

Occupational airborne contact dermatitis caused by thyme dust

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The aim of the study was to assess occupational hazards to the farmer's skin associated with processing thyme (*Thymus vulgaris* L.). 46 farmers were studied during the threshing of dried thyme. They were questioned about work-related skin problems and examined before and after work. In all persons, serum thyme-specific IgE was measured. Skin prick tests, the Ouchterlony test and the migration inhibition test were carried out with allergens of airborne bacteria and fungi present in the working environment. Of the 46 farmers studied, 4 showed skin symptoms after 5–30 min of exposure to thyme dust. Thyme-specific IgE was found in 1 person with work-related symptoms, but also in 2 asymptomatic farmers. Therefore, the importance of IgE seems to be questionable in eczema related to thyme dust. Skin and blood tests with microbial allergens also showed no significant differences between the symptomatic and asymptomatic farmers. To our knowledge, this is the 1st description of occupational airborne contact dermatitis caused by thyme dust. The etiology of thyme-related skin symptoms remains obscure, although an irritant mechanism seems probable.

Key words: thyme (*Thymus vulgaris* L.); farmers; work-related symptoms; occupational airborne contact dermatitis; organic dust; microflora; plants; agriculture. © Munksgaard, 2001.

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Thyme (*Thymus vulgaris* L.) is an aromatic, shrubby herb of the mint (Labiatae) family. The dried leaves and flowering tops of the plant are widely used as a culinary spice and in the production of cosmetics and drugs. Infusions and essential oils of thyme possess antiseptic, astringent, antispasmodic, expectorant, stimulant and carminative properties. In natural medicine, they are commonly used internally in the treatment of respiratory and digestive ailments and externally in the treatment of skin infections. The medical effects of thyme are attributed to its volatile oil composed mostly of phenols; its major and most active constituent is thymol, with lesser amounts of carvacrol, borneol, geraniol, linalol, thymol methyl ether and alpha-pinene. The other constituents of the thyme herb include flavonoids (apigenin, luteolin), polyphenolic acids (caffeic acid), triterpene acids (ursolic acid, rosmarinic acid), terpinene, tannins, saponins, etc. (1).

In recent years, many farmers in eastern Poland have specialized in producing thyme, as well as other medical plants, for the pharmaceutical industry. Before supplying the thyme to the industry, the farmers thresh the dried plant in order to obtain a coarse powder. This activity is carried out indoors and is associated with a high exposure to plant dust.

Our study was aimed at assessing the potential health hazards to skin from exposure to thyme dust. Besides the potential allergenic and/or irritant action of thyme, we have also considered in this study the possible adverse effects of epiphytic microorganisms present in thyme dust. In past decades, it has been documented that bacteria and fungi may occur abundantly in airborne organic dusts and cause allergic and/or immunotoxic diseases of the respiratory tract, skin and conjunctiva (2–4). In recent studies, large quantities of airborne bacteria, fungi and bacterial endotoxin were found during thyme threshing, within ranges of 10^4 – 10^5 colony forming units/m³ (CFU/m³), 10^3 – 10^4 CFU/m³, and 10^1 – 10^3 µg/m³, respectively (5, 6). Accordingly, in this study the patients were also examined for sensitivity to the dominant microbial antigens.

Materials and Methods

Study population

Farmers growing thyme (*Thymus vulgaris* L.) for the pharmaceutical industry were examined in a prospective study, carried out in 1998. All farms visited were located east of Lublin (eastern Po-

land). Because of the favourable climate, many farmers in this region specialize in growing hops and medicinal plants for local industry. A total of 46 farmers were examined (22 male and 24 female), aged 19–74 years, with duration of employment in agriculture ranging from 6 to 57 years.

On-site examinations

On the day of study, before the farmers started threshing the dried thyme plant, they were questioned using a special questionnaire for collecting epidemiological data focused on work-related skin symptoms described previously (7). Special attention was paid to past skin symptoms related to thyme dust exposure. The farmers also underwent dermatological assessment before and after threshing the dried thyme. All subjects were prick tested and blood samples were taken for laboratory tests. After completing the examinations, farmers were instructed to start their work and report to the research team in the case of skin symptoms appearing during work.

