



Shoe Dermatitis: Causes, Prevention, and Management

Here's an update for the podiatric physician.

Objectives

- 1) Appreciate the clinical data regarding the causes of shoe "contact" dermatitis as found in the literature.
- 2) Recognize key features present during the presentation of shoe dermatitis.
- 3) Appreciate the management and prevention of shoe dermatitis.

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Following this article, an answer sheet and full set of instructions are provided (p. 200).—**Editor**

By Robert G. Smith, DPM, MSc, RPh

Introduction

At least seven pairs of shoes are purchased by American families annually. Podiatric physicians have come to realize that there is a variety of footwear styles: casual, formal, work, and athletic shoes made all over the world from leather, rubber, and other synthetic materials. For this reason, it is impossible to identify precisely all of their constituents. A vast variety of potentially sensitizing chemicals are used during shoe manufacturing and finishing. A medical condition referred to as "shoe dermatitis" is a form of con-

tact dermatitis caused by the contact of the foot with parts of the shoe due to these chemicals.^{1,3} Despite a warm and humid environment inside shoes, shoe dermatitis is relatively uncommon. Shoe dermatitis is a diagnostic and therapeutic challenge and is a common type of contact dermatitis affecting children and adults regardless of race. For this reason, it is imperative that the foot and ankle physician become familiar with recognizing signs and symptoms of shoe dermatitis so that patients can be accurately diagnosed and appropriately treated to avoid secondary infections and disability.

This review will first present

causative factors for the etiology of shoe contact dermatitis supported by clinical based evidence as found in the medical literature.^{2,3} Secondly, a description of the signs and symptoms of shoe contact dermatitis will be presented in a narrative fashion.^{2,3} Finally, both treatment options and preventative measures to avoid shoe dermatitis will be offered to the podiatric clinician.

Causes of Shoe "Contact" Dermatitis

Allergic contact dermatitis is caused by the body's reaction to something that directly contacts the

Continued on page 190

Shoe Dermatitis...

skin. Many different substances, called "allergens", can cause allergic contact dermatitis. Cronin reports that historically in the 1930s and 1940s, leather and dyes caused most of the presenting cases of shoe contact dermatitis.⁴

By the 1950s and 1960s, rubber allergens became the most common identifiable cause of foot dermatitis.^{3,4} Today, shoe dermatitis may occur if a person is sensitive to the rubber or elastic compounds in shoes, form inserts, or elastic glues used to bind shoe components. The other identifiable causes of shoe dermatitis are cements, dichromates used in tanning, dyes, anti-mildew agents, formaldehyde, and nickel

eyelets or nickel arch supports.

The allergen is usually a rubber accelerator or antioxidant used in the manufacture of rubber rather than rubber or latex. Rubber continues to be blamed as a common cause of shoe dermatitis, especially when the antioxidant monobenzyl hydroquinone is present.^{3,5} This antioxidant may also cause hypopigmentation of the skin.⁵

The paraphenylenediamine group of rubber additives are an important cause of industrial dermatitis. Shoe dermatitis is usually caused by the rubber adhesive used to glue the parts together. Moreover, adhesives, both rubber and non-rubber, can cause problems so much so that even leather shoes may contain products that cause shoe dermatitis.

Chromates

Chromates are compounds that contain chromium and are commonly responsible for allergic contact dermatitis from contact with cement, leather, some matches, paints and anti-rust compounds. Chromates are used to tan leather for shoes and clothing. Chromium is gradually liberated from leather collagen by the action of hydroxyl acids in sweat, especially when shoes are worn without stockings.⁵

Athletic running shoes, as well as swim fins, contain rubber accelerators, antioxidants, and other rubber additives that are common causes of foot dermatitis.⁶ These compounds include: thioureas, thiram, carbamates, N-isopropyl-N-phenyl-p-

Continued on page 191

TABLE 1
The Most Common Allergens in Shoe Dermatitis Found in the Literature

Study	Year	Patient #	Method	Common Allergens
Saha et al.	1993	50	Patch test	Potassium dichromate, colophony
Freeman	1997	55	Interview	Rubber, chromate, para-tert-Butylphenol formaldehyde, colophony
Shackelford and Belsito	2002	704 70*	Patch test	Rubber components, chromated leather adhesives
Rani et al.	2003	119	Patch test	para-tert-Butylphenol formaldehyde, cobalt chloride, glues
Lazzarini et al.	2004	1027 53*	Patch test	para-tert-Butylphenol formaldehyde, chromate, rubber chemicals, dyes
Holden and Gawkröder	2005	3337 230*	Patch test	Chromate, rubber chemicals, paraphenylenediamine
Nardelli et al.	2005	8543 474*	Patch test	Potassium dichromate, cobalt chloride, paraphenylenediamine, rubber components para-tert-Butylphenol formaldehyde, colophony
Chowdhuri and Ghosh	2007	640 155*	Patch test	Potassium dichromate, cobalt chloride
Warshaw et al.	2007	10,061 109*	Patch test	para-tert-Butylphenol formaldehyde, Potassium dichromate, carba mix
Bajaj et al	2007	1000 310*	Patch test	Potassium dichromate, mercaptobenzthiazole, mercapto mix

* Accounts for the number of patients with contact dermatitis from footwear

Shoe Dermatitis...

phenylenediamine, and mercapto-benzothiazole.⁶ As with other footwear, the dye found in the in-soles of certain running shoes has caused contact dermatitis in runners.

