

Immunoadjuvant properties of glove cornstarch powder in latex-induced hypersensitivity

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Summary

Background Cornstarch powder present in medical gloves plays an important role in latex-induced hypersensitivity as allergen carrier either, by the inhalation route, by skin contact or by direct contact with mucous membranes.

Objective Our objective was to test the hypothesis that cornstarch could act as an immunoadjuvant in immediate type-I latex-induced hypersensitivity.

Methods Guinea-pigs were sensitized by intraperitoneal route with two different antigens (latex proteins and ovalbumin) with or without cornstarch powder. Airway responsiveness after specific bronchial provocation was evaluated and specific IgG and IgG₁ levels were determined by enzyme-linked immunosorbant assay (ELISA). Controls were treated with cornstarch powder or saline alone.

Results Animals sensitized with latex proteins ($n = 7$ in each group) showed significant bronchoconstriction ($P < 0.03$) and higher anti-latex antibody levels than the controls ($P < 0.005$). Guinea-pigs sensitized with latex-contaminated cornstarch had higher levels of specific antibodies than those sensitized with latex alone ($P < 0.05$). Animals sensitized to latex mixed with cornstarch showed higher bronchospasm than those treated with latex alone ($P < 0.003$). Animals sensitized to ovalbumin mixed with cornstarch also showed higher antibody and bronchoconstriction levels ($P < 0.05$) than those immunized with ovalbumin alone but antibody titres were significantly lower than those of the animals treated with ovalbumin and Freund's complete adjuvant ($P < 0.01$; $n = 5$ in each group).

Conclusion Our findings show that cornstarch powder increases antigen-induced bronchoconstriction and antibody production. This role of immunoadjuvant is not antigen-specific. The cornstarch powder used as donning agent in latex gloves is an allergen carrier and it can enhance latex-induced hypersensitivity.

Keywords airway hyper-responsiveness, cornstarch glove powder, guinea-pig, IgG₁, immunoadjuvant, latex, latex allergy

Submitted 29 April 2002; revised 26 July 2002; accepted 14 October 2002

Introduction

Within the last 20 years, the prevalence of immediate IgE-mediated type I hypersensitivity to natural rubber latex (NRL) has dramatically increased [1]. Health care workers (HCW) are the group most at risk because of the increasing use of latex gloves and other products containing NRL [2–4]. Patients, particularly children who have undergone multiple surgical procedures for spina bifida, are also affected [5–8].

The mechanism of sensitization to NRL is not clearly established. Three routes are likely:

skin

respiratory tract: because of the switch from talc to cornstarch (CS) powder as a donning agent in NRL medical gloves, this

route may be predominant for HCW. Sensitization could occur through inhalation of airborne CS particles that are known to adsorb the NRL proteins responsible for IgE-mediated hypersensitivity. Furthermore, the use of non-powdered gloves by HCW has led to a decrease in the occurrence of the NRL hypersensitivity reactions [9–11].

mucous membranes: this route is considered to be important for patients resulting from direct contact of latex medical devices on these membranes during surgical and other procedures [12].

NRL itself is capable of inducing a strong immunological response, including the production of IgE antibodies when administered intraperitoneally, intranasally or by the tracheal route to experimental animals [13–16]. The involvement of CS powder in NRL sensitization as allergen carrier is also well documented, but its role as adjuvant in latex-induced hypersensitivity has not been established [17].

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The aim of the present study was to investigate the property of CS as potentiator of latex-induced hypersensitivity reaction features such as specific antibody production and bronchoconstriction (BC) after antigen challenge. The role of CS powder as potentiator of immediate hypersensitivity reactions was also studied with an ovalbumin (OV) experimental model of sensitization that is easier and more widely studied.

Methods

Animals

Male albino Dunkin–Hartley guinea-pigs (weight 300–350 g) were purchased from the Elevage Saint Antoine, Pleudaniel, France. The animals were maintained on a standard diet in the animal facility of the UFR Biomédicale des Saints-Pères, Université Paris V, France. Utmost care was taken to avoid undue pain to the animals.

The guinea-pig was chosen as the experimental model because its respiratory tract morphology is similar to that of humans [18]. This animal is considered as a very good airway hyper-responsiveness model and exhibits analogous airway responsiveness and antibody-mediated reactions to those occurring in humans [19–22].

Antigen sources

OV used in this study was a commercial reagent from Serlabo, France. NRL used was non-ammoniated latex kindly provided by Dr R.G.O. Kekwick (Department of Biochemistry, University of Birmingham, UK). The fresh latex fluid, obtained from a *Hevea brasiliensis* tree in Thailand, was collected and immediately ultracentrifuged. The liquid phase containing the majority of the proteins (C-serum) was then separated and lyophilized. The C-serum contained 240 mg protein/g of lyophilisate, as determined by the EN455–3-modified Lowry method [23].

