# Sensitisation to natural rubber latex: an epidemiological study of workers exposed during tapping and glove manufacture in Thailand

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**Abstract**

***Objectives*—To estimate the prevalence of sensitisation to natural rubber latex in latex tappers and latex glove factory workers, and to relate this to airborne exposure to latex.**

***Methods*—Five hundred workers employed in three latex glove factories, 314 tappers, and 144 college students (control group) were studied. The workers in the glove factories were classified into three exposure groups; high, moderate, and low. Personal exposures to natural rubber latex aeroallergens were measured by immunoassay. Symptom questionnaires and skin prick tests with latex allergens (Stallergènes 1:200 w/v) and other common environmental allergens were performed. The criterion for positivity was a wheal reaction at least 3 mm in diameter greater than that to a diluent control.**

***Results*—The geometric mean (GM) concentration of latex in air was 15.4 µg/m$^3$ for those employed in glove stripping, glove inspections, and packing of powdered gloves. The moderate exposure glove manufacturing group and the tappers had GM concentrations of 2.3 and 2.4 µg/m$^3$ respectively, compared with United Kingdom users of latex powdered gloves,who had GM concentrations of 0.5 µg/m$^3$. The prevalence of sensitisation to latex in the tappers and latex glove factory workers was 1.3% and 1.7% respectively. No positive cases were found among the college students. Workers who showed a positive skin prick test to latex were more likely to be atopic. Work related respiratory and dermatological symptoms were found in about 20% of each population studied, but were not related to the presence of positive latex prick tests.**

***Conclusions*—This study suggests that in the Thai latex industries, latex sensitisation is rare despite high concentrations of airborne exposure and is less prevalent than in the healthcare sector in Europe where skin exposure is greater.**

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Keywords: natural rubber; latex; allergy; glove factory; healthcare

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The use of natural rubber latex gloves began early in the 1900s,[1] and today they are regarded as indispensable in surgical procedures. Their use has increased with the rising awareness of acquired immune deficiency syndrome (AIDS), and has been associated with an increase in allergic reactions to their ingredients.[2–7] In the first two decades after latex gloves were introduced, it became apparent that rubber products can induce contact dermatitis. As well as irritant dermatitis due to the effects of glove occlusion, delayed type allergy to accelerators, particularly the thiuram group, has been recognised as a major effect from the use of rubber gloves for decades. Little was known about other consequences of latex allergy before 1979, when Nutter[8] reported the first case of immediate contact urticaria on the hands after the use of latex household gloves. It soon became evident that contact urticaria from rubber gloves not only causes itching but can even give rise to life threatening symptoms.[9–11] The prevalence of latex sensitisation amongst healthcare workers ranges from 3% to 22%, much of the variability being due to the use of non-standardised allergen extracts.[5 12–21] This could also be due to the use of gloves with different concentrations of allergen as there are great variations between allergen concentrations in gloves from different manufacturers. There are three studies in glove manufacturers: the prevalence of positive latex skin prick tests (SPT) was 11% in Canada[22] (4.7% if a >3 mm rather than >2 mm wheal was used); 2% in various factories in Malaysia;[23] and a small study showed that one out of 17 had a skin prick test positive to latex and had symptoms compatible with occupational asthma.[24] All used non-standardised extracts. There are no reports of the prevalence of sensitisation to natural rubber latex in tappers. These rates are low compared with the prevalence in healthcare workers who are exposed to subjectively lower concentrations of aeroallergens . We set out to compare the level of latex sensitisation with a well standardised allergen extract with concentrations of latex in air among latex glove manufacturers and latex tappers.

## Methods

### STUDY POPULATION

This is a cross sectional study of the current employees of three factories that manufactured natural rubber latex examination gloves and a group of workers from 10 rubber plantations in Thailand. A group of vocational college students in Thailand was also included as a control. Ten factories manufacturing examination gloves that employed over 50 workers were identified from Ministry of Industry lists in

Rayong and Chonburi; the three nearest to Mabtaphut without known health problems were selected for study. The original protocol included a group of healthcare workers in the United Kingdom. Their consent rate to skin prick testing was only 16%, so their results have been omitted from this paper, but their air measurements are included for comparison.

A total of 475 rubber plantation workers (tappers) were recruited. They are involved in the tapping and collecting of fresh latex and mixing it with ammonia. The fresh latex from these rubber plantations is tapped from the *Hevea brasiliensis*, clone RRIM 600 (Rubber Research Institute of Malaysia 600).

All 583 workers in the three latex factories where examination gloves were made were invited to participate in the study. These workers included both production and non-production workers. The production workers mainly manipulated latex gloves by stripping gloves from the glove moulds, inspecting the gloves, and packing them into branded boxes. Almost all other production processes were mechanised.