Review of the Literature

A review of the medical literature reveals a number of case reports, retrospective observations, random control trials, and practice guidelines that identify the potential antigens responsible for shoe dermatitis.⁶⁻²⁸ Shoe contact dermatitis resulting from shoe linings was first noted in 1877 and has appeared as a recent case report in which the cause was attributed to para-tertiary-butylphenol formaldehyde.^{12,15,19} The most common allergens responsible for causing shoe dermatitis as found in the literature are presented graphically as Table 1.

Saha, et al. conducted a study to determine the prevalence and clinical patterns of footwear dermatitis.¹⁰ Fifty patients with suspected shoe dermatitis and thirty control subjects were patch-tested with 22 allergens.¹⁰ While seventy percent of patients showed sensitivity to these footwear allergens, both potassium dichromate and colophony were identified as the most common sensitizers.¹⁰ The validity of this observational design study is strengthened by the investigators' use of matched controls to avoid observer bias. These investigators stress that there should be footwear screening to detect responsible allergens and call upon both manufacturers and research institutions to assist with such screenings in order to provide non-allergenic footwear to the public.¹⁰

Observational results reported by Freeman in 55 patients with chronic foot dermatitis revealed "rubber" as the most the common allergen, followed by chromate, p-tertiary-butylphenol-formaldehyde resin and colophony responsible for causing chronic footwear dermatitis.^{3,9} In this study, the incidence of shoe dermatitis was almost equal in both genders. A hallmark observation identified by Freeman was that during a differential diagnosis, all parts of the foot were affected except the inter-digital areas and hyperhidrosis was found in all subjects.⁹

At the center of this report is the foremost intention of the investigator to analyze interventional data from subjects retrospectively. Freeman's patient improvement (the resolution of symptoms of 87.5%) was attributed to successfully finding suitable footwear secondary to patch testing that identified the principle causative antigen.^{3,9} However, the relatively small representative sample size in this study does impact the magnitude of precision as it relates to likelihood estimates when used and applied to generalize populations. Therefore, the effectiveness of the intervention of empowering patients with allergen awareness may not be fully appreciated because of bias.

Shackelford and Belsito demonstrated that rubber components were the most common allergens contributing to the etiology of allergic-appearing dermatitis.^{3,7} The continued and increased frequency with which rubber components act as causative allergens in shoe dermatitis is a reflection of their continued use, further accentuated by Belsito.^{3,8}

Shackelford and Belsito used a five-year retrospective investigational method on 704 patients who were patch-tested. Ten percent of these patients demonstrated a clinical presentation suggestive of allergic contact dermatitis.⁷ Because this was a retrospective design, verifying the existence of risk factors or outcome conditions to the same degree as seen in prospective study design is difficult. It is possible that this investigation may have both elements of recall and or selection bias.

Most athletic shoes increase the probability of perspiration because of the combination of the impermeable nature of their construction.^{3,8,11} Rubber allergens will penetrate the skin at a greater rate because of this increase in perspiration and will result in increased skin exposure and sensitization of these materials.^{3,8,11}

A prospective investigation conducted by Rani, et al. included 119 patients (21 males and 98 females) suspected of having contact dermatitis due to shoe allergens.¹⁶ Both shoe series and European Standard series patches were applied on the upper back of each subject and removed after forty-eight hours.¹⁶ Seventy-three percent (n=87) reacted positively to a variety of allergens. These

authors determined quantifiably that glues and para-tert-butylphenol formaldehyde resin were the leading causes of shoe dermatitis.¹⁶ Glues (33.6%) were the leading cause of shoe dermatitis, followed by leather allergens (26.4%), rubber allergens (7.6%), and dyes (7.6%).

Rani, et al. determined that the maximum incidence of shoe dermatitis observed in this study was in the 20-50 year age group.¹⁶ This finding validates Saha, et al.'s results because a similar pattern of prevalence was observed in this investigation.¹⁰ Rani, et al. acknowledge that their observed prevalence of footwear dermatitis may be influenced by differences in geographic location, social disparity, and climate.¹⁶ The present study indicates that patients with suspected shoe dermatitis should be patch-tested with the shoe series in addition to a standard series.¹⁶

Another investigation was conducted by Lazzarini, et al. on fifty-three patients with eczematous dermatitis.¹⁷ Patch testing was performed using the Brazilian series.¹⁷ Thirty-seven (70%) had at least one positive patch test reaction.¹⁷ The compounds causing positive reactions were rubber-vulcanizing agents, followed by either metals or topical medications.¹⁷ This prospective study detailed both inclusion and exclusion criteria for their study subjects. Also, the presence of dermatosis on the dorsal region of the foot in the majority of the patients with a positive test result was statistically significant.¹⁷ The use of statistical data enriches this investigation by demonstrating that their results are not due to random chance.

Holden and Gawkrödger reported their experience of ten years of patch-testing on 230 patients to identify which allergens are important in determining the cause of shoe dermatitis.¹³ Forty-four subjects of the group showed relative allergic positive reactions to the allergens in the British Contact Dermatitis Society's standard series. Only 13 patients had relevant positive results to one or more allergens from the shoe series.¹³

The current shoe series consists of 17 allergens, including two from the rubber series. One percent of the

Continued on page 192

Shoe Dermatitis...