Different sources of glove donning CS powders were used in this study: (i) cornstarch (Agenasorb 9020, Agrana Stärke GMBH, Wien, Austria) which is habitually used for powdering latex gloves had never been in contact with any NRL source; (ii) NRLCS₁ is a mixture of CS mentioned in (i) with NRL in saline solution: 0.4 g CS were suspended in 1 mL of NRL 1 mg/mL in saline solution; (iii) NRLCS₂ is a CS powder bearing NRL proteins which was collected in the slurry tank on the glove production line of a latex glove manufacturing plant in Thailand. NRLCS₂ contained 228 µg of proteins/g of dry powder (EN 455–3).

NRL, CS, NRLCS₁ and NRLCS₂ samples were assayed by enzyme-linked immunosorbent assay (ELISA) and radioallergosorbent test (RAST) inhibition methods as previously described, to determine antigenic and allergenic NRL protein contents [24, 25]. These data were used to calculate the total dose given to the animals (Table 1).

The endotoxin content in CS, NRLCS₂ and OV + CS solutions was determined by using the kinetic chromogenic quantitative *Limulus* amoebocyte lysate assay (BioWhittaker) according to the *European Pharmacopoeia*. The assay revealed an endotoxin content of 1.3 ng/g cornstarch in CS, 324 ng/g for NRLCS₂ and 7.6 ng/mL in the OV + CS suspension (Prof. J.C. Darbord, Laboratoire des Contrôles Biologiques, PCH, Paris, France).

Sensitization protocol

Sensitization of guinea-pigs with NRL or OV was conducted according to the schedule described in Fig. 1.

Five groups ($n = 7$ in each group) were sensitized to latex by one subcutaneous (s.c.) injection on day D1 and four intraperitoneal (i.p.) injections on days D3, D5, D8 and D10 of the sensitization protocol (Fig. 1a). The NRL group received 0.5 mL of NRL 1 mg/mL diluted in sterile 0.9% NaCl solution per injection. The NRLCS₁ group received 0.5 mL per injection of the NRLCS₁ suspension. The NRLCS₂ group received 0.2 g of NRLCS₂ powder suspended in 0.5 mL of saline solution. The NaCl group received 0.5 mL of saline solution alone and the CS group received 0.2 g of CS alone suspended in 0.5 mL of saline solution (controls).

Three groups ($n = 5$ in each group) were sensitized with OV by one s.c. injection on day D1 and two intramuscular (i.m.) injections on days D3 and D5 of the sensitization protocol (Fig. 1b) as previously described [26]. OV group received 5 mg OV in 0.5 mL of sterile 0.9% NaCl solution per injection. OV + CS group received 5 mg OV + 0.33 g of CS in 0.5 mL of the saline solution. OV + FCA group (Freund's complete adjuvant, Difco Laboratories, Detroit, MI, USA) received 5 mg OV + 0.25 mL of FCA + 0.25 mL of saline solution.

Table 1. Total dose of latex proteins received by the guinea-pigs sensitized to latex, determined by the modified Lowry method according to the EN455–3 norm, CIALP (competitive immunoassay for antigenic latex proteins) and RAST (radioallergosorbent test) inhibition methods

Groups	Cornstarch (g)	Total proteins (µg)	Antigenic proteins (µg)	Allergenic proteins (µg)
NaCl	–	ND	ND	ND
CS	1	ND	ND	ND
NRL	–	582	143	127
NRLCS ₁	1	582	143	127
NRLCS ₂	1	228	2	9

NaCl, saline alone; CS, cornstarch alone; NRL, natural rubber latex; NRLCS₁, NRL mixed to CS; NRLCS₂, latex-contaminated cornstarch; ND, not detected.

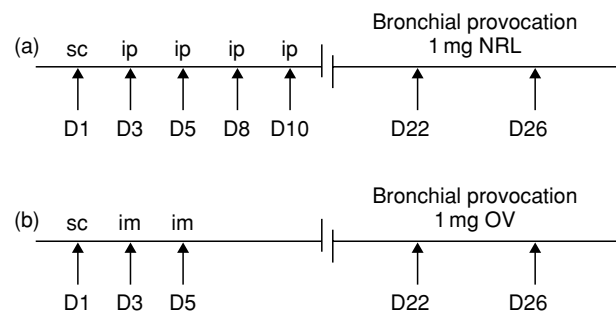


Fig. 1. Sensitization protocol. (a) Guinea-pigs separated in five groups ($n = 7$ in each) received five injections (one s.c. and four i.p.) of NRL, NRLCS₁, NRLCS₂, NaCl or CS. (b) Guinea-pigs separated in three groups ($n = 5$ in each) received three injections (one s.c. and two i.m.) of OV alone, OV + CS or OV + FCA. Both NRL and OV challenges were performed between D22 and D26. s.c., subcutaneous; i.p., intraperitoneal; NRL, natural rubber latex; NRLCS₁, NRL mixed to CS; NRLCS₂, latex-contaminated cornstarch; CS, non-contaminated cornstarch; i.m., intramuscular injection; OV, ovalbumin; FCA, Freund's complete adjuvant.

