

The manufacture of gloves from natural rubber latex

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Gloves that will provide a barrier of protection from infectious organisms are an essential feature of medical practice for the protection of both patients and medical personnel. Natural rubber latex has consistently been the most satisfactory raw material for the manufacture of gloves. Certain latex proteins, carried over into the finished product by inadequate manufacturing processes, may pose a risk of provoking allergic reactions in some patients and medical workers. As with any allergy, the risk depends on the route of exposure and dose. Hence, the method of manufacture, including the means used to coat gloves to make donning easy, can influence the eventual exposure of sensitive people to latex allergens. In this article, we describe the several processes in use and their effects on latex protein content. (*J Allergy Clin Immunol* 2002;110:S3-14.)

Key words: Latex products, dry rubber products, residual extractable proteins, allergenicity, powdered and powder-free gloves, barrier protection

Section A

Because of the very good physical properties of the natural rubber elastomer, natural rubber (NR) products have been used preferentially worldwide for many years. This is particularly so for latex-dipped products, such as gloves and condoms, which are known for their excellent barrier protection against microorganisms including bacteria and viruses, as well as infectious fluids. The recent emergence of latex protein allergy (type I hypersensitivity), associated with the use of medical gloves and some other latex products, is of great concern to clinical professionals and the manufacturers. Prevalence has been reported to be less than 1% of the general population,^{1,2} although it appears to be higher among selected risk groups, such as employees in the health care sector. Research and development projects focusing on product improvement have been undertaken by latex glove manufacturing countries throughout the world, especially Malaysia, to address the problem. The objective of this article is to provide a better understanding of NR prod-

Abbreviations used

EP: Extractable protein
NR: Natural rubber
RRIM: Rubber Research Institute of Malaysia

ucts, particularly medical gloves and their association, if any, with latex protein allergy.

NR LATEX

NR products are derived from *Hevea brasiliensis* latex, a milky fluid obtained by tapping the bark of *Hevea* trees (Fig 1). Like all plant materials, latex contains growth-related substances such as proteins, carbohydrates, and other organic and inorganic constituents. The rubber hydrocarbon particles (the elastic component sought in all NR products) comprise 25% to 45% of the latex system. The nonrubber substances constitute only a small percentage of the latex system. When subjected to ultracentrifugation at approximately 59,000g, latex can be separated into 3 main fractions³ (Fig 2): (1) top rubber hydrocarbon particle phase; (2) ambient C-serum in which all latex particles are suspended; and (3) denser bottom fraction of nonrubber particles, particularly luteoids, which contain yet another serum (B-serum).

Proteins comprise about 1% to 1.5% of this latex system,⁴ with about 27% of this being found in the rubber phase, 48% in the C-serum, and 25% in the bottom fraction. A study of these proteins with sodium dodecylsulfate-polyacrylamide gel electrophoresis revealed that there are two major surface-bound proteins of 14 kd and 24 kd in the rubber particle phase.⁵ Although the soluble proteins in C-serum ranged from as low as 7 kd to as high as 133 kd, those in the B-serum showed a narrower molecular weight range, varying from less than 14 kd to about 45 kd.

The bulk of these proteins are removed when the latex is processed into its products. Only a small fraction remains in the product⁶ as the residual extractable proteins (EPs) implicated in the allergy reactions. Thus, although about 10 proteins have been identified to be potential allergens in latex,^{7,8} it is doubtful whether all of them could survive the stringent manufacturing processes and remain as part of an extractable fraction in latex products. Information regarding the status of allergenic proteins in latex products is presently incomplete.

Owing to their water solubility, most of the residual EPs can be leached out by washing. Thus, the quantity of this fraction, though small, does vary from product to product, depending on processing conditions used during manufacturing.

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0091-6749/2002 \$35.00 + 0 1/0/124499

doi:10.1067/mai.2002.124499



FIG 1. NR latex collected in a cup after skillful tapping of the bark of a *Hevea brasiliensis* tree.

TYPES OF NR PRODUCT

Hevea latex is usually converted into two major types of raw material from which products are made. They are the liquid latex concentrate and solid dry rubber.

For the preparation of liquid latex concentrate, latex collected from the trees is concentrated generally by centrifugation to remove part of the unwanted serum. This concentrates the rubber content (polyisoprene) of about 60% (vol/vol). NR latex is preserved with ammonia to combat bacterial growth when harvested from the tree and again after centrifugation. Latex concentrate is the starting material for NR latex products.

Dry rubber, on the other hand, is produced by a different route. The NR latex is coagulated, creped, crumbled, and washed extensively before being thoroughly dried at above 100°C. This raw material is available in the form of solid bales (eg, standard Malaysian rubber grades) and sheets (eg, ribbed smoked sheet grades), used in the production of NR dry rubber products.

NR latex products

Latex concentrates are mixed with various compounding chemicals before being processed into gloves, condoms, balloons, catheters, baby soothers, or dental dams. Production methods may involve dipping formers into latex, foaming into foam or sponge, or extrusion into latex thread or "elastic."

For dipped products,⁹ formers (molds) of the desired shapes are dipped into the compounded latex to enable the deposition of a thin film of latex. Dipping can be done either in the presence or absence of a destabilizing chemical (ie, coagulant or straight dips, respectively). The product is generally washed (the "wet-gel" or "pre-cure" leach) to remove the excess chemicals before it is

Distribution of Proteins (59,000 gmax)

Fresh Hevea Latex

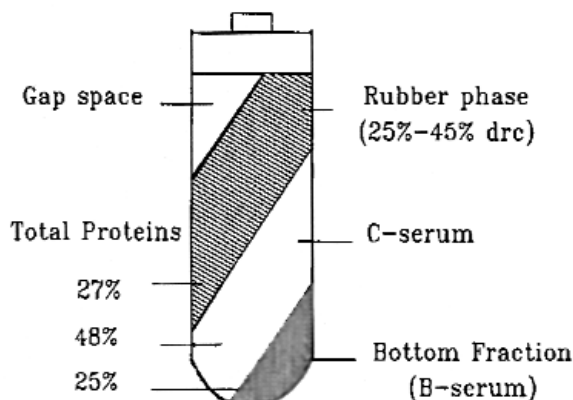


FIG 2. Freshly collected *Hevea brasiliensis* latex separated into its 3 main fractions on ultracentrifugation at 59,000g.

vulcanized in ovens at 100°C to 120°C. Leaching is also done after vulcanization, termed the *dry-gel* or *postcure leach*. In view of the protein allergy problem, emphasis is now placed on the application of optimized leaching protocols to remove as much as possible of the soluble allergenic proteins. Before the products are stripped from the formers, the gloves are dipped in a slurry tank where powder is applied to the products.

