

# **LATEX PROTEIN ALLERGY AND YOUR GLOVES**

**Ong Eng Long, Esah Yip and Lai Pin Fah  
Rubber Research Institute of Malaysia  
Malaysian Rubber Board**

**Malaysian Rubber Board (MRB)  
Monograph No. 1 (September 1998)**

# ***Latex Protein Allergy and Your Gloves***

## **INTRODUCTION**

Natural rubber gloves were first introduced about 100 years ago. In the early days, thin rubber gloves were made by macerating bale rubber with added chemicals, followed by dissolving the mixture in solvent naphtha. Moulds were then coated with the resulting fluid mixture, which was subsequently dried and vulcanised in heated chambers containing highly toxic sulphur chloride vapour. This process was both very lengthy and expensive. It was replaced in about 1930 by the cheaper and faster method of latex dipping. Today, this latter process is adopted almost exclusively for the manufacture of all medical gloves.

Natural rubber latex gloves have been and still are being used extensively worldwide as an effective method of minimising healthcare workers' exposure to contaminated blood and body fluids, as well as for reducing cross-infection during surgery. The use of such gloves has indeed become an essential and important practice especially in the healthcare settings. In fact billions of latex gloves are being used for protection every year all over the world, and with that, loss of millions of lives have been prevented. However, they have been reported in recent years to give rise to certain allergies in some individuals. This has certainly caused great concern to both the medical profession and the latex product manufacturers, particularly in the case of the latex protein allergy. Origin of the problem is not clearly known, but it appears to have been triggered by the sudden upsurge in the use of latex gloves due to the AIDS scare in the late eighties, when some gloves with high levels of allergenic proteins were produced. Although the problem is real, it is somewhat 'circumscribed' affecting only a small number of people.

To address the problem, a great deal of research has been carried out in the manufacturing countries especially in Malaysia, as well as in consumer countries in the West. Whilst studies in Europe and USA largely concern the development of suitable diagnostic tests and management of the affected people, much effort has been made in Malaysia to further improve quality of the products. Intensive R&D by the Rubber Research Institute of Malaysia (RRIM) of the Malaysian Rubber Board (MRB) has enabled Malaysian glove factories to produce gloves with superior qualities with low protein / allergen content. The use of such gloves will help to reduce the possibility of further sensitisation.

This monograph is written to redress the negative and often misinformed comments in the news media and on the Internet concerning latex protein allergy. We hope to present a more balanced account of the subject by giving full weight not only to the problem, but also to the efforts, which have been and are being made to improve the situation.

## How is Natural Rubber Latex Made into its Products?

*What is latex?* Latex or natural rubber latex (NRL) is obtained from the *Hevea brasiliensis* tree when its bark is tapped. It is a milky fluid comprising 30% - 40% of the rubber hydrocarbon particles suspended in a serum together with a few percent of other non-rubber substances such as proteins, lipids, carbohydrates, sugars and some metals (non-rubber fraction). The remaining major component is water.

*Raw materials.* *Hevea* latex collected from the trees is processed *via* two quite separate routes to produce the raw materials from which its products are made.

Latex concentrate. Latex collected in the field is concentrated (generally by centrifugation, to remove part of the unwanted serum) to a dry rubber content of about 60%. It is then preserved with ammonia to combat bacterial growth. This becomes the starting material for all natural latex products, whether produced by dipping (gloves, balloons, condoms, catheters, baby soothers and dental dams) or other processes such as foaming (latex foam or sponge) or extrusion (Latex thread, more commonly known as 'elastic').

Dry rubbers. Latex is coagulated with acid, creped, crumbled and washed extensively to remove surplus acid (among other things) before being dried at above 100°C. Some latex that has autoaggregated in the field while awaiting collection is also processed in this way. This *dry rubber* is then the raw material for the production of tyres, tubings, hoses, footwear, automotive components, engineering parts, adhesives, and some household appliances. Some rubber thread is also made in this way. Many of these products are manufactured from a combination of natural rubber and various types of synthetic rubber.

*Natural rubber (NR) products.*

Production of latex goods. Liquid latex concentrate is first mixed with various compounding chemicals, after which formers of desired shape are dipped into the latex-mix to enable the deposition of a thin film of latex. Dipping can be done either in the presence or absence of a destabilising chemical (coagulant dip or straight dip, respectively). Generally leaching is carried out at a certain stage of the process, and the product is cured at about 100'-120'C. In view of the protein allergy issue, more emphasis is now placed on improved leaching of the gloves to remove as much as possible of the soluble allergenic proteins during processing. This can be achieved, for instance, by adding extra leaching facilities.

Production of dry rubber goods. The process generally involves mixing and compounding of the solid dry rubber with various chemicals. In tyres, for example, carbon black fillers are incorporated for the purpose of reinforcement. Subsequent fabrication into products often involves processes such as moulding, injection moulding, extrusion and calendaring. The choice of process used depends on the type of product to be manufactured. Vulcanisation of the rubber products is then carried out at high temperatures (140' to 160'C).

## Synthetic Rubber Products

Synthetic rubber products are produced by exactly similar methods, both from latices and dry rubbers. These do not contain proteins, but they do contain the same range of curative and protective chemicals which can cause irritant contact dermatitis as well as Type IV chemical hypersensitivity (see below).