230 cases were positive for five allergens.¹³ Chromate was identified as the top allergen during this investigation. These authors conclude from their observation that nickel is rarely a relevant allergen for foot dermatitis, unless an obvious source of metal buckles is present.¹³

Nardelli, et al. report the results of a thirteen-year retrospective study that was conducted to identify the relationship between the causative allergens in shoes and localization of foot dermatitis.¹⁴ This study determined that 474 patients presenting with foot dermatitis had a positive reaction to one or more substances related to footwear. The most common allergens in decreasing order of frequency in this study were potassium dichromate and cobalt chloride, followed by p-phenylenediamine, rubber components, colophony, and p-tert-butylphenol formaldehyde.¹⁴ Potassium dichromate and cobalt chloride were most often found in relation to dermatitis of the whole foot.¹⁴ Rubber chemicals were associated with dermatitis of the soles of the feet.¹⁴

Chowdhuri and Ghosh conducted an epidemio-allergological investigation of 640 patients identifying 155 cases of footwear dermatitis.²⁰ After a detailed history and clinical examination of a total of 640 patients, patch testing was performed.²⁰ Patch test units were comprised of ointment forms, liquid forms, strips, discs, and chambers. Those patients with foot dermatitis only were tested for footwear allergens with controls.²⁰

Statistical analysis of data obtained from history, clinical features, and allegro-logical findings by correlation and follow up was performed.²⁰ Post-patch test counseling was employed and the results were clinic-allergologically correlated.²⁰ Fortunately, this later prospective investigation's results allows for validation of Freeman's earlier observations on the benefit of patient allergen awareness. Chowdhuri and Ghosh identified potassium dichromate and cobalt chloride as the commonest allergens causing footwear dermatitis.²⁰

Warshaw, et al. retrospectively analyzed data from 10,061 patients

between 2001 to 2004.²⁴ These investigators set forth four goals as objectives for this study: to determine the frequency of allergens associated with a shoe source in North American Contact Dermatitis Group patients with footwear allergic contact dermatitis, compare their results to allergen frequencies from other published studies, quantify the number of shoe-related reactions that were not identified on the North American Contact Dermatitis Group standard series, and identify relevant allergens not included on the North American Contact Dermatitis Group standard series, based on data from other studies.²⁴

It was determined that in 109 North American Contact Dermatitis

*The most common individual shoe allergen was p-tertiary butylphenol formaldehyde resin, and as a group, rubber chemicals were most common, a finding consistent with those of other investigations.*²⁴

Group patients with allergic contact dermatitis of the foot and allergens the most common allergen was from a shoe source p-tertiary butylphenol formaldehyde resin, an adhesive, which accounted for 24.7% of positive patch test results, followed by potassium dichromate (17.5%) and carba mix (11.7%).²⁴

North American Contact Dermatitis Group patients were statistically more likely to have positive patch test reactions to p-tertiary butylphenol formaldehyde resin and statistically less likely to have a positive patch test reaction to potassium dichromate than patients represented in pooled data studies.²⁴ A determined final conclusion from their analysis was in North American Contact Dermatitis Group patients.

The most common individual shoe allergen was p-tertiary butylphenol formaldehyde resin, and as a group, rubber chemicals were most common, a finding consistent with those of other investigations.²⁴ This investigation is superior to the other investigations because of its through comparative analysis of results to previously published literature findings.²⁴

Bajaj, et al. reported their experience with patch-testing of 1,000 patients.²⁵ Patients with suspected allergic contact dermatitis were involved in this retrospective analysis.²⁵ The Indian Standard Series was used for patch-testing. The age range of this cohort was eight to 87 years, with a median age of 35.9 years.²⁵ Suspected footwear dermatitis was the commonest clinical pattern found in 310 patients.²⁵ Among these 310 patients, 190 (61.3%) showed positivity to one or more allergens.²⁵

Chemicals such as potassium dichromate (34.2%), mercaptobenzthiazole (30%), and mercapto mix (28%) were the leading allergens in patients with footwear dermatitis.²⁵ Interestingly, there were no statistically significant differences in sensitization rates between males or females.²⁵ These authors suggest that wearing thick absorbent socks and using other non-chromate chemicals for tanning and curing leather can minimize chromium exposure from leather footwear.²⁵

Case Studies

As a point of completeness, case studies describing shoe dermatitis as they appear in the medical literature are presented. Oztas, et al. report shoe dermatitis from para-tertiary butylphenol formaldehyde in a 38 year old woman.¹⁵ Onder, et al. further present four cases of footwear dermatitis emphasizing that rubber is still the most common shoe allergen reported.¹⁸

Verma, et al. describe a case report of a 29-year-old male with purpuric contact dermatitis from footwear.²¹ This report notes that there exist variations in individual allergen sensitivity with shoe dermatitis because of differences in chemical composition of footwear or individual susceptibility.²¹

Interestingly, Hartmann and Hunzelmann offer a case report of a

Continued on page 193

Shoe Dermatitis...

47-year-old man with a vesicular dermatitis on both soles from cinnamon as an odour-neutralizing agent in shoe insoles.²² Patch-testing revealed a positive reaction to cinnamic aldehyde and cinnamic alcohol, despite a social history described by the patient of often eating food flavored with cinnamon.²²

Most recently, a case report describing allergic contact dermatitis to Crocs™ has been cited in the literature.²⁶ Castanedo-Tardan, et al. present the case of a 14-year-old boy with a two-year history of pruritic erythematous plaques on both the dorsal and ventral surface of his feet.²⁶ Patch-testing was performed to the North American Contact Dermatitis Standard series and to a punch plug of the patient's Crocs™ with positive results.²⁶

Discontinuation of the Crocs™ and the use of sneakers resulted in clearance of his foot dermatitis.²⁶ These authors assert the importance of testing shoe components and the need to obtain the individual ingredients from the shoe product manufacturer to enable clinicians to identify potential allergens.²⁶