Determination of thyme-specific IgE levels

Thyme-specific IgE levels in sera of farmers were determined using UniCAP[®] System (Pharmacia & Upjohn Diagnostics AB, Sweden) with thyme allergen (Rf273), results being expressed in CAP classes 0–6.

Preparation of microbial antigens

All antigens were produced in our department from the strains of bacteria and fungi prevalent in the air during thyme threshing (5) and known to possess allergenic and immunotoxic properties (2, 3). Antigens for all the tests were prepared according to unified procedure as described earlier (8, 9) and used in different concentrations, depending on the test. In all tests lyophilised saline extracts of bacterial or fungal cell mass were used. In the case of mesophilic, non-branching bacteria these were harvested from nutrient agar cultures, while actinomycetes and fungi were harvested from sugar broth cultures. The mass was then homogenized and extracted in saline (0.85% NaCl) in the proportion 1:2 for 48 hrs at 4°C, with intermittent disruption of cells by 10-fold freezing and thawing. Afterwards, the supernatant was separated by centrifugation, dialyzed against distilled water for 24 h, concentrated by evaporation to 0.1–0.15 of previous volume and lyophilized.

Skin tests

The tests were carried out by prick method with the antigens of *Pantoea agglomerans* (synonyms: *Erwinia herbicola*, *Enterobacter agglomerans*), *Saccharopolyspora rectivirgula* (synonyms: *Microspolyspora faeni*, *Faenia rectivirgula*), *Streptomyces albus* and *Aspergillus fumigatus*. The antigens were dissolved in phosphate buffered saline (PBS, Biomed, Kraków) at a concentration of 5 mg/ml, sterilized by filtering and checked for sterility and lack of toxicity. The test was performed on the forearm with the antigenic extract and PBS as a control. The test sites were observed after 20 min. Wheal-and-erythema reactions of 3 mm or more in diameter were regarded as positive (9).

Test for inhibition of leukocyte migration (MIF) in the presence of specific antigen

The test was performed with the antigens of *Pantoea agglomerans*, *Arthrobacter globiformis*, *Saccharopolyspora rectivirgula*, and *Aspergillus fumigatus*, by the whole blood capillary microculture method according to Bowszyc et al. (10). Patient's blood and Parker's culture medium was added in volumes of 0.5 ml and 0.12 ml, respectively, to 2 silicon test tubes. Then, 0.12 ml of the antigen solution at the concentration of 25 µg/ml was added to 1 tube, while to the other 0.12 ml of the diluent (PBS) was added as a control. Both suspensions were incubated for 30 min at room temperature and thereafter distributed to heparinized glass capillaries 75×1 mm. Capillaries were sealed at both ends with a 4:1 mixture of liquid paraffin and petrolatum, centrifuged for 10 min at 1500 rev/min and fastened tangentially on microscopic slides with sticky tape at an angle of 10°. These microcultures were then incubated for 4 h at 37°C in a humid chamber. The leukocyte migration distances, visible as distinct white zones, were measured under the binocular microscope. The results were expressed as a migration index (MI), i.e., the ratio of the mean migration distance of leukocytes in microcultures with antigen, to the analogous distance in microcultures without antigen. The test was considered as positive at an MI equal to 0.790 or lower (8).

Agar-gel precipitation test

The test was performed with 12 bacterial and fungal allergens (*Acinetobacter calcoaceticus*, *Alcaligenes fecalis*, *Pantoea agglomerans*, *Arthrobacter globiformis*, *Bacillus subtilis*, *Saccharopolyspora rectivirgula*, *Thermoactinomyces vulgaris*, *Streptomyces albus*, *Alternaria alternata*, *Aspergillus can-*

didus, *Aspergillus fumigatus*, *Penicillium citrinum*) by Ouchterlony double diffusion method in purified 1.5% Difco agar. The undiluted serum separated from the blood sample of the examined subject was placed in the central well and antigens at a concentration of 30 mg/ml, in the peripheral wells. The plates were incubated for 6 days at room temperature, then washed in saline and in 5% sodium citrate solution (to prevent false-positive reactions), and stained with azocarmine B (8, 9, 11).

