretics said from the platter.
They argued it long and they argued it strong,
And I hear they are arguing now;
But of all the choice spirits who lived in the cheese,
Not one of them thought of a cow.

This witty poem mirrors man’s inability to eradicate the scabies mite, which has survived for thousands of years despite Bonomo’s conclusive proof in 1687 of the causative organism, how scabies could be spread and its effective treatment.

INCIDENCE

Scabies is not a small, global problem, because 300 million cases annually are suspected worldwide with US incidence approximating 1 million. The UK mean prevalence is 2.27 per 1000 in boys and men and 2.81 in 1000 in girls and women, where 1 in 1000 people consult their family physician about the intense itching.

This politically correct organism is nondiscriminatory, affecting both sexes, every social class, and all ages and races, although African Americans have been shown to have a lower prevalence.

CONTRIBUTING FACTORS

Scabies develops through personal contact. Whether it is from the few minutes a caregiver has contact with the scabetic patient or whether the personal contact has to do with sexual contact, the patient develops an itch—sometimes euphemistically known as the 7-year itch. Mellenby, during World War II noted that 1 volunteer of 127 who slept in a bed, which had been used the previous night by someone with scabies, would contract the infestation. A higher incidence has been found in the winter than the summer in several countries, which may be due to overcrowding in cold conditions. Some dispute a wax or wane cycle, although Downs reported 15- to 20-year peaks.

ENTOMOLOGY

Sarcoptes scabiei var. Hominis is an ectoparasite that belongs to the Arachnida class and has 8 legs (Figure 1). It is microscopic with a 4-stage, 4-week life cycle. After fertilization, the female mite, which reaches up to 0.45 mm, remains fertile for life. It burrows into the epidermal layer; releases proteases, which break down the stratum corneum, upon which it subsequently feeds; and then plants its eggs in the stratum granulosum. Sarcoptes scabiei live for around 3 to 4 weeks in the host’s skin with the females burrowing their eggs. Only a maximum of 10% of these eggs will survive to adulthood. Contrary to common thought, the scabies mite can live for up to 72 hours with no human contact.

CLINICAL FEATURES

Clinical features typically appear after 48 hours if the patient has had scabies in the past and between 2 and 10 weeks for a first exposure.

The classical picture involves red papules in the finger webs (Figure 2), on the penis (Figure 3) and/or the breast, or with scattered lesions on the body, each causing nocturnal pruritus. The face is spared, except for in immunocompromised patients, children, and the elderly. Explanations for this distribution are inconclusive. A more intense infestation is seen in patients who
Figure 1. The scabies mite, showing 8 legs.

Figure 2. The characteristic red papules on the finger webs.

Figure 3. Red papules on the penile corona indicating scabies, until proven otherwise.

Figure 4. Crusted scabies in an older man who had neglected himself.

Usually, 10 to 20 females can be observed in the burrows; however, it has been reported that this number can be much higher. There may be up to 2 million in a patient with crusted scabies, with some communities, eg, Aboriginal communities in Australia, having an endemic of crusted scabies. Investigations include dermatoscopy, scraping of burrows, or biopsy for microscopic examination.

TREATMENT

Treatment is far easier than the past use of vapor baths and sulfur ointments. Contemporary therapy involves topical permethrin applied over the body for 12 hours, which has supplanted the long-time standard of topical lindane. More recently, oral ivermectin has been used. Because a patient may be asymptomatic and infectious for up to 10 weeks, all contacts should be treated to eliminate the infestation. If the patient does not regularly change clothing, sheets, or towels, then bed linen and clothing should be machine-washed at >140°F or kept in storage for up to 2 weeks.

There is always concern regarding resistance; however, this has not been documented with the current regimens. More
often than not, lack of compliance or re-infestation has been considered resistance, which it is not.  

CONCLUSIONS

Scabies is a significant worldwide infection, affecting 5% of the global population. Effective topical and oral therapies are available, but the mite has not been eliminated. Overcrowding, unsanitary conditions, and sexual promiscuity may increase the risk of infection. To manage scabies successfully, the goal should be to address these risk factors and adequately treat all patients and their contacts.

Poor Giovanni Bonomo,
Would be filled with such woe,
To have this tiny little mite,
Still causing affliction by its bite.

REFERENCES

Erlotinib is a highly specific epidermal growth factor receptor tyrosine kinase inhibitor that is used to treat various metastatic cancers. It acts by targeting the overexpressed EGFRs on cancer cells, which have been related to chemoresistance and poor prognosis. The most commonly reported side effects in patients receiving erlotinib are dermatitis and diarrhea. We present two cases of erlotinib-induced severe scalp perifolliculitis.

CASE 1

The patient was a 75-year-old woman who was administered erlotinib 150 mg daily for metastatic non–small cell lung cancer. She was referred to our department because of a 2-week appearance of extensive, thick, greenish and yellowish, crusted lesions of the scalp (Figure 1 and Figure 2). Folliculitis with perifollicular inflammation, green exudate, and diffuse scaling were present, along with an intense foul-smelling odor. The lesions began to develop within the first week after commencement of erlotinib therapy. No preexisting scalp condition was reported.

A 3-mm punch biopsy was performed by her physician and an inflammatory cell infiltrate with perifollicular distribution was demonstrated. Mycologic examination from scaling and smears of pus was negative, while bacteriologic examination revealed the presence of methicillin-resistant *Staphylococcus aureus*. The diagnosis of erlotinib-induced folliculitis with impetiginization was made. The patient continued to receive erlotinib, and doxycycline 100 mg twice daily for 14 days was added based on the antibioticogram with daily application of mupirocin ointment 2% to the nares and external auditory canals. In addition, a sunscreen of sunburn protection factor 30 or higher was suggested. The lesions subsided within 2 weeks and no relapse was seen 2 months after doxycycline discontinuation.

CASE 2

The patient was a 70-year-old African American woman who developed a tender “burning” scalp eruption 2 weeks after starting oral erlotinib 150 mg daily for metastatic non–small cell lung carcinoma. She presented with numerous pustules and thick yellow-green crusting of the scalp (Figure 3). Culture results for fungi and bacteria were negative. Skin biopsy revealed a perifollicular accumulation of inflammatory cells, lymphocytes, and neutrophils. Oral doxycycline 100 mg twice a day was administered for 3 weeks, at which point the eruption was completely clear (Figure 4) and the medication was discontinued, with no recurrence at 3-month follow-up visit despite continuation of erlotinib therapy.

DISCUSSION

The EGFR is implicated in a variety of malignancies, and its expression is associated with advanced disease and poor prognosis. Agents targeting the EGFR have emerged as a promising therapy against cancer. Erlotinib is indicated for the treatment of chemotherapy-resistant non–small cell lung cancer. When compared with standard chemotherapy, this targeted therapy has fewer nonspecific toxicities and is devoid of hematopoietic side effects.

In spite of their increased specificity, the use of EGFR inhibitors (EGFRIs) leads to the development of a papulopustular eruption on the face and upper aspects of the trunk in 45% to 100% of patients, and may result in anticancer drug dose decrease, interruption, or discontinuation. A similar eruption is seen on 75% to 79% of patients treated with erlotinib. Its pathogenesis...
is poorly understood. Erlotinib interacts with EGFRs that are expressed in epidermal keratinocytes, sebaceous and eccrine glands, and hair follicle epithelium. It inhibits the EGFR tyrosine kinase, leading to growth arrest and inflammation. It also alters keratinocyte proliferation, probably resulting in occlusion of the hair follicle due to a lack of differentiation and favoring bacterial overgrowth, thus exacerbating inflammation.²

Although it is commonly referred to as acne or an acneiform eruption, these designations are inaccurate based on clinical and histological findings. Clinically, the eruption is devoid of comedones and the lesions are pruritic or tender. Patients frequently report a “burning” sensation, which is exacerbated by the use of some acne therapies, such as retinoids or alpha-hydroxy acids. Histologically, the sebaceous glands are not affected, and comedones are not observed; however, topical and/or oral anti-inflammatory acne treatments may be beneficial.²

In distinguishing this type of eruption from the typical acneiform eruption of the face, neck, chest, and back that is associated with EGFRIs,⁴ both our patients developed an eruption from erlotinib that consisted of pustules with perifollicular inflammation and yellow-green crusts of the scalp. They were also distinct from the single case report of a psoriasiform scalp dermatitis reported previously.⁵ The unique presentation in our patients is puzzling, as it cannot be easily explained why the eruption was confined to the scalp and why it did not extend to the neck and trunk. It has been suggested that the erlotinib-induced eruption improves despite continuation of treatment; nevertheless, if the reaction is quite severe, it may lead to discontinuation of treatment.² Physicians, including dermatologists, should recognize the event, counsel patients about the various aspects of developing an erlotinib eruption, and treat it appropriately.

REFERENCES


Figure 1. Case 1: Thick, malodorous, greenish and yellowish, crusted lesions on the scalp.

Figure 2. Case 1: Thick yellow-green crusts on the scalp.

Figure 3. Case 2: Numerous pustules covered with thick yellow-green crusts on the scalp before treatment.

Figure 4. Case 2: Same patient after 3 weeks of therapy with oral doxycycline.
NEW FINDINGS IN DELUSIONS OF PARASITOSIS

Michael J. Fellner, MD

ABSTRACT

Two new cases are presented with delusions of parasitosis. Both were women, one middle-aged and one elderly, and exhibited classic symptoms of parasites and "strings" in the skin indicative of Morgellons disease. Each had an additional psychiatric disorder: drug addiction to cocaine and senile dementia. They also illustrate the difficulty encountered by the dermatologist in providing adequate therapy because of resistance to psychiatric referral as well as to standard accepted medication. Newer psychotropics, such as risperdal and lexapro, show promise in helping these patients and add to the therapeutic armamentarium of pimozide. (SKINmed. 2012;10:72–74)

ORIGINAL CONTRIBUTION

New Findings in Delusions of Parasitosis

Michael J. Fellner, MD

Two new cases are presented with delusions of parasitosis. Both were women, one middle-aged and one elderly, and exhibited classic symptoms of parasites and "strings" in the skin indicative of Morgellons disease. Each had an additional psychiatric disorder: drug addiction to cocaine and senile dementia. They also illustrate the difficulty encountered by the dermatologist in providing adequate therapy because of resistance to psychiatric referral as well as to standard accepted medication. Newer psychotropics, such as risperdal and lexapro, show promise in helping these patients and add to the therapeutic armamentarium of pimozide. (SKINmed. 2012;10:72–74)

CASE 1

A 44-year-old African American woman presented with the complaint of “stuff crawling on the skin.” She described in great detail that strings were coming out of her eyelids and eyelashes, causing her great distress. She felt the need to constantly brush off the strings from the eyes with her hands, which caused her hands to feel irritated as well as her face. In addition, she described that “parasites come out of my ears.” She said the parasites made a fuzzing noise in her ears, which she described as resembling the fuzz sound of soda poured into a glass.

She indicated that the onset of the symptoms began approximately 1 year previously, which coincided with abandonment by her lover of 6 years as well as the loss of her job as a social worker. Her medical history revealed that she had been addicted to crack cocaine as well as heroin in the past. She admitted to smoking crack as recently as 3 weeks before the initial visit. In addition, she was taking methadone, which was prescribed by the hospital’s mental health clinic.

She reported to be in otherwise good health expect for an allergy to iodine. After the relationship breakup, she was briefly treated for depression with an antidepressant by a mental health clinic. She refused to return to the mental health facility due to her perception of stigma over mental illness.

Physical examination revealed mild scaling of the scalp consistent with mild seborrheic dermatitis, scaling of palms and soles, and dystrophic toe nails. The remainder of the physical examination including the face, back, trunk, arms, and legs were within normal limits.

Results from all laboratory tests including complete blood cell count and complete metabolic panel were within normal limits. The patient refused to have a urine toxicology examination.

Treatment was initiated with fluocinolone solution to the scalp as well as the head and shoulders, ciclopirox cream twice a day to the feet for tinea pedis, and permethrin cream to the body for itch.

She had previously used Sarna lotion and hydroxyzine 25 mg every night at bedtime and had her apartment exterminated, with no relief. At the first visit she was started on escitalopram 10 mg every night at bedtime. She refused a psychiatric consultation.

At the second follow-up visit 2 weeks later, the patient reported no improvement in symptoms and, if anything, reported that the “strings” were worse than ever and the parasites were crawling out of her ears and onto her face. She was very angry that she was prescribed a selective serotonin reuptake inhibitor (SSRI). Examination revealed no change compared with the first visit.

The patient was encouraged to ventilate about her problems. Lidocaine/prilocaine cream was prescribed for dysesthesias and feelings of formication and she was encouraged to increase the dose of escitalopram to 20 mg at night.
CASE 2

A 90-year-old woman was referred from a major medical dermatology center with a diagnosis of delusions of parasitosis. On the first visit she described worms and strings coming out of her body including the skin, eyes, and mouth. She reported the onset as September 2009 following a bout of diarrhea during the summer that lasted for 2 months. She was treated with albendazole by a noted parasitologist for trichuris infection. The diarrhea abated with the treatment.

By September 2009, she had described worms and strings coming out of her body, causing her great discomfort. She first went to her primary care physician at the medical school center. He examined the material she brought and told her there were no parasites or strings but only mucous. This angered her and she refused to return to the physician. She brought a drawing of the worms and strings on her first dermatology visit (Figure 1).

Examination revealed a thin elderly woman in no acute distress whose stream of thought was verbose and rambling. The skin showed a reddened and ulcerated area on the right thigh (Figure 2). The remainder of the physical examination was within normal limits. Results from laboratory tests were within normal limits. The patient was given mupirocin ointment for the ulcer and ammonium lactate 12% lotion for the skin on the body and was reassured there was some possibility that the disturbance might abate.

On follow-up 2 weeks later, she claimed the parasites had started in June 2009, contradicting her previous statement that they had started in September 2009. She now claimed slight improvement with the treatment. There were, however, new lesions on the right thigh (Figure 3). Once again she was unclear about whether these resulted from the parasites. She indicated that the strings and worms were coming out of her ears, eyes, nose, and skin on the face.

She was encouraged to take doxepin 25 mg at night and continue with ammonium lactate 12% lotion and mupirocin ointment. She was also encouraged to ventilate about her multiple social problems, including her family, her will, and her eating problems. She said she weighed 87 pounds because she was unable to eat any carbohydrates since she believed the parasites lived on sugars. She said she was in the process of getting assistance in daily-living activities at home.

Figure 1. The patient’s drawing of string and parasite coming out of her skin.

Figure 2. The patient’s thigh lesion on first visit.

Figure 3. The patient’s thigh lesions on second visit.
On third follow-up, she said she felt considerably better (2 weeks after second visit) using emollients. She did not mention parasites, but said the problem was improving. She was encouraged to seek psychologic or psychiatric counseling but was not accepting of this suggestion. She said she was going to make an appointment for a visit at a nearby medical center geriatric unit to help her with nutrition and memory problems. She was encouraged to take doxepin at bedtime and to use emollients.