## What is Latex Protein Allergy?

The three types of adverse reactions associated with latex gloves affecting some users are shown in *Table 1*. While irritant contact dermatitis and Type IV hypersensitivity have been known for many years, that of Type I hypersensitivity emerged only in the late eighties.

It is important to point out that none of the above reactions is caused by the rubber hydrocarbon itself, as quite frequently misunderstood by many people. Furthermore, it may be worth noting that the Type I hypersensitivity is not confined to NR latex products. Indeed, Type I hypersensitivity is quite frequently caused in some individuals by penicillin, other antibiotics, wasp- and bee-stings, and even some foods such as fruits and peanuts.

TABLE 1. TYPES OF REACTION AFFECTING SOME INDIVIDUALS THROUGH USE OF NATURAL / SYNTHETIC LATEX GLOVES

Reaction type	Symptoms	Cause
Irritant contact Dermatitis (Non-allergic)	Skin rash, dry flaky skin with papules, cracks and sores	Residual soaps, hand cream, powder, temperature and pH extremes, disinfectants and incomplete hand rinsing
Type IV – Chemical Hypersensitivity (Cell-mediated allergy)	Eczema, appears at 48 hours to 96 hours post exposure by skin contact	Residues of chemicals used for processing of gloves, particularly, the thiurams and carbamates
Type I – Latex Protein Hypersensitivity (IgE mediated allergy)	Immediate localized itching, burning or discomfort, urticaria (hives) within 5 to 60 minutes after contact, rhinitis, asthma and in very serious cases, anaphylaxis (happens only rarely)	Residual extractable proteins found in natural rubber latex products

## Who is at Risk?

Of the three types, Type I hypersensitivity is considered to be the most serious one. The prevalence of this type of allergy among the general population is not exactly known, but estimates of less than 1% have been given. However, higher incidence of occurrence has been reported when a number of selected groups were studied (*Table 2*).

Atopy seems to be a principal pre-determinant for sensitisation, believed to be due to exposure *via* cutaneous or mucosal contact or even *via* aerosolised allergens. It is interesting to note that, however, the prevalence among potential high risk groups in natural rubber producing countries such as Malaysia and Thailand is only 2% and about 3%, respectively<sup>14,8</sup>, despite repeated exposures to latex and latex products.

TABLE 2. PREVALENCE OF VARIOUS POTENTIAL HIGH RISK GROUPS  
(ASSESSED BY SKIN-PRICK TESTING)

Potential high risk group	Prevalence (%)	References
Healthcare workers	2.8 - 16.9	1 - 7
<i>Spina bifida</i> / multi-operated children	32 - 50.6	8, 9
Hairdressers and housekeepers	8 - 9.7	10, 11
Rubber industry workers	2 - 11	12 - 14

## Diagnosis of Latex Protein Allergy

A complete medical history is an important indicator. The skin-prick test is a sensitive and simple test for the allergy. It is in fact considered to be the 'golden standard' test, although it could sometimes cause allergic reaction if not properly performed. It involves pricking the skin, usually on the forearm, through a drop of test liquid containing the allergenic materials. It should only be carried out at medical centres with staff who are experienced and equipped to handle severe reactions. A positive reaction is indicated by swelling or redness at the test site within minutes of application. Blood tests can also be conducted by measuring the specific IgE antibodies in the serum using techniques such as the radioallergosorbent test (RAST). However, such tests lack high sensitivity and specificity of the clinical skin test, and their use could sometimes give rise to false positive or negative results.

Once a positive diagnosis is determined, then the most sensible remedy is avoidance of NR latex proteins. It must be emphasised that proper diagnosis should be done and all hypersensitive persons should be identified so that they would not continue to expose themselves to the allergens which they are sensitive to. Otherwise, very unpleasant or serious consequences could result.

## What are Residual Extractable Proteins?

If latex is ultracentrifuged, the latex system can be separated into three fractions, namely, (a) the least dense upper fraction of rubber hydrocarbon particles, (b) the ambient serum in the middle, and (c) the bottom fraction comprising the non-rubber particles. Fraction (a) forms the main ingredient of all rubber products. Fractions (b) and (c) are usually removed to a great extent during processing.

*Hevea* latex contains about 1% of total proteins. About 1/4 of these are associated with surfaces of the rubber particles of fraction (a), the remaining 3/4 are in the non-rubber phase [fractions (b) and (c)] of the latex, and they are water soluble. When processed into latex concentrate, considerable amounts of these soluble proteins are removed. Further conversion of latex into a film, such as gloves, condoms or balloons, removes more of the soluble proteins, during leaching and washing steps, so that the remaining levels are very low. These residual proteins in the latex products are those which are implicated in the allergy.

Not all proteins in the residual extractable fraction cause the allergic reaction. So far, about eight of the potential allergens present in the latex<sup>1</sup> have been identified. This subject, together with the study of changes in proteins from latex to the product, are being intensively investigated.