All animals were challenged with NRL or OV between days D22 and D26. The animals were bled after bronchial challenge. The blood was centrifuged (15 min at 1500 *g*) and the serum was collected and stored at -20°C until assayed.

Bronchial provocation

The degree of BC after NRL or OV challenge was evaluated by a modification of the method originally described by Konzett and Rössler [27], that is, by measuring variations in pulmonary insufflation pressure (PIP). Guinea-pigs were anaesthetized with urethane i.p. (1.5 g/kg) and the left jugular vein and the right carotid artery were catheterized. The carotid artery was connected to an arterial pressure transducer (DPT 700–500, NARCO Biosystems, Houston, TX, USA). The animals were tracheotomized and connected to an artificial respiration pump (Braun, Melsungen, Germany) and a differential pressure transducer (PM5, Statham, Los Angeles, CA, USA). The ventilation parameters (volume and frequency) of each animal were calculated according to the Kleinman and Radford table [28]. Anaesthetized animals were pre-treated with propranolol (2 mg/kg i.p.) (Sigma, St Louis, MO, USA) at least 10 min before challenge to prevent possible bronchodilatation induced by catecholamines [29]. Then, challenge was performed by instillation of 1 mg NRL or OV in 20 μL of saline solution directly into the lungs via the trachea. PIP variations and arterial pressure were recorded during 15 min with the differential pressure captor connected to a Physiograph E & M (NARCO Biosystems).

Determination of latex-specific IgG and IgG₁

Anti-latex IgG and IgG₁ were determined in the guinea-pig sera by direct ELISA methods. NRL 50 $\mu\text{g}/\text{mL}$ in bicarbonate buffer 0.1 M pH 9.6 was used to coat the wells of microplates (Maxisorp™, NUNC, Roskilde, Denmark) overnight at 4°C . Phosphate-buffered saline (PBS) 0.1 M pH 7.4 + 0.05% Tween-20 + 1% bovine serum albumin (BSA; Sigma) was used as blocking buffer (overnight at 4°C).

For total anti-latex IgG determinations, 150 μL of serial dilutions in EIA buffer [phosphate-buffered saline (PBS) + 0.05% Tween-20 + 0.1% BSA] of the serum samples were incubated overnight at 4°C . Wells were washed with PBS + 0.05% Tween-20, then 150 μL of rabbit anti-guinea-pig IgG peroxidase-labelled (Sigma) 1:10 000 diluted in EIA, were added to the wells and incubated 1 h at 37°C . Colour development was read at 405 nm wavelength with an automated microplate reader (MRX, Dynex, Issy-les-Moulineaux, France) 30 min after addition of the peroxidase substrate *o*-phenylenediamine dihydrochloride (Sigma).

To determine the titres of guinea-pig anti-latex IgG₁, 150 μL of the serum dilutions were incubated overnight at 4°C . The wells were then washed and 150 μL of 1:1000 rabbit anti-guinea-pig IgG₁ (heavy chain-specific, Bethyl Laboratories, Montgomery, TX, USA) were added to the wells and incubated overnight at 4°C . After four washes, 150 μL of 1:10 000 mouse monoclonal anti-rabbit peroxidase-labelled (Sigma) were added and incubated 1 h at 37°C . Colour development was performed as described above.

Three sera from control guinea-pigs were also assayed for latex-specific IgG and IgG₁ determination then the mean dilution curve was calculated (OD values plotted against the corresponding dilutions).

Individual titres of anti-latex IgG and IgG₁ were calculated from their dilution curve. The titre, expressed in ELISA units (EU), is the reverse dilution value corresponding to the intersection point between the dilution curve and the mean dilution curve +2SD (standard deviation) of the sera of three control guinea-pigs.

Determination of ovalbumin-specific IgG and IgG₁

OV-specific IgG and IgG₁ antibody titres in the guinea-pig sera were determined as described above but, instead of NRL, microplates were previously coated with OV 20 $\mu\text{g}/\text{mL}$ in bicarbonate buffer 0.1 M pH 9.6. Anti-OV antibodies titres were calculated according to the method described above for calculation of the anti-latex antibody titres.

Data analysis

Results were expressed as the mean of the group $\pm$ standard error of the mean (SEM). For comparison between specific antibody titres and PIP variations, the area under the curve (AUC), expressed in $\text{cmH}_2\text{O} \times \text{min}$, was calculated for each animal. The results of specific antibody measurements and PIP variations were compared using the Mann–Whitney *U*-test. Correlation between IgG and IgG₁ titres and PIP variations were calculated using the non-parametric Spearman correlation test. For all statistical tests, a $P < 0.05$ was considered as significant.

