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Vulval allergic contact dermatitis: Medicaments are a common cause

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Running Title: Vulval allergic contact dermatitis

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Article type : Research Letter

Title: Vulval allergic contact dermatitis: medicaments are a common cause

When patch tested, women with vulval dermatoses and/or symptoms have been found to have a high prevalence of both contact allergy (38-81%) and vulval allergic contact dermatitis (ACD) (16– 58%) (1-7).

Indeed, vulval ACD often arises as a secondary condition caused by treatments for vulval symptoms (3, 6, 7). Its diagnosis can therefore be challenging. However, it is important to identify allergens, in order to ensure that treatments (prescribed or otherwise) are not causing further harm.

The aim of this study was to determine which allergens were most responsible for vulval ACD in our tertiary referral centre in Melbourne.

We conducted a retrospective analysis of patch test data from 2004 – 2017. We included all women with a history suspicious for vulval ACD, who had at least one positive patch test result.

The study was deemed to be a low-risk retrospective analysis of our database, and was reviewed in-house by the XXX (now XXX) Quality Assurance Committee.

Patients were patch tested to an extended European baseline series until 2012. From 2012, the Australian Baseline Series was tested (8). Additional series and/or allergens were selected according to exposure history. Readings were performed on days 2 and 4 according to the International Contact Dermatitis Research Group guidelines. Relevance was based on

a positive patch test reaction to an allergen ($\geq 1+$), a compatible clinical history of contact dermatitis, and exposure to the allergen.

Forty-one women were referred to the patch-testing clinic with vulval rashes over the 13-year study period. Three of the 41 were excluded from our study, because there was insufficient information in their records to confirm whether their positive patch test reactions were relevant. Of the remaining 38 women, 18 (47.4%) had at least one positive patch test result, and 8 (21.1%) had at least one relevant positive patch test result. They shared a total of 50 positive and 11 relevant positive patch test results (Table 1).

These 18 women were aged 20 – 68 years (median 51). Five (27.8%) were atopic. Pre-existing anogenital conditions were common. These included lichen planus (5 cases), lichen sclerosus (LS) (2 cases, one of whom also had haemorrhoids), vulvovaginal candidiasis (1 case), anal fissure (1 case), and pressure urticaria (1 case). The remaining 8 women had no other dermatoses, other than the dermatitis being investigated.

Nickel sulfate was the most common positive allergen, with 5 positive patch test results. However, it was only deemed to be relevant in one case, which related to a vulval piercing.

The 11 allergens assessed as being relevant are listed in Table 1. Each was assessed as being relevant once.

The most common causes of ACD were medicaments, including the treatments used for patients' pre-existing anogenital conditions. One woman with LS had a relevant positive reaction to her Diprosone OV[®] cream, although the exact allergen was unclear. Another woman with haemorrhoids had a relevant positive reaction to tixocortol-21-pivalate, a marker for hydrocortisone allergy, which was present in her Xyloproct[®] ointment. One woman with an anal fissure had relevant positive tests to multiple local anaesthetics including cinchocaine, and her Proctosedyl[®] ointment which contained cinchocaine. Yet another woman, with vulvovaginal candidiasis which she treated with Daktarin[®] cream, was found to have a positive relevant reaction to miconazole.

The finding that medicaments are among the most common causes of vulval ACD is consistent with numerous other studies (1-7, 9). However, in contrast to previous studies (1-4, 9), we did not find fragrances and preservatives to be common causes of vulval ACD, with only once case of fragrance causing ACD. Three cases were excluded, where it was unclear how their fragrance or preservative reaction was relevant.

The limitations of this study include its small sample size, retrospective design, long study period dating back to 2004 and incomplete data in three cases.

In conclusion, we have found that vulval ACD is not uncommon among women presenting for patch testing with vulval dermatoses, and can arise as a secondary phenomenon following topical treatments containing culprit allergens. It is important to be aware that medicaments can aggravate pre-existing conditions. Timely patch testing can be helpful, so that these women and their clinicians can confidently choose treatments while avoiding allergens.

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Table 1: List of allergens causing relevant reactions

Allergen	Number of positive reactions*	Number of relevant reactions*	Category (medication, preservative, fragrance, etc.)	Allergen source
Tixocortal-21-pivalate	2	1	Medication (corticosteroid)	Xyloproct® ointment
Nickel sulfate	5	1	Metal	Piercing
Lanolin alcohol (wool alcohol)	2	1	Emollient/emulsifier	Cleanser (applied to groin area)
Amerchol L 101	2	1	Emollient/emulsifier	Cleanser (applied to groin area)
Betadine® antiseptic	1	1	Medication (antiseptic)	Betadine® antiseptic
Betamethasone dipropionate	1	1	Medication (corticosteroid)	Diprosone OV cream®
Cinchocaine	1	1	Medication (local anaesthetic)	Proctosedyl® ointment
Lignocaine	1	1	Medication (local anaesthetic)	Lignocaine and nifedipine cream
Lyrall	1	1	Fragrance	Fragranced body wash
Miconazole	1	1	Medication (antifungal)	Daktarin® cream

Toluene sulfonamide formaldehyde resin	1	1	Resin	Nail polish
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*Patients could have multiple positive reactions and multiple relevant reactions; therefore, the total number of reactions exceeds the number of patients.