Corazza, et al. describe a case presentation of a 72-year-old man with the rarely reported contact sensitization to an amputation prosthesis.²⁷ This man presented with an erythematous-edematous scaly dermatitis involving his left foot stump extending to the leg with extension to his right foot and leg.²⁷ A cutaneous biopsy from his left leg was performed revealing histological findings consistent with chronic eczematous dermatitis.²⁷

This patient wore an orthopedic shoe with its mobile plastic prosthesis device covered with leather.²⁷ Patch-testing revealed positive results to para-tertiary-butylphenol-formaldehyde resin, cobalt chloride, nickel sulfate, and potassium dichromate.²⁷ The patient's dermatitis healed with oral antihistamines, systemic and topical steroids, replacing the old prosthesis with chromate-free and para-tertiary-butylphenol-formaldehyde resin-free shoes and wearing extra pairs of socks.²⁷

The last case report centers on a 64-year-old woman with the presentation of unilateral contact dermati-

tis caused by footwear.²⁸ Clinical examination revealed linear erythema on the dorsum of her right foot with two flaccid blisters on the side of her right foot.²⁸ History revealed the patient noticed the lesions and believed they were related to her shoes that had been dyed two months earlier.²⁸ Patch testing was performed with positive results to rubber and dyed leather.²⁸ It was concluded that she had experienced shoe dermatitis after the lesions resolved when the patient stopped using the shoes.²⁸ An important fact acknowledged by these authors is that the atypical presentation of this condition delayed this patient's diagnosis.²⁸

The podiatric clinician is encouraged to determine if these literature citations are relevant and valid to their specific patient populations. First, the number of subjects is crucial to determine whether accurate statistics can be generated from the

**Shoe dermatitis
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collected data. Krejcie and Morgan have suggested that a good rule of thumb is that 400 subjects will provide reliable statistics that can be applied to general populations.²⁹

Indeed, seven of the ten reviewed investigations have greater than 400 subjects. On the other hand, when examining the sub-populations of subjects with foot dermatitis, only one investigation allows for the sample sizes to be precisely visualized by explaining in detail entry and exclusion criteria, ensuring a homogenous study sample population. The methods of all these investigations are described in detail and were designed to answer the investigators' research question.

All the studies do clearly state and define their primary outcome and how it was measured. Only one investigation addresses confounding variables regarding the presentation of shoe dermatitis. Finally, a few of these investigations specifically state statis-

tical significance, but it must be remembered that statistical significance only minimizes the possibility that the results could have occurred by chance alone. It implies nothing about the actual importance or clinical significance of these results. The findings of all the investigations do offer needed clinical information regarding the most common allergens responsible for causing shoe dermatitis.

Signs and Symptoms of Shoe Dermatitis

Usually, the substances that cause shoe contact dermatitis pose no trouble for most people, and may not even be noticed the first time a person is exposed. Once the skin becomes sensitive or allergic to any of the etiological substances, any exposure will produce a rash.^{3,5} The rash usually does not start until a day or two later, but can start as soon as hours, or as late as a week.⁵ The history of onset of symptoms and absence of any previous history of skin disease and the possible temporal relationship to wearing new shoes can aid the healthcare professional in distinguishing shoe dermatitis from other forms of dermatological diseases.

Shoe dermatitis usually shows as redness, swelling and water blisters. The size of these blisters range from tiny to large. Also, these blisters may break and form crusts and scales. Untreated, the skin may darken and become leathery and cracked. Allergic contact dermatitis can be difficult to distinguish from other rashes, especially after it has been present for a while. The dermatitis can occur on the weight-bearing parts, heels, sides of the foot, and other pressure and friction areas.¹²

The most common site first involved with shoe dermatitis is the dorsal surface of the big toe and on the insteps (Figures 1a b). Later, it extends by spreading to the other toes and dorsal aspect of the foot.⁵ Skin lesions may be acute, presenting as red, blistering, oozing, and usually symmetrical.^{3,5}

The clinical symptoms of shoe contact dermatitis can range from mild, itchy rash to severe itching with swelling and small blisters.³ On the other hand, chronic lesions are

Continued on page 194

Shoe Dermatitis...

dry, lichenified, and in severe cases, open sores may present and can result in secondary bacterial infections.^{3,5}

Finally, an important diagnostic parameter used by physicians is the presence of normal skin not in contact with shoes between eczematous areas.³ The design of the footwear determines to a large extent the appearance of shoe dermatitis.¹² The podiatric physician may keep this observation in mind when referred a patient for medical evaluation. If untreated, a secondary infection may result, which presents as swelling, tenderness and pus formation.

