

Latex Allergy in Dental Students: A Cross-Sectional Study

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Background: Latex allergy is a major occupational health problem in health care workers who regularly use latex gloves. Dentists are one of the high risk groups for latex allergy and sensitization as it is generally found that healthcare workers (HCW) have 3 times greater prevalence of latex allergy. There are very few studies of latex allergy in HCW in Thailand.

Objective: To study the prevalence of latex-related symptoms, latex-sensitization and possible risk factors in dental students.

Material and Method: A cross-sectional study was performed on all dental students of the Faculty of Dentistry, Chulalongkorn University, during Dec 2007 to May 2008, using questionnaires and skin prick tests (SPT), using 3 latex extracts prepared from Proglove, Doctor Plus gloves and a commercial latex allergen (Stallergenes, France). SPT was done only in those who were willing and signed informed consents.

Results: There were 617 completed questionnaires (87.3%). The mean age of the volunteers was 20.9 ± 1.7 years with 29.3% male and 70.7% female. The prevalence of latex glove-related symptoms was 5.0%. These symptoms were all local, cutaneous symptoms, ranging from hand pruritus (64.5%), hand eczema (19.4%) and contact urticaria (16.1%). Eight subjects (1.3%) reported pruritus or urticaria on exposure to other rubber products while 12 subjects (1.9%) reported reactions to some fruits. The risk factors for latex-glove allergy were personal history of allergic diseases (atopic dermatitis, urticaria, pruritus and rubber allergy), duration of using gloves more than 18 hours per week, more than 3 pairs of gloves used per day and timing of glove exposure. The 4th to 6th year students were observed significantly more prevalence of symptoms than the 1st to 3rd year students (OR, 3.69; 95% CI, 1.73-7.87; $p = 0.0003$). SPT for 3 extracts of latex was done in 247 cases (40.0%); overall latex sensitization rate was 14.2%. The commercial extract had higher incidence of latex sensitization compared to the 2 gloves extract. The 1st year students had the lowest percentage of latex sensitization (3.2%) and positive skin test was significantly found in the 2nd year students (20.8%; OR, 6.46; 95% CI, 1.87-47.98; $p = 0.04$).

Conclusion: The prevalence of latex allergy in dental students is 5% and the signs and symptoms were local cutaneous reaction; pruritus, eczema and contact urticaria. The latex sensitization rate in dental students was 14.2%, which is higher than the general population. The possible risk factors included personal history of allergic diseases, duration and frequency of exposure. Therefore, primary prevention of the occupational latex allergy should be carefully considered especially concerning high risk factors.

Keywords: Latex allergy, Latex sensitization, Risk factors, Dental students

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Allergy to natural rubber latex has been known for more than 20 years. Latex allergy is a major occupational health problem in health care workers (HCW), who regularly use latex gloves^(1,2). The systemic review of the prevalence of latex allergy is 3 times higher among HCW than in the general population (4.32% vs. 1.37%)⁽³⁾. Dentists are at increased risk for latex sensitivity because they use regularly the latex gloves.

There is also a report of "Latex-fruit syndrome" in which cross-reaction with latex was observed in some fruits⁽⁴⁾. There are very few studies about the prevalence of latex allergy in HCW in Thailand^(5,6).

Objective

1. To study the prevalence of latex allergy, latex sensitization in dental students.
2. To find the risk factors for latex allergy.

Material and Method

A cross-sectional study using self-administered questionnaires in dental students at the

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Faculty of Dentistry, Chulalongkorn University was done during December 2007 to May 2008. Additional skin prick test (SPT) was performed in selected dental students.

Target population

The 707 dental students, 1st-6th year, Faculty of Dentistry, Chulalongkorn University were included. The number of the students in first, second, third, fourth, fifth and sixth year were 132, 139, 130, 105, 105 and 96 respectively. All students were included in the questionnaires part with no exclusion criteria besides those who were not willing to.

