# Epidemiology of latex sensitization and allergies in health care workers

**David H. Garabrant, MD, MPH,[a] and Sarah Schweitzer, MS[b]** *Ann Arbor, Mich*

**Although it is often claimed that health care workers are at increased risk of latex sensitization and type I allergies, there has been no systematic analysis of the epidemiologic studies that are relevant to this conclusion. A systematic analysis of the epidemiologic literature found that, in the past 14 years, there have been 48 epidemiologic studies of type I latex allergy among health care workers. Of these, 2 cohort studies estimated the incidence of latex sensitization by skin prick testing at between 1% and 2.5% per year. Neither compared the risk to that in the general population. The prevalence of sensitization in health care workers varied between 0% and 30%, yet this large variation was unexplained. Increased risk of sensitization was not clearly associated with the duration of work in health care, the time spent wearing latex gloves, the frequency of exposure, the specific job categories, the use of powdered versus nonpowdered latex gloves, the use of latex versus nonlatex gloves, or any measurements of ambient exposure to latex proteins. The epidemiologic studies do not support a conclusion that health care workers are at clearly increased risk of latex sensitization or type I allergies compared to other occupations in the United States. The role of latex gloves in causing latex sensitization and type I allergic symptoms remains poorly defined because of the inconsistent results across studies. Future epidemiologic studies are needed that include measured exposures to latex antigens, that compare health care workers to appropriate referent groups, and that address confounding by atopy, age, sex, and race. (J Allergy Clin Immunol 2002;110:S82-95.)**

***Key words:*** *Allergy, sensitization, latex rubber, occupation, health care industry, epidemiologic*

The relation between health care work and risks of type I allergic sensitization and allergic symptoms to natural rubber latex remains controversial. Although many authors conclude that the risks of latex sensitization and allergy are elevated among health care workers, few studies have directly compared these risks to the risks in other occupations or in the general public. Similarly, internal comparisons of the risks of these conditions among specific groups of health care workers have given conflicting results about the role of latex gloves. Hence, there is a need for a systematic review of the epidemiologic studies to summarize the evidence that health care workers are at increased risk of latex sensitization and allergy and to assess the evidence that these medical conditions are associated with exposure to latex gloves.

The use of natural latex rubber gloves in the health care industry increased throughout the 1980s in response to the recognition of human immunodeficiency virus as a transmissible agent. The adoption of universal precautions in the United States in 1987[1] led to further increases in glove use, as did the implementation of the Occupational Safety and Health Administration bloodborne pathogen standard in 1992. Type I latex allergy among hospital personnel was recognized in Finland in 1987[2] and has been followed by numerous epidemiologic studies that have measured the prevalence of latex sensitization and allergic symptoms among health care workers. This review summarizes those studies, with particular reference to the evidence that health care workers are at increased risk of either sensitization or allergic symptoms, and the evidence that exposure to latex gloves is associated with increased risk of these conditions.

## METHODS

### Inclusion and exclusion criteria

The scientific literature was searched on MedLine to identify published epidemiologic studies of health care workers in which either the incidence or prevalence of latex sensitization was reported or in which the incidence or prevalence of type I allergic symptoms (contact urticaria, allergic rhinoconjunctivitis, asthma, or anaphylaxis) was reported. Case reports of individuals who underwent clinical evaluations for latex allergy because of known or suspected exposure to latex products were excluded if they contained inadequate information to estimate the risk of latex sensitization or latex allergy.

### Data extraction and classification

Study characteristics, measurements of exposure to latex gloves, estimates of the risks of sensitization, estimates of the risks of allergic symptoms, measures of relative risk, confidence intervals, and probability values were abstracted from the studies when they were available. Results were grouped according to the methods for estimating exposure to latex gloves: duration of exposure, frequency of exposure, job titles or work locations that implied exposure, use of powdered versus powder-free latex gloves, use of latex versus non-latex gloves, and measurements of ambient latex protein levels. Preva-

From [a]Occupational Medicine, University of Michigan School of Public Health and University of Michigan School of Medicine, and the [b]Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor.

Dr Garabrant has served as an expert witness on behalf of defendants in litigation concerning allergy to latex products. Ms Schweitzer has no significant financial interest in the commercial sponsors of this publication. She attests that there is no commercial or personal conflict of interest.

Reprint requests: David H. Garabrant, MD, University of Michigan School of Public Health, 1420 Washington Heights, Ann Arbor, MI 48104; e-mail: dhg@umich.edu.

© 2002 Mosby, Inc. All rights reserved.

0091-6749/2002 $35.00 + 0 **1/0/124967**
doi:10.1067/mai.2002.124967

lences, incidence rates, odds ratios, confidence intervals, and probability values were calculated in instances in which data were reported adequately to allow this to be done, if they were not done by the authors. Calculations were performed with the use of SAS 8.0 (SAS Institute, Cary, NC), EpiInfo 2000 (Centers for Disease Control and Prevention, Atlanta, Ga), and Microsoft Excel 2000 (Microsoft Corporation, Redmond, Wash).

## RESULTS

Forty-eight epidemiologic studies of type I allergic sensitization to latex or latex allergy among health care workers were identified, which included 28,097 subjects (of which approximately 21,000 were health care workers; Table I).[2-49] Two cohort studies measured the incidence of latex sensitization,[17,43] and 1 cohort study measured the incidence of contact dermatitis and urticaria.[23] The remainder were cross-sectional studies that measured the prevalence of sensitization or type I allergic symptoms.

All 48 studies reported the study design, the number of subjects, the study population, and the presence or absence of a referent group. Seventeen studies reported the prevalence of latex-specific IgE; 32 studies reported either the prevalence or incidence of skin prick test (SPT) positivity to latex, and 8 studies reported neither. Twenty-six studies reported symptom prevalence. Participation rates in the survey phase of these investigations varied considerably from a low of 3% among volunteers who were screened at a dental convention[20] to 100% among newly hired hospital house officers.[34] Fifteen of these studies did not report the participation rates,* which raises concerns about the degree to which the studies provide reliable prevalence estimates. Only 5 of the studies included a comparable referent group outside of the healthcare industry.[14-17,23] There were substantial variations in the methods and measurements made in each study. Latex sensitization was assessed with various in vitro methods that included the CAP radioimmunoassay, the CAP immunoassay system (Pharmacia, Uppsala, Sweden), the AlaSTAT radioimmunoassay, the AlaSTAT electroimmunoassay, the AlaSTAT microplate assay (Diagnostic Products Corporation, Los Angeles, Calif), the HY-TEC electroimmunoassay (Hytech Biomedical, Irvine, Calif), the radioallergosorbent test from Kallestad, and other methods that were less clearly specified. Latex sensitization was assessed in many studies through SPTs or scratch chamber tests with a variety of latex antigen sources. SPTs were performed with gloves or glove eluates in 23 of 32 studies, and the number of glove or glove eluates that were used ranged from 1 (8 studies), 2 (6 studies), 3 (2 studies) and 4 (3 studies) to 5 (4 studies). In addition, SPTs were performed with commercial latex samples (Bencard Allergie GmbH, München, Germany; Le Groupe Stallergènes, Antony, France; Guthrie Research Institute, Sayre, Pa; The Goodyear Tire & Rubber Company, Akron, Ohio; Pharmacia Corporation, Peapack, NJ; and Baxter Healthcare Corporation, Deerfield, Ill) in 18 studies; the number of samples that were used ranged from 1 to 5. Two studies gave no information about the material used for SPTs. Commercial latex varied substantially, not only in its source and methods of derivation but also in the different types of latex samples (nonammoniated raw latex, low-ammoniated latex, and high-ammoniated latex) in different studies. The extent to which these variations altered the antigen content of the samples was neither known nor described in most studies. In addition, the extent to which the prevalence of SPT positivity varied across studies as a result of variation in the number of tests performed is unknown.

