

Anogenital allergic contact dermatitis, the role of spices and flavour allergy

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Background: In patients with vulval or anogenital dermatitis, irritant contact dermatitis is more common than allergic contact dermatitis. The reported frequency and relevance of contact sensitivity in anogenital dermatitis varies greatly.

Objective: To determine the frequency and relevance of contact sensitization in a Dutch group of female patients with chronic anogenital complaints.

Methods: We reviewed patch test results of 53 women with chronic anogenital complaints, with sole vulval symptoms in 29 women and sole perianal in 5, in whom inflammatory skin diseases like lichen sclerosus, lichen planus, psoriasis, as well as infectious diseases were unlikely or excluded as a cause of their symptoms. All women were tested with the European baseline series plus additional test series according to their personal history.

Results: Thirty-five patients (66%) showed one or more positive test reactions. Seven of these patients (20%) had one or more clinically relevant positive reactions, most often to flavours and spices.

Conclusion: A considerable number of patients with anogenital dermatitis have a contact sensitization. Clinically relevant reactions were mainly found to spices and flavours. This is in contrast to the data reported in the literature that shows most contact allergies in vulval patients to ingredients of topical medication.

Key words: allergic contact dermatitis; anogenital dermatitis; flavours; spices; vulva. © Blackwell Munksgaard, 2008.

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As previously shown, allergens may play an important role in vulval or anogenital dermatitis (1–4). Vulval skin differs from other cutaneous epithelia in structure, morphology, and biophysical characteristics. The skin of the labia majora, for example, is more hydrated, more occluded, and more exposed to friction, which increases the susceptibility to irritants, as well as contact sensitizers (5). These features of the vulva may explain the high occurrence of contact sensitization in studies looking at patients with vulval dermatitis (5). However, allergic contact dermatitis may only be considered late in the patient's history leading to an unnecessary delay in making the diagnosis and adequate treatment advice (6).

The prevalence of contact sensitization in the anogenital area is unclear; previous studies indicate a high incidence of clinically relevant sensi-

zation to topical medication (2). About 20–30% of the women attending a vulval clinic in Oxford, UK, in 2000 suffered from vulval dermatitis, 26% of them had positive patch tests that were thought to be relevant with regard to their vulval dermatitis (3). Lewis et al. described that 49% of women with vulval pruritus had one or more relevant test reactions (4). Allergens that are commonly detected in previous studies include topical medication, preservatives, emollients, fragrances, and rubber products.

Our objective was to determine the frequency and relevance of contact sensitization in a Dutch group of female patients with chronic anogenital complaints in whom inflammatory skin diseases like lichen sclerosus, lichen planus, psoriasis as well as infectious diseases like a candida or herpes infection were unlikely or excluded as a cause of

their complaints. Furthermore, we wanted to evaluate the most frequently involved allergens to give a guide with regard to the kind of allergens that may be useful to test in a vulval disease clinic.

Subjects and Methods

Fifty-three women with a clinical diagnosis of chronic anogenital dermatitis were included in our study. The vulval region was involved in 48 women (91%) and the perianal region in 24 (45%) women, with sole vulval symptoms in 29 women and sole perianal in 5. They were retrospectively recruited from a departmental patch test register or included prospectively attending a vulval clinic. Patients with a distinct inflammatory or infectious skin disease like lichen sclerosus, lichen planus, psoriasis, a candida or herpes infection were excluded. A biopsy or culture to exclude or confirm a particular diagnosis was only performed if the clinical picture was indecisive. The women had a mean age of 35.3 years (range 16–64, median 32.5) at the onset of their symptoms. The mean duration of the anogenital complaints was 6.4 years (range 0.5–21, median 5) at the time the patients were included in the study in 2006. Twenty-seven of 53 patients (51%) had a personal history of an atopic background.

All patients have been patch tested between January 2002 and May 2006. Patch tests were performed on the upper part of the back with Van der Bend square chambers[®] on Fixomull stretch[®] (Beiersdorf, Hamburg, Germany). All patients were tested with the European baseline series and an additional routine series of 20 allergens. Patients were further tested, depending on their personal history, with fragrances, flavours, and spices, textile finishes and dyes, topical drugs, a series with glues and/or rubber additives, as well as their own products. To test the spices, we have used standardized patch test preparations of 30% spices in petrolatum. We have experience with those concentrations for many years and they are available in our departmental routine diagnostic programme (7). Tests were read and graded on D2, D3, and D6 or D7 according to the recommendations of the International Contact Dermatitis Research Group.

