

Latex Protein Allergy: A Prevalence Study of Factory Workers

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This paper concerns the study of prevalence of Type I latex protein allergy among workers in various latex glove factories in Malaysia. A total of 149 subjects (108 females and 41 males) with a mean age of 30.6 years were examined both by questionnaires and by skin prick test (SPT). In the absence of a standardised SPT latex allergen mixture, the clinical test was carried out using six glove extracts with extractable protein content varying from 0.02 mg/g to 0.75 mg/g of gloves (or 20 µg/g to 750 µg/g), as measured by the RRIM modified Lowry microassay.

Only three subjects were found to show wheal size ranging from 2–4 mm when tested with glove extracts with extractable protein content of > 0.6 mg/g. Such reaction, was however not detected in all cases when protein levels were at 0.1 mg/g or lower. This prevalence as compared to those reported in the West is relatively low.

Natural rubber products have been used widely for over a hundred years. Although their use has been known to be associated with Type IV allergy in some users for more than sixty years¹, no serious incidence has occurred through their usage. While this type of allergy is brought about by some residual chemicals^{2,3}, added to the latex during processing, the Type I allergy reported recently⁴⁻⁷ is caused by the presence of some residual soluble proteins in latex products⁸. Unlike the Type IV reaction which is of cell-mediated delayed hyper sensitivity, the Type I allergy is of immediate

hypersensitivity and is IgE-mediated⁹. Absorption of the allergenic proteins is mainly via cutaneous and mucosal routes. Symptoms involve urticaria, rhinitis, conjunctivitis, asthma and, only very rarely, anaphylaxis. The onset of this type of allergy is believed to be due to a myriad of factors, one of which is the sudden demand in the late 1980s for latex products such as gloves and condoms, which are very good protective barriers against viral diseases, particularly AIDS. It is thought that the increased exposure to latex products has resulted in sensitisation of, especially, the atopic individuals.

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For diagnosis of the Type I hypersensitivity, various methods¹⁰⁻¹⁴ have been used by different people. The most preferred method, by far, is the skin prick test (SPT), despite the lack of a standardised latex allergen-containing reagent. This test is very sensitive, and when performed with proper reagent preparation and the prick technique, it provides a very simple, convenient and safe diagnostic method.

To-date, the prevalence of Type I latex protein allergy in the general population is still unknown, although the risk appears to be higher among the atopic than the non-atopic individuals. The high risk groups identified in the West among the predominantly latex product users, are the healthcare workers and children with *spina bifida* and urogenital abnormalities. To a lesser extent, the rubber industry workers are also included. Using mainly the SPT and the radio-allergosorbent test (RAST), a number of prevalence studies have been carried out mostly among healthcare workers¹⁵⁻¹⁸ and the *spina bifida* children¹⁹⁻²¹, and to a lesser extent, the rubber factory workers²². In Malaysia, (the world's largest producer of latex products) the group of people who are constantly exposed to latex or rubber are the rubber tappers, rubber factory workers and the latex product manufacturing plant workers. Prevalence of Type I latex protein allergy among these groups of people has, however, not been studied yet. Work was thus undertaken to do this. This paper concerns the study of latex factory workers.

MATERIALS AND METHODS

149 workers from a number of latex glove manufacturing plants in the states of Selangor, Negeri Sembilan and Malacca

were examined. All workers were interviewed with the guide of a prepared questionnaire for information regarding age, sex, duration of time working in an occupationally exposed area, history of various allergies and family history of allergy, if any. Each subject was then skin prick tested in a hospital.

Glove Extracts (Test Reagents)

Six different brands of latex medical gloves were obtained commercially. Glove pieces from each brand, weighing 1 gram, were cut into 1 cm² and extracted in 5 ml of phosphate buffered saline (PBS) at pH 7.2 at room temperature for 1 h. The resulting extracts were centrifuged at 1600 × g for 10 min to remove any particulate contamination, to give clear test extracts.