**DISCUSSION**

These cases are the first to exhibit findings of Morgellons disease and delusions of parasitosis at the same time. Morgellons is a pattern of dermatologic symptoms very similar, if not identical, to those of delusions of parasitosis, and many patients with Morgellons are diagnosed with another psychosomatic illness.2 In delusional parasitosis, patients hold a delusional belief that they are infested with parasites. They may experience formication, the sensation that insects are crawling under the skin. It is a common symptom in cocaine abusers as well. Individuals who experience this condition may develop elaborate rituals of inspection and cleansing to locate and remove parasites and fibers, resulting in a form of self-mutilation; they injure themselves in attempts to be rid of the “parasites” by picking at the skin, causing secondary lesions. Continuous picking of the lesions prevents healing. Patients with delusional parasitosis often present at the doctor’s office with what physician’s term the matchbox sign, a medical sign characterized by the patient making collections of fibers and other foreign objects supposedly retrieved from the skin, and, because of “unshakeable delusional ideation,” strongly reject diagnoses that do not involve parasites. The Morgellons Research Foundation, a nonprofit organization, considers Morgellons to be a newly emerging infectious disease, but the medical community disagrees, noting that the described symptoms of Morgellons are associated with the psychotic disorder known as delusional parasitosis.2

Due to the second patient’s age, it was deemed inappropriate to give pimozide or treatment with an SSRI medication since sudden death in the elderly has been reported.3 The treatment plan was to gain the patient’s confidence before attempting to refer her for psychologic or psychiatric care, since there did not appear to be any insight on her part at the first 2 visits.

Therapy is often unsuccessful because many patients, such as those reported here, refuse consultation with a psychiatrist either because they believe the problem is organic or because they fear mental illness and the stigma of psychiatry. In extremely severe cases, suicide has been reported, illustrating the urgency of corrective medication and prompt psychiatric referral.4 Standard treatment with pimozide risks substantial side effects.3 This has led to trial with additional psychotropic agents. Recent success has been reported with the use of risperdal5 and olanzapine.6

Nowhere have these diseases been more graphically illustrated than in the Oscar-nominated 2010 film “Black Swan” wherein the heroine played by Natalie Portman suffers from the delusion that parasites and strings are coming out of her skin. This is a must-see film for dermatologists and psychiatrists alike.

**REFERENCES**


REVIEW

Wound Care in Short-Term Rehabilitation Facilities and Long-Term Care: Special Needs for a Special Population

E. Foy White-Chu, MD; Madhuri Reddy, MD, MSc

ABSTRACT

Chronic wounds can pose a challenging diagnostic and treatment dilemma in the older frail adult population. The benefits of short-term rehabilitation and long-term care settings are the access to interdisciplinary resources. Rehabilitative specialists, dieticians, and skilled nurses are readily available to meet the patients’ needs as they transition to home or remain in a long-term care setting for their higher level of care needs. This article follows 3 cases: a skin tear complicated by venous ulceration, a pressure ulcer with fever, and arterial ulcers in a patient who opts for comfort care. The cases illustrate the higher needs of this population and emphasize the attention that must be paid to respect nursing-time intensiveness, incorporate realistic goals of care for wound healing, and ensure excellent communication with the team members, patients, and family. (SKINmed. 2012;10:75–81)

CASE 1: SKIN TEAR THAT IS SLOW TO HEAL

The wound care team was asked to examine an 80-year-old woman for a skin tear that was slow to heal. The skin tear occurred with a leg scratch while donning compression stockings. The wound became infected, leading to her hospitalization and subsequent short-term rehabilitative stay. Her wound infection resolved, but the wound remained. She reported a significant medical history of chronic myelomonocytic leukemia and myelodysplastic disorder, for which she took hydroxyurea and prednisone. Her examination revealed venous stasis changes, pitting edema, and 2+ palpable pulses bilaterally. Her wound was tender to any touch. A lidocaine/prilocaine mixture cream was applied with an occlusive dressing 1 hour prior to bedside debridement. She tolerated the debridement well, and the results are seen in Figure 1. A local dressing of a thin film of silver sulfadiazine with a nonadherent foam dressing was applied to the wound. The leg was wrapped with a multilayer compression wrapping (Figure 2). The patient and nursing staff were educated on proper wrapping technique. The physical therapy team coordinated an intense walking program with the patient while the dietician optimized her nutrition. Wound healing expectations were presented to the patient, explaining that her hematologic diseases and need for immuno-suppressive medications will slow wound healing, but that the wound did have the potential to heal.

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not cause pressure ulcers. The intervention to promote healing in a skin tear in this location is different from the approach for pressure ulcers. Due to the high litigious factor surrounding pressure ulcers in long-term care settings, it is important that the clinician document clearly whether a wound is a pressure ulcer or not.

The majority of skin tears will heal in 7 to 21 days. For a skin tear that takes longer to heal, the clinician needs to re-evaluate the underlying conditions that are delaying wound healing. For skin tears on the lower extremities, a physical examination must be completed to evaluate for concomitant arterial and/or venous disease. Table I lists the do’s and don’ts of skin tear prevention.

VENOUS ULCERS
Venous ulcers have a higher incidence and prevalence in long-term care facilities than in the community. As in all wounds, healing the venous ulcer takes an interdisciplinary approach. Nurses educate patients on the importance of edema control with compression bandaging. Rehabilitative therapists coordinate a walking program. Studies suggest that walking improves the calf pump muscle function and thus increases the venous ejection fraction. Worse calf pump muscle function is related to more severe ulcers. Clinicians evaluate pain management and titrate medications as appropriate. As needed, acetaminophen or low-dose opioids may be necessary to facilitate the patient’s ability to exercise and/or tolerate compression. Venous ulcers can be painful, and studies suggest that pain is undertreated.

Compression is the most important aspect for the prevention and treatment of venous leg ulcers. Offering various levels of compression based on the patient’s tolerances and coexisting peripheral arterial disease is recommended. Compression can be safely applied as long as there is not significant arterial disease and the patient does not have uncompensated congestive heart failure. A greater number of layers allow for tighter compression, and tighter compression leads to an increased likelihood of venous ulcer healing. Lower compression may be indicated

Table I. Prevention of Skin Tears

<table>
<thead>
<tr>
<th>Do</th>
<th>Don’t</th>
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<tbody>
<tr>
<td>Advise moisturizers</td>
<td>Wear very tight clothing</td>
</tr>
<tr>
<td>Review medication list to minimize falls</td>
<td>Forget to check friction prone areas in chair/bed bound patient (eg, occiput, elbows, knees, and heels)</td>
</tr>
<tr>
<td>Use paper tape or soft silicone for wounds</td>
<td>Use regular tape for occlusive dressings</td>
</tr>
<tr>
<td>Consider shin pads/padding furniture</td>
<td>Hesitate to form an interdisciplinary care plan with nursing staff on transfers</td>
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</tbody>
</table>
because of patient preference, especially with older adults. Some compression is better than none at all.\textsuperscript{13,14}

For patients who have some peripheral arterial disease but significant edema, the edema may cause further compromise of arterial flow. These patients still benefit from some form of compression.\textsuperscript{19} Assess the patients’ arterial flow by palpating pedal pulses. If no pulses are palpated, but there is significant edema in the feet, then attempt mild compression with a compression \textit{stocking} (ie, elasticized tubular bandage) rather than wrapping. Thromboembolic stockings are used only for bedfast patients and are not considered a form of compression stockings.\textsuperscript{16} Coordinate with nurses to follow pain levels and discoloration of the toes and to remove the stocking if any complications arise.

For patients who have palpable pulses, offer elastic compression wrapping. This is made up of 2 to 3 layers of compression wrapping—cotton-absorbent (gauze) layer, followed by an elastic wrap, followed by an elastic self-adherent bandage. Each layer is laid down at 50% stretch with 50% overlap. If the patient’s ankle is <18 cm in circumference, or if the patient finds the 3 layers to be uncomfortable, omit the second layer. Care must be taken to not overstretch each layer, as this can cause new areas of breakdown. If ballooning of the foot occurs, this is because of too much compression at the ankle. Avoid the use of a nonelastic system (eg, Unna boot) because this is a form of support that exerts high pressure with walking only.\textsuperscript{17} Many patients who are either just out of the hospital or live in long-term care are not ambulatory, and thus would not benefit from a nonelastic system for edema management.

To determine the vascularity of the foot wound in order to determine the wound’s ability to heal, consider collaboration with a vascular surgeon who does toe photoplethysmography. Ankle-brachial indices (ABIs) may not be specific in older patients or patients with diabetes because of vessel calcification and non-compressible vessels (ie, they may overestimate the amount of blood flow).\textsuperscript{10} Toe photoplethysmography, also known as toe pressure, is performed in most tertiary care center vascular laboratories in addition to the ABIs. Toe pressures provide a much more accurate determination of vascularity in a person with diabetes. Toe pressures 50 mm Hg are considered adequate for healing, 30 mm Hg to 50 mm Hg are considered borderline for healing, and 30 mm Hg is likely inadequate for healing to take place. Palpable dorsalis pedal pulses usually indicate a toe pressure of 80 mm Hg, and no further noninvasive testing may be necessary.\textsuperscript{18}

Wound drainage impacts the frequency of dressing and wrapping changes. For the majority of wounds, the wrapping and dressing may be changed no more than every 3 days. This allows for edema management without decompression of the leg with frequent unwrapping. Considering how nursing-intensive these wrappings can be, changing every 3 days lowers the nursing burden and ensures better wrapping technique. For highly exudating wounds, an incontinence garment can be used over the wound product, followed by the compression wrapping. These dressings are changed daily until the drainage has decreased to where it can be changed less frequently. A Cochrane review of dressings for venous leg ulcers found that there was inadequate data to support one form of dressing over another; therefore, they recommended choosing a dressing based on local costs and provider or patient preferences.\textsuperscript{17} The challenges and treatments of venous ulcers are mentioned in Table II.

### Case 2: Stage IV Pressure Ulcer and Fever

The wound care team was asked to see a 68-year-old woman regarding a stage IV pressure ulcer and fever. She had a significant medical history of diabetes mellitus and end-stage renal disease (on hemodialysis). The wound developed at home when she refused to participate in rehabilitative therapy after her femoral fracture, which occurred at least 6 months prior to her admission to the short-term rehabilitative facility. The patient was not adherent to her rehabilitative regimen, stating she was too tired. To address this, her sedating medications were reduced by the geriatrician, and her dialysis regimen was optimized by the nephrologist to curtail low blood pressures. She continued not to engage in therapy, and the patient insisted on sitting up in bed or in a chair.

### Table II. Venous Ulcer Challenges and Treatments

<table>
<thead>
<tr>
<th>PROBLEM</th>
<th>APPROACH</th>
</tr>
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<tbody>
<tr>
<td>Edema</td>
<td>Compression bandaging (as much as patient can tolerate or is medically acceptable) until and for 2 weeks after wound has completely healed, then lifelong compression stockings. Medical contraindications to compression include: severe peripheral arterial disease and unstable congestive heart failure.</td>
</tr>
<tr>
<td>Impaired calf muscle pump function</td>
<td>Walking: range of motion exercises for the ankle</td>
</tr>
<tr>
<td>Pain</td>
<td>As needed acetaminophen or low dose opioids may be necessary to facilitate patient’s ability to exercise and/or tolerate compression. In acute lipodermatosclerosis, non-steroidal anti-inflammatory may be helpful short-term.</td>
</tr>
<tr>
<td>Donning compression stockings after healing</td>
<td>Utilize stocking aids. Consider custom stockings with zippers or Velcro—although more expensive they will be easier to apply.</td>
</tr>
</tbody>
</table>

*SKINmed. 2012;10:75–81*
for most of the day. Per standard of care at this facility, she had a specialized wheelchair cushion and powered mattress put in place, along with friction reducing devices for transfers in her bed.

The initial state of this increasingly painful wound is pictured in Figure 3. There was a foul odor present and the granulation tissue was friable and bled easily. Intravenous antibiotics were started, since most likely the fever was caused by this wound. Because the wound could not be adequately offloaded as a result of the patient’s nonadherence to rehabilitative therapies, the wound was temporarily treated as a wound without the potential to heal. The wound was packed with povidone-iodine-soaked gauze throughout the wound. Mirrors were set up in the patient’s room so she could see the wound during our examination. It was shortly after this intervention that the patient began to actively participate in rehabilitative therapies. Her plastic surgeon was contacted for further operative debridement of the wound, because her blood cultures continued to demonstrate bacteremia. Once she returned to the short-term rehabilitative unit, the patient’s wound care orders were changed to reflect a wound that had the potential to heal, and moist wound healing was implemented. The patient engaged in therapy and maintained good diabetic nutrition under the guidance of a dietician. The patient was eventually discharged to another facility prior to her transition to home. The patient was followed by the wound care team in the outpatient clinic, and 7 months after initial consultation, the wound continued to improve, as shown in Figure 4. This patient’s wound eventually healed entirely without any need for surgical repair.

PRESSURE ULCERS

In the United States, since October 2008, the Centers for Medicare and Medicaid Services no longer reimburses acute care facilities for treatment of pressure ulcers that have developed in-house. This legislation was based on the belief that pressure ulcers are largely preventable. A recent consensus statement from the National Pressure Ulcer Advisory Panel stated that not all pressure ulcers are avoidable and that the condition of skin failure does exist.19,20 Although it remains to be seen how this legislative decision will impact pressure ulcer prevention and treatment, it does emphasize the importance of skin surveillance and protection. Incidence rates of pressure ulcers in long-term care facilities range from 2% to 23%. In comparison, incidence rates in acute care range from 2.2% to 38% and 0% to 17% in home care.21,22 Pressure ulcers can be problematic in not just the patient, but also to the facilities, as failure to heal or prevent them can lead to litigation.23 Pressure ulcers primarily present over bony prominences, including the sacrum, heels, hips, and elbows. They can also occur anywhere that skin is damaged by excessive pressure, friction or shear, or excess moisture.24 This is illustrated by the striations from the negative pressure device tubing on the posterior thighs, as seen in Figure 3. Risk factors are numerous, but primarily include immobility. Malnutrition also plays an important role.22 Determining the exact cause of the pressure ulcer is essential to enhance healing.24,25

Confirm with the facility whether they use a nonpowered specialized mattress. For pressure ulcers that are in stage III or IV, a powered overlay or mattress may be ordered. Rehabilitative therapists can evaluate wheelchairs and cushions every 2 years for patients who are primarily wheelchair users. Any skin breakdown that can be attributed to sitting should also prompt an evaluation of the chair and cushion. Specialized wheelchair cushions—gel, gel-foam, or air-filled—can be implemented after the therapist has evaluated the wheelchair. Strict
bed rest is not recommended, as this may lead to worsening failure to thrive, depression, deconditioning, pneumonia, deep venous thrombosis, and more pressure ulcers. These recommendations regarding bed rest, powered devices, and specialized wheelchair cushions are based on the National and European Pressure Ulcer Advisory Panel Guidelines. The evidence, as reviewed by the panel and also in recent systematic reviews, did not find that powered mattresses were superior to nonpowered mattresses either for prevention or treatment. Rather, the guidelines were based on expert opinion. Support surfaces are important for offloading of pressure, but they do not address the other ulcer causes, such as friction, shear, and moisture. In short, nothing can replace good personal attendant care with frequent turning, incontinence care, and lifting and transfers that minimize friction and shear.