Control subjects were recruited from a vocational college in Udornthani province, in an area without a latex industry, and with only one rubber plantation tapped for the first time in the year of the study. All 144 students studying commerce, clothing and textiles, and home economics participated.

### EXPOSURE GROUPS

Airborne exposure categories were derived from factory walk through surveys and discussions with workers, supervisors, and managers. Workers were classified into the high air exposure group when all of the following criteria were met: manipulating many gloves, continuously working on the same tasks throughout the working shift, working in an environment where high levels of powder dust were visible, working in areas without local exhaust ventilation. High exposure included glove stripping, inspection, powdered glove packaging, turning gloves inside out, and curing. No workers were wearing adequate respiratory protective devices, those without any respiratory protective device in the moderate exposure areas were reclassified to high exposure. The moderate exposure group included other production tasks—such as non-powdered glove packaging and laboratory work. Workers employed in the offices, the stores, or employed as drivers and office housekeepers were classified into the low exposure group. All the rubber plantation workers were classified as belonging to the moderate exposure group. Skin exposure was subjectively much lower than in healthcare workers to all jobs. Tapping involved some exposure as did packaging and turning gloves inside out; however, in no case was latex applied directly to the skin as is the case in glove users.

### AIR SAMPLING AND ANALYSIS

Personal air samples for natural rubber latex aeroallergens were collected by drawing air through polytetrafluoroethylene (PTFE) filter cassettes. A 25 mm PTFE filter with a pore size of 1 μm supplied by Millipore Limited (Milton Keynes, UK) was loaded in an Institute of Occupational Medicine (IOM) sampling head attached to a medium flow rate pump (SKC, USA). The air samples were drawn at the flow rate of 2 l/min. Samples were obtained from 22 workers in two plantations and 61 workers from the three glove factories.[25] Fourteen personal sample air measurements were collected from nurses in high exposure areas (operating theatres, and intensive care) and 12 from workers in general wards in the United Kingdom hospital. Eight control blanks were also incorporated. After the collection of air samples, the sampled filters were eluted and a competitive inhibition radioimmunoassay was employed to measure latex aeroallergens, with a pool of serum from healthcare workers with latex sensitisation.[25]

### SKIN PRICK TESTING

Skin prick tests were performed by a trained nurse with (*a*) natural rubber latex reagent (Stallergènes, SA, Fresnes, France 1:200 w/v); (*b*) common inhalable allergens; cat allergen; mixed grass allergens and *Dermatophagoides pteronyssinus* (Allergopharma Joachim Ganzer KG, Germany); (*c*) histamine hydrochloride (1 mg/ml); and (*d*) a diluent control. A reading on the maximal wheal diameter on a wheal diameter reading plate (Bio Diagnostics Limited, Worcestershire, UK) was made after 15 minutes. A wheal 3 mm larger than the diluent control with a positive histamine reaction was considered a positive response. Also recorded were 2 mm latex wheals. Workers with a >3 mm wheal to at least one of the common inhalant allergens were defined as atopic.

### QUESTIONNAIRE

A questionnaire in Thai was modified from the European standard questionnaire for occupational respiratory diseases and occupational asthma (European Community respiratory health survey-screening questionnaire, 1986). It included questions to determine symptoms of rhinitis, conjunctivitis, and asthma with supplementary questions to detect urticaria and dermatitis. Other questions including personal history of atopic disease, smoking, history of symptoms related to latex products, and frequency of domestic use of rubber gloves were also included. Symptoms were considered to be work related if they were stated to improve over weekends or during holidays. Work related breathlessness or wheezing was regarded as work related asthma. Symptoms of itchy, irritated, or watery eyes were regarded as conjunctivitis. For urticaria, the symptoms described in the questionnaire were itchy red rash.

### DATA HANDLING AND STATISTICAL ANALYSIS

The SPSS-PC statistical program (a registered trademark of SPSS UK) was used to analyse all data. Data were analysed for the point prevalence of latex sensitisation with a 95% confidence interval (95% CI) with the descriptive statistics module. Comparison between

