

Severe adverse reactions during specific subcutaneous immunotherapy

ADVERSE reactions during specific subcutaneous immunotherapy (IT) seem in theory to be a more and more frequent inconvenience. According to a study carried out in France in 1980 by Vervloet et al. (1), 0.2% of pollen allergenic extract injections provoked organ reactions. In 1988, Vervloet et al. (2) reported a notably higher frequency, i.e., 1.8% of pollen extract injections and 2.5% of mite extract injections. In a retrospective study of the period 1968-92, Andri & Betteli (3) reported organ reactions in 0.063% of patients, taking into consideration a total of 278 000 injections. According to Vervloet et al.'s study in 1980 (1), anaphylactic shock occurred as a result of pollen allergenic extract subcutaneous injections in 0.024% of cases, whereas in 1988 (2) he reported its occurrence in 0.04% of subjects after pollen and mite allergenic extract injections. In a retrospective study carried out in the USA between 1945 and 1985, Lockey et al. (4) noted 24 cases of fatal shock during IT, while Reid et al. (5), in a recent study, also carried out in the USA between 1985 and 1989, reported 17 cases of fatal shock. In the UK, a similar study (6) revealed 26 cases followed by fatal shock in the period 1957-86.

The authors intend to demonstrate, on the basis of their experience, the low incidence of organ or systemic reactions if IT is carried out by qualified staff and in suitably equipped premises. Between 1984 and 1993, in the Department of Diagnosis and Treatment of Allergic Diseases of Messina University, about 3000 patients were treated with IT, reaching a total of 150 000 subcutaneous injections. Apart from the most common local reactions (erythema and edema) exclusively at the injection site, the authors noted only 16 cases (0.01%) of organ reactions (two cases of glottis angioedema and 14 cases of bronchoconstriction), which regressed after pharmacologic treatment and did not reappear during successive injections. The allergens which caused the reactions were mite allergenic extracts (*Dermatophagoides pteronyssinus* and *D. farinae*) in 11 cases and *Parietaria* pollen allergenic extract in five cases. Anaphylactic shock

occurred in only one case (0.0006%), that of a 14-year-old boy with a maintenance dose of mite IT, who therefore needed immediate treatment with the drugs usually used in an allergologic emergency. No cases of fatal anaphylaxis were reported.

In conclusion, the authors affirm that specific IT remains essential in the treatment of respiratory allergies and does not present any great risk to patients as long as it is carefully monitored and carried out by specialized staff.

Hyposensitization is essential for allergy but must be handled with care.

L. RICCIARDI, S. ISOLA, S. GANGEMI, M. CILIA, C. LEVANTI
PROF. F. PURELLO D'AMBROSIO
Policlinico Universitario Pad. H
98125 Messina
Italy

Accepted for publication 24 November 1995

REFERENCES

1. Vervloet D, Khairallah E, Arnaud A, Charpin J. A prospective national study of the safety of immunotherapy. *Clin Allergy* 1980;10:59-64.
2. Vervloet D, Birnbaum J, Charpin J. Désensibilisation spécifique. In: Charpin J, Vervloet D, editors. *Allergologie*. 3rd ed. Paris: Flammarion, 1992:1005-15.
3. Andri L, Betteli C. L'immunoterapia specifica. In: Atti Convegno "La rinite e la congiuntivite allergica" (Verona, 5 October 1990). Lofarma, Milano, 1990:85.
4. Lockey RF, Benedict LM, Turkeltaub PC, Bukantz SC. Fatalities from immunotherapy (IT) and skin testing (ST). *J Allergy Clin Immunol* 1987;79:660-77.
5. Reid MJ, Lockey RF, Turkeltaub PC, Platts-Mills TAE. Survey of fatalities from skin testing and immunotherapy 1985-1989. *J Allergy Clin Immunol* 1993;92:6-15.
6. Committee on Safety in Medicine. Desensitizing vaccines. *BMJ* 1986;293:948.

Allergic contact dermatitis from estradiol in a transdermal therapeutic system

ESTRADERM® TTS (transdermal therapeutic system) (Ciba-Geigy, SA, Barcelona, Spain) is a thin adhesive patch, consisting of a drug reservoir containing estradiol as an ethanolic gel with hydroxypropyl cellulose acetate, a rate-controlling micro-

porous membrane, and an adhesive layer. The most common adverse reaction to transdermal estradiol consists of erythema and irritation at the application sites (1, 2). Allergic contact dermatitis from estradiol has rarely been described (3).

■ A 36-year-old woman with a history of oophorectomy had been using Estraderm® TTS 50, one patch twice weekly, at varying sites on the buttocks. After 4 months, she began to develop itchy, discoid patches of papules and vesicles at the site of application of the Estraderm patches. For that reason, therapy was discontinued.

