Dear Reader,

As the year draws to a close, many people will be busy participating in holiday festivities — dressing up to attend parties in their fanciest footwear or dressing down to travel home, often to cold climates where warmth will be the biggest concern. With the selection of footwear for so many occasions on the minds of so many, it seems an appropriate time to focus an issue of this newsletter on shoe dermatitis—its causes, its prevention, and its management.

Shoe dermatitis is a complicated yet necessary diagnosis because the best bet for successful treatment is identifying the underlying allergen so that an avoidance strategy can be devised for the patient. The complexity mainly arises for two reasons. First, the many chemicals present in footwear and other products that contact the feet make it challenging to identify the culpable allergen. Second, shoe manufacturing and marketing are complicated international processes and imports abound. Consequently, it can be difficult to determine the substances that may be present in any given pair of shoes and to identify alternative products that are allergen-free.

As you will learn in this issue, however, patch testing with both commercial allergens and a patient’s own footwear products is the surest way to good outcomes, especially with a little help from your friends here at Smart Practice. We all extend our warm wishes for a happy, safe, and dermatitis-free holiday season!

Sincerely,

Dr. Curt Hamann
President & CEO, SmartPractice

Shoe dermatitis is relatively common. Estimates of its prevalence among patch-tested patients range from 1.5 to 24.2%. And no wonder. The environment within a shoe—warm and occlusive—is perfect for promoting perspiration. In turn, the moist conditions help leach and disseminate the many potential sensitizers from shoe materials. Concomitantly, the moisture facilitates skin absorption. The friction that shoes impose on the feet further favors the development of allergic contact dermatitis (ACD). It’s almost difficult to conceive of a situation more optimal for promoting sensitization and for inhibiting healing of dermatitis.

People have probably developed contact dermatitis from their footwear since shoes were invented because tanning leather has always involved chemicals. However, the major related shoe allergens have changed with changes in manufacturing processes. In 1877 the first case of allergic contact dermatitis from shoe linings was noted in a treatise on skin disease. In the 1930s and 1940s, most cases of shoe contact dermatitis were attributed to leather and dyes. By the 1950s and 1960s, rubber allergens were recognized as the most common identifiable cause of foot dermatitis. Based on a retrospective review of patients with foot dermatitis from the North American Contact Dermatitis Group (NACDG) published in 2007, the adhesive p-tert-butylphenol-formaldehyde resin (PTBP-FR) discussed in the previous issue of this newsletter, was the most common shoe allergen followed by potassium dichromate. However, a long list of potential allergens, including other elastic and potentially allergenic compounds used to glue the parts of shoes together, can underlie shoe dermatitis. Besides adhesives, other major identifiable causes of shoe dermatitis include rubber and rubber additives, tanning agents, dimethyl fumarate, dyes, metals, and aldehydes. Indeed, an almost bewildering number of allergens are associated with shoe dermatitis.

Both natural and synthetic rubber and sometimes a combination of both may be found in shoes. Rubber box-toe shoes/boots have been reported as the most common cause of shoe dermatitis, but rubber is also used in other footwear such as sneakers, tennis shoes, slippers, boots, sandals, and flip-flops. Furthermore, rubber cements are used in joining shoe uppers, the outer leather and linings. Most rubber allergens are related to chemicals added during the processing of the latex—typically oxidants to slow degradation of the polymer and accelerators to speed the rate of vulcanization. In the NACDG study of shoe dermatitis, rubber chemicals considered as a group, which included carba mix, thiuram mix, mercaptobenzothiazole, mercapto mix, mixed dialky ureas, and black rubber mix, were the most common cause of shoe dermatitis (40.4%). Likewise, rubber chemicals are common shoe allergens in Brazil, Australia, and Britain. Other chemical accelerators to test for in patients with shoe dermatitis include thioureas, diphenylguanidine, diamino diphenylmethane, 4,4-dithiodimorpholine, cyclohexylidithiophthalimide, and hydroquinone monobenzylether.