The symptoms assessed by the investigators were not standardized, nor were the methods for ascertaining their presence. In most instances, symptoms were self-reported without objective confirmation. In some instances, queries were made whether symptoms were related to latex exposure, although in others this was not asked. Individual symptoms (such as hand urticaria) were reported in most instances (26 studies), although groups of symptoms (such as hand dermatitis or type I allergic symptoms) were reported in few (6 studies). In summary, there was great diversity among studies in the measurements made and the methods used to report the measurements. The extent to which these variations influenced the apparent relationship between exposures and outcome could not be quantified. To examine risk factors for latex sensitization and allergic symptoms, studies were grouped according to the measures of exposure that were reported in each study. Results are summarized in Tables II through VII.

### Duration of exposure to latex gloves

Fifteen studies reported the prevalence of latex sensitization among health care workers, 8 of which reported quantitative results (Table II). Two studies did not report results, even though data were collected from which such results were obtainable.[17,43] Five studies reported that there was either "no association" or "no significant association" between sensitization and the duration of work with latex gloves but gave no further details regarding the findings.[6,9,13,26,29] Among the 8 studies that reported quantitative results, the findings were inconsistent and showed no clear association between the duration of exposure and latex sensitization. DeGroot et al[12] showed that the risk of sensitization (both latex-specific IgE and SPT responses) decreased with increasing duration of exposure to latex gloves. Similarly, Konrad et al[27] and Mace et al[33] showed that the duration of exposure to latex gloves was higher among nonsensitized subjects than among latex-sensitized subjects, based on SPT results. Four studies found weakly positive associations between the duration of latex glove use and sensitization, either based on IgE or SPT.[2,15,24,49] None of these studies showed any statistically significant relationships. A single study found a significantly increasing trend in the prevalence of positive SPT responses among dental students as they progressed through 4 years of dental

*2,8,10,11,13,18,21-23,26,31,33,44,49,50

**TABLE I.** Epidemiologic studies of latex allergy in health care workers

| Study | Study type | No. of subjects | Non–health care worker referents | Participation (%) | Incidence (I)/ prevalence (P) |
|---|---|---|---|---|---|
| Allmers et al (1998)[3] | Cross-sectional | 90 | None | 43 | P |
| Amin et al (1998)[4] | Cross-sectional | 460 | None | 74 | P |
| Arellano (1992)[5] | Cross-sectional | 201 | Atopic allergy clinic patients | 56 | P |
| Baur et al (1998)[6] | Cross-sectional | 145 | None | 60 | P |
| Berky et al (1992)[7] | Cross-sectional | 1043 | None | 64 | P |
| Brehler et al (1997)[8] | Cross-sectional | 500 | None | Not stated | P |
| Brown et al (1998)[9] | Cross-sectional | 168 | None | 98 | P |
| Bubak et al (1992)[10] | Cross-sectional | 49 | None | Not stated | P |
| Charous et al (1994)[11] | Cross-sectional | 47 | Asymptomatic atopic volunteers | Not stated | P |
| de Groot et al (1998)[12] | Cross-sectional | 66 | None | 67 | P |
| Douglas (1997)[13] | Cross-sectional | 140 | None | Not stated | P |
| Fishwick et al (1997)[14] | Cross-sectional | 1609 | Australian general population | 64 | P |
| Garabrant et al (2001)[15] | Cross-sectional | 5524 | United States general population | 86 | P |
| Gautrin et al (1997)[16] | Cross-sectional | 110 | Other trade students without latex exposure | 77 | P |
| Gautrin et al (2000)[17] | Prospective cohort of dental hygiene apprentices | 769 | Pastry-making & animal handler apprentices | 90 | I |
| Geller (1998)[18] | Cross-sectional | 50 | Nonatopic community members | Not stated | P |
| Grzybowski et al (1996)[19] | Cross-sectional | 741 | None | 91 | P |
| Hamann et al (1998)[20] | Cross-sectional | 1071 | None | 3 | P |
| Hunt and Fransway (1995)[21] | Cross-sectional | 342 | None | Not stated | P |
| Iacobelli et al (1993)[22] | Cross-sectional | 104 | None | Not stated | P |
| Jolanki et al (1999)[23] | Incidence | 1079 | Finnish general population | Not stated | I |
| Kaczmarek (1996)[24] | Cross-sectional | 381 | None | 42 | P |
| Katelaris (1996)[25] | Cross-sectional | 177 | None | 77 | P |
| Kibby and Akl (1997)[26] | Cross-sectional | 135 | None | Not stated | P |
| Konrad et al (1997)[27] | Cross-sectional | 101 | None | 86 | P |
| Kujala and Reijula (1995)[28] | Cross-sectional | 534 | None | 64 | P |
| Lagier et al (1992)[29] | Cross-sectional | 248 | None | 93 | P |
| Leung (1997)[30] | Cross-sectional | 1472 | None | 74 | P |
| Levy et al (1998)[31] | Cross-sectional | 83 | None | Not stated | P |
| Liss (1997)[32] | Cross-sectional | 1351 | None | 66 | P |
| Mace et al (1993)[33] | Cross-sectional | 247 | None | Not stated | P |
| Miller et al (1998)[34] | Cross-sectional | 291 | None | 100 | P |
| Page et al (1998)[35] | Cross-sectional | 532 | None | 83 | P |
| Palczynski et al (1999)[36] | Cross-sectional | 2867 | None | 77 | P |
| Safadi (1996)[38] | Cross-sectional | 34 | None | 97 | P |
| Safadi et al (1996)[37] | Cross-sectional | 93 | None | 85 | P |
| Schopf et al (1998)[39] | Cross-sectional | 759 | None | 92 | P |
| Sinha and Harrison (1998)[40] | Cross-sectional | 1827 | None | 23 | P |
| Smedley et al (1999)[41] | Cross-sectional | 372 | None | 48 | P |
| Sussman et al (1995)[42] | Cross-sectional | 435 | None | 70 | P |
| Sussman (1998)[43] | Prospective cohort | 50 | None | 91 | I |
| Tarlo (1997)[44] | Cross-sectional | 203 | None | Not stated | P |
| Turjanmaa (1987)[2] | Cross-sectional | 512 | Patients from the allergy department | Not stated | P |
| Vandenplas et al (1995)[45] | Cross-sectional | 273 | None | 94 | P |
| Watts et al (1998)[46] | Cross-sectional | 122 | None | 71 | P |
| Wrangsjo et al (1994)[47] | Cross-sectional | 233 | None | 87 | P |
| Wrangsjo and Osterman (1994)[48] | Cross-sectional | 233 | None | 90 | P |
| Yassin et al (1994)[49] | Cross-sectional | 224 | None | Not stated | P |

**TABLE II.** Duration of exposure to latex gloves versus latex sensitization or type I allergic symptoms among health care workers