For foam products,¹⁰ the process usually involves incorporation of air into the compounded latex concentrate, usually with the use of a foamer. A gelling agent is then introduced, and the foamed latex is allowed to gel in a mold. Curing is carried out at 100°C, after which the product is washed and dried.

Latex threads¹¹ are prepared by continuous extrusion of a suitably compounded latex concentrate through appropriate nozzles of certain diameters into a bath of latex coagulant. The latter is usually an aqueous solution of acetic acid of an appropriate concentration. The extruded threads are washed, cured, dried, and lubricated.

NR dry rubber products

Raw dry rubber is the raw material for the production of tires, tubing, hoses, footwear, automotive components, engineering parts, adhesives, rubber-cut thread, and some household articles. The manufacture of these products generally involves mixing and compounding of the solid raw dry rubber with various chemicals, as well as with carbon black fillers as in the case of tires. Subsequent fabrication into products often involves processes such as molding, injection molding, extrusion, and calendaring. The choice of process used depends on the type of product manufactured. Vulcanization of rubber products is then carried out at high temperatures (140°-160°C).

NR LATEX PRODUCTS AND PROTEIN ALLERGY

Because the presence of residual EPs containing the allergens in latex products gives rise to a potential for an allergic reaction in sensitized individuals, the quantity of this fraction has gained much interest among users and manufacturers. Much of the protein allergy prevalence reported is related to NR latex products, especially gloves.

A survey of EP levels in medical gloves with the use of the modified Lowry test¹² revealed that glove EP levels could vary from as low as <20 µg/g to >1000 µg/g. A similar wide variation was reported by Yunginger et al,¹³ who measured the EP level by a modified triketohydrindene hydrate method and determined the allergen content by using serum of individuals with latex allergy in an immunologic inhibition assay. It should be pointed out that the absolute protein values generated by different tests for a given sample are not comparable^{14,15} because of differences in methodology and calibration standards used. The gloves with low EP content that were surveyed were undoubtedly the well-leached and properly processed or chlorinated powder-free gloves, whereas those with high EP content were the inadequately manufactured ones.

Other latex products generally have relatively lower EP content than gloves because of variations adopted in the processing conditions. This is particularly true for chlorinated products, such as catheters and many household gloves in which the EP content is $<100 \mu\text{g/g}$, often lower than $50 \mu\text{g/g}$ as measured by the modified Lowry test method. Testing of a number of commercially available toy balloons has also indicated a similarly narrower EP range from about $30 \mu\text{g/g}$ to $300 \mu\text{g/g}$. However, the modified Lowry test has been shown to be an inappropriate method for determining the residual proteins of foam products because of the interfering action of the gelling agents used, such as diphenyl guanidine, which often produces false readings. There is evidence that only about 10% to 20% of the EP readings obtained by this method are actually due to the presence of EP in the foam samples (Yip 1998, unpublished findings). Further investigations are needed to improve EP measurement methods for these products.

Risk indicators

In view of the wide range of EP content seen in gloves, it is of great interest to know how this parameter is related to the potential allergenicity of these products, because not all EPs are allergenic. A study to evaluate this relationship was undertaken by Yip et al.,¹⁶ who used the skin prick testing procedure for latex products developed by Turjanmaa et al.¹⁷ A total of 39 lots of commercially available medical gloves and gloves produced under different processing conditions were analyzed by using the modified Lowry test (Rubber Research Institute of Malaysia [RRIM]), and the extracts were also clinically skin prick tested on a total of 59 latex-sensitive subjects in Finland. Allergic responses were evaluated against a positive control histamine reference.

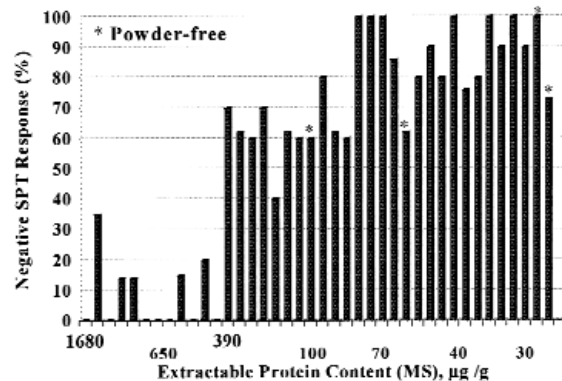


FIG 3. EP content of latex gloves and percentage of negative skin prick test responses shown by latex-sensitive subjects. (Reprinted with permission from Ong EL, Yip E, Lai PF. Latex protein allergy and your gloves. Kuala Lumpur: Rubber Research Institute of Malaysia, Malaysian Rubber Board; 1998. Monograph No. 1.)

Results showed that high EP levels are invariably associated with positive skin prick test responses, whereas low EP levels tend to show reduced allergic reactions. The study also revealed that when the EP level was $<400 \mu\text{g/g}$, more than 60% of the subjects with latex allergy did not have a positive response. At sufficiently low EP levels of about $100 \mu\text{g/g}$ and less, the percentage of non-responders generally increased and in some cases reached 100%, regardless of whether the gloves were powdered or powder-free (Fig 3).

A similar study,¹⁸ carried out in a group of 30 latex-sensitive individuals in a Canadian population with the use of 30 latex medical gloves, confirmed a significant relationship between EP content and allergenicity of latex gloves. Although the European study showed a correlation coefficient of 0.87, the Canadian study indicated a value of 0.94. The apparently high nonresponse level at $<100 \mu\text{g/g}$ (determined by modified Lowry test [RRIM]) observed in the Canadian study supported findings of the European study.