Diagnosis of Shoe Dermatitis

The physician and patient will discuss the materials that touch the person's skin at work and home, and try to identify the allergen. Given that history and physical examination alone are not sufficient to con-

firm the diagnosis of allergic contact dermatitis, Freeman recommends that all patients with foot dermatitis which does not respond to treatment should be patch tested to exclude shoe allergy.^{2,9}

A foot and ankle physician may detect the skin sensitizer responsible for shoe dermatitis by performing a "patch test."^{2,5} First described by Josef Jadassohn in 1895, patch testing is a safe and quick way to diagnose contact allergies and remains the gold standard for diagnosing allergic contact dermatitis.^{30,31} A small amount of the suspected allergen is applied to the skin for a fixed time.^{2,5}

Commercial patches are available that contain common allergens that are known to cause contact dermatitis.^{2,3} Two methods for patch-testing exist. The first is the 24-component, thin layer, rapid-use, epicutaneous test screening tool.³² The second method is comprehensive patch testing, which involves creating customized patch-tests based on the history of the patient.³²

Patch-testing can also be done using pieces of the shoe soaked in water and applied under occlusion to the medial forearm or back for 48 hours. Finally, patch testing of solid objects may be performed by trimming off a small sample between 0.5–1 cm² and applying the sample to the skin. The ability to select specific allergens gives more power as a diagnostic tool because of the ability to have a higher rate of identifying the relevant allergen, which would have been missed by using a limited screening tool.^{2,32}

Patch testing is not the test of choice for diagnosis of Type-I allergy.³⁰ After these patches are re-

moved, the treating physician can check for a positive reaction over a few days.^{2,3} A positive significant allergen will produce a reaction with pruritus, erythema, edema, and even vesiculation. If indeed, the patient tests positive for shoe contact dermatitis, the physician must document this allergy within the patient's chart and ensure and provide patient instructions to stop wearing the shoes causing this reaction.^{2,3,5}

Management and Prevention of Shoe Dermatitis

Patient empowerment through education to assist in avoidance of the affecting antigen is the primary goal as well as the cornerstone of shoe dermatitis management.

Unfortunately, patient avoidance of these antigens is often difficult to implement, which ultimately results in a presentation of shoe dermatitis. Once a diagnosis of shoe dermatitis has been confirmed, treatment management goals include alleviation of pruritus and treating the inflammation. The podiatric physician should emphasize basic good skin care with the use of soap-free hydrating cleansers and emollients to patients as an important adjunct to the treatment of shoe dermatitis.³²

Treatment should begin with a non-pharmacological approach and incorporate prescription medications, when necessary. In order to treat shoe dermatitis, the physician must achieve an understanding of the mechanism and pathophysiology of allergic contact dermatitis. First, contact dermatitis results from exposure to exogenous agents. Then Zellar and Warshaw's classification system for contact dermatitis can be used to identify if the reaction is one of two types: nonimmunologic and immunologic.³⁰

Shoe dermatitis has been identified as allergic contact dermatitis which is a delayed, cell-mediated, immunologic reaction requiring prior sensitization to the offending antigen.³⁰

Allergens are processed by antigen-presenting cells known as Langerhans cells with receptors specific for the antigen which recognize the antigen, bind to it, and become activated.³⁰ Subsequent contact between the antigen and the skin trig-

Continued on page 195



Figures 1a and b: The most common site first involved with shoe dermatitis is the dorsal surface of the big toe and on the insteps. Later, it extends by spreading to the other toes and dorsal aspect of the foot. (Photo Courtesy of G. Dock Dockery, DPM, Seattle, WA.)

Shoe Dermatitis...

gers an inflammatory cascade that manifests clinically within 24 to 72 hours.³⁰

Skin affected by allergic contact dermatitis will demonstrate inflammation corresponding to the degree of potency and immune reaction from the allergen.³² Summaries of both non-pharmacological and pharmacological approaches will be offered with an emphasis on mechanism of actions, potential adverse effects, and patient consideration.^{2,3,32-37}

First, moist compresses may be used to enhance the drying of well-localized, acute, weeping lesions. Cool moist soaks applied for five to ten minutes, followed by air-drying, may significantly reduce drainage from the affected foot. Secondly, even though the exact mechanism is unknown, an absorbent cloth moistened with isotonic physiologic saline, aluminum sulfate-calcium acetate astringent solution, silver nitrate or tap water applied for 20-30 minutes, several times a day, can be utilized to reduce inflammation and provide relief from the irritating symptoms of shoe dermatitis.^{2,32}

Finally, inflamed lower extremity skin that is dry, hot, and indurated may benefit from a thin layer of white petrolatum followed by a cold compress.^{2,32}

Moisturizing emollients have been prescribed to treat shoe dermatitis, providing both occlusion and humectance.³² The occlusion property of emollients provides a sealant layer on the surface of the skin to reduce water loss.³² On the other hand, the humectance property is one of increasing the "water-holding capacity" of the stratum corneum and therefore increasing skin hydration.^{2,32} Lipids known as ceramides have been added to moisturizing emollients to improve the skin barrier in inflamed skin by enhancing the structural lipid bilayer of the stratum corneum.^{2,32}

Finally, urea, glycerin, pyrrolidone carboxylic acid, alpha-hydroxy acids, as in lactic acid and glycolic acid are examples of low molecular weight humectants that have been added to emollients.^{2,32}

The prescribing and application of topical corticosteroids is a medical standard of care in the treatment of

shoe dermatitis.^{2,3} Corticosteroids are known to interfere with inflammatory response. The major therapeutic role of corticosteroids in treating allergic contact dermatitis is their ability to inhibit T-cell activation and leukocyte migration.³³

A recently published literature account using contact hypersensitivity mouse models has suggested that corticosteroid therapeutic effects and cell targets for immune suppression in contact allergies, may also involve both macrophages and neutrophils.^{32,34}

Topical glucocorticoids (corticosteroids) are adrenocorticosteroid derivatives incorporated into a vehicle formulated to be applied to the skin and external mucous membranes.^{2,3} Corticosteroids tend to penetrate human skin slowly, leading to a reservoir effect.^{2,3,35}