Exclusion criteria for SPT

- History of anaphylactic reaction from latex-glove allergy: vertigo, hypotension, face or eye edema.
- Having underlying diseases that need regular medications.
- Fever or illness on the day of testing.
- On anti-allergic drugs within the past 7 days

The dental students, 1st-6th year, were enrolled. Informed consent was obtained before answering the questionnaires and SPT. The questionnaires included basic demographic information, year of study, prior allergic symptoms, family history, latex-exposed allergic symptoms, details of latex exposure, history of other rubber products allergy and fruit-related latex allergy.

SPT was performed using 3 kinds of extracts (2 kinds extracted from normally used gloves in the Faculty: Proglowe, Doctor Plus and the other commercial latex allergen (*Hevea brasiliensis*), Stallergenes, France). Histamine base and normal saline solution were used for positive control and negative control. The glove extracts were prepared by Turjanmaa and Fink's method^(7,8). The wheal size ≥ 3 mm or equal/bigger than the positive control was defined positive. The standby Emergency Department staff and emergency kits were available for immediate resuscitation in case of anaphylaxis or serious complications after the SPT.

Statistical analysis

Data analysis was done by using SPSS for window version 10.0 and Epi Info version 3.3.2. Chi-square test and t-test was used for continuous variable data. P-value < 0.05 was considered statistically significant.

Results

A total of 617 (87.3%) out of 707 of dental

students completed the questionnaires and among these students, 247 (40%) had SPT done (Fig. 1). There were 87.3% male and 29.3% female. The male: female ratio was 1:2.4. The mean age was 20.9 ± 1.7 years old. The percentage of students, 1st-6th year, who completed the questionnaires were 92.4, 91.4, 93.6, 97.1, 61.9 and 82.3% respectively, and for SPT were 25.4, 37.8, 42.6, 44.1, 58.5 and 41.8% respectively (Fig. 1). History of allergic diseases, allergic rhinitis, urticaria, atopic dermatitis, drug allergy, asthma, food allergy, allergic conjunctivitis, fruit-related latex allergy and rubber allergy were found in 54%, 65.2%, 28.2%, 22.5%, 14.1%, 9.9%, 8.7%, 7.8%, 3.6% and 2.4%, respectively. Thirty-one students (5.0%) reported latex allergy (Table 1) and the reactions reported were only cutaneous reactions as 20 (64.5%) hand pruritus with or without rash, 6 (19.4%) hand eczema and 5 (16.1%) contact dermatitis (Table 2).

Comparison between those with and without latex glove allergy is shown in Table 3. There were significant differences in age ($p < 0.0001$), underlying allergic history ($p = 0.002$), atopic dermatitis ($p = 0.0004$), urticaria ($p = 0.028$), pruritus ($p < 0.0001$), timing of glove exposure, more than 18 hours per week ($p < 0.0001$), number of gloves used, more than 3 pairs per day ($p = 0.002$) and year of study, more observed in 3rd year up ($p < 0.0001$).

Skin prick test (SPT)

Two hundred and forty-seven out of 617 students (40.0%) underwent skin prick test. Positive skin test (latex sensitization) was reported 14.2% (at least 1 kind of latex extract), 11.3% with commercial

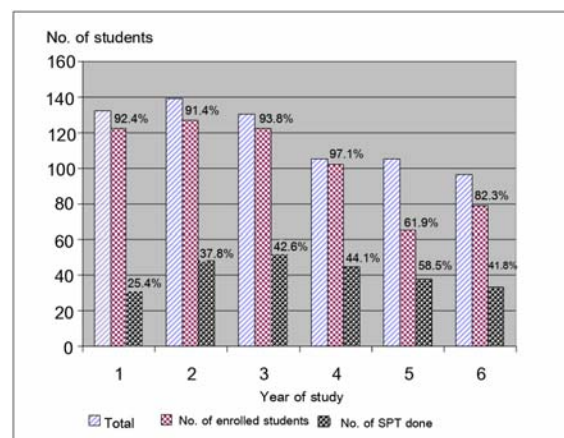


Fig. 1 Numbers of students enrolled and underwent skin prick test distributed by year of study