The markedly reduced allergenicity observed at EP levels $\leq 100 \mu\text{g/g}$ is also consistent with the assessment of allergen content, as determined by the IgE latex-specific ELISA-inhibition test, of 46 widely marketed medical latex gloves¹⁹ (Fig 4). Although the threshold level for sensitization is unknown, these findings have provided useful guidelines for the manufacture of gloves associated with reduced risk.

EP content reduction

Assuming that gloves with high EP content may elicit adverse reactions in sensitized users, many manufacturers, especially in Malaysia, are making concerted efforts to reduce the protein content in their products to a sufficiently low level. In fact, new and improved technologies are now available to achieve this. These include:

- Use of low-protein lattices (specially processed raw lattices)
- Proper optimized “precure” and “postcure” leaching protocols

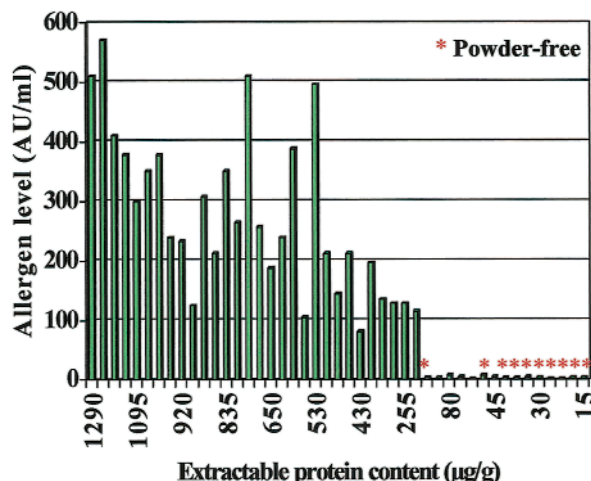


FIG 4. EP content and allergen level of 46 lots of latex gloves, as determined by modified Lowry test and IgE latex-specific ELISA-inhibition, respectively. (Reprinted with permission from Ong EL, Yip E, Lai PF. Latex protein allergy and your gloves. Kuala Lumpur: Rubber Research Institute of Malaysia, Malaysian Rubber Board; 1998. Monograph No. 1.)

- Chemical or enzymatic deproteinization
- Chlorination (powder-free)
- Polymer coating (powder-free)

Low-protein latices. The preparation of low-protein latices involves reduction of proteins during the liquid latex stage or reduction at the source. There are several ways for doing this, but the two approaches often adopted are physical means and enzymatic treatment.

1. Physical means: Latex concentrate (raw or prevulcanized) is diluted and re-centrifuged to further remove the soluble proteins in the serum phase.²⁰ Alternatively, a creaming and re-creaming process with a creaming agent can be used.
2. Enzymatic treatment: *Hevea* field latex or latex concentrate is treated with a proteolytic enzyme, after which the treated latex is centrifuged to remove the broken-down protein in the serum phase.²¹⁻²⁴ In such a preparation, a suitable stabilizing system, usually involving a surfactant, is required to maintain the colloidal stability of the latex. If left unstable, the latex could produce poor-quality film products.

Leaching protocol. Studies have shown that residual EPs on the surface of the gloves are concentrated on the donning side (or the surface away from the former during processing).^{25,26} This is largely due to migration of the soluble proteins within the wet latex film during the manufacturing process. This migration begins when latex gloves are first subjected to leaching at the wet-gel stage and continues during curing and drying in the vulcanization ovens. Thus, leaching both during the wet-gel/pre-cure stage and after the drying/postcure stage is strongly recommended to effect substantial removal of these residual proteins.²⁰

Chemical or enzymatic deproteinization. Instead of treating raw latex with a suitable chemical or proteolytic enzyme, this method involves dipping latex gloves in

enzyme solutions during processing under appropriate conditions.²⁷ The enzyme-treated gloves are then often subjected to further washing to remove the unwanted proteins (including the digested and fragmented latex proteins and enzymes), as well as chemical residues.

Chlorination. The process of chlorination is used to produce powder-free latex articles²⁸ because it can reduce the tackiness of latex film surfaces without the addition of lubricating powders. Chlorination usually involves pre-washing of powdered latex gloves to remove excess powder before their treatment with a suitable concentration of chlorine. This is followed by neutralization and further washing for the removal of surface residues. Chlorinated products generally have greatly reduced EP levels.

Polymer coating. Polymer coating provides an alternative way to reduce surface tackiness of powder-free latex gloves. The process involves the coating of glove surfaces with a polymer, which may be hydrogel, acrylic polyurethane, silicone polymer, or a polymer blend. The type of polymer used depends on the intended use of the device, device material, and other processing requirements. A dual approach is often adopted: (1) coating of the donning side and (2) chlorination of the gripping side of the glove.

Each of these processes, used under suitable processing conditions, is capable of reducing the EP content of latex gloves. The use of a combination of low-protein latex with precure and postcure leaching procedures has been shown to produce very effective EP content reduction.²⁰

Powdered and powder-free gloves

According to a report by the Food and Drug Administration,²⁹ 65% of medical gloves used in the United States in 1997 were powdered latex gloves, and only 35% of them were powder-free latex gloves. Because of the awareness of latex protein allergy and the possibility that powder from powdered gloves can become an aeroallergen, the trend of glove use has since been reversed. The percentage of powder-free gloves is now on the increase, whereas that of powdered gloves is on the decrease. The Food and Drug Administration has, in fact, forecast that the market share of powder-free gloves will increase to 80% in 4 years' time and that of powdered gloves will decrease to 20% in the same period. Is glove powder really a problem?

Cornstarch powder is presently used in the manufacture of gloves to facilitate easy donning and to keep the sides of gloves from sticking together. During processing, the finished gloves, while still attached to the formers, are generally powdered by dipping them into a powder slurry tank, after which they are dried and stripped from the formers. It is in the slurry tank that the uptake of any unremoved residual EPs from gloves by the powder particles occurs. Hence, powder particles from poorly processed gloves with high EP content are likely to be heavily laden with the undesirable proteins, which could become aeroallergens when the powder particles become airborne. However, if the EP content of gloves were low, the uptake by powder would also be expected to be low.