Results

Fifty-three patients underwent patch testing; the results are summarized in Table 1, 2, and 3. Thirty-five of the 53 patients tested (66%) had positive reactions; 17 of 53 patients (32%) had multiple positive reactions; 7 of 53 patients (13%) had clinically relevant positive test reactions.

Table 1. Summary of patch test results

Summary of patch test results	n (%)
Patients tested	53
Patients with positive reactions	35 (66.0)
Patients with one positive reaction	18 (34.0)
Patients with multiple positive reactions	17 (32.1)
Patients with relevant positive reactions	7 (13.2)
Patients with multiple relevant reactions	3 (5.7)
Total number of implicated allergens	34
Relevant implicated allergens	11 (32.4)

The most common allergen found to be positive was nickel [18/53 patients (34%)]. Probably none of our 53 patients had a clinically relevant nickel sensitization with regard to their vulval or anogenital complaints.

We found 17 positive patch test reactions to fragrance mix I and other fragrance markers in nine different patients (17%). These reactions were judged to be relevant in one patient. This patient had positive reactions to fragrance mix I, hydroxyisohexyl 3-cyclohexene carboxaldehyde,

Table 2. Number of positive and clinically relevant test reactions (patients *n* = 53)^a

Group	Allergens	P	R
Metals	Nickel sulfate 5%	18	
	Cobalt chloride 1%	3	
Fragrances	Fragrance mix I 8%	8	1
	Hydroxyisohexyl 3-cyclohexene carboxaldehyde 5%	2	1
	Jasmine absolute 2%	1	
	Narcissus absolute 2%	1	
	Lemon grass oil 2%	1	
	Evernia prunastri 2%	1	
	Lavender absolute 2%	1	
	Colophonium 20%	1	
	<i>Myroxylon pereirae</i> 25%	1	
	Curry mix (Djawa [®]) powder 30%	4	2
Spices	Pepper (white) powder 30%	3	
	Cayenne pepper powder 30%	2	
	Nutmeg powder 30%	2	1
	Coriander powder 30%	2	1
	Peppermint oil 2%	1	1
	Onion powder 30%	1	1
	Benzoic acid 5%	1	
	Methyldibromo glutaronitrile 0.3%	3	1
Preservatives	2-phenoxyethanol 1%	2	
	Sodium metabisulfite 5% aqua	1	
	Thimerosal 0.1%	1	
	Compositae mix 5%	2	
Plants	Primin 0.01%	1	1
	Sesquiterpene lactone mix 0.1%	1	
Dyes	Paraphenylene diamine 1%	2	
	Disperse blue 106 1%	1	
Rubber	Thiuram mix 1%	1	
Glues	<i>p</i> - <i>t</i> -butylphenolformaldehyde resin 1%	1	
Own products	Aluminium starch octenyl succinate 'as is'	1	
	Clearsun [®] day/night cream 'as is'	1	
	Sanex [®] bodymilk 'as is'	1	1

P, number of positive reactions; R, number of definitely or probably relevant positive reactions.

^aAll allergens were solved in petrolatum if not stated otherwise.

Table 3. Patients with clinically relevant positive patch test reactions^a

Relevant allergens	Relevancy
Fragrance mix I	Improvement of vulval dermatitis while avoiding perfumed products (I)
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	Improvement of vulval dermatitis while avoiding perfumed products (I)
Sanex [®] bodymilk	Improvement of vulval dermatitis while avoiding perfumed products (I)
Methyldibromo glutaronitrile	Avoidance of moist toilet paper containing methyldibromo glutaronitrile led to a marked improvement (II)
Primin	Patient works with primula; hand-vulva leads probably to vulval dermatitis (patient lost for follow-up) (III)
Peppermint oil	Avoidance of peppermint oil in herbal tea led to an improvement, provocation leads to symptoms within 2 days (IV)
Nutmeg powder	Avoidance of nutmeg leads to a considerable improvement (V)
Coriander powder	In one patient, a positive reaction to coriander and curry was found; avoidance gives a slight improvement (VI)
Curry mix (Djawa [®]) powder	In one patient, a positive reaction to onion and curry was found; avoidance of spices led to an improvement (VI)
Onion powder	In one patient, a positive reaction to onion and curry was found; avoidance of spices led to an improvement (VII)

^aPatients $n = 7$ (numbered I–VII).