Table 1. Demographic data of all participants and students with/without SPT

Characteristics		Participants n = 617	SPT done n = 247 (40.0%)	SPT- not done n = 370 (60.0%)	p-value
1. Gender:	Male	181 (29.3%)	79 (32.0%)	102 (27.6%)	0.238
	Female	436 (70.7%)	168 (68.0%)	268 (72.4%)	
2. Mean age (years)		20.87 ± 1.79	21.20 ± 1.73	20.65 ± 1.81	0.203
3. Previous allergic diseases					
Yes		333 (54.0%)	139 (56.3%)	194 (52.4%)	0.348
Asthma		33 (9.9%)	12 (8.6%)	21 (10.8%)	0.658
Allergic rhinitis		217 (65.2%)	84 (60.4%)	133 (68.6%)	0.621
Allergic conjunctivitis		26 (7.8%)	15 (10.8%)	11 (5.7%)	0.060
Atopic dermatitis		75 (22.5%)	25 (18.0%)	50 (25.7%)	0.206
Urticaria		94 (28.2%)	43 (30.9%)	51 (26.3%)	0.220
Pruritus		27 (8.1%)	11 (7.9%)	16 (8.2%)	0.939
Drug allergy		47 (14.1%)	17 (12.2%)	30 (15.5%)	0.574
Food allergy (except fruit)		29 (8.7%)	11 (7.9%)	18 (9.3%)	0.813
Rubber allergy		8 (2.4%)	3 (2.2%)	5 (2.6%)	0.747
Fruit related-latex allergy		12 (3.6%)	9 (6.5%)	3 (1.5%)	0.008*
4. Allergic diseases in family					
Yes		286 (46.4%)	116 (47.0%)	170 (45.9%)	0.804
5. Latex-glove allergy					
No		586 (95.0%)	233 (94.3%)	353 (95.4%)	0.550
Yes		31 (5.0%)	14 (5.7%)	17 (4.6%)	
6. Year of study (1 st -6 th year)		3.16 ± 1.65	3.45 ± 1.58	2.97 ± 1.66	0.346

*significant

Table 2. Results of skin prick test in volunteers with different symptoms of latex allergy

Symptoms	SPT done n (%)	Result of SPT	
		SPT +ve (%)	SPT -ve (%)
1. Hand pruritus with or without rash	9 (29.0)	1 (7.14)	8 (57.14)
2. Hand eczema	2 (6.5)	1 (7.14)	1 (7.14)
3. Contact urticaria	3 (9.7)	1 (7.14)	2 (14.3)
Total n = 31	14 (45.2)	3 (21.42)	11 (78.58)

latex extract, 4.1% with extract from “PROGLOVE”, 3.2% with “DOCTOR PLUS” and 0.8% with all 3 kinds of extracts (Table 4). In 31 students with latex allergy symptoms, only 14 students had SPT done (45.2%) and only 3 had positive SPT (21.4%) (Table 2). Comparison of those with positive and negative SPT, there were no significant differences in demographic data such as age, gender, allergic history (including family history), duration of glove exposure, number of gloves used per day and year of study (Table 5). There was no serious complication during the testing.

The relationship between the prevalence of latex-glove allergy, latex sensitization and year of study was observed (Fig. 2). The prevalence of latex-glove allergy in students in 1st-3rd yrs and 4th-6th yrs were 2.4% and 8.9% respectively (OR 3.69, 95% CI 1.73-7.87, p = 0.0003). Latex sensitization increased significantly between 1st yr and 2nd year students (OR = 6.46, 95%CI 1.57-47.98, p = 0.04). There was no significant difference in latex sensitization with other years of study, 2nd-6th year.