Results

Sensitization with NRL

An increase of the PIP variations after latex challenge was observed in the animals sensitized with latex, i.e. NRL, NRLCS₁ and NRLCS₂, compared to the controls (Fig. 2a). The groups treated with NRL containing CS powder had higher PIP variations than the group sensitized with NRL alone ($61.3 \pm 10.7 \text{ cmH}_2\text{O} \times \text{min}$ for NRLCS₂ and $91.4 \pm 5.3 \text{ cmH}_2\text{O} \times \text{min}$ for NRLCS₁ vs. $36.7 \pm 9.0 \text{ cmH}_2\text{O} \times \text{min}$ for NRL group) (Fig. 3). But the BC level was significantly higher than NRL only with those treated with NRLCS₁ ($P < 0.003$). The PIP variations observed on the control groups, i.e. guinea-pigs that received only NaCl ($14.3 \pm 5.8 \text{ cmH}_2\text{O} \times \text{min}$) or CS ($11.1 \pm 4.3 \text{ cmH}_2\text{O} \times \text{min}$), were not significantly different.

Sensitization with latex proteins induced significant anti-latex IgG and IgG₁ production compared to the control groups ($P < 0.005$; Fig. 4). No difference was observed between NRL (IgG: $788 \pm 190 \text{ EU}$ and IgG₁: $677 \pm 239 \text{ EU}$) and NRLCS₁ group (IgG: $367 \pm 66 \text{ EU}$ and IgG₁: $1479 \pm 437 \text{ EU}$). But guinea-pigs treated with NRLCS₂ had significantly higher IgG and IgG₁ titres (IgG: $2124 \pm 670 \text{ EU}$, $P < 0.03$ and IgG₁: $4607 \pm 1352 \text{ EU}$, $P < 0.005$) than those immunized with NRL alone. There was a highly significant correlation between the anti-latex IgG and IgG₁ titres ($r = 0.94$, $P < 0.0001$). A significant correlation between PIP variations and latex specific IgG ($r = 0.64$, $P < 0.001$) and IgG₁ ($r = 0.68$, $P < 0.001$) was also observed.

Sensitization with OV

Sensitization with OV + CS or OV + FCA resulted in higher BC to OV after bronchial challenge compared to OV alone

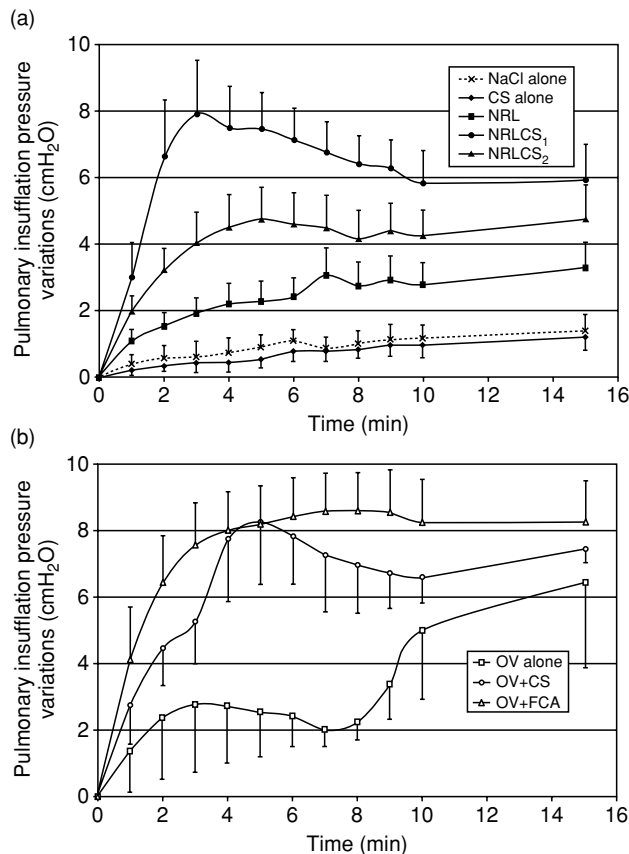


Fig. 2. Pulmonary insufflation pressure (PIP) variations measured on guinea-pigs after bronchial provocation. (a) Guinea-pigs ($n = 7$ for each group), previously treated with NRL (■), NRLCS₁ (●), NRLCS₂ (▲), NaCl (x) or CS (•), were challenged with 1 mg of NRL. (b) Guinea-pigs were pre-treated with OV alone (□), OV + CS (○) or OV + FCA (△, $n = 5$ each) and were challenged with 1 mg OV. Data are expressed as the mean of the group $\pm$ SEM.

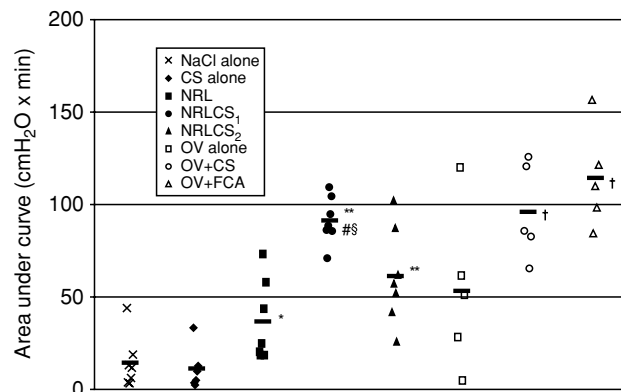


Fig. 3. Bronchoconstriction level expressed as the AUC calculated for each guinea-pig after bronchial provocation with 1 mg NRL or 1 mg OV. The mean of the group ($n = 7$ or 5 in each) is represented as the '—' symbol. * $P < 0.03$ and ** $P < 0.005$ compared to control groups, # $P < 0.003$ compared to NRL group, \$ $P < 0.04$ compared to NRLCS₂ group and † $P < 0.05$ compared to OV group. NRL (■), NRLCS₁ (●), NRLCS₂ (▲), NaCl (x) or CS (•), OV alone (□), OV + CS (○) or OV + FCA (△).