The absorption of the drug into the skin is a function of the nature of

*A variety of
topical corticosteroids
are available
in various potency
and vehicles.*

the drug, the behavior of the vehicle, and the status of the skin. Drug absorption is increased with an increase of water content of the stratum corneum.^{2,3}

The differences in rate of absorption of different topical drugs, or the same drug in a different vehicle, rely on three variables: the concentration of drug in the vehicle, the partition coefficient of the drug between the stratum corneum and the vehicle, and the diffusion coefficient of the drug in the stratum corneum.³

The diffusion coefficient is the extent to which the matrix of the barrier restricts the mobility of the drug.³ Increases in molecular size of the drug will increase the frictional resistance and decrease the diffusion coefficient.³

Topically applied corticosteroids diffuse across cell membranes to interact with cytoplasmic receptors located in both dermal and intradermal cells. The primary therapeutic

effects of topical corticosteroids are due to their non-specific anti-inflammatory activity. Glucocorticoids enhance or repress the transcription of genes contained in almost every cell involved in the immune and inflammatory responses through interaction of cell receptors located in the cell membrane and its cytoplasm.^{3,36}

The anti-inflammatory action of steroids is mediated by its action of cortisol, as it induces production of lipocortins through the glucocorticoid receptor mechanism to inhibit the activity of phospholipase A2.³ This action impairs production of prostaglandins and leukotrienes, the mediators of inflammation, through the action of cyclooxygenase on arachidonic acid.^{3,36}

A variety of topical corticosteroids are available in various potency and vehicles. The relative potency of a product depends on several factors including the characteristics and concentration of the drug and vehicle used.^{2,3} Vasoconstriction assays are used to measure the relative potency of available commercial products.^{2,3} The podiatrist should be familiar with the classifications of relative potencies of available products as they are presented in Table 2.

Once the selection of a topical corticosteroid agent is considered, the clinician must decide on the most appropriate delivery system; thus the choice of vehicle in a topical formulation is of great importance.^{2,3}

The ideal vehicle has the following characteristics: easy to apply and remove, acceptable cosmetically without odor and non-greasy, non-irritating, compatible with the active ingredient, and readily releasing the active drug.³ Topical corticosteroids are available in vehicles such as gels, lotions, solutions, creams, and ointments.^{3,36}

An advantage of using creams or oil-in-water emulsions is that they are absorbable and are vehicles that may be drying.^{2,3} Water-miscible creams may be more appropriate for moist or weeping lesions.^{2,3} Ointment bases are compounded as either water-insoluble bases like petrolatum or water-soluble bases like polyethylene glycol, or they can be emulsified with water.^{2,3}

Continued on page 196

Shoe Dermatitis...

An ointment is a water-in-oil emulsion. It is noted as being the most effective hydrating agent. It is considered more potent and effective due to its occlusive, nature-enhancing corticosteroid penetration.^{2,3} Ointments are the most effective vehicle for treating thick, fissured, lichenified and dry, scaly eruptions.^{2,3}

Lotions are formulated as a powder in a water suspension and are considered less lipophilic suspending agents.^{2,3} Lotions are used to treat superficial dermatoses, especially if there is slight oozing. Gels are semi-solid polymers containing pockets of liquids that tend to allow for greater

penetration when compared to lotions. Gels are most useful when applied to hairy areas or other areas where it is considered cosmetically unacceptable to have residue of a vehicle remain on the skin.^{2,3}

Both gels and ointment formulations are considered more potent than creams and lotions, because ointments and gels restrict water loss and preserve hydration of the stratum corneum.^{2,3}

Although topical corticosteroids are generally well-tolerated for short term use, the sophisticated method of delivering topical corticosteroids is not void of producing adverse effects. Long-term widespread use can result in adverse effects grouped into four categories: cutaneous

changes, cutaneous infections and infestations, eye effects, and systemic effects.^{2,3}

Systemic adverse effects include hypothalamic-pituitary-axis suppression, hyperglycemia, and avascular necrosis.^{2,3,32} Therefore, alternative therapeutic interventions for treating shoe dermatitis must be considered.

Topical immune modulators have been investigated as a treatment option for inflammatory skin disorders.^{2,32} Both tacrolimus ointment and pimecrolimus cream act by inhibiting the protein calcineurin, which subsequently prevents the dephosphorylation of the nuclear factor of activated T-cells, a transcription factor. This causes signal transduction pathways in T-cells to be blocked and inflammatory cytokine production is inhibited.^{2,32,37}

Experimentally, both tacrolimus and pimecrolimus have demonstrated efficacy in treating allergic contact dermatitis induced by nickel.^{2,32} Tacrolimus and pimecrolimus should be limited to short-term use. Adverse reactions associated with tacrolimus included pruritis, a sensation of burning skin, and alopecia. Adverse effects associated with pimecrolimus use include a sensation of burning skin, headache, and risk of infection. These agents should be considered when conventional therapies have failed. Both these agents do carry a block box warning emphasizing their potential for cancer risks.^{2,32}

Systemic therapy may be reserved for severe and chronic allergic contact shoe dermatitis. Systemic treatments may include the use of the following oral agents: H1-antihistamines, systemic corticosteroid, azathioprine, methotrexate, and mycophenolate mofetil.^{2,32}

Oral antihistamines have an effect on severe pruritis by competing with free histamine by binding at H1-receptor sites. The most common antihistamines used to treat allergic dermatitis include cetirizine, hydroxyzine, diphenhydramine, chlorpheniramine, and loratadine. Adverse effects of antihistamines include dry mouth and drowsiness.