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These Boots are Made for Walking...and Causing Shoe Dermatitis

As the end-of-the-year holiday parties approach, everyone will be wearing their fanciest footwear. And as winter settles in for the duration, they will also be pulling on their toastiest boots. Will they also be inducing, eliciting, or exacerbating a case of shoe dermatitis?

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The adhesives used to bind the various parts of shoes together, such as PTBP-FR mentioned above, are another group of shoe allergens. While its prevalence as an allergen is reportedly high in North America and also in Pakistan, PTBP-FR has been a relatively unimportant allergen in studies from Brazil and Britain. Colophony, a tree sap used in natural rubber latex cement and another potential adhesive allergen found in shoes, has been associated with positivity rates as high as 9%. Epoxy resins are also known shoe allergens. These resins are polymerized with diglycidyl ether of bisphenol A or bisphenol F, both of which have been associated with shoe dermatitis. Bisphenol A is usually considered the stronger sensitizer and may be encountered in footwear such as flip flops. The glue catalyst and plasticizer, benzyl peroxide, is a potential shoe allergen included in some patch test shoe series. Workers in a factory producing shoes from polyvinyl chloride have developed an occupational allergy to the plasticizer dibutylphthalate.

The process of preparing the leather used in shoes introduces allergens related to tanning. Chromate salts, particularly trivalent salts (e.g., chromic acid, chromic sulfate, and chrome trichloride), are often used to tan leather. These compounds act by binding to the collagen in leather and stabilizing it. During the tanning process, however, the trivalent salts may oxidize to hexavalent chromium (Cr(VI)). These forms bind poorly to proteins, which increases their bioavailability. When feet perspire in chromate-tanned shoes, the potent contact allergen can be leached from the leather setting the stage for sensitization. Potassium dichromate is the hexavalent form typically used in patch testing, and it has been found to be a common shoe allergen around the world. In the NACDG study of shoe dermatitis, potassium chromate was the most common allergen, followed by dithranol, followed by dithranol, followed by dithranol.

Unfortunately, the list of allergens associated with dermatitis of the feet does not end here. The many allergens that may be present in shoes include arsenic, cadmium, copper, lead, zinc, and mercury. Other substances used to tan leather are used to make shoes and can provide relief for chromate-sensitized individuals. However, these alternate tannins may also be allergens. Shoes made from vegetable tannins are a popular substitute for patients with a chromate allergy. Vegetable tannins may be extracted from the bark, leaves, wood, fruits or roots of many types of trees and plants. One of the oldest vegetable tannins is derived from chestnut. Another common tannin is extracted from an Argentinian hardwood evergreen known commonly as quebracho. Its name, quebracho, reflects the hardness of its wood. The term is a composite of two Spanish words—quebrar, meaning to break, and hacha, meaning ax—that is, the ax breaks. Yet another vegetable tannin comes from mimosa, an extract from the bark of the black wattle tree, an Acacia species originally from Australia. Black wattle is also grown in large plantations in Brazil, China, Vietnam, South Africa, Kenya, and India. The vegetable tannin myrobalan, from the ground nuts of the Terminalia chebula tree, which grows in Nepal, India, Sri Lanka, Burma, Thailand, Indochina and south China, is also used in tanning shoe leather. A mixture of these vegetable tannins may be used for tanning, and a secondary wattle tanning can follow tanning with chrome. Formaldehyde, a less common shoe allergen, is used in the tanning of white leather shoes. In one case the pattern of foot dermatitis in a woman who was patch-test positive to formaldehyde corresponded to the areas of contact between her feet and a pair of white pumps. Glutaraldehyde, another recognized allergen, also may be used in tanning leather, but its role in foot dermatitis is thought to be minimal.

Dyes, particularly paraphenylenediamine (PPD) and 4-aminoazobenzene, can be shoe allergens. Other dyes reported to have caused shoe allergies include disperse orange 3, acid yellow 36, disperse red 1, and disperse blues 106 and 124. It is prudent to remember that many other textile dyes may be present in socks.