(Fig. 2b). BC level was significantly higher with OV + CS or OV + FCA treatment (respectively 95.9 ± 11.7 cmH₂O × min and 114.2 ± 12.2 cmH₂O × min, $P < 0.05$) compared to OV

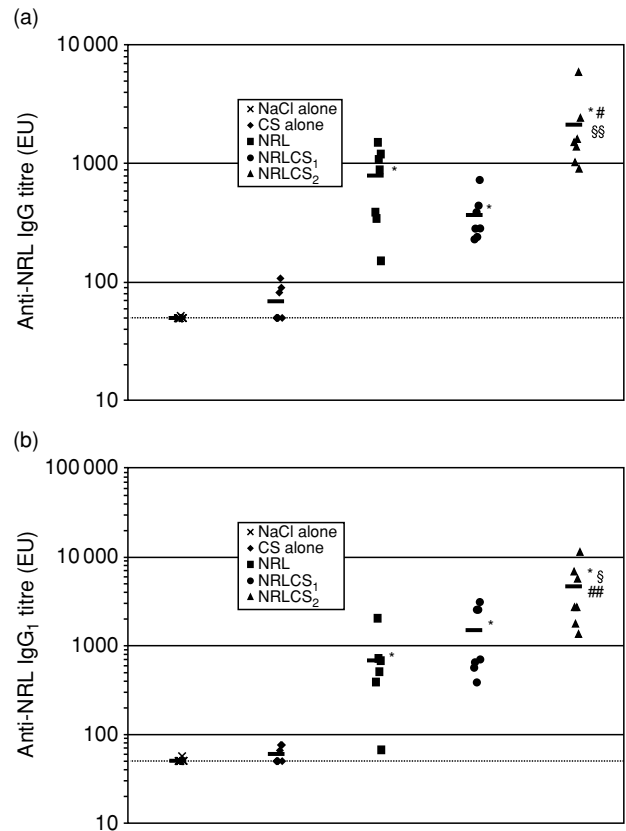


Fig. 4. Latex-specific antibody levels determined by ELISA on the guinea-pigs sera after bronchial provocation. (a) Anti-latex IgG, (b) anti-latex IgG₁. Data are presented as individual titres and expressed in ELISA units (EU). The mean of the group ($n = 7$ in each) is represented as the '—' symbol. * $P < 0.005$ compared to the control groups, # $P < 0.03$ and ## $P < 0.005$ compared to the NRL group and \$ $P < 0.04$ and §§ $P < 0.002$ compared to NRLCS₁ group. NRL (■), NRLCS₁ (●), NRLCS₂ (▲), NaCl (x) or CS (•).

alone (53.0 ± 19.4 cmH₂O × min; Fig. 3). BC level was not different between OV + CS and OV + FCA treatment.

All the guinea-pigs sensitized with OV demonstrated specific IgG production (Fig. 5). Those treated with OV + FCA showed higher antibody titres for both anti-OV IgG and IgG₁ (respectively $107\,198 \pm 19\,124$ EU, $P < 0.01$ and $267\,464 \pm 75\,975$ EU, $P < 0.01$) compared to those treated with OV alone (IgG: $13\,885 \pm 5101$ EU; IgG₁: $36\,497 \pm 15\,405$ EU). The animals sensitized with OV + CS also produced higher but not significant anti-OV IgG and IgG₁ levels (respectively $23\,906 \pm 4197$ EU and $67\,117 \pm 11\,634$ EU) than those of the animals immunized with OV alone (IgG: $13\,885 \pm 5101$ EU; IgG₁: $36\,497 \pm 15\,405$ EU). Anti-OV IgG and IgG₁ titres were very well correlated ($r = 0.97$, $P < 0.001$). Neither IgG nor IgG₁ titres correlated with the PIP variations.

Discussion

Guinea-pigs immunized with NRL proteins by repeated i.p. injections demonstrated BC induced by bronchial challenge with NRL as shown by a significant increase of the PIP variations compared to the control animals. These animals also demonstrated significant levels of NRL-specific IgG and IgG₁.

