Bacitracin

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Bacitracin is an antibiotic widely used by both the medical profession and the general public. It is most commonly found in a variety of topical ointments and creams used after surgical procedures, for acute skin injuries, and for chronic wounds. The incidence of allergy to this agent has been increasing over the last 10 years, probably because of more frequent use. This article reviews basic information about bacitracin as an allergen, including sources of exposure, chemical composition, types of allergic reactions, and patch testing.

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Case Report

A 21-year-old woman with a history of malignant melanoma excision with skin graft and a strong family history of atopy presented with dermatitis in the antecubital fossae that had persisted for one year and had spread to the medial lower legs. She had pruritic papules complicated by secondary infection, which she was managing with bacitracin, hydrocortisone, and Eucerin® Moisturizing Lotion. She also was being treated with oral ciprofloxacin, cetirizine, and diphenhydramine. In addition, she used some facial and hair care products. Results of biopsies performed by the referring dermatologist suggested contact allergy with secondary bacterial infection. Findings of the skin examination included eczematous papules coalescing into annular lesions on bilateral antecubital fossae (Figure); the surrounding skin showed hypopigmentation. Similar eczematous papules and patches and postinflammatory pigmentation were evident on the medial lower legs.

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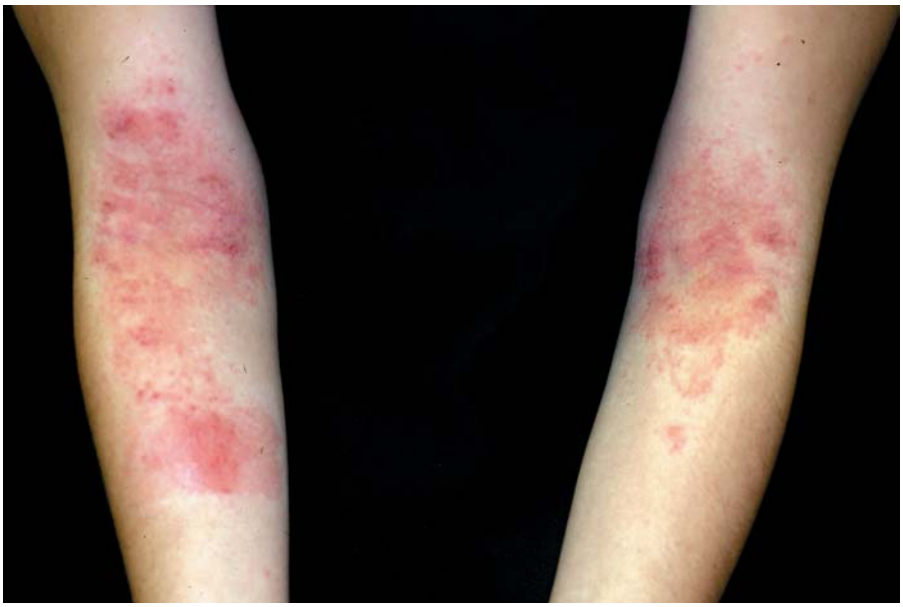
Patch testing was performed with the North American Contact Dermatitis Group 2002 allergen series. Test results at 96 hours revealed a 2+ reaction to bacitracin, 2+ reaction to neomycin, and 2+ reaction to lanolin. The patient reported using neomycin and bacitracin at the time of her melanoma excision and continuing to use bacitracin on her eczema. She did not recall having any problem other than a "tape allergy" at her surgical site. Lanolin was an ingredient in the moisturizing cream she was using.

Comment

Allergen Aspects—Bacitracin is derived from the Tracey I strain of *Bacillus subtilis*. Because the bacteria used to derive bacitracin was initially recovered from damaged tissue and "street debris" debrided from a compound fracture of a 7 year old named Margaret Tracey, the agent was called "bacitracin."[1] Originally tested for parenteral use, bacitracin was abandoned after discovery of severe nephrotoxicity with internal administration.