There were 8 students (1.3%) having a history

Table 3. Demographic data of students with and without latex-glove allergy

Characteristic		Latex glove allergy n = 31	No latex glove allergy n = 586	OR	95% CI	p-value
1. Gender:	Male	5 (16.1%)	176 (30.0%)	2.16	0.18, 1.19	0.097
	Female	26 (83.9%)	410 (70.0%)			
2. Mean age (years)		22.03 ± 1.64	20.81 ± 1.78		-1.87, -0.58	< 0.0001*
3. Previous allergic history						
Yes		23 (74.2%)	310 (52.9%)	2.45	1.11, 5.4	0.02*
Asthma		1 (4.3%)	32 (10.3%)	0.59	0.08, 4.19	1.0
Allergic rhinitis		11 (47.8%)	206 (66.5%)	1.01	0.49, 2.08	0.97
Allergic conjunctivitis		1 (4.3%)	25 (8.1%)	0.76	0.11, 5.34	1.0
Atopic dermatitis		10 (43.5%)	65 (21.1%)	3.44	1.69, 7.02	0.0004*
Urticaria		9 (39.1%)	85 (27.4%)	2.28	1.08, 4.79	0.028*
Pruritus		6 (26.1%)	21 (6.8%)	5.24	2.35, 11.7	< 0.0001*
Drug allergy		3 (13.0%)	44 (14.2%)	1.30	0.41, 4.12	0.723
Food allergy (except fruit)		4 (17.4%)	25 (8.1%)	3.00	1.13, 8.02	0.051
Rubber allergy		3 (13.0%)	5 (1.6%)	8.16	3.11, 21.41	0.005*
Fruit allergy		1 (4.3%)	11 (3.5%)	1.68	0.25, 11.33	0.464
4. Allergic diseases in family						
Yes		17 (54.8%)	269 (45.9%)	1.41	0.71, 2.80	0.331
5. Duration of latex exposure						
hr/wk		18.58 ± 12.0	10.03 ± 11.29		-12.72, -4.38	< 0.0001*
6. Number of gloves use						
Pairs/day		2.92 ± 1.77	1.79 ± 1.98		-1.85, -0.39	0.002*
7. Skin prick test						
skin test +ve		17 (54.8%)	353 (60.2%)	1.65	-1.81, -0.64	0.43
8. Year of study (1 st -6 th)		4.32 ± 1.51	3.09 ± 1.63			< 0.0001*

*significant

Table 4. Skin prick test of 3 kinds of latex extracts (n = 247)

Kinds of latex extracts	Number of positive	% of SPT-positive
Latex extract "DOCTOR PLUS"	8	3.2
Latex extract "PROGLOVE"	10	4.0
Commercial latex extract	28	11.3
All 3 extracts	2	0.8
At least 1 extract	35	14.2

of other rubber products allergy, of which 3 also had latex-glove allergy (only 1 has positive SPT) (Table 6). Twelve students (1.9%) reported fruit-related latex allergy. Fruit-related latex allergy was kiwi, papaya, chestnut, dragon fruit, pineapple and longan; 9 out of 12 students underwent SPT and the results were all negative (Table 7).

Discussion

The prevalence of latex allergy in dental

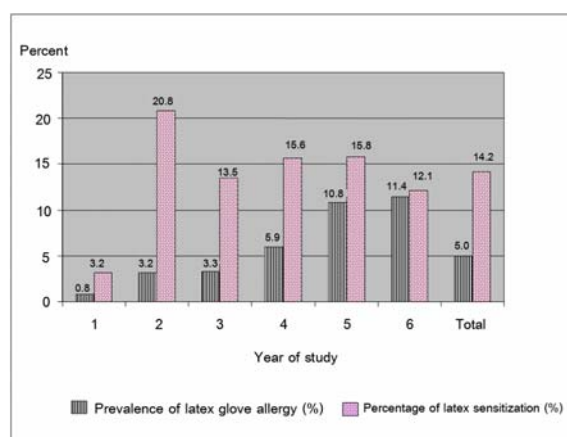
practitioners was 9-24%⁽⁹⁻¹¹⁾ and 6.2-18.5% in dental students^(12,13). Tarlo et al reported 24% in prevalence of latex allergy and 10% in latex sensitivity in dental students and staff in Canada⁽⁹⁾. In Thailand, Chalitangkul G reported 7.6% in dental students, 4th-6th yr at Mahidol University⁽⁵⁾. The present study showed 5.0% prevalence of latex allergy in dental students in 1st-6th yr and 8.9% in students 4th-6th yr, which is higher than the previous study, but lower than other studies done in dental professionals, which means that timing