## Allergic Potential of Latex Gloves

Since the amount of residual extractable proteins present in latex products prepared from the same latex concentrate can vary, depending on the processing conditions they are subjected during manufacturing, not all gloves have the same amount of residual extractable proteins. For example, gloves that have been subjected to more thorough leaching during processing will have less extractable proteins than those that have not, although the latex used for both may have originated from the same source of supply. A sensitive and accurate method is needed to evaluate the allergic potential of these products. However, at present, there is no universally agreed method for doing so. In fact, the tests adopted currently are of two main types: (i) measurement of total extractable proteins; and (ii) assessment of allergenicity or allergen content.

### *(i) Total extractable proteins.*

- Colorimetric measurements: (a) RRIM modified Lowry (*MS 1392:96P*)  
(b) ASTM modified Lowry (*D 5712-95*)  
(c) prEN 455-3 modified Lowry  
(d) Bradford microassay
- Chromatographic analysis: (e) RRIM SE-HPLC method  
(f) Amino acid analysis by HPLC
- Immunoassay (g) LEAP (measurement of antigenic proteins)

There is no common standard reference for all these test methods. Therefore, protein values generated by them for a given sample are different (*Table 3*). This is also the case even with all the three modified Lowry microassays (a, b, and c). Differences in the resulting protein values are mainly due to variations of the modified Lowry procedure adopted by the three tests. It is therefore important to point out that for an accurate comparison between samples, protein values must be based on a *single* test method only.

(ii) *Allergenicity/Allergen content.*

- |                    |  |
|--------------------|--|
| Clinical test:     | (a) Skin-prick test                      |
| Serological tests: | (b) IgE latex specific RAST-inhibition   |
|                    | (c) IgE latex specific ELISA-inhibition. |

TABLE 3. MEASUREMENT OF TOTAL EXTRACTABLE PROTEINS OF A GIVEN GLOVE SANTLE BY DIFFERENT TEST METHODS<sup>16</sup>.

Test method	Total extractable proteins (EP), (µg/g)
(a) RRJM modified Lowry (Calibration standard: bovine serum albumin)	103
(b),4STA,f modified Lowry (ovalbumin)	91
(d) Bradford colorimetric assay (bovine serum albumin)	56
(e) SE-HPLC (latex serum proteins)	301
(g) LEAP - total antigenic proteins <sup>a</sup> (latex film extracts)	64

<sup>a</sup>IgG antibodies used in the test are not specific to latex allergens, hence measurement is in the form of total extractable proteins.

Test (c): prEN455-3 was at the early draft stage when this work was carried out. Since the analytical condition had not been finalised, it was not considered appropriate to include in this study. Similarly, Test (f) was not available during the time of the study, hence no value.

Values by the RRIM modified Lowry (EP<sub>RRIM</sub>) have been reported to be very well correlated with those by ASTM (EP<sub>ASTM</sub>)<sup>17</sup>, SE-HPLC<sup>18</sup> and reasonably well with those by the Bradford assay.

These tests have more specificity for latex allergens than those of the extractable protein measurements. Of the three, the skin-prick test is most appropriate since it evaluates the allergic reactions *in-vivo*. One drawback of this test, however, is the availability of latex hypersensitive individuals, and their willingness to be tested. For this reason, the two serological *in-vitro* tests are often preferred, since they require only their blood serum containing the latex specific IgE antibodies. Nevertheless, in view of the lack of standardised reference mixtures for both the IgE serum pool and latex allergens, which are essential for the two tests, results generated by different laboratories for the same test sample can differ. Furthermore, procedures of both tests are relatively sophisticated and very tedious to perform, besides being very costly.

Generally for routine testing, the much simpler and faster total extractable protein methods are used. As mentioned earlier, these tests are not specific to latex allergens. Therefore, for meaningful indication of the allergic potential, it is important that the EP values produced, by whichever test used, should show significant correlation with the allergic response or the allergen contents of the samples analysed. This may not always be the case, depending on the adequacy of the protein measurements by the various tests concerned. Such relationships have been demonstrated by the EP<sub>RRIM</sub> values<sup>19-21</sup> thus making the RRIM modified Lowry test a very useful one.

### **EP Levels of Gloves and Other Latex Products?**

Extractable protein content of latex gloves has been found to vary from as low as less than 20 µg/g of glove to as high as more than 1000 µg/g (as measured by the RRIM modified Lowry test). While the well leached powdered gloves and the powder-free gloves usually have low EP content, those of the poorly leached gloves have high EP content. On the other hand, other latex products such as condoms, latex thread, balloon bags and teats have a narrower EP range, varying from less than 20 µg/g to about 200 µg/g. Chlorinated products such as catheters and most powder-free gloves always have very low EP values of below 100 µg/g.

### **Are There 'Safe' EP Levels?**

For already sensitised and hypersensitive individuals, the only course is one of avoidance of latex. Some individuals who experience allergic reactions to latex proteins also show cross-reactive responses to proteins in food (such as various fruits and nuts). These food should also be avoided.

For the rest of the population, threshold levels for sensitisation is not known, but it is possible to obtain indications on extractable protein levels of low risk by identifying levels at which a great number of latex hypersensitive individuals do not react.