Sanex[®] bodymilk, as well as to *p*-phenylene diamine. The sensitization to fragrance and related materials (hydroxyisohexyl 3-cyclohexene carboxaldehyde and Sanex[®] bodymilk) was clinically relevant for her vulval dermatitis (this patient had sole vulval symptoms). Avoiding perfumed products including her own perfumed Sanex[®] bodymilk led to a marked improvement of the vulval complaints. The reaction to *p*-phenylene diamine seemed to play no role with regard to her vulval dermatitis.

Positive reactions to flavours and spices were found in 15 of 53 patients (28%). Reactions to the five flavours or spices, such as peppermint oil, nutmeg, coriander, curry, and onion, were thought to be clinically relevant in four patients. One of these patients, with a positive reaction to peppermint oil, experienced a dramatical improvement of her anogenital dermatitis avoiding herbal tea containing peppermint oil (1). The other patients with positive reactions to various spices and flavours (Tables 2 and 3) noticed an improvement of the dermatitis when avoiding them. The degree of improvement ranged from mild to obvious.

Positive test reactions to preservatives were found in six patients. The reaction to methyldibromo glutaronitrile in one patient was clinically relevant. The patient used moist toilet paper containing methyldibromo glutaronitrile. Avoiding this toilet paper led to a marked improvement of the vulval dermatitis (this patient had sole vulval symptoms).

Patients' own products led to positive patch test reactions in five patients; only one of these patients had a clinically relevant reaction (Sanex[®] bodymilk), as described above.

Positive reactions to plants occurred in three patients of which the one to primin was judged to be relevant as she worked with primula; no

more details are available as she is lost for follow-up. Finally, we found a few reactions to rubber additives, glue, dyes, and some other allergens, which were not thought to be relevant with regard to the anogenital dermatitis (Table 2).

Discussion

Sixty-six per cent of our patients with vulval or anogenital dermatitis had one or more positive patch test reactions. This is in line with other reports of vulval dermatitis as summarized by Margesson et al.; positive test reactions varied between 39% and 78% (2). The prevalence of positive patch test reactions in patients with anogenital dermatitis is usually higher compared with the general female adult population (8). Dotterud et al. tested 1236 adults of a general population to 24 allergens (TRUE test[®]), 56% were women and 35% of them were sensitized to at least one allergen. Carlsen et al. determined the frequency of contact sensitivity in a population of 14 998 patients with eczema using the European baseline series. About 35% had at least one positive test reaction; 40% of the tested women had a positive reaction compared with 25% of the men (9). As the prevalence of contact sensitization in patients with anogenital dermatitis is comparable to or perhaps even higher than in patients with eczema at other sites, it seems important to perform patch tests early in the course of the disease.

However, not all positive test reactions will be clinically relevant with regard to the anogenital dermatitis. Thirty-five of 53 patients in our study (66%) had positive patch test reactions to 36 allergens; 20% (7 of 35) of those had definite or probable clinically relevant reactions. This percentage

is somewhat lower compared with previous studies (2–4). Thirty-four per cent of our patients were sensitized to nickel. This is in line with the prevalence found in a population of vulval patients reported by Lucke et al. (10), but is higher compared with most reports of the general female population, varying between 20% and 28% (8, 10–12, departmental data not published). Lucke et al. found a nickel sensitization in 31% of 55 women with vulval pruritus, burning, and pain (10). About 50% of the patients experienced improvement of their symptoms avoiding direct contact to nickel. One patient experienced an improvement only when she also followed a nickel-free diet. The investigators conclude that nickel is a more important allergen in vulval dermatitis than generally thought. We did not find any clinically relevant nickel sensitization in our patients; direct contact to nickel at the anogenital site could not be established ('hand–anogenital region contact'). However, we did not advise our patients to follow a nickel-free diet nor did we perform a nickel analysis of the urine. Menné et al. described four females with a chronic intermittent dyshidrotic eruption of the hands who were sensitive to nickel (13). There was an association between an increased excretion of nickel and the outbreak of vesicles. These results support the idea that the chronic condition was maintained by ingestion of nickel. Further studies are needed to evaluate if nickel ingestion plays a role in anogenital dermatitis.