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Baur et al[6]: Duration of exposure to NRL | "No significant association" | Results not stated* | "No significant association" |
| Brown et al[9]: Duration of exposure to latex gloves | "Not shown to increase the risk for latex sensitization" | "Not shown to increase the risk for latex sensitization" | |
| de Groot et al[12]: No. of years worked with latex gloves vs latex-specific IgE and SPT response | | | |
| 0-5 Y | OR, 1.0† | OR, 1.0† | |
| >5 Y | OR, 0.6 ($P$ = 1.0) | OR, 0.3 ($P$ = .37) | |
| Douglas et al[13]: Years worked as a nurse vs SPT response | | "No significant difference" | |
| Garabrant et al[15]: Work in health care jobs compared with other occupations in US population | | | |
| Current job in health care with glove use vs other occupations | OR, 1.17 (95% CI, 0.51-2.65) | | |
| Longest held job in health care vs other occupations | OR, 1.49 (95% CI, 0.92-2.40) | | |
| Gautrin et al[17]: Cumulative hours of exposure to NRL gloves | | Results not stated* | |
| Kaczmarek et al[24]: Number of years employed vs latex IgE prevalence | | | |
| <10 Y | Prevalence, 5% | | |
| ≥10 Y | Prevalence, 7% | | |
| Kibby and Akl[25]: Length of service among hospital employees | Results not stated* | "No significant difference between latex reactors and non-reactors" | Results not stated* |
| Konrad et al[27]: Average years of exposure to NRL gloves | Results not stated* | | |
| Non-latex sensitized | | 10.3 ± 7.4 Y | |
| Latex sensitized | | 8.0 ± 5.3 Y | |
| | | ($P$ > .05) | |
| Lagier et al[29]: Operating room nurses who wore latex gloves; years of operating room experience | | "No relationship was observed between skin test positivity and years of operating room experience" | "The length of exposure did not influence the prevalence of symptoms" |
| Mace et al[33]: Duration of use of latex gloves vs prevalence of SPT response | | | |
| SPT positive | Results not stated* | Years of use, 17.4 | |
| SPT negative | | Years of use, 17.6 | |
| Sinha and Harrison[40]: Length of time exposed to latex | | | "May not be a significant factor" |
| Sussman[43]: Years since first exposure to latex gloves | | Results not stated* | |
| Tarlo[44]: Prevalence of latex SPT sensitization and symptoms in dental students and staff | | | |
| Year 1 & 2 students | | Prevalence, 0% | Asthma, 0% |
| Year 3 students | | Prevalence, 6% | Asthma, 0% |
| Year 4 students | | Prevalence, 10% | Asthma, 4% |
| Staff(duration not stated) | | Prevalence, 25% | Asthma, 9% |
| | | (trend $P$ = .02) | (trend $P$ = .02) |
| Year 1 & 2 students | | | Rhinoconjunctivitis, 5% |
| Year 3 students | | | Rhinoconjunctivitis, 8% |
| Year 4 students | | | Rhinoconjunctivitis, 11% |
| Staff (duration not stated) | | | Rhinoconjunctivitis, 16% |
| | | | (trend $P$ = .05) |
| Year 1 & 2 students | | | Urticaria, 4% |
| Year 3 students | | | Urticaria, 0% |
| Year 4 students | | | Urticaria, 6% |
| Staff (duration not stated) | | | Urticaria, 2% |
| | | | (trend $P$ = not significant) |
| Turjanmaa[2]: Duration of latex glove use vs scratch chamber test/SPT response (odds ratio for positive scratch chamber and SPT) | | | |
| 0-5 Y of use | | OR, 1.0† | |
| 6-10 Y of use | | OR, 1.1 (95% CI, 0.2-2.8) | |
| >10 Y of use | | OR, 1.5 (95% CI, 0.4-5.0) | |
| Yassin et al[49]: Years of hospital employment vs SPT response to any of 4 glove extracts | | | |
| SPT positive | | Years employed, 5.2 | |
| SPT negative | | Years employed, 5.0 | |

*OR*, Odds ratio; *NRL*, natural rubber latex.
*Results were not reported by authors, even though data were collected.
†Reference level or group.

school.[44] However, this study had extremely poor participation, particularly among first-year dental students, none of whom completed SPTs and only 11% of whom completed the questionnaire survey. Prevalence estimates that are based on such data should be interpreted cautiously. In summary, this large number of studies provides no clear indication whether the risk of latex sensitization increases or decreases with the duration of exposure to latex gloves.

Four studies examined the risks of type I allergic symptoms in relation to the duration of latex exposure.[6,29,40,44] Three of these studies reported no significant associations but gave no further details regarding the findings.[6,29,40] The single study by Tarlo[44] found significantly increasing trends in symptoms of asthma and rhinoconjunctivitis but not urticaria, among dental students. However, the lack of information on the participation rate in this study raises concerns about the reliability of these findings. Overall, it is unclear whether the prevalence of type I allergic symptoms increases or decreases with increasing duration of exposure to latex gloves.

## Frequency of exposure to latex gloves or number of gloves worn per day

Thirteen studies examined the prevalence of latex sensitization according to the number of hours per day latex gloves were worn or the number of latex gloves worn per day (Table III). Five of these studies reported nonsignificant associations but gave no further details regarding these findings.[2,13,29,32,45] Two studies gathered relevant data but did not report the findings.[41,43] The other studies gave inconsistent findings, showing either weakly positive associations[12,27,32,33,44,49] or weakly negative associations.[24,32,33,35,46,49] The study by Liss[32] gave conflicting results. In that study, when glove use was measured as the number of pairs of latex gloves used per day per person, nonsensitized subjects used significantly more gloves than sensitized subjects. When exposure was measured in hours per day of latex glove wearing, there were no differences between those who were and were not allergic to latex. When departments were categorized into tertiles by glove consumption and the departmental SPT prevalence was categorized as either above or below the average across departments, there was a significant association between higher SPT prevalence and higher consumption of sterile latex gloves. In contrast, there was no such association with latex examination gloves. Yassin et al[49] found a strong association between SPT response to glove extracts and latex glove use, which showed that subjects who used latex gloves always or most of the time were at significantly increased risk of sensitization compared to those who used latex gloves occasionally. However, this study should be interpreted cautiously because the participation rate was not reported and subjects whose glove use was unknown were all SPT negative. This latter observation suggests that glove use may have been reported more reliably among those who were SPT positive. Of importance, 2 studies reported an exposure index that combined the frequency and duration of latex glove use.[35,45] Neither study found that the glove exposure index was important in the explanation of the risk of sensitization. In summary, these 16 studies provide no clear evidence that any measure of the frequency of latex glove use was associated with increasing risk of sensitization.

Three studies reported on type I symptom prevalence in relation to the frequency of latex glove use.[29,30,41] Two of these studies found that hand symptoms were strongly associated with latex glove use, although neither differentiated between urticaria and other hand symptoms.[29,30] The third study combined all type I symptoms (hand urticaria, puffiness around the eyes or mouth, chest tightness, wheezing, and anaphylaxis) and found that they were associated with increasing numbers of gloves used per day (trend, $P = .06$), but not with the duration of glove wearing each day or with time spent working in the presence of others who were wearing gloves.[41] These studies, in the aggregate, suggest that hand symptoms (not necessarily type I allergies) are associated with latex glove use and provide limited evidence that suggests that type I symptoms are associated with increasing glove use.

## Job titles, departments, and work locations that imply exposure to latex gloves

The 18 studies that reported risks of sensitization and type I symptoms by job title, department, or work location are difficult to summarize because of the lack of uniformity in subject group definitions (Table IV). The pattern of results does not suggest that any definable occupational group, department, or work location is clearly at increased risk over others. The studies also indicate that, within any occupational or departmental group, the prevalence of sensitization varies widely across studies. Four of the studies reported no significant influence of work area or occupation on the prevalence of sensitization, but gave no further details regarding these findings.[10,26,27,35] Both Turjanmaa[2] and Smedley et al[41] reported that operating theater personnel were at increased risk of sensitization compared to examination and laboratory personnel or outpatient nurses, respectively. In contrast, Grzybowski et al[19] found operating room nurses to be the lowest risk group among all nursing specialties in their study, and Wrangsjo et al[47,48] found even lower prevalences of sensitization among operating theater staff than in any of these other studies. The cross-sectional study by Liss[32] and the subsequent incidence study of the same population reported by Sussman[43] reported the highest risks of sensitization among laboratory workers. These findings were not confirmed in the studies of Safadi,[38] Turjanmaa,[2] or Yassin et al[49] who found laboratory workers to be at moderate to relatively low risk. The prevalence of sensitization among physicians ranged from 5% to 9% and was not clearly high or low compared to other health care professions.[24,40,49] Overall, there was no discernable pattern of increased risk in any occupation, department, or location of work among health care workers.