The RRIM, in collaboration with Dr. K. Turjanmaa of the Department of Dermatology, Tampere University in Finland, have shown<sup>20</sup> that when a group of latex hypersensitive subjects were skin tested with latex gloves of varying content of EP<sub>RRIM</sub>, about 60% of them indicated no allergic response at levels less than 400 µg/g (*Figure 1*). Up to hundred percent of negative responses were observed at EP<sub>RRIM</sub>

lower than about 100 µg in this study. Subsequent collaborative work with Dr. T. Palosuo of the Department of Immunobiology, Institute of National Public Health in Helsinki, using ELISA-inhibition technique (which has been validated by the skin-prick test) confirmed that gloves with EPRRIM of about 100 µg and less also have very low allergen content" (*Figure 2*). Although threshold levels of allergenic proteins needed for sensitisation are unknown, these findings provide useful guidelines for the manufacturing of low protein/ low allergenicity gloves.

The Food and Drug Administration (FDA) of the USA has allowed 'Low Protein Labelling' claim for the 510(k) submission by glove manufacturers since March 1995. However, no maximum EP levels have yet been specified, although claim on label below 50 µg (sensitivity limit of the ASTM modified Lowry test) is not permitted. It is recently learned that a maximum EP level of 1200 µg per glove would be suggested in their Proposed Rule, which is expected to be published soon.

### **Production of Low Protein Gloves**

Recognising the protein allergy problem, much effort has been made by many manufacturers in Malaysia to reduce the EP levels of their products. Approaches taken include:

- Adoption of improved leaching protocols during processing, as recommended by RRIM<sup>22</sup>
- Use of low protein latices
- Chlorination<sup>23</sup>
- Polymer coating.

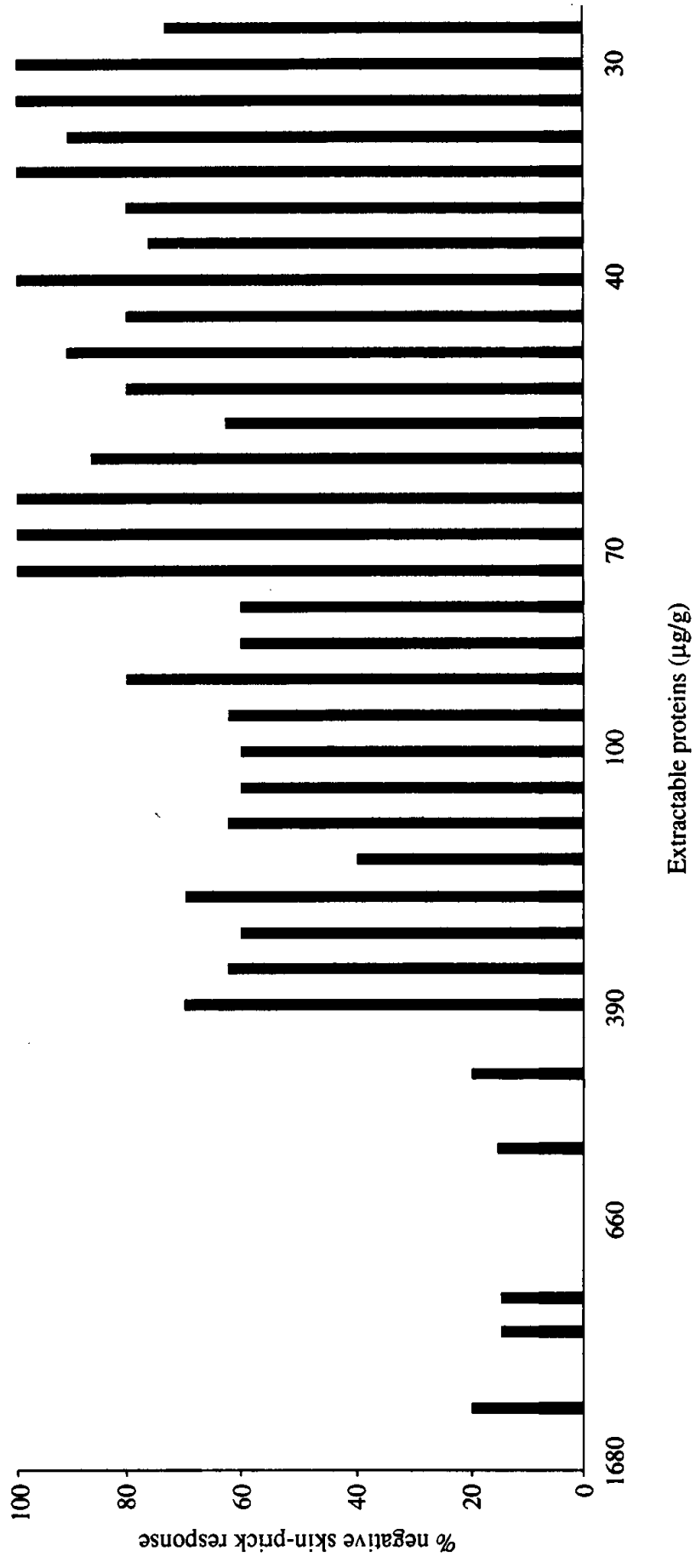


Figure 8. Negative skin-prick responses to allergens by a total of 88 latex hypersensitive subjects when skin prick tested with 20 µg of natural latex gloves with different Fluorocon concentrations (as determined by the RCM method) (Lowy, 1987)