Tomazic et al,³⁰ in their study of glove powder, reported that glove powder particles do absorb glove proteins, but the amount is very small. Their results also indicated that such uptake of proteins by powder is much reduced when gloves of low EP content are analyzed. Furthermore, Yip et al,^{16,18,19} in their studies of the relationship between EP and allergenicity, as well as that between EP and allergen content of gloves, observed that powdered latex gloves with low EP levels can have very low or negligible allergenicity or allergen content, similar to that of low-protein powder-free gloves (Fig 5). Therefore, powder need not be a serious allergy issue when properly manufactured low-protein powdered gloves are used. Nevertheless, gloves with excessive powder should be avoided.

Powder-free gloves, on the other hand, have provided users a choice of latex gloves with very little or no lubricating powder. Those currently available in the market are largely prepared by chlorination. The process, while oxidizing the outer rubber surface of the glove to reduce tackiness, also markedly reduces the EP content. This is essentially attributed to the extensive washing procedure, as well as to a certain degree of insolubilization of proteins just below the surface of the gloves, which is thought to reduce migration to the surface. However, the chlorination process must be well controlled; otherwise, discoloration and inferior aging properties of the product could result.²⁸

Polymer-coated gloves provide another type of powder-free gloves. The function of the polymer coat is to replace powder as the donning lubricant. However, durability and donning capability of the coated gloves are influenced by both the bonding characteristics and the elasticity of the coating polymer. Poor bonding or vast differences in elasticity between NR and the coating material could result in the tendency of the latter to crack during processing and donning. EP levels of these gloves are generally low, but variation has also been observed as a result of differences in the processing conditions.

Choice of gloves

Because the fundamental function of gloves is to protect both the wearer and the patient against the transmission of infectious microorganisms, the most important criterion for selection of gloves for safe use should be barrier performance. With the onset of latex protein allergy affecting certain genetically predisposed individuals, the risk of sensitization and allergy-triggering reactions in these already allergic users should also be considered.

Properly manufactured NR latex gloves are known for their excellent barrier property, high strength, good elasticity, tactile sensitivity, comfort, fit, and durability. This is particularly so with powdered gloves. Over the years, manufacturers of synthetic gloves have attempted to simulate these NR properties. It is not unreasonable to say that today, these properties are still unsurpassed (in full) by any of the synthetic gloves currently manufactured.³¹

With the present availability of low-protein, powder-free, and low-powder latex gloves, users are now given a choice of latex gloves that can meet both the barrier and allergy selection criteria. To assist glove users in select-

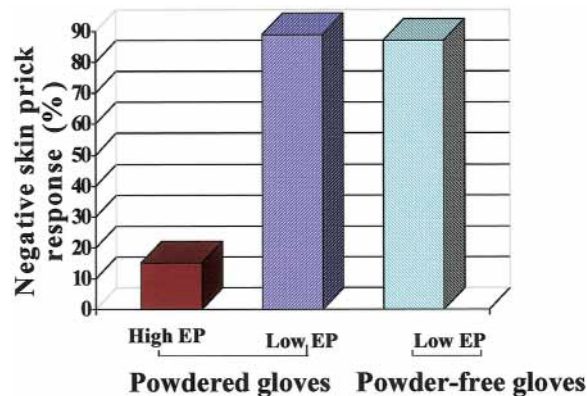


FIG 5. Negative allergic response by latex-sensitive persons when skin prick—tested with powdered gloves of high EP content (>600 µg/g) and low EP content (<100 µg/g), as compared with powder-free gloves with similarly low EP content. (Reprinted with permission from Ong EL, Yip E, Lai PF. Latex protein allergy and your gloves. Kuala Lumpur: Rubber Research Institute of Malaysia, Malaysian Rubber Board; 1998. Monograph No. 1.)

TABLE I. “In-use” barrier performance: A comparison between vinyl and natural rubber latex gloves

Date	Method used	Glove failure (%)		Reference
		NR latex	Vinyl	
1989	Dye	3.3	53	Korniewicz et al ³³
1990	Virus φX174	7	63	Korniewicz et al ³⁴
1990	Virus lambda	<1*	22*	Klein et al ³⁵
		<1†	56†	
1993	Bacteria, Gram-negative	9	43	Olsen et al ³⁶
1994	Dye/water leak test	4.1	51.3	Korniewicz et al ³⁸
		3.8‡	19.7‡	
1999	Water leak test	0-4	26-61	Rego and Roley ³⁹
			12-20§	

*No alcohol contact.

†Pretreatment with 70% alcohol.

‡Double gloving.

§Stretch vinyl.

ing the right latex gloves, Malaysia has developed a standard Malaysian glove program,³² whereby all certified gloves would provide users with effective barrier protection and minimum risk for development of latex allergy. It should be stressed that under no circumstances should inadequately manufactured latex gloves with high protein or high allergen content and excessive powder be used if further sensitization among the users is to be prevented or minimized.

Latex-sensitive individuals must choose gloves made of synthetic materials, because their best treatment is avoidance of the allergens to which they are sensitive. However, it is important to point out that in raising awareness of the allergy and seeking preventive measures, proper and balanced recommendations must be given. Because the majority of glove users are not thought to be likely to experience allergic reactions to latex, substitution of latex gloves with synthetic gloves should only be done with caution for the following reasons:

TABLE II. Latex allergen activity and extractable protein level of different grades of natural rubber dry rubbers and dry rubber products,⁵⁵ as evaluated by the IgE latex-specific RAST-inhibition and the modified Lowry tests

NR rubber sample	EP content ($\mu\text{g/g}$)*	Relative latex allergen activity (RLU/mL) [†]
SMR CV (raw rubber)	<20	6
SMR CV (compound mix)	<20	1
SMR L (raw rubber)	<20	4
SMR L (compound mix)	<20	3
SMR 20 (raw rubber)	<20	2
SMR 20 (compound mix)	<20	2
Cut thread A	<20	<1
Cut thread B	29	1
Cut thread C	<20	4
Hot water bottle	<20	<1
Diver's flippers	34	2
Reference: nonammoniated latex serum proteins		100,000
Control: latex gloves X	695	438
Control: latex gloves Y	689	431
Control: vinyl gloves	—	<1

Standard IgE antibody mixture was pooled from sera of 31 confirmed latex-sensitive subjects. Relative allergen activity: >100, very high; 100-50, high; 50-10, medium; 10-5, low; <5, very low or no activity. Latex gloves X and Y were two latex glove samples shown to have positive allergenicity.

