

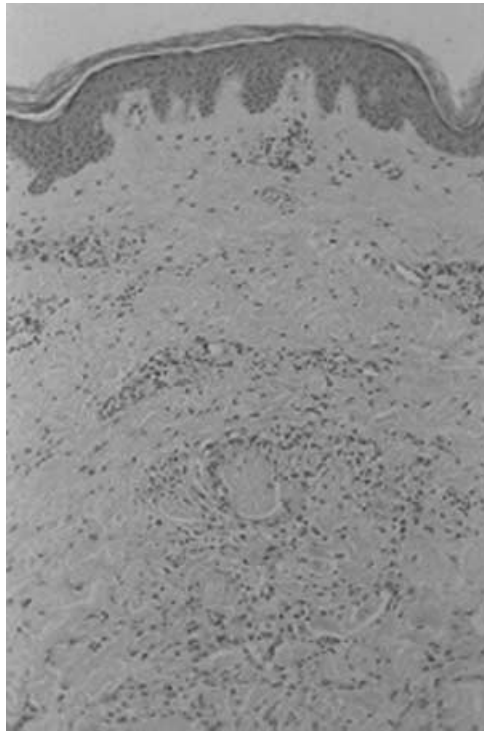


fig. 2 Focal areas of collagen degeneration in the upper dermis accompanied by a deposit of basophil material. The infiltrate is composed of histiocytes and lymphocytes, and several epithelioid and multinucleated cells (H&E, $\times 100$).

epithelioid and multinucleated cells (fig. 2). Warthin–Starry stain for *B. Burgdorferi* was negative and PCR on paraffin sections failed to detect *B. Burgdorferi* DNA.

Because of the peculiar histological features and the negative microbiological results, prednisone 25 mg/day and diaminodifenil-sulphone 100 mg/day were introduced, which resulted in the lesions clearing. The patient is still on this treatment.

Our patient is very likely to have been infected by *B. Burgdorferi*. Although *B. Burgdorferi* serology was initially negative, it turned positive within 3 months and western blot was positive. In addition, Liguria is a highly endemic region and tick bites may well go undetected.

The interstitial GA pathology is unusual in the lesions of Lyme's disease.² It has been described recently in 11 cases of late-phase *B. Burgdorferi* infection,³ mostly corresponding clinically to a peculiar setting of morphea and, quite surprisingly for a late phase, in a few cases to the typical erythema chronicum migrans. The histopathological findings consisted of an interstitial inflammatory infiltrate mostly composed of histiocytes dispersed among the collagen bundles, and focal areas of small pseudorosette formation characterized by small histiocytes disposed

radially around thick collagen bundles, and occasionally a few intermingled plasma cells.

In our case, the lesions were clinically similar to those of erythema chronicum migrans, differing from those of Moreno *et al.*³

The appearance of interstitial GA is an unusual presentation of Borreliosis, occurring in clinically different lesions and at different stages of the disease. What causes some patients to develop such pathology is unclear. It may be speculated that *B. Burgdorferi* antigens persist in the lesion and that the granuloma formation is meant to circumscribe them. In our opinion, *B. Burgdorferi* serology, immunoblotting and PCR should be performed in any patient with the interstitial type of GA.

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References

- 1 Dabski K, Winkelmann RK. Generalized granuloma annulare: histopathology and immunopathology. *J Am Acad Dermatol* 1989; **20**: 28–39.
- 2 Steere AC, Grodzicky MS *et al.* The spirochetal etiology of Lyme disease. *N Engl J Med* 1983; **308**: 733–740.
- 3 Moreno C, Kutzner H *et al.* Interstitial granulomatous dermatitis with histiocytic pseudorosettes: a new histopathologic pattern in cutaneous borreliosis. Detection of *Borrelia burgdorferi* DNA sequences by a highly sensitive PCR-ELISA. *J Am Acad Dermatol* 2003; **48**: 376–384.

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Linking allergy to mercury to HLA and burning mouth syndrome

Editor

Burning mouth syndrome (BMS) is a small-fibre neuropathy.¹ Its hallmarks include a burning sensation in the mouth in the absence of visible oral lesions. The literature links BMS with nutritional deficiency, hormonal imbalance, emotional disorders, and allergy to dental materials.^{1,2,4–6} Women are more commonly affected than men.^{1,3}

We hypothesized that HLA-class II molecules have a role in allergy sensitization to mercury, causing adverse events in oral tissues.^{7–9}

Here, we describe two Italian, Caucasian, unrelated women who represent a rare and outstanding example of interactions between extreme allergy to mercury, HLA class II molecules and BMS.