■ A 49-year-old, postmenopausal woman began using Estraderm TTS 50. Within 7 months, she began to experience erythematous and itching lesions at each application site, leading to discontinuation of the treatment.

Patch tests were carried out in both patients with Estraderm TTS 50 and with a placebo patch (Estraderm TTS 50 without estrogen) supplied by Ciba-Geigy, SA, Barcelona, Spain. Additional patch tests with Oestraclin® gel (estradiol) and its excipients, carbopol, triethanolamine, and ethanol (provided by Seid SA, Barcelona, Spain), were performed.

Estradiol in "hormone patch therapy" might cause allergy.

Only Estraderm TTS 50 (Fig. 1) and Oestraclin revealed a positive reaction, with papules, erythema, and vesicles at 48 and 96 h. Patch test results with placebo and excipients were negative. The results of the patch tests are shown in Table 1.

Closed patch tests with the European standard series were negative.

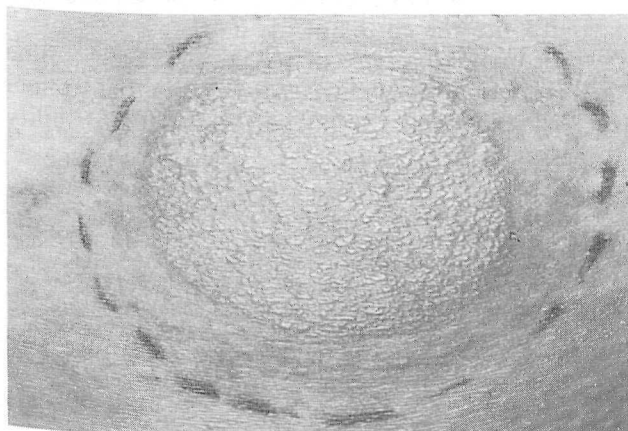


FIGURE 1 Eczematous reaction on buttocks after application of patch test.

Table 1. Patch test results (readings at day 3)

Patch test	Patient 1	Patient 2
Estraderm TTS 50	+++	++
Placebo patch	-	-
Oestraclin gel	+++	++
Carbopol 1% pet	-	-
Triethanolamine 2% pet	-	-
Ethanol as is	-	-

+++ : erythema, papules, vesicles; ++ : erythema, papules; pet: petroleum.

■ Transdermal therapeutic systems (TTS) represent an important advance in the evolution of hormonal replacement therapy. However, local irritant skin reactions may occur with these systems (1, 2). Components of the Estraderm TTS including hydroxypropyl cellulose (4), ethanol (5) in the reservoir, and the adhesive (6) have been implicated as causes of allergic contact dermatitis. Estradiol has rarely been reported to be a potential allergen of delayed contact sensitivity (3). Autoimmune estrogen dermatitis has been described in patients with skin problems before each menstrual period (7). To our knowledge, cross-reactivity with other estrogens has not been reported.

In our cases, patch test results suggest that skin reactions were probably due to estradiol as a cause of allergic contact dermatitis.

S. QUIRCE, A. GARDE, G. BAZ, P. GONZALEZ
DRA. MARÍA DOLORES ALONSO DÍAZ DE DURANA
Servicio de Alergología
Hospital Obispo Polanco
Avda Ruiz Jarabo s/n
44002 Teruel
Spain

Accepted for publication 14 September 1995

ACKNOWLEDGMENT

We thank Seid Laboratories for providing some of the patch test materials.

REFERENCES

- Balfour JA, Heel RC. Transdermal estradiol. A review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy in the treatment of menopausal complaints. *Drugs* 1990;40(4): 561-82.
- Hogan DJ, Maibach HI. Adverse dermatologic reactions to transdermal drug delivery systems. *J Am Acad Dermatol* 1990;22: 811-14.
- Carmichael AJ, Foulds IS. Allergic contact dermatitis from oestradiol in oestrogen patches. *Contact dermatitis* 1992;26:194-5.
- Schwartz BK, Clendenning WE. Allergic contact dermatitis from hydroxypropyl cellulose in a transdermal estradiol patch. *Contact Dermatitis* 1988;18:106-7.
- Pecquet C, Pradalier A, Dry J. Allergic contact dermatitis from ethanol in a transdermal estradiol patch. *Contact Dermatitis* 1992;27:275-6.
- McBurney EI, Boustany S, Collins JH. Contact dermatitis to transdermal estradiol system. *J Am Acad Dermatol* 1989;20:508-10.
- Shelley WB, Shelley ED, Talanin NY, Santoso-Pham J. Estrogen dermatitis. *J. Am Acad Dermatol* 1995;32:25-31.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.