*Table 1 Characteristics of the participants*

| | Tappers | Glove factory 1 | Glove factory 2 | Glove factory 3 | Students |
|---|---|---|---|---|---|
| Total population | 475 | 273 | 80 | 230 | 144 |
| Number seen | 314 | 221 | 75 | 204 | 144 |
| Response rate (%) | 66.1 | 80.9 | 93.8 | 88.7 | 100 |
| Age (y, mean (SD)) | 38.4 (11.2) | 26.8 (8.9) | 25.3 (8.4) | 22.5 (6.5) | 16.3 (1.1) |
| Female (n (%)) | 183 (58.3) | 182 (82.4) | 67 (89.3) | 183 (89.7) | 138 (95.8) |
| Duration of exposure (y, mean (SD)) | 14.4 (10.5) | 2.9 (2.7) | 2.5 (2.3) | 1.0 (1.2) | NA |
| Smoking (n (%)): | | | | | |
| Current smoker | 51 (16.4) | 53 (24) | 10 (13.3) | 32 (15.7) | (0) |
| Ex-smoker | 11 (3.5) | 2 (0.9) | 0 | 4 (1.9) | (0.9) |
| Non-smoker | 252 (80.1) | 166 (75.1) | 65 (86.7) | 168 (82.4) | (99.1) |
| Atopy (%) | 98 (31) | 45 (22) | 18 (25) | 75 (37) | 20 (14) |

NA=not applicable.

*Table 2 Characteristics of the participating factory workers by exposure group*

| | Exposure group: High | Moderate | Low |
|---|---|---|---|
| Number (%) | 323 (64.6) | 114 (22.8) | 63 (12.6) |
| Age (y, mean (SD)) | 24.3 (7.5) | 24.7 (7.3) | 27.4 (9.4) |
| Female | 310 (96.0) | 79 (69.3) | 43 (68.3) |
| Duration of exposure (y, mean (SD)) | 2.04 (2.3) | 1.9 (2.3) | 2.2 (2.6) |
| Smoking (n (%)) | | | |
| Current smoker | 36 (11.1) | 31 (27.2) | 28 (44.4) |
| Ex-smoker | 2 (0.6) | 3 (2.6) | 1 (1.6) |
| Non-smoker | 285 (88.2) | 80 (70.2) | 34 (54.0) |
| Atopy (skin prick test, n (%)) | 84 (26.0) | 29 (25.4) | 25 (39.7) |

groups was made by $\chi^2$ tests with Mantel-Haenszel $\chi^2$ for linear by linear association and Fisher's exact test for categorical variables. A value of $p \leq 0.05$ was considered to be significant.

The study protocol was approved by the ethics committee of the South Birmingham Health Authorities. All workers gave consent for the study.

## Results

### PARTICIPANTS

The characteristics of the populations under study and the response rates are shown in table 1. The overall response rate was 80%. The groups were not well matched for several of the variables. The tappers were older than the glove manufacturers who were older than the college students. There were more men than women among tappers than the other groups. There were few smokers in any group; college students were less atopic than the other groups, therefore at least smoking was well matched. Table 2 shows characteristics of the participating glove factory workers by exposure group. Most workers were in the high exposure group (64.6%). The mean age was similar in the three exposure groups. There were more women in the high exposure group and more smokers and atopic people in the low exposure group. Workers in all exposure groups had similar duration of exposure.

*Table 3 Measurement of latex allergen in air*

| Workplace | Exposure group | Samples n | Natural rubber latex aeroallergen (µg/ml): Geometric mean | GSD |
|---|---|---|---|---|
| Glove manufacturers | High | 40 | 15.4 | 2.46 |
| | Moderate | 15 | 2.3 | 3.09 |
| | Low | 6 | 1.0 | 4.18 |
| Rubber plantations | Moderate | 21 | 2.4 | 2.02 |
| United Kingdom hospital | High | 12 | 0.4 | 3.3 |
| | Low | 15 | 0.5 | 2.6 |

*Table 4 Positive skin prick tests to latex*

| | Exposure group | Wheal ≥ 3 mm n (%) | Wheal ≥ 2 mm n (%) |
|---|---|---|---|
| Glove manufacturers | High | 4 (1.3) | 27 (8.8) |
| | Moderate | 4 (2.4) | 7 (6.3) |
| | Low | 0 | 5 (7.9) |
| Rubber plantations | Moderate | 4 (1.3) | 21 (6.7) |
| College students | None | 0 | 2 (1.4) |

### MEASUREMENTS OF LATEX IN AIR

The air measurements were not normally distributed and geometric mean values by exposure group are shown in table 3. The result confirmed the correct categorisation of workers into the three different exposure groups. The concentrations were all high compared with areas of high powdered glove use in the United Kingdom hospital. The tappers had similar concentrations of exposure in air to the moderate group of glove manufacturers.