Table 5. Comparison between students with SPT-positive and SPT-negative

Characteristic	SPT-positive n = 35	SPT-negative n = 212	OR	95% CI	p-value
1. Gender: Male	10 (28.6%)	69 (32.5%)	1.18	0.59, 2.33	0.64
Female	25 (71.4%)	143 (67.5%)			
2. Mean age (years)	21.51 ± 1.70	21.14 ± 1.73		-0.96, 0.20	0.20
3. Previous allergic history			1.04	0.56, 1.93	0.91
Yes	20 (57.1%)	119 (56.1%)			
4. Allergic history in family			0.66	0.36, 1.24	0.19
Yes	20 (57.1%)	96 (45.3%)			
5. Duration of glove exposure hr/wk	13.91 ± 11.89	11.95 ± 11.71		-6.01, 2.09	0.34
6. Number of gloves used pairs/day	1.90 ± 1.33	2.11 ± 2.0		-0.47, 0.90	0.54
7. Reported symptom related to wearing gloves			1.56	0.54, 4.47	0.43
Yes	3 (8.6%)	11 (5.2%)			
8. Year of study (1 st -6 th)	3.66 ± 1.49	3.40 ± 1.60		-0.79, 0.28	0.35

Table 6. Allergic reaction from other rubber products

Rubber products	n = 8	Symptoms	Latex allergy n = 3	SPT n = 3
Elastic band	2 (25%)	Itching	1	not done
Rubber band	1 (12.5%)	Contact urticaria	-	positive
Plaster	1 (12.5%)	Rash, itching	-	not done
Rubber shoes	2 (25%)	Contact itching	1	positive (not done 1)
Elastic in lingerie	2 (25%)	Urticaria	1	negative (not done 1)

**Fig. 2** Year of study distribution of latex allergy prevalence and latex sensitization

of exposure is an important risk factor to develop allergic symptoms. Reported clinical manifestations of latex

allergy included cutaneous reactions, which is the most common (irritant contact dermatitis, allergic contact dermatitis, contact urticaria), rhino-conjunctivitis, asthma and anaphylaxis⁽¹⁵⁻²³⁾, but only cutaneous reactions were observed in the present study.

The risk factors for latex glove allergy in the present study were similar to other studies^(5,9,13,14). This included previous history of atopy, eczema and longer exposure to latex gloves. The present study showed latex allergy is related to its exposure, *i.e.* duration of using gloves more than 18 hours per week, more than 3 pairs of gloves used per day and timing of glove exposure. Prevalence of latex-glove allergy was increased with years of study (Fig. 2). Percentage of latex-glove allergy in 4th-6th year students was significantly increased compared with 1st-3rd year students (OR = 3.69, 95% CI 1.73-7.87, *p* = 0.0003). It is because the 4th-6th year is a clinic course and pre-clinic course in 1st-3rd year. In 1st-3rd year, the number of gloves

Table 7. Allergic reactions with fruit-related (negative-SPT in 9 cases)

Fruit	n = 12 (%)	Symptom	Latex-glove allergy n = 1
Kiwi fruit	4 (33.3%)	Mouth, throat itching	
Papaya	4 (33.3%)	Lip, throat itching, lip swollen (1 case)	Hand urticaria (1 case)
Chestnut	1 (8.3%)	Not specified	
Dragon fruit	1 (8.3%)	Body itching	
Pineapple	1 (8.3%)	Throat itching	
Longan	1 (8.3%)	Lip, palate itching	

used per day is 0-2 pairs, and duration of using gloves 0-10 hours/week, compared with 2-5 pairs/day and duration 10-35 hours/week in the 4th-6th year students.

