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Allergic Reactions and Risk of Vulvodynia

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Abstract

A recent histological study of vestibular tissue from women with localized vulvodynia found universal presence of mast cells compared to no presence in vestibular tissue among controls. Since histamine is generated by mast cells, and mast cells contribute to the production of cytokines during chronic inflammation, we assessed the association between conditions that elicit a clinically-relevant histamine response and vulvodynia.

Methods—We studied 239 women with and 239 women without vulvodynia to assess the influence of self-reported allergic reactions antecedent to first development of vulvar pain symptoms among cases, and a matched reference age among controls.

Results—Women with self-reported hives prior to first report of vulvar pain or reference age among controls were 2.5 times more likely to develop vulvodynia (95% CI 1.7–4.4). Those reporting a history of allergic reactions to insect bites were 2.1 times more likely (95% CI 1.1–4.0), and those reporting a history of seasonal allergies were 2.0 times (95% CI 1.3–3.2) more likely to develop vulvodynia. Findings were similar in a restricted subset of clinically-confirmed cases and matched controls.

Conclusions—An altered immuno-inflammatory response to environmentally-induced allergic reactions may predispose women to the development of vulvodynia or may be markers of an already heightened immuno-inflammatory response.

Introduction

Little is known about the etiology of vulvodynia, a condition of unexplained vulvar pain characterized by burning, rawness, or localized pain that occurs spontaneously or through direct contact (1). This debilitating condition may affect between 3% and 7% of women during their reproductive years (1,2).

Vulvodynia may result from an immuno-inflammatory response. Recent clinical- and laboratory-based studies have shown that vulvodynia patients exhibit lower serological levels of interleukin-1 receptor antagonist, suggesting that these women may be at a greater risk of a proinflammatory immune response as a consequence of their inability to terminate an inflammatory event involving IL-1 production (3). Higher frequency of certain alleles in interleukin-1B and interleukin-1 receptor antagonist polymorphic genes have also been reported among women with vulvodynia (4,5).

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Allergic hypersensitivities are immuno-inflammatory processes that may lead to vulvodynia. Allergic reactions are consistent with pathology studies that have confirmed the presence of subepithelial hyperinnervation in women with vulvodynia, and these women present with increased number and activity of mast cells (6). It has also been hypothesized that C-fiber nociceptors, which can be sensitized through excessive histamine reactions, may be one neuronal pathway by which women experience vulvodynia. C-fibers (7,8).

We sought to determine whether allergic conditions that elicit a histamine response could be related to the development of chronic vulvar pain. Using data from our case-control study, we examined whether a history of allergies and allergic reactions were associated with an increased risk of vulvodynia.

Materials and Methods

This study was approved by the Human Subjects Research Committee at Brigham and Women's Hospital and at the University of Minnesota. Written informed consent was obtained from all participating women.

Target Population

Using Massachusetts Town Books (annual census publications that list residents by name, age, and address), we randomly selected 450 women ages 18–64 each month, for 55-months from three ethnically diverse Boston neighborhoods (defined geographically by zip code) and six suburban communities. The monthly sample was weighted to the age and community distribution of all communities combined based on U.S. census data and included only women with a verifiable telephone number.

A short questionnaire assessed whether women in the general population had experienced chronic vulvar pain for three months or longer including burning, knife-like sharp pain, or pain on contact during intercourse, at the time of tampon insertion or during a pelvic exam. This questionnaire was mailed to a sample of 24,750 subjects, and 2,059 were returned as undeliverable with no forwarding address. After three mailings and telephone follow-up, 3,443 subjects could not be confirmed as residing at the mailed household, and 745 subjects could not complete the questionnaire due to a language barrier. Of the remaining 18,503 subjects, 12,435 (67.2%) completed the initial screener questionnaire (see Fig. 1). Our response was somewhat lower for inner-city neighborhoods (64.6%) compared to west suburban communities (68.2%), but the mean age of responders and non-responders was identical.

Of 12,435 women that returned the initial questionnaire, 662 reported chronic vulvar pain and were eligible for further screening as potential vulvodynia cases. There were 1,851 women with chronic itching and/or other non vulvodynia-related symptoms who were excluded from further consideration, and 9,922 women with no history of vulvar pain symptoms who comprised the pool of eligible controls.

Selection of cases and controls

Women reporting symptoms suggestive of vulvodynia (N=662, Fig. 1) were asked to participate in a telephone interview to assist in ruling out the presence of other vulvar conditions including sexually transmitted diseases (STDs), yeast/bacterial infections, vulvar skin problems, misclassified pelvic disorders, estrogen-related dyspareunia, and inflammatory vaginitis. Questions included the effectiveness of vaginal creams in alleviating symptoms, nocturnal awakenings, use of self-treatments, specific pain location, consistency of pain since the start of sexual intercourse, use of and effectiveness of lubricants, and use of hormone replacement therapy. As shown in Figure 1, 444 potential cases (67.1%) agreed to complete

the telephone assessment. A similar proportion of telephone interviewed participants compared to non-participants reported pain on contact (78% versus 82%), knife-like pain (33% versus 36%) and vulvar burning (22% versus 20%). Based on the telephone and initial self-administered interviews, our clinical expert, Dr. Elizabeth G. Stewart, selected as eligible cases women with vulvodynia-related symptoms likely to meet the International Society for the Study of Vulvovaginal Disorders (ISSVD) criteria for vulvodynia (N=256). Dr. Stewart has been diagnosing vulvodynia for more than 20 years and has been involved in the development of the vulvodynia diagnostic criteria for the ISSVD. Women with symptoms consistent with conditions other than vulvodynia (i.e. infection, dermatosis, etc) were excluded (N=188). Of the 256 eligible cases, 194 (75.8%) agreed to participate in interviews that assessed medical, psychiatric, sexual histories, and childhood victimization. The mean duration of symptoms was 136 months with less than 5% reporting ≤ 1 year of symptoms, and 25% reporting symptoms for ≥ 18 years.

All cases were offered a free clinical examination to confirm their diagnosis and a recommended course of therapy. Clinical confirmation involved a pelvic exam that applied Friedrich's diagnostic criteria (9). For localized vulvodynia, cases were clinically confirmed by absence of signs or symptoms of any known cause of vulvar pain and by the presence of pain on touch by a cotton swab in the vestibule. For generalized vulvodynia, cases were clinically confirmed by absence of signs or symptoms of any known cause of vulvar pain and by the patient's description of burning, stinging, pain or rawness with or without allodynia in the affected area. Localized and generalized vulvodynia were combined for our analysis.

Seventy-three cases agreed to the clinical examination and 56 (77%) were clinically-confirmed as vulvodynia. The remaining 17 women had no disorder (n=3), lichen sclerosis (n=2), vaginal infections (n=2), pelvic pain disorder (n=8), vaginismus (n=1) and irritable bowel syndrome (n=1) and were excluded. There were 121 women classified as cases that were not clinically-confirmed. Clinically-confirmed population-based cases were slightly older (mean age=38) than non-clinically-confirmed population-based cases (mean age=36) and were equally likely to be non-Caucasian (14%). The proportion of clinically- and non-clinically-confirmed cases was similar in those reporting burning, pain on contact, and knife-like sharp pain for three months or longer. In addition, mean duration of symptoms for clinically and non-clinically confirmed cases was similar as well (141 versus 133 months, respectively). In addition to the 177 cases identified from the general population, we also included a consecutive series of 65 clinically-confirmed cases from a clinic specializing in vulvovaginal disorders. These women resided in similar communities as those identified from the general population.

For each of the 242 identified cases, we randomly selected age-matched controls ($\pm$ five years) from similar communities. All controls had no history of chronic vulvar pain. We approached 520 controls in order to obtain 242 participants. On average, participating and non-participating controls were similar in age (mean ages 36 and 37, respectively), but participating controls were slightly less likely to be non-Caucasian (15% versus 17%, respectively). For each control woman, we assigned a "reference age" that reflected the age at first onset of chronic vulvar pain in her matched case.

Assessment of Allergy-Related Data

Cases and controls participated in a telephone interview (separate from that used to screen cases) to provide detailed information about their reproductive and medical history. Allergy-related data included details about seasonal allergies, allergic reactions to insect stings and bites, and a history of hives (urticaria). The cause of the hives was not obtained. For each of these exposures, we assessed age at first onset and frequency of episodes. In addition, we separated episodes that occurred before and after age at first onset of vulvar pain symptoms and the matched reference age among controls. Detailed ages allowed us to assess whether

episodes of allergic reactions preceded or followed the development of vulvodynia in cases, or reference age in controls.

Statistical Analysis

Our analyses are based on 239 pairs of cases and controls. Three case-control pairs were excluded due to missing information critical to the evaluation of allergic reactions. One of these cases was from the general population and all three cases had been clinically confirmed. Thus, our analyses are based on 176 population-based matched pairs, and 118 clinically-confirmed matched pairs.

Conditional logistic regression models were used to estimate the odds of allergic reactions among those with and without subsequent vulvodynia. Age, education, and history of childhood physical or sexual abuse were included as covariates in all logistic regression models. Although sexual and reproductive history variables have been shown to be associated with vulvodynia, they did not appear to be related to allergic reactions and were therefore not included as covariates in the logistic regression models. Pain with first tampon use was assessed as both a confounder and effect modifier. When assessing effect modification, we used unconditional logistic regression, due to loss of matched pairs, with matching factors (age and township) included as covariates.

To assess the impact of the proximity of the allergic reaction to the first onset of vulvar pain, we identified the median number of years between first onset of an allergic reaction and the first onset of vulvar pain in cases or reference age in controls. We then assessed associations among those exposed prior to and subsequent to the median number of years within this interval.

In addition to analyzing the data in all cases and matched controls, we conducted sensitivity analyses in two subsets of cases and controls according to how cases were identified. First, we assessed the associations in the subset of population-based cases and controls only. Our earlier analyses showed that women with vulvodynia identified from the general population had different patterns of exposures, such as oral contraceptive use, than those who chose to seek clinical care (10). It has been previously observed that 40% of women with vulvar pain choose not to seek care. Therefore, the representativeness of population-based samples is crucial. Secondly, since a true diagnosis of vulvodynia requires clinical confirmation, we also present our findings using only the subset of clinically-confirmed cases and their matched controls. Thus, results presented in all tables are shown separately for three groups of cases: population-based cases, clinically-confirmed cases, and all cases.

Results

The proportion of cases and controls were similar with respect to age (as expected due to matching), race, religion, and education (Table 1). Cases were, however, more likely to experience pain and difficulty with first tampon use, and also to have experienced childhood victimization ($p < 0.01$ for both associations).

Cases were 2–3 times more likely to report a history of hives prior to first onset of vulvar pain symptoms compared to controls (OR=2.7, 95%CI 1.7–4.4), regardless of the source of the vestibulodynia case (population-based, clinically confirmed, any case, Table 2). The association of hives with vulvodynia increased with greater number of hives episodes: 1 antecedent episode was associated with a 1.1-fold odds ratio, while ≥ 2 episodes was associated with a nearly 3-fold odds of vulvodynia. Among all cases and the subset of population-based cases, the association was stronger with more distant exposure to hives prior to first onset of

vulvar pain in cases and reference age in controls. This was not observed among the subset of clinically confirmed cases and matched controls.

Cases were also more likely to report a history of an allergic reaction to an insect bite or sting. Much of the association between a history of allergic response to a bite or sting and vulvodynia was confined to those women with exposure prior to reference age, and this was observed in each case category. No differences in associations were observed by the interval between first exposure and first onset of vulvar pain. Lastly, cases more commonly reported a history of seasonal allergies compared to controls. When the age at onset of seasonal allergies was stratified by median years between first episode and first onset of vulvar pain, the association was stronger for seasonal allergies that began more distantly from age at first onset of vulvar pain among population-based cases but not among clinically confirmed cases in comparison to their matched controls.

We examined other dermatological conditions that may have a proinflammatory response (rash, psoriasis, acne, removal of a mole). As shown in Table 3, self-reported histories of skin rashes, clinical diagnosis of psoriasis, and treatment for acne was not associated with vulvodynia. However, the removal of a mole was significantly more often reported among cases. These largely null associations did not vary when stratified by antecedent or subsequent exposure to vulvar pain in cases or reference age in controls, nor did they vary by the interval between first onset of the skin condition and first onset of vulvar pain in cases or reference age among controls (data not shown).

Discussion

Our data suggest that women with a history of urticaria, seasonal allergies or reaction to insect stings appear to be more prone to later development of vulvodynia than women with no history of these allergic reactions. We also showed that this association was largely confined to exposures that occurred before the first onset of vulvar pain, suggesting that allergenic exposures could be involved as, or a marker of, factors involved in the development of vulvodynia. We also observed that a history of other skin conditions, not as strongly related to an immune response, generally were not associated with the risk of vulvodynia.

In evaluating our findings, a concern was that our controls were selected based on no history of vulvar pain or itching. However, our cases all experienced vulvar pain consistent with vulvodynia, but some may also have reported co-morbid vulvar itching. This raised the possibility that the lack of a history of vulvar itching among our controls, but not necessarily cases, could have explained our associations with respect to allergic reactions. We therefore reanalyzed our data using a subset of cases with no co-morbid vulvar itching and their matched controls. We found that the associations reported in Tables 2 and 3 were nearly identical within this subset of cases and matched controls. Thus, the elimination of co-morbid itching from both cases and controls had little impact on our overall results.

To our knowledge, ours is the first epidemiological study to report an association between allergic reactions and vulvodynia. A case report in 1993 reported dermatographism in 2 patients with vulvodynia (11), and a second in 1997 reported on a 25 year old woman with urticaria for 8 years concomitant with persistent burning sensation around the vaginal introitus (12). A case series of 18 women with vulvodynia found minimal allergenic responses after patch testing (13). However, the authors noted that all 18 cases had an absence of tenderness on pressure with a cotton swab at the time of examination suggesting that these women may not have met the diagnostic criteria for vulvodynia, or were cases with non-localized symptoms that constitute a minority of women that meet the ISSVD criteria for this condition. A more recent

case series reported that over a 17-month period, 14 women were seen with factitious urticaria and vulvodynia (14).

Our study supports the immunological findings from a clinical study of 7 cases of women with localized vulvodynia undergoing vestibular excision in comparison to 7 age-matched controls undergoing corrective or cosmetic vestibular surgery in the absence of vulvar pathology (7). Vestibular tissue samples were obtained and histologically examined for the presence of mast cells, heparanase expression, and subepithelial and intraepithelial innervation. The vestibular tissue in all 7 cases showed the presence of mast cells and heparanase expression whereas these findings were absent in all 7 controls. Higher levels of innervation were observed among cases relative to controls as well. The authors suggest that neurotrophins excreted by the mast cells may lead to the presence of localized hyperinnervation and hyperalgesia. Thus, our findings of a higher prevalence of antecedent allergenic exposures among cases suggests that allergic hypersensitivity could be involved in the pathogenic mechanism of vulvodynia. However, whether a proinflammatory state is a consequence of the vulvodynia pathogenesis, or rather a consequence of environmental exposures that induce this immune response and lead to the onset of vulvar symptoms, is unknown.

As with most interview-based case-control studies, we cannot rule out that case women might have differentially recalled their history of allergic reactions more so than controls. Given that urticaria and seasonal allergies are common disorders (observed in approximately 28% and 43% of controls, respectively), and that allergic reactions have not been commonly linked to vulvodynia, it is less likely that cases would have differentially reported the presence of these exposure compared to controls, and more likely that any reporting bias would have been non-differential leading to an attenuation of any true association. In addition, we did not observe an association with other skin conditions such as rashes, acne, or psoriasis, suggesting that cases were not necessarily over reporting all skin condition exposures. Another observation that would suggest that recall bias was not driving the association was the fact that we did not see a stronger association by allergic reactions that were more proximal to the time of first onset of vulvar pain. Lastly, the allergic reactions evaluated in this analysis, although self-reported, are not subjected to poor diagnostic criteria that might influence differential recall between cases and controls.

A second limitation is that not all of our cases of vulvodynia were clinically confirmed. However, we stratified results by clinically-confirmed status and found no major variation in risk estimates. Thus, although we acknowledge the potential of case status misclassification, our sensitivity analyses suggest that misclassification could not have accounted for much of the observed associations. Also associated with our lack of universal case confirmation is the inability to differentiate between generalized and localized vulvodynia, which may be insightful to the etiology of this condition. However, of those clinically confirmed, the large majority in this study were localized vulvodynia.

An important strength of our study was our attempt to assess the temporal relationship between the allergenic exposures and age at first onset of vulvar pain in cases (or reference age in controls). Our results indicate that most of the associations observed occurred among women who had developed allergic hypersensitivity prior to first onset of vulvar pain. An important next step is to confirm these findings in a clinically-confirmed population-based sample of cases and controls and then determine how these epidemiologic findings fit within the pathogenic mechanism of vulvodynia.

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Figure 1. Flow chart of general population screening by which cases and controls were identified from the Boston Metropolitan area, 2000–2005

*An additional 65 cases were enrolled from a clinic specializing in vulvovaginal disorders.

Table 1

Demographic and menstrual characteristics of women with and without vulvodynia

	Population based cases		Validated cases*		All cases	
	Cases (N=176) %	Controls (N=176) %	Cases (N=118) %	Controls (N=118) %	Cases (N=239) %	Controls (N=239) %
Age at interview						
<30	30.7	30.7	39.0	39.0	35.2	35.2
30–39	26.7	26.7	24.6	24.6	27.6	27.6
40–49	28.4	29.0	23.7	23.7	23.4	23.8
≥50	14.2	13.6	12.7	12.7	13.8	13.4
Reference age [†]						
<20	29.0	30.7	28.0	27.1	28.5	29.3
20–24	24.4	23.3	26.2	26.3	25.9	25.1
25–30	25.0	25.6	22.9	24.6	23.4	24.3
>30	21.6	20.4	22.9	21.0	22.2	21.3
Race						
White	88.6	83.0	93.2	90.7	90.3	85.4
Hispanic	7.4	3.4	4.2	0.8	5.9	2.9
African American	2.9	9.7	0.9	6.8	2.5	8.4
Other	1.1	4.0	1.7	1.7	1.3	3.3
Religion						
Catholic	54.0	59.1	45.8	57.6	50.6	57.3
Jewish	10.2	12.5	20.3	14.4	13.8	12.6
Protestant	17.0	14.8	14.4	11.9	15.9	14.2
Other	18.8	13.6	19.5	16.1	19.7	15.9
Education						
College	26.1	31.3	23.7	25.4	25.1	31.8
College graduate	43.2	37.5	44.9	46.6	44.4	38.5
Graduate school	31.7	31.2	31.4	28.0	30.5	29.7
Pain and difficulty with 1 st use of tampons						
Little or no difficulty and pain	8.5	13.1	24.6	12.7	15.9	13.8
Difficulty but no pain	17.0	27.3	13.6	33.0	16.7	29.3
Difficulty and pain	50.6	33.5	43.2	31.4	46.5	32.6
Never used tampons	23.9	26.1	18.6	22.9	20.9	24.3
History of childhood abuse						
Never	26.7	39.8	28.8	35.6	28.0	38.5
Moderate	35.8	40.9	47.5	47.5	40.2	41.9
Severe	31.8	14.2	18.6	11.8	26.4	14.2
Not reported	5.7	5.1	5.1	5.1	5.4	5.4

* Validated cases include the clinically identified cases and the population-based cases that were clinically confirmed.

[†] Age at first onset of vulvar pain symptoms among cases and matched reference age for controls to ensure comparable exposure assessments.

Table 2

Self-reported hives, reactions to insect stings, and seasonal allergies in women with and without vulvodinia

	Population-based cases			Clinically-confirmed cases			All cases		
	Cases	Controls	OR [†] (95%CI)	Cases	Controls	OR [†] (95%CI)	Cases	Controls	OR [†] (95%CI)
	group)	group)	%	group)	group)	%	group)	group)	%
Hives									
No history of hives	54.0	75.6	1.0	55.1	66.9	1.0	54.0	71.6	1.0
Any history of hives	46.0	24.4	3.2 (1.8-5.7)	44.9	33.1	2.0 (1.1-3.7)	46.0	28.4	2.5 (1.6-3.9)
Any hives prior to ref age [*]	35.8	15.3	3.6 (2.0-6.8)	32.2	22.9	2.0 (1.0-3.8)	34.7	18.4	2.7 (1.7-4.4)
1 episode	11.4	5.7	3.3 (1.4-8.1)	8.5	11.0	1.1 (0.4-2.7)	10.9	7.9	2.0 (1.0-3.9)
2 or more episodes	24.4	9.6	3.8 (1.9-7.7)	23.7	11.9	2.9 (1.3-6.5)	23.8	10.5	3.3 (1.8-5.9)
>Median yrs between 1st episode and ref age	23.3	5.1	6.1 (2.7-13.9)	17.0	11.9	1.7 (0.8-3.9)	20.9	8.4	3.2 (1.7-5.8)
<Median yrs between 1 st Episode and ref age	12.5	10.2	1.8 (0.8-4.2)	15.2	11.0	2.3 (0.9-5.8)	13.8	10.0	2.2 (1.1-4.3)
Allergic reaction to insect sting									
Hives only after ref age	10.2	9.1	2.2 (0.9-5.2)	12.7	10.2	2.0 (0.8-5.2)	11.3	10.0	1.9 (1.0-3.8)
No history of allergic reaction	83.5	92.6	1.0	87.3	93.2	1.0	84.9	93.3	1.0
Any history of allergic reaction	16.5	7.4	2.7 (1.3-5.6)	12.7	6.8	2.3 (0.9-5.8)	15.1	6.7	2.6 (1.4-4.9)
Stings prior to ref age [*]	13.7	7.4	2.3 (1.1-5.0)	9.3	6.8	1.4 (0.5-3.9)	12.1	6.7	2.1 (1.1-4.0)
>Median yrs between 1st episode and ref age	7.4	3.4	2.3 (0.8-6.6)	5.1	2.6	1.9 (0.4-8.2)	6.7	2.9	2.3 (0.9-5.9)
<Median yrs between 1 st Episode and ref age	6.3	4.0	2.0 (0.7-5.6)	4.2	4.2	1.2 (0.3-4.5)	5.4	3.8	1.8 (0.7-4.4)
Seasonal Allergies									
Stings only after ref age [*]	2.8	0		3.4	0		3.0	0	
No history of allergies	46.0	55.7	1.0	40.7	57.6	1.0	48.1	56.9	1.0
Any history of allergies	54.0	44.3	1.5 (1.0-2.5)	59.3	42.4	2.6 (1.3-5.0)	51.9	43.1	1.5 (1.0-2.3)
Any allergies prior to ref age [*]	38.1	25.0	2.1 (1.2-3.6)	43.2	26.3	3.1 (1.5-6.4)	38.1	25.1	2.0 (1.3-3.2)
>Median yrs between 1st episode and ref age	23.3	10.8	3.3 (1.6-7.0)	16.1	13.6	2.3 (0.9-5.8)	20.9	12.1	2.6 (1.4-4.9)
<Median yrs between 1 st Episode and ref age	14.8	14.2	1.2 (0.6-2.5)	27.1	12.7	3.9 (1.7-9.0)	17.2	13.0	1.6 (0.9-2.9)
Allergies only after ref age [*]	15.9	19.3	1.0 (0.5-1.8)	16.1	16.1	1.7 (0.7-4.1)	13.8	18.0	0.8 (0.5-1.5)

* Age at first onset of vulvar pain symptoms among cases and matched reference age for controls to ensure comparable exposure assessments.

[†] Adjusted for age, education, childhood physical victimization, and pain with first tampon use.

Table 3

Other self-reported skin conditions in women with and without vulvodynia

	Population-based cases			Clinically-confirmed cases			All cases		
	Cases Controls (N=176 per group)	%	OR (95%CI)	Cases Controls (N=118 per group)	%	OR* (95%CI)	Cases Controls (N=239 per group)	%	OR* (95%CI)
Skin rash*	51.1	58.0	1.0	52.5	61.9	1.0	54.0	59.8	1.0
No history of skin rash	48.9	42.0	1.4 (0.9 – 2.3)	47.5	38.1	1.4 (0.8 – 2.3)	46.0	40.2	1.3 (0.9 – 1.9)
Any history of skin rash	64.2	73.9	1.0	64.4	72.0	1.0	66.1	74.5	1.0
No history of mole removed	35.8	26.1	2.1 (1.2 – 3.7)	35.6	28.0	1.5 (0.8 – 2.6)	33.9	25.5	1.7 (1.1 – 2.6)
Any history of mole removed	95.5	96.0	1.0	93.2	96.6	1.0	96.2	96.2	1.0
Psoriasis diagnosed by doctor	4.5	4.0	1.2 (0.4 – 3.5)	6.8	3.4	2.2 (0.6 – 8.0)	3.8	3.8	1.1 (0.4 – 2.9)
No history of psoriasis	47.2	51.1	1.0	51.7	61.0	1.0	49.0	55.2	1.0
Any history of psoriasis	52.8	48.9	1.1 (0.7 – 1.9)	48.3	39.0	1.7 (0.9 – 3.1)	51.0	44.8	1.3 (0.9 – 2.0)
Treatment for pimples or acne									
No history of treatment									
Any history of treatment									

* Question phrased: "Have you ever had a skin rash (contact dermatitis) that was clearly related to some chemical or plant exposure? (Please include any reactions to soaps, perfumes, lotions, or plants such as poison ivy)"

† Adjusted for age, education, childhood physical victimization, and pain with first tampon use.