Systemic corticosteroid therapy has demonstrated high efficacy in the treatment of acute allergic dermatitis by dramatically improving

Continued on page 197

TABLE 2
Relative Potency of Corticosteroids

Potency	Generic Names	Strengths (%)
Lowest	Dexamethasone sodium	0.1
	Hydrocortisone acetate	0.5, 1
	Methylprednisolone	0.25-1
Mild	Aclometasone dipropionate	0.05
	Desonide	0.05
	Dexamethasone sodium	0.1
Medium	Betamethasone benzonate	0.025
	Clocortolone pivalate	0.1
	Desoximetasone	0.05
	Hydrocortisone butyrate	0.1
	Hydrocortisone valerate	0.2
	Triamcinolone acetaonide	0.02
	Fluocinolone acetonide	0.025
	Flurandrenolide	0.05,0.025
	Fluticasone propionate	0.05
Mometasone furoate	0.1	
High	Amcinonide	0.1
	Betamethasone dipropionate	0.05
	Betamethasone dipropionate (augmented)	0.05
	Betamethasone valerate	0.1
	Diflorasone diacetate	0.05
	Desoximetasone	0.05,0.25
	Fluocinolone acetonide	0.2
	Fluocinonide	0.05
	Halcinonide	0.1
	Hydrocortisone 17-butyrate	0.1
	Triamcinolone acetonide	0.5
	Very High	Betamethasone dipropionate (augmented)
Clobetasol propionate		0.05
Diflorasone diacetate		0.05
Halobetasol propionate		0.05

TABLE 3 Management and Prevention of Shoe Dermatitis

Non-pharmacological

- Moist compressions or cool moist soaks
- Moisturizing emollients or humectants

Pharmacological

- Topical corticosteroids
- Topical immune modulators
- Systemic corticosteroids
- Oral antihistamines
- Steroid-sparing systemic immunosuppressant therapy

The foremost part of treatment plan for shoe dermatitis is avoidance of the sensitizer (allergen) once known

Offer an educational initiative

stances. Adams suggests that measures to control sweating may be very helpful for the patient who suffers from shoe dermatitis.¹²

Medicated powders, administered once or twice a day to control foot perspiration, may be helpful in preventing shoe dermatitis. Podiatric clinicians can suggest stockings made of absorbent cotton that should always be worn by the patient who is recovering from an episode of shoe dermatitis.^{2,3} Further, the foot and ankle physician could suggest changing socks two or three times a day, and the wearing of different shoes for work and home to prevent dermatitis.¹²

An insight may be gleaned from a recent report by Borghesan and Bellotti describing successful treatment of a contact allergic dermatitis in a fifty year old construction worker with "barrier socks."³⁸ These authors describe both an improvement in their patient's quality of life as well as a comparative reduction in costs incurred when comparing their observations with traditional topical therapy.³⁸

Finally, Srinivas, et al. offer a method to reduce the allergenic hexavalent chromium in leather.³⁹ These authors acknowledge their perspective that chromium is the most common allergen in leather footwear.^{10,39} Further, they recount that hexavalent chromium penetrates the skin and causes an allergic reaction; however, as the reduced trivalent chromium form, it is less allergenic.³⁹ These investigators prepared a 5% vitamin C solution to be used as a soaking solution for a piece of leather overnight.

After soaking this piece of leather, as well as a control piece of leather soaked in distilled water, these samples were stuck to the inner surface of the heels of two volunteers' shoes and to the inner surface of the sandal strap of a third volunteer.³⁹ The pieces of leather were left in place for one week.³⁹ The results of this observational case control study proved that freshly prepared vitamin C solution was capable of making leather hypo-allergic by converting the hexavalent chromium to trivalent chromium.³³

Continued on page 198

Shoe Dermatitis...

skin inflammation; however, they also cause the same adverse effects as topical corticosteroids. In the attempt to avoid adverse effects from repeated doses of corticosteroids in patients with chronic dermatitis, steroid-sparing systemic immunosuppressant therapy was investigated.^{2,32}

The selection of these agents depends on the clinical presentation of the patient as well as the patient's general health and presenting contra-indications. Azathioprine is a cell cycle-specific antimetabolite that affects natural killer cell function, T-cell signaling, prostaglandin production and neutrophil activity. Azathioprine has been studied in allergic contact dermatitis induced by parthenium revealing resolution of disease.^{2,32}

Methotrexate exerts cytotoxic activity through a cell cycle, S-phase-specific antimetabolite, which causes inhibition of neutrophil chemotaxis and inhibition of TNF-alpha, IL-1, IL-6, and IL-8. Mycophenolate mofetil selectively and non-competi-

tively inhibits the enzyme inosine 5'-monophosphate dehydrogenase, preferentially blocking the type II isoform, in the de novo purine synthesis pathway. Both methotrexate and mycophenolate mofetil have been recognized as effective treatment options for immune-mediated skin disease.^{2,32}

The foremost part of a treatment plan for shoe dermatitis is the avoidance of the sensitizer (allergen), once it is known. The podiatric physician can offer expertise in footwear by providing education to patients with the selection of footwear without materials that may cause shoe dermatitis. Substitute products made of different materials that do not cause allergic reactions will lessen the likelihood of future episodes of shoe dermatitis. Treatment and management suggestions are summarized in Table 3.

Secondly, the podiatric physician may offer an educational initiative to the patient to avoid re-dyed shoes.^{2,3,5} Patients with shoe dermatitis can use special types of shoes prepared from non-sensitizing sub-

Shoe Dermatitis...