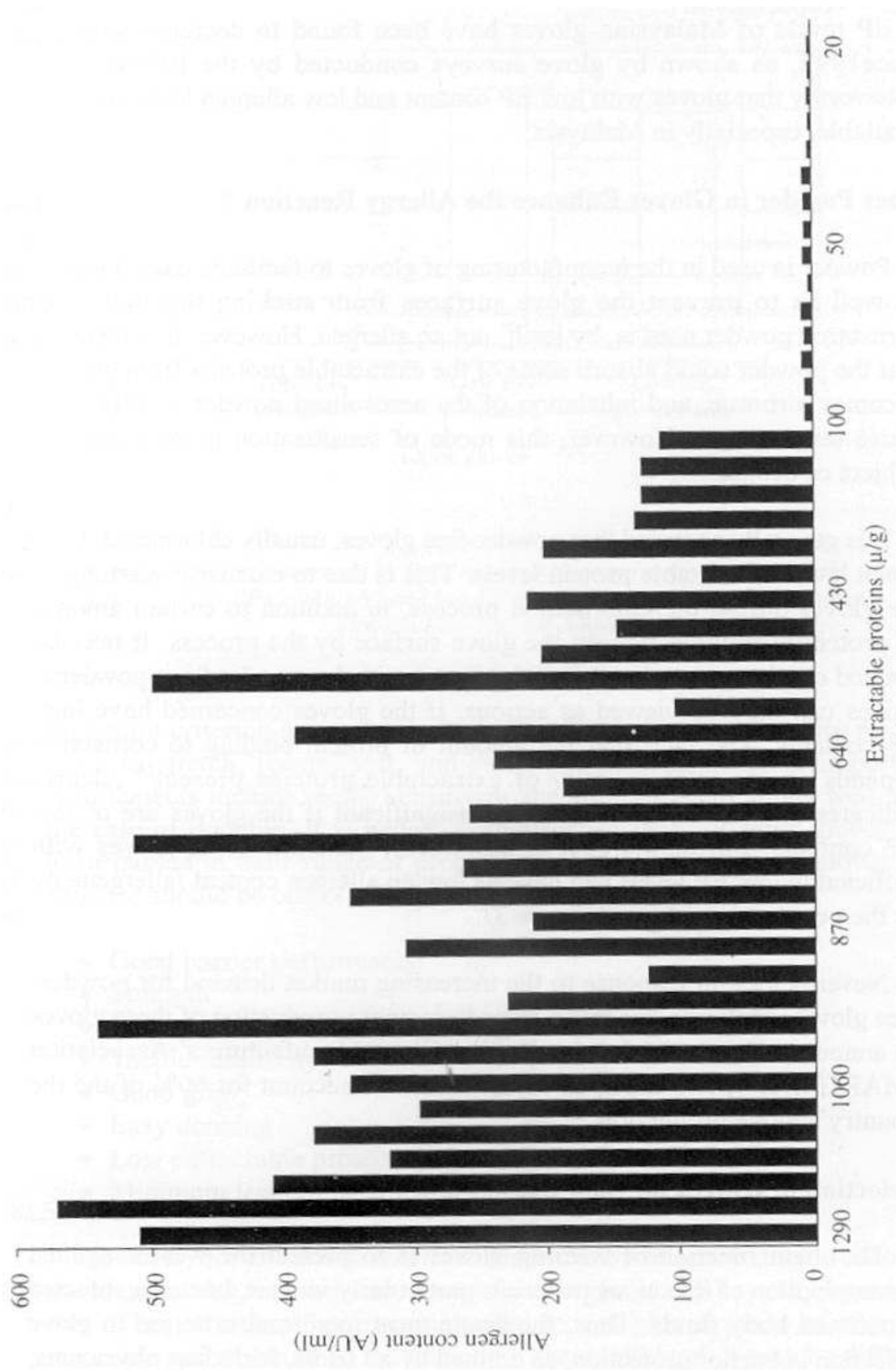


Figure 2. Total extractable proteins (EP) and its relationship by the total amount of allergen content (AU/ml) in the corresponding allergen content as measured by the allergen specific IgE in the allergen test for the patients of allergic rhinitis.

EP levels of Malaysian gloves have been found to decrease steadily since 1992, as shown by glove surveys conducted by the RRIM. It is noteworthy that gloves with low EP content and low allergen level are now available, especially in Malaysia.

### **Does Powder in Gloves Enhance the Allergy Reaction?**

Powder is used in the manufacturing of gloves to facilitate easy donning as well as to prevent the glove surfaces from sticking together. The cornstarch powder used is, by itself, not an allergen. However, it is believed that the powder could absorb some of the extractable proteins from gloves, become airborne, and inhalation of the aerosolised powder is alleged to cause sensitisation. However, this mode of sensitisation is very much a subject of debate.

It is generally accepted that powder-free gloves, usually chlorinated, have much lower extractable protein levels. This is due to extensive washing of the gloves during the chlorination process, in addition to certain amount of protein insolubilisation on the glove surface by the process. It may be pointed out that absorption of allergenic proteins by powder from powdered gloves can only be viewed as serious, if the gloves concerned have high EP contents. The fact that the amount of protein binding to cornstarch depends on the total quantity of extractable proteins present<sup>24</sup> clearly indicates that absorption should be insignificant if the gloves are of low EP contents. Furthermore, it is noteworthy that powdered gloves with sufficiently low EP levels can have as low an allergen content /allergenicity as the powder-free gloves (Figure 3).

