

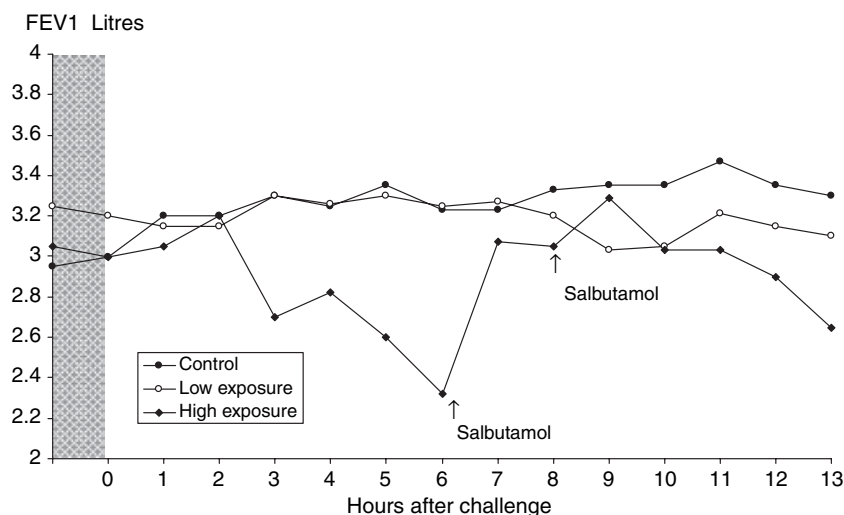


Figure 2. Case B challenge with aerosolized vitamin mixture. Control challenge aerosolized saline. Two active challenge days represent low and high exposure to the aerosolized solution containing raw vitamin as provided by the cereal company.

We believe these two cases are the first reports of occupational asthma related to the use of thiamine in an industrial setting. The production of a fine aerosol of vitamin mixture facilitates the pulmonary deposition. Both cases are confirmed by occupational challenge, which demonstrated predominantly late asthmatic reactions.

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C1-INH and C3/C4 levels do not correlate with long-term danazole dosage and HAE-1 attack-free interval

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Key words: C1-INH; C3; C4; danazole; hereditary angioedema.

Patients with hereditary angioedema are rare in clinical practice and thus therapeutic experience is rather based on individual cases. A

Long-term follow-up showed no correlation between C3/C4/C1-INH, danazole dosage and absence of HAE-attacks.

46-year old man was first diagnosed to have hereditary angioedema type-1 (HAE-1) on the basis of clinical history and serological findings in March 2002. He presented in casualty with a recent onset of spontaneously evolving, angioedema at various sites, triggered sometimes by manual labor such as gardening work. Complement C4 and C1-esterase inhibitor (C1-INH) levels were found to be far below the normal baseline. A functional assay of C1-INH came back as normal and thus the diagnosis HAE-1 was confirmed.

As attack frequency was high, continuous therapy was needed. In absence of any contraindications, and facing a male patient, we decided to start danazole 200 mg/day according to the Budapest protocol, as the second drug of choice Tranexamic acid is regarded as less effective and the patient was worried about the particular side effects (1). As expected, the attacks ceased within a few days. The dosage was reduced step-by-step over time as shown in Fig. 1A, based on absence of clinical symptoms. The patient's compliance was high, follow-up was every 3–4 months until today. Monitoring included routine biochemistry, yearly abdominal ultrasound, full blood count and control of serum levels for C3, C4 and C1-INH. Up to today no side effects of danazole became evident. In April 2004, the patient ran out of medication for 2 weeks and suddenly HAE attacks relapsed, but stopped again within 2 weeks of restarting danazole 50 mg/day. In January 2005 the minimum maintenance dose of 50 mg/d 5 days a week was reached (1). As evident from our time course analysis of serum C3, C4 and C1-INH levels shown in Fig. 1B there was no evident correlation between the values of these three parameters and the clinical success of therapy in our patient. The serum C4 gradually went back to normal, C3 was always normal and C1-INH stayed below the normal range for the whole monitored time of 3 years. This observation is in accordance with the small study ($n = 8$) by Zimmermann (2), who found similar long-term patterns for C4 and C1-INH. Gelfand described in the first danazole study in 1976 an initial increase of C1-INH and C4 within the first days of