NR, Natural rubber; EP, extractable protein; SMR, standard Malaysian rubber; CV, constant viscosity.

*Determined by RRIM modified Lowry test.

[†]Determined by RAST inhibition.

- Synthetic gloves, particularly vinyl, have inferior properties. Their poor barrier performance during use is well documented³³⁻³⁹ (Table I). If gloves of other materials^{39,40} are to be considered, it is important that they be able to provide effective barrier protection under conditions of use.
- Although the currently available synthetic gloves may be protein-free, they are not allergy-free. Instances of type IV allergic reactions caused by residual chemicals,⁴¹⁻⁴⁷ and even type I hypersensitivity (vinyl^{48,49} and nitrile⁵⁰), have been reported. Japan has recently issued a directive against the use of vinyl gloves with phthalates in the handling of food because of the leaching of harmful chemical residues from the gloves into food during handling.⁵¹
- Unlike disposal of NR latex gloves, which are biodegradable,⁵²⁻⁵⁴ disposal of most synthetic gloves by incineration emits hazardous and toxic substances.⁵⁵ Unless the process is well controlled, disposal on a large scale may adversely affect the environment.

NR DRY RUBBER PRODUCTS

In contrast to the wide range of EP content found in NR latex gloves, the amount of residual EP fraction in both raw dry rubbers and dry rubber products has been found to be extremely low. Yip, Turjanmaa, and Mäkinen-Kiljunen⁵⁶ studied 27 raw dry rubber samples from 9 differently processed dry raw rubber grades obtained from a number of different sources. Results showed that EP levels are generally <50 $\mu\text{g/g}$ and are in fact very often found to be <20 $\mu\text{g/g}$ (modified Lowry test [RRIM]). Subsequent vulcanization and fabrication processing of the dry rubber into its final product forms often involve high tem-

peratures and do not appear to have any adverse effects on the EP content, which remains low.

This low EP content is mainly attributed to the processing of raw rubber, whereby these proteins were either rendered insoluble by the acid used for coagulation or leached out by the extensive and continuous washing used throughout the procedure. Subsequent high-temperature drying and product fabrication methods often cause further reduction of the remaining protein. Assessments of both in vitro and in vivo allergen activities of a number of dry rubber and dry rubber products by IgE latex-specific RAST-inhibition immunoassay and skin prick testing, respectively, have confirmed the negligible allergenicity of dry rubber products⁵⁶ (Tables II and III).

The inhibition of IgE binding to NR latex proteins, reported for extracts of worn and contaminated tires,⁵⁷ may not necessarily be due to NR latex antigens. Some of the inhibition may be due to cross-reactive antigens also present in the extracts.^{58,59}

CONCLUSION

It appears that NR dry rubber products with their extremely low levels of residual EP and latex allergen are not likely to affect the majority of the population, although one can never exclude those who are allergic to NR latex. For NR latex gloves, in which the EP level has been found to vary widely, effective reduction of the residual EP fraction is now possible with the new and improved manufacturing technologies. Low-protein, low-powder and low-protein, powder-free NR latex gloves are now produced with the intent of preventing or minimizing sensitization among users, which may be glove-associated.

TABLE III. Residual extractable proteins of various grades of dry rubbers and dry rubber products and allergic responses to skin prick testing elicited in latex-hypersensitive persons⁵⁵

NR samples	EP content (μg/g)*	Allergic response by skin prick testing (%)		
		Negative	2+	3+/4+
SMR CV (raw rubber)	<20	100	0	0
SMR CV (compound mix)	<20	100	0	0
SMR CV (vulcanizate)	<20	100	0	0
SMR L (raw rubber)	<20	90	10	0
SMR L (compound mix)	<20	100	0	0
SMR L (vulcanizate)	22	100	0	0
SMR 10 (vulcanizate)	<20	100	0	0
SMR 20 (raw rubber)	<20	90	10	0
SMR 20 (compounded mix)	<20	100	0	0
SMR 20 (vulcanizate)	<20	100	0	0
RSS (raw rubber)	<20	88	0	12
RSS (vulcanizate)	27	100	0	0
DPNR: normal grade (raw)	22	90	10	0
DPNR: food grade (raw)	<20	100	0	0
Cut thread A	<20	100	0	0
Cut thread B	29	90	10	0
Cut thread C	<20	100	0	0
Hot water bottle	<20	100	0	0
Diver's flippers	34	100	0	0
Latex glove A	647	0	30	70
Latex glove B	655	0	23	77
Latex glove C	686	0	0	100

Latex gloves A, B, and C were known to show positive allergic responses. Compounded mix: American Chemical Society 1. Vulcanizate: with American Chemical Society formulation 1 for rubber gum mix, cured at 140°C for 40 minutes. A total of 31 subjects with latex hypersensitivity were clinically tested. Allergic responses: 4+, strong positive reaction; 3+, clear positive reaction; 2+, weak positive reaction; Negative, no positive reaction.

NR, Natural rubber; EP, extractable protein; CV, constant viscosity; SMR, standard Malaysian rubber; L, light-color grade; RSS, ribbed smoked sheet; DPNR, deproteinized natural rubber.

*Determined by modified Lowry test.

Glove powder does not need to be an allergy problem if gloves with low EP content are used. Although NR latex gloves, when properly manufactured, are the best protective devices available, the use of inadequately processed high-protein latex gloves with excessive powder should be avoided.

Only a small percentage of the population is allergic to NR latex. These individuals must wear synthetic gloves. For the much larger, unaffected majority of glove wearers, extreme caution must be exercised if the switch to synthetic protection is being considered. Incorrect choice of gloves could result in more serious health risks to all concerned. This is particularly so when diseases such as HIV, hepatitis, and other potentially lethal infectious agents can be transmitted to anyone if the gloves used have inferior barrier protection. All possible exposures and vulnerabilities must be taken into account in a risk-benefit analysis.