Nevertheless, in response to the increasing market demand for powder-free gloves, Malaysia has taken steps to increase production of these gloves as announced by the Malaysian Rubber Glove Manufacturers' Association (MARGMA)<sup>25</sup>, two-thirds of whose members account for 60% of the country's glove production.

### **Selection of Gloves for Safe Use**

The main function of wearing gloves is to protect the wearer against contamination of infectious materials particularly viruses, bacteria, infected blood and body fluids. Thus, the single most important criterion in glove selection is barrier protection, as defined by all users, including physicians, dentists, medical and non-medical workers and researchers. The next most

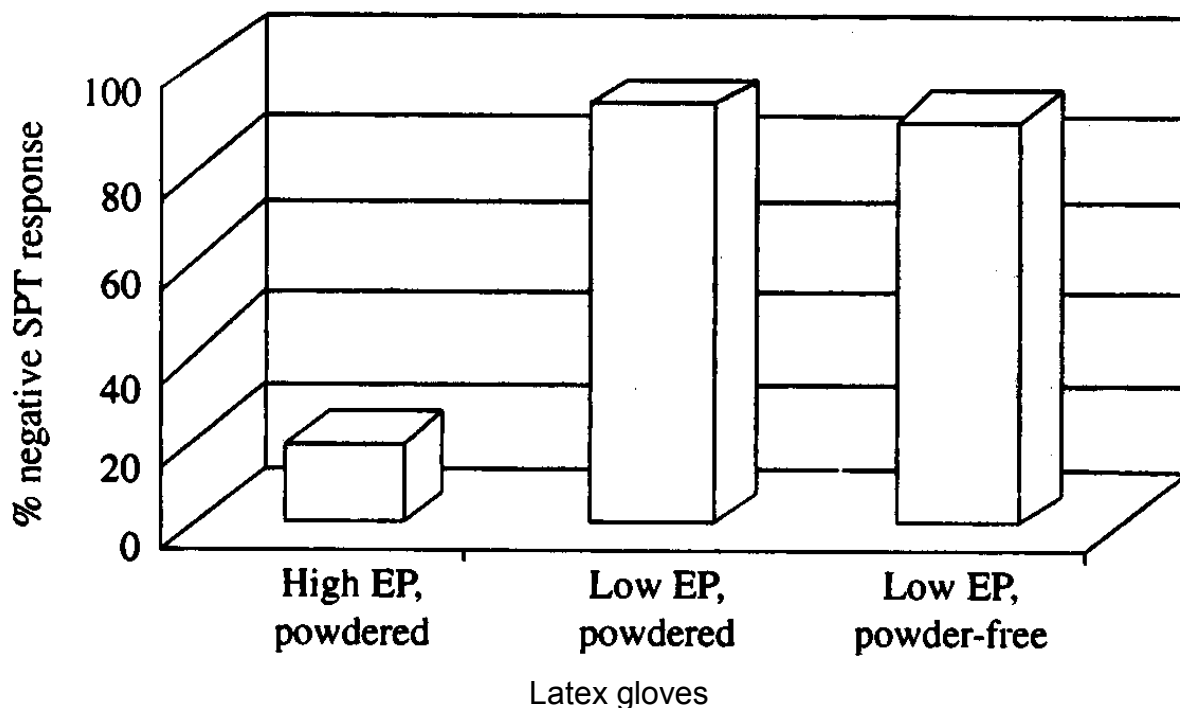


Figure 3. Negative allergic response by latex hypersensitive persons when skin-prick tested with powdered gloves of high EP (>500pg/g) and low EP of <100  $\mu$ /g, as compared to powder-free glove with similarly low EP content.

important criterion are strength, fit and comfort, that is, the ability for the glove to stretch, remain soft, and conform to the hand. Other important requirements include tactile sensitivity, the ability to grip things well, and the ease of donning. It is widely acknowledged that NR latex gloves are unsurpassed in their range of properties<sup>26</sup>. Hence, selection of gloves for safe use should be one of NR with the following properties:

- Good barrier performance
- Strength
- Fit and comfort
- Tactile sensitivity
- Good grip
- Easy donning
- Low extractable protein content
- Minimum level of chemical residues.

However, for the *latex sensitive individuals*, selection should also be based on similar requirements, except that the gloves will have to be *protein-free*. They are therefore recommended to use gloves made of non-NR materials and it should be the choice for them, although it may be difficult to find an alternative to latex that matches it in terms of its superior physical properties<sup>27</sup>. Although some have claimed to possess comparable properties, they have however, not yet withstood the test of time, unlike the NR latex gloves. In addition, the synthetic options currently available are 5 to 10 times more costly.