Protein Concentration of Glove Extracts

Protein concentration was determined essentially by the RRIM modified Lowry method²³. Soluble proteins were first extracted from glove pieces of each brand of glove in PBS (pH 7.2) at 23°C for 3 h. After removal of the glove powder by centrifugation, protein in each clear extract was precipitated prior to measurements using trichloroacetic acid (resulting concentration of 5%) and phosphotungstic acid (resulting concentration of 0.22%). The resulting suspensions were centrifuged, and the sedimented protein from each sample was redissolved in minimum quantity of 0.2 M sodium hydroxide. Protein concentration was then measured by the Lowry colorimetric microassay. Absorbance values at 750 nm were read against a curve calibrated using bovine serum albumin (BSA) standard.

Skin Prick Test

A drop of test extract was introduced onto the volar surface of the forearm. A flap of the skin was gently lifted with a sterile lancet (2.4 mm, Beckton Dickinson, New Jersey) through the drop, allowing the allergens to penetrate into the skin. Reaction was observed after 15 min. Positive reactions appearing as wheals were recorded, and the wheal size measured. Histamine (1 mg/ml) and PBS (pH 7.2) were used as positive and negative controls, respectively. Wheal size was graded according to the Bencard Skin Test Reaction Chart (Bencard Allergy Diagnosis, UK) as indicated below:

- : no wheal and absent erythema or erythema less than 1mm in diameter
- + : wheal absent or very slight erythema present and not more than 3 mm
- ++ : wheal size not more than 3 mm diameter with associated erythema
- +++ : wheal size between 3 mm to 5 mm diameter with associated erythema
- ++++ : any larger reaction possibly with pseudopodia.

Reaction showing wheal size equal or larger than ++ was considered to be positive. All glove extracts used were freshly prepared.

RESULTS

The 149 workers examined consisted of 108 females and 41 males. Their mean age was 30.6

years, ranging from 17 to 54 years. All have been working in the glove manufacturing plants for a mean duration of 4.5 years. Twenty-two (14.8%) had worked for more than 5 years in the plants. Fifty-eight (39%) had history of various allergies and thirty-two (21.5%) had strong family history of atopy. Nine complained of hand dermatitis since working in the factories (*Table 1*).

The six different brands of glove used for skin testing were shown to have extractable protein content ranging from 0.02 mg/g to 0.75 mg/g of glove (or 20 µg/g to 750 µg/g). Of the 149 subjects tested, only three (2 females and 1 male) showed positive skin test reaction. Their wheal size varied from undetectable to as large as 4 mm when tested with the extracts from gloves with increasing content of extractable proteins (*Table 2*). All three were non-atopic, with no history of hand dermatitis and have worked in the glove plants for 1-5 years. In addition, they have not experienced any Type I allergic reactions to latex products.

DISCUSSIONS

Although skin prick testing has been found to be the most sensitive diagnostic tool for detecting latex protein allergy, both the allergen reagent and the wheal size evaluation for positive reaction have not yet been universally standardised. In view of this, our study was conducted using extracts from latex gloves which were expected to contain most allergens commonly encountered by affected users. For evaluation of wheal size, the method of Bencard was adopted. According to the Bencard grading, which made no reference to the wheal size shown by the

TABLE 1 PARTICULARS OF LATEX GLOVE WORKERS
SUBJECTED TO SKIN PRICK TEST

Item	Number
Number of workers tested	149
Age range (Mean)	17 – 54 yrs. (30.6 yrs.)
No. of female workers	108 (72.5%)
No. of male workers	41 (27.5%)
Mean duration of work in latex glove factories	4.5 yrs.
No. of workers with > 5 yrs. of duration	22 (14.8%)
No. of workers with history of allergies	58 (38.9%)
No. of workers with strong family history of allergies	32 (21.5%)
No. of workers with hand dermatitis	9 (6.0%)