The latex sensitization (positive-skin prick test) was 14.2% (at least 1 extract). The positive-SPT in the 2 kinds of normally used gloves was 7.3%, even though the authors extracted the gloves by using the reliable method recommended by Turjanmaa and Fink. The positive-SPT increased to 11.3% with standard commercial extract. This suggests that the commercial extract is more sensitive to detect the reaction. Among 31 students with latex allergic symptoms, 14 (45.2%) had SPT done and only 3 (21.4%) had positive-SPT. This was because SPT detected IgE-mediated reaction, but the presented students had cutaneous reactions which was non IgE-mediated reaction. The 1st year students had the lowest percentage of latex sensitization (3.2%) with 20.8% in 2nd year students ($p = 0.04$), but not different with other years (Fig. 2). The 1st year students had less clinical courses and the 2nd year students were starting their clinical courses. This suggests that latex sensitization begins at the 2nd year of study.

Comparison with positive-SPT and negative-SPT students, there was no correlation with other risk factors for latex sensitization in the present study (Table 5). This is because the number of SPT done was only 40.0% and the most common cutaneous reaction: irritant contact dermatitis and allergic contact dermatitis, which are non-IgE-mediated reaction that makes negative-SPT, or level of latex-specific IgE is too low in mild cases that makes negative-SPT.

Clinical implication

Latex allergy is a major occupational health problem in health care workers, especially dentists and surgeons. For those with IgE-mediated latex-glove reaction, they have to use non-latex glove which is more expensive and has less elasticity than latex-

glove⁽¹⁶⁾. Free-powdered or low protein latex-glove are recommended in those with having contact dermatitis or no symptoms to prevent and decrease latex sensitization^(24,25).

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Potential conflicts of interest

None.

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การศึกษาการแพ้ภูมิตัวเองของนิสิตคณะทันตแพทยศาสตร์

มุกดา หวังวิวัฒนา, จินตนา ศิริกุล, ทศลาภา แดงสุวรรณ

ภูมิหลัง: การแพ้ภูมิตัวเองเป็นปัญหาสำคัญในบุคลากรทางการแพทย์ซึ่งมีการใช้ภูมิตัวเองในการทำงานเป็นประจำ ความชุกของการแพ้ภูมิตัวเองในบุคลากรทางการแพทย์พบสูงเป็น 3 เท่าของประชากรทั่วไป ทันตแพทย์เป็นบุคคลที่มีความเสี่ยงในการเกิดอาการแพ้ภูมิตัวเองและ latex sensitization ทำให้มีการศึกษาและนำวิธีการป้องกันตั้งแต่วัยยังไม่เกิดปัญหาในขณะที่เป็นนักศึกษาทันตแพทย์ แต่การศึกษาความชุกของการแพ้ภูมิตัวเองในกลุ่มนี้ยังมีไม่มากนักในประเทศไทย

วัตถุประสงค์: เพื่อศึกษาความชุกของอาการแพ้ภูมิตัวเอง latex sensitization และปัจจัยเสี่ยงในนิสิตคณะทันตแพทยศาสตร์

วัสดุและวิธีการ: ทำการศึกษาแบบ cross-sectional study ที่คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ระหว่างเดือนธันวาคม พ.ศ. 2550 ถึง พฤษภาคม พ.ศ. 2551 โดยการตอบแบบสอบถาม และทำการทดสอบผิวหนังด้วยวิธีสะกิด (skin prick test) ด้วยน้ำยาสกัดจากภูมิตัวเอง 2 ชนิดที่นิสิตใช้เป็นประจำและน้ำยา commercial latex extract (Stallergenes, France)

