papules proximally on both inner thighs and sporadic lesions on the lower part of the trunk and lower legs. A tiny stab wound could be seen at the top of some of the papules. The lesions were strictly demarcated by the edges of his underwear and no lesions at all were found in the pubic area. Although there was no itching or excoriations, clinically it looked like multiple bites from fleas. Light microscopic examination of the parasite showed that it was not the pubic louse and the parasite was classified as a larva of the tick *I. ricinus* (performed by Alice Olesen, Danish Pest Infestation Laboratory) (Fig. 1).

The patient was followed for 2 months but no signs of erythema chronicum migrans were found and two serum samples performed after 2 and 8 weeks for antibodies against *Borrelia burgdorferi* proved negative.

DISCUSSION

The developmental cycle of the common tick *I. ricinus* (a mite) is generally 3 years, with a duration of each developmental stage (larva, nymph, adult) of 1 year (1, 4, 5). After engorgement, the female oviposits and lays about 2000 eggs (6, 7). When the larvae are hatched, 300 to 400 can be found within an area of 20 to 30 cm^2 (personal communication, Peter Gjelstrup, Curator at the National Historic Museum, Aarhus). The larvae have 6 legs (Fig. 1) and measure about 1 mm, while the larger nymphs and adults have 8 legs (2, 3). The larvae are found in the vegetation very close to the ground, the nymphs slightly higher, while the adults may be found about 1 meter above the ground. Therefore, larvae in general feed on small rodents (6), while larger animals, and humans, are hosts for the nymphs and adults. The peak of spring larval activity in European countries occurs in late May (5). We, therefore, believe that our patient had been sitting on the top of myriads of larvae being in their host-seeking phase.

Although probably seldom encountered, we suggest that bites from larvae of the tick *I. ricinus* should be kept in mind in cases of multiple 'insect' bites and especially in May–June and August–September, which are the peak periods of tick activity (1, 5). The differential diagnosis is important because the larvae may cause infection with the spirochete *Borrelia burgdorferi* (8).

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Start and End of the Effects of Terfenadine and Astemizole on Histamine-induced Wheals in Human Skin

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A study was made of effects of two antihistamines, terfenadine (60 mg twice daily) and astemizole (10 mg once daily) on wheals induced by histamine dihydrochloride (10 mg/ml) in the prick test on the upper back of 15 healthy students. The suppressive effects of terfenadine on the histamine wheal appeared earlier (2 h), and disappeared earlier (within 1 day) than those of astemizole (3 days and 28 days, respectively). No difference between the maximal effects of the two drugs was seen. ***Key words: Prick testing; Histamine H_1 antagonists.***

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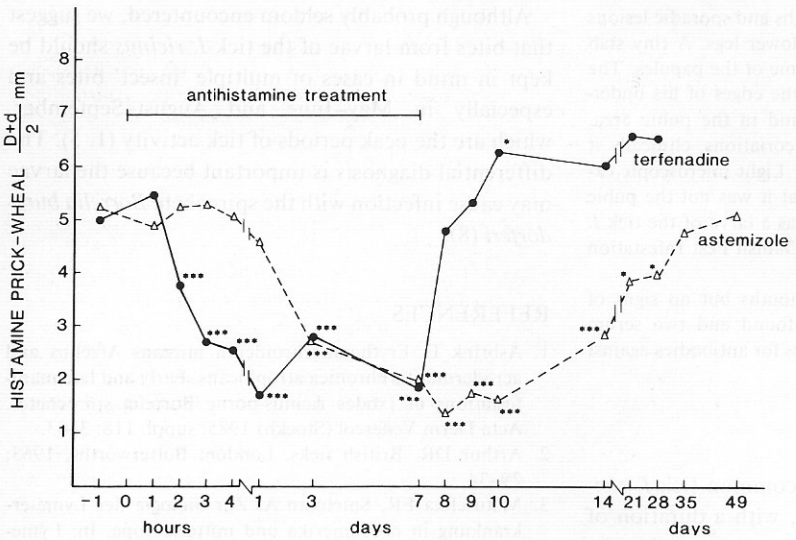

Fig. 1. Effect of peroral terfenadine (60 mg twice daily) and astemizole (10 mg once daily) on histamine-induced wheals in the prick test on the upper back in two groups of 15 healthy voluntary medical students. $*p<0.05$, $***p<0.001$.

In this study, the appearance and disappearance of the antihistamine effect of two non-sedating antihistamines, terfenadine and astemizole, were investigated using inhibition of the wheal in the histamine prick test as a marker for the antihistamine effect.

MATERIAL AND METHODS

The volunteer test subjects were healthy medical students. Terfenadine (Teldanex®, Draco, Lund, Sweden) 60 mg twice daily (in the morning and in the evening) was given to 15 subjects (8 females and 7 males, mean age 22.5 years) and astemizole (Hismanal®, Orion, Espoo, Finland, under licence from Jansen Pharmaceutica, Beerse, Belgium) 10 mg once daily (in the morning) also to 15 subjects (9 females and 6 males, mean age 23.5 years). Both drugs were given perorally for 7 days, and no dietary restrictions concerning the daily meals were given. The first dose of the drug was given in the test laboratory between 10.00 a.m. and noon.

Histamine dihydrochloride (Sigma Chemical Co., St. Louis, Mo, USA; 10 mg/ml in physiol. NaCl) was used in the skin prick tests performed on the upper back. The size of the wheal was measured 15 min later, and expressed as the mean of the maximum diameter and the maximum diameter perpendicular to it. Each test site was used only once.

The histamine prick test was performed before and 1, 2, 3 and 4 h after the first antihistamine dose; 1, 3 and 7 days after beginning of the antihistamine treatment and; 1, 2, 3, 7, 14, 21 (last test in the terfenadine group), 28 and 42 days after stopping the treatment, at the same time each day.

Statistical analysis of the resluts was performed using the *t*-test for paired observations.

RESULTS

A significant decrease in the size of the histamine wheal was noticed 2 h after the first terfenadine dose (Fig. 1). The level of antihistamine effect reached within 3 h did not alter significantly during the 7-day treatment period. One day after the last dose, the antihistamine effect of terfenadine had disappeared and after 3 days, a slight increase ($p<0.05$) in the wheal size was noted.

Astemizole caused a significant decrease in the histamine wheal size within 3 days after the first dose (Fig. 1). The maximum effect was reached 1 day after stopping medication ($p<0.01$ compared wheal size on 7th day). The antihistamine effect had disappeared 4 veeks after the last astemizole dose.

DISCUSSION

The use of the histamine skin test as an indicator for antihistamine effect is a safe and reproducible method (1, 2, 3). In previous studies, it has been demonstrated that the maximum effect of terfenadine of the histamine-induced wheal is reached 4 h after a single 60 mg dose (4, 5), a result that agrees with the present results. Contrary to an earlier report where the suppressive effect of terfenadine was significantly greater than that of astemizole on the 7th day of treatment (3), no such difference between these two drugs were recorded in this study.

The serum half-life values for the two antihistamines tested are different: for terfenadine it is 3–4 h (6) and for astemizole, 2 weeks (7). The tissue binding of astemizole in the guinea pig is 4–6 days (8). These pharmacokinetic differences are the most probable explanations for the differences between terfenadine

and astemizole in the appearance and disappearance of the antihistamine effect.

According to the results of this study, a reasonable period to wait after stopping the treatment before performing skin tests for immediate-type allergy would be 1–2 days for terfenadine and at least 4 weeks for astemizole.

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