TABLE 2 DEMOGRAPHIC DATA OF THE 3 SUBJECTS (OF A TOTAL OF 149) WITH POSITIVE SKIN TEST REACTIONS
TO EXTRACTS FROM LATEX GLOVES WITH VARYING CONTENT OF EXTRACTABLE PROTEINS

Sex/Age	Atopy	Skin prick test: Allergic response (wheal size in mm)						
		Histamine (1 mg/ml)	Extractable protein content of gloves (mg/g glove)					
			0.75	0.69	0.64	0.11	0.07	0.02
F/29	N	4 mm	NR	NR	++ 3 mm	NR	NR	NR
F/20	N	3 mm	+++ 4 mm	+++ 4 mm	++ 2 mm	+ 1 mm	NR	+ 1 mm
M/20	N	4 mm	++ 3 mm	NR	++ 2 mm	NR	NR	NR

Allergic response :

NR : no reaction, no wheal or erythema < 1 mm

+ : wheal absent, or very slight erythema < 3 mm

++ : wheal < 3 mm with associated erythema

+++ : wheal between 3–5 mm with associated erythema

++++ : larger reaction possibly with pseudopodia

Reaction showing wheal size equal or larger than ++ was considered to be positive.

F : female worker

M : male worker

N : no history of atopy

histamine (1 mg/ml) control, the three cases with wheal size of 2–4 mm encountered in the present investigation, were considered positive. This gives a prevalence of 2%. It may be mentioned that the preferred assessment according to Turjanmaa¹³ was not used due to the unavailability of histamine (10 mg/ml) required, at the time of the study.

Although atopy and pre-existing hand dermatitis have been reported to be factors underlying an individual's risk in developing latex protein allergy, the three positive cases found did not experience any immediate allergic reaction to latex products. They were neither associated with any form of atopy (allergic rhinitis, asthma, eczema or urticaria), nor had prior hand eczema or dermatitis. Furthermore, the positive responses were not related to the length of time they spent in the manufacturing plants. One may therefore speculate that such positive reactions could well be associated with IgE cross-reactivity involving latex proteins and certain foods^{24–27}, which were, however, not investigated in this study.

Compared to the 11% prevalence reported by Tarlo *et al.*²², who skin tested 81 workers in a surgical glove factory in Canada, a prevalence of 2% shown in this study is comparatively low. Although not included, similarly low incidence has also been observed among other high risk groups in Malaysia, such as the healthcare workers, and the rubber tappers²⁸. This is indeed in contrast to the comparatively high prevalence reported for the high risk groups in the West, which showed a variation of 2.8% to 16.9% among the healthcare workers^{29,30}, and 32% to 51% among the *spina bifida* children^{31–33}.

It is noteworthy that wheal size and hence allergic response shown by the positive subjects (*Table 1*) increased with increasing concentration of extractable proteins tested. Generally, very little or no response was demonstrated by these allergic persons at extractable protein content of 0.11 mg/g (or 110 µg/g) or lower. This is highly consistent with the findings by Yip *et al.*³⁴ which showed a well correlated relationship between the residual extractable proteins in latex gloves and the allergic responses elicited by them in latex hypersensitive persons. More importantly, extractable protein content of 0.1 mg/g or 100 µg/g and lower, (by the same RRIM modified Lowry method) were shown to be associated with very little or no allergic responses as assessed by the skin prick test. It is often wondered if sensitisation were solely due to frequent exposure to latex products, how is it that high risk groups in Malaysia, who are exposed frequently to latex and latex products, demonstrated such low prevalence, if at all? Various explanations have been proposed, one of which referred to the genetical differences between people in the West and in Malaysia. In view of the recent awareness in cross-reactivity shown by allergens from foods and latex, differences in diets of people concerned have also been suggested to be yet another possible cause. While much work is needed to further understand the allergy reactions, it may be worth noting that the Rubber Research Institute of Malaysia has developed various methods³⁵ for effective removal of the undesirable residual proteins from latex products, to prevent further sensitisation among users.

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