Moist wound healing is widely employed in ulcer management; however, in some clinical situations, moist wound healing may increase bacterial burden and infection risks. In these situations, antiseptics may be necessary to prevent wound worsening. Povidone-iodine is a very broad-spectrum antimicrobial with in vitro activity against gram-positive and gram-negative bacteria, including methicillin-resistant Staphylococcus aureus, fungi, and protozoa. Because antiseptics have fallen out of favor by many wound practitioners and have been prohibited altogether in some facilities, it is important to document the potential healability of the wound. If a wound does not have the potential to heal, then this should be clearly stated, including the reasons for poor healability. This documentation will support the use of an antiseptic and will allow the facility to utilize the antiseptic without getting cited by state surveyors.

CASE 3: TOE ULCERS AND REFRACTORY PAIN

A 97-year-old woman with a significant medical history of lymphedema, coronary artery disease, and atrial fibrillation who had lived at the long-term care facility for 8 years was seen for pressure ulcers on her heels. The patient reported significant pain at rest and at night in her bilateral legs that was relieved with dependency. She could not tolerate any compression wrapping, and she preferred to sit in her wheelchair most of the day. On examination she had multiple ischemic ulcerations on her toes, as well as purplish discoloration on her heels and a large, painful skin tear on her right leg. No palpable pulses and no signal via Doppler were found. In the past, the patient had preferred comfort care measures, including do not hospitalize; however, the patient and family opted for hospital transfer to address the refractory ischemic pain.

The wound care team contacted the vascular surgeon prior to hospital referral to clarify the patient’s goals of care and objectives of intervention, if any, to help with the pain. Noninvasive studies revealed severe lower-extremity arterial disease that may only be amenable to a bypass procedure. Both the patient and her family declined surgery, again opting for comfort care, and the patient returned to the long-term care facility with a palliative care consultation.

Modalities to help the pain, including oral opiates, nitroglycerin patch on the dorsum of her foot, and allowing her to hang her legs dependently were all offered to the patient. She developed a coccyx pressure ulcer from the prolonged sitting, despite a specialized cushion and wheelchair to offload the area. The patient’s family was informed of the skin breakdown; they requested to follow the patient’s wishes to stay sitting for most of the day as a pain relief modality and also quality-of-life enhancer. As the patient’s pain worsened with progression of the peripheral arterial disease, including pain with any passive movement for hygiene, so did her wounds (Figure 5). The palliative care team advised increasing pain and anxiety medications and to time these with hygiene care. The patient died within 1 month of the initial consultation.

PALLIATIVE WOUND CARE

Due to the frailty of older patients, some may opt to not have aggressive measures. Their experiences with repeated hospitalizations and interventions prove to be traumatic, and the patients may find themselves worse off after a hospitalization. As part of the provider’s assessment, the goals of care should be addressed with the patient and/or family. The provider should discuss—and document—the potential healability of a wound and what measures must be taken to increase healability.

Pain management for arterial ulcers is challenging. A palliative care specialist can facilitate communication with the family on

Figure 5: Worsening arterial ulcers. Photo courtesy of E. Foy White-Chu, MD.
the natural progression of disease, assess nonpharmacologic modalities for comfort, and offer advice on oral medications, such as opiates or gamma-aminobutyric acid analogs (e.g., gabapentin). Topical locally applied nitroglycerin patch application can sometimes be useful for pain management. Nitroglycerin patches should only be used in ulcers that do not have the potential to heal. Ischemia is a very potent vasodilator, and there is some concern that the calf muscle blood supply will dilate further and “steal” the blood from the foot.36 There are some studies that suggest topical nitroglycerin to ameliorate pain in patients with diabetic neuropathy and other ischemic processes.37,38 A 2-week trial of a locally applied (dorsum of foot), low-dose nitroglycerin patch 0.1 mg/h to 0.2 mg/h may be attempted. The patient, family, and long-term care staff should be educated that this medication is for pain management only and not for wound healing. If there is no improvement in pain after 2 weeks, then the medication should be discontinued.

Keeping the ischemic extremities dependent can also improve pain. As in this patient, prolonged sitting can put a patient at risk for pressure ulcers, specifically in the coccyx and ischial regions. Rehabilitative specialists, in collaboration with nurses and personal care attendants, can recommend specialized wheelchairs and cushions that offload the pressure points but maintain the patient’s pain control of the ischemic extremities.

CONCLUSIONS

The short-term rehabilitative and long-term care settings are unique opportunities for wound care. The patients have the advantages of an interdisciplinary team that can approach wound healing from multiple angles: optimizing nutrition, offloading with rehabilitative therapies, assistance in personal care and turning, and titration of medications as appropriate. The outside provider, who is seeing these patients in their clinic, should pay special attention to the patient’s goals of care, the optimization of wound healing without conflicting with the patient’s daily activities and rehabilitative sessions, and the nursing intensiveness of dressing changes. Most importantly, the provider must be available to the primary team. After each patient visit, a brief phone call to the charge nurse or primary care provider can go a long way in facilitating excellent communication and care for the patient.

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REFERENCES

SELF-TEST REVIEW QUESTIONS

W. Clark Lambert, MD, PhD, Section Editor

Instructions: For each of the following numbered questions, choose the appropriate lettered response(s). Unless directed to choose only one lettered response, all, some, or none of the responses may be correct.

1) The most common object and location associated with skin tears in elderly patients are: (Choose the single best response.)
   a. bedrails, with injuries sustained in hospital intensive care facilities.
   b. geriatric recliners, with injuries sustained in doctors’ offices and waiting rooms.
   c. geriatric recliners, with injuries sustained in hospital intensive care facilities.
   d. wheelchairs, with injuries sustained in doctors’ offices and waiting rooms.
   e. wheelchairs, with injuries sustained in the patient's bedroom.

2) A skin tear in an elderly patient should be expected to heal in approximately: (Choose the single best response.)
   a. seven days.
   b. fourteen days.
   c. seven to twenty-one days.
   d. one month to six weeks.
   e. three months.

3) Which of the following statements regarding treatment of venous leg ulcers is (are) correct? (Answer as many as apply.)
   a. Compression is the most important aspect for prevention.
   b. Elevation is the most important aspect for treatment.
   c. Arterial disease is not a contraindication for treatment with compression.
   d. Uncompensated congestive heart failure is a contraindication for treatment with compression.
   e. An Unna boot exerts high pressure with walking only.
   f. Thromboembolic stockings are an excellent choice for compression treatment.

4) Ankle-brachial indices (ABIs) may overestimate the amount of blood flow in: (Choose the single best response.)
   a. elderly patients.
   b. patients with diabetes mellitus.
   c. patients with non-compressible vessels.
   d. patients with vascular calcifications.
   e. all of these are correct.

5) Nitroglycerin patches should be applied: (Answer as many as apply.)
   a. early in management of all symptomatic ulcers in patients over 85 years of age.
   b. early in management of all symptomatic ulcers in patients who smoke more than one pack of cigarettes per day.
   c. for pain management only.
   d. only in ulcers caused by negative pressure devices.
   e. only in ulcers that have been judged not to have the potential to heal.

ANSWERS TO SELF-TEST REVIEW QUESTIONS:

1) e 2) c; 3) a, d, e; 4) e; 5) c, e
Cutaneous Tuberculosis: A Diagnostic Dilemma—Laboratory Inputs

Virendra N. Sehgal, MD; Prashant Verma, MD; Sambit N. Bhattacharya, MD; Sonal Sharma, MD; Navjeevan Singh, MD; Nishant Verma, MD

Bacterial cultures are the gold standard for diagnosing cutaneous tuberculosis, but there are limitations, despite the advances embracing the innovative technologies, including interferon-γ release assays, enzyme-linked immunosorbent assay, and molecular diagnostics, in addition to conventional skin tests and microscopic pathology. The results and their interpretation of cultures are reviewed for use in day-to-day practice.

Cutaneous tuberculosis (TB) is a challenge to clinical diagnosis. It may warrant the application of several novel techniques, which are now available for use, despite the exorbitant cost, both in developing and developed nations. Occasionally, limited resources may prove an impediment; nevertheless, the appraisal of newer modalities is significant and should be used wherever appropriate.

DIAGNOSTIC MODALITIES

SKIN TESTS

Tuberculin Test

The tuberculin test is based on the principle that individuals who have been infected with the tubercle bacilli respond to a delayed-type hypersensitivity reaction at the test site. The interpretation of the test may be complicated by cross-sensitivity, induced by environmental mycobacteria and/or Bacille Calmette-Guérin (BCG) vaccination. Standard tuberculin purified protein derivative (PPD) test is considered useful in the developing world. It involves the intradermal injection of 1 tuberculin unit PPD RT23 with Tween 80 on the mid-volar aspect of the forearm and measurement of the maximum transverse diameter of induration after 3 days, with a proviso that the larger the size of the induration, the higher the probability of its being a tuberculous infection. A size ≥15 mm may be due to infection with tubercle bacilli, irrespective of BCG vaccination status; however, induration <5 mm indicates absence of tuberculin sensitivity. Induration in the range of 5 mm to 9 mm is usually of a nontuberculous nature, while induration of 10 mm to 14 mm is equivocal, requiring a careful interpretation. To confuse the issue even more, the size of induration in an infected individual may be diminished in the presence of immunosuppressive conditions.¹

A patient with a tuberculous chancre usually becomes tuberculin test-positive around the time when lymphadenopathy is apparent, which correlates with T-cell sensitization.²,³ A patient with scrofuloderma most often shows a positive tuberculin skin test (TST),² whereas the test may or may not be positive in a patient with TB cutis orificialis.³ The TST is typically negative in a disseminated miliary TB patient due to anergy,⁴ while it is variable in a patient with a metastatic TB gumma.⁵,⁶ An individual’s TST is usually positive in lupus vulgaris.⁶⁷ Patients with tuberculids are usually in good health but show a positive TST.⁶

Mycobacterial Antigen, MPB64 Transdermal Patch Test

This antigen has been formulated for delivery in a transdermal patch for use as a diagnostic skin test reagent to detect active TB. The test may be useful to distinguish patients with active TB from patients who are TB-infected but asymptomatic. The MPB64 transdermal patch may be useful in monitoring successful chemotherapy.⁸ Unfortunately, there is hardly a report on its use in cutaneous TB thus far.⁹

INTERFERON-γ RELEASE ASSAYS

Quantiferon-TB Gold Test

It is an in vitro diagnostic aid that measures a component of cell-mediated immunity to Mycobacterium tuberculosis and is
based on the quantification of interferon-γ (IFN-γ) released from sensitized lymphocyte. The US Food and Drug Administration (FDA) approved Quantiferon-TB Gold test (QFT-G) in 2005 for the diagnosis of both latent and active TB infections. The antigens used in QFT-G are not shared by the BCG vaccine strain or by a nontuberculous mycobacterium. According to the Centers for Disease Control and Prevention 2005 guidelines, QFT-G can be used in place of the TST, as it has increased specificity, has a lack of cross-reactivity to BCG, and is convenient for both the patient and provider. The concordance rate between TST and QFT-G ranges from 60% to 90%. The usefulness of this test to monitor the efficacy of anti-TB therapy is controversial. A recent study suggested that the QFT-G adds no significant information for treatment monitoring when applied in routine clinical practice in a low prevalence setting. Kinetics of T-cell responses on TB treatment and reversion and conversion thresholds need to be adequately addressed. Diversity of IFN-γ responses among patients of different geographic origins is an issue for further investigation. For IFN-γ release assays (IGRAs) to measure IFN-γ response accurately, a fresh blood specimen that contains viable white blood cells is needed. This requirement limits the use of early IGRAs to facilities in which trained laboratory technicians could begin testing blood within a few hours of its collection. The Quantiferon-TB Gold In-Tube test (QFT-GIT) was developed to address this limitation. QFT-GIT was approved by the FDA as an aid for diagnosing M tuberculosis infection.

**T-SPOT.TB TEST**

Early secretory antigenic target-6 (ESAT-6) and culture filtrate protein 10 (CFP-10) are secreted antigens encoded by a region of difference-1 of M tuberculosis. These antigens elicit IFN-γ secretion by peptide-specific T cells. Accordingly, diagnostic tests have been developed to measure T-cell responses to these antigens. T-Spot.TB (Oxford Immunotec, Inc, Marlborough, MA) is an ex vivo enzyme-linked immune-spot assay that uses overlapping peptide panels to stimulate IFN-γ secretion by ESAT-6 and CFP-10–specific T cells. T-Spot.TB assay showed positive results in 29 of 31 patients with extrapulmonary TB, where the sensitivity was found to be 93.5%. Another recent study assessed the performance of the QFT-GIT and the T-SPOT.TB tests in the immunodiagnosis of active pulmonary TB in adult patients. This study analyzed the T-cell IFN-γ responses during treatment in patients who recovered after curative treatment and also self-healed TB patients. When analyzing patients only included at the beginning of treatment, the sensitivity was 83.3% for T-SPOT.TB and 69.4% for QFT-GIT. In contrast, when evaluating patients during treatment, the sensitivity of the T-SPOT.TB and QFT-GIT decreased to 69.8% and 48.8%, respectively.

The response to the specific antigens increased after finishing the treatment compared with the values during the treatment. The T-SPOT.TB was found to be more sensitive in diagnosing active TB than the QFT-GIT. The IFN-γ tests could be used as a complementary method in the diagnosis of active TB; however, the studies are lacking in extrapulmonary cutaneous TB.

QFT-G, QFT-GIT, T-SPOT, and TST each measure different aspects of the immune response and use different antigens and interpretation criteria. As a result, test results might not be interchangeable. Different tests can yield different results. In addition, as with TST, live virus vaccines might affect IGRA test results; however, the effect of live virus vaccination on IGRA has not been studied.

**MICROSCOPIC PATHOLOGY**

**FINE-NEEDLE ASPIRATION CYTOLOGY**

Fine-needle aspiration cytology (FNAC) is a semi-invasive procedure that is currently being used in office practice. This, along with a biopsy, was used in 30 cases of cutaneous TB in which the specimens were also subjected to Ziehl-Neelsen and periodic acid-Schiff staining. Cohesive epithelioid cell granulomas were identified in 8 of the 9 (88.8%) patients with lupus vulgaris, while acid-fast bacilli (AFB) could be demonstrated in only 2 (22.2%) patients on cytology and none on histopathologic study. A total of 15 (79%) of the 19 specimens from scrofuloderma patients showed caseation necrosis with or without granulomas (Figure 1A and 1B). Two (10.5%) specimens revealed granulomas with acute inflammatory infiltrates. AFB were demonstrated in 15 (78.9%) cases on cytology, as compared with 3 (15.8%) on histopathology. A case from a patient with tuberculosis verrucosa cutis and one with lichen scrofulosorum were inconclusive; hence, FNAC may obviate the need for biopsy especially in cases of scrofuloderma. Because FNAC of skin lesions seldom yields a diagnostic aspirate, FNAC of the regional lymph nodes may be undertaken to establish a probable etiological diagnosis in cutaneous TB. The percentage of AFB positivity declines with more epithelioid cell granulomas. In remote places, where facilities for a proper histopathological examination are lacking, FNAC may be an ideal alternative.

