

cells and immunocomplex formation. On the other hand, chronic allergic mucositis probably due to food allergy, which caused turbinate hypertrophy, could have triggered headache. Whatever the pathogenetic mechanism, the most important finding was the patient's response to ED and DBPCFC, which indicated a strong cause-and-effect relationship. Headache is a very common disorder, often requiring repeated pharmacologic therapy, while an ED is relatively easy to achieve. Since food exclusion may be a better therapy than drugs, AFR should always be kept in mind.

Key words: food allergy, egg and milk; headache.

G. F. STEFANINI\*, L. MARSIGLI, F. G. FOSCHI, F. EMILIANI, M. BISELLI, F. CAPUTO, G. H. LEEFIELD, E. CASTELLI, G. GASBARRINI  
\*Patologia Medica I  
Policlinico S. Orsola  
Via Massarenti 9  
40138 Bologna  
Italy

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## Systemic contact dermatitis to copper-containing IUD

**A**LLERGOLOGIC features due to exposure to some of the most common metals such as nickel, cobalt, and chromium appear to be on the increase. Hypersensitivity to these metals can appear with a typically eczematous picture of contact dermatitis (1) or as systemic contact dermatitis (2) (after oral, inhalant, or parenteral contact with the allergen), characterized by various clinical pictures such as dyshidrosis, widespread eczema (Shannon's pseudoatopy), urticaria, and, in some cases, polymorphic or purpuric erythema.

Copper, or, more precisely, its salt, copper sulfate, can cause the above reported clinical pictures (3, 4);

in the literature, the cases reported of monovalent sensitivity to copper are rare (5).

Intrauterine devices (IUD) are made of copper sulfate, and, to date, few cases of contact dermatitis and urticaria in women wearing IUD have been reported (6, 7). Our report documents a case of endometritis and urticaria-angioedema syndrome we observed in the allergology outpatient department, in a woman wearing a copper-containing IUD who, as a result, became monosensitized to copper sulfate.

A 32-year-old housewife had had the clinical features of widespread urticaria together with angioedema of the eyelids and of the labia majora and minora for about 6 months; corticosteroids and H<sub>1</sub>-antagonists provided only intermittent, temporary relief.

The patient's clinical history showed that she had presented persistent symptoms characterized by pre- and postmenstrual hematic stillicidium and leukorrhea for about 6 months. Numerous systemic antibiotics and anti-inflammatory drugs had not caused any remission of the symptoms. The patient also reported that she had been wearing a copper-containing IUD for the past 12 months.

A 72-h patch test with the routine series of the International Contact Dermatitis Research Group, including copper sulfate, was performed and revealed marked positivity to 1% copper sulfate in water. The patch test also was positive with further dilution of the solution (0.5 and 0.01% sulfate in water); 48-h application of the copper spiral to the patient's forearm was also positive and provoked a crop of dyshidrotic vesicles, preceded by erythema and itching. Plasma copper and ceruloplasmin were normal.

We also performed an *in vitro* lymphocyte-stimulating test with copper, which was positive too. The test had a typical crescendo reaction.

Histologic examination of the endometrial biopsy showed vulvovaginitis with hyperplasia of the cervical canal and T-cell and eosinophilic granulocyte infiltration.

Removal of the copper-containing IUD caused complete remission of both the widespread urticaria and the eyelid and genital angioedema.

Copper sulfate is a metal in the form of turquoise crystals. It is in common use because it is a very efficient conductor of both electricity and heat. It is present in bronze and brass, in coins, in denatured

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*In rare cases, copper-containing intrauterine contraceptive devices can cause generalized dermatitis.*

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alcohol as a coloring agent, and in IUDs. It is also used as a pesticide and a fertilizer.

Its sensitizing capacity is extremely low: in addition to external professional exposure (8), internal exposure to copper sulfate, with the appearance of systemic contact dermatitis, has become increasingly significant. Hoher et al. (9) reported a case of interstitial nephritis due to a copper-containing IUD.

Zabel et al. (4) and Hausen & Hohlbaum (10) performed allergologic examinations on several women who exhibited different degrees of cutaneous complaints after wearing a IUD, and who had a low incidence of positivity to the copper sulfate patch test; in all women, removal of the IUD caused remission of the symptoms.

Systemic contact dermatitis is an allergic disease that can be caused by various immunoreactions; however, T-cell-mediated reactions are involved (11). In experimental animals (12), it has been shown, with a radioactively labeled copper IUD, that small amounts of the metal are absorbed through the mucous membrane and carried to the cutis via the blood or lymph; in the cutis, the allergen is intercepted from antigen-presenting cells and recognized by T cells which migrate to the lymph nodes with blastic transformation, proliferation of cytotoxic lymphocytes, and production of cytokines. These are able to recall neutrophils and eosinophils to the reaction site and cause capillary dilation and increased permeability, resulting in a cutaneous allergic inflammation which may be responsible for the urticaria/angioedema features.

In conclusion, although there is a relatively low incidence of cases reported in the literature describing allergy to copper sulfate, it is advisable to bear the possibility of this disorder in mind, especially in fertile young women wearing a copper-containing IUD.

**Key words:** copper sulfate; intrauterine contraceptive device; systemic contact dermatitis.

F. PURELLO D'AMBROSIO\*, L. RICCIARDI, S. ISOLA, S. GANGEMI, M. CLIA, C. LEVANTI, A. MARCAZZO  
\*Policlinico Universitario  
Pad. H, Viale Gazzi  
98100 Messina  
Italy

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## Cutaneous delayed reaction to ranitidine

**R**ANITIDINE is a histamine H<sub>2</sub>-receptor antagonist used in the therapy of gastric and duodenal ulcers, gastroesophageal reflux, and hypersecretory states. Chemically, it is a furan derivative with a molecular weight of 350.9 Da. Ranitidine is a well-tolerated drug. Many patients have been treated, and much experience has been accumulated on the safety of this drug. Headaches, tiredness, dizziness, and mild gastrointestinal disturbance are among the most frequent complaints (1). Hypersensitivity reactions and dermatologic effects have rarely been associated with ranitidine therapy (2-8).

We report on a patient who developed a cutaneous delayed reaction after taking ranitidine, a rare adverse reaction to this drug.

In February 1994, a 43-year-old woman was treated with ranitidine (Zantac<sup>®</sup>, Glaxo, UK) 300 mg once daily as the sole treatment for a duodenal ulcer. Forty-eight hours after starting treatment, she developed papular eruption on her arms and legs. Papules were very itchy, measured 2-5 mm, and cleared completely within 2 weeks of the drug's being withdrawn. The patient did not recall a prior exposure to ranitidine. Similar clinical reactions with the same evolution were observed in April 1994 and October 1995 after reexposure to ranitidine. The patient had neither a personal nor a family history of atopy. She gave her written, informed consent before the study.

Cutaneous sensitivity to ranitidine, other H<sub>2</sub>-receptor antagonists (cimetidine, famotidine, and nizatidine), and a furan derivative (nitrofurantoin) was evaluated by prick and intradermal tests at 10 mg/ml, and by patch tests at 1% and 10% in petrolatum. Drugs used in test preparations were obtained as pure products from the trade-name

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