The bacitracin molecule consists of a thiazolidine ring and a polypeptide chain and acts by inhibiting bacterial cell wall synthesis by complexing with the carrier protein C55-prenol pyrophosphatase. This protein assists in transfer of polysaccharides, liposaccharides, and peptidoglycans to the growing cell wall.[2] Bacitracin is chemically unrelated to a frequent co-allergen, neomycin.[3] Despite differing chemical structures, cross-reactivity of bacitracin with polymyxin B has been hypothesized because they are produced by similar bacteria, *B subtilis* and *Bacillus polymyxa*, respectively.[4,5]

Sources and Exposure—Bacitracin is available in several forms for external use and has a wide antibiotic spectrum. A water-soluble form has a shelf life of 2 years, and bacitracin complexed with approximately 7% zinc forms a stable and less water-soluble form with a shelf life up to 5 years.[6] Gram-positive cocci and bacilli, *Neisseria species*, *Haemophilus influenzae*, and *Treponema pallidum* are



Acute eczematous papules on the bilateral antecubital fossae caused by allergy to bacitracin.

all sensitive to bacitracin in doses equivalent to 0.1 U/mL. *Actinomyces* and *Fusobacterium* are less sensitive but are affected by doses between 0.5 and 5 U/mL. The Enterobacteriaceae family of bacteria, as well as genera *Pseudomonas*, *Candida*, *Nocardia*, and *Cryptococcus*, are resistant to bacitracin.[6] In a prospective study, bacitracin was found to be effective in eradicating nasal *Staphylococcus aureus* in only 44% of healthcare workers tested.[7]

Topical use of bacitracin is widespread. It is one of the most commonly used preparations by the general public and medical professionals for postoperative and general wound care.[5] Bacitracin, which is found in many topical medicaments available over the counter, is often compounded with neomycin and polymyxin B in a triple antibiotic for use on acute skin injuries and perceived infections. Bacitracin also is commonly used as an additive to irrigation fluid for intraoperative use and as a soaking agent for a variety of implants. It also is used in a number of prescription eye and ear preparations, both in drop and ointment forms.

Keeping the skin moist and occluded has been shown to assist in wound healing and early reepithelialization compared with exposing the skin to air.[8,9] A topical antibiotic, commonly bacitracin, is frequently used within the medical profession as a topical postsurgical wound treatment. In a study by Smack et al,[10] results of topical application of white petrolatum were compared prospectively with the results obtained with bacitracin ointment in surgical wounds. The investigators found no significant difference in wound healing, rate of infection, or incidence of allergic contact dermatitis between the 2 groups. When comparing the 2 groups of patients in whom postsurgical infections occurred, the investigators found a statistically significant increase ($P=.004$) in infections by antibiotic-sensitive *S aureus* in patients using white petrolatum. In the group using white petrolatum, 8 of 9 infections were due to these gram-positive organisms, whereas none of the 4 infections in the group treated with bacitracin were caused by gram-positive pathogens. All infections in the patients treated with bacitracin were caused by gram-negative organisms.[10] Gram-positive wound infections can usually be treated with inexpensive oral antibiotics, as compared with the more expensive antibiotics required to cover gram-negative organisms. One can argue that using white petrolatum for surgical wound management is adequate to promote wound healing and that wound infections that do occur can be easily and inexpensively treated.

Skin reactions to bacitracin include contact allergy, contact urticaria, and even anaphylaxis. Bacitracin is commonly used on chronic skin wounds, such as venous stasis ulcers. In that context, it has been shown to cause a high rate of contact allergy, 22% in one series.[11] In the North American Contact Dermatitis Group biannual reports, the incidence of type IV allergic reactions to bacitracin (tested as a 20% concentration in petrolatum) has risen from 7.8% (272/3482) of patients tested in the 1992-1994 period[12] to 9.1% (280/3079) in 1994-1996 period,[13] 8.7% (357/4103) in the 1996-1998 period,[14] and 9.2% of 5812 patients in the 1998-2000 period.[15] There also have been 18 reports of immediate hypersensitivity

reactions, including anaphylaxis, induced by topical bacitracin. In sensitive patients, surgical irrigation fluid containing bacitracin has been reported to cause anaphylaxis.[16] Anaphylaxis from direct application of bacitracin to "varicose ulcers" was reported as early as 1967.[17]

Patch Testing and Preventive Measures—The use of bacitracin, initially thought to be a rare sensitizer, has grown over the past decade. Owing to this increased use, bacitracin has become a significant cause of allergic contact dermatitis in North America. It was featured as the "contact allergen of the year" in 2003 by the *American Journal of Contact Dermatitis*.[5] Despite its propensity to cause allergic contact dermatitis, bacitracin is not included on the T.R.U.E. Test® series. It is not tested on the European Standard series or the International Standard Series,[5] but the infrequent use of bacitracin in Europe and internationally may not warrant its inclusion on those standard patch testing trays. In the United States, the high prevalence of allergy warrants including bacitracin in a screening patch test series. Bacitracin is patch tested in 5% to 20% concentrations in petrolatum. If there is a clinical suspicion of an immediate, immunoglobulin E–mediated type I allergic reaction (eg, anaphylaxis, contact urticaria) believed to be related to bacitracin contact, testing must be performed cautiously by a clinician or allergist trained in resuscitation and the treatment of anaphylaxis because serious risks exist with type I allergic reactions.