## **How do Non-latex Gloves Perform as Compared to Natural Rubber Latex Gloves?**

Although non-latex gloves may be protein-free, it must however be remembered that the most important function of gloves is to provide barrier protection for the users, to avoid contact with infectious materials. Thus far, latex gloves have been proven to have excellent barrier protective capability, and other superior physical properties. On the other hand, non-latex synthetic gloves are generally known to lack the comfort and fit, as well as to have lower strength and endurance as compared to the latex gloves. Above all, their barrier properties are often inferior to those of latex gloves, as demonstrated in the case of vinyl glove<sup>28, 29</sup>. Furthermore, it may be emphasised that non-latex gloves are not free from eliciting allergic reaction in some users. The fact that the same chemical compounding chemicals are used in their processing, they can also cause Type IV hypersensitivity. Therefore, unless one is latex sensitive, the glove of choice should clearly be that of latex.

### **Maximum Performance of Latex Gloves**

For maximum performance of latex gloves, care should be taken to ensure proper storage and correct usage of the products. Rubber tends to deteriorate with prolonged ageing, especially in warm climate. Therefore, they should be kept in containers and stored in a cool dry place. Storage for an unnecessarily long period is not recommended. As soon as signs of deterioration appear (e.g. tackiness, brittleness and acrid odour), the gloves should be destroyed.

Correct usage of latex gloves is also important. For long operational procedures, there is a need to change gloves at regular intervals to prevent accumulation of fluids in the gloves. For challenging surgical procedures, which could sometime result in holes and cuts, the use of double gloving is recommended to provide maximum protection. Contact with oil-based antiseptics, phenols and their derivatives, petroleum-based grease, kerosene and other related organic compounds, should be avoided.

### **Do Dry NR Rubber Products Pose a Protein Allergy Problem?**

Dry rubbers and dry rubber products are prepared and manufactured by very different processes from those of latex-dipped goods. Owing to the extensive washing during the processes, followed by high temperature drying and product fabrications, most of the residual extractable proteins are removed or rendered insoluble in these dry rubber products. Their 'nonallergenicity' has been demonstrated by Yip, Turjanmaa and Mäkinen-Kiljunen<sup>30</sup>, who showed that they not only have extremely low extractable protein levels ( $EP_{RRIM} < 50 \mu\text{g}$ , very often lower than  $20 \mu\text{g}$ ) but also negligible allergen activity (as shown by RAST-inhibition) and very little allergic response when skin tested on latex hypersensitive persons. Hence, dry rubber products are generally not affected by the latex protein allergy problem.

## REFERENCES

1. TURJANMAA, K. (1987). Incidence of Immediate Allergy to Latex Gloves in Hospital Personnel. *Contact Dermatitis*, 17, 270.
2. ARELLANO, R., BRADLEY, J. AND SUSSMAN, G. (1992) Prevalence of Latex Sensitisation among Hospital Physicians Occupationally Exposed to Latex Gloves. *Anesthesiology*, 77, 314.
3. LAGIER, F., VERVLOET, D., LBERMET, I., POYEN, D. AND CHARPIN, D. (1992) Prevalence of Latex Allergy in Operating Room Nurses. *J Allergy Clin. Immunol.*, 90, 319.
4. YASSIN, M., LIERL, M., FISCHER, T., O'BRIEN, K., CROSS, J. AND STEINMETZ, C. (1994) Latex Allergy in Hospital Employees. *Ann. Allergy*, 72, 245.
5. WRANGSJO, K., OSTERMAN, K. AND VAN HAGE-HAMSTEN, M. (1994) Glove-related Skin Symptoms among Operating Theatre and Dental Care Unit Personnel (II). Clinical Examination, Tests and Laboratory Findings Indicating Latex Allergy. *Contact Dermatitis*, 30, 139.
6. VANDENPLAS, O., DELWICHE, J.P., EVRARD, G., AIMONT, P, VANDERBRENTT, X., JAMART, J. AND DELAUNOIS, L. (1995) Prevalence of Occupational Asthma Due to Latex among Hospital Personnel. *Am. J Resp. Critic Care Medicine*, 151, 54.
7. TURJANMAA, K., CACIOLI, P., THOMPSON, R., SINLOTE, P. AND LOPEZ, M. (1995) Frequency of Natural Rubber Latex Allergy among US Operating Room Nurses Using Skin Prick Testing . (Abstract). *J Allergy Clin. Immunol.*, 95, 214.
8. TE-ERARTKUL, A., DANGSUWAN, T., WITTITSUWANNAKUL, R., KERDSOMNUK, S., SAWAENGSAKDI, L., ROENGRAK, S., WITITSUWANNAKUL, D. AND VICHANOND, P. (1997) Epidemiology of Latex Allergy among Healthcare Personnel at Siriaj Hospital. *Siriaj Hosp Gaz.*, 49(9) , 837.
9. MONFRFT-VAURPJN, D.A., BEAUDOUINE, E., WIDNIEP, S., MOUTON, C., KANNY, G., PRESTAT, F., KOHLEP, C. AND FELDMANN, L. (1993) Prospective Study of Risk Factors in Natural Rubber Latex Hypersensitivity. *J Allergy Clin. Immunol.* 92, 668.
10. KELLY, K., KURUP, V, ZACHARISEN, M., RESNICK, A. AND FINK, J. (1993) Skin and Serologic Testing in the Diagnosis of Latex Allergy. *J Allergy Clin. Immunol.*, 91, 1140.
11. SUSSMAN, G.L., BEEZHOLD, D., LISS, G. AND DOUGLAS, A. (1994) Latex Allergy in Housekeeping Personnel. ( Poster Paper ) *Latex Allergy Symposium, Toronto, Canada.*