### PREVALENCE OF POSITIVE SKIN PRICK TEST TO NRL

Among those surveyed 96% of glove factory workers and all tappers and unexposed college students underwent skin prick testing. Among 795 skin prick tested workers, 12 (1.5%, 95% CI 0.67 to 2.35) workers had a positive reaction to the latex reagent. These comprised eight glove factory workers (1.7%, 95% CI 0.5 to 2.8) and four tappers (1.3%, 95% CI 0.5 to 2.0). None of the college students showed a positive reaction. The percentages with wheals of more than 2 mm and 3 mm are shown in table 4. There were no significant relations between wheal diameter and any of the exposure groups, smoking, age, sex, or family history of allergy. There were significantly more 2 mm reactors who were atopic (10.6% *v* 6.3%, $\chi^2_1=4.46$, p=0.04), however, most workers sensitised to latex had a negative reaction to grass pollen. Although not significant, the prevalence of a >2 mm wheal to latex increased with duration of employment in the glove manufacturers from 6.8% for those employed for less than 1 year, to 9.5% for those employed for 1–5 years and 11.3% for those employed for more than 5 years. No relation between duration of employment and latex wheal positivity was found in the plantation workers.

### PREVALENCE OF WORK RELATED SYMPTOMS

Work related symptoms were common in all groups, and particularly common in the college students (table 5). There were no significant differences between the exposure groups for any symptom. The low exposure glove manufacturers were the least symptomatic for breathlessness, cough, eye irritation, runny nose, and urticaria.

## Discussion

This is the first study of a representative sample of latex glove factory and plantation workers in which aeroallergen measurements and a standardised natural rubber latex allergen extract were used. The response rate was high. The

*Table 5 Work related symptoms*

| | Exposure group | | | | |
|---|---|---|---|---|---|
| | Glove manufacturers | | | Rubber plantation | College students |
| Work related symptom (%) | High | Moderate | Low | Moderate | None |
| Wheeze | 21.1 | 21.9 | 22.2 | 22.9 | 29.9 |
| Breathlessness | 19.8 | 28.1 | 11.1 | 18.8 | 20.1 |
| Cough | 26.6 | 29.8 | 19.0 | 21.7 | 39.8 |
| Eye irritation | 36.2 | 48.2 | 34.9 | 41.1 | 38.2 |
| Runny nose | 22.9 | 28.1 | 12.7 | 27.4 | 45.1 |
| Eczema | 27.9 | 26.3 | 17.5 | 21.3 | 16.0 |
| Itchy red rash | 25.4 | 28.9 | 12.7 | 19.1 | 16.7 |

latex allergen concentrations in air were high,[25] but despite this the rate of sensitisation, as assessed by skin prick testing, was very low.

Stallergènes latex skin prick test reagents were used in this study. This reagent has been standardised and the concentration of 1:200 w/v, showed a 93% sensitivity and 100% specificity, 100% negative predictive value (NPV), and 96% positive predictive value (PPV).[26] Turjanmaa *et al*[26] stated that it contains most of the important allergens including proteins of about 14, 20, 27, 30, and 45 kDa. It should therefore be able to detect latex sensitisation if present. The ability to produce a wheal response in the Thai population was shown by the positive histamine wheals and their response to common environmental allergens. The largest wheal of latex reaction was 4.2 mm. The same bottle of latex skin prick tests produced wheals up to 8 mm in United Kingdom hospital workers, where 14.6% of those tested had at least a 3 mm wheal.[27] If the criterion for a positive test was relaxed to greater than 2 mm, a positive test occurred in 8.1% of glove factory workers, 6.7% of tappers, and 1.4% of college students. These figures are still less than the 11% found in the Canadian glove factory reported by Tarlo *et al*[22] who used an unstandardised allergen and reported wheals greater than 2 mm as positive. Even lower results have been reported from Malaysia, where the prevalence of a 2 mm or greater wheal among glove factory workers was 2%[23] and 4.7% among tappers (Shahnaz M, personal communication). The latex skin test reagent used in the Malaysian study was also unstandardised.

The Thai workers studied were exposed to high concentrations of latex in air with median concentrations 30 times higher than in the United Kingdom hospital studied,[25] and yet had a low prevalence of strongly positive skin prick tests to latex. This difference highlights the need to consider other factors which may be different between the Thai workers and the United Kingdom hospital staff. Most sensitised healthcare workers have had extensive skin exposure to latex, which is likely to be the predominant route of sensitisation in them. Occlusive skin exposure did not occur in the Thai workers studied. Once sensitised healthcare workers often react to airborne latex resulting in rhinitis and asthma. This may include the nature of the allergens in Thailand and the ability of the Thai workers to form IgE antibodies to latex allergens. It is possible that very high concentrations of exposure lead to a degree of tolerance and that lower concentrations might paradoxically be associated with greater levels of sensitisation. Factors which may reduce atopy are infection, poor hygiene, and large family size, and a factor which might block the IgE response is high concentrations of IgE in response to parasitic infection.