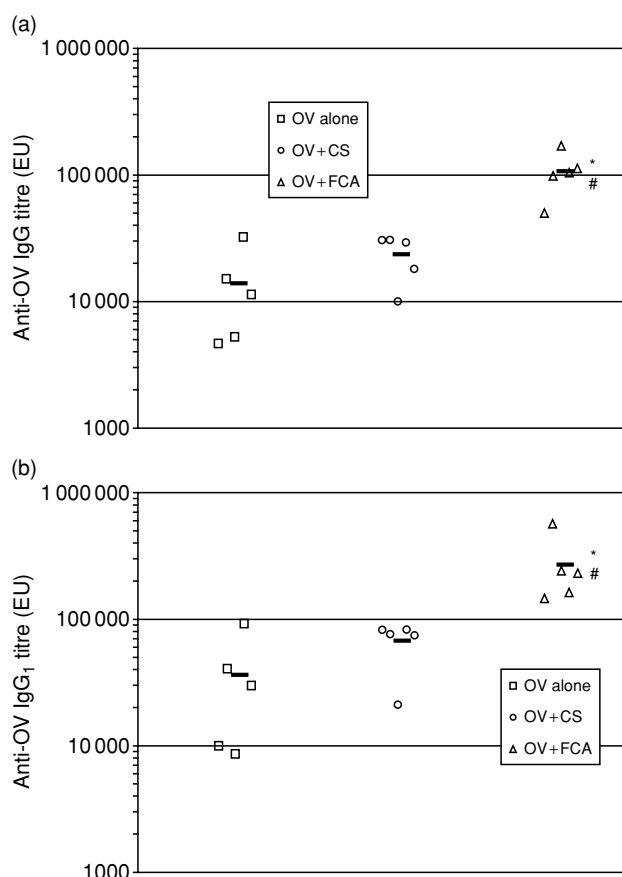


Fig. 5. OVA-specific antibody levels determined by ELISA on the guinea-pigs sera after bronchial provocation. (a) Anti-OVA IgG, (b) anti-OVA IgG₁. Data are presented as individual titres and expressed in ELISA units (EU). The mean of the group ($n = 5$ in each) is represented as the '—' symbol. * $P < 0.01$ compared to OV alone and # $P < 0.01$ compared to OV + CS. OV alone (□), OV + CS (○) or OV + FCA (Δ).

Guinea-pig IgG₁ antibodies are responsible for the basophil histamine liberation. This leads to an immediate hypersensitivity reaction that, in the guinea-pig, is characterized by agitation and severe acute respiratory distress and that may terminate in fatal anaphylaxis [21].

Sensitization to latex with NRL mixed to CS (NRLCS₁ group) resulted in a significant higher BC level compared to the treatment with NRL alone but no significant increase of antibody level was observed. It has been found that multioperated children who have undergone corrective surgical procedures become sensitized only after repeated latex exposure [8]. Instead of this, treatment with NRL-contaminated CS (i.e. NRLCS₂ group), in which the conditions were similar to those of patient exposure by peritoneal route during surgical procedures, resulted in an increase of antibody titre but not of BC level after latex challenge. The difference between NRL and NRLCS₂ groups was the dose of latex antigenic proteins given which was about 70 times lower for NRLCS₂ group (see Table 1). A previous study in guinea-pigs demonstrated the importance of the sensitization regimen in the pattern of the immunological response [30]: sensitization with small amounts of antigen (1–10 µg) with adjuvant conducted to IgE and IgG₁ production but sensitization with large amounts of antigen induced only IgG₁ production. In our experiments,

sensitization with NRLCS₂ induced higher IgG₁ production than with NRL alone.

In the present study, CS appeared to play a dual role, serving both as a carrier of antigen, allowing direct contact between peritoneal membrane and NRL antigens, and also as an immunoadjuvant, potentiating the antigenicity of these antigens [9]. In addition, all the animals treated with CS (NRLCS₁, NRLCS₂ and CS groups) presented abdominal adhesions that were not observed in the other groups (data not shown). These adhesions are induced by a peritoneal injury caused by the abrasion, or other trauma, of the mesothelial lining of the peritoneum [31]. Brehler et al. showed that the high pH of CS glove powder may be responsible for the dermal irritation that occurs in individuals who wear latex gloves [32]. Furthermore, previous reports showed that CS powder is able to induce inflammatory responses in guinea-pigs [33, 34]. The alkalinity of the CS powder used in our experiments (pH 10–10.8) may have been one of the causes of the peritoneal inflammation we observed. Damaged peritoneal surfaces lead to post-traumatic inflammation characterized by an influx of macrophages. These cells become activated, ingest the CS particles and act as antigen-presenting cells [35]. It is reasonable to believe that activated macrophages are able to ingest antigen-bearing CS particles more efficiently than they would ingest soluble NRL proteins, which could explain the immunoadjuvant activity that we observed.

In the present study we studied the effects of two different sources of NRL-contaminated CS. NRLCS₂ was tested because it reproduces the exposure by peritoneal contact during surgery procedures as this CS was collected from a glove production line. The NRL dose given to the NRLCS₁ group was about 70 times more elevated than to the NRLCS₂ group. This can explain that the responsiveness after bronchial challenge was higher for NRLCS₁ group. On the other hand, NRLCS₁ was constituted by an aqueous mixture of NRL proteins and CS but, for NRLCS₂, the NRL proteins were adsorbed on the CS matrix. This difference between the NRLCS sources can explain why with NRLCS₂ we observed a higher antibody production. The sensitization with NRLCS₂ may also lead to a production of antibodies directed to different epitopes than with NRLCS₂. This hypothesis will be studied further.