Results

Of the 46 farmers examined, 4 gave a history of previous skin symptoms related to threshing thyme; all were female, aged 25–54. They are presented in detail in Table 1. 3 of them also complained of a similar rash when performing other work associated with exposure to organic dust on the farm. None of the 4 subjects complained of

any skin problems not related to work. All the 4 persons were free from skin symptoms during the initial examination, and presented to the research team with rash within 5–30 min of starting work. In these patients pruritus, erythema and a slight swelling of uncovered skin (face, neck, hands) was found, typical of acute airborne contact dermatitis. Symptoms of rhinitis were found in 2, and of conjunctivitis in 1. Among the 4 farmers with thyme dust-related skin symptoms, thyme-specific IgE was found in 1, prick tests with airborne bacteria allergens were positive in 2 (in both cases with actinomycetal allergens), and precipitins against airborne bacteria and fungi were found in all 4. For technical reasons, leukocyte migration inhibition test was carried out in 3 of 4 symptomatic subjects, with positive results to *A. fumigatus* in 2 and to *S. rectivirgula* in 1 person (Table 1).

In the remaining 42 farmers without skin symptoms, thyme-specific IgE was found in 2; prick

Table 1. Results in patients with eczema provoked by thyme dust

Patient	Years of farm working	Health problems when previously exposed to thyme dust	Symptoms during work on day of examination	Other work-related skin symptoms	Positive skin prick tests	Thyme-specific IgE	Serum precipitins against:	MIF positive to:
F, 25 years	6	since 5 years rash and sneezing; for 1 preceding year no symptoms on exposure	after approx. 30 min erythema on face and neck, sparse papules, burning sensation, sneezing	rash of uncovered skin when exposed to dust of grain, flax, other herbal plants	<i>S. rectivirgula</i>	CAP class 0	<i>P. agglomerans</i> <i>A. fumigatus</i>	none
F, 33 years	10	since 10 years rash, lacrimation, sneezing, rhinorrhoea, dyspnea; the symptoms appeared immediately after starting thyme plantations	after approx. 5 min erythema on face and neck, moderate oedema, burning sensation	rash of uncovered skin when exposed to dust of grain, hay, flax, other herbal plants	none	CAP class 2	<i>P. agglomerans</i> <i>P. citrinum</i> <i>A. faecalis</i>	<i>S. rectivirgula</i> <i>A. fumigatus</i>
F, 52 years	38	since 5 years rash and burning, dyspnea; for approx. 15 preceding years no symptoms on exposure to thyme	after approx. 30 min erythema on face, neck, and décolleté, burning sensation, itching of conjunctivae and nose	not present	none	CAP class 0	<i>P. agglomerans</i> <i>A. calcoaceticus</i>	not tested
F, 54 years	40	since approx. 10 years rash and itching, dyspnea; for approx. 15 preceding years no symptoms on exposure to thyme	after 10–15 min erythema and oedema on mental and submandibular area, burning sensation	rash and dyspnea when exposed to melissa dust	<i>S. albus</i>	CAP class 0	<i>P. citrinum</i>	<i>A. fumigatus</i>

tests with allergens of airborne bacteria and fungi gave positive results to *Pantoea agglomerans*, *Saccharopolyspora rectivirgula*, *Streptomyces albus* and *Aspergillus fumigatus*, in 7, 3, 1 and 2 persons respectively. Precipitating antibodies against airborne bacteria and fungi *Acinetobacter calcoaceticus*, *Alcaligenes fecalis*, *Pantoea agglomerans*, *Arthrobacter globiformis*, *Bacillus subtilis*, *Saccharopolyspora rectivirgula*, *Thermoactinomyces vulgaris*, *Streptomyces albus*, *Alternaria alternata*, *Aspergillus candidus*, *Aspergillus fumigatus* and *Penicillium citrinum* were found, respectively, in 4, 13, 27, 1, 1, 1, 1, 2, 1, 0, 13 and 2 persons. For technical reasons, leukocyte migration inhibition test was completed in 32 of 42 asymptomatic subjects. In this group, inhibition of leukocyte migration induced by antigens of *Pantoea agglomerans*, *Arthrobacter globiformis*, *Saccharopolyspora rectivirgula* and *Aspergillus fumigatus* was found in 5, 8, 8, and 5 persons, respectively.