The low level of sensitisation in the current study may be related to the short period of exposure of many of the workers. Most glove factory workers had been exposed to latex for less than 1 year. The prevalence of latex sensitisation (wheal >2 mm diameter) increased with increasing duration of exposure in the glove manufacturers. The highest prevalence of latex sensitisation was found among those exposed between 5 and 10 years (11.3%). As about 50% of workers had been exposed to latex for 1 year or less, the present study is likely to have underestimated potential sensitisation. By contrast, Azizah *et al*[23] found no relation between the duration of time the workers spent in latex glove factories and the presence of sensitisation to latex defined by a positive skin prick test to latex. However, the workers in that study were not randomly or systematically selected and as such, the results reported might not be representative. Sensitisation may develop soon after first exposure; for example workers in the sanding section of a doll factory all developed latex allergic symptoms with the positive skin prick tests confirmation within 3 years.[28] Although the exposure times were much higher among the rubber tappers than among the glove factory workers in the present study, the prevalence of latex sensitisation was also small and even smaller than among the glove factory workers. This implies that the duration of exposure alone may not explain the low sensitivity to latex among the Thai workers exposed to it.

The relation between the prevalence of sensitisation and exposure to latex allergens can be modified by host factors. Host factors related to atopy are associated with latex sensitisation.[16 17 29–32] In the present study, the prevalence of atopy defined by skin prick tests positive to one or more common inhalable allergens was 29.7% in the Thai workers, which was significantly more than the Thai college students (13.9%). The prevalence of atopy seemed to increase with increasing age unlike other studies,[33–35] which reported the reverse effect. The prevalence of atopy in Thai workers seems to be close to the general prevalence of atopy in the United Kingdom working population, which is 25% to 33%.[36] Unfortunately, data on the prevalence of atopy among the Thai working population has not been reported; therefore comparison can only be made with other groups of the Thai population. The prevalence of atopy, defined as having a history of atopic disease and positive skin prick tests to common inhalable allergens, in the general population in north and north east Thailand was about 20%.[37] Among the Thai latex workers studied who had a positive skin prick test to latex (wheal >2 mm), 42% had

atopy. This compares with other latex sensitisation studies which reported that 64% to 85% of the subjects sensitised to latex were atopic.

The latex particle size may be different in the Thai workers than the healthcare workers, where corn starch powder is the major carrier of latex allergens. Little is known of any variation in particle size of the corn starch between different manufacturers. The two studies which have measured particle size have produced inconsistent results; one showing that the corn starch was 1–3 μm[38] and the other that particles carrying latex allergens were mainly greater than 7 μm.[39] In hospital studies the latex allergen has been shown to be tightly bound to corn starch.[38] Replacement of talc, to which latex is less firmly bound, is one of the possible explanations for the increasing prevalence of latex allergy.[40]

There are no standardised respiratory or occupational questionnaires available in Thai. The questionnaire used in this study was developed in English, and produced results indicating increasing work related symptoms with increasing exposure to latex gloves in a United Kingdom hospital. It is possible that the questions were interpreted in a different manner by the Thai subjects studied. In particular the college students came from an area without rubber plantations. They were studying commerce, home economics, and textiles and were not exposed to latex products at college; despite this they had the highest level of work related symptoms. Glove manufacturers are exposed to chlorine and tappers to acetylene from their headlamps (tapping is done at night), providing alternative causes for some of their symptoms. The group with medium exposure in air had more symptoms than those with high exposure. This could be due to selective loss of symptomatic workers from the high exposure group but it is more likely to be due to the lack of specificity of the questionnaire as symptoms were usually high in the unexposed college students. A study on Malaysian workers in a latex glove factory found that none of the workers sensitised to latex had any adverse reactions on exposure to latex.[23] Lagier *et al*[5] have also reported a poor correlation between at least one self reported symptom related to latex gloves and response to skin prick tests with only a positive predictive value of only 18.6%. Therefore, the findings of the present study and other previous reports suggest that self reported symptoms may be non-specific for latex sensitisation.

## Conclusion

The study shows that sensitisation to well defined latex allergen extract was infrequent among the Thai workers studied despite concentrations in air much higher than in the United Kingdom hospital. It is likely that sensitisation is often by cutaneous exposure but that once sensitisation has occurred air concentrations of latex induce asthma and rhinitis. Control of air concentrations alone, for instance by limiting powder in the hospital, is unlikely to control sensitisation in healthcare workers without also reducing skin absorption by reducing extractable antigen from latex gloves.

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