

2. Himsworth H. *Report of the enquiry into the medical and toxicological aspects of CS (orthochlorobenzylidene malononitrile)*. Part 2. *Enquiry into toxicological aspects of CS and its use for civil purposes*. London: HMSO 1971. (Cmnd 4775).
3. Trigwell P. CS gas has been used as a chemical restraint in mentally ill person. *BMJ* 1997; 314: 444.
4. Gray P J. CS gas is not a chemical means of restraining a person. *BMJ* 1997; 314: 1353.
5. Finn D H, Hogg M A P, Crichton D. Improvement in apparatus for controlling riots. 1960; CS Patent No 967660.
6. Ballantyne B, Swanston D W. The irritant potential of dilute solutions of ortho-chlorobenzylidene malononitrile (CS) on the eye and tongue. *Acta Pharmacol Toxicol* 1973; 32: 266–277.
7. Parneix-Spake A, Theissen A, Roujeau J C, Revuz J. Severe cutaneous reactions to self-defence sprays. *Arch Dermatol* 1993; 129: 913.
8. Fuchs T, in der Wiesche M. Zur Frage der Kontaktallergien auf CN und CS ('Tränengas') bei Demonstrationsteilnehmern. *Z Hautkr* 1990; 65: 288–292, 295.
9. Kanerva L, Tarvainen K, Pinola A, Leino T, Granlund H, Estlander T, Jolanki R, Förström L. A single accidental exposure may result in a chemical burn, primary sensitization and allergic contact dermatitis. *Contact Dermatitis* 1994; 31: 229–235.
10. Shmunes E, Taylor J S. Industrial contact dermatitis. Effect of the riot control agent ortho-chlorobenzylidene malononitrile. *Arch Dermatol* 1973; 107: 212–216.
11. Jones G R N. Are CS sprays safe? *Lancet* 1997; 350: 605–606.
12. Lancet Editorial. 'Safety' of chemical batons. *Lancet* 1998; 352: 159.

Contact dermatitis from clotrimazole with positive patch-test reactions also to croconazole and itraconazole

S. ERDMANN, M. HERTL AND H. F. MERK

Department of Dermatology, University Hospitals RWTH Aachen, Pauwelsstrasse 30, D-52074 Aachen, Germany

Key words: allergic contact dermatitis; antimycotics; azoles; clotrimazole; cross-sensitivity; medicaments. © Munksgaard, 1999.

Case Report

A 52-year-old man presented with contact dermatitis in the genital area spreading to the lower abdomen and upper thighs. He had applied a cream containing clotrimazole 1% and dexamethasone acetate 0.1% (Baycuten® N). This antimycotic had been prescribed to him 1 year before and at that time successfully cured a tinea. After withdrawing the topical medication, and with additional oral treatment with prednisone 0.5 mg/kg, the skin rapidly recovered completely.

2 months later, he was patch tested with a standard series, a drugs series including clotrimazole 5% pet., all

the constituents of Baycuten® N cream, and a series of azole antimycotics (1% and 5% pet., 1% eth.). He reacted to clotrimazole and Baycuten® N, clotrimazole being the only constituent of Baycuten® N to react. Furthermore, patch tests to itraconazole (triazole) and to croconazole (imidazole) were also positive (Table 1).

Discussion

Contact allergies to modern imidazole antimycotics are comparatively rare, considering their high prescription rates. They may be caused by either vehicle components or the active ingredient. The most common sensitizers in the vehicle are cetearyl alcohol and propylene glycol (18); of the active ingredients, miconazole, econazole, tioconazole, and isoconazole have most frequently been reported (3–9, 12, 16, 22), but these are also the most frequently prescribed. Contact allergies to clotrimazole are relatively rare (1, 10, 15, 17, 20, 23).

Imidazoles can be divided into phenethyl (ketoconazole, miconazole, tioconazole, isoconazole, enilconazole, econazole, sulconazole, sertaconazole, oxiconazole) and phenmethyl (clotrimazole, croconazole, bifonazole). Itraconazole was the only triazole antimycotic in our test series, and is used exclusively for oral treatment. Cross-sensitivity was first proposed between the 2,4-dichlorophenylethyl imidazoles (13). Baes (2) then introduced the concept of ortho-chloro cross-sensitivity. Cross-sensitivity has been suggested between the phenethyl imidazoles miconazole, econazole, and isoconazole, between sulconazole, miconazole, and econazole.

Table 1. Patch test results

		D2	D3	D7
itraconazole	1% eth.*	—	+	+
croconazole	1% eth.*	—	+	+
bifonazole	1% eth.*	—	—	—
sertaconazole	1% eth.*	—	—	—
miconazole	1% eth.*	—	—	—
oxiconazole	1% eth.*	—	—	—
tioconazole	1% eth.*	—	—	—
ketoconazole	1% eth.*	—	—	—
Baycuten® N	as is	++	++	++
clotrimazole	1% eth.*	++	++	++
dexamethasone	1% pet.	—	—	—
other constituents of Baycuten® N		—	—	—

* Also tested at 1% and 5% pet.

zole, and between isoconazole and tioconazole (3, 11, 14). Cross-sensitivity has rarely been reported between clotrimazole and other structures, bifonazole and other structures, or ketoconazole (also a phenylethyl imidazole) and other structures (3).