**HISTOPATHOLOGIC UNDERTONES**

Granuloma is its mainstay and may either be specific or nonspecific, according to its clinical variant.

**SCROFULODERMA**

Typical tubercle surrounding wedge-shaped necrosis is scrofuloderma’s hallmark. It is possible to demonstrate AFB in the lower portion of the dermis, as well as in the walls of the ulcer and abscess.
**TB Cutis Orificialis**
Ulceration surrounded by a nonspecific inflammatory infiltrate and extensive caseation necrosis is the pre-eminent microscopic feature of TB cutis orificialis. The presence of granulomas containing epithelioid and Langhans'-type giant cell in the dermis may be present. Usually, Ziehl-Neelsen-stained AFB are detected.20

**TB Verrucosa Cutis**
Its microscopic pathology is characterized by marked pseudoeptitheliomatous hyperplasia of the epidermis with hyperkeratosis and a dense inflammatory cell infiltrate, consisting of neutrophils, lymphocytes, and giant cells. Granulomatous infiltrates are key to its diagnosis (Figure 2). Typical tuberculous foci with caseating necrosis are uncommon.22

**Lupus Vulgaris**
Its histopathology is conspicuous and is formed by a granuloma, containing prominent epithelioid cells, Langhan's giant cells, and a mononuclear infiltrate (Figure 3). Caseation necrosis is minimal/absent. AFB are also rare. The variations in tissue histology may be expected due to secondary changes of abscess formation, ulceration, atrophy, and scarring.

**Lichen Scrofulosorum**
It is necessary to establish its microscopic pathology, which is primarily characterized by a collection of epithelioid cells in the upper part of the dermis and/or around the hair follicle. An occasional giant cell may be identified in the granuloma. Caseation necrosis, however, is conspicuous by its absence (Figure 4).23
ERYTHEMA INDURATUM OF BAZIN

Three of the four microscopic findings, namely septal panniculitis, fat necrosis, small/large vessel vasculitis, and presence of granulomas, are considered essential for entertaining its diagnosis, the details of which are illustrated in Figure 5.

PAPULONECROTIC TUBERCULIDS

Lesions show a wedge-shaped necrosis of the upper aspect of the dermis, extending to and involving the epidermis. Epithelial cells and, infrequently, Langhan’s giant cells are seen. An obliterative granulomatous vasculitis with fibrin present in vessel walls and lumen is typical.

IMMUNOHISTOCHEMISTRY

Immunohistochemistry has gained prominence as a diagnostic supplement. Accordingly, the presence of M tuberculosis antigen was demonstrated in 68% of the 50 cases examined in a series by immunohistochemical staining procedures using anti-M tuberculosis antisera. The antigen could be detected within the giant cells and also in an extracellular location, interspersed between the mononuclear cell infiltrate. In another study, immunohistochemistry was used to detect the secreted mycobacterial antigen MPB64 on 55 formalin-fixed tissue biopsies from suspected tuberculous lymph nodes. This antigen has not been detected in nontuberculous mycobacteria. Polymerase chain reaction (PCR) for amplification of IS6110 from DNA obtained from the biopsies was used as a gold standard. The observed agreement between PCR and immunohistochemistry was 87%. In another study employing the anti-BCG immunostain, positive results were reported in 100% of 27 cases of mycobacterial infections such as TB, lepromatous leprosy, and atypical mycobacterial infections. Regular skin structures, cellular debris, and necrotic material were not immuno-stained by the anti-BCG antibody. This stain cross-reacts with many bacteria and fungi and produces minimal background staining. In conclusion, the anti-BCG immunostain may be particularly effective in the detection of organisms, when obscured by a dense round cell infiltrate and macrophages.

Figure 3. Lupus vulgaris: Section showing epithelioid cell granulomas with conspicuous prominent giant cells extending to mid-dermis along with hyperplastic epithelium depicting hyperkeratosis and acanthosis (hematoxylin-eosin stain, original magnification ×40). Inset: hematoxylin-eosin stain, original magnification ×100.

Figure 4. Lichen scrofulosorum: Section showing perifollicular epithelioid cell granulomas with relative sparing of arrector pili muscle (hematoxylin-eosin stain, original magnification ×100).

Figure 5. Erythema induratum: Section showing septal panniculitis, vascular damage, neutrophil and macrophage infiltrate in the vessel wall, and thrombosis (hematoxylin-eosin stain, original magnification ×40). Inset: hematoxylin-eosin stain, original magnification ×400.
ISOLATION AND IDENTIFICATION OF M TUBERCULOSIS, IN VITRO CULTURE AND GUINEA PIG INOCULATION

IN VITRO RECOVERY OF M TUBERCULOSIS

This method is used to determine the presence of mycobacteria and their sensitivities; however, it has limitations due to low yield and often a several-week delay in producing results.\textsuperscript{27–29}

Culture sensitivity for the solid, egg-based L-J medium, is much lower than specificity, with sources ranging from 80% to 85% and 98.5%, respectively.\textsuperscript{29,30} Growth on solid media usually takes 3 to 8 weeks. In addition to the conventional culture, efforts to improve upon/ensure the recovery of the organism and several sophisticated modifications have been made available for use.

BACTEC SYSTEM

The radiometric BACTEC 460 TB culture (BACTEC) system has shown better isolation rates in pulmonary TB. It has demonstrated an improved mycobacterial isolation rate and substantially reduced detection time, when compared with L-J medium, in cutaneous TB. The combined isolation rate on both media is greater than that of either used separately.\textsuperscript{31}

BACTEC MGIT 960 SYSTEM

This system is a fully automated, nonradiometric instrument that is suitable for the detection of growth of TB and mycobacteria other than TB. It is characterized by detection times that are even shorter than that of the BACTEC 460 system. This is the only automated system that offers susceptibility testing for 5 anti-tubercular drugs at a time; however, the contamination rate is higher than that for the radiometric BACTEC 460 system.\textsuperscript{32}

MB-REDOX

This is yet another manual culture system for the recovery of mycobacteria. It consists of a liquid medium (modified Kirchner medium) containing a redox indicator, a colorless tetrazolium salt, which is reduced to colored formazan by actively growing mycobacteria. In a multicenter study,\textsuperscript{33} the MB-Redox was found to be a reliable, nonradiometric system for growth and detection of mycobacteria. When used in combination with a solid medium, it proved to be an effective replacement for BACTEC 460. The MB-Redox system is a labor-intensive method that requires much handling during the visual reading procedures.

MB CHEK (BIPHASIC MEDIUM)

The recovery rate of M tuberculosis on biphasic medium was 44 (95.65%) and 35 (76.08%) on L-J. Similar rates were recorded in another study in which MB chek was found to be superior to BACTEC.\textsuperscript{34} In contrast, BACTEC was shown to be superior (91.9%) to MB chek (79.7%) in another study,\textsuperscript{35} while same recovery rates of M tuberculosis by both MB chek and BACTEC have been noted by others.\textsuperscript{36}

GUINEA PIG INOCULATION

The record of guinea pig inoculations, carried out at the London Hospital during a 5-year period, was reviewed. Guinea pig inoculation was done in a total of 677 clinical specimens, of which only 34 were found to be positive, both in vitro culture and guinea pig in vivo. In addition, 22 and 5 were positive on culture and guinea pig alone, respectively. Cost, safety, and animal welfare considerations suggest that the practice of routine inoculation of suspected tuberculous tissue specimens in guinea pigs should be discontinued.\textsuperscript{37} Another study, where extrapulmonary specimens were inoculated into guinea pigs, gave fewer positive results than did cultures.\textsuperscript{38} Two cases of erythema induratum of Bazin have been confirmed using guinea pig inoculation.\textsuperscript{39} This cumulative information, coupled with cost, safety, and animal welfare issues, also warrants its exclusion from routine diagnostic procedures.\textsuperscript{38}

IMMUNOCROMATOGRAPHY

Recently, a simple culture confirmation test for M tuberculosis complex has been develop by using lateral flow immune chromatographic assay to detect MPB64 antigen with anti-MPB64 monoclonal antibody. This low-tech, rapid test with high sensitivity and specificity could provide a viable alternative to currently available identification methods, particularly for recently introduced nonradiometric liquid culture systems such as the mycobacteria growth indicator tube (MGIT), to differentiate M tuberculosis from mycobacteria other than TB.\textsuperscript{40}

HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

High-performance liquid chromatography (HPLC) of mycolic acids for the identification of AFB from culture is now available. The method is accurate and versatile, because many species can be identified with a single inexpensive test (identification and quantitation of M tuberculosis directly from clinical specimens by fluorescence detection HPLC).\textsuperscript{41}

ENZYME-LINKED IMMUNOSORBENT ASSAY

A 60 antigen–based enzyme-linked immunosorbent assay (ELISA) test (A-60 TB) for TB is currently available. Its sensitivity, specificity, and positive predictive value are estimated at 76%, 98%, and 95%, respectively, in pulmonary TB.\textsuperscript{42} In a recent study\textsuperscript{43} on clinicohistopathologically diagnosed cases of cutaneous TB, the ELISA test was positive in 60% of patients despite the failure to detect AFB on tissue specimens and culture negativity. In addition, mycospot–ELISA, a lipoarabinomannan-based test, was used in 22 randomly selected specimens of clinicohistopatho-
logically suspected cutaneous TB. All were AFB smear and culture negative, and 9 of the 22 sera reacted to the test (40.8%). Efficacy and sensitivity were found to be 47.8% and 43.4%, respectively. The negative predictive value was only 7.1%.44

The preceding tests should, therefore, form a component of the battery of investigations.

**Molecular Diagnosis**

The advent of molecular diagnostics has added innovative dimensions to current practice, the majority revolving around: (1) detection of nucleic acids, DNA, and RNA, that are specific to *M tuberculosis* by PCR, including other amplification techniques; and (2) detection of mutations in the genes that are associated with drug-resistant *M tuberculosis*, by either sequencing or nucleic acid hybridization.

*M tuberculosis* species identification by 16S rRNA gene sequence analysis oligohybridization and strain typing are in use for direct and rapid detection of mycobacteria, as well as for drug susceptibility pattern.45 In contrast to pulmonary samples, PCR performed on extrapulmonary samples may be less sensitive due to small sample volume and an irregular dispersion of the organisms in paucibacillary specimens.46

The presence of PCR inhibitors, especially in extrapulmonary specimens, may produce false-negative results. The inherent sensitivity of PCR may lead to amplification of nonspecific sequences and contaminants,47 compounded by the inability to differentiate between live and dead organisms. PCR has been found to be the most sensitive (88%) and specific (83%) test for the diagnosis of cutaneous TB,48 corroborated by another study,49 in which 75% of lupus vulgaris, 62.2% of TB verrucosa cutis, and 50% of scrofuloderma, were found to be PCR positive. In addition, one case each of lichen scrofulosorum and erythema induratum tested positive. A PCR-based assay for *M tuberculosis* was evaluated in 60 formalin-fixed tissue specimens, the target for the amplification being a segment of IS6110 in the bacterial chromosome. A total of 57 of the 60 specimens showed granulomatous inflammation, and 53 were recovered in vitro, of which 10 were positive for *M tuberculosis* and 3 for other mycobacteria; 15 of 60 specimens demonstrated AFB. When performed comparatively on a positive culture for *M tuberculosis*, PCR was 100% sensitive and 93% specific, having a positive predictive value of 76.9% and negative predictive value of 100%. PCR for *M tuberculosis* DNA done on tissue samples was positive in 14 of 19 patients who had a clinical diagnosis of TB, negative for all the 6 patients with nontuberculous mycobacterial infections, and negative for all 33 patients who had a diagnosis of a disease other than mycobacterial infection. When compared with the clinical diagnosis of TB, PCR for *M tuberculosis* DNA in these patients’ tissues was 73.6% sensitive and 100% specific, having a positive predictive value of 100% and negative predictive value of 88.6%.50 In addition, several anecdotal reports of the utility of PCR in the diagnosis of cutaneous TB are available. These data indicate that PCR amplification is useful for detecting *M tuberculosis* DNA in formalin-fixed tissue specimens and that it can be used to increase diagnostic accuracy in patients who have a diagnostic dilemma.49

**Real-Time PCR Technique**

This is considerably simpler and faster with respect to the standard PCR technique; however, some problems of sensitivity when the samples contain small amounts of *M tuberculosis* DNA may arise. It could be a useful method for assessing treatment response in patients with TB. Real-time PCR assay has shown a high degree of specificity, sensitivity, and especially rapidity of detection of TB, the latter being a very important factor in patient management in terms of initiating appropriate antitubercular therapy.51

**DNA Probes**

Based on information about specific gene sequences, well-defined oligonucleotide probes for identification of various clinically relevant mycobacteria have been developed14–20 and are readily available. These include probes for identification of *M tuberculosis*, *Mycobacterium avium*, and several other mycobacteria. These probes are being used in several countries for rapid confirmation of the identity of mycobacterial isolates. When utilized along with newer methods of detection of the early growth, BACTEC, Septi-Chek, and MGIT, these probes are of great help in rapidly confirming the diagnosis, as the identity of an isolate can be established within 1 to 2 days with gene probes as compared to a much longer time required with classical biochemical tests.52

**Ribosomal rRNA-Based Probes**

In recent years, ribosomal RNA gene region has been extensively explored for designing systems for ribosomal DNA fingerprinting and for development of probes, as well as gene amplification assays for various mycobacterial species including *M tuberculosis*, *Mycobacterium leprae*, and *M avium*.52,53 These probes are 10- to 100-fold more sensitive than DNA targeting and may be used to confirm the diagnosis directly in the clinical specimens in a good proportion of cases; the lowest detection limit is around 100 organisms. At present, these are useful mainly for rapid identification of mycobacterial isolates.

**Gene Amplification Methods for Identification**

Molecular techniques may also be used for confirmation of the identity of isolates. The original inoculum needs to be kept in
mind, different strategies to identify the isolates from cultures and directly from the clinical specimens include amplification of specific gene regions followed by hybridization with species-specific probes, sequencing, and restriction fragment length polymorphism (RFLP) analysis, such as hsp 65 kDa gene, katG, and rRNA genes. These PCR-RFLP assays help in the quick identification of pathogenic mycobacteria including \( M \) tuberculosis from the culture isolates as well as directly from the clinical specimen.

**Antitubercular Therapy as a Diagnostic Adjunct**

The diagnosis of cutaneous TB may pose a challenge due either to a lack of sensitivity of culture or to an inability to take up the molecular diagnostics as a result of limited resources in developing countries or to equivocal laboratory results. To this end, a therapeutic trial of the 4-drug antitubercular treatment may be a valid diagnostic method in uncertain cases of cutaneous TB. Four-drug antitubercular therapy comprising isoniazid, rifampicin, pyrazinamide, and ethambutol may be started, with 6 weeks being an adequate duration to assess the clinical response. In the event of an unfavorable response, either the diagnosis should be reconsidered or the possibility of multidrug-resistant TB should be considered. Patients with tuberculosis and those with minimally active disease may take longer than 6 weeks to respond. As a result, it may be worthwhile to prolong the therapeutic trial in such cases before considering alternative diagnoses.

**Conclusions**

Diagnostic dilemma continues to loom large in cutaneous TB, leading to requisition of several laboratory innovations, which are required to be made use of during its discourse.

**References**

30. Diagnostic Standards and Classification of Tuberculosis in Adults and Children. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. Am J Respir Crit Care Med. 2000;161:1376–1395.
37 Pallen MJ. The inoculation of tissue specimens into guinea-pigs in suspected cases of mycobacterial infection does it aid diagnosis and treatment? Tubercle. 1987;68:51–57.

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Cutaneous Tuberculosis
Sometimes It Takes Darkness to See the Light: Pitfalls in the Interpretation of Cell Proliferation Markers (Ki-67 and PCNA)

Carmen Castilla, BS; Patrick McDonough, BA; Gizem Tumer, MD; Peter C. Lambert, BA, MS; W. Clark Lambert, MD, PhD

“[Clarity], like a photograph, develops in the dark.—Yousuf Karsh

The degree of cell proliferation in a tumor is often associated with metastatic risk and mortality. Proliferating cell nuclear antigen (PCNA) and Ki-67 are proliferation markers that can be used to assess malignant potential in cutaneous lesions and pathological cell proliferation in psoriasis. These markers are elevated during periods of cell proliferation; however, they are also upregulated following UV irradiation. This upregulation may be problematic, as many skin lesions are subject to sun exposure in an everyday setting.

Ki-67 (the name of which was derived from the town in which it was discovered, Kiel, Germany, and the number of the original clone in well plate 96) is a large protein with two isoforms generated by alternative mRNA splicing. It is closely associated with cell proliferation and is only present in dividing cells. Ki-67 is thought to work in conjunction with regulators of the cell cycle to manage progression of S phase and to determine commencement and termination of mitosis. Because Ki-67 can be found in both normal and neoplastic cells during cell proliferation, it has been used to assess growth fraction in a designated cell population. An increase in the Ki-67 labeling index, the fraction of tumor cells positive for Ki-67, has been found to portend a worse prognosis in cutaneous malignancies, such as melanoma and Merkel cell carcinoma (Figure 1A and Figure 1B). In addition, an increase in Ki-67-positive cells has been shown to correlate with an increase in the psoriasis area and severity index, with higher scores indicating worse disease. This correlation has prompted some researchers to use Ki-67 to evaluate the effectiveness of medications in the treatment of psoriasis.

UV radiation has been shown to affect epidermal cells on a molecular level by activating pathways that induce cell proliferation (Figure 2). Because Ki-67 is closely associated with cell proliferation, it is also upregulated following UV irradiation. Possibly, it may also play a role in DNA repair following UV irradiation. As a result, patients can have a UV radiation–induced increase in Ki-67, which can be mistakenly interpreted to indicate a higher-grade neoplasm or, in the case of psoriasis, suboptimal treatment.

CHARACTERISTICS

Proliferating cell nuclear antigen (PCNA) is a circular, homotrimeric protein that associates with DNA polymerases delta and epsilon, which are involved in DNA synthesis and repair. PCNA functions as a sliding clamp, holding the DNA polymerase around the DNA strand and increasing the efficiency of nucleotide addition (Figure 3). When UV radiation induces pyrimidine dimers, PCNA and DNA polymerase delta are upregulated, performing nucleotide excision repair to restore the integrity of the DNA. Much like Ki-67, PCNA has been used as a marker of cell proliferation in assessing cutaneous neoplasms. In normal skin, PCNA-positive cells are only located around hair follicles and in the basal layer of the epidermis, while in neoplasms, PCNA-positive cells can be found anywhere in the tumor. In human skin, UV exposure has been shown to induce PCNA

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Figure 1. (A) Multiple nests of melanocytes are shown in malignant melanoma. (B) Ki-67 immunostain showing increased reactivity. Black arrowhead indicates a melanin pigment. Red arrowheads indicate increased Ki-67 labeling in or above the basal layer, indicative of cell proliferation or of ultraviolet exposure within the previous 24 hours. Full black arrows indicate a hypocellular dermis, indicative of long term ultraviolet exposure.

Figure 2. Normal skin adjacent to the melanocytic lesion showing increased Ki-67 proliferation index above the basal layer (arrowheads) due to ultraviolet exposure.

Figure 3. DNA replication fork illustrating DNA synthesis along the leading and lagging strand. Proliferating cell nuclear antigen (PCNA) is shown in pink acting as a clamp to secure polymerase delta (shown in green) and polymerase epsilon (shown in teal) to the DNA strand, allowing for greater efficiency of nucleotide addition.
expression in suprabasal cells. As a result, skin biopsies taken from patients who were recently exposed to the sun, or other sources of UV radiation, can appear to contain rapidly proliferating cells when in fact the cells are only repairing UV-induced damage. Without a good history from the clinical dermatologist, the dermatopathologist may misinterpret these PCNA-positive cells as indicative of a higher-grade malignancy.

CONCLUSIONS

Dermatopathologists must be aware of the possibility of upregulation of Ki-67 and PCNA following UV exposure. This elevation can lead to incorrect tumor grading or psoriasis rating and subsequent projected prognosis. In an ideal setting, patients should avoid UV exposure before the biopsy of a suspected cutaneous malignancy; however, this is not always practical. We recommend that clinicians routinely ask patients about their recent UV exposure before a skin biopsy and report this information to the dermatopathologist to avoid misinterpretation of Ki-67 and/or PCNA levels.

REFERENCES

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*In vitro activity does not necessarily correlate to in vivo activity.*
A 52-year-old African woman presented with multiple 2-mm to 8-mm dermal papules that had been evolving over several weeks. They were primarily over the ears (Figure 1), dorsal surface of the hands, extensor surface of the forearms, distal aspects of the lower extremities, and dorsal surface of the feet (Figure 2). In addition, the patient had indurated plaques over the earlobes and forehead (Figure 3), with moderate loss of the eyebrows. There was a mild sensory deficit over the left distal aspects of the arms and right distal aspects of the lower extremity on monofilament testing. A dermal nodule was noted over Erb’s point on the left side of the neck. The patient denied problems with her vision or a history of previous genital ulcers. She had recently immigrated to the United States from Tanzania. She had no significant medical history and was not taking any medication. Several full-thickness punch biopsies were obtained and changes were seen consistent with a mycobacterial infection. Results from a Fite-Faraco–modified acid-fast stain were positive, and a presumptive diagnosis of leprosy was made. Upon consultation with the National Hansen’s Disease Clinical Center, the patient was started on a multidrug regimen (clofazimine, dapsone, and rifampin) for a total of 24 months.

Leprosy (Hansen’s disease) is a chronic infectious disease caused by the bacillus *Mycobacterium leprae*. It is rarely fatal, but it is associated with disabling sequelae. The chronic granulomatous infection preferentially affects the skin and peripheral nerves. The keys to effective treatment are early diagnosis and rapid institution of multidrug therapy.

Although leprosy has a worldwide distribution, it is most prevalent in India, Brazil, the Democratic Republic of Congo, Tanzania, Nepal, Mozambique, Madagascar, Angola, and the Central African Republic. In the United States, cases of leprosy are primarily seen in immigrants (as in the case presented), although multiple cases are reported in individuals native to the United States. The National Hansen’s Disease Registry reported 166 cases in the United States in 2005, 75% of which were identified as immigrants.

Transmission of the disease is predominantly via nasal and oral droplets from an infected individual and, less frequently, from cutaneous sites. Solitary short-term contact with an infected patient is usually insufficient for transfer of the bacillus. The risk of infection in the general population has been approximated at 0.02%, whereas it increases to 25% in individuals who have long-term close contact with infected persons.

**DIAGNOSIS**

Leprosy is a difficult diagnosis to make, primarily due to the rarity of this disease in the United States. This suggests that a high index of suspicion is required for making the correct diagnosis. It is important for the practitioner to understand the range of clinical manifestations and available diagnostic tools. With earlier detection, appropriate multidrug therapy may be instituted and morbidity reduced.

**CLINICAL PRESENTATION**

Leprosy has two classification systems. The Ridley-Jopling System divides leprosy into 6 categories according to clinical and histopathologic findings and number of bacteria in the lesions (Table I), whereas the World Health Organization (WHO) has created a more pragmatic system that divides leprosy into three groups: (1) paucibacillary, single-lesion; (2) paucibacillary leprosy (2–5 lesions); and (3) multibacillary leprosy (>5 lesions).

The clinical manifestations are dependent on the host’s immune response to the bacillus. Tuberculoid leprosy (TT) occurs when cell-mediated immunity prevails (Th1 cytokines); however, if there is primarily an antibody response (Th2 cytokines), lepromatous leprosy (LL), as seen in this case, is the clinical presentation. The borderline forms of the disease denote the spectrum of immunologic responses between the purely cell-mediated and antibody-mediated responses seen in TT and LL, respectively.

*M leprae* primarily affects the skin and peripheral nerves. In LL, one can see numerous poorly defined macules, papules, or plaques primarily over the face, distal extremities, and buttocks. If there is diffuse infiltration, leonine facies can be appreciated. Additional clinical signs can include thickening of the earlobes, loss of the eyelashes and eyebrows (madarosis), lower
extremity edema, and acquired ichthyosis of the lower extremities. In TT, there is a single or very few lesions. They are well-defined, erythematous to hypopigmented macules or plaques with a raised edge (the preferred site for biopsy). Often, the lesions are hairless with hypesthesia or anesthesia.

Neural involvement can result in sensory, motor, and autonomic impairment. Granulomatous inflammation can lead to palpable thickening of the nerves, most commonly the posterior tibial nerve. These palpable nerves can be painful and are at an increased risk of becoming damaged. Sequelae of nerve involvement are similar to those seen in any peripheral neuropathy, including traumatic ulceration and infection.

Another manifestation of leprosy is type I and type II reactions. Most commonly seen after beginning antimicrobial therapy, they are also seen with stressors such as infections and pregnancy. Type I reactions (or reversal reactions) occur when the immunologic response to *M. leprae* changes, i.e., from a cell-mediated (Th1) to a humoral (Th2) response, or vice versa. Most commonly, this presents as acute inflammation in skin lesions and/or nerves. Type II reactions are primarily seen in LL (and borderline lepromatous) patients. It is principally a cutaneous small vessel vasculitis caused by an exuberant humoral response. The most common manifestation is erythema nodosum leprosum. These patients

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**Figure 1.** Multiple, 2–8 mm dermal papules over the ears.

**Figure 2.** Multiple, 2–8 mm dermal papules over the dorsal surface of the feet.

**Figure 3.** Indurated plaques over the forehead with moderate loss of the eyebrows.
have tender, red papules or nodules over the face and extensor extremities. A severe variant of the type II reaction is Lucio’s phenomenon, described as a necrotizing vasculitis associated with vascular thrombosis and subsequent ischemic necrosis.

**Diagnostic Tools**

The diagnosis of leprosy is primarily clinical, although multiple investigations are available.

If possible, a skin biopsy should always be performed (preferentially, from the active edge). The two most important findings on histopathologic study are *M. leprae* in the tissue and granulomatous inflammation around the nerves. The bacilli are most commonly stained with the Fite-Faraco technique, although Ziehl-Neelsen and Wade can also be used. Another means for identifying bacilli is slit-skin smears. A small slit is made in an involved area and smeared on a glass slide. The slide is stained and examined for bacilli. The slit-skin is positive in nearly 100% of cases of LL, 75% of borderline leprosy, and 5% of TT.

Serologic testing for *M. leprae* includes antiphenolic glycolipid-I (anti-PGI) antibody, neopterin, and lipoarabinomannan. As one might expect, the levels of anti-PGI antibodies are higher in the multibacillary patient (compared with paucibacillary). A recent report proposed following anti-PGI antibody trends and may be useful in monitoring response to treatment in LL patients. Additionally, several molecular biologic techniques have been developed, including molecular probes targeting both DNA and RNA of *M. leprae* and polymerase chain reaction techniques. rRNA and rDNA probes may be helpful in evaluating smear-negative, evolving multibacillary disease and response to treatment. Unfortunately, the utility of these investigations in clinical practice is minimal. The main detractor is that in the most difficult to diagnose forms of leprosy, ie, TT and borderline tuberculoid, these tests do not reliably detect *M. leprae.*

Finally, the lepromin (or Mitsuda) test is performed by injecting heat-killed *M. leprae* intradermally. A test result is deemed positive when a nodule forms at the injection site approximately 3 to 4 weeks later, indicating a cell-mediated response. This test is positive in TT and borderline tuberculoid leprosy. Although it has some prognostic value, it has no diagnostic value and is not routinely performed.

**TREATMENT**

The current treatment of leprosy is centered on multidrug therapy. In the United States, the National Hansen’s Disease Clinical Center in Baton Rouge, Louisiana, is an important resource (http://www.hrsa.gov/hansens/clinicalcenter.htm). It serves as a source of information and medications. In endemic countries, the WHO spearheads the effort in delivering free multidrug therapy to patients.

The WHO recommendations on leprosy are based on the number of skin lesions and bacilli noted on examination (Table II). These guidelines are controversial, and many still recommend 24 months of treatment for multibacillary disease (whereas current WHO guidelines recommend 12 months). Multidrug therapy was started in 1982 after drug therapy with a single agent was associated with dapsone resistance. Although resistance continues to be a concern, multidrug therapy leads to only rare treatment failures. Relapse rates have been approximated to range from 0.7 to 20 of 1000-person-years. Additional agents
that are active against *M. leprae* (other than those mentioned in Table II) are clarithromycin and fluoroquinolone antibiotics, especially pefloxacin (not available in the United States).

Treatment of type I reactions is with oral prednisone. The aim is to decrease the inflammation and eye/nerve damage. The treatment for type II reactions (erythema nodosum leprosum) is immunosuppression. The most common therapy is thalidomide (300 to 400 mg daily). In severe reactions, prednisone may be needed.

**CONCLUSIONS**

Leprosy is a chronic infection that has become quite rare in the United States; therefore, the practitioner must have a high index of suspicion in order to make the appropriate diagnosis. With earlier detection and rapid induction of multidrug therapy, the extreme morbidities associated with long-standing infection can be avoided.
Actinomycetoma

Ncoza C. Dlova, MBChB, FCDerm; Anisa Mosam, MBChB, FCDerm

An 8-year-old boy presented with a 6-month history of asymptomatic multiple nodules, papules, and some ulcerated plaques involving the groin and right foot. Occasional draining sinuses were observed. The patient was human immunodeficiency virus negative. Skin biopsy and fungal culture confirmed actinomycetoma caused by *Norcadia brasiliensis*.