**TABLE III.** Frequency of exposure to latex gloves or number of latex gloves worn/day versus latex sensitization or type I latex allergic symptoms among health care workers

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| de Groot et al[12]: Average hours/day worked with latex gloves vs SPT response | | | |
| SPT negative | | 1.1 Hr/d | |
| SPT positive | | 2.2 Hr/d | |
| Douglas[13]: Prevalence of latex SPT response versus hours gloved each day, hours worked each week, and no. of glove changes/day | | "No significant difference" | |
| Kaczmarek[24]: Number of hours worked/week vs latex IgE prevalence | | | |
| <40 Hrs/wk | Prevalence, 6% | | |
| ≥40 Hrs/wk | Prevalence, 5% | | |
| Konrad et al[27]: Average hours/day exposed to NRL gloves | Results not stated* | | |
| Non-latex sensitized | | 1.8 ± 1.6 Hrs/d | |
| Latex sensitized | | 2.1 ± 1.7 Hrs/d ($P > .05$) | |
| Lagier et al[29]: Prevalence by frequency of latex glove use among operating room nurses | | "No relationship between SPT positivity and glove wearing time" | |
| Prevalence of hand symptoms (redness, itching, and urticaria) among everyday users vs occasional users | | | Prevalence, 48% vs 24% ($P < .0005$) |
| Leung[30]: Prevalence of symptoms among hospital staff (from multivariate logistic regression) | | | |
| History of daily glove use vs glove dermatitis | | | OR, 50.1 (95% CI, 15.9-151.1) |
| History of daily glove use vs latex allergy | | | "Not significant" |
| Hours/day wearing gloves vs glove dermatitis | | | "Not significant" |
| Hours/day wearing gloves vs latex allergy | | | "Not significant" |
| Glove changes/day vs glove dermatitis | | | "Not significant" |
| Glove changes/day vs latex allergy | | | "Not significant" |
| Liss[32]: Comparison of whether departmental prevalence of positive SPT exceeds the overall average prevalence of positive SPT (in all departments) vs departmental glove consumption per worker | | Departments exceeding average SPT prevalence | |
| Sterile latex glove consumption: | | | |
| Lowest tertile departments | | 1/10 | |
| Medium tertile departments | | 9/10 | |
| Highest tertile departments | | 8/10 ($P = .0004$) | |
| Bulk (examination) glove consumption per worker: | | | |
| Lowest tertile departments | | 6/13 | |
| Medium tertile departments | | 5/13 | |
| Highest tertile departments | | 8/13 ($P = .49$) | |
| SPT response vs number of pairs of latex gloves used per day per person | | | |
| Latex SPT positive | | Mean ± SD gloves/d, 5.4 ± 10.1 | |
| Latex SPT negative | | Mean ± SD gloves/d, 6.6 ± 11.6 ($P = .04$) | |
| Prevalence of SPT response vs hours that latex gloves were worn each day | | "No differences… (data not shown)" | |
| Mace et al[33]: Hours/day of use of latex gloves vs prevalence of SPT response | | | |
| SPT positive | Results not stated* | 4.5 Hrs/d of use | |
| SPT negative | | 4.7 Hrs/d of use | |
| Prevalence of use of latex gloves for ≥6 hrs/d vs SPT response | | | |
| SPT positive | Results not stated* | Prevalence of use, 35.3% | |
| SPT negative | | Prevalence of use, 34.3% | |
| Page et al[35]: Association between latex glove use and sensitization | | | |
| No latex glove use | OR, 1.0 (95% CI, reference level†) | | |
| Wearing more than 18 pairs of latex gloves daily | OR, 0.9 (95% CI, 0.3-2.1) | | |
| Cumulative index (frequency times duration) of exposure to latex gloves | | | |
| 0 Pair-hours of latex glove use daily | OR, 1.0 (95% CI, reference level†) | | |
| >7 Pair-hours of latex glove use daily | OR, 0.8 (95% CI, 0.3-2.2) | | |

(*Continued on next page*)

(**TABLE III.** Continued)

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Smedley et al[41]: Risk of symptoms in the past month suggestive of type I allergy (hand urticaria, puffiness around eyes or mouth, chest tightness, wheezing, or anaphylaxis) in relation to wearing latex gloves | | | |
| Wearing gloves >1 hr/d | Results not stated* | Results not stated* | |
| No | | | OR, 1.0 |
| Yes | | | OR, 0.8 (95% CI, 0.3-1.8) |
| Working in room >1 hr/day where others wear gloves | Results not stated* | Results not stated* | |
| No | | | OR, 1.0 |
| Yes | | | OR, 1.5 (95% CI, 0.6-4.0) |
| No. of gloves used per day | Results not stated* | Results not stated* | |
| 1-4 Prs/d | | | OR, 1.0 |
| 5-19 Prs/d | | | OR, 2.6 (95% CI, 0.8-8.4) |
| ≥20 Prs/d | | | OR, 3.5 (95% CI, 0.9-13.0; trend, $P = .06$) |
| Sussman[43]: Association between latex glove use and sensitization | | | |
| No. of latex gloves worn/day | | Results not stated* | |
| Hours/day spent wearing latex gloves | | Results not stated* | |
| Tarlo[44]: SPT sensitization among dental students and staff | | | |
| Hours/week in clinic | | | |
| SPT positive | | 24.0 Average hrs/wk | |
| SPT negative | | 23.5 Average hrs/wk ($P$ = NS) | |
| Time gloved/week | | | |
| SPT positive | | 63 Hrs | |
| SPT negative | | 61 Hrs ($P$ = NS) | |
| Turjanmaa[2]: Hours/day of latex glove use vs scratch chamber test/SPT response | | "No significant difference" | |
| Vandenplas et al[45]: Prevalence of positive SPT among hospital staff; cumulative index of exposure (based on frequency and duration of latex glove use) | | "Cumulative index of exposure had only minimal explanatory value ($P = .06$)" | |
| Watts et al[46]: Latex glove use in pairs/12-hour shift vs SPT response among ICU workers | | | |
| Sensitized subjects (n = 17) | | 20 Gloves/shift | |
| Nonsensitized subjects (n = 105) | | 28 Gloves/shift ($P = .30$) | |
| Yassin et al[49]: Use of latex gloves at work vs SPT response to any of 4 latex glove extracts | | | |
| Always use latex gloves | | OR, 0.96 (95% CI, 0.4-2.1) | |
| Most of time use latex gloves | | OR, 1.0 (reference level†) | |
| Occasionally use latex gloves | | OR, 0.08 (95% CI, 0-0.5) | |
| Missing information (16 subjects missing info, all SPT negative) | | OR, 0 ($P = .04$) | |
| Daily use of latex gloves in household | | | |
| Yes | | OR, 0.3 (95% CI, 0.06-1.1) | |
| No | | OR, 1.0 | |

*OR*, Odds ratio; *NRL*, natural rubber latex; *NS*, not significant.
*Results were not reported by authors, even though data were collected.
†Reference level or group.

Symptoms of type I allergies were reported in 8 studies according to job title. The study by Fishwick et al[14] examined asthma risks across occupations in the general population of New Zealand and found no evidence of increased risk of asthma among nurses compared with all other occupations. In contrast, Smedley et al[41] found significantly increased risks of type I allergic symptoms in operating department professionals and theater nurses compared with outpatient nurses. Although each of the other studies reported on symptom prevalence in various groups of health care workers, there was no consistent pattern of increased risk across studies.*

## Powdered versus powder-free latex gloves

There have been 4 studies in which the risks of sensitization among users of powdered latex gloves were com-

*25,30,38,40,45,47,49

**TABLE IV.** Job titles/work locations that imply exposure to latex gloves versus latex sensitization or type I latex allergic symptoms among health care workers

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Bubak et al[10]: Occupations among health care workers antibody increase was not associated with…occupation" | "Magnitude of the IgE | | |
| Fishwick et al[14]: Prevalence of asthma among nurses compared with other occupations in general population (adjusted for age, sex, and smoking) | | | |
| Asthmatic symptoms (n = 54) | | | OR, 1.05 (95% CI, 0.60-1.83) |
| Bronchial hyperreactivity (n = 39) | | | OR, 0.54 (95% CI, 0.25-1.15) |
| Bronchial hyperreactivity/wheezing (n = 36) | | | OR, 0.55 (95% CI, 0.25-1.40) |
| Grzybowski et al[19]: Prevalence of latex IgE by nursing specialty | Prevalence, "No overall difference" | | |
| Medical, surgical (n = 284) | Prevalence, 9.5% | | |
| Emergency department (n = 67) | Prevalence, 10.4% | | |
| Labor/delivery (n = 22) | Prevalence, 13.6% | | |
| Intensive care (n = 242) | Prevalence, 8.3% | | |
| Operating room (n = 126) | Prevalence, 6.3% | | |
| All nurses (n = 741) | Prevalence, 8.9%(95% CI, 6.7-10.8) | | |
| Kaczmarek[24]: Prevalence of latex IgE by occupation | | | |
| Nurses (n = 208) | Prevalence, 5% | | |
| Physicians (n = 64) | Prevalence, 5% | | |
| Aides (n = 25) | Prevalence, 0% | | |
| Other/unknown (n = 84) | Prevalence, 8% | | |
| Katelaris[25]: Prevalence of hand urticaria by job among dental workers | | | |
| Chair-side assistants (n = 64) | | | Prevalence, 13% |
| Dentists (n = 45) | | | Prevalence, 9% |
| Kibby and Akl[26]: Prevalence of sensitization in hospital employees (n = 135); location of work among hospital employees; job title of hospital employees | Results not stated* | "No significant difference between latex reactors and non-reactors" | Results not stated* |
| Konrad et al[27]: Comparison of work areas of sensitized and nonsensitized anesthesia staff (n = 101) | Results not stated* | "Work area showed no significant influence on prevalence" | |
| Leung[30]: Prevalence of symptoms among hospital staff from multivariate logistic regression (n = 1472) | | | |
| Occupation as a nurse vs glove dermatitis | | "Not significant" | OR (95% CI), |
| Occupation as a nurse vs latex allergy | | "Not significant" | OR (95% CI), |
| Liss[32]: Prevalence of SPT positivity to latex by job category | | | |
| Laboratory workers (n = 65) | | Prevalence, 16.9% | |
| Nurses/physicians (n = 788) | | Prevalence, 13.3% | |
| Housekeepers (n = 78) | | Prevalence, 11.5% | |
| Therapists/technicians (n = 145) | | Prevalence, 7.6% | |
| Others (n = 231) | | Prevalence, 9.5% ($P$ = .15) | |
| Page et al[35]: Prevalence of sensitization by job category | "Sensitization was not associated with job category ($P$ = .3)" | | |
| Safadi[38]: Prevalence by job category among dental professionals | | | |
| Prevalence of sensitization | | | |
| Dentists/fellows/residents (n = 10) | | Prevalence, 30% | |
| Dental assistants/dental hygienists (n = 14) | | Prevalence, 0% | |
| Support staff/laboratory technicians (n = 10) | | Prevalence, 10% | |
| Prevalence of skin symptoms (dryness, redness, itching, swelling) | | | |
| Dentists/fellows/residents (n = 10) | | | Prevalence, 30% |
| Dental assistants/dental hygienists (n = 14) | | | Prevalence, 36% |
| Support staff/laboratory technicians (n = 10) | | | Prevalence, 20% |

(*Continued on next page*)

(**TABLE IV.** Continued)

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Prevalence of upper respiratory symptoms (sneezing, rhinitis, watering eyes) | | | |
| Dentists/fellows/residents (n = 10) | | | Prevalence, 10% |
| Dental assistants/dental hygienists (n = 14) | | | Prevalence, 28% |
| Support staff/laboratory technicians (n = 10) | | | Prevalence, 0% |
| Sinha and Harrison[40]: Prevalence of "symptoms suggestive of latex allergy" | | | |
| Nurses (n = 1329) | | | Prevalence, 7% |
| Doctors (n = 191) | | | Prevalence, 8% |
| Pathology staff (n = 58) | | | Prevalence, 14% |
| Radiographers (n = 36) | | | Prevalence, 14% |
| Physiotherapists (n = 42) | | | Prevalence, 2% |
| Domestic personnel (n = 141) | | | Prevalence, 1.5% |
| Ward clerks (n = 30) | | | Prevalence, 13% |
| Smedley et al[41]: Lifetime prevalence of symptoms suggestive of type I allergy (hand urticaria, puffiness around eyes or mouth, chest tightness, wheezing, or anaphylaxis) in relation to wearing latex gloves | Results not stated* | Results not stated* | |
| Nurses in outpatient/infectious disease department (n = 7; referent group) | | | OR, 1.0 |
| Surgeons (n = 13) | | | OR, 0.3† (95% CI, 0.5-3.2) |
| Anesthetists (n = 6) | | | OR, 1.7 (95% CI, 0.6-4.8) |
| Theater nurses (n = 29) | | | OR, 2.6 (95% CI, 1.2-5.6) |
| Operating department professionals (n = 10) | | | OR, 5.4 (95% CI, 2.4-12.4) |
| Sussman[43]: Incidence of SPT conversion per year | | | |
| Physicians/nurses (n = 268) | | Incidence, 1% | |
| Therapists (n = 49) | | Incidence, 0% | |
| Laboratory workers (n = 23) | | Incidence, 4% | |
| Others (n = 94) | | Incidence, 1% | |
| Turjanmaa[2]: Prevalence of sensitization (scratch chamber) test/SPT response by occupation | | | |
| Operating room personnel (n=145) | | Prevalence, 6.2% | |
| Examination/laboratory personnel (n = 367) | | Prevalence, 1.6% ($P < .01$) | |
| Vandenplas et al[45]: Prevalence of work related symptoms by occupation in hospital workers | | | |
| Nurses (n = 201) | | | Asthma, 3% |
| Cleaning staff (n = 50) | | | Asthma, 0% |
| Technologists (n = 38) | | | Asthma, 0% |
| Nurses (n = 201) | | | Rhinoconjunctivitis, 10% |
| Cleaning staff (n = 50) | | | Rhinoconjunctivitis, 8% |
| Technologists (n = 38) | | | Rhinoconjunctivitis, 5% |
| Nurses (n = 201) | | | Urticaria, 8% |
| Cleaning staff (n = 50) | | | Urticaria, 4% |
| Technologists (n = 38) | | | Urticaria, 5% |
| Wrangsjo et al[47,48]: Prevalence of sensitization among Swedish operating theater staff and dental staff | | | |
| Operating theater staff (n = 57) | Positive, 4% | Positive, 4% contact urticaria, 7% | Prevalence of self-reported |
| Dental staff (n = 176) | Positive, 1% | Positive, 1% contact urticaria, 0% | Prevalence of self-reported |
| Yassin et al[49]: Job group vs SPT response to any of 4 latex glove extracts | | | |
| Nurses (n =136) | | Positive, 18% | |
| Doctors (n = 11) | | Positive, 9% | |
| Laboratory technicians (n = 41) | | Positive, 17% | |
| Dental assistants/residents (n = 36) | | Positive, 38% | |
| Respiratory therapists (n = 6) | | Positive, 17% | |
| Housekeeping personnel/clerks (n = 17) | | Positive, 0% | |

*OR*, Odds ratio.
*Results not stated, results were not reported by authors even though data were collected.
†Authors did not explain the discrepancy between the odds ratio and the 95% CI.

**TABLE V.** Studies of powdered versus powder-free latex gloves worn versus latex sensitization or type I latex allergic symptoms among health care workers

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Brehler et al[8]: Powdered vs nonpowdered latex gloves used | | | |
| Nonpowdered | OR, 1.0* | | |
| Powdered | OR, 1.5 (95% CI, 0.6-4.0) | | |
| Page et al[35]: Prevalence of sensitization by type of glove used | | | |
| Used powdered latex gloves | Prevalence, 4.7% | | |
| Used powder-free latex loves | Prevalence, 7.0% ($P$ = .4) | | |
| Levy et al[31]: Prevalence of sensitization among dental students | | | |
| Powdered latex glove users | | Prevalence, 15% | |
| Nonpowdered latex glove users | | Prevalence, 0% ($P$ = .053) | |
| Sussman[43]: Incidence of SPT conversion per year | | | |
| Powdered latex glove users | | Incidence, 1% | |
| Nonpowdered latex glove users | | Incidence, 1% | |

*OR*, Odds ratio.
*Reference level or group.

pared with risks among users of powder-free latex gloves (Table V). These studies do not suggest that powdered gloves are associated with increased risk of sensitization. Brehler et al[8] found that users of powdered gloves were at moderately increased risk of sensitization (odds ratio, 1.5; 95% CI, 0.6-4.0), although Page et al[35] found the prevalence of sensitization was higher among users of powder-free latex gloves (7%) than powdered latex gloves (4.7%; $P$ = .4). Sussman[43] found the incidence of sensitization was virtually identical at 1% per year among both powdered and powder-free glove users. Only Levy et al[31] reported (in an abstract) an appreciable difference in the prevalence of sensitization (15% among powdered glove users compared to 0% among nonpowdered users; $P$ = .053). In summary, the risk of sensitization is not clearly increased among users of powdered latex gloves compared with users of powder-free gloves in these 4 studies.

## Latex versus non-latex gloves

Four studies have examined the risks of sensitization among users of latex gloves compared with the risks among users of non-latex gloves (Table VI). Grzybowski et al[19] reported that the risk of sensitization was significantly lower among users of latex gloves than among users of non-latex gloves (odds ratio, 0.2; $P < .001$). Similarly, Tarlo[44] reported that the prevalence of sensitization was significantly lower among users of latex gloves (7%) than among users of non-latex gloves (36%; $P <$ .001). However, this latter result should be interpreted cautiously because of the absence of information in that report about the participation rate among subjects. Turjanmaa[2] reported that there was no significant difference in the prevalence of sensitization according to the type of glove used (latex versus vinyl versus both). Page et al[35] reported virtually identical prevalences of sensitization (approximately 6%) among current users of latex versus non-latex gloves and among ever users versus never users of latex gloves. The study by Baur et al[6] collected data about the type of glove used but did not report the results. Overall, these studies do not support a conclusion that latex glove use is associated with increased risk of sensitization compared to non-latex glove use.

Three studies have examined the risks of type I allergic symptoms among users of latex gloves compared with the risks among users of non-latex gloves. Page et al[35] found that self-reported hand dermatitis, rhinoconjunctivitis, and hand urticaria were significantly more common among users of latex gloves than among users of non-latex gloves, that general urticaria was also more common (but not significantly), and that asthma prevalence was not meaningfully different. The interpretation of these findings, in the absence of evidence that sensitization was associated with latex glove use, suggests that such symptoms may not have been mediated through latex sensitization. Baur et al[6] found that subjects with symptoms that were related to latex contact were more likely to use non-latex gloves but gave no further details about this finding. Kujala and Reijula[28] found no association between glove type and skin symptoms when other factors were taken into the logistic regression model. However, this latter study was not limited to type I allergic hand symptoms (urticaria), and the results should be interpreted cautiously.

## Measures of exposure to latex rubber based on environmental samples

Of all the studies reviewed, only 3 studies reported measurements of latex proteins in the air, and 1 study reported latex protein concentrations on surfaces (Table VII). Sussman[43] reported the incidence of sensitization in areas in which the latex proteins ranged between 5 and 83 ng/m$^3$ of the air in summer and between 40 and 616 ng/m$^3$ of air in the winter, compared to areas in which

**TABLE VI.** Studies of latex versus non-latex gloves worn versus latex sensitization or type I latex allergic symptoms among health care workers

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Baur et al[6]: Latex vs non-latex glove use | Results not stated* | Results not stated* | Subjects with symptoms more likely to use non-latex gloves |
| Grzybowski et al[19]: Latex vs non-latex glove use by nurses | | | |
| Non-latex | OR, 1.0† | | |
| Latex | OR, 0.2 ($P \leq .001$) | | |
| Kujala and Reijula[28]: Logistic regression of skin symptoms as a function of glove type (latex vs vinyl) | | | "No association between glove type and skin symptoms when other factors were taken into the model" |
| Page et al[35]: Prevalence by type of glove used | | | |
| Prevalence of sensitization | | | |
| Current latex glove users vs current non-latex glove users | Prevalence, 6.1% vs 6.3% ($P = .9$) | | |
| Ever used latex gloves vs never used latex gloves | Prevalence, 6.3% vs 5.1% ($P = .6$) | | |
| Prevalence of work related symptoms: latex glove users vs non-latex glove users | | | |
| Hand dermatitis | | | Prevalence, 23.4% vs 4.9% ($P < .01$) |
| Rhinoconjunctivitis | | | Prevalence, 16.3% vs 7.9% ($P < .01$) |
| Hand urticaria | | | Prevalence, 9.9% vs 2.1% ($P < .01$) |
| Work-related asthma | | | Prevalence, 1% vs 2% ($P = .44$) |
| General urticaria | | | Prevalence, 5% vs 2% ($P = .08$) |
| Tarlo[44]: Use of latex or non-latex gloves vs prevalence of SPT sensitization among dental students and staff | | | |
| Latex glove users | | Prevalence, 7% | |
| Non-latex glove users | | Prevalence, 36% ($P = .001$) | |
| Turjanmaa[2]: Glove type (latex/vinyl/both) vs scratch chamber test/SPT response | | "No significant difference" | |

*OR,* Odds ratio.
*Results were not reported by authors, even though data were collected.
†Reference level or group.

exposures ranged from undetectable to less than 1 ng/m$^3$ of air. The incidence rate of sensitization was virtually identical at 1% in both areas. Page et al[35] reported exposures in work areas of sensitized and nonsensitized subjects and found that levels were higher in the areas of the nonsensitized subjects. This was evident for airborne latex, for surface latex sampled from the backsides of ceiling tiles, and for dust samples taken from air handling filters in the work areas. The air samples showed very low levels of latex proteins in all areas (the highest measurement being 3.3 ng/m$^3$), which raises concern that aerosol exposures in this facility may have been too low to affect the sensitization rates. However, more than 316,000 pairs of powdered latex, 370,000 pairs of powder-free latex, and 47,000 pairs of non-latex gloves were used annually in the clinical areas that were studied, which indicates that the use of and contact with latex gloves was extensive.[51] Baur et al[6] reported the prevalence of sensitization and symptoms from a study in which the aerosol exposures to latex proteins were dichotomized as above or below 0.6 ng/m$^3$. They found that all sensitized subjects (and all symptomatic subjects) worked in areas where exposure was above 0.6 ng/m$^3$. It is difficult to reconcile these results with those of Page et al[35] who found sensitized and symptomatic subjects working in areas well below the threshold in the report by Baur et al, or with those of Sussman, who found the incidence of sensitization to be virtually identical at exposure levels well above and below the threshold in the report by Baur et al. In summary, these studies do not support the existence of an exposure threshold for sensitization or symptoms, nor do they support conclusions

**TABLE VII.** Intensity of exposure from quantitative environmental measurements (ambient exposure levels to natural rubber latex [NRL]) versus latex sensitization or type I latex allergic symptoms among health care workers

| Study and explanation | Latex-specific IgE | SPT response | Type I allergic symptoms |
|---|---|---|---|
| Baur et al[6]: Prevalence of IgE/symptoms higher among subjects exposed to latex aeroallergen below 0.6 ng/m$^3$ compared to those exposed above 0.6 ng/m$^3$ | $P < .02$ (data not reported) | Results not stated | $P < .05$ (data not reported) |
| Page et al[35]: Comparison of geometric mean levels of environmental NRL proteins among sensitized vs nonsensitized subjects | | | |
| Airborne latex (ng/m$^3$) | Geometric mean NRL concentration, 0.34 vs 0.47 ($P < .05$) | | |
| Surface latex (ng/cm$^2$) | Geometric mean NRL concentration, 124.9 vs 172.2 | | |
| Filter latex (ng/g of dust) | Geometric mean NRL concentration, 14,308 vs 25,279 | | |
| Sussman[45]: Incidence of SPT conversion vs personal samples of latex protein in air | | | |
| Exposures: 5-83 ng/m$^3$ (summer) and 40-616 ng/m$^3$ (winter) | | Incidence, 1% | |
| Exposures from undetectable to <1 ng/m$^3$ | | Incidence, 1% | |

that the risks of sensitization or symptoms increase as aerosol exposure increases.

## DISCUSSION

This body of scientific literature has a number of limitations that indicate that conclusions regarding the risks of latex sensitization, allergic symptoms, or risks that are associated with latex glove exposure among health care workers should be drawn cautiously. Most of the studies are cross-sectional, from which estimates of prevalence (but not incidence) have been made.

The participation rates in these studies vary widely, and the possibility of selection bias is a concern in those studies with participation substantially below 70%. Studies with high participation should be viewed as generally less likely to be influenced by selection bias, other factors being equal. Differences in the measurements being made are substantial across these studies, including the tests used to measure latex-specific IgE, the identity and number of reagents used in SPTs, the criteria for positive responses to these tests, the methods by which symptoms were reported, and the verification of symptoms through physical examinations, tests for sensitization, or challenge tests with latex samples. Similarly, measures of exposure to latex gloves varied widely (Tables II-VII).

Numerous studies have indicated that atopy is strongly associated with latex sensitization or allergic symptoms.* Many of the studies did not collect or report information on important confounding factors, including atopy, age, sex, and race. The extent to which these factors may have distorted the associations between indices of latex glove exposure (or work in specific jobs or areas) and measures of sensitization is unknown.

Numerous studies reported "no significant associations" but give no further details regarding the findings; other studies collected relevant data but did not report the findings. Such reporting practices limit the interpretation of the pattern of results from this extensive body of literature and raise concerns that selective reporting of findings may have occurred.

There is a willingness on the part of some investigators to speculate that the lack of association between various measures of exposure and sensitization or symptoms is due to preferential movement of subjects out of exposed jobs or settings. However, few of the studies measured such movement and the validity of such assumptions remains unknown. The single cross-sectional study that assessed job changes found no evidence that subjects who were sensitized and symptomatic preferentially left the workplace.[35] It is difficult to infer the sequence of events from cross-sectional data, such as whether subjects who become symptomatic tend to leave exposed jobs, or conversely, whether subjects who are symptomatic tend to choose nonexposed jobs in the first place. In contrast, prospective studies tend to have far greater ability to identify the time sequence of events, typically because sensitization is assessed at entry into the study and the incidence rate among nonsensitized subjects is measured as exposure occurs over time. Here, the studies by Gautrin et al[17] and Sussman[43] are important. Sussman found no difference in the rate of sensitization (1% per year) among users of powdered and nonpowdered latex gloves. Gautrin found that latex sensitization was more common (2.5% per year) among dental hygiene apprentices than among 2 other apprentice occupations. Both studies indicate that the risk

*5,9,12,26,29,31-33,42,43,46

of sensitization is relatively low and that the estimates are unlikely to be affected appreciably by job migration.

This review has not addressed the issues that are related to the amelioration or resolution of type I latex allergies after cessation of exposure. Although it has been demonstrated that individual patients have allergic responses to latex exposures at work and that cessation of exposure is associated with clinical improvement, no quantitative estimates of the risks of latex sensitization or allergy that are related either to work in health care or to glove exposure are provided. We chose not to review this topic because of the lack of quantitative information regarding risk factors.

### Recommendations for future epidemiologic studies

Defined eligibility criteria and uniform methods for subject enrollment are critical to the validity of epidemiologic studies. Cross-sectional studies that are based on convenience samples that are not known to be representative of any definable populations are difficult to interpret and may not give reliable measures of risk. High participation rates are essential to reduce the possibility of selection bias and participation rates must be reported.

Appropriate comparison groups are critically important. Few of the studies reviewed herein included appropriate referent groups that would allow comparisons of health care workers to other population groups. As a result, it is unclear whether health care workers are at increased risk of latex sensitization or of type I allergic symptoms, compared with the general population. Efforts should be made to standardize the methods for the measurement of outcomes to insure comparability across studies, especially with respect to latex-specific IgE and SPTs. Similarly, efforts should be made to standardize the assessment of symptoms in terms of how symptoms are queried, the definitions of symptoms that are felt to represent type I allergies, and whether the symptoms are perceived to be related to latex exposure.

This review highlights the paucity of environmental air and surface measures of latex antigen exposure, which are critical to the assessment of risk. Measures of the duration, frequency, intensity, and route of exposure (both skin and inhalation) to latex antigens are invaluable and should have a prominent place in future studies. Further progress in the differentiation of latex antigens from other latex protein in aerosols will allow more refined estimates of risks that are related to exposure. Assessments of the patterns of use and of skin contact with gloves have been made commonly, and many studies have included good estimates of the number of pairs of gloves, the hours per day, the pair-hours, and the types of gloves worn. These will continue to be essential components of well-conducted studies.

It is evident that atopy is strongly related to the risk of latex allergy and that age, sex, and race may also be determinants of latex allergy. Insofar as these factors may also influence which jobs people take, they should be regarded as potential confounders that must be addressed either in the study design or in the data analysis. Failure to do so may result in biased estimates of the association between jobs (and their correlates such as latex glove use) and type I allergic disorders.

## CONCLUSIONS

This large body of scientific literature indicates that the prevalence of sensitization to natural rubber latex among health care workers ranges widely (between 0% and 30%), depending on the definition of the group studied and the methods by which sensitization is assessed. Most of the estimates fall in the range of 5% to 17%. The literature also supports a conclusion that the incidence of sensitization is in the range of 1% to 2.5% per year. The single study that directly compared the prevalence of sensitization in health care workers to that in the general population found that health care workers were at little, if any, increased risk.[15] Numerous investigations have examined the risks of sensitization and type I allergic symptoms that are related to latex glove use and have reported great variation in the risks of sensitization and symptoms that are related to each measure of exposure that has been studied. The evidence that is available at this time does not support a conclusion that the risk of sensitization is associated with any measure of exposure to latex gloves. Similarly, the risk of type I allergic symptoms is not clearly associated with any measure of exposure to latex gloves, with the possible exception of hand symptoms. A number of studies have demonstrated that hand symptoms are associated with latex glove use, but these studies have failed to differentiate type I allergic symptoms adequately from other types of symptoms (type 4 allergy and irritant contact dermatitis).

The extent to which the variation in risks of sensitization and type I symptoms among studies reflects true differences in risk or is explained by the different methods used in these studies (selection bias related to poor participation, incomplete reporting of findings, or confounding by extraneous factors) cannot be determined. There is a need for well-designed studies of latex-exposed populations to explore the risks of sensitization and type I allergic disorders in relation to measured exposures to latex antigens, in which these extraneous factors have been adequately addressed. Although claims are common that health care workers are at increased risk of latex sensitization and type 1 allergy, few of the epidemiologic studies that have been published to date support such conclusions; most studies do not. Most studies show no clear pattern of risk that is associated with any specific aspect of health care work, with latex glove use, or with powdered latex gloves, in particular.

#### REFERENCES

1. Centers for Disease Control. Recommendations for prevention of HIV transmission in health-care settings. MMWR Morb Mortal Wkly Rep 1987;36:3-18.
2. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. Contact Dermatitis 1987;17:270-5.
3. Arellano R. Prevalence of latex sensitization among hospital physicians occupationally exposed to latex gloves. Anesthesiology 1992;77:905-8.
4. Amin A, Palenik CJ, Cheung SW, Burke FJT. Latex exposure and aller-

gy: a survey of general dental practitioners and dental students. Int Dent J 1998;48:77-83.
5. Allmers H, Brehler R, Chen Z, Raulf-Heimsoth M, Fels H, Baur X. Reduction of latex aeroallergens and latex-specific IgE antibodies in sensitized workers after removal of powered natural latex gloves in a hospital. J Allergy Clin Immunol 1998;102:841-6.
6. Baur X, Chen Z, Allmers H. Can a threshold limit value for natural rubber latex airborne allergens be defined? J Allergy Clin Immunol 1998;101:24-7.
7. Berky ZT, Luciano WJ, James WD. Latex glove allergy: a survey of the US Army Dental Corps. JAMA 1992;268:2695-7.
8. Brehler R, Kolling R, Webb M, Wastell C. Glove powder: a risk factor for the development of latex allergy. Eur J Surg 1997; 163(suppl):23-5.
9. Brown RH, Schauble JF, Hamilton RG. Prevalence of latex allergy among anesthesiologists. Anesthesiology 1998;89:292-9.
10. Bubak ME, Reed CE, Fransway AF, Yunginger JW. Subspecialty clinics: allergic diseases: Allergic reactions to latex among health-care workers. Mayo Clinic Proc 1992;67:1075-9.
11. Charous BL, Hamilton RG, Yunginger JW. Clinical aspects of allergic disease: occupational latex exposure: characteristics of contact and systemic reactions in 47 workers. J Allergy Clin Immunol 1994;94:12-8.
12. deGroot H, de Jong NW, Duijster E, van Wijk RG, Vermuelen A, van Toorenenbergen AW, et al. Prevalence of natural rubber latex allergy (type I and type IV) in laboratory workers in the Netherlands. Contact Dermatitis 1998;38:159-63.
13. Douglas R. Prevalence of IgE-mediated allergy to latex in hospital nursing staff. Aust N Z J Med 1997;27:165-9.
14. Fishwick D, Pearce N, D'Souza W, Lewis S, Town I, Armstrong R, et al. Occupational asthma in new Zealanders: a population based study. Occup Environ Med 1997;54:301-6.
15. Garabrant DH, Roth HD, Parsad R, Ying GS, Weiss J. Latex sensitization in health care workers and in the US general population. Am J Epidemiol 2001;153:515-22.
16. Gautrin D, Infante-Rivard C, Dao TV, Magnan-Larose M, Desjardins A, Malo JL. Specific IgE-dependent sensitization, atopy, and bronchial hyperresponsiveness in apprentices starting exposure to protein-derived antigens. Am J Resp Crit Care Med 1997;155:1841-7.
17. Gautrin D, Ghezzo H, Infante-Rivard C, Malo JL. Incidence and determinants of IgE-mediated sensitization in apprentices. Am J Resp Crit Care Med 2000;162:1222-8.
18. Geller M, Paiva TCB, Geller P. Latex allergy in a surgical center [abstract]. J Allergy Clin Immunol 1998;101(suppl):S204.
19. Grzybowski M, Ownby DR, Peyser PA, Johnson CC. The prevalence of anti-latex IgE antibodies among registered nurses. J Allergy Clin Immunol 1996;98:535-44.
20. Hamann CP, Turjanmaa K, Rietschel R, Siew C, Ownby DR, Gruninger SE, et al. Natural rubber latex hypersensitivity: incidence and prevalence of type I allergy in the dental profession. J Am Dent Assoc 1998;129:1-12.
21. Hunt LW, Fransway AF. An epidemic of occupational allergy to latex involving health care workers. J Occup Environ Med 1995;37:1204-9.
22. Iacobelli AM, McCullough JA, Ownby DR. The prevalence of latex allergy in high risk medical personnel. J Allergy Clin Immunol 1993;91:1-2.
23. Jolanki R, Estlander T, Alanko K, Savela A. Incidence rates of occupational contact urticaria caused by natural rubber latex. Contact Dermatitis 1999;40:329-31.
24. Kaczmarek RG. Prevalence of latex-specific IgE antibodies in hospital personnel. Ann Allergy Asthma Immunol 1996;76:51-6.
25. Katelaris CH. Prevalence of latex allergy in a dental school. Med J Aust 1996;164:711-4.
26. Kibby T, Akl M. Prevalence of latex sensitization in a hospital employee population. Ann Allergy Asthma Immunol 1997;78:41-4.
27. Konrad C, Fieber T, Gerber H, Schuepfer G. The prevalence of latex sensitivity among anesthesiology staff. Anesth Analg 1997;84:629-33.
28. Kujala VM, Reijula KE. Glove-induced dermal and respiratory symptoms among health care workers in one Finnish hospital. Am J Ind Med 1995;28:89-98.
29. Lagier F, Verloet D, Lhermet I, Poyen D. Prevalence of latex allergy in operating room nurses. J Allergy Clin Immunol 1992;90:319-22.
30. Leung R. Prevalence of latex allergy in hospital staff in Hong Kong. Clin Exp Allergy 1997;27:167-74.
31. Levy DA, Allouache S, Brion M, Valantin C, Walikow M, Buck D, et al. Effect of powdered vs. nonpowdered latex gloves on the prevalence of latex allergy in dental students [abstract]. J Allergy Clin Immunol 1998;101(suppl):S148.
32. Liss GM. Latex allergy: epidemiological study of 1351 hospital workers. Occup Environ Med 1997;54:335-42.
33. Mace SR, Sussman GL, Liss G, Stark DF. Latