

The Association Between Acne Vulgaris, Acne Vulgaris with Nonspecific Facial Dermatitis, and Demodex Mite Presence

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Background: *Demodex* mites can lead to various skin disorders, from non-specific dermatitis to conditions that mimic other diseases, making it challenging to diagnose accurately. Additionally, it has been reported that *Demodex* mites can cause skin conditions such as perioral dermatitis, pustular folliculitis, pityriasis folliculorum, blepharitis, and rosacea. Due to conflicting studies, there is a debate regarding the link between *Demodex* mites and acne vulgaris. This study aims to determine the prevalence of *Demodex* mites on the faces of individuals with acne vulgaris, acne with nonspecific facial dermatitis, and healthy facial skin to clarify the association.

Materials and Methods: This observational case-control study involved 120 participants aged 18–37: 40 individuals with acne vulgaris only, 40 with acne and nonspecific facial dermatitis, and 40 healthy controls. The same dermatologist examined and diagnosed all participants to ensure accuracy before being grouped. The Standardized Skin Surface Biopsy (SSSB) method was used to detect *Demodex* mites in all three study groups. Furthermore, additional samples were collected randomly from acne lesions using the Superficial Needle Scraping (SNS) method in the two acne groups.

Results: The study found no significant difference in *Demodex* prevalence and high *Demodex* density rate between patients with only acne vulgaris and the control group ($p > 0.05$). However, acne patients with nonspecific facial dermatitis had a higher rate of *Demodex* prevalence and high *Demodex* density rate than the only acne vulgaris and control group ($p < 0.05$). The clinical symptoms of nonspecific facial dermatitis in acne patients strongly associated with *Demodex* mites are patchy red, dry, scaly skin, roughness, insect bite-like papules, and flushing.

Conclusion: *Demodex* prevalence and high *Demodex* density rate are not associated with acne vulgaris. Still, it is associated with acne and nonspecific facial dermatitis, particularly in patients with patchy redness, dry, scaly skin, roughness, insect bite-like papules, and flushing.

Keywords: acne vulgaris, demodicosis, *Demodex* mite, *Demodex folliculorum*, *Demodex brevis*

Introduction

Demodex mites are ectoparasites belonging to the family *Demodicidae* of the order Acari of the class *Arachnida*. Only two species are found in humans, *D. folliculorum* in the hair follicles and *D. brevis*, principally in the sebaceous glands. *Demodex* mites were found in most people over 60 years old (84% of the tested population) and in all people over 70 (100%).¹ The prevalence of *Demodex* mites differs in various studies based on the sensitivity of the detection method.² Studies have found that abnormal *Demodex* mite proliferation is more common in individuals who are obese, have high blood sugar levels, suffer from end-stage chronic renal failure, or have a weakened immune system. Moreover, repeated application of topical steroids and other immunomodulators on the face has been reported to increase the number of *Demodex* mites.³

An abnormal increase in the density of *Demodex* mites can cause several skin disorders grouped under the term demodicosis. Clinical presentations can vary in appearance, ranging from nonspecific facial dermatitis, such as dry, itchy, and sensitive skin, to mimicking other known skin diseases, such as eczema, seborrheic dermatitis, folliculitis, and acne vulgaris.^{3–9} This is why it is often misdiagnosed or underdiagnosed. Additionally, it has been reported that *Demodex* mite proliferation is a cause of multiple skin diseases such as pityriasis folliculorum, perioral dermatitis, pustular folliculitis, blepharitis, and rosacea.^{1,3,9–13}

The role of *Demodex* mites in acne vulgaris is still controversial. While many studies show a positive relationship between acne vulgaris and *Demodex* mite infestation, some studies deny this relationship.^{14–22} The studies showed significant heterogeneity due to differences in study design, sample size, population, and detection methods. Additionally, the subjects were not screened for nonspecific facial dermatitis other than acne vulgaris, which could have resulted in inaccurate findings because demodicosis can present with nonspecific facial dermatitis and coexist with acne vulgaris.²³

This study aims to clarify the association between acne vulgaris and *Demodex* mites by determining the prevalence of *Demodex* mites and high *Demodex* density rate on the face of individuals who have only acne vulgaris and those who have acne with nonspecific facial dermatitis in comparison to participants who have healthy facial skin.

Patients and Methods

Study Population

The study group consisted of 80 patients aged 18–37 who visited our clinic seeking consultation for acne vulgaris. All patients underwent a skin examination by a dermatologist to diagnose acne and detect coexisting nonspecific facial dermatitis. The diagnosis of acne vulgaris is based on the clinical presentation of blackheads, whiteheads, inflammatory papules, nodules, and scarring. Patients who did not have comedones were excluded. Nonspecific facial dermatitis is an abnormality of the facial skin that exhibits at least one of the following symptoms: patchy red, flushing, telangiectasia, dry, scaly skin, roughness, insect bite-like papules, itching, and stinging sensation. After conducting the skin examination, acne patients were divided into two groups of 40 each. One group presented with acne vulgaris only, while the other had acne with nonspecific facial dermatitis. The control group consisted of 40 healthy participants aged 18–37. The same dermatologist examined the facial skin of all the healthy participants, as in the case of the acne group, to ensure that they had normal facial skin and did not have acne vulgaris and nonspecific facial dermatitis.

Clinical Grading of the Acne Lesions

In both acne groups, the Investigator's Global Assessment (IGA) was used to evaluate the severity of acne vulgaris.^{24,25} This system is graded from 0–4 depending on the descriptive criteria of facial acne only. Grade 0 (Clear) indicates the absence of acne lesions, although some residual hyperpigmentation and erythema may still be present. Grade 1 (almost clear) means a few scattered comedones and small papules can be found. Grade 2 (mild) indicates less than half of the face is affected with comedones, papules, and pustules. If more than half of the face is affected with many comedones, papules, and pustules, along with one nodule, it is considered Grade 3 (moderate). Grade 4 (severe) is when the entire face is covered with comedones, numerous papules and pustules, and a few nodules and cysts.

Demodex Detection

All three study groups underwent *Demodex* mite detection using the Standardized skin surface biopsy (SSSB) method. The procedure involved collecting two samples from both cheeks by placing a 1 cm² square marked slide coated with cyanoacrylate glue onto each cheek for 60 seconds before removal. Afterward, immersion oil was applied to a slide and covered with a cover slip for microscopic examination. After examining slides from both cheeks to count mites, the average number per square centimeter was calculated by dividing the total by two.

Additionally, in the two acne groups, samples from acne lesions were randomly collected using the Superficial needle scraping (SNS) method by gently scraping five pustules with the convex surface of a number 18 needle and smearing them onto a slide. The preparation was stained with methylene blue and examined under a light microscope at 40× and 100× magnification.

A positive result of *Demodex* detection is observed under a microscope by scanning for the presence of eggs, larvae, nymphs, or adults of *D. folliculorum* or *D. brevis*. High *Demodex* density is defined as a density of *Demodex* mites higher than 5 mites/cm² observed on SSSB¹¹ or 3 mites/5 pustules on SNS.²⁶

Statistical Analysis

Descriptive data was reported in frequency and percentage. Chi-square or Fisher's exact tests were used to compare the acne vulgaris only group, acne with nonspecific facial dermatitis group with normal healthy skin group (the control). Logistic regression analysis was tested to predict *Demodex* presence and high *Demodex* density based on SSSB and SNS tests.

Results

A total of 120 participants were enrolled in this study: 40 patients with acne vulgaris only, 40 patients with acne and nonspecific facial dermatitis, and 40 healthy controls. All participants were aged 18–37 years, with 69 females and 51 males. Of 80 acne patients, 21 had mild acne, 37 had moderate acne, and 22 had severe acne, according to the IGA criteria. The common features of skin disorders in acne with nonspecific facial dermatitis group are patchy redness, dryness, scaliness, roughness, insect bite-like papules, and itchy skin, respectively. The results of SSSB and SNS reveal that the prevalence rate was 34.2%, and the high *Demodex* density rate was 20%, as shown in Table 1.

The results in Table 2 show that the group of acne with nonspecific facial dermatitis had a significantly higher *Demodex* prevalence rate (62.5%) compared to the groups with only acne vulgaris (22.5%) and the control group (17.5%) with $p < 0.001$. No significant difference was observed between the group with only acne vulgaris and the control group ($p = 0.576$).

Consistent with the *Demodex* prevalence rate, the acne with nonspecific facial dermatitis group had a significantly higher high *Demodex* density rate (40%) compared to the groups with only acne vulgaris (12.5%) and the control group

Table 1 Clinical Characteristics and *Demodex* Prevalence

Characteristics	Total (n)	Frequency	Percentage
Ranges of age (years)			
○ 18–22	120	32	26.7
○ 23–27	120	28	23.3
○ 28–32	120	35	29.2
○ 33–37	120	25	20.8
Gender			
○ Male	120	51	42.5
○ Female	120	69	57.5
Acne severity grading			
○ Mild	80	21	26.3
○ Moderate	80	37	46.2
○ Severe	80	22	27.5
Acne with nonspecific facial dermatitis			
○ Patchy red	40	32	80.0
○ Dry, scaly skin	40	22	55.0
○ Roughness	40	21	52.5
○ Insect bite-like papules	40	9	22.5
○ Itching	40	9	22.5
○ Stinging	40	7	17.5
○ Telangiectasia	40	6	15.0
○ Flushing	40	6	15.0
<i>Demodex</i> prevalence			
○ SSSB ≥ 1 mite/cm ²	120	40	33.3
○ SNS ≥ 1 mite/5 pustules	80	11	13.8
○ Combined SSSB and SNS	120	41	34.2
High <i>Demodex</i> density			
○ SSSB ≥ 6 mite/cm ²	120	23	19.2
○ SNS ≥ 3 mite/5 pustules	80	8	10.0
○ Combined SSSB and SNS	120	24	20.0

Abbreviations: SSSB, Standardized Skin Surface biopsy; SNS, Superficial Needle Scraping.

Table 2 Comparison of *Demodex* Prevalence and High *Demodex* Density Between Normal Healthy Skin, Acne Vulgaris Only, and Acne with Nonspecific Facial Dermatitis Group, Based on SSSB and SNS

SSSB / SNS	Normal Healthy Skin (n=40)	Acne Vulgaris Only (n=40)	Acne with Nonspecific Facial Dermatitis (n=40)	P value*	P value**	P value***
Demodex prevalence, n (%)						
○ SSSB ≥ 1 mite/cm ²	7(17.5)	9(22.5)	24(60.0)	0.576	<0.001	0.001
○ SNS ≥ 1 mite/5 pustules	–	3(7.5)	8(20.0)	–	–	0.096
○ SSSB and SNS	7(17.5)	9(22.5)	25(62.5)	0.576	<0.001	<0.001
High Demodex density, n (%)						
○ SSSB ≥ 6 mite/cm ²	3(7.5)	5(12.5)	15(37.5)	0.356	0.001	0.010
○ SNS ≥ 3 mite/5 pustules	–	2(5.0)	6(15.0)	–	–	0.132
○ SSSB and SNS	3(7.5)	5(12.5)	16(40.0)	0.356	0.001	0.005

Notes: P value* - Comparison between normal healthy skin group with acne vulgaris only group. P value** - Comparison between normal healthy skin group with acne and nonspecific facial dermatitis group. P value*** - Comparison between acne vulgaris only group with acne and nonspecific facial dermatitis group. Chi-square or Fisher's exact tests were used for hypothesis testing.

Abbreviations: SSSB, Standardized Skin Surface biopsy; SNS, Superficial Needle Scraping.

(7.5%), with p-values of 0.001 and 0.005, respectively. While no statistically significant differences existed between the group with only acne vulgaris and the control group ($p=0.356$).

SNS positivity was detected in 11 acne patients, of which 3 cases were from the group of patients with acne vulgaris only, and 8 cases were from the group with acne and nonspecific facial dermatitis. Among the patients with acne, 11 tested positive for SNS, out of which 10 were also positive for SSSB. Moreover, 8 cases showed high *Demodex* density. Only one case tested negative for SSSB.

Table 3 shows the logistic regression analysis results indicating no significant difference in the prevalence of *Demodex* between females (39.1%) and males (27.4%), with a p-value of 0.184. Same as the high *Demodex* density rate among females (24.6%) and males (13.7%) was also not significantly different, with a p-value of 0.145. When comparing different age groups, no significant difference was found in the rates of *Demodex* prevalence and high *Demodex* density rate among participants aged 18–37 ($p>0.05$).

In the group of acne with nonspecific facial dermatitis, patchy redness ($p<0.001$), dry and scaly skin ($p<0.001$), roughness ($p=0.001$), insect bite-like papules ($p=0.006$), and flushing ($p=0.02$) were strongly associated with *Demodex* prevalence (Figures 1–5). However, there was no significant statistical association found in clinical features such as telangiectasia ($p=0.091$), stinging ($p=0.146$), or itching ($p=0.296$).

Discussion

Demodex infestation may cause various skin disorders, with rough, dry skin with follicular scales, papules, and pustules as common clinical features.^{3,4,17} Whether *Demodex* mites are responsible for many common skin diseases is still debated. Many studies have shown a significant association between *Demodex* infestation and rosacea.^{11,27} On the other hand, dermatologists still have controversy about the role of *Demodex* mites in the development of acne, as only a limited number of studies have been conducted to establish their association.^{14–22}

This observational case-control study examined 120 participants aged 18–37: 80 patients (40 with acne vulgaris only, 40 with acne and nonspecific facial dermatitis) and 40 healthy controls.

According to this study, the prevalence rate of *Demodex* mites detected by SSSB in all three study groups was 33.3%. However, when SSSB and SNS were used together, the rate increased slightly to 34.2%. This outcome is consistent with previous studies that have reported the overall prevalence of *Demodex* mite to be around 34.8%, 40.36%, and 43%.^{15,17,20}

It was found that 13.7% of acne patients exhibited positive results for SNS. This finding is aligned with research by Huang et al, which revealed that positive SNS was observed in 14.0% of acne patients compared to 83.0% of patients

Table 3 Results of Logistic Regression Analysis of *Demodex* Prevalence and High *Demodex* Density

Characteristics	<i>Demodex</i> Prevalence n (%)	OR (95% CI)	P-value*	High <i>Demodex</i> Density n (%)	OR (95% CI)	P-value**
Range of Age (years)						
○ 18–22	9(28.1)	Reference	–	7(21.9)	Reference	–
○ 23–27	9(32.1)	1.2(0.4–3.7)	0.735	5(17.9)	0.8(0.2–2.8)	0.698
○ 28–32	11(31.4)	1.2(0.4–3.4)	0.768	7(20.0)	0.9(0.3–2.9)	0.850
○ 33–37	12(48.0)	2.4(0.8–7.1)	0.126	5(20.0)	0.9(0.2–3.2)	0.863
Gender						
○ Male	14(27.4)	Reference	–	7(13.7)	Reference	–
○ Female	27(39.1)	1.7(0.8–3.7)	0.184	17(24.6)	2.1(0.8–5.4)	0.145
Clinical characteristics in the acne with nonspecific facial dermatitis group, compared with the control group						
○ Control (healthy skin)	7(17.5)	Reference	–	3(7.5)	Reference	–
○ Patchy red	21(65.6)	9.0(3.0–26.9)	<0.001	14(43.8)	9.6(2.4–37.7)	0.001
○ Dry, scaly skin	15(68.2)	10.1(3.0–33.9)	<0.001	11(50.0)	12.3(2.9–52.2)	0.001
○ Roughness	13(61.9)	7.7(2.3–25.4)	0.001	7(33.3)	6.2(1.4–27.2)	0.016
○ Insect bite-like papules	6(66.7)	9.4(1.9–47.1)	0.006	5(55.6)	15.4(2.6–89.9)	0.002
○ Flushing	4(66.7)	9.4(1.4–62.0)	0.020	2(33.3)	6.2(0.8–48.6)	0.084
○ Telangiectasia	3(50.0)	4.7(0.8–28.4)	0.091	2(33.3)	6.2(0.8–48.6)	0.084
○ Stinging	3(42.9)	3.5(0.6–19.4)	0.146	1(14.3)	2.1(0.2–23.2)	0.560
○ Itching	3(33.3)	2.4(0.5–11.8)	0.296	1(11.1)	1.5(0.1–16.8)	0.722

Notes: *Demodex* prevalence was defined as SSSB ≥ 1 mite/cm² or SNS ≥ 1 mite/5 pustules. High *Demodex* density was defined as SSSB ≥ 6 mites/cm² or SNS ≥ 3 mites/5 pustules. P value* - Logistic regression analysis was tested to predict *Demodex* prevalence with reference group. P value** - Logistic regression analysis was tested to predict high *Demodex* density with reference group.

Abbreviation: OR, odds ratio; 95% CI or confidence interval.

with papulopustular rosacea ($P < 0.001$).²⁶ The results of SNS are lined up with those of SSSB. Of 11 SNS-positive acne patients, 10 tested positive for SSSB, and 8 had high *Demodex* density. Only one case tested negative for SSSB.

Previous studies have shown conflicting results regarding *Demodex* detection rates among males and females. Some studies show a higher prevalence of *Demodex* in males,¹⁵ while others show a higher prevalence in females.²⁸ However,



Figure 1 The left cheek has an erythematous patch with multiple small inflammatory papules and comedones. (SSSB = 9.5 mites/cm², SNS = negative /5 pustules).



Figure 2 The right cheek has dry, scaly skin with multiple whitehead comedones and inflamed papules. (SSSB = 13.5 mites/cm², SNS = negative /5 pustules).



Figure 3 The right cheek has rough skin with comedones, and some indurated inflamed papules. (SSSB = 14 mites/cm², SNS = 3 mites/5 pustules).

our study indicates no significant difference between males and females in the prevalence of *Demodex* and high *Demodex* density rate. This finding is consistent with many studies.^{15,18,19}

In terms of age, our study and Akçınar et al found no significant difference in *Demodex* detection rates across age groups.^{19,21} However, many studies found a higher prevalence of *Demodex* among older individuals.^{17,18,22,28} These different findings may be due to the different sample sizes, mean age, and age ranges of the subjects in each study.

This study reveals a significantly higher prevalence of *Demodex* in the group of acne with nonspecific facial dermatitis (62.5%) compared to the group of acne vulgaris only (22.5%) and control (17.5%). Although the prevalence of *Demodex* in the group of only acne vulgaris is higher than in the control group, it is not significantly different.

When focusing on the high *Demodex* density rate, the group of acne with nonspecific facial dermatitis still had a significantly high *Demodex* density rate of 32.5% compared to the only acne vulgaris and control group with 12.5% and 7.5%, respectively. While no statistically significant differences were found in the acne vulgaris only group and the control group.



Figure 4 The right cheek has small papules resembling insect bites, comedones, inflamed papules, and areas of hyperpigmentation from prior acne. (SSSB = 15.5 mites/cm², SNS = 4 mites/5 pustules).



Figure 5 The right cheek has comedones, inflammatory papules, and flushing. (SSSB = 10 mites/cm², SNS = negative /5 pustules).

From this information, the prevalence of *Demodex* and high *Demodex* density rate showed a strong association with the group of acne with nonspecific facial dermatitis, while no association was found in the group of acne vulgaris only.

Compared to previous research, Okyay et al found that the prevalence of *Demodex* was not significantly different between patients with acne (20.7%) and those without acne (38.6%).¹⁵ A study by Manoyana et al discovered no significant difference

in *Demodex* mite density between the acne and the control groups ($P = 0.313$).²⁰ Similarly, Skrlin et al found no significant difference in *Demodex* prevalence between the acne and control groups, with 12% in both groups.²⁹

However, a study by Zhao et al demonstrated that *Demodex* infestation was the most influential factor for developing acne vulgaris (OR = 5.565, 95% CI: 2.384–12.99 and $p < 0.001$).¹⁷ A study by Akçınar et al revealed a statistically significant difference in the prevalence of *Demodex* between the group with acne and the group without acne at 42.6% vs. 12.3% ($p < 0.001$).²¹

Regarding the high *Demodex* density rate, Maldonado-Gómez et al revealed that severe acne vulgaris was significantly associated with the high *Demodex* density rate ($P = 0.001$).³⁰ A Meta-analysis study conducted by Zhao et al concluded that acne vulgaris is associated with *Demodex* infestation and suggested examining *Demodex* mites and using acaricidal therapies if regular acne treatments are ineffective.¹⁸

Studies about the association between *Demodex* mites and acne vulgaris exhibited significant heterogeneity due to variations in sample size, study design, country, population, detection method, and performing technique. This study found no significant association between *Demodex* mite and acne vulgaris. Although some previous studies have shown a significantly higher prevalence of *Demodex* in patients with acne vulgaris, this does not necessarily mean that *Demodex* mite is a causative factor for acne vulgaris. The reasons for the high prevalence of *Demodex* in acne patients remain unknown.