*Figure 1. Actinomycetoma of the right foot.*

*Figure 2. Actinomycetoma of the groin.*
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A 68-year-old Caucasian man presented with a suspicious lesion near the left axilla during a full skin examination that was performed for a presentation for dermatitis. The patient stated that he had the lesion for several decades but that it may have become more raised over the past few months. He did not think much of the changes, however, because it was to him, “just a birthmark.” The patient had no personal or family history of melanoma. On examination, the patient had a 4.5-cm by 1.2-cm oval light tan patch studded with multiple hyperpigmented macules regularly distributed within the lesion. In addition, at the lateral aspect of the lesion, the patient had a 0.9-cm irregularly pigmented black papule that was suspicious for melanoma (Figure 1). A deep saucerization biopsy of the lesion was performed, and histopathological examination revealed malignant melanoma, with a Breslow depth of 1.13 mm (Figure 2 and Figure 3). It was recommended that the patient have a wide local excision of the biopsy site and the adjacent remaining portions of the nevus spilus. A sentinel lymph node biopsy and an oncologic evaluation were also performed. The sentinel lymph node biopsies, as well as a computed tomographic scan performed by oncology, showed no evidence of metastatic disease. Since the procedure, the patient has shown no signs of disease recurrence.

Nevus spilus (NS), also commonly referred to as speckled lentiginous nevus, is a skin lesion composed of a tan-to-brown pigmented patch spotted by several smaller, darker melanic macules or papules. These lesions are found in 0.2% to 2.3% of the overall population. Even though NS is classically regarded as a benign lesion, there have been several cases reported in the literature of malignant melanoma developing within this entity. At this time, however, the precise risk for malignancy within NS has yet to be determined. The NS lesion is typically a single, nonhairy lesion with a background pigmented patch a few centimeters in diameter and that is dotted by multiple smaller, darker macules or papules usually measuring 1 to 3 mm in diameter. Although most NS lesions are described as small (<1.5 cm) or medium (1.5–19.9 cm), there have also been reports of giant lesions, as well as those in a zosteriform distribution. NS can be found anywhere on the body, but most reported lesions are found on the trunk or extremities. These lesions occur fairly equally in men and women. Although studies have found that NS occurs with equal prevalence within different races, case reports tend to feature Caucasian patients.

There has been some debate as to whether NS is an acquired or congenital lesion. Support for the theory that these lesions are acquired comes from a study that found no evidence of these lesions in 1058 newborns and another study that found only two cases of NS in a group of 1118 newborns. The background NS lesion is most commonly found during the first year of life, if not later, and the spotted macules or papules have been observed to develop even later between the ages of 6 and 39 years. Despite these findings, some authors make the argument that NS is a subtype of congenital melanocytic nevi. Other investigators argue that the following factors all support the idea that these lesions can in fact be considered a type of congenital melanocytic nevi and not an acquired entity: (1) NS spots have been found at or soon after birth in several recent studies; (2) the distribution patterns show embryonic development; and (3) histologic features of NS are similar to those of congenital melanocytic nevi, the hamartomatous behavior of these NS lesions, as well as several cases of NS lesions developing into more classic congenital melanocytic nevi. NS is presented as a “melanocytic garden” that can give rise to a variety of different lesions based on the way in which melanocytes differentiate. One expert supports NS as the “roots of the melanocytic garden.” It is thought that NS arises from a localized defect in neural crest melanoblasts, which may be influenced by both genetic and environmental factors. The melanocytic stem cells develop into melanocytes in the embryonic dermis, and their progeny then migrate into the epidermis. These melanocytes can differentiate into a variety of redundant lesions below the epidermis, which could explain the great variation in character found amongst NS lesions. This investigator supports the idea of others that a congenital lesion
is one which develops within the first 2 years of life because these lesions are programmed from birth, but the mature progeny of the melanocytes take time to reach the surface of the skin. Overall, there is evidence supporting NS as both an acquired and a congenital lesion, and it has been suggested that NS are acquired lesions that can be found in association with congenital nevi.26

Histologically, the background lesion of NS is lentigo simplex,13 with hyperpigmentation of the basal layer of the epidermis as a result of an increase in melanocyte number or an increase in the melanin in keratinocytes.1,2 The spots have been found to be either junctional,3 compound, or dysplastic nevi.9,13 Investigators propose the theory that NS lesions can be further divided based on whether they have macular or papular spots. Macular NS is composed of lesions with uniformly flat dots in a checkerboard pattern. Histologically, the macular-type spots show an elongation of the interpapillary ridges with an increased number of melanocytes as well as increased melanin pigment in the basal layer of the epidermis. Nests of melanocytes can also be found at the dermoepidermal junction of the tips of the papillae. The background pigmentation has increased melanocytes only in the basal epidermal layer and increased melanin deposits in the keratinocytes. Papular NS is characterized by a background macule that is superimposed by multiple papules or nodules also in a checkerboard pattern. The papules have melanocytic nests in the papillar and reticular dermis, resulting in either a dermal or compound melanocytic nevi pattern. The background macule consists of elongated interpapillary ridges as well as elevated amounts of melanin and melanocytes in the basal layer of the epidermis.1 Although the macular form of NS is more likely to degenerate into melanoma, both forms have the ability to undergo malignant transformation.

More than 20 cases of NS degenerating to malignant melanoma, including a few fatal cases,9,14,15 have been reported; however, the exact risk for malignant degeneration is currently unknown. Investigators have found that there is no significantly elevated incidence of malignant melanoma in a population with NS

**Figure 1.** Oval tan patch studded with hyperpigmented macules and melanoma at the margin of lesion.

**Figure 2.** Superficial spreading melanoma (hematoxylin and eosin, original magnification ×10).

**Figure 3.** Superficial spreading melanoma (hematoxylin and eosin, original magnification ×40).
lesions as compared with a control group of general dermatology outpatients, implying that NS does not possess a particularly high risk of malignant potential. The risk of NS degenerating into malignancy does not seem to be associated with sex, age, or race; however, most reported cases of malignant transformation have been found in Caucasian or black patients.\(^6,9\) One risk factor for malignancy is the size of the NS lesion. The majority of melanomas reported in the literature are found on medium (1.5–19.9 cm) or large NS lesions.\(^8,9\) Investigators recently reported that 24% of melanomas developed on zosteriform NS and 16% developed on giant lesions. Because these types of lesions are much less common than the small or medium NS lesions, the giant and zosteriform lesions have a higher relative risk of malignant transformation.\(^9\)

Another factor suggested as a possible precursor to malignant melanoma is dysplasia within the nevus. Researchers describe intraepidermal melanocytic dysplasia as a common feature in precursor lesions of melanoma. Using flow cytometry, other studies show nuclear aneuploidy in the melanoma as well as in the darker spots of the NS lesion. Studies of these dysplastic NS lesions show alterations to the stroma as well as increased vascularization and light inflammatory infiltration of the dermis.\(^3,12,13\)

**CONCLUSIONS**

Because many questions remain surrounding the malignant potential of NS, the management of these lesions has not been precisely defined. Careful observation for changes that could indicate the development of melanoma is recommended.\(^4,10\) Patient education about self-examination is of utmost importance in the management of patients affected with this skin lesion. Once a melanoma develops, it has a similar prognosis and management as compared with other melanomas.\(^9\) Overall, individualized management of each case is recommended due to the lack of established guidelines for these cases.\(^4\) We recommend our patients to have the lesion examined by a dermatologist every 2 to 3 years. NS is an entity that requires further study, given its well-defined malignant potential. With our case, we add to the known information regarding this lesion with the hope that with time it will come to be more completely understood. We also remind the clinician that although rare, malignant degeneration of NS is possible, and clinicians should consider this fact in evaluating patients with this unusual skin lesion.

**REFERENCES**

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Case Study

Pseudocyst of the Auricle: An Uncommon Entity of the Ear
Alexis Sheaffer, BS; Joya Sahu, MD; Jason B. Lee, MD

A 48-year-old white man presented with a 2-month history of a lump on his right ear following purported exposure to the cold. The patient denied any history of trauma, rubbing, insect bite, or inflammation at the site. The patient was otherwise healthy and was not taking any medications. The lesion was completely asymptomatic, as the patient denied any pain, tenderness, or change in size since the lesion appeared. Physical examination revealed a 1.1-cm × 1-cm skin-colored, slightly fluctuant, rubbery, nonmobile dermal nodule on the right scaphoid fossa (Figure 1). No erythema, warmth, tenderness, or drainage was noted. A review of systems was noncontributory. A punch biopsy performed at the site of the cyst yielded clear, serous drainage. The cystic lesion was drained completely and decompressed. Histological examination revealed the surface of an intracartilaginous cystic space lined by degenerated cartilage, consistent with a diagnosis of pseudocyst of the auricle (Figure 2 and Figure 3). The lesion, although much smaller than at the time of presentation, persisted at the 3-week follow-up visit. It remained asymptomatic, without pain or irritation. At that time, the patient declined re-excision with bolster dressing. At 7-month follow-up, he reported the lesion to be stable.

Pseudocyst of the auricle is an uncommon, benign entity most commonly seen in young men, aged 20 to 60 years.1-5 It is also referred to as an intracartilaginous cyst, endochondral pseudocyst, idiopathic cystic chondromalacia, and pseudouricular seroma.6,7 The lesion usually presents as an asymptomatic, spontaneous, fluctuant, unilateral swelling on the helix or antihelix with little or no history of antecedent trauma.2,6,7 Drainage of the cyst yields a sterile, viscous, straw-colored, glycosaminoglycan-rich fluid.3,5 Despite numerous medical and surgical treatments available, auricular pseudocysts usually have a chronic, relapsing course.

HISTOLOGY

Histologic examination of auricular pseudocysts reveals an intracartilaginous cystic space, characteristically devoid of an epithelial lining.2,4,8-10 The walls contain eosinophilic, amorphous material often with small clefts. There is focal fibrosis at the cyst edges, which is thought to increase proportionally with pseudocyst duration.5,9 The dermis and epidermis are relatively normal appearing.10 Cartilage adjacent to the cyst area exhibits degenerative changes with minimal inflammation.5,9,10 Recently, several studies have reported an inflammatory infiltrate consisting predominately of lymphocytes.1,2,8,11 In a case series of 16 patients, investigators reported a perivascular lymphocytic inflammation superficial to the site of auricular cartilage degeneration.8 Additionally, early signs of granulation tissue and fibroplasia were seen within days of clinical presentation, becoming increasingly prominent in older lesions.8,10

THEORIES

Although many theories have been proposed to explain the etiology of auricular pseudocysts, a definitive cause has yet to be elucidated. Initially, this was described in 1966, when it was proposed that extracellular lysosomal enzymatic activity induced pseudocyst formation.4 Subsequent studies, however, found no evidence of increased lysosomes on both electron microscopy and pseudocyst fluid analysis, disproving this early hypothesis.5,12

A subsequent theory suggested that an embryological defect left residual planes of tissue in the auricle, predisposing individuals to pseudocyst formation. This defect made the auricle inherently susceptible to shearing forces of minor trauma, leading to expansion of residual tissue planes with subsequent fluid accumulation.5,12,13

After noting lymphocytic perivascular infiltration on histologic examination, experts proposed an underlying inflammatory cascade as the etiology of pseudocyst formation.11 A lymphocytic infiltrate in excised pseudocyst specimens was similarly reported.1

This, however, has been refuted by others who describe pseudocysts as noninflammatory, noting sparse perivascular lymphocytic infiltrate on histologic examination1,3,9,10.
One hypothesis that has garnered strong support proposes that chronic low-grade trauma has a significant role in pseudocyst formation. Authors suggest that chronic friction from daily activities such as the carrying of a sack on one's shoulder or lying on a hard pillow overnight leads to the overproduction of glycosaminoglycans, which causes compressive ischemic cartilage necrosis. The resultant microcysts coalesce to form pseudocysts. It should be noted, however, that few, if any, patients, including our reported case, recall a traumatic event or daily source of friction to support this theory.

Similarly, others propose that the constant friction of the ear against the skull caused by the use of motorcycle helmets or earphones causes perichondral ischemia and subsequent cartilaginous degeneration and pseudocyst formation. Elevated levels of lactate dehydrogenase (LDH) 4 and 5, as well as hemosiderin found in pseudocyst fluid, support this theory. In auricular cartilage, LDH 4 and 5 are the main enzymatic components, and thus daily trauma of the cartilage results in their release and subsequent damage to the surrounding tissue.

Recently, a hormonal basis has been suggested to account for the male predominance of patients with pseudocysts of the auricle. The authors propose that sex-specific hormonal modulation influences cytokine induction potential in response to chronic low-grade trauma in men and women. Testosterone has been shown to induce interleukin (IL) production from monocytes, most notably IL-1β. This IL, found in pseudocystic fluid, is known to play a major role in the inflammatory cascade. In contrast, estradiol and progesterone have an inhibitory effect on similar inflammatory mediators, blunting the response to low-grade trauma in women. This hormonal inhibition prevents the immunologic cascade attributed to cartilaginous destruction, protecting women from developing this entity.

**TREATMENTS**

Despite numerous treatment options for pseudocyst of the auricle, there remains a high recurrence rate in patients. Additionally, some treatments carry the risk of cartilage damage or visible distortion of the auricle. Delaying treatment, however, may also lead to significant auricular deformity, so intervention must be strongly considered. The goals of treatment are, therefore, to have recurrence-free resolution of the pseudocyst while preserving auricular architecture.

Corticosteroid injection therapy has been used to treat pseudocysts of the auricle with modest success. The risks of atrophy and permanent deformity of the auricle limit the use of this treatment. Another potential injectable agent is minocycline, which...
acts as both a sclerosant and as an anti-inflammatory agent via suppression of LDH 4 and 5.6,17 Although a single case series demonstrates efficacy with minocycline, review of the literature reveals limited long-term success.1,7

Needle aspiration is one of the more common surgical approaches used to treat pseudocysts of the auricle. If performed independently, however, the lesion typically recurs within 1 week.1,7,10 In order to decrease the high recurrence rate, a compression dressing is used in conjunction with aspiration. In a small case series of 10 patients, a plaster of Paris cast was applied for compression to the ear for 2 weeks following pseudocyst aspiration. At 1-year follow-up, complete resolution was seen in all cases.13

Others report only moderate success with the use of compression dressings following surgical intervention, leading to persistence and pseudocyst recurrence.1,6,7,10 Another similar method, surgical button bolstering, entails suturing a sterile button to the anterior and posterior side of the auricle in order to compress the elevated loose tissue following decompensation of the cartilage. The button is kept in place for a period of 5 to 7 days in order to prevent pseudocyst recurrence.1,6 This approach decreased the recurrence rate by more than 60%,1 but recurrence was still seen in patients usually within 1 week of surgery. Additionally, increased ear thickness was seen in a significant number of patients as a result of the surgical intervention.1 Others have reported perichondritis, fibrosis, decreased cartilaginous strength, and cauliflower ear deformity following similar procedures.1,6,10

Deroofing the pseudocyst following incision and drainage is a simple, safe, and effective alternative that has improved the rates of resolution in patients who have experienced failed conservative treatments.1,19 Investigators used this treatment in 20 patients, many with refractory lesions following aspiration and surgical buttonging dressing procedures. Performed with local anesthesia, the base of the pseudocyst is carefully curetted and cauterized. This removes degenerated cartilage, thought to be the nidus of recurrence.1 These investigators reported complete resolution in all 20 patients using this technique, at 1 to 3 months of follow-up. It should be noted, however, that this requires an additional commitment of time as well as resources for both the patient and physician.