Patients with confirmed contact dermatitis should avoid products containing bacitracin. Patients with bacitracin sensitivity should be taught to read labels, specifically to look for the presence of bacitracin in both prescription and over-the-counter wound care products; moisturizing ointments; adhesive bandages; and skin, eye, ear, and nose preparations. It also may be present in veterinary products, and sensitive persons should apply such products on their animals with caution. If bacitracin is used on postoperative wound and biopsy sites, it seems wise to advise patients to apply only a small amount to the wound itself, not to the surrounding skin, and to use it for a limited number of days. The astute clinician on the lookout for contact allergy or an aggravated dermatitis will ask about bacitracin use and advise patients with dermatitis or wound healing problems to discontinue it.

Bacitracin allergy may masquerade as cellulitis or wound infection. One key clinical clue to allergy is itching, rather than pain, in the involved erythematous skin. It is a common cause of scattered generalized dermatitis. Physicians should inquire about the chronic use of bacitracin on diseased or damaged skin, such as in venous stasis disease, leg ulcers, atopic dermatitis, or other chronic dermatoses, and discourage such use.

REFERENCES

1. Meleney FL, Johnson BA. Bacitracin. *Am J Med*. 1949;7:794-806.
2. Hsu S, Quan LT. Topical antibacterial agents. In: Wolverton SE, ed. *Comprehensive Dermatologic Drug Therapy*. 1st ed. Philadelphia, Pa: Saunders; 2001:472-496.
3. Binnick AN, Clendenning WE. Bacitracin contact dermatitis. *Contact Dermatitis*. 1978;4:180-181.
4. Grandinetti PJ, Fowler JF. Simultaneous contact allergy to neomycin, bacitracin, and polymyxin. *J Am Acad Dermatol*. 1990;23:646-647.
5. Sood A, Taylor JS. Bacitracin: allergen of the year. *Am J Contact Dermat*. 2003;14:3-4.
6. Katz BE, Fisher AA. Bacitracin: a unique topical antibiotic sensitizer. *J Am Acad Dermatol*. 1987;17:1016-1024.
7. Soto NE, Vaghjimal A, Stahl-Avicolli A, et al. Bacitracin versus mupirocin for *Staphylococcus aureus* nasal colonization. *Infect Control Hosp Epidemiol*. 1999;20:351-353.
8. Hinman CD, Maibach HI. Effect of air exposure and occlusion on experimental human skin wounds. *Nature*. 1963;200:377-378.
9. Agren MS, Karlsmark T, Hansen JB, et al. Occlusion versus air exposure on full-thickness biopsy wounds. *J Wound Care*. 2001;10:301-304.
10. Smack DP, Harrington AC, Dunn C, et al. Infection and allergy incidence in ambulatory surgery patients using white petrolatum vs bacitracin ointment. *JAMA*. 1996;276:972-977.
11. Zaki I, Shall L, Dalziel KL. Bacitracin: a significant sensitizer in leg ulcer patients? *Contact Dermatitis*. 1994;31:92-94.
12. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group standard tray patch test results (1992 to 1994). *Am J Contact Dermat*. 1995;6:160-165.
13. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. *J Am Acad Dermatol*. 1998;38:911-918.
14. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch-test results, 1996-1998. *Arch Dermatol*. 2000;136:272-273.
15. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch-test results, 1998-2000. *Am J Contact Dermat*. 2003;14:59-62.
16. Antevil JL, Muldoon MP, Battaglia M, et al. Intraoperative anaphylactic shock associated with bacitracin irrigation during revision total knee arthroplasty. *J Bone Joint Surg*. 2003;85A:339-342.
17. Comaish JS, Cunliffe WJ. Absorption of drugs from varicose ulcers: a cause of anaphylaxis. *Br J Clin Pract*. 1967;21:97-98.