

Allergic Contact Dermatitis of the Vulva

Susan M. O’Gorman, MB, BCh* and Rochelle R. Torgerson, MD, PhD†

Background and Objectives: Allergic contact dermatitis (ACD) of the vulva arises as a primary condition or develops secondary to topical agents. We aimed to describe the incidence of ACD in patients presenting with vulvar symptoms and to identify the allergens of most importance.

Patients and Methods: Using a database of the patch testing results from 3 geographically distinct sites, we identified patients tested to a gynecologic series between 2003 and 2010. Patients had patch testing to the standard European battery and a gynecologic series. Patch testing was in line with accepted universal methods: application on day 1, allergen removal and initial reading on day 3, and final reading on day 5.

Results: Ninety patients were included. Thirty-five (39%) had a relevant positive result. The 5 allergens with the highest number of cases with a relevant reaction were natural fragrance mix 2%, balsam of Peru, benzocaine 5%, fragrance mix 8%, and quaternium 15 1%. The most common gynecologic series allergen to cause a relevant reaction was terconazole.

Conclusions: Allergic contact dermatitis is a frequent finding in patients presenting with vulvar symptoms. We identified a relevant positive result to patch testing in 39%. We found fragrances, medicaments, and preservatives to be of most relevance.

Troubling vulvar symptoms, such as pruritus, may signal an allergic contact dermatitis (ACD). This can affect the vulva as a primary condition or can occur in the presence of a preexisting vulvar dermatosis. This condition was first described in 1990 by Doherty et al¹ but since then has been widely reported, its incidence in the literature varying from 16% to 44% in patients who undergo patch testing for vulvar symptoms.^{2,3} The vulva presents a unique field of contact allergy,^{4,5} with an epithelium that differs from the skin.⁶ Its exposures differ from elsewhere on the body, as does the environment, with increased heat and occlusion. Exposures unique to the vulva include sanitary napkins, tampons, and over-the-counter preparations for vulvar pruritus. Before women seek dermatologic advice for their vulvar symptoms, most have tried numerous topical preparations, which in some cases exacerbate the initial symptoms.

Given these unique features of ACD affecting the vulva, it is not surprising that numerous studies have found that many relevant allergens have been identified outside the standard European series, thus supporting extended patch testing in these patients.²

Studies have identified a higher incidence of ACD in certain subgroups of patients presenting with vulvar symptoms, such as those using multiple topical treatments and those with severe pruritus.² Conversely, a lower rate of ACD has been identified in patients with a baseline diagnosis of vulvodynia.⁷ These are interesting findings, suggesting a predictably higher yield from patch testing in certain subgroups.

In the current study, we aimed to determine the incidence of ACD in patients presenting to our institute with vulvar symptoms over an 8-year period. We aimed to identify which allergens are most important. We also aimed to determine the relevance of previously reported associations between ACD and patient demographics, such as baseline dermatologic conditions, atopy, and the number of previously used topical agents. A further aim of our study was to determine the association between the presenting symptom and rate of relevant patch test results.

PATIENTS AND METHODS

This study was approved by the institutional review board. A database of the patch testing service at our center was used to identify all patients who were patch tested to the gynecologic series in addition to the standard series between 2003 and 2010. Not all allergens in each series were used in all cases, and this decision was at the discretion of the treating dermatologist. All patients who had not consented to research participation were excluded. Patients were also excluded if they did not have predominant vulvar symptoms or if they were followed up elsewhere for interpretation of patch test results. Baseline demographic data, the allergens to which each patient was tested, and the results of

From the Departments of *Internal Medicine and †Dermatology, Mayo Clinic, Rochester, MN.

Address reprint requests to Rochelle R. Torgerson, MD, PhD, Department of Dermatology, Mayo Clinic, 200 First St SW, Rochester, MN 55905. E-mail: torgerson.rochelle@mayo.edu.

The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0b013e318284da33

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TABLE 1. Patient Demographic Characteristics

Characteristic	Total Patients (n = 90)
Ethnicity, n (%)	
White	82 (91)
Black	2 (2)
Other/unknown	6 (7)
Age at application, mean (SD), y	52.2 (18.2)
Duration of symptoms, median (IQR), mo	30 (12–84)

the patch testing were extracted from the database. The staff at our biostatistics department undertook database extraction and analysis.

Additional data on patients' presenting symptoms, duration of symptoms, previous topical treatments, baseline dermatoses affecting the vulva, visible changes affecting the vulva at baseline, and history of atopy were gathered from the electronic medical record.

TABLE 2. Standard Series (Results by Allergen)

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
7	Hexahydro-1,3,5- <i>tris</i> (2-hydroxyethyl)triazine 1%	90	0 (0)	0 (0)
9	1H Benzotriazole 1%	11	0 (0)	0 (0)
11	2-Bromo-2-nitropropane-1,3-diol 0.25%	60	1 (2)	0 (0)
68	2- <i>tert</i> -Butyl-4-methoxyphenol (BHA) 2%	11	0 (0)	0 (0)
70	2,6-di- <i>tert</i> -Butyl-4-cresol (BHT) 2%	89	0 (0)	0 (0)
74	Bacitracin 20%	90	1 (1)	0 (0)
76	Balsam of Peru 25%	90	8 (9)	5 (6)
83	Benzalkonium chloride 0.1% aqueous	87	3 (3)	1 (1)
85	Benzocaine 5%	59	7 (12)	5 (8)
86	Benzoic acid 5%	90	3 (3)	0 (0)
91	2-Hydroxy-4-methoxybenzophenone 10%	2	0 (0)	0 (0)
120	Black rubber mix 0.6%	90	0 (0)	0 (0)
125	Budesonide 0.1%	61	0 (0)	0 (0)
150	Carba mix 3%	90	1 (1)	1 (1)
182	Cinnamic aldehyde 1%	70	0 (0)	0 (0)
187	Cobalt chloride 1%	90	8 (9)	1 (1)
189	Cocamidopropyl betaine 1% aqueous	77	1 (1)	1 (1)
191	Coconut diethanolamide (cocamide DEA) 0.5%	59	0 (0)	0 (0)
192	Colophony 20%	89	0 (0)	0 (0)
197	DMDM hydantoin 1%	89	0 (0)	0 (0)
210	Diazolidinyl urea 1% aqueous	90	0 (0)	0 (0)
222	Dimethylol dihydroxyethylene urea 4.5% aqueous	58	0 (0)	0 (0)
232	Disperse blue no. 106 1%	90	3 (3)	3 (3)
233	Disperse blue no. 124 1%	90	3 (3)	3 (3)
241	Disperse orange no. 3 1%	90	3 (3)	2 (2)
261	Epoxy resin 1%	90	0 (0)	0 (0)
264	Ethyl acrylate 0.1%	90	1 (1)	0 (0)
268	Ethylenediamine dihydrochloride 1%	90	3 (3)	2 (2)
270	Ethyleneurea-malamin formaldehyde mix 5%	90	0 (0)	0 (0)
281	Formaldehyde 1% aqueous	90	3 (3)	2 (2)
282	Fragrance mix 8%	90	8 (9)	4 (4)
292	Glutaraldehyde 0.2%	90	0 (0)	0 (0)
295	Glyceryl thioglycolate 1%	90	1 (1)	1 (1)
302	Gold sodium thiosulfate 0.5%	89	19 (21)	3 (3)
310	Hexachlorophene 1%	31	0 (0)	0 (0)
314	Hexylresorcinol 0.25%	90	1 (1)	0 (0)
319	Hydrocortisone 17-butyrate 1% alcohol	89	0 (0)	0 (0)
329	Imidazolidinyl urea 2%	90	0 (0)	0 (0)
330	Imidazolidinyl urea 2% aqueous	90	1 (1)	1 (1)
333	Isopropyl myristate 20%	90	0 (0)	0 (0)
353	MCI/MI 100 ppm	11	0 (0)	0 (0)
354	MCI/MI 100 ppm aqueous	90	5 (6)	3 (3)

TABLE 2. (Continued)

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
355	Methyldibromo glutaronitrile/phenoxyethanol 1.5%	90	4 (4)	3 (3)
364	Mercapto mix 1%	90	0 (0)	0 (0)
373	Methyl methacrylate 2%	90	0 (0)	0 (0)
381	Mixed dialkyl thioureas 1%	90	0 (0)	0 (0)
411	Neomycin sulfate 20%	90	3 (3)	2 (2)
415	Nickel sulfate hexahydrate 2.5%	90	9 (10)	2 (2)
437	<i>p</i> -Phenylenediamine 1%	89	4 (4)	1 (1)
439	4- <i>tert</i> -Butylphenol formaldehyde resin 1%	90	2 (2)	1 (1)
449	Paraben mix 16%	90	2 (2)	1 (1)
462	Phenoxyethanol 1%	11	0 (0)	0 (0)
477	Potassium dichromate 0.25%	90	1 (1)	0 (0)
497	Quaternium 15 1%	90	6 (7)	4 (4)
518	Sesquiterpene lactone mix 0.1%	90	0 (0)	0 (0)
526	Sorbic acid 2%	59	0 (0)	0 (0)
532	Stearyl alcohol 30%	90	0 (0)	0 (0)
582	Thiuram mix 1%	90	0 (0)	0 (0)
590	Tixocortol-21-pivalate 1%	90	1 (1)	1 (1)
594	Toluenesulfonamide formaldehyde resin 10%	90	1 (1)	1 (1)
597	Triamcinolone acetonide 1%	90	0 (0)	0 (0)
604	Triclosan 2%	90	0 (0)	0 (0)
608	Triethanolamine 2%	90	0 (0)	0 (0)
681	Mercaptobenzothiazole 1%	90	0 (0)	0 (0)
682	Wool alcohols (lanolin alcohol) 30%	89	0 (0)	0 (0)
684	Diazolidinyl urea 1%	90	0 (0)	0 (0)
686	Propylene glycol 10%	74	1 (1)	1 (1)
687	Chloroxylenol (PCMX) 1%	90	0 (0)	0 (0)
688	DMDM hydantoin 1% aqueous	31	2 (6)	2 (6)
691	Phenol formaldehyde resin 1%	90	0 (0)	0 (0)
692	Clioquinol 5%	11	0 (0)	0 (0)
693	Cetyl alcohol 5%	90	0 (0)	0 (0)
695	Chlorquinaldol 5%	11	0 (0)	0 (0)
701	Tocopherol (vitamin E) 10%	31	0 (0)	0 (0)
722	2-Hydroxy-4-methoxybenzophenone 3%	87	0 (0)	0 (0)
740	Clobetasol-17-propionate 1%	59	0 (0)	0 (0)
754	Dermatophagoides mix 0.1%	11	0 (0)	0 (0)
757	Iodopropynl butylcarbamate 0.1%	20	0 (0)	0 (0)
794	Lidocaine 5%	89	0 (0)	0 (0)
804	Gold sodium thiosulfate 0.25% in petrolatum	43	4 (9)	1 (2)
805	(+/-)- α -Tocopherol 100% (vitamin E)	56	0 (0)	0 (0)
806	Compositae mix 5%	55	1 (2)	0 (0)
807	DMDM hydantoin 2% in petrolatum	1	0 (0)	0 (0)
808	DMDM hydantoin 2% in aqueous	59	0 (0)	0 (0)
924	Fragrance mix II	40	1 (2)	1 (2)
933	2-Bromo-2-nitropropane-1,3-diol 0.5%	30	1 (3)	0 (0)
936	Budesonide 0.01%	29	0 (0)	0 (0)
2045	Natural fragrance mix 2%	74	7 (9)	6 (8)
2050	Caine mix III	31	0 (0)	0 (0)
2058	Amidoamine 0.1% aqueous	74	0 (0)	0 (0)
100028	Propylene glycol 20% in water	16	0 (0)	0 (0)
100050	Gold sodium thiosulfate 2%	16	6 (38)	2 (12)

DEA indicates diethanolamide; DMDM, Dimethylol-5,5-dimethyl hydantoin 1,3; MCI/MI, methylisothiazolinone + methylchlorisothiazolinone; PCMX, parachlorometacresol.

TABLE 3. Gynecologic Series (Results by Allergen)

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
68	2-tert-Butyl-4-methoxyphenol (BHA) 2%	90	0 (0)	0 (0)
86	Benzoic acid 5%	90	3 (3)	0 (0)
105	Benzyl alcohol 1%	90	0 (0)	0 (0)
273	Eucalyptus oil 2%	90	0 (0)	0 (0)
314	Hexylresorcinol 0.25%	90	1 (1)	0 (0)
333	Isopropyl myristate 20%	90	0 (0)	0 (0)
375	Methyl salicylate 2%	89	0 (0)	0 (0)
449	Paraben mix 16%	90	2 (2)	1 (1)
464	Phenylmercuric acetate 0.01% aqueous	90	0 (0)	0 (0)
526	Sorbic acid 2%	90	0 (0)	0 (0)
527	Sorbitan monooleate (Span 80) 5%	90	0 (0)	0 (0)
532	Stearyl alcohol 30%	90	0 (0)	0 (0)
674	Quinine sulfate 1%	16	0 (0)	0 (0)
686	Propylene glycol 10%	74	1 (1)	1 (1)
692	Clioquinol 5%	90	0 (0)	0 (0)
693	Cetyl alcohol 5%	90	0 (0)	0 (0)
721	Petrolatum 100%	90	0 (0)	0 (0)
775	Estradiol 1%	74	0 (0)	0 (0)
776	Progesterone 4%	73	0 (0)	0 (0)
778	Testosterone 0.4%	73	0 (0)	0 (0)
779	Clindamycin phosphate 2%	73	1 (1)	1 (1)
780	Metronidazole 0.75%	73	0 (0)	0 (0)
781	Clotrimazole 1%	74	1 (1)	1 (1)
782	Miconazole 1% alcohol	89	1 (1)	0 (0)
783	Terconazole as is	56	4 (7)	4 (7)
784	Tioconazole as is	73	1 (1)	1 (1)
785	Butoconazole nitrate as is	58	0 (0)	0 (0)
786	Conjugate estrogen 0.625 mg/g	74	1 (1)	1 (1)
788	Replens as is	89	1 (1)	0 (0)
789	Nonoxyl-9 0.5% aqueous	74	0 (0)	0 (0)
790	Polysorbate 60 (Tween 60) 10%	73	0 (0)	0 (0)
791	Sodium lauryl sulfate 0.1% aqueous	74	1 (1)	1 (1)
792	Glycerin (glycerol) 1% aqueous	74	0 (0)	0 (0)
793	Quinine hydrochloride 1% aqueous	74	0 (0)	0 (0)
931	Terconazole 3 cream 0.8%	34	3 (9)	2 (6)
100010	Metronidazole 1%	16	0 (0)	0 (0)
100019	Butoconazole nitrate 3 as is	3	0 (0)	0 (0)
100020	Nystatin 2%	20	0 (0)	0 (0)
100021	Ketoconazole cream 2% as is	20	0 (0)	0 (0)
100023	Clotrimazole 5%	16	0 (0)	0 (0)
100024	Tween 80 10%	16	0 (0)	0 (0)
100028	Propylene glycol 20% in water	16	0 (0)	0 (0)
100029	Clindamycin phosphate 10%	16	0 (0)	0 (0)
100037	Sodium lauryl sulfate 0.5%	16	0 (0)	0 (0)
100038	Tioconazole 1%	16	0 (0)	0 (0)
100044	Conjugate estrogen cream 0.625 mg/g as is	16	0 (0)	0 (0)

For patch testing, we used aluminum chambers on porous surgical paper tape (Finn chambers on Scanpor, Smart Practice, Phoenix, AZ). Patch testing was conducted in line with accepted universal methods, with patients presenting for application on day 1. On day 3, allergens were removed, and an initial reading was undertaken.

On day 5, patients returned for a final reading and interpretation. Reactions were graded from 0 to 4 (++++). Reactions of grade 2 (++), 3 (+++), and 4 (++++), were considered positive. Grade 1 (+) reactions were only considered positive if the treating dermatologist considered them relevant to the patient's vulval symptoms.

TABLE 4. Reactions to Metal Allergens*

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
187	Cobalt chloride 1%	90	8 (9)	1 (1)
302	Gold sodium thiosulfate 0.5%	89	19 (21)	3 (3)
415	Nickel sulfate hexahydrate 2.5%	90	9 (10)	2 (2)
804	Gold sodium thiosulfate 0.25% in petrolatum	43	4 (9)	1 (2)
100050	Gold sodium thiosulfate 2%	16	6 (38)	2 (12)

*All metal allergens were from the standard series.

Distributions between groups were compared using the Wilcoxon rank sum test for continuous variables and the χ^2 test for dichotomous variables.

RESULTS

Ninety patients were identified who met the inclusion criteria. The demographic data of all patients are outlined in Table 1. Eighty-two patients (91%) reported their ethnicity as white. The mean age at application was 52.2 years (range, 12.9–84.3 years). The median duration of symptoms was 30 months [interquartile range (IQR), 12–84 months]. Patients were tested to allergens in the standard and gynecologic series. The allergens with which the patients were tested to and the positive results are shown in Tables 2 and 3.

Sixty-two patients (69%) had a positive result, and 35 (39%) patients had a positive result that was considered relevant to their presentation with vulvar symptoms. Forty-one patients (46%) had multiple positive results. In the 62 patients with a positive reaction, the average number of positive reactions was 2.5, and the average number of relevant reactions was 1.25.

There were 140 positive reactions to allergens in the standard series, and of these, 67 (47.9%) were considered relevant. The

TABLE 5. Reactions to Steroid Allergens*

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
125	Budesonide 0.1%	61	0 (0)	0 (0)
319	Hydrocortisone 17-butyrate 1% alcohol	89	0 (0)	0 (0)
590	Tixocortol-21-pivalate 1%	90	1 (1)	1 (1)
597	Triamcinolone acetonide 1%	90	0 (0)	0 (0)
740	Clobetasol-17-propionate 1%	59	0 (0)	0 (0)
936	Budesonide 0.01%	29	0 (0)	0 (0)

*All steroid allergens were from the standard series.

TABLE 6. Reactions to Antibiotic Allergens

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
74	Bacitracin 20%	90	1 (1)	0 (0)
411	Neomycin sulfate 20%	90	3 (3)	2 (2)
779	Clindamycin phosphate 2%*	73	1 (1)	1 (1)
780	Metronidazole 0.75%*	73	0 (0)	0 (0)
100010	Metronidazole 1%*	16	0 (0)	0 (0)
100029	Clindamycin phosphate 10%*	16	0 (0)	0 (0)

*Allergen from gynecologic series.

5 allergens from the standard series to cause a positive reaction in most cases, in descending order, were gold sodium thiosulfate 0.5%, nickel sulfate hexahydrate 2.5%, balsam of Peru 25%, fragrance mix 8%, and cobalt chloride 1%. The top 5 allergens from the standard series to cause a positive reaction considered relevant to the presentation of vulval symptoms, in descending order, were natural fragrance mix 2%, balsam of Peru 25%, benzocaine 5%, fragrance mix 8%, and quaternium 15 1%.

There were 21 positive reactions to allergens from the gynecologic series of which 13 (62%) were considered relevant. The allergens from the gynecologic series with the highest rates of positive reactions, in descending order, were terconazole as is,

TABLE 7. Reactions to Antifungal Allergens*

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
692	Clioquinol 5%	11	0 (0)	0 (0)
695	Chlorquinaldol 5%	11	0 (0)	0 (0)
692	Clioquinol 5%†	90	0 (0)	0 (0)
781	Clotrimazole 1%†	74	1 (1)	1 (1)
782	Miconazole 1% alcohol†	89	1 (1)	0 (0)
783	Terconazole as is†	56	4 (7)	4 (7)
784	Tioconazole as is†	73	1 (1)	1 (1)
785	Butoconazole nitrate 3 as is†	58	0 (0)	0 (0)
931	Terconazole 3 cream 0.8%†	34	3 (9)	2 (6)
100019	Butoconazole nitrate 3 as is†	3	0 (0)	0 (0)
100020	Nystatin 2%†	20	0 (0)	0 (0)
100021	Ketoconazole cream 2% as is†	20	0 (0)	0 (0)
100023	Clotrimazole 5%†	16	0 (0)	0 (0)
100038	Tioconazole 1%†	16	0 (0)	0 (0)

*Clioquinol 5% appears twice in the above list as it was present in both the standard and gynecologic series.

†Allergen from gynecologic series.

TABLE 8. Reactions to Anesthetic Allergens*

Code No.	Allergen	No. Tested	Result, n (% of Total Tested)	
			Positive	Relevant
85	Benzocaine 5%	59	7 (11.9)	5 (8.5)
794	Lidocaine 5%	89	0 (0)	0 (0)
2050	Caine mix III	31	0 (0)	0 (0)

*Anesthetic allergens were all from standard series.

terconazole cream 0.8%, benzoic acid 5%, and paraben mix 16%. All other allergens from the gynecologic series that elicited a positive reaction elicited it in only 1 case, and of them, the reactions considered relevant were to propylene glycol 10%, clindamycin phosphate 2%, clotrimazole 1%, tioconazole as is, conjugate estrogen 0.625 mg/g, and sodium lauryl sulfate 0.1% aqueous.

The reactions seen to metal allergens in our patients can be seen in Table 4. Gold sodium thiosulfate was the metal allergen that was associated with the highest rate of positive results. There was no clear history of direct contact of the metal with the vulva in any case. One patient reacted to cobalt, gold sodium thiosulfate 0.5%, and gold sodium thiosulfate 0.25%, and it was thought to be relevant because of contact with zippers and fasteners.

Reactions to steroid allergens are summarized in Table 5. We saw only 1 positive reaction to a steroid allergen in our series, and this was to tixocortol-21-pivalate 1%. This reaction was considered relevant.

Antibiotic preparations included in our series were clindamycin phosphate 2%, clindamycin phosphate 10%, metronidazole 0.75%, metronidazole 1%, bacitracin 20%, and neomycin sulfate 20%. Neomycin sulfate 20% was the antibiotic allergen in our series that had the highest rate of relevant positive reactions (Table 6).

We included several topical antifungals in our testing with members of the imidazole family, including clotrimazole 1%, miconazole 1%, terconazole, tioconazole, and butoconazole nitrate. We also included nystatin 2%, clioquinol 5%, and chlorquinadol 5%. Most of these antifungal allergens were components of the gynecologic series rather than the standard series. The antifungal in our series most associated with ACD of the vulva was terconazole (Table 7).

TABLE 9. Reactions Related to Atopy

Reactions	No. Patients	Positive Patch Test Rate, %	Relevant Patch Test Rate, %
Personal history of atopy*			
Yes	26	77	42
No	56	66	38
Family history of atopy†			
Yes	25	72	40
No	54	68	41

*Data on personal history of atopy were missing or unknown in 8 patients.

†Data on family history of atopy were missing or unknown in 11 patients.

TABLE 10. Reactions Related to Occupation*

Occupation	Total (n = 90)	Positive Patch Test Rate, %	Relevant Patch Test Rate, %
Missing/other	41	68	32
Homemaker	22	73	41
Manager	3	67	67
Medical assistant	2	50	50
Nurse	5	60	20
Nurse's aide	2	0	0
Retired	10	90	80
Secretary	2	50	50
Student (beyond high school)	2	50	0
Teacher	2	100	0

*Totals may sum to more than 100% because some patients had multiple occupations.

Occupations for which there was only 1 patient were grouped in "other" category.

Benzocaine was the only topical anesthetic to elicit a positive response, and it did so in a substantial number of patients tested to it (Table 8).

Of the preservative allergens, quaternium 15 had the highest rate of relevant positive results.

Although a higher rate of positive and relevant positive results was seen in those with a personal history of atopy, this rate was not statistically significant. Likewise, a family history of atopy was not a good predictor of positive or relevant results (Table 9).

The most frequently occurring occupation in our patient sample was homemaker, and this subgroup had a rate of positive and relevant results that was just marginally higher than the rate for the group as a whole. A subgroup in which a substantially higher rate of positive results was seen described themselves as retired (Table 10).

A higher rate of relevant results was seen in those older than 70 years compared with those younger than 70 years (62% vs 32%). In those older than 80 years, 100% had a relevant positive result (Table 11).

The most frequently occurring presenting symptom in those with a relevant positive result was pruritus, with 80% of patients with a relevant positive patch test result reporting this as a major presenting symptom. This compares with vulvar burning in 66%,

TABLE 11. Age at Patch Test Application and Results

Age at Application, y	No. of Patients	Positive Patch Test Rate, %	Relevant Patch Test Rate, %
<20	1	100	0
20–39	25	72	40
40–59	33	64	24
60–79	27	67	48
≥80	4	100	100

TABLE 12. Presenting Vulvar Symptom Related to Results*

Presenting Symptom	Patients (n = 90), n (%)	Patients With This Symptom and Positive Result, %	Patients With This Symptom and Relevant Result, %	Patients With Positive Result and This Presenting Symptom, %	Patients With Relevant Result and This Presenting Symptom, %
Pruritus	63 (71)	71	44	73	80
Burning	43 (48)	79	53	55	66
Vulvar pain	47 (52)	72	45	55	60
Discharge	14 (16)	79	50	18	20

*Totals may sum to more than 100% because most patients had more than 1 presenting symptom.

vulvar pain in 60%, and vulvar discharge in 20%. Most patients had more than 1 presenting symptom (Table 12).

The median duration of symptoms in the group with a positive result was longer than in the group with all negative results [36 months (IQR, 12–84 months) vs 24 months (IQR, 6.8–78 months); $P = 0.32$].

Patients with a prior diagnosis of vulvar disease were more likely than those without a prior diagnosis to have a positive result (75% vs 66%, $P = 0.40$). Regarding specific prior diagnoses, patients with baseline vulvodynia had the highest rate of positive results, whereas patients with lichen sclerosis had the highest rate of relevant positive results (Table 13).

A greater number of topical agents were used in the group with a positive patch test result, with a median use of 3.5 agents (IQR, 2–5 agents) vs 3 agents (IQR, 2–4 agents) in the negative group, but this finding was not statistically significant (rank sum $P = 0.44$). Notably, an increased rate of positive results was seen in patients with a prior treatment of a vulvar yeast infection, with 71% of those with a prior history of a treated yeast infection having a positive result vs 56% of those without a prior history of a yeast infection having a positive result. This was not statistically significant ($P = 0.20$).

DISCUSSION

It is now well accepted that ACD is a notable consideration in patients presenting with recalcitrant vulvar symptoms.⁸ The association was first published by Doherty et al¹ in 1990. Since then, multiple studies have testified to the relevance of ACD in these

patients; however, difficulties in interstudy comparison arise in several ways. Many of the studies assessed anogenital symptoms and hence included male patients.^{4,5,9} Furthermore, although some studies reported positive results,¹⁰ other studies reported only positive results that were considered relevant to the vulvar symptoms.⁵ What constituted relevancy was often at the discretion of the authors and differed between studies.

Our finding of a positive patch test reaction in 69% of our patients is higher than that typically reported, which ranges from 38% to 65.5%.^{7–14} Some of the difference observed here may relate to changes in the extent of patch testing performed, changes particularly marked between the current and older studies. In our study, the total number of allergens included was 127, and the median number of allergens with which patients were tested to was 105 (IQR, 102–106). In the study by Marren et al,¹³ the maximum number of allergens included was 67. Nardelli et al¹⁴ included patch and prick testing and reported results of testing to a total of 58 allergens. Bauer et al⁹ reported results to testing with 41 allergens. The extension of patch testing reflects the increased recognition of the vulva as a unique environment in patch testing practice.

Our percentage of patients with at least 1 relevant result, at 39%, falls within the range in the published literature of 16% to 44%.^{2,3} This finding supports a recommendation to have a low threshold for performing patch testing in patients with recalcitrant vulvar symptoms.

Patients who were retired had a high rate of positive but also relevant results. An associated finding was that those older than 80 years had a high rate of relevant positives. The small numbers in this group limit interpretation of this finding. In elderly patients, coexisting morbidities such as urinary incontinence can lead not only to irritant contact dermatitis but also, due to disruption of the vulvar skin's barrier function, to ACD. This may explain the high rate of relevant positives seen in patients older than 80 years.

Patients with a positive result had a history of using more topical products than those with no positive result, and this finding mirrors that in previous studies.^{13,16}

In our study, we found that although the diagnosis in most of the cases was elicited by testing with the standard series, the gynecologic series was an important addition for completeness of testing. Also of note, a positive reaction to an allergen from the gynecologic series was more likely to be relevant to the presentation

TABLE 13. Baseline Vulvar Dermatoses Related to Result

Baseline Condition	Patients (n = 90), n (%)	Positive Patch Test Rate, %	Relevant Patch Test Rate, %
Any	28 (31)	75	32
Visible	61 (68)	70	43
Lichen simplex chronicus	4 (4)	75	25
Vulvodynia	10 (11)	80	30
Lichen sclerosis et atrophicus	10 (11)	60	40
Lichen planus	4 (4)	75	25

with vulvar symptoms than a positive reaction to an allergen from the standard series ($P = 0.23$).

We saw a higher rate of positive patch testing results in patients with a personal history of atopy ($P = 0.32$), in keeping with previous studies.² In the study by Haverhoek et al,² patients with a history of atopy were more likely to have a positive result but not more likely to have a relevant positive result. In our study, patients with a personal history of atopy had a marginally higher rate of having a relevant result.

Our finding of neomycin as the most frequent antibiotic allergen implicated in ACD of the vulva is in keeping with published data.^{4,9} This finding suggests that the use of neomycin for vulvar dermatoses should be avoided. Several topical antibiotics are believed to cross-react with neomycin, including tobramycin, kanamycin, gentamicin, streptomycin, and bacitracin.

Our rate of steroid sensitivity, at 1%, was lower than that reported in similar studies.^{5,13,15} In the study by Marren et al,¹³ 5 (11.9%) of 42 patients tested with steroid allergens had a positive reaction. One positive reaction was to tixocortol pivalate, and 4 were to clobetasol propionate.¹³ This may reflect differing prescribing practices. The positive reaction in our study was to tixocortol pivalate, an indication of sensitivity to hydrocortisone.

Two classes of topical anesthetic are well known, esters and amides, and of these, the former is more frequently associated with ACD. Our series included an ester anesthetic, benzocaine 5%, and an amide anesthetic, lidocaine 5%. Our finding that lidocaine is less frequently associated with ACD than other caine anesthetics is supported in previous studies.⁹ Our finding that benzocaine is a frequent culprit in vulvar ACD also supports previously published data.^{5,10} Included in our series was caine mix III, a combination of 3 anesthetics—2 ester anesthetics, benzocaine and tetracaine, and an amide anesthetic, dibucaine—and this elicited no positive reactions in testing with 31 patients. The North American Contact Dermatitis Group and a study by Bauer et al in Germany have previously reported a high rate of positive reactions to dibucaine.^{5,9}

Quaternium 15 1%, a formaldehyde-releasing preservative frequently found in cosmetics, shampoos, and soaps, was 1 of the top 5 allergens in our standard series to cause a relevant reaction. Ethylenediamine dihydrochloride 1% is a chemical stabilizer used in various topical creams and ointments. We found it to be a relevant allergen in our series. Our finding of a substantially high rate of positive and relevant reactions to the preservatives methylchloroisothiazolinone/methylisothiazolinone 100 ppm aqueous and methylidibromo glutaronitrile is in keeping with published data.⁹ These are known to be present in some brands of toilet tissue and may be particularly relevant as allergens in the setting of moistened toilet tissue. The importance of preservatives in genital ACD is well documented.^{5,13}

Our finding that nickel frequently elicited a positive reaction is in keeping with previous studies of vulvar ACD.^{7,11,15} Although 9 patients had a positive reaction to nickel, only 2 of these cases were deemed of relevance to the vulvar symptoms. In 1 patient, it

was deemed relevant because of a clear history of reacting to costume jewelry, but there was no clear history of direct contact with the vulva. Although nickel seems to be consistently a major cause of positive reactions, most studies have found a low rate of relevancy to vulvar symptoms.^{11,15} Other authors have felt it to be relevant in this setting, in part because of dietary nickel.⁷ It seems most accurate to conclude that the implication of nickel as a relevant allergen in ACD of the vulva remains controversial. It is likely that some of the controversy relates to differing interpretations of the relevancy of the positive results. Whether transfer occurs, for example, on a patient's hands, from jewelry worn elsewhere and sensitizes the vulva remains unclear. Interestingly, as noted in previous studies, nickel may be a component in toilet tissue made from recycled paper.^{9,10}

The high incidence of positive reactions to fragrance seen in our study was in keeping with previous studies as was the high rate of relevancy.^{4,5,11} These findings support the implication of scented products, such as soaps, shower products, and scented toilet tissue, in the initiation and continuation of troubling vulvar symptoms. Our findings support a recommendation for patients with vulvar symptoms to avoid using fragranced products.

Studies have suggested that there is a low rate of positive patch test results in patients presenting with a known diagnosis of vulvodynia, and some have concluded that patch testing may not be helpful in these patients.^{7,17} Our study demonstrated a positive patch test result in 80% of patients with baseline vulvodynia, with 30% having at least 1 relevant result. This rate of positive results was higher than that in patients with background of lichen sclerosus et atrophicus, lichen simplex chronicus, or lichen planus. In the aforementioned study by Nunns et al,¹⁷ 30 patients with vulvodynia were chosen at random to be patch tested, and with 5 positive results, none of which was considered relevant. Nunns et al¹⁷ concluded that ACD did not appear to be a primary or propagating factor in vulvodynia. In our study, the patients were patch tested on the basis of a clinical suspicion for ACD, and therefore, the patients differed substantially from those described by Nunns et al.¹⁷ That said, we did find a high rate of positive results in patients with vulvodynia, and so ACD should be a consideration in these patients.

Our finding of a relevant positive patch test result in 40% of those with a background of lichen sclerosus and in 25% of patients with baseline lichen planus or lichen simplex chronicus was in keeping with previous reports.^{13,14}

CONCLUSIONS

Our study found that ACD is an important consideration in the investigation of recalcitrant vulvar symptoms. We found fragrances, medicaments, and preservatives to be of most relevance. The relevance of metals in vulvar symptoms remains unclear.

We detected a higher rate of positive results in patients with a personal history of atopy, a longer duration of symptoms, preceding use of more topical agents, and a known vulvar dermatosis

at baseline. We saw a high rate of relevant results in retired patients.

The most frequently occurring symptom in patients with a relevant reaction was pruritus.

More than 91% of our patients reported their ethnicity as white, and therefore our results may not be applicable to patients of other ethnicities.

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American Contact Dermatitis Society Core Allergen Series: Erratum

In the article that appeared on page 7 of the January/February 2013 issue, a Core Allergen was printed incorrectly in Table 1 on page 8. In #43, Hydroxymethyl should read as follows:

Hydroxyethyl

REFERENCE

1. Schalock PC, Dunnick CA, Nedorost S, et al. American Contact Dermatitis Society Core Allergen Series. *Dermatitis* 2013;24(1):7–9.