Ten (28%) of our tested allergens (Table 3) seemed to be clinically relevant; those were mainly flavours and spices. Twenty per cent of our patients with positive patch tests had clinically probable or definite relevant sensitizations to fragrance mix, hydroxyisohexyl 3-cyclohexene carboxaldehyde, Sanex[®] bodymilk, methyl dibromoglutaronitrile, primin, peppermint oil, nutmeg, coriander, curry (Djawa[®]) or onion. However, the true rate of clinically relevant hypersensitivity in positive patch test reactions remains for a great part unknown. If a positive patch test reaction is found, an attempt should be made to connect it with the information obtained from the history and clinical examination (14). In one of the patients, we were able to demonstrate the relevance of sensitization to peppermint oil by performing a provocation after elimination of the suspected allergen (1). The allergen was probably excreted in the urine and/or the faeces, leading to an allergic contact dermatitis of the anogenital region. However, we cannot exclude that the anogenital localization of the dermatitis in our patients may be caused by a systemic contact dermatitis.

Positive reactions to fragrances and *Myroxylon pereirae* are often thought to be clinically relevant in patients with genital dermatitis (15–18). How-

ever, Bauer et al. found no higher sensitization rate to fragrances in patients with genital complaints compared with a control group (19). We found a respectable amount of sensitizations to fragrances (17%) that is high compared with other studies investigating the prevalence of fragrance allergies in the general adult population and in other eczema populations (8, 9, 20, 21).

However, the relevance of this sensitization for vulval or anogenital complaints in our study group was only demonstrated in one patient (Table 3). Nevertheless, we think that fragrances are important to be tested in patients with anogenital dermatitis. According to our results, spices and flavours play an important role in allergic contact dermatitis of the vulva. We suggest testing patients with an anogenital dermatitis with the European baseline series and additional series containing spices and flavours. The fragrance mix, *Myroxylon pereirae* and colophony are regarded as markers for spices (22). One should, however, keep in mind that an absent reaction to a spice marker does not rule out sensitivity to spices and flavours.

Previous studies report topical medicaments like local anaesthetics, antibiotics, corticosteroids, and preservatives in topicals to be the most important sensitizers in the genital area (2, 16–19). Kügler et al. compared patch test results in patients with anogenital dermatoses with a general patch test population, the latter standardized for age and sex using data of the Information Network of Departments of Dermatology (IVDK) (23). They found a significantly higher frequency of sensitization to the local anaesthetics cinchocaine, and benzocaine, and bupivacaine. They recommend to patch test patients with anogenital dermatoses with the baseline series plus major sensitizers like local anaesthetics and patients' own products. In contrast, in our group of patients, we did not find any contact sensitization to topical drugs.

An explanation for this discrepancy may be that there are differences in exposure to topical medications in different countries. In the Netherlands, there has been a great reduction of over-the-counter products containing benzocaine and related anaesthetics during the past years because of the high frequency of contact allergies caused by topical anaesthetics. Nevertheless, creams containing benzocaine to treat for example haemorrhoids are still available over the counter, but the overall exposure to these products is probably low.

Furthermore, the use of different patch test series might also explain the different results. We tested with flavours and spices, while in previous studies, patch tests with flavours and spice series

are not explicitly mentioned to be performed (3, 10, 17–19, 23). Many different spices are used in the Netherlands because of a mixed population of various ethnic groups that like to eat spicy food.

Finally, most patch test studies of patients with vulval diseases included patients with various diseases like lichen sclerosus, lichen planus, psoriasis, vestibulitis, and vulvodynia (4, 10, 17–19). This may also explain the difference in the detected allergens, with a higher frequency of contact allergies to topical drugs.

We conclude that in patients with chronic vulval or anogenital dermatitis, the possibility of an allergic contact dermatitis should be considered early in the course of the disease, especially in patients that do not respond well to treatment. We want to stress that it is important to take a detailed history in patients with anogenital dermatitis to discover relevant allergens. We recommend to initially perform patch tests with the European baseline series, additional series with spices and flavours and the patients' own products. It should be kept in mind that not only locally applied products may lead to a contact dermatitis (product–anogenital region contact and hand–anogenital region contact) but also orally administered products may cause the disease after excretion through the urine and/or the faeces.

References

- Vermaat H, van Meurs T, Rustemeyer T, Bruynzeel D P, Kirtschig G. Vulval allergic contact dermatitis due to peppermint oil in herbal tea. *Contact Dermatitis* 2008; 57: 1–2.
- Margesson L J. Contact dermatitis of the vulva. *Dermatologic Therapy* 2004; 17: 20–27.
- Crone A M, Stewart E J, Wojnarowska F, Powell S M. Aetiological factors in vulvar dermatitis. *Eur Acad Dermatol Venereol* 2000; 14: 181–186.
- Lewis F M, Shah M, Gawkrödger D J. Contact sensitivity in pruritus vulvae: patch test results and clinical outcome. *Am J Contact Dermat* 1997; 8: 137–140.
- Farage M F. Vulvar susceptibility to contact irritants and allergens: a review. *Arch Gynecol Obstet* 2005; 272: 167–172.
- Salim A, Powell S, Wojnarowska F. Allergic contact dermatitis of the vulva—an overlooked diagnosis. *J Obstet Gynaecol* 2002; 22: 447.
- Bruynzeel D P, Prevoo R L. Patch tests with some spices. *Dermatol Clin* 1990; 8: 85–87.
- Dotterud L K, Smith-Sivertsen T. Allergic contact sensitization in the general adult population: a population-based study from Northern Norway. *Contact Dermatitis* 2007; 56: 10–15.
- Carlsen B C, Menné T, Johansen J D. 20 Years of standard patch testing in an eczema population with focus on patients with multiple contact allergies. *Contact Dermatitis* 2007; 57: 76–83.
- Lucke T W, Fleming C J, McHenry P, Lever R. Patch testing in vulval dermatoses: how relevant is nickel? *Contact Dermatitis* 1998; 38: 111–112.
- Schnuch A, Uter W, Geier J, Gefeller O; IVDK study group. Epidemiology of contact allergy: an estimation of morbidity employing the clinical epidemiology and drug-utilization research (CE-DUR) approach. *Contact Dermatitis* 2002; 47: 32–99.
- Schäfer T, Böhler E, Ruhdorfer S, Weigl L, Wessner D, Filipiak B, Wichmann H E, Ring J. Epidemiology of contact allergy in adults. *Allergy* 2001; 56: 1192–1196.
- Menné T, Thorboe A. Nickel dermatitis–nickel excretion. *Contact Dermatitis* 1976; 2: 353–354.
- Bruze M. What is a relevant contact allergy? *Contact Dermatitis* 1990; 23: 224–225.
- Marren P, Wojnarowska F, Powell S. Allergic contact dermatitis and vulvar dermatoses. *Br J Dermatol* 1992; 126: 52–56.
- Lewis F M, Harrington C I, Gawkrödger D J. Contact sensitivity in pruritus vulvae: a common and manageable problem. *Contact Dermatitis* 1994; 31: 264–265.
- Brenan J A, Dennerstein G J, Sfameni S F, Drinkwater P, Marin G, Scurry J P. Evaluation of patch testing in patients with chronic vulvar symptoms. *Australas J Dermatol* 1996; 37: 40–43.
- Goldsmith P C, Rycroft R J, White I R, Ridley C M, Neill S M, McFadden J P. Contact sensitivity in women with anogenital dermatoses. *Contact Dermatitis* 1997; 36: 174–175.
- Bauer A, Geier J, Elsner P. Allergic dermatitis in patients with anogenital complaints. *J Reprod Med* 2000; 45: 649–654.
- Schnuch A, Lessmann H, Geier J, Frosch P J, Uter W, IVDK. Contact allergy to fragrances: frequencies of sensitization from 1996 to 2002. Results of the IVDK*. *Contact Dermatitis* 2004; 50: 65–76.
- Bruynzeel D P, Diepgen T L, Andersen K E et al. Monitoring the European baseline series in 10 centres 1996–2000. *Contact Dermatitis* 2005; 53: 146–149.
- van den Akker T W, Roesyanto-Mahadi I D, van Toorenenbergen A W, van Joost T. Contact allergy to spices. *Contact Dermatitis* 1990; 22: 267–272.
- Kügler K, Brinkmeier T, Frosch P J, Uter W. Anogenital dermatoses–allergic and irritative causative factors. Analysis of IVDK data and review of the literature. *J Dtsch Dermatol Ges* 2005; 3: 979–986.

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