SUMMARY

NR products are derived from *Hevea brasiliensis* latex, about 1% of which is protein. Only a very small fraction of these proteins remains in the product as residual EP implicated in NR latex allergic reactions. Much of the protein is removable by various leaching processes. Thus, the quantity of EP can vary from product to product, depending on the processing conditions used.

Latex gloves have EP levels varying from <20 μg/g to >1000 μg/g (modified Lowry test); other latex products generally have a relatively lower and narrower range. Although the threshold level for sensitization is unknown, studies have provided guidelines for the manufacturing of low-protein gloves with reduced risk, especially for the unaffected majority of users.

With improved technologies, powdered gloves can now have markedly reduced EP content and allergenicity that may reach levels often associated with powder-free gloves, which generally have very low EP content, particularly because of the chlorination process.

Properly manufactured NR latex gloves are known for their excellent "in-use" barrier protection against transmission of viruses and other infectious agents. Substitution of these gloves with protein-free synthetic gloves with less superior barrier properties for the unaffected majority should only be attempted with caution.

The amount of residual EP in both dry and crumbled rubber and their products is extremely small, generally <50 μg/g. This is attributed to differences in the processes involved. Assessments of both in vitro and in vivo allergen activities of a number of dry rubbers and rubber products by RAST-inhibition immunoassay and skin prick testing, respectively, have confirmed their minimal allergenicity.

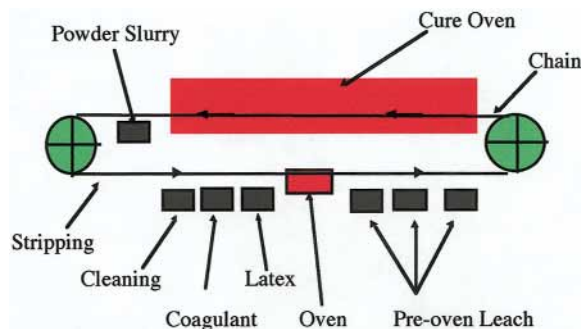


FIG 6. Batch machine.

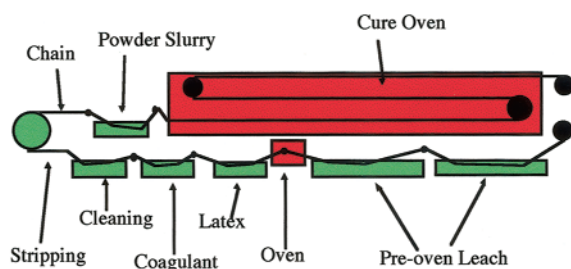


FIG 7. Continuous chain machine.

Therefore, NR dry rubber products are not likely to affect the majority of the population.

Section B

GENERAL MANUFACTURING PROCESSES AND MACHINE TYPES

For the manufacture of natural rubber or even synthetic gloves, there are basically two styles of machines.⁶⁰ These are the batch style and the continuous chain or drag line machines. For each grouping, there are a variety of subsets of designs because manufacturers often design and build their own machines or can purchase machines from machine fabricators. To keep the presentation simple, I will only refer to the more common style machines.

The operation of batch machines (Fig 6), more commonly used for surgical gloves, can best be described as a group of formers indexing their way through a series of dipping tanks. These machines tend to be very flexible because the parameters for each dipping function can be independently set and are not fixed to the parameters of the other dip tanks, as is the case with the continuous chain machines. Each dipping function is only limited by the slowest preceding dipping operation (Fig 7).

The design of a continuous chain machine is much more critical than that of a batch machine. The speed of the chain movement, the length of the dip tanks, and the individual distances between each dipping point are all heavily interdependent. An example of this is: if the soak time in a leach tank needs to be adjusted, it cannot be done without affecting all the other soak times. The only way to make such an adjustment is to physically alter path lengths or increase the length of the leach tank.

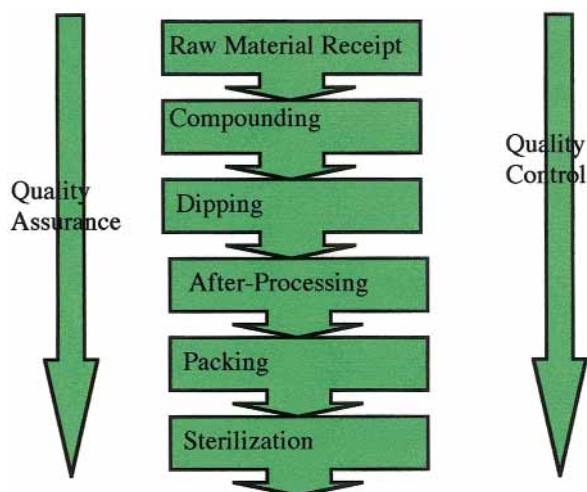


FIG 8. Overall process flow.

Batch machines are generally used for the manufacture of surgical gloves, and chain machines are used to make both surgical and examination gloves.

GENERIC MANUFACTURING PROCESS

Although manufacturers have many proprietary features to their own manufacturing processes, they generally follow a standard sequence (Fig 8).

The formers or molds on which the gloves are shaped are generally made of porcelain⁶¹ but can be made of plastics capable of withstanding high temperatures. The former surface needs to be maintained in a clean state to obtain an even and continuous deposition of the latex. Consequently, the first step in most processes is former cleaning. A variety of cleaning agents can be used, including alkaline solutions, acidic solutions, oxidizing agents, surfactants, and a combination of these.

Once the former surface has been cleaned, the next step is to coat the former with a coagulant,⁶² which will assist in controlling the amount of latex that will be deposited on the mold and eventually determine the thickness of the glove. Several coagulants can be used, with the most common being calcium nitrate. The coagulant solution may also contain some type of parting agent, which will prevent the rubber from adhering to the porcelain surface and allow the cured glove to be stripped off the former. Calcium carbonate is generally used as a parting agent. In some of the powder-free processes, other salts and even some polymers can be used as the mold release agent.