Dimethyl fumarate (DMF) is a somewhat surprising shoe allergen. This methyl ester form of fumaric acid was first recognized as a cause of ACD because of its use in furniture manufactured in China. A potent allergen, DMF is found not in shoes themselves, but in sachets in shoe boxes. The presence of DMF prevents the growth of mold during storage but in so doing permeates the leather. The location of symptoms may reflect the concentration of the DMF in shoe. In a Spanish study, most patients’ symptoms primarily began with erythema involving the dorsum of the toes and feet followed by the entire foot and then bottom of the leg. In March 2009 the European Commission limited the amount of DMF in products to no more than 0.1 mg/kg.

These Boots are Made for Walking…and Causing Shoe Dermatitis…continued
Shoe dermatitis is easily misdiagnosed and must be differentiated from a host of other conditions that can affect the feet: infections, atopic dermatitis, nummular foot dermatitis, irritant contact dermatitis resulting from friction in the moist, occlusive microenvironment, juvenile plantar dermatoses, pompholyx, psoriasis, lichen planus, and even allergic contact dermatitis (ACD) related to a nonshoe allergen (e.g., cosmetic or body care product). When limited to the feet, acral psoriasis, palmoplantar pustulosis, and pityriasis rubra pilaris can be confused with shoe dermatitis. Although infections may be recognized more easily, a Dermatophyte infection should still be ruled out in patients suspected of ACD involving the feet. The presence of more than one dermatitic condition simultaneously—so-called hybrid dermatitis—can further complicate the diagnosis. Health care providers may be more prone to make certain misdiagnoses in particular populations. In athletes, for instance, shoe dermatitis may be mistaken for tinea pedis. What is the best approach for diagnosing—the key to management—the underlying cause of shoe dermatitis?

Differentiation of shoe dermatitis from conditions that have similar clinical manifestations begins with recognizing the most common pattern of symptoms. Shoe dermatitis may manifest with a mild, itchy rash, but severe pruritis associated with swelling and small blisters also occurs. In chronic cases, dry, lichenified lesions may be present. In severe cases open sores can lead to secondary bacterial infections, while painful fissures can impair gait and be quite disabling. Although a unilateral outbreak is possible, the classic eczematous pattern of contact dermatitis from shoes is symmetrical, involving the dorsal foot and ankle. The interdigital spaces, however, are spared—a diagnostic hallmark. The dorsal surface of the big toe and the instep are often the first sites involved. The dermatitis may later spread to other toes and to the dorsal aspect of the foot. Over time it may reach the ankle—a clue that the disease process is ACD—especially when it shifts from being stable and well-localized and spreads in a poorly localized fashion. Overall, the dermatitis involves the weight-bearing parts of the foot where friction and pressure from the shoes occur. Consequently, the pattern of foot dermatitis reflects the design of the responsible shoe(s).

As with any contact dermatitis, patch testing is the gold standard for diagnosis. Patients who have no reaction to allergens on baseline series but are suspected of having shoe dermatitis can be tested with expanded series of petrolatum footwear allergens, which are available commercially for the purpose. As noted in a recent review of shoe dermatitis published in the journal, Dermatitis, 29 of the 35 allergens on the ready-to-use T.R.U.E. TEST® are potentially relevant allergens for shoe dermatitis. Therefore, T.R.U.E. TEST can simplify patch testing for shoe dermatitis by reducing the number of petrolatum allergens that must be purchased, stored, and prepared. The convenience applies to testing with both baseline and expanded series.

Studies indicate that expanded patch testing for shoe dermatitis is important. The need in cases suspected of having shoe dermatitis is underscored by a finding from the North American Contact Dermatitis Group (NACDG): The NACDG baseline series failed to detect a relevant allergen in almost 13% of the patients with foot dermatitis. As part of extended patch testing, most practitioners also advocate patch testing with pieces of a patient’s own footwear—shoes and socks. A recent case of a patient with persistent dermatitis who wore shoes labeled as “chromium-free” underscores the challenges associated with identifying the sensitizers in shoes. Despite a negative spot test for Cr(VI), the shoes were analyzed by x-ray fluorescent spectroscopy and found to contain chromium. When such advanced testing is unavailable to identify the sensitizers in a shoe, patch testing with shoe samples at least allows patients to know which shoes should be removed from their wardrobe.