Discussion

Thyme-specific IgE has been found in patients with pollen allergy (12), although Type-I reactions after ingestion of thyme are uncommon (13). Oil of thyme is known as a rubefacient and has been reported to cause hyperemia and inflammation when used in bath preparations (14). Thymol, the main constituent of thyme oil, is capable of producing irritation of the skin and has been reported to cause dermatitis in dentists, and, when used in toothpaste may provoke cheilitis and glossitis (14). Le Roy et al. (15) found contact allergy to thyme oil in 5% of 100 patients with leg ulcers; the probable source of allergen were wound dressings containing thyme oil.

Until now, only scant attention has been paid to thyme as a potential occupational hazard. Lemiere et al. have described a butcher with occupational asthma caused by aromatic herbs (16), and demonstrated a significant reduction in FEV₁ and increased methacholine reactivity after a challenge with thyme powder. However, in this case, thyme-specific IgE could not be found in RAST. Mackiewicz et al. (6) described a case of allergic alveolitis in a female farmer exposed to thyme herb dust. The disease was characterized by typical symptoms, radiological changes in the lower parts of the lungs and the dominance of CD8+ lymphocytes in bronchoalveolar lavage (BAL) fluid. The authors concluded that some microbiological factors associated with thyme dust, particularly *Pantoea agglomerans*, may contribute to the adverse effects of the dust. To the best of our knowledge, no skin changes caused by occupational exposure to thyme herb dust have previously been described.

The short time of onset of the skin symptoms (5–30 min) in the 4 reactive persons in our study may suggest either a Type I allergy or an irritant reaction. We had the opportunity to test 1 of these persons (M. M.) in our allergy laboratory after the study. Prick test and patch test with the thyme extract (made of commercially available dried thyme herb) and patch test with thyme oil (purchased from a local pharmacy) were carried out. No reactions were observed in prick and patch tests with the extract, whereas the patch test with thyme oil gave a classical irritant reaction (on day 2 there was a moderate erythema sharply restricted to the contact area). A similar skin reaction was also found in 2 healthy controls. This observation seems to support an irritant mechanism, even though thyme-specific IgE (CAP class 2) was found in 1 person with rash after thyme dust exposure (patient P. B.). Thyme-specific IgE was also found, however, in 2 other farmers, 1 of whom (male, 35 years, CAP class 3) denied any skin symptoms at all, and the 2nd (female, 19 years, CAP class 1) complained of "sun allergy"; photodermatitis may sometimes be mistaken for airborne contact dermatitis, though this patient did not show any skin reaction while threshing thyme. All 3 patients denied any symptoms after ingesting thyme as a food additive or medicine in the past. Therefore, the importance of IgE seems to be questionable in eczema related to thyme dust. Also, skin and blood tests with microbial allergens did not show significant differences between the symptomatic and asymptomatic farmers. Nevertheless, it cannot be excluded that bacterial and fungal allergens, as well as bacterial endotoxin, may aggravate the effects of thyme herb constituents. To summarize, the etiology of thyme-related skin symptoms remains obscure, although in the opinion of the authors, they may suggest an airborne irritant contact dermatitis.

Only 1 of the patients described had sought medical help for her skin problems in the past, which suggests that awareness of the problems of occupational health in Polish farmers is unsatisfactory.

Conclusions

Thyme dust is capable of inducing occupational airborne contact dermatitis. As yet, no specific etiologic factor has been identified, though our observations suggest an irritant mechanism.

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