There are two possible explanations for this association. One possibility is that *Demodex* mites and acne vulgaris are causally related due to several mechanisms that suggest a connection. *Demodex* mites may cause acne by blocking hair follicles. The waste products and the associated bacteria may trigger a delayed hypersensitivity reaction, eventually leading to acne development.²¹ The other possibility is that acne vulgaris causes an abnormal proliferation of *Demodex* mites. While genetics is a significant factor in *Demodex* infestation, other potential causes exist. Bacterial infections could create an environment that promotes the growth of *Demodex* and weaken the immune response by decreasing the number of NK cells or lymphocytes. These cells control the mite population in the host, and their depletion could increase *Demodex* infestation.^{3,16,31,32}

However, further studies are required in these regards.

Demodicosis can present in various ways and may be mistaken for other skin conditions. The appearance of the symptoms can range from non-specific facial dermatitis to more severe manifestations, depending on personal genetics, immunity, and the density of mites.^{2,18,31} In many cases, it may only present as nonspecific facial dermatitis, leading to underdiagnosis or misdiagnosis. This is why demodicosis has a lower incidence than it should be despite many people being infested with *Demodex* mites.^{3,18}

In this study, all participants were examined by the same dermatologist to ensure accuracy. *Demodex* infestation can be presented with nonspecific facial dermatitis and coexist with acne vulgaris, leading to inaccurate outcomes. The clinical symptoms of nonspecific facial dermatitis in acne patients that are strongly associated with *Demodex* infestation, including patchy red (OR = 9.0, 95% CI: 3.0–26.9 and $p < 0.001$), dry, scaly skin (OR = 10.1, 95% CI: 3.0–33.9 and $p < 0.001$), roughness (OR = 7.7, 95% CI: 2.3–25.4 and $p = 0.001$), insect bite-like papules (OR = 9.4, 95% CI: 1.9–47.1 and $p = 0.006$), and flushing (OR = 9.4, 95% CI: 1.4–62.0 and $p = 0.020$).

Acne patients can be infested with *Demodex* mites as the general population. Moreover, demodicosis can coexist with acne vulgaris, making diagnosis more challenging. If acne patients experience nonspecific facial dermatitis such as patchy red, dry, scaly skin, roughness, insect bite-like papules, or flushing, they should consider getting tested for *Demodex* mites because acne treatment may not improve these symptoms and can worsen demodicosis, making treatment more complicated.

There are limitations in this study that need to be taken into consideration. Firstly, the sample size is relatively small. Secondly, we only compared the prevalence and high-density rates of *Demodex* mites in different groups rather than the average *Demodex* density as in some studies. Thirdly, we did not use ether cleaning before SSSB or the two consecutive SSSB methods, which are more efficient at detecting mites than the SSSB method alone.³³ This is because Thai patients with demodicosis commonly experience irritation, bleeding, and post-inflammatory hyperpigmentation after using these methods. Additionally, this study aims to use the SSSB results for comparison with previous studies that employed this method. Lastly, the study did not separate acne patients on whether they had previously received treatment, which could possibly impact the prevalence of *Demodex* mite observed.

Conclusion

The study revealed that patients with acne vulgaris only and the control group had no significant difference in *Demodex* prevalence and high *Demodex* density rates. Patients with acne and nonspecific facial dermatitis showed significantly higher *Demodex* prevalence and high *Demodex* density rates compared to acne vulgaris only and control groups.

Therefore, *Demodex* mite is not associated with acne vulgaris. However, acne with nonspecific facial dermatitis is associated with *Demodex* mite, particularly when symptoms such as patchy redness, dry, scaly skin, roughness, insect bite-like papules, and flushing occur.

Data Sharing Statement

Unavailable data, but the reader can personally request to access the data via the personal email of the authors.

Statement of Ethics

The present study was conducted in accordance with the World Medical Association Declaration of Helsinki. All subjects had given their written informed consent, and the study protocol was reviewed and approved by the Ethical Research Committee of Mae Fah Luang University, approval number COA 140/2023.

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Disclosure

All authors had no conflicts of interest.

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