CS powder also potentiated the immunological response to OV. The level of BC was similar to that obtained with OV + FCA but the antibody level was lower. The results obtained after both NRL and OV sensitization demonstrated that CS acts as an adjuvant, increasing BC level. Similar results were found in a previous report where polystyrene particles had an adjuvant effect on the production of IgE in mice [36]. When associated with allergens, lipopolysaccharide (LPS) may be an important factor in the pathogenesis of asthma [37]. Williams and Halsey showed that NRL gloves, particularly non-sterile powdered NRL gloves, were contaminated with large amounts of endotoxin, i.e. LPS [38]. They also found a high level of LPS contamination in a sample of CS collected in a latex glove production line. In contrast, the amount of LPS was very low in their virgin CS powder and it was similar to the amount found in the CS used in the present study. However, our NRLCS₂, which was collected in a production line slurry tank, contained 200 times less LPS than theirs, for which we have no clear explanation. Slater et al. found that LPS was a powerful immunoadjuvant for the development of allergic reactions to NRL proteins in mice [39]. They sensitized mice by

the intranasal route to LPS-contaminated recombinant latex allergen Hev b 5 in the presence or absence of LPS. The mice sensitized without LPS received a dose of endotoxin (324 ng) that was similar to that we administered to the guinea-pigs treated with latex-contaminated CS (NRLCS₂; 450 ng).

In the present study, we demonstrated that CS powder can act not only as an allergen carrier but also as an immunoadjuvant in latex-induced allergic reactions. These findings support the hypothesis that CS powder is an important factor in the pathogenesis of latex allergy after peritoneal contact. Further studies will allow testing of its implications in airway sensitization to latex proteins. It would be also useful to compare the immunoadjuvant effects of talc and cornstarch [40].

Acknowledgements

We thank Dr R.G.O. Kekwick, Department of Biochemistry, University of Birmingham, Edgbaston, U.K and Mr H. de Livonnière, CIRAD-CP, Paris, France, for providing latex extract and cornstarch powders, Prof. J.C. Darbord, Laboratoire des Contrôles Biologiques, PCH, Paris, France, for the endotoxin measurements and Mss. M. Legoy and B. Viginier for their excellent technical work.