CONCLUSIONS

Pseudocyst of the auricle is an uncommon, benign entity seen in men ranging in age from 20 to 60 years. The pseudocyst presents as an asymptomatic, spontaneous, fluctuant, unilateral swelling that has characteristic histologic findings. Although there are many proposed theories to explain the formation of these cysts, the complete etiology is still unknown. Despite the numerous types of treatments available, these cysts often have a chronic relapsing course. Treatment options are numerous and include observation, intralesional injections with corticosteroids, minocycline, and trichloroacetic acid, aspiration with or without bolster dressing, incision and drainage with bolstering, and incision and drainage with or without subsequent deroofing. Despite the numerous treatment options available, the outcome in the majority of interventions is still unsatisfactory. Additional understanding of the pathophysiology of pseudocyst of the auricle is, therefore, critical in order to enhance the effectiveness of the treatment of this unique and rare entity.

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A 71-year-old man presented to our dermatological clinic with a 3-month history of a wound on his leg. He complained of weakness for the past few months. On his dermatological examination he had a 3×3-cm necrotic ulcer on his left tibia (Figure 1). On physical examination, there was 1×1-cm axillary lymphadenopathy. There was no other lymph node enlargement, hepatosplenomegaly, or gingival hypertrophy. Peripheral blood results showed 2.4×10^3/mm^3 leukocytes (normal range 4–11×10^3/mm^3) with 66% neutrophils. The hemoglobin value was 10.1 g/dL (13–18 g/dL), and the platelet count was 63×10^3/mm^3 (150–440×10^3/mm^3). No blasts were detected in a peripheral blood smear. His lactate dehydrogenase level was 567 U/L (240–480 U/L). All other results of blood chemistry were within normal limits. Punch biopsy of the skin lesion showed ulceration and dense dermal acute and chronic inflammation. There was a superficial and deep perivascular and periadnexal infiltrate of neoplastic cells composed of relatively abundant eosinophilic cytoplasm and large nuclei with blastic chromatin and occasional small nucleoli (Figure 2). Mitotic figures were prominent. Immunohistochemical stains were performed, and the neoplastic cells were CD3, CD20, CD138, and S100 protein negative. Myeloperoxidase and CD68 were positive. The histopathological findings were consistent with leukemic infiltration. Examination of bone marrow biopsy revealed that the blasts were constituted more than 20% of the bone marrow cellularity. Cytogenetic analysis of bone marrow aspiration with fluorescence in situ hybridization was negative for inversion 16, t(8;21) and t(15;7). Histochemical stains for myeloperoxidase, sudan black, periodic acid-Schiff, and alpha naphthyl acetate were also negative. Blastic cells were DR, CD13, CD117, and CD34 positive and CD5, CD7, CD10, CD14, CD19, CD20, CD33, CD41, CD56, CD64, and CD79 negative according to flow cytometry immunophenotyping. Blastic cells were 35% in the bone marrow. Based on the findings of bone marrow examination, the patient was diagnosed as having acute myeloblastic leukemia (AML) with minimal differentiation (subtype M0) according to French-American-British and World Health Organization classification. The examination of abdominal ultrasonography and thoracic and abdominal computed tomography revealed no metastases. The patient was treated with chemotherapy that consisted of cytarabine and daunorubicin. After chemotherapy, the lesion regressed. One month after chemotherapy, the patient presented to the hospital with a complaint of fever. He was diagnosed with febrile neutropenia. He died of cardiac failure 12 months after appearance of skin infiltration.

Neoplasms are dependent on angiogenesis and blood supply for continued and stable growth. When growth exceeds vascular supply, ulcers occur within neoplasms. It is generally recommended to perform biopsies on leg ulcers that have failed to heal. Although the timing of the biopsy is uncertain, some clinicians suggest performing biopsies on nonhealing ulcers after 2 or 3 months. Cutaneous involvement in patients with leukemia is classified into two groups: nonspecific and specific lesions. Nonspecific lesions do not contain neoplastic cells and occur in up to 40% of leukemic patients. Infections, drug reactions, vasculitis, and hemorrhagic diathesis are common examples of nonspecific lesions. Specific lesions of leukemia cutis (LC) are characterized by infiltration of the skin with neoplastic cells. Incidence rates vary from >5% to 40% depending on the type of leukemia. LC-induced skin lesions may take several different forms. While erythematous to violaceous papules and nodules are most frequent, infiltrated hemorrhagic plaques, perifollicular acniform papules, and generalized erythematous maculopapular eruption and necrosis may also exist. In our case, an uncommon manifestation, necrosis was prominent.

LC’s prevalence among AML is 2% to 9%. LC is most frequent among AML subtypes M4 and M5. LC is rare in AML-M0. To our knowledge, only four cases of LC with AML-M0 have been reported. Investigators defined one case of LC among 17 AML-M0 patients. Other experts defined another case of LC among 9 AML-M0 patients. Another report of a patient with LC had a cutaneous nodular eruption. As in our case, LC represented the first clinical manifestation of AML-M0. Investigators reported a 55-year-old woman diagnosed with AML-M0. She had one nodule as the manifestation of LC.
LC is more common in patients with known hematologic disease. Less frequently, however, LC might appear as the first symptom of leukemia. In the latter case, it becomes harder to diagnose LC, hence making the histopathology and immunophenotyping more important in accurate diagnosis.

On histopathological evaluation, the degree of infiltration varies from small perivascular deposits to dense diffuse infiltrates completely filling the dermis and often extending into the subcutaneous fat. Malignant myeloid cells tend to appear cytologically monotonous. Nuclei are round to oval and chromatin may be evenly dispersed. Immunohistochemistry is generally required for confirmation, as well as examination of peripheral blood and bone marrow. Cells are positive for myeloperoxidase. Myeloid cells do not express B-lineage or T-lineage markers. Some experts claim that CD68 and lysozyme immunostains are the most sensitive immunostains in the detection of myeloid leukemia cutis. Myeloperoxidase immunostain is useful, but immunostains for CD117 and CD34 are insufficiently sensitive. In another study, lysozyme and myeloperoxidase were found to be sensitive markers of myeloid lineage.

**CONCLUSIONS**

LC is accepted as a sign of poor prognosis. The treatment is directed at the leukemia itself.

Treatment response of LC is in line with the treatment response of the hematologic disease.

This case was unique because the patient consulted our clinic with a necrotic ulcer without prior history of myeloid leukemia or other hematologic disorder. Necrosis is an unusual presentation of LC and it is even harder to diagnose without a hematologic disorder.

We also want to emphasize the importance of examining the histopathology of long-standing leg ulcers and blood testing (hemography, peripheral blood smear) of patients who complain of weakness or weight loss.

**REFERENCES**

**HISTORICAL DIAGNOSIS & TREATMENT**

*Diagnosis and treatments have advanced over the past century. This feature depicts conditions from a collection of stereoptical cards published in 1910 by The Stereoscopic Skin Clinic, by Dr. S. I. Rainforth.*

**SYPHILIS PRIMARIA:** Sclerosis syphilitica et oedema indurativum.

A few days after the appearance of the chancre it is not uncommon to palpate a few hard painless cords which vary in thickness from that of a pin to that of a match and extend from the neighborhood of the chancre toward the base of the penis. They are lymphatic vessels which have become specifically indurated, plugged with agglutinated leucocytes or compressed by perilymphangitic infiltration. They disappear usually with the induration of the chancre, that is in four to six weeks. Occasionally the lymphatic involvement is so extensive that it causes considerable edema of the prepuce, which differs from an ordinary inflammatory edema however, in that it is very firm and elastic, like caoutchouc, and does not pit on pressure, its border is rather abrupt in its substance the hard lymphatic cords can often be felt, the skin over the affected area is nearly always dusky red, and the swollen tissues are painless and not at all or only slightly tender. The form swelling usually causes phimosis and thus completely conceals any chancre located on the inner fold of the prepuce or in the coronary sulcus. The same lesion is more common in women associated with a chancre on a labium majus. It does not differ from the indurated edema of the penis except that the thickened lymphatics can rarely be palpated owing to their less accessible position. The swelling is usually quite sluggish, persists for weeks or months and even under treatment disappears very gradually, but without leaving any traces. Although a comparatively rare accompaniment of the primary sore this peculiar form of edema, when it is well marked, is a distinctive a specific lesion as the chancre itself. Nevertheless it is not advisable to begin constitutional treatment with mercury until the diagnosis has been confirmed by the finding of Spirochaeta pallida or the appearance of secondary manifestations.
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CASE STUDY

Inflammatory Linear Verrucous Epidermal Nevus With Genital Involvement

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An 18-year-old woman was admitted to our clinic complaining of pruritic lesions on her inguinal and genital areas that had been present since birth. She had previously used topical steroids and a combination of topical steroids and calcipotriol for approximately 6 months; however, the treatment was unsuccessful. Her medical history was unremarkable. On dermatologic examination, mild erythematous, lichenified, and verrucous papules occurring in a linear pattern on the right inguinal area and on the region extending from the right labium majus to the perianal area were noted (Figure). Additionally, an erythematous area with central erosion surrounded by maceration was noted on the intergluteal area. Two separate punch biopsy samples were obtained from the erythematous, lichenified, verrucous, papular lesion on the inguinal area and from the erythematous, eroded, macerated lesion on the intergluteal area. Histopathological examination of both biopsy specimens revealed a thin orthokeratotic layer and scattered parakeratotic layers, as well as papillomatosis and acanthosis of the epidermis with a slight hyperpigmentation of the basal layer. A mild, perivascular, chronic inflammatory cell infiltration was noted in the dermis. Based on the clinical and histopathological findings, the patient was considered to have inflammatory linear verrucous epidermal nevus, and cryotherapy was initiated. At the 2-week follow-up after the first application, it was observed that the itching complaint decreased substantially and the eroded lesions in the intergluteal area were re-epithelialized. On clinical follow-up, no improvement was observed in the papular component of the lesion after 4 sessions of cryotherapy. The patient voluntarily discontinued the follow-up after 4 sessions of cryotherapy.

Epidermal nevus is a hamartoma of the epidermis and papillary dermis, and may be keratinocytic, follicular, sebaceous, apocrine, or eccrine in origin. It usually appears during infancy, but rarely may be present at birth, or may develop in late childhood and even in adulthood.1–3 Verrucous epidermal nevus is the most common form of an epidermal nevus. The described clinical variants of verrucous epidermal nevus include localized verrucous epidermal nevus, systematized verrucous epidermal nevus, nevus unius lateris, ichthyosis hystrix, and inflammatory linear verrucous epidermal nevus (ILVEN).1 ILVEN occurs as a result of increased interleukin 1, interleukin-6, and tumor necrosis factor, as well as intercellular adhesion molecule levels; however, the exact etiology is unknown.3 In 1971, investigators first described ILVEN and established the following diagnostic criteria for ILVEN: early age at onset, female predominance, pruritus, a distinctive inflammatory histological appearance, and persistent skin lesions resistant to treatment.4 ILVEN usually appears at birth or during adolescence, and manifests as localized or widespread lesions.1,2 In a 23-case series, experts reported that the lesion was present at birth in 39% of the patients and that the age of onset ranged from 3 months to 6 years.3 ILVEN is usually sporadic, and familial cases are rare.2 In our patient as well, the lesion was present at birth and there was no family history. The most prominent complaint is itching.1–3,5 Despite the fact that itching was the main complaint in the present case, the patient was also concerned with the cosmetic appearance.

ILVEN usually consists of inflammatory papules that coalesce into unilateral, pruritic, erythematous, and verrucous plaques, occurring in a linear pattern along the lines of Blaschko.1–3 ILVEN is usually unilateral and localized to the lower extremities and gluteal area; however, the arms, genital area, and other parts of the body may also be involved.2 ILVEN with genital involvement has rarely been reported in the literature.5–7 A total of 15 ILVEN cases were diagnosed among a 233-case series of epidermal nevus, and of these, involvement of the inguinogenital area was noted in only 3 cases.7 In a study conducted on 23 cases of ILVEN, inguinal involvement was noted in 3 cases, while ILVEN was located on the penis, scrotum, labium major, and vulvae in 5 cases.5 In the present case, the ILVEN lesions
Figure. Linear erythematous, lichenified, verrucous papules on the right inguinal area and right labium majus.

case study

Chronic Lymphocytic Leukemia Revealed by a Granulomatous Zosteriform Eruption

Sondes Trojjet, MD; Houda Hammami, MD; Inès Zaraa, MD; Alia Bouzguarrou, MD; Meriem Joens, MD; Slim Haouet, MD; Amel Ben Osman, MD; Mourad Mokni, MD

A word (Granulomatous) in the title of this Case Study was incorrectly presented on the cover.

REFERENCES


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The histopathological appearance of ILVEN includes alternating parakeratotic and orthokeratotic areas. Psoriasiform epidermal hyperplasia with elongation of rete ridges, spongiosis, and exocytosis are present together with hyperkeratosis, acanthosis, and papillomatosis; moreover, perivascular lymphohistiocytic inflammatory infiltrate is noted in the upper part of the dermis. In the present case, histopathological examination revealed orthokeratosis, parakeratosis, papillomatosis, and acanthosis, which was consistent with the typical histopathology of ILVEN.

CONCLUSIONS

The treatment of ILVEN is difficult and usually unsuccessful. ILVEN is characteristically resistant to topical treatments, and maintenance of treatment is required for symptomatic recovery. Topical treatments include dithranol, corticosteroids applied under occlusion, tretinoin, calcipotriol, podophyllin, and intraleisional steroid application. Potent steroid and intralesional steroid injections provide temporary symptomatic relief. Dermabrasion and cryotherapy frequently result in recurrence. Better results have been achieved by carbon dioxide laser. On the other hand, successful results with the use of systemic retinoids have been reported, but lifelong treatment is required. In another report, a patient with complete recovery following 6 months of systemic etanercept therapy was reported. Surgical excision is the most definitive treatment for ILVEN. Our patient had previously received topical potent steroids and calcipotriol therapy, although the treatment was of no benefit. Cryotherapy was initiated and applied for 4 sessions. At the 2-week follow-up after the first application, it was observed that the lesions partially responded to the treatment; moreover, it was noted that the associated itching almost completely resolved and the eroded lesions in the intergluteal area were completely re-epithelialized. No regression was noted in the papular components of the lesions. The patient voluntarily discontinued the follow-up after 4 sessions of cryotherapy.
CASE STUDY

Oral Frictional Hyperkeratosis (Morsicatio Buccarum): An Entity to Be Considered in the Differential Diagnosis of White Oral Mucosal Lesions

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A 55-year-old man presented with desquamating lesions on his bilateral buccal mucosa intermittently for approximately 3 years. The alteration in texture within his mouth created an uncomfortable sensation and, at times, the lesions spontaneously peeled away requiring him to spit repeatedly. The patient denied any history of trauma, cheek biting, or use of tobacco products. On initial examination, the patient was asymptomatic and the oral mucosa had no abnormal findings, but on repeat examination when symptoms were present, the patient had shaggy white plaques on the bilateral buccal mucosa limited to the line of dental occlusion (Figure 1). The plaques could be easily peeled away from the underlying skin with a cotton swab without any pain, leaving behind normal underlying mucosa. A review of the prior biopsy of the affected mucosa revealed an irregularly hyperplastic epithelium with foci of ballooned epithelial cells within the upper layer, parakeratosis, and bacterial overgrowth (Figure 2). Microscopic examination of fragments of mucosa peeled away from the affected area revealed fragments of parakeratotic cornified material colonized by numerous bacteria (Figure 3). Results from periodic acid–Schiff stain revealed no fungal elements. The diagnosis of oral frictional hyperkeratosis was established based on the clinical and microscopic findings. It was concluded that the hyperkeratosis was likely caused by bite trauma or grinding of the teeth while the patient was asleep. Triamcinolone 0.1% ointment in Orbase and tretinoin 0.05% gel were ineffective. The patient found that rinsing with hydrogen peroxide solution was most helpful in reducing the lesions. A bite guard was recommended by an oral and maxillofacial surgeon, but the patient has yet to use it.