After the former has been coated and dried, it is immersed in a latex solution.⁶³ The latex can be either synthetic or natural and will generally have been mixed or compounded with curatives, antioxidants, and stabilizers. It may also be prevulcanized.⁶⁴ Pre vulcanization is a process by which the curing process is partially accomplished before dipping.

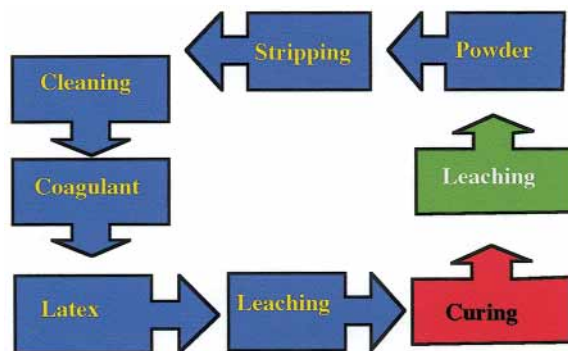


FIG 9. Powdered glove manufacture, post-oven leach.

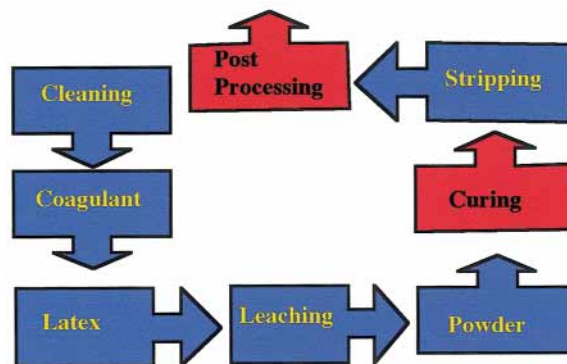


FIG 10. Powdered glove manufacture, off-line powdering.

The latex that has now been deposited on the former is allowed to build up some wet-gel strength before leaching. The leaching process⁶⁵ before the vulcanization step is effective in removing residual calcium nitrate and does remove some soluble protein. Hot water is used, and the tanks are usually regularly replenished with fresh water.

The leached latex now enters a vulcanizing oven where the rubber will achieve its final strength. Exit from the oven is the point at which processes can vary significantly.

POWDERED GLOVE MANUFACTURE

Three basic manufacturing routes can be used at this stage.⁶⁶

1. The gloves can be dipped into a powder slurry and then stripped and packed.
2. The gloves can be leached again and then powdered with a powder slurry.
3. The gloves can be stripped, washed, dried, and powdered.

Process 1 is the simplest and possibly the most commonly used approach. The glove is stripped from the former and packed. The glove surface would be expected to contain high levels of residual materials.

Process 2 is what is commonly referred to as a *post-oven leaching process*. During the vulcanization process, the water entrapped in the latex film is turned into steam and escapes through the film. As the steam passes through the film, it will carry with it any residual nitrates, curatives, and soluble proteins. This is similar in essence to a steam distillation. Consequently, the surface of the latex glove as it exits the vulcanizing oven is rich in these materials. Presentation of this surface, with its high concentration of chemicals and protein, to a leach tank containing clean hot water enables the surface to be easily washed and effectively reduces the concentration of the aforementioned materials. It is crucial that the water in the leach tank be continually refreshed; otherwise, the concentration of the extractable material increases to a point at which contaminants are added rather than removed from the glove surface (Fig 9).

In process 3 the gloves are post-processed. The gloves, after they are stripped from the formers, are placed in a commercial washer where they are subjected to a hot

water and detergent wash, followed by hot water rinsing. This washing is very effective in removing residual chemicals such as nitrates and certain curatives, and it also dramatically reduces the protein levels (Fig 10). Not all glove formulations lend themselves to washing in this manner, and consequently, some development work is required to make this change to an existing process that does not use post-processing.

It is important to note that the leaching process for the removal of water-soluble protein is only critical for gloves made from NR latex and not for synthetic gloves.

Powder-free processing

Today, a variety of methods are available for the production of powder-free gloves. These are (1) chlorination, (2) coatings, and (3) powder-free coagulants and coatings.

Chlorination

Chlorination is probably the most widely used method for the manufacture of powder-free gloves.⁶⁷ The double bonds in the polyisoprene polymer contained within NR latex are very susceptible to the addition of chlorine. The effect of the chlorine on the surface of the glove is to stiffen and detackify the rubber surface; in fact, chlorination is a type of accelerated aging. The chlorine is detrimental to the physical properties of the glove. For this reason, it is important that the chlorination process be carefully controlled because over-chlorination will result in gloves that have shorter shelf-lives and poorer physical properties. The NR gloves will also become discolored and have a bad odor. Some synthetic gloves may also be detackified by means of chlorination.

Chlorination of gloves can be done in several ways.

The gloves can be produced in the standard way that powdered gloves are produced and subjected to a batch chlorination process. The most common piece of equipment used to chlorinate gloves is a rotating drum chlorinator, which is commercially available.

A chlorination cycle may involve the following steps:

1. Prewashing
2. Exposure to a chlorine solution
3. Neutralization
4. Rinsing
5. Drying

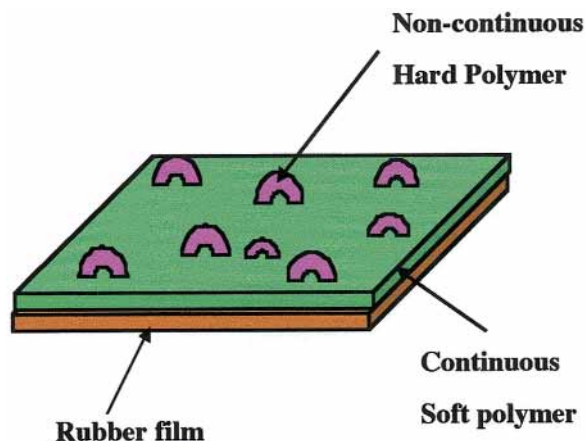


FIG 11. Powdered glove manufacture, coatings.