Optimally, samples from all footwear should be tested on the patient's back. The materials, which should be about 1 cm² and less than 2 mm thick, should be soaked in water for 15 minutes before application. Thin pieces help avoid inducing false-positive irritant reactions. To avoid false-negative results some experts recommend leaving the personal samples in place for 4 or 5 days. (The other allergens, however, are worn for the usual 48 hours.) When a patient has a negative reaction to patch testing but suspicion remains strong, allergen extraction from a shoe sample using an ultrasonic bath may concentrate the sensitizer enough to elicit a response.

Sometimes when a patient has a positive patch test reaction to an allergen, determining whether it is the relevant allergen can still be challenging. In general, there are no requirements for detailed labeling of the chemical composition of footwear. Second, shoes are often imported, which further complicates discovering the chemical components used in the manufacturing process. In particular, the United States has been the world's largest importer of shoes, and China has been its biggest supplier. Furthermore, regional differences exist in the allergens that dominate a given market—so footwear allergens that are common in one country might be rare in another. For example, PTBP-FR is a frequent allergen related to shoe dermatitis in North America, Pakistan, and Portugal with a reported prevalence of greater than 20% in all three countries. In contrast, the prevalence of PTBP-FR as a shoe-related allergen in studies from Canada, Brazil, and Britain has been less than 5%. Although gas chromatography and mass spectroscopy have been used to identify potential chemical allergens in shoes, their practicality in a typical clinical practice is probably limited.

This recalcitrant condition can be chronic and difficult to treat without identification of the underlying allergen—information needed to guide shoe selection. Nonetheless, a good prognosis is associated with aller-
gen avoidance. In one report, for example, a mean of 2.9 years after patch testing, shoe dermatitis had improved or resolved in 87.5% of the patients. Atopy, however, may be associated with a poor prognosis. In these patients existing dermatitis does not always clear even with allergen avoidance.

When possible, patients should wear shoes that do not contain the allergen causing their shoe dermatitis. Patients allergic to the chromate used to tan leather will benefit from wearing chromium-free leather shoes. If such shoes cannot be obtained, switching to a new pair of leather shoes every few months has been recommended as has wearing two pairs of socks and alternating shoes. Vegetable-tanned shoe insoles are another alternative, and shoes from synthetic materials are readily available. An option for patients with rubber allergies is to replace the insoles of their shoes with cork, composite or felt applied with a non-rubber cement. Although expensive, custom-made shoes are available from a variety of sources. Sachets that come with the shoes may contain dimethyl fumarate and should be removed upon purchase.

Socks may be worn as a barrier, but it is best if they are changed frequently. A special MicroAir® Barrier Sock is now available. The two outer layers of the socks are made from a knit polyester microfiber constructed with a raised woven design and the inner layer is a microporous membrane. They are designed to be impermeable to liquids, ions, and gas while wicking away moisture at a high rate. Good outcomes were obtained in a small study of the efficacy of these barrier socks, especially when patients complied with the protocol by wearing the socks every time they wore shoes. However, the socks appear somewhat bulky, and some patients reported physical and social discomfort when wearing them. Favorable case reports have also been published. Successful use of barrier creams has been reported, but such creams have also been reported to worsen dermatitis.

Good skin care that includes moisturizing emollients or humectants is an important adjunct to avoidance. Measures to control sweating of the feet may be helpful—hyperhidrosis may be present in many patients who develop shoe dermatitis. Over-the-counter products should be used before escalating treatment to prescription medications. Typically systemic corticosteroids would be used only after more conservative treatment has failed. Treatment with an antibiotic may be needed if the skin becomes infected. As with any contact dermatitis, however, the most important part of management is perhaps patient education, and we at SmartPractice are here to help you insure that your patients are comfortable about kicking off their shoes and dancing in their dermatitis-free feet at all those holiday galas and beyond!

References
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