Patient 1. In 2001, a 71-year-old woman reported BMS. Symptoms started after oral rehabilitation with gold-based crowns and dental amalgams. BMS was accompanied by glossodynia, pharyngitis, and dysphagia.

Oral examination revealed multiple macular pigmentations on the oral mucosa, histologically diagnosed as lentigo simplex. There was no evidence of folic acid and cobalamin deficiency. Tissue transglutaminase antibodies of IgA-class were normal (1.5 U/mL). Allergic sensitization to metallic mercury was detected (score +++).

We inferred that recent dental metal rehabilitation was related to the patient's symptoms. Clinical features and patch-testing supported a diagnosis of BMS type-3.¹⁰ Treatment was amalgam removal and after 1 month her symptoms resolved. At follow-up at 4 years she is currently symptom-free.

Patient 2. In 2001, a 65-year-old woman presented with a painful and burning sensation in the mouth. Patch-testing showed evidence of allergy to mercury (score +++). We diagnosed a typical BMS type-3. A detailed case report has been published elsewhere.⁶

To gain insight into the genetic relationship between the two patients, we decided to identify the molecular histocompatibility complex (MHC) genotypes.

HLA class I and II alleles were typed from genomic DNA by standard PCR-based methods (PCR-SSP and reverse PCR-SSO; Dynal Invitrogen Corporation, Bromborough, UK).

Interestingly, both patients shared the two haplotypes HLA-DRB1*0701; DQA1*0201; DQB1*0202/DRB1*11; DQA1*0505; DQB1*0301 (Table 1). The combined presence of these two haplotypes is associated with the incidence of coeliac disease, because of the presence of the DQA1*05, DQB1*02 heterodimer encoded in cis-trans.

It is tempting to speculate that the DQA1*05, DQB1*02 heterodimer, encoded by the shared haplotypes of the two patients, presents an, as yet, undefined hapten antigen to specific T cells. This mechanism has been shown to operate in patients affected by coeliac disease.

Our immunogenetic observations suggest a possible correlation between MHC and allergic sensitization to mercury, implying that genetic susceptibility factors may confer a major adverse reaction to mercury.

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References

- 1 Lauria G, Majorana A, Borgna M *et al.* Trigeminal small-fiber sensory neuropathy causes burning mouth syndrome. *Pain* 2005; **115**: 332–337.
- 2 James J, Ferguson MM, Forsyth A. Mercury allergy as a cause of burning mouth. *Br Dent J* 1985; **159**: 392.
- 3 Zakrzewska JM, Glenney AM, Forssell H. Interventions for the treatment of burning mouth syndrome: a systematic review. *J Orofac Pain* 2003; **17**: 293–300.
- 4 Alanko K, Kanerva L, Jolanki R, Kannas L, Estlander T. Oral mucosal disease investigated by patch-testing with a dental screening series. *Contact Dermatitis* 1996; **34**: 263–267.
- 5 Dutree-Meulenberg RO, Kozel MM, van Joost T. Burning mouth syndrome: a possible etiologic role for local contact hypersensitivity. *J Am Acad Dermatol* 1992; **26**: 935–940.
- 6 Pigatto PD, Guzzi G, Persichini P, Barbadillo S. Recovery from mercury-induced burning mouth syndrome due to mercury allergy. *Dermatitis* 2004; **15**: 75–77.
- 7 Sato K, Kusaka Y, Zhang Q *et al.* Investigation of the association between mercury sensitization and HLA-DR6. *Contact Dermatitis* 1996; **34**: 295.
- 8 Prochazkova J, Bartova J, Ivaskova E *et al.* HLA association in patients with intolerance to mercury and other metals in dental materials. *Dis Markers* 2000; **16**: 135–138.
- 9 Guzzi G, Mazzi B, Tomasi S, Fleischhauer K, Pigatto PD. Association between HLA-class II and mercury sensitization. 7th International Conference of Mercury as a Global Pollutant. *RMZ Materials Geoenvironment* 2004; **51**: 136–140.

Table 1 HLA typing of two patients with type 3 burning mouth syndrome associated with allergy to mercury

	A*	B*	Cw*	DRB1*	DRB3*	DRB4*	DQA1*	DQB1*	DPB1-
Patient 1	24	18	12	0701		0101101	0201	0202	0401
	32	1401	08	1104	0202		0505	0301	0402
Patient 2	02	07	07	0701		0101101	0201	0202	0401
	11	18	12	1101	0202		0505	0301	1701

10 Lamey PJ, Lamb AB, Hughes A, Milligan KA, Forsyth A.
Type 3 burning mouth syndrome: psychological and allergic
aspects. *J Oral Pathol Med* 1994; **23**: 216–219.

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Silicon in hair loss: a preliminary SEM microanalysis study

Editor

Hair composition has been studied by microanalysis performed by scanning electron microscopy (EDX analysis),^{1,2} but data about the trace elements in telogen effluvium in otherwise healthy subjects are lacking in the literature.³

Among essential elements, increasing evidence suggests that silicon (Si) is important in maintaining optimal hair condition. Skin, connective tissue collagen, bone and cardiovascular apparatus need adequate amounts of this element.^{4–6}

We evaluated the presence of Si in the hair of patients with telogen effluvium and in control subjects.

Twenty female subjects (mean age: 42.35 years, range 14–77) with telogen effluvium and a group composed of 20 healthy female controls, homogeneous to the group of patients in terms of age and place of residence, were enrolled on the study.

Samples of untreated scalp hair obtained by pull test were collected from the patients and from the controls and were prepared for analysis. Segments (1 cm long) cut from the proximal end of the hairs were mounted on aluminium stubs and coated with carbon in evaporator (Emitech K 950, CAMBRIDGE Stereoscan 360, Cambridge Instruments Ltd, Cambridge, UK).

The proximal part only of the untreated scalp hair was analysed to reduce environmental exposure and cosmetic contamination in the concentration of the detected elements.

Energy-dispersive X-ray microanalysis (EDX analysis) was performed by scanning electron microscopy (Cambridge Stereoscan S 360, OXFORD Instruments INCA Energy 300, High Wycombe, UK) with a microanalysis device (Oxford Instruments INCA 3000, EMITECH K950, Ashford, UK) (fig. 1).

Data obtained, i.e. weight percentage of calcium (Ca), sulphur (S) and silicon (Si), from the patients were compared with sex and age-matched controls. The Student's *t*-test was used for statistical evaluation.

Mean values of Si, Ca and S hair concentration (weight percentages) are summarized in Table 1. Si was found in 5% of the patients and in 35% of the controls ($P < 0.05$), which was statistically significant. Ca was found in 70% of the patients and in 85% of the controls ($P > 0.05$; not significant). S was found in 100% of both patients and controls.

As regards the skin, Si probably plays a role in the thickness or elasticity of the epidermis and dermis; it

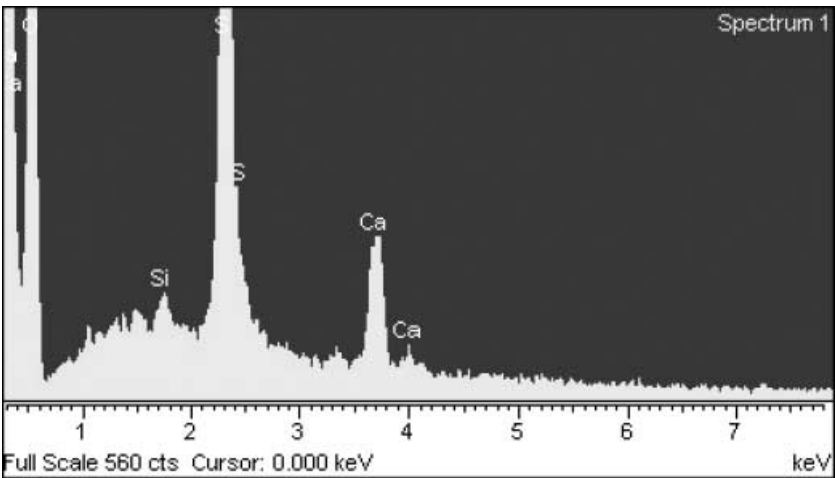


fig. 1 X-ray emission spectrum obtained with EDX analysis of control no. 10, which reveals the presence of Si.

Element	Mean value (DS) in patients (% weight)	Mean values (DS) in controls (% weight)	t-test
Ca	0.42 (0.43)	0.64 (0.54)	$P > 0.05$ (n.s.)
S	5.80 (0.69)	5.35 (0.91)	$P < 0.05$ (s)
Si	0.01 (0.04)	0.09 (0.20)	not computable (n.s.)*

*n.s., not statistically significant; s, significant.

Table 1 Mean values (standard deviation) of hair Ca, S and Si in patients and controls