Oral frictional hyperkeratosis (OFH), also referred to as morsicatio buccarum or morsicatio mucosae oris, is a white lesion in the mouth that results from chronic trauma as a result of long-standing rubbing or biting by the teeth.1 This entity is well-recognized among oral and maxillofacial specialists and dentists, but is less frequently encountered, and possibly under-recognized, by dermatologists. Patients often seek help on discovering an irregularity of the oral mucosa, sometimes complaining of areas of peeling or shredding of tissue. Although this condition is usually self-induced, the patient may not be aware of his or her habit, which is often the result of grinding of the teeth during sleep. A 2009 study of 2552 dental outpatients revealed 0.9% of patients with frictional hyperkeratosis.2 Sites of involvement include the buccal mucosa and, less commonly, the labial mucosa and the tongue—all areas within reach of the teeth.3 The differential diagnosis of these lesions includes contact stomatitis, white sponge nevus, lichen planus, candidiasis, and oral leukoplakia, especially when lesions are present on the

Figure 1. Whitish plaque with an irregular surface on the left mucosa near the line of dental occlusion.
CONCLUSIONS

Depending on the causative factors, treatment may include the use of a bite guard during sleep to prevent the grinding of teeth; dental evaluation for the treatment of rough, sharp, or malpositioned teeth; or other psychological therapy to help break the habit of biting.

Awareness of this relatively common and benign condition of the oral mucosa will allow for greater recognition of OFH based on clinical features, obviating the need for an invasive biopsy. The clinical diagnosis can be confirmed by examination of desquamating tissue obtained painlessly from the patient with the use of a cotton swab. A biopsy may be indicated in cases of OFH with atypical clinical features.

REFERENCES

CASE STUDY

Vesicular Palmoplantar Pityriasis Rosea

Varinder Singh, MD;1 Meghna Sharma, MD;1 Tarun Narang, MD;1 Manas Madan, MD2

A 16-year-old young man presented with intensely itchy erythematous dermatitis on the body for 1 week and vesicular lesions on the palms and soles for 4 to 5 days. Lesions on the palms and soles were accompanied by severe burning and itching. The patient gave a history of sore throat and fever, 1 week prior to the onset of lesions. A general physical examination was normal, and cutaneous examination revealed multiple, well-defined erythematous scaly plaques with collarette scaling on the trunk and extremities (Figure 1). Vesicular lesions were seen on the palms and soles (Figure 2). The differential diagnoses we considered were pityriasis rosea and secondary syphilis. The possibility of dermatophytid, vesicular pityriasis rosea, and pompholyx was limited to the palms and sole lesions. Complete blood cell count was within normal limits. Results from antistreptolysin O titer, potassium hydroxide mount, and venereal disease research laboratory were negative. Skin biopsies were taken from the back and left palm. The biopsy specimen from the back revealed focal spongiosis, lymphocyte exocytosis, vacuolar changes in the basal layer, and perivascular lymphocytic infiltrate in the dermis (Figure 3). The biopsy obtained from the vesicular lesion on the left palm revealed an intraepidermal vesicle with no evidence of acanallolytic process (Figure 4). A diagnosis of pityriasis rosea was made and the patient was started on clarithromycin 500 mg once a day for 7 days, along with antihistamines and emollients. The lesions faded dramatically in a very short period, and there was significant involution of almost all of the lesions after 7 days of clarithromycin. During the 6 months of follow-up, no recurrence was observed.

Pityriasis rosea (PR) is an acute self-limiting dermatitis with a natural course that lasts from 4 to 6 weeks.1 Although no etiology has been proven, infectious agents, autoimmunity, drugs, and stress have been proposed as possible etiological factors.1,2 Recent studies have shown a probable etiological role for human herpesvirus (HHV) 6 and HHV-7 or both in PR. The detection of HHV-7 and HHV-6 DNA or both in peripheral mononuclear cells, tissues, and cell-free plasma of PR patients supports a causal relationship; however, proving a viral origin is a complex problem, especially for diseases associated with HHVs with a high prevalence in the general population.2

Typical PR is a clinical diagnosis for atypical eruptions without a definite diagnosis; however, it is safer to consider skin biopsy and other investigations to rule out other differential diagnoses.2,3 Histopathological characterization of PR is not specific but can help to diagnose atypical variants. Histopathological findings of PR include absence or decrease of the granular cell layer, extravasation of red blood cells in the papillary dermis and partly into the epidermis, dyskeratosis, liquefaction of basal cells, homogenization of papillary collagen, and intraepidermal vesicles in apparently dry skin.4 The vesicular lesions are caused by severe spongiosis, exocytosis, and intraepidermal vesicles. Some studies have also observed multinucleated giant cells and acantholysis in the epidermis. Electron microscopic studies have detected virions resembling HHV-6 and HHV-7 in the epidermis and dermis close to the blood vessels, suggesting that the virus invades the extravascular dermal spaces and damages the dermal and epidermal tissues either directly or by its interaction with the host immune mechanism.4

Vesicular PR is rare; there are few reports of vesicular PR in the literature. Investigators have reported an incidence of 0.5% in a study of 380 PR cases.3 It is seen more frequently in children and young adults, may be severely pruritic and extensive, and tends to persist longer than the common variant of PR.6 The lesions may either preceede the classic eruption of PR or appear simultaneously.7 Vesicular PR may be mistakenly diagnosed as dishidrosis, dermatophytid, scabies, drug eruption, or varicella. Generally, no treatment is required in asymptomatic cases because of the self-limiting nature of the disease.6 A recent Cochrane collaboration paper suggested that there is inadequate evidence for the efficacy of all topical medications, and agents that have not been found to be significantly beneficial include sunlight, artificial UV therapy, systemic antihistamines and corticosteroids, antiviral agents, and intravenous glycerylizin. Although there are reports of high doses of acyclovir being useful in PR, there is some evidence that oral erythromycin may shorten the course of the rash and alleviate pruritus.6,8 Clarithromycin has also been
used successfully in one study.\textsuperscript{10} Our patient responded well to clarithromycin, wherein lesions started regressing within 7 days and he had no relapse until 6-month follow-up.

The excellent response in our case with clarithromycin may be caused by the anti-inflammatory and immunomodulatory effects of clarithromycin,\textsuperscript{11} or it could indirectly suggest involvement of pathogens such as streptococci, mycoplasma, legionella, and chlamydia\textsuperscript{12} in causing or triggering PR in our patient, which respond well to clarithromycin.

**CONCLUSIONS**

Clinicians should be aware of the wide spectrum of PR variants so that appropriate management and reassurance can be offered. Despite the rarity of vesicular PR, physicians should include this entity in the differential diagnosis of sudden-onset vesicular eruptions. More analytical studies on viral and bacterial etiology are needed to settle the issue of etiopathogenesis.
REFERENCES


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**BOOK REVIEW**

Noah S. Scheinfeld, MD, JD, Section Editor

**Hall's Manual of Skin as a Marker of Underlying Disease**

Edited by John C. Hall and Brian J. Hall. 300 pages. Shelton, CT; People’s Medical Publishing House–USA; 2011. $89.95. ISBN 1607951029

Some day all skin diseases, I think, will be understood by physicians as nosological moebius strips. That is, infectious diseases will be seen as aberrations of immunity and reifications of mutated DNA. Cancer will be viewed as a phenomenological Venn diagram of mutations, viral interpolations, and immunological underachievement. Diseases of immuinity will be understood as a collection of infections and neoplastic sins that cannot be undone. Until that time and perhaps even in that time, the physician will be well advised to carry and review Hall’s Manual of Skin as a Marker of Underlying Disease, a skillfully edited book with an international talent show of contributors.

This dermatologic text, which reads like a roman à clef, takes its place with the other necessary works that have addressed dermatology and systemic disease by Braverman,1 Callen,2 and Provost.3 In one important way, Hall’s book surpasses them. Hall’s price point is under $100, which means that Hall’s book can be presented by the pharmaceutical companies as an educational aid.

Just as a Jewish scholar keeps a Mishnah Torah authored by the Rambam on his desk, the Tur (Arba’ah Turim) by Jacob ben Asher in his archive, Rabbi Yitzchak Alfasi’s the intelligent digest “the Rif” in the appendix sections of his Talmud and the Shulcan Aruch by Yosef Karo on his wall with the handy glosses of the Rema, Moses Iserles on Karo’s pages, the scholar is advised if he can to keep all these 4 books on systemic disease within arm’s length. Hall’s book covers the topics of internal diseases and skin in a brief but effective fashion, with sections on neurological, infectious, pediatric, genetic, and other topics divided into chapters on the manifestation of the specific disease states. Each chapter is unique and replete with excellent information.

I particularly enjoyed the section on neurological diseases and the skin. I found the discussion on reflex sympathetic dystrophy (RSD) enlightening. I confess that I had never parsed RSD into its 3 stages until I read the chapter in Hall’s book. These stages are:

- **Stage one**: RSD characterized by severe burning pain at the site of the injury, with muscle spasm, joint stiffness, restricted mobility, rapid hair and nail growth, and vasospasm.

- **Stage two**: RSD characterized by more intense pain. The swelling spreads, hair growth diminishes, nails become cracked, brittle, grooved, and spotty, osteoporosis becomes severe and diffuse, joints thicken, blisters form, and muscle atrophy occurs.

- **Stage three**: RSD characterized by irreversible changes in the skin and bones, while the pain becomes unyielding and may involve the entire extremity. There is marked muscle atrophy.

I vividly recall while I was a resident seeing a patient in the palliative care unit of Beth Israel Hospital near Stuyvesant Park Manhattan who had chronic pain and blisters on his feet. I could not make the diagnosis at the bedside. With the help of PubMed, I eventually was able to make this diagnosis. Not until I had read Hall’s book did I know how to stage RSD.

The pictures are commendable and added to my visual memory. In particular, the chapter on eye diseases has great images. In the sections on endocrine diseases, I learned a bit; however, some of the information in the chapter on diabetes I came to believe was more founded in the author’s opinions rather than in recognized fact. In particular, I think the author’s suggestion that lichen planus and granuloma annular can be associated with diabetes is one such example. I enjoyed the discussion and pictures involved with nutritional disorders and thought the color plates memorable. The discussion of lupus was a bit muddled as evidenced by a chart parsing lupus into many categories and subcategories, but then the current understanding of lupus is muddled and resembles Ptolomey’s complex system utilizing a physical realization of the universe as a set of nested spheres rather than Relativity’s austere truth. The discussion of graft vs host disease would benefit from a discussion of the use of UV-A1 and imatinib as treatments, which I mention because dermatologists should more carefully understand these therapies.

This book fills the reader with wonderment and is easy to read. The audience will be at once the seasoned dermatologist as well as the resident in need of levening, each of whom will benefit from reading this book and referring to it, frequently. The reasonable price means that it will actually get into hands and in front of the eyes of dermatologists, hopefully everywhere.

**REFERENCES**


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and bilateral papilledema. Manifestations of adrenal suppression in pediatric patients
include low plasma cortisol levels to an absence of response to ACTH stimulation.

Topical corticosteroids. At the first follow up visit, approximately one month after the conclusion of
treatment, 65 days post-treatment. Subjects did not develop any other signs or symptoms of HPA axis suppression.
The exception of one subject. This last subject recovered adrenal function by
the second post treatment visit, 65 days post-treatment.

Corticosteroids could result in sufficient systemic absorption to produce detectable
other untoward effects. It is not known whether topical administration of
corticosteroids has been shown to be teratogenic after dermal application in
laboratory animals. There are no adequate and well-controlled studies in
pregnant women. Therefore, Locoid Lipocream should be used during pregnancy
only if the potential benefit justifies the potential risk to the fetus.

Please refer to full prescribing information for detailed information regarding
systemic embryofetal development studies.

Pediatric Use
Safety and efficacy in pediatric patients below 3 months of age have not been
established.

Because of higher skin surface-to-body-mass ratios, pediatric patients are at a
greater risk than adults of HPA axis suppression when they are treated with topical
corticosteroids. They are therefore also at a greater risk of glucocorticosteroid
insufficiency if Locoid Lipocream is applied to large surface areas or used
under occlusion. If HPA axis suppression is noted, reduce the application frequency,
discontinue use, or switch to a lower potency corticosteroid.

Systemic effects of topical corticosteroids may also include manifestations of
Cushing’s syndrome, hyperglycemia, and glucosuria. Pediatric patients may be more susceptible to systemic toxicity due to their larger
skin surface-to-body-mass ratios.

Initiate appropriate therapy if concomitant skin infections develop.
Discontinue use if irritation develops.

Adverse Reactions
The most common adverse reactions (>1%) are HPA axis suppression and
applying corticosteroids on the face, under arms, or groin areas unless
constitute occlusive dressings.
Do not use Locoid Lipocream in the diaper area, as diapers or plastic pants may
preclude occlusive dressings.

Avoid contact with the eyes.
Do not bandage, otherwise cover, or wrap the affected skin area so as to be
occlusive unless directed by your physician.

Do not use Locoid Lipocream in the diaper area, as diapers or plastic pants may
preclude occlusive dressings.

Do not use Locoid Lipocream on the face, underarms, or groin areas unless
directed by your physician.

If no improvement is seen within 2 weeks, contact your physician.

Do not use other corticosteroid-containing products while using Locoid Lipocream
without first consulting your physician.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP Controlled
Room Temperature]. Protect from freezing. Keep out of the reach of children.

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Locoid Lipocream is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses, including the treatment of mild to moderate atopic dermatitis in patients 3 months of age and older. Safety and effectiveness in pediatric patients below 3 months of age have not been established.

Reversible HPA axis suppression may occur, with the potential for corticosteroid insufficiency. Consider periodic evaluations for HPA axis suppression if applied to large surface areas or used under occlusion. Systemic effects of topical corticosteroids may also include manifestations of Cushing’s syndrome, hyperglycemia, and glucosuria. Pediatric patients may be more susceptible to systemic toxicity due to their large skin surface-to-body-mass ratios. Initiate appropriate therapy if concomitant skin infection develops. Discontinue use if irritation develops. Please see full Prescribing Information on adjacent page.

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