The case reported here is unique in that the patient showed positive reactions to croconazole and itraconazole, besides clotrimazole, and had apparently used only 1 azole. Croconazole, belonging to the phenmethyl imidazoles like clotrimazole, was first marketed in Japan and Korea in 1986 and was introduced to the European market only recently. There are a number of publications on hypersensitivity to it (8, 9, 21) and cross-sensitivity between croconazole, isoconazole, bifonazole, and clotrimazole was reported in 1988 (8). Croconazole seems to owe its position as the only strong sensitizer among the azole derivatives to its methylene group (7).

References

- Balato N, Lembo G, Nappa P, Ayala F. Contact dermatitis from clotrimazole. *Contact Dermatitis* 1985; 12: 110.
- Baes H. Contact sensitivity to miconazole with ortho-chloro cross sensitivity to other imidazoles. *Contact Dermatitis* 1991; 24: 89–93.
- Dooms-Goossens A, Matura M, Drieghe J, Degreef H. Contact allergy to imidazoles used as antimycotic agents. *Contact Dermatitis* 1995; 33: 73–77.
- Foged E K, Hammershøy O. Contact dermatitis due to miconazole nitrate. *Contact Dermatitis* 1982; 8: 284.
- Gibson G, Buckley A, Murphy G M. Allergic contact dermatitis from tioconazole without cross-sensitivity to other imidazoles. *Contact Dermatitis* 1994; 30: 308.
- Guidetti M S, Vincenzi C, Guerra L, Tosti A. Contact dermatitis due to imidazole antimycotics. *Contact Dermatitis* 1995; 33: 282.
- Hausen B M, Angel M. Studies on the sensitizing capacity of imidazole and triazole derivatives. Part II. *Amer J Contact Dermatitis* 1992; 3: 95–101.
- Higashi N. Contact dermatitis from imidazole derivatives. *Hifubyoh-Shinryoh* 1988; 10: 713–716.
- Higashi M, Isonomaki M, Hazano S. 3 cases of contact dermatitis from topical imidazole antimycotics. *Skin Res* 1990; 32: (suppl) 149–154.
- Kalb R E, Grossman M E. Contact dermatitis to clotrimazole. *Cutis* 1985; 36: 240–242.
- Izu R, Aguirre A, Gonzales M, Diaz-Perez J L. Contact dermatitis from tioconazole with cross-sensitivity to other imidazoles. *Contact Dermatitis* 1992; 26: 130–131.
- Jelen G, Tennstedt D. Contact dermatitis from topical imidazole antifungals: 15 new cases. *Contact Dermatitis* 1989; 21: 6–11.
- Motley R J, Reynolds A J. Contact allergy to 2,4-dichlorophenylethyl imidazole derivatives. *Contact Dermatitis* 1988; 19: 381–382.
- Nishioka K, Kurata K, Asagami C. Experimental study of the potential for contact sensitization and cross-reaction of imidazole antifungals. *Contact Dermatitis* 1991; 25: 39–44.
- Nöhle M, Szliska C, Uter W, Schwanitz H-J. Spättyp-Sensibilisierung gegen ausgewählte Antimykotika. *Z Hautkr* 1997; 72: 934.
- Perret C M, Happle R. Contact allergy to miconazole. *Contact Dermatitis* 1988; 19: 75.
- Raulin C, Frosch P J. Kontaktallergie auf Clotrimazol und Azidamphenicol. *Dermatosen in Beruf und Umwelt* 1987; 16: 39–40.
- Raulin C, Frosch P J. Contact allergy to imidazole antimycotics. *Contact Dermatitis* 1988; 18: 76–80.
- Raulin C, Frosch P J. Contact allergy to oxiconazole. *Contact Dermatitis* 1987; 16: 39–40.
- Roller J A. Contact allergy to clotrimazole. *Br Med J* 1978; 2: 737.
- Shono M, Hayashi K. Contact dermatitis to croconazole hydrochloride. *Skin Res* 1987; 29 (suppl): 231–236.
- Stubb S, Heikkilä H, Reitamo S, Förström L. Contact allergy to tioconazole. *Contact Dermatitis* 1992; 26: 155–158.
- Valsecchi R, Pansera B, Di Landro A, Cainelli T. Conubial contact sensitization to clotrimazole. *Contact Dermatitis* 1994; 30: 248.

Contact dermatitis due to diethyl sebacate

MIZUHO KIMURA¹ AND AKIRA KAWADA²

¹Department of Dermatology, Murayama Hospital, Asahigaoka 1-7-7, Asaka City, Saitama 351-0035, Japan

²Department of Dermatology, Teikyo University School of Medicine, Ichihara Hospital, Anesaki 3426-3, Ichihara City, Chiba 299-0111, Japan

Key words: allergic contact dermatitis; diethyl sebacate; patch testing technique; emulsifiers; topical medications. © Munksgaard, 1999.

A 28-year-old woman was seen in June 1998 with pruritic erythema on both feet. She had started using an antimycotic over-the-counter preparation, 0.2% pyrrolnitrin and 0.4% clotrimazole ointment (Pyroace W[®], Fujisawa Co. Ltd. Osaka, Japan) about 2 weeks before, and a few days later developed erythema. She then changed to New Eurax G[®] (OTC) (Fujisawa), but the eruption did not improve.

We performed patch tests with Pyroace W[®] ointment (as is) and New Eurax G (as is) initially. Positive reaction was seen to Pyroace W[®] ointment (as is). Secondly, the patient was patch tested with 1% and 10% pet. of pyrrolnitrin, clotrimazole, and 6 other constituents (crotamiton, white beeswax, isopropyl myristate, polyoxyethylene lauryl ether, and diethyl sebacate). Only diethyl sebacate showed a positive response on D2 at 10% pet. and on