ผลการศึกษา: นิสิตเข้าร่วมการวิจัยโดยการตอบแบบสอบถาม 617 ราย (ร้อยละ 87.3) เป็นเพศหญิงร้อยละ 70.7 เพศชายร้อยละ 29.3 อายุเฉลี่ย 20.9 ± 1.7 ปี ความชุกของอาการแพ้ภูมิตัวเองเท่ากับร้อยละ 5.0 อาการที่พบทั้งหมดเป็นอาการทางผิวหนัง โดยพบอาการคันที่มือมากที่สุด คือร้อยละ 64.5 รองลงมาคือ ผื่นคันที่มือ (hand eczema), ผื่นลมพิษจากการสัมผัส (contact urticaria) พบร้อยละ 19.4 และ 16.1 ตามลำดับ พบผู้ที่มีอาการแพ้ผลิตภัณฑ์อื่นที่ทำด้วยยาง 8 ราย (ร้อยละ 1.3) โดยมีอาการคันและผื่นลมพิษเมื่อสัมผัสผลิตภัณฑ์จากยาง และพบผู้ที่มีปฏิกิริยาเมื่อรับประทานผลไม้บางชนิด 12 ราย (ร้อยละ 1.9) ปัจจัยเสี่ยงต่อการเกิดอาการแพ้ภูมิตัวเอง ที่พบได้แก่ประวัติการเป็นโรคภูมิแพ้มาก่อนที่จะเข้ามาเป็นนิสิต โดยเฉพาะโรค atopic dermatitis, ลมพิษ คันที่ผิวหนังโดยไม่มีผื่น และประวัติการแพ้ผลิตภัณฑ์ที่ทำด้วยยาง ระยะเวลาที่ใช้ภูมิตัวเองมากกว่า 18 ชั่วโมงต่อสัปดาห์ จำนวนภูมิตัวเองที่ใช้มากกว่า 3 คู่ต่อวัน และระยะเวลาที่มีโอกาสสัมผัสภูมิตัวเองโดยพบว่า นิสิตชั้นปีที่ 4 ถึง 6 มีความชุกของอาการแพ้ภูมิตัวเองสูงกว่านิสิตชั้นปีที่ 1 ถึง 3 อย่างมีนัยสำคัญ (OR, 3.69; 95% CI, 1.73-7.87; $p = 0.0003$) มีการทดสอบผิวหนังในนิสิต 247 ราย (ร้อยละ 40.0) อัตราการเกิด latex sensitization เท่ากับร้อยละ 14.2 อัตราการเกิด latex sensitization ในนิสิตชั้นปีที่ 1 ต่ำที่สุด คือร้อยละ 3.2 แตกต่างจากนิสิตชั้นปีที่ 2 ซึ่งมีอัตราการเกิด latex sensitization ร้อยละ 20.8 อย่างมีนัยสำคัญทางสถิติ (OR, 6.46; 95% CI, 1.87-47.98; $p = 0.04$)

สรุป: ความชุกของการแพ้ภูมิตัวเองในนิสิตคณะทันตแพทยศาสตร์เท่ากับร้อยละ 5 อาการแพ้เป็นอาการทางผิวหนังทั้งหมดคือ อาการคัน ผื่นและลมพิษบริเวณที่สัมผัส พบอัตราการเกิด latex sensitization ร้อยละ 14.2 ซึ่งสูงกว่าในประชากรทั่วไปปัจจัยเสี่ยงที่ทำให้เกิดอาการแพ้ภูมิตัวเอง คือ ประวัติการเป็นโรคภูมิแพ้มาก่อนที่จะเข้ามาเป็นนิสิต ระยะเวลาการทำงานที่ใช้ภูมิตัวเอง ดังนั้นควรจะได้พิจารณาถึงวิธีการป้องกันโดยเฉพาอย่างยิ่งในกลุ่มที่มีความเสี่ยงเพื่อมิให้เกิดปัญหาที่รุนแรงต่อไป