References

- Turjanmaa K, Alenius H, Mäkinen-Kiljunen S, Reunala T, Palosuo T. Natural rubber latex allergy. *Allergy* 1996; 51:593–602.
- Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* 1992; 90:319–22.
- Sussman GL. Latex allergy: its importance in clinical practice. *Allergy Proc* 1992; 13:67–9.
- Liss GM, Sussman GL, Deal K et al. Latex allergy: epidemiological study of 1351 hospital workers. *Occup Environ Med* 1997; 54:335–42.
- Cremer R, Kleine-Diepenbruck U, Hoppe A, Bläker F. Latex allergy in spina bifida patients: prevention by primary prophylaxis. *Allergy* 1998; 53:709–11.
- Ylitalo L, Alenius H, Turjanmaa K, Palosuo T, Reunala T. IgE antibodies to prohevein, hevein, and rubber elongation factor in children with latex allergy. *J Allergy Clin Immunol* 1998; 102:659–64.
- Nieto A, Estornell F, Mazón A, Reig C, Nieto A, García-Ibarra F. Allergy to latex in spina bifida: a multivariate study of associated factors in 100 consecutive patients. *J Allergy Clin Immunol* 1996; 98:501–7.
- Porri F, Pradal M, Lemièrre C et al. Association between latex sensitization and repeated latex exposure in children. *Anesthesiology* 1997; 86:599–602.
- Levy DA, Allouache S, Chabane MH, Leynadier F, Burney P. Powder-free protein-poor natural rubber latex gloves and latex sensitization. *JAMA* 1999; 281:988.
- Swanson MC, Buback ME, Hunt LW, Yunginger JW, Warner MA, Reed CE. Quantification of occupational latex aeroallergens in a medical center. *J Allergy Clin Immunol* 1994; 94:445–51.
- Newsom SWB, Shaw M. A survey of starch particle counts in the hospital environment in relation to the use of powdered latex gloves. *Occup Med* 1997; 47:155–8.
- Ruëff F, Kienitz A, Schöpf P et al. Frequency of natural rubber latex allergy in adults is increased after multiple operative procedures. *Allergy* 2001; 56:889–94.
- Kurup VP, Kumar A, Choi H et al. Latex antigens induce IgE and eosinophils in mice. *Int Arch Allergy Immunol* 1994; 103:370–7.
- Aamir R, Safadi GS, Mandelik J et al. A guinea pig model of hypersensitivity to allergenic fractions of natural rubber latex. *Int Arch Allergy Immunol* 1996; 110:187–94.
- Reijula KE, Kelly KJ, Kurup VP et al. Latex-induced dermal and pulmonary hypersensitivity in rabbits. *J Allergy Clin Immunol* 1994; 94:891–902.
- Xia JQ, Rickaby DA, Kelly KJ, Choi H, Dawson CA, Kurup VP. Immune response and airway reactivity in wild and IL-4 knockout mice exposed to latex allergens. *Int Arch Allergy Immunol* 1999; 118:23–9.
- Tomazic VJ, Shampaine EL, Lamanna A, Withrow TJ, Adkinson NF Jr, Hamilton RG. Cornstarch powder on latex products is an allergen carrier. *J Allergy Clin Immunol* 1994; 93:751–8.
- Schreider JP, Hutchens JO. Morphology of the guinea pig respiratory tract. *The Anat Record* 1980; 196:313–21.
- Martin JG. Modèles animaux d'hyperréactivité bronchique. *Rev Mal Resp* 1994; 11:93–9.
- Morley J, Chapman ID, Hoshiko K, Mazzoni L. Acute airway hyper-reactivity in the guinea pig. *Eur Respir Rev* 1995; 29:202–10.
- Neveu T. Les différentes hypersensibilités chez le cobaye. Méthodes d'analyse: comparaisons. *Sci Tech Anim Laboratory* 1985; 10:251–9.
- Bice DE, Seagrave JC, Green FH. Animal models of asthma: Potential usefulness for studying health effects of inhaled particles. *Inhalation Toxicol* 2000; 12:829–62.
- Association Française de Normalisation. EN455–3. Medical Gloves for Single Use – Part 3: Requirements and Testing for Biological Evaluation. S 97-003. AFNOR, Paris 2000.
- Chabane MH, Barbara J, Hrabina M, Leynadier F. Competitive immunoassay for antigenic latex protein measurement: rabbit antiserum-based assay compared to modified Lowry and human IgE-inhibition methods. *J Invest Allergol Clin Immunol* 1999; 9:372–9.
- Palosuo T, Mäkinen-Kiljunen S, Alenius H, Reunala T, Yip E, Turjanmaa K. Measurement of natural rubber latex allergen levels in medical gloves by allergen-specific IgE-ELISA inhibition, RAST-inhibition, and skin prick test. *Allergy* 1998; 53:59–67.
- Advenier C, Mallard B, Santais MC, Ruff F. The effects of atropine in anaphylactic shock in the guinea pig. *Agents Actions* 1982; 12:103–7.
- Konzett H, Rössler R. Versuchsanordnung zu untersuchungen an der bronchialmuskulatur. *Arch Exp Path Pharmacol* 1940; 195:71–4.
- Kleinman LI, Radford EP. Ventilation standards of small mammals. *J Appl Physiol* 1964; 19:360–2.
- Lau WAK, Rechtman MP, Boura ALA, King RG. Synergistic potentiation by captopril and propranolol of bradykinin-induced bronchoconstriction in the guinea pig. *Clin Exp Pharmacol Physiol* 1989; 16:849–57.
- Andersson P. Antigen-induced bronchial anaphylaxis in actively sensitized guinea pigs. Pattern of response in relation to immunization regimen. *Allergy* 1980; 35:65–71.
- Holmdahl L. Making and covering of surgical footprints. *Lancet* 1999; 353:1456–7.
- Brehler R, Voss W, Müller S. Glove powder affects skin roughness, one parameter of skin irritation. *Contact Dermatitis* 1998; 39:227–30.
- Grant JB, Davies JD, Verrier Jones J. Starch dermatitis: evidence of immunogenicity of surgical glove powder in the guinea pig. *Br Exp J Pathol* 1975; 56:396–401.
- Grant JB, Davies JD, Jones JV. Allergic starch peritonitis in the guinea pig. *Br J Surg* 1976; 63:867–9.
- Grant JB, Davies JD. Ascitic starch phagocytosis in experimental guinea pig peritonitis. *Br J Exp Pathol* 1981; 62:407–10.

- 36 Granum B, Gaarder PI, Eikeset A, Stensby BA, Løvik M. The adjuvant effect of particles: importance of genetic background and pre-sensitization. *Int Arch Allergy Immunol* 2000; 122:167–73.
- 37 Eldridge MW, Peden DB. Allergen provocation augments endotoxin-induced nasal inflammation in subjects with atopic asthma. *J Allergy Clin Immunol* 2000; 105:475–81.
- 38 Williams PB, Halsey JF. Endotoxin as a factor in adverse reactions to latex gloves. *Ann Allergy Asthma Immunol* 1997; 79:303–10.
- 39 Slater JE, Paupore EJ, Elwell MR, Truscott W. Lipopolysaccharide augments IgG and IgE response of mice to the latex allergen Hev b 5. *J Allergy Clin Immunol* 1998; 102:977–83.
- 40 Lundberg M, Wrangsjö K, Johansson SGO. Latex allergy from glove powder: an unintended risk with the switch from talc to cornstarch? *Allergy* 1997; 52:1222–8.