12. VAN DER WALLE, H. AND BRUNSVELD, V (1995) Latex Allergy among Hairdressers. *Contact Dermatitis*, 32, 177.
13. TARLO, S., WONG, L., ROOS, J. AND BOOTH, N. (1990) Occupational Asthma Caused by Latex in a Surgical Glove Manufacturing Plant. *J Allergy Clin. Immunol.*, 85, 626.
14. AZIZAH, M.R., SHAI-INAZ, M., HASMA, H., MOK, K.L., ESAH YIP AND NASURUDDIN, B.A. (1997) Latex Protein Allergy: A Prevalence Study of Factory Workers. *J nat. Rubb. Res.* 11(4), 240.
15. PALOSUO, T (1996) Identifying and Quantifying Natural Rubber Latex Protein Allergens. *Proc. International Conference on 'Latex Protein Allergy: Managing the Issue', Amsterdam*, 11.
16. ESAH YIP (1994) Total Extractable Proteins of Latex Gloves as Measured by Different Tests. (Unpublished results). Rubber Research Institute of Malaysia, Kuala Lumpur.
17. ESAH YEP (1997) Measurements of Total Extractable Proteins in Latex Gloves: A Comparative Study of the RRIM and ASTM Tests. *Proc. International Rubber Conference, Kuala Lumpur*, 353.
18. ESAH YEP (1994) Determination of Extractable Proteins in Latex Products by High Performance Liquid Chromatography (BPLC). *Latex Proteins and Glove Industry*. Kuala Lumpur: Rubber Research Institute of Malaysia, 4 1.
19. PALOSUO, T., MAKINEN-KILJUNEN, S., ALENIUS, H., REUNALA, T., ESAH YIP AND TURJANMAA, K. (1997) Measurement of Natural Rubber Latex Allergen Levels in Medical Gloves by an Allergen-specific IgE ELISA-inhibition, RAST-inhibition, and Skin-prick testing. To be published.
20. ESAH YIP, TURJANMAA, K., NG, K.P. AND MOK, K.L. (1995) Residual Extractable Proteins and Allergenicity of Natural Rubber Products. *Proc. International Conference on 'Latex Protein Allergy: The Latest Position, Paris*, 33.
21. ESAH YIP, PALOSUO, T., ALENIUS, H. AND TURJANMAA, K. (1997) Correlation between Total Extractable Proteins and Allergen Levels  
|  
of Natural Rubber Latex Gloves. *J nat. Rubb. Res.*, 12(2), 120.
22. NG, K.P., ESAH YIP AND MOK, K.L. (1994) Production of Natural Rubber Latex Gloves with Low Extractable Protein Content: Some Practical Recommendations. *J nat. Rubb. Res.* 9(2), 87.
23. NOR AISAH AB. AZIZ (1994) Formulations for Heat Resistant Chlorinated Natural Rubber Latex Films. *J nat. Rubb. Res.*, 9(2) 109.

24. TOMAZIC, VJ., SHAWAINE, E.L., LAMANNA, A., WITHROW, TJ., ADKINSON N.F. JR., AND HAMILTON, R.G. (1994) *J Allergy Clin. Immunol.*, 93(4), 753-758.
25. Towards Powder-free Low-protein Latex Gloves (1997) *Malaysian Rubber Glove Manufacturers' Association Newsletter*, 2nd. Quarter (Editorial).
26. LAI, RF. (1997) Benefits *versus* the Risk of Using Natural Rubber Latex Gloves. *Proc. International Rubber Conference, Kuala Lumpur*, 370.
- 27 MORRIS, M.D. (1994) Health Considerations of Synthetic Alternatives to Natural Rubber Latex. *J nat. Rubb. Res.*, 9(2), 121.
28. KORNIIEWICZ, D.M., LAUGHON, B., CYR, H., LYTLE, D. AND LARSON, E. (1990) Leakage of Virus through Used Vinyl and Latex Examination Gloves. *J Clin. Microbiol.*, 28, 787.
29. KORNIIEWICZ, D.M-., KIRWIN, M., CRESCI, K., TIAN SING, TAY ENG CHOO, WOOL, M. AND LARSON, E. (1994) Barrier Protection with Examination Gloves: Double *versus* Single. *A. JL C*, 22(1), 12.
30. ESAH YEP, TURJANMAA, K. AND MAKINEN-KELJUNEN, S. (1995) The 'Non-allergenicity' of NR Dry Rubber Products, with Reference to Type I Protein Allergy. *Rubber Developments*, 48(3/4), 48.

### **ACKNOWLEDGEMENTS**

The authors wish to thank the Director General of the Malaysian Rubber Board (MRB) for permission to publish this document. Deep appreciation is also extended to the members of the Latex Protein Allergy Task Force for their very helpful comments during the preparation of the monograph.

### **Disclaimer**

<p>This document is for information and educational purposes only. For medical advice, please consult your doctors/physicians.</p>
--