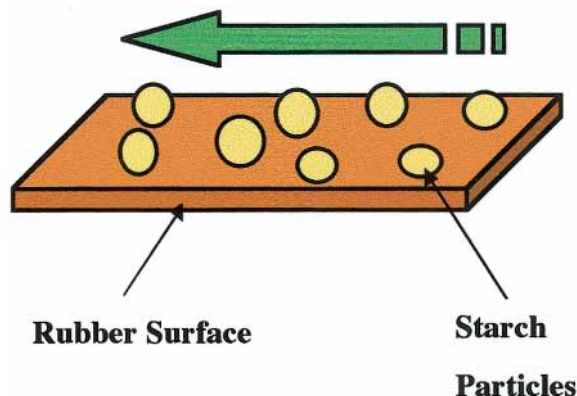


FIG 12. Powder-free glove manufacture, powdered surface.

TABLE IV. Physical properties

Nonchlorinated			Aged			
Original						
Modulus	Tensile	Elongation	Modulus	Tensile	Elongation	Protein
2.8	36.3	873	2.4	34.0	935	155 µg/g

The powdered gloves can be placed directly in the chlorinator, and with the use of high concentrations of chlorine, the gloves are chlorinated on the inside and outside, with the outside receiving a heavier dose. Gloves processed in this way are usually badly discolored and have a distinct odor. They also tend to have lower values for tensile strength and show a marked decrease in their aged tensile properties (Table IV).

An alternative process is to manually invert the gloves to expose the inner surface and chlorinate them by using a lower-strength solution. The gloves are then re-inverted. They can be dried at this stage, or they can be subjected to a further chlorination cycle to reduce the surface tack. Gloves that are not chlorinated a second time usually have good grip characteristics but tend to stick to each other in the box, which makes dispensing difficult. Gloves that are double-chlorinated have a smoother feel but will not block in the packaging. The processes in which lower chlorine concentrations are used produce gloves that have better physical properties than those produced with high chlorine concentrations.

Another technique is use of on-line chlorination. The advantages of using this method are that the outside of the glove is chlorinated and can then become the inner surface for donning when inverted at stripping. Post-dip chlorination is then performed very lightly on the outer surface (after inversion). These processes aid in maintaining better physical properties. Further, donning is improved and gloves will not block in packaging.

Coatings

Coating the inner surface of the glove, followed by chlorination of the outer surface, is becoming the more

common technique to render gloves powder-free. An example of gloves produced by this method is the Ansell Perry Encore line of gloves (Ansell Perry, Massillon, Ohio). Coatings offer the opportunity for manufacturers to enhance or improve the donnability of gloves. Some coatings provide excellent dry hand donning, whereas others provide both dry and damp or wet hand donning. Typical coating materials are polyacrylates, polyurethanes, and combinations of the two. The coatings can be classified as hydrogels⁶⁸ and nonhydrogels.^{69,70} Hydrogel coatings are composed of materials that absorb water many times their weight and become swollen and slippery so that a glove is easily donned. Nonhydrogels repel water, and the topography of the coating mimics the characteristics of a powdered surface.

These coatings allow good donnability because they usually provide a topography to the glove inner surface that contains hard spherical protrusions embedded in a soft binding matrix (Fig 11). This topography closely resembles a powdered surface on which the spherical powder particles act like "ball bearings" and allow the hand to glide over the surface of the glove (Fig 12).

There are two methods of applying coatings to gloves: on-line and after-processed. On-line coating applications occur during the glove-making operation just before final oven drying. The coating is applied as an overdip on the wet-gel glove. Priming⁶⁸ of the wet gel is sometimes used to ensure good adhesion of the coating to the glove surface. Primers are generally acids or salts that are applied as an overdip and activate the surface of the glove for better binding of coating material.

After-processed coatings refer to washing the finished gloves in a batch washer and at the same time treating the

gloves with a coating material. Materials typically used are the same as those used in on-line coating applications. The wet, coated gloves are then dried in batch dryers. A drawback to this technique is that both sides of the glove can be coated; this affects the grip of the outside surface and often does not provide adequate donnability.

Powder-free coagulants and coatings

Several glove manufacturers are using glove processes that do not involve powders. The technique uses the previously mentioned coatings coupled with a powderless coagulant.⁷¹ Typically, a coagulant contains a release agent (powder) to facilitate stripping, or removal, of the finished glove from the glove former. Powder-free coagulants that do not require powder to release the glove from the former have been developed. Organic release agents are being used as substitutes for the powder. Tack and grip can be controlled to provide the glove user with the desired characteristics.

In some cases, modifications to the latex formulation and/or processing produce a dryer, less tacky rubber, eliminating the need for all powders.

The nonuse of powder in the glove manufacturing process has eliminated the need for washing and chlorination. However, this may affect the latex protein content of NR gloves, because washing and chlorination are excellent techniques for reducing extractable allergenic materials.

SUMMARY

Manufacturers use a variety of machines and processes to produce both surgical and examination gloves.⁶⁰ The most popular style of machine for the production of examination gloves, and to some extent surgical gloves, is the continuous chain or drag-line machine.

Powdered gloves are typically produced by means of an on-line powdering process in which the gloves are dipped into a slurry made from modified cornstarch.⁶⁶ Some manufacturers have used off-line processes in which the gloves are washed, dried, and powdered. The powdering can be accomplished by either a wet or dry process.

The most widely used method for the production of powder-free gloves is subjection of the gloves to a chlorination process.⁶⁷ Chlorine is used to chemically modify the NR surface. This modification reduces the surface tack of the rubber and allows the glove to be donned without the use of powder. However, this treatment is not sufficient to allow the glove to be donned when the user's hand is damp or wet.

This shortfall in the performance of the gloves led to the development of polymeric coatings, which when applied to the rubber surface, allowed the user to don the gloves not only with dry hands but also with damp or wet hands. This feature is particularly important for surgical gloves because intraoperative changes may be necessary.

The coatings are made from a variety of materials.⁶⁸⁻⁷⁰ Acrylates, urethanes, and even nitriles have been used as surface coatings for medical gloves. The methods of application to the rubber surface range from on-line coatings to off-line washing processes.

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