Conclusion

Shoe contact dermatitis presents as a diagnostic and therapeutic challenge for the podiatric physician. Rubber compounds continue to be blamed as a common cause of shoe dermatitis. As an important member of the healthcare team, the podiatric physician must be familiar with recognizing signs and symptoms of shoe dermatitis so patients can avoid secondary infections and disability. This review presents causative factors for the etiology of shoe contact dermatitis supported by clinical-based evidence as found in the medical literature. ■

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See answer sheet on page 201.

1) According to this review what substance is not among the most common allergens responsible for causing shoe dermatitis?

- A) Potassium dichromate
- B) Para-tert-Butylphenol formaldehyde
- C) Thiamine
- D) Rubber components

2) Cronin reports that historically in the 1930s and 1940s _____ and _____ caused most of the presenting cases of shoe contact dermatitis.

- A) Rubber and elastic
- B) Leather and dyes
- C) Rubber and leather
- D) Dyes and Rubber

3) What was a hallmark observation identified by Freeman's observations during a differential diagnosis?

- A) No subjects had hyperhidrosis.
- B) 50% of subjects had hyperhidrosis.
- C) 33% of subjects had hyperhidrosis.
- D) 100% of subjects had hyperhidrosis.

4) A safe and quick way to diagnosis contact allergies, which remains the gold standard for diagnosing allergic contact dermatitis is _____?

- A) antibiotics
- B) radiology
- C) patch test
- D) family history

5) Treatment of shoe "contact" dermatitis should begin with a _____.

- A) non-pharmacological approach

- B) contact isolation
- C) broad spectrum antibiotics
- D) systemic corticosteroids

6) Which of the following corticosteroid(s) have the lowest relative potency?

- A) Dexamethasone sodium 0.10%
- B) Hydrocortisone acetate 0.5%, 1%
- C) Methylprednisolone 0.25%-1%
- D) All of the above products have low potency.

7) In shoe dermatitis, allergens are processed by antigen-presenting cells, known as _____.

- A) Keratinocytes
- B) Fibroblasts
- C) Langerhans cells
- D) Platelets

8) According to this review, what may determine, to a large extent, the appearance of shoe dermatitis?

- A) The patient's age
- B) The patient's social history
- C) The design of the footwear
- D) The patient's physiology

9) Patch-testing is not the test of choice for diagnosis of _____.

- A) Type II allergy
- B) Type I allergy
- C) Type III allergy
- D) Type IV allergy

10) Topical corticosteroids' primary therapeutic effects are due to their _____.

- A) Moisturizing emollient activity
- B) Anti-infective properties
- C) Water-holding capacity
- D) Non-specific anti-inflammatory activity

11) Chowdhuri and Ghosh identified _____ and _____ in their investigation as the most common allergens causing footwear dermatitis.

- A) Potassium dichromate and cobalt chloride
- B) Rubber components and colophony
- C) Potassium dichromate and leather
- D) Cobalt and leather

12) Two topical immune modulators investigated as treatment options for inflammatory skin disorders are _____ and _____.

- A) Humectants and emollients
- B) Azathioprine and mycophenolate
- C) Tacrolimus ointment and pimecrolimus
- D) Methotrexate and hydroxyzine

13) Shoe "contact" dermatitis skin lesions may be acute, presenting as red, blistering, oozing and _____.

- A) Always contagious
- B) Usually symmetrical
- C) Never itch
- D) Always interdigital

14) Castanedo-Tardan, et al. present the case of a 14-year-old boy with a two-year history of pruritic erythematous plaques on both the dorsal and ventral surface of his feet from _____.

- A) Contact sensitization to the amputation prosthesis
- B) Dyed leather shoes
- C) Crocs™ with positive patch test results
- D) Positive reaction to cinnamic aldehyde and cinnamic alcohol

Continued on page 200

(cont'd)

15) Borghesan and Bellotti describe successful treatment of a contact allergic with _____.

- A) Systemic emollients
- B) Systemic corticosteroids
- C) Collagenase products
- D) Barrier socks

16) All of the following are common antihistamines used to treat allergic dermatitis except _____.

- A) Diphenhydramine
- B) Fluocinolone acetonide
- C) Loratadine
- D) Hydroxyzine

17) Srinivas, et al. offer a method to reduce the allergenic hexavalent chromium in leather by using a 5% solution of _____.

- A) Thiamine
- B) Pyridoxine
- C) Ascorbic acid
- D) Folic acid

18) The patch test was first described by _____ in 1895.

- A) Josef Jadassohn
- B) Shanmuga Sundaram
- C) A.K. Bajaj
- D) Abir Saraswat

19) Chromates are compounds that contain _____ and are commonly responsible for allergic contact dermatitis.

- A) Silver
- B) Mercury
- C) Chromium
- D) Lead

20) Long-term widespread use of topical corticosteroids can produce which of the following adverse effects:

- A) Hypothalamic-pituitary axis suppression.
- B) Hyperglycemia.
- C) Avascular necrosis.
- D) All the above are adverse effects.

See answer sheet on page 201.

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Therapeutic Hosiery: An Essential Component of Footwear for the Pathologic Foot (Richie)

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- 1. A B C D 11. A B C D
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3. A B C D 13. A B C D
4. A B C D 14. A B C D
5. A B C D 15. A B C D
6. A B C D 16. A B C D
7. A B C D 17. A B C D
8. A B C D 18. A B C D
9. A B C D 19. A B C D
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EXAM #9/08

Shoe Dermatitis: Causes, Prevention, and Management (Smith)

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