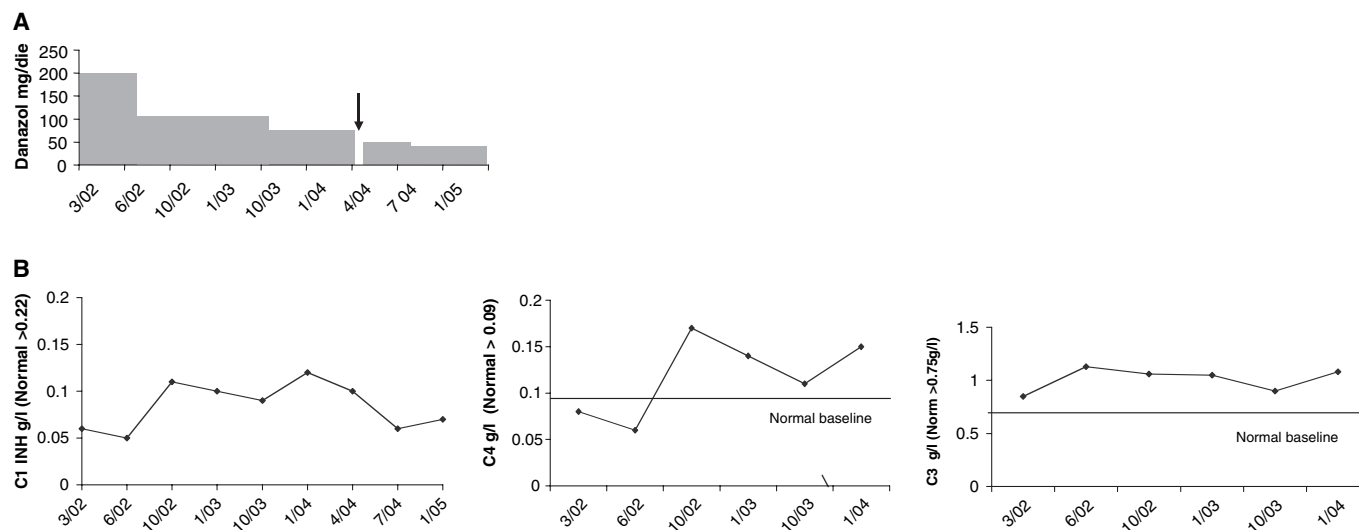


Figure 1. (A) Danazole dose over the last 3 years since starting the medication. The arrow points the only medication gap of 2 weeks in 3 years during which HAE attacks relapsed. (B) Time course of C1-INH, C4 and C3 levels in serum (laboratory: clinical chemistry, University of Ulm).

starting the drug, but did not perform a long-term survey (3). The mechanism of action for the attenuated steroid danazole is not known but it seems to depend on its 17α alkylation (4). In summary neither of the three monitored values could be regarded as valuable for clinical decisions about dosage reduction of danazole in our patient, these relied purely on the clinical history obtained at each follow-up visit. Long-term low dose danazole therapy, as expected (3), proved to be very effective for disease control and a maintenance dose of 50 mg 5x/week was enough to suppress the HAE attacks completely. For dosage determination there is still no biochemical marker available, as the diagnostically relevant C3, C4 and C1-INH levels did neither in the previously published eight patients (2) nor in our case provide any valuable clinical information for follow-up and C1–C1-INH complexes monitored by Cicardi did also not prove to be useful for this purpose (5). At present only studies with a few patients looking at long-term effects of danazole, such as liver neoplasms and androgenetic effects, exist (6). However, despite the concern of side effects, which are serious for women because of the endocrinological interference, experience with low dose treatment for more than 15 years supports the status of danazole as a first line therapy for HAE-1 (2).

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Linear urticarial streaks associated with opioid administration

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Key words: mast cell; opioids; urticaria.

A 40-year-old male was admitted to the hospital with an ischemic lower limb. He was given 50 mg of Demerol® (meperidine) intravenously for pain control. Just minutes after being given the Demerol, the patient was noted to develop a rash along the

Intravenous opioids cause linear urticarial streaks.