

Anogenital Dermatitis in Patients Referred for Patch Testing

Retrospective Analysis of Cross-sectional Data From the North American Contact Dermatitis Group, 1994-2004

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Objectives: To characterize patients with anogenital dermatitis referred for patch testing by the North American Contact Dermatitis Group, to identify common allergens, and to explore sex associations.

Design: Retrospective, cross-sectional analysis of the North American Contact Dermatitis Group database, 1994-2004.

Patients: Five hundred seventy-five patients with anogenital signs or symptoms were referred for patch testing; 347 had anogenital disease only.

Main Outcome Measure: Currently relevant allergic patch test reaction in patients with anogenital signs or symptoms.

Results: Sex percentages and mean age were not significantly different in patients with anogenital involvement only compared with those without anogenital involvement. In patients with anogenital involvement only, a final diagnosis of "other dermatoses" was statistically significantly more common in female patients compared with male patients ($n=347$; relative risk, 1.99; 95% confidence interval, 1.37-

2.91), but the diagnosis of allergic contact dermatitis was not associated with sex. Specific allergens that were statistically significantly more common in patients with anogenital involvement included cinnamal (or cinnamic aldehyde), dibucaine, benzocaine, hydrocortisone-17-butyrate, and budesonide (all $P < .005$). Those that were statistically significantly less frequent included quaternium-15, cobalt chloride, formaldehyde, *p*-phenylenediamine, and thiuram mix (all $P < .04$). Seventy-three patients had anogenital allergic contact dermatitis, defined as anogenital involvement only, allergic contact dermatitis as the only diagnosis, and at least 1 positive reaction of current clinical relevance. In that subgroup, the most common allergen sources were cosmetics, medications, and corticosteroids.

Conclusion: In patients in the North American Contact Dermatitis Group with anogenital involvement only, male and female patients were equally likely to have allergic contact dermatitis but female patients were more likely to have other dermatoses. Common allergens and sources consisted of those likely to have contact with the anogenital area.

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ANOGENITAL DERMATOLOGIC disorders may be less common than other skin conditions but often have substantial effects on quality of life.¹⁻³ Contact dermatitis of the anogenital area may be irritant or allergic.

*For editorial comment
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Allergic contact dermatitis (ACD) may be caused by anogenital-specific products including feminine hygiene products and contraceptive agents or by nonanogenital products that inadvertently are transferred to the anogenital area.⁴⁻⁶

Current clinical relevance (eg, an allergen in a source used by the patient in the anogenital area) is critical in interpreting patch test results. A positive reaction to thimerosal may indicate exposure to vaccines during childhood but have no current relevance to a patient's anogenital dermatitis if this ingredient cannot be verified in products currently being used by the patient.⁷⁻⁹ While several studies have listed positive reactions (which are often of past relevance) in patients with anogenital dermatoses, few studies have reported current clinical relevance and only 1 included both men and women (**Table 1**). The largest study, by Bauer et al,¹⁰ included 1008

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Table 1. Published Studies of Patch Test Results in Patients With Genital Dermatoses

Source, Country, Study Period	No. of Patients Patch Tested (% Female)	Study Population	Mean Age, (Age Range), y	No. of Patients With at Least 1 Positive Reaction	No. of Patients With at Least 1 Clinically Relevant Reaction (% of Total)
Bauer et al, ¹⁰ Germany, Switzerland, and Austria, 1992-1997	1008 (48.2)	Patients with anogenital signs/symptoms	65 (40)>40	483	NR
Goldsmith et al, ¹¹ United Kingdom, 14 years	201 (100)	Women with vulvar and/or perianal dermatoses	NR	79	NR
Marren et al, ¹² United Kingdom, 1986-1990	135 (100)	Women with persistent vulvar symptoms	51 (14-88)	63	39 (29)
Nardelli et al, ⁵ Belgium, 1990-2003	92 (100)	Women with vulvar dermatitis	49 (7-92)	35	15 (16.5)
Virgili et al, ¹³ Italy, 1993-2000	61 (100)	Women with vulvar lichen simplex chronicus (40 vulvar only, 21 vulvar and perianal)	45.6 (23-85)	29	16 (26)
Lucke et al, ¹⁴ Scotland, 1992-1997	55 (100)	Women with vulvar dermatoses	50.3 (14-78)	36	16 ^a (72.7)
Brenan et al, ¹⁵ Australia, 1993-1994	50 (100)	Women with vulvodynia	38.8 (NR)	21	NR
Crone et al, ⁴ United Kingdom, 1997	32 (100)	Women with vulvar dermatitis	45 (22-66)	15	9 (26)

Abbreviation: NR, not reported.

^aRelevant reactions defined in the context of the outcome of disease (improvement when patient stopped applying the agent). Only 22 patients had followed up.

^bRelevant.

patients in Germany, Austria, and Switzerland who were referred for patch testing because of anogenital signs or symptoms. Although approximately half of these patients had positive reactions, clinical relevance was not reported. The other 7 studies included fewer patients or women only and recruited subjects primarily from clinics that treated vulvar disorders.^{4,5,11-15} None of the previously reported studies included patients in North America.

The objectives of this study were to characterize patients in North America with anogenital dermatitis referred for patch testing by the North American Contact Dermatitis Group (NACDG), to identify common allergens in individuals with anogenital ACD, and to explore associations of ACD with sex.

METHODS

NACDG DATABASE

Between July 1, 1994, and December 31, 2004, 22 025 patients underwent patch testing using the NACDG standard series of 50 to 65 allergens, as previously described.^{7-9,16,17} These allergens and general data from 4 study periods have been previously reported.^{7-9,16,17} In the 1996-1998 database, some individuals underwent the TRUE Test (Thin-layer Rapid Use Epicutaneous Test; Allerderm Laboratories, Inc, Phoenix, Arizona) instead of or in addition to the NACDG standard allergen patch test series. For these analyses, any reaction to either an NACDG standard allergen or a TRUE Test allergen was considered a positive reaction; if the reaction was to the same antigen, however, it was counted only once. Data collected included the following: demographics (age, sex, and race/ethnicity), occupation, site of dermatitis, relevant irritants, and allergens (relevancy, source, and relationship to occupation). Relevance and source codes were linked to specific allergens, whereas site codes (up to 3 sites) and final diagnoses (up to 3 diagnoses) were linked to patients but not to specific allergens. For these analyses, patch test reactions coded as "definite" (positive repeat open application test or patch test reaction to the product contain-

ing the positive allergen), "probable" (positive allergen identified in known skin contactants in the patient), or "possible" (skin contact with materials known to contain the positive allergen) were considered currently clinically relevant. Reactions graded as having "past" or "unknown" relevance were excluded. Allergen-related source data were not collected for the 1994-1996 database but were subsequently collected as a single-digit code corresponding to defined categories until 2001, when a detailed 3-digit coding system was adopted. The presence of an "other" relevant allergen along with the source was collected, but the name of the specific other relevant allergen was not collected as part of this database. At the time of collection, all data were manually entered into a computerized database (Access 2003; Microsoft Corp, Redmond, Washington) and checked for quality assurance at a central location.

STUDY POPULATION AND SUBGROUPS

This analysis of deidentified NACDG data was approved by the Minneapolis Veterans Affairs Medical Center Subcommittee on Human Studies. Several subgroups were identified including the following: patients referred for patch testing who had anogenital involvement only (group 1), patients referred for patch testing who were without anogenital involvement (group 2), and patients with "anogenital ACD," defined as individuals with anogenital involvement only, ACD as the only diagnosis, and at least 1 positive reaction of current clinical relevance (group 3) (**Figure**).

ANALYTICAL METHODS

Statistical analyses were performed using commercially available software (SAS version 8.2; SAS Institute Inc, Cary, North Carolina). Counts and percentages were used to describe demographic and patch test data. The χ^2 test was used to compare selected demographic data and the prevalence of positive patch test reactions to the most common allergens. The Fisher exact test (2-tailed) was used whenever appropriate. Statistical tests and corresponding *P* values were 2-sided; *P* < .05 was considered statistically significant. No

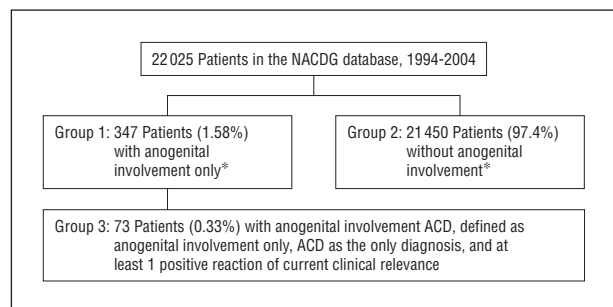


Figure. North American Allergic Contact Dermatitis Group (NACDG) study population, with subgroups. *Excludes 228 patients (1.05%) with involvement of the anogenital area in addition to another body site. The percentages do not total 100% because group 3 is a subgroup of group 1. ACD indicates allergic contact dermatitis.

adjustments for multiple comparisons were used in this exploratory analysis.

RESULTS

PATIENTS REFERRED FOR PATCH TESTING WITH AND WITHOUT ANOGENITAL INVOLVEMENT (GROUPS 1 AND 2)

Demographic Data

In the 22 025 patients tested, the anogenital area was involved in 1 of up to 3 sites in 575 patients (2.61%) and as the only site in 347 patients (1.58%; group 1; Figure). The mean (SD) age of the patients in group 1 was 47.2 (17.2) years (age range, 0-92 years) and was not significantly different from that of patients without anogenital involvement (group 2; $P = .67$). Of patients with anogenital involvement, 60.5% were female, compared with 64.7% of patients without anogenital involvement ($P = .10$; relative risk, 1.39; 95% confidence interval, 0.94-2.04). Individuals with anogenital involvement were 1.9 times more likely to be white compared with those without anogenital involvement ($P = .001$; 95% confidence interval, 1.24-2.77). Individuals without anogenital involvement were 1.4 times more likely to have atopy, defined as a personal history of eczema, asthma, or hay fever, compared with those with anogenital involvement ($P = .003$; 95% confidence interval, 1.12-1.79).

Final Diagnoses in Patients Having Anogenital Involvement Only (Group 1)

Allergic contact dermatitis, other dermatoses, dermatitis not otherwise specified, and irritant contact dermatitis were the most common final diagnoses in patients having anogenital involvement only (Table 2). Analysis of the 4 most frequent final diagnosis codes by sex found that there were no statistically significant associations of ACD, other types of dermatitis, or irritant contact dermatitis with sex. Female patients, however, were twice as likely as male patients to have a final diagnosis of other dermatoses ($P < .001$; relative risk, 1.99; 95% confidence interval, 1.37-2.91).

Table 2. Final Diagnoses in Patients Having Anogenital Involvement Only (Group 1)^a

Diagnosis	No. (%)		
	Total Diagnoses (n=347)	Diagnoses in Male Patients (n=137)	Diagnoses in Female Patients (n=210)
Allergic contact dermatitis	153 (44.1)	68 (49.6)	85 (40.5)
Other dermatoses	114 (32.9)	29 (21.2)	85 (40.5)
Other dermatitis ^b	75 (21.6)	31 (22.6)	44 (21.0)
Irritant contact dermatitis	74 (21.3)	36 (26.3)	38 (18.1)
Atopic dermatitis	9 (2.6)	5 (3.6)	4 (1.9)
Seborrheic dermatitis	7 (2.0)	7 (5.1)	0
Psoriasis	6 (1.7)	1 (0.7)	5 (2.3)
Nummular eczema	3 (0.9)	2 (1.5)	1 (0.5)
Stasis dermatitis	1 (0.3)	0	1 (0.5)

^aNumber of diagnoses divided by the number of patients in each category; total percentage is more than 100% because up to 3 diagnoses could be identified per patient.

^bOther eczematous dermatitides such as lichen simplex chronicus or chronic eczematous dermatitis not otherwise specified.

Most Common NACDG Allergens in Patients With Anogenital Involvement Only (Group 1)

Of individuals with anogenital involvement only, 220 (63.4%) had at least 1 positive reaction of current clinical relevance. Frequency of the most common 24 allergens in patients with anogenital involvement only is given in Table 3. Allergens that were statistically significantly more frequent in patients with anogenital involvement only (group 1) compared with patients without anogenital involvement (group 2) included cinamal (or cinnamic aldehyde), dibucaine, benzocaine, hydrocortisone-17-butyrate, and budesonide. Allergens that were statistically significantly less frequent included quaternium-15, cobalt chloride, formaldehyde, *p*-phenylenediamine, and thiuram mix.

PATIENTS WITH ANOGENITAL ACD (GROUP 3)

Only 73 patients met our definition of anogenital ACD, which required the following 3 criteria: anogenital involvement only, ACD as the only diagnosis, and at least 1 positive reaction of current clinical relevance. Thirty-four patients were male and 39 were female. Table 4 summarizes the most common (≥ 4 reactions) currently relevant allergens in patients with anogenital ACD (group 3). These results were similar to those in patients with anogenital involvement only (group 1; Table 3). No reactions were occupationally related.

The 3 most common sources of allergens in patients with anogenital ACD (group 3) were medications ($n = 47$), corticosteroids ($n = 31$), and other or unknown agents ($n = 32$). The most common sources of irritant contact dermatitis included miscellaneous health aids, cosmetics, corticosteroids, soaps and cleansers, and other or unknown agents.

Table 3. Most Common Allergens in Patients With Anogenital Involvement Only (Group 1) Compared With Patients Without Anogenital Involvement (Group 2)

Allergen	Group 1		Group 2		Group 1 vs Group 2	
	No. of Patients Tested	Clinically Relevant Reaction, No. (%) ^a	No. of Patients Tested	Clinically Relevant Reaction, No. (%) ^a	P Value ^b	RR (95% CI)
Fragrance mix, 8% petr	346	40 (11.56)	21 353	2011 (9.42)	.18	1.23 (0.91-1.65)
<i>Myroxylon pereirae</i> (balsam of Peru), 25% petr	347	39 (11.24)	21 419	1953 (9.11)	.17	1.23 (0.91-1.66)
Nickel sulfate, 2.5% petr	347	20 (5.76)	21 387	1847 (8.64)	.06	0.67 (0.44-1.02)
Cinnamic aldehyde, 1% petr	265	13 (4.91)	20 786	392 (1.89)	.001	2.60 (1.52-4.46)
Neomycin sulfate, 20% petr	345	15 (4.35)	21 393	913 (4.27)	.94	1.02 (0.62-1.68)
Dibucaine, 2.5% petr	146	6 (4.11)	9763	7 (0.07)	<.001	57.32 (19.50-168.46)
Propylene glycol, 30% aq	301	12 (3.99)	19 380	622 (3.21)	.45	1.24 (0.71-2.17)
Benzocaine, 5% petr	342	13 (3.80)	20 796	121 (0.58)	<.001	6.53 (3.72-11.46)
Hydrocortisone-17-butyrate, 1% petr	146	5 (3.42)	9765	41 (0.42)	<.001	8.16 (3.27-20.34)
Quaternium-15, 2% petr	347	11 (3.17)	21 415	1712 (7.99)	.001	0.40 (0.22-0.71)
Bacitracin, 20% petr	344	9 (2.62)	21 346	807 (3.78)	.26	0.69 (0.36-1.32)
Budesonide, 0.1% petr	339	9 (2.65)	21 157	226 (1.07)	.005	2.49 (1.29-4.80)
Methyldibromo glutaronitrile and phenoxyethanol, 2.0% petr	231	6 (2.60)	15 406	570 (3.70)	.38	0.70 (0.32-1.55)
Lanolin alcohol, 30% petr	343	8 (2.33)	20 796	445 (2.14)	.81	1.09 (0.55-2.18)
Tixocortol-21-pivalate, 1% petr	345	8 (2.32)	21 346	487 (2.28)	.96	1.02 (0.51-2.03)
Carbamate mix, 3% petr	347	7 (2.02)	21 416	861 (4.02)	.06	0.50 (0.24-1.05)
Paraben mix, 12% petr	346	7 (2.02)	21 362	226 (1.06)	.08	1.91 (0.91-4.03)
2-Bromo-2-nitropropane-1,3-diol, 0.5% petr	343	6 (1.75)	21 317	413 (1.94)	.79	0.90 (0.40-2.00)
Cobalt chloride, 1% petr	343	6 (1.75)	21 368	827 (3.87)	.04	0.45 (0.20-1.00)
Formaldehyde, 1% aq	347	5 (1.44)	21 421	1353 (6.31)	.001	0.23 (0.10-0.55)
Methylchloroisothiazolone/methylisothiazolone, 100 ppm aq	346	5 (1.45)	21 294	454 (2.13)	.38	0.68 (0.28-1.63)
p-Phenylenediamine, 1% petr	347	5 (1.44)	21 409	626 (2.92)	.1	0.49 (0.21-1.18)
Budesonide, 0.01% petr	68	5 (7.35)	5011	64 (1.28)	<.001	5.76 (2.39-13.85)
Thiuram mix, 1% petr	347	5 (1.44)	21 413	919 (4.29)	.009	0.34 (0.14-0.80)

Abbreviations: aq, aqueous; CI, confidence interval; petr, petrolatum; RR, relative risk, compares clinically relevant patch test results in individuals.

^aClinically relevant: definite, probable, or possible relevance; excludes tests with reactions with past or unknown relevance.

^bGroup 1 vs group 2.

COMMENT

Of 22 025 patients referred to NACDG members between 1994-2004, 347 (1.6%) were identified as having anogenital involvement only. Despite this relatively small number, 220 patients (63.4%) in this group (group 1) had at least 1 positive reaction of current clinical relevance. This analysis is the first, to our knowledge, to characterize male and female patients with anogenital involvement referred for patch testing in North America and to identify clinical relevance of positive reactions.

We hypothesized that sensitization rates could vary between male and female patients on the basis of biostructural differences.^{18,19} While the density of Langerhans cells during the menstrual cycle does not seem to fluctuate,²⁰ Edwards and Morris²¹ reported a statistically significant difference in the number of Langerhans cells in the keratinized vs nonkeratinized areas of the vulva. The skin overlying the penis is believed to facilitate the absorption of allergens and, in turn, to facilitate the development of dermatoses and ACD,^{22,23} and there is some evidence that circumcision decreases the risk of inflammatory dermatoses.²⁴

Our results showed no statistically significant difference in the percentage of male and female patients referred for patch testing who had anogenital involve-

ment only. Final diagnosis differed only for the category of other dermatoses, which was statistically more common in female patients, likely because of women with vulvodynia, for which there is no direct male correlate (red scrotal syndrome is less common than vulvodynia). The frequency of the final diagnosis of ACD was similar in male and female patients. However, in patients with anogenital ACD (group 3), the frequency of specific allergens differed by sex. Frequency of relevant allergy to dibucaine, neomycin, propylene glycol, ethylenediamine, cinnamal, bronopol (2-bromo-2-nitropropane-1,3-diol), and all corticosteroids except tixocortol pivalate was at least 3 times higher in male than in female patients. The few reactions to each allergen, however, precludes meaningful clinical interpretation.

Allergens that were statistically significantly more common in patients with anogenital involvement were those that are more likely to be found in products for use in the anogenital area. The most common allergens in patients in the most restrictive group, those with anogenital ACD (group 3), consisted of 3 fragrances, 5 preservatives, 4 medications, 2 vehicles, 5 corticosteroids, 1 metal, and 1 rubber compound.

The relevance of systemic exposure of nickel in patients with nickel sensitivity and anogenital dermatitis is controversial. Lucke et al¹⁴ documented improve-

Table 4. Most Common Clinically Relevant Allergens^a in Patients With Anogenital ACD (Group 3)

Allergen	No. of Clinically Relevant Reactions/No. of Patients With Anogenital ACD, No. (%)		
	Total	Men	Women
Fragrances			
<i>Myroxylon pereirae</i> (balsam of Peru), 25% pet	18/73 (26.7)	7/34 (20.6)	11/39 (28.2)
Fragrance mix, 8% petr	15/73 (20.6)	6/34 (17.7)	9/39 (23.1)
Cinnamal (or cinnamic aldehyde), 1% pet	4/73 (5.5)	3/34 (8.8)	1/39 (2.6)
Preservatives and stabilizers			
Quaternium-15, 2% pet	10/73 (13.7)	6/34 (17.7)	4/39 (10.3)
Paraben mix, 12% pet	6/73 (8.2)	4/34 (11.8)	2/39 (5.1)
Methylchlorisothiazolone/methylisothiazolone, 100 ppm aq	5/73 (6.9)	3/34 (8.8)	2/39 (5.2)
Ethylenediamine dihydrochloride, 1% pet	4/72 ^b (5.7)	3/33 ^b (9.1)	1/39 (2.6)
2-Bromo-2-nitropropane-1,3-diol, 0.5% pet	4/73 (5.5)	3/34 (8.8)	1/39 (2.6)
Medicaments			
Benzocaine, 5% pet	9/72 ^b (12.5)	5/33 ^b (15.2)	4/39 (10.3)
Dibucaine, 2.5% pet	5/37 ^b (13.5)	4/20 ^b (20)	1/17 ^b (5.9)
Neomycin sulfate, 20% pet	7/72 ^b (9.7)	6/33 ^b (18.2)	1/39 (2.6)
Bacitracin, 20% pet	4/73 (5.5)	1/34 (2.9)	4/39 (10.3)
Vehicles			
Propylene glycol, 30% aq	7/68 ^b (10.3)	6/34 ^b (17.7)	1/39 ^b (2.7)
Lanolin alcohol, 30% pet	5/73 (6.9)	3/34 (8.8)	2/39 (5.2)
Corticosteroids			
Budesonide, 0.01% pet	5/19 ^b (26.3)	5/12 ^b (41.7)	0/7 ^b (0)
Hydrocortisone-17-butyrate, 1% pet	5/37 ^b (13.5)	4/20 ^b (20)	1/17 ^b (5.9)
Clobetasol-17-propionate, 1% pet	4/37 ^b (10.8)	3/20 ^b (15)	1/17 ^b (5.9)
Budesonide, 0.1% pet	7/72 ^b (9.7)	7/33 ^b (21.2)	0/39 (0)
Tixocortol-21-pivalate, 1% pet	5/73 (6.9)	2/34 (5.9)	3/39 (7.7)
Metals			
Nickel sulfate, 2.5% pet	6/73 (8.2)	0/34 (0)	6/39 (15.4)
Rubber chemicals			
Carba mix, 3% pet	5/73 (6.9)	3/34 (8.8)	2/39 (5.2)

Abbreviations: ACD, allergic contact dermatitis; aq, aqueous; petr, petrolatum.

^aFour reactions or more. Clinically relevant: definite, probable, or possible relevance; excludes reactions of past or unknown relevance.

^bDenominator differs because some allergens were not tested in all study years.

ment in 1 patient with nickel sensitivity and vulvar dermatitis after dietary restriction of nickel. In our study, currently relevant nickel allergy occurred much more frequently in female than in male patients (group 3, 15.4% vs 0%). Of individuals with source codes, jewelry was the relevant source in at least 1 patient.

Fragrances were common allergens in our and previous studies.^{4,11-15} The sources of these allergens were broad; cosmetics and medications were the most common sources identified in our study. Products used to cleanse the anogenital area such as soaps and douches could contain fragrances including those present in fragrance mix, cinnamal, and *Myroxylon pereirae* (balsam of Peru).²⁵ Balsam of Peru may be found in hemorrhoidal creams. Systemic sensitization including baboon syndrome²⁶ is also possible. Salam and Fowler²⁷ reported the results in 45 patients allergic to balsam of Peru or fragrance who were given a balsam-free diet; 14 (31%) had anogenital involvement.

There was a high rate of current clinically relevant reactions to preservatives in our study, similar to findings in previous studies.^{4,5,10-13} Preservatives were most often identified in cosmetics and medications. These products could be used directly on the anogenital area or transferred from the hands. In addition, parabens may be used in lubrications on condoms.²⁸ Other allergens that may be found in condoms include carbamates and thiurams. There was no

specific NACDG source code for condoms and contraceptive devices. Therefore, it is possible that the source of carbamate allergies in our study coded as "other" could have represented condoms or diaphragms.^{28,29}

In our study, there was a high rate of ACD from medications including topical corticosteroids, neomycin, bacitracin, dibucaine, and benzocaine, which can be found in hemorrhoid and vaginal medications.^{30,31} This finding is consistent with those of previous studies.^{4,10-15} Bauer et al¹⁰ also found high rates of allergic reactions (relevance not reported) to dibucaine and benzocaine but lower rates of allergic reactions to neomycin, bacitracin, and corticosteroids.

Allergy to corticosteroids was common in our study, similar to most previously reported studies.^{4,5,11,14} This finding could be explained by either the frequent use of corticosteroids to treat anogenital conditions or by enhanced penetration.^{18,19,32,33} Feldmann and Maibach³⁴ showed that carbon 14 hydrocortisone penetrates the scrotum at a rate 42 times higher than in the ventral forearm. Similarly, Britz et al³⁵ showed that 7.7% of topically applied hydrocortisone cream penetrated vulvar epithelium compared with 1.3% used on forearm skin.³⁵

This study has several limitations. First, the data were cross-sectional; therefore, causal relations cannot be determined. Second, the study sample was drawn from pa-

tients who were referred for patch testing; as such, they are representative of neither the general population nor the general dermatology population. Third, there were few patients with anogenital ACD. Our strict definition excluded patients with more than 1 diagnosis (ACD plus other dermatoses). This was necessary to confidently identify allergens related to the anogenital area. Fourth, most of the patients were white, which limits generalizations to individuals of other races/ethnicities. Fifth, while previous studies have differentiated reactions on the basis of genital and/or anal involvement, our data grouped these 2 body sites into 1 category.

In summary, although relatively few patients in this study had anogenital involvement only, distribution of sex was not significantly different from patients without anogenital involvement. Similar numbers of male and female patients had anogenital ACD; however, other dermatoses were twice as likely in female compared with male patients. For patients with anogenital ACD, sources were consistent with those likely to have contact with the anogenital region. More research is needed to further elucidate relevance, important nonstandard allergens, and detailed sources in patients with anogenital dermatoses.

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Author Contributions: Dr Warsaw had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Warsaw, Furda, Fowler, and Zug. *Acquisition of data:* Warsaw, Maibach, Rietschel, Fowler, Belsito, Zug, DeLeo, Marks, Mathias, Pratt, Sasseville, Storrs, and Taylor. *Analysis and interpretation of data:* Warsaw, Furda, Maibach, Rietschel, Fowler, Belsito, and Zug. *Drafting of the manuscript:* Warsaw, Furda, Belsito, and Zug. *Critical revision of the manuscript for important intellectual content:* Warsaw, Furda, Maibach, Rietschel, Fowler, Belsito, Zug, DeLeo, Marks, Mathias, Pratt, Sasseville, Storrs, and Taylor. *Statistical*

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Notable Notes

The Clinical and Histopathological Description of Geometric Phagedenism (Pyoderma Gangrenosum) by Louis Brocq One Century Ago

Pyoderma gangrenosum is an idiopathic, rapidly evolving, severely debilitating neutrophilic dermatosis, typically characterized by an inflammatory ulcer with a purulent infiltrated border.¹ About two-thirds of pyoderma gangrenosum are associated with systemic diseases, mostly inflammatory bowel diseases (either ulcerative colitis or Crohn disease), but also with monoclonal gammopathies and myeloproliferative disorders.

Brunsting, et al,² (from the Mayo Clinic, Rochester, MN), first coined the term pyoderma (echthyma) gangrenosum in 1930. In their seminal article, 4 of 5 patients presented with ulcerative colitis and one had idiopathic chronic purulent pleurisy.² At that time, the term *pyoderma* was used by dermatologists to refer to "purulent skin diseases due to infectious agents."^{1(p459)} Brunsting et al first introduced the term *gangrenosum* to address the necrotic and rapidly extensive features of this dermatosis.²

In 1908, Louis Brocq, MD (**Figure**), reported a series of patients with typical features of the entity later named pyoderma gangrenosum by Brunsting et al.¹ As a meticulous semiologist, Brocq discerned three components of the skin ulcer^{3(p25)}: (1) the ridge, "the most prominent part of the ulcer's edge, featuring a regular, geometric, circular or elliptic pattern"; (2) the external slope of the border, sometimes painful, featuring erythema and infiltration, which decreases steadily and fades "between 4 and 20 mm from the ridge"; and (3) the internal slope of the border, typically vertical and "as sharp as a cliff," with "a height of 3 to 12 mm" and "dimpled by purulent cavities," which shows a "marked tendency of undermining."

Brocq also described two evocative aspects of the histopathological picture³: (1) the presence of a necrotic inflammatory infiltrate with a predominance of neutrophils; and (2) the marked depth of this infiltrate, usually involving the hypodermis. Moreover, he demonstrated that the reported ulcerative dermatosis was neither related to syphilis nor transmissible to animals.³ Finally, he emphasized that the main differential diagnosis was infectious cellulitis.³

Brocq named this dermatosis *geometric phagedenism*, to underscore both the geometrical pattern of the ridge and the necrotic and rapidly extensive nature of the ulcer (*phageton* [Greek], meaning food, consumption). Even though the former term is no longer used, there is no doubt that geometric phagedenism as described by Brocq and pyoderma gangrenosum as described by Brunsting et al are the same disease.¹

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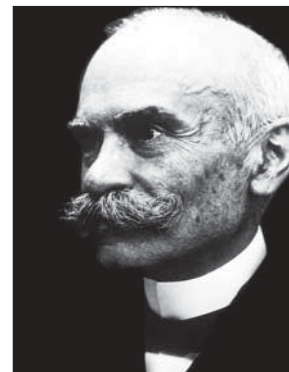


Figure. Louis Brocq, MD (1856-1928), cofounder of the French Society of Dermatology and Syphiligraphy in 1899, was the head of the Department of Dermatology and Venereology at Saint Louis University Hospital (Paris, France) from 1906 to 1921 and was one of the co-authors of the first French dermatological encyclopedia in 1900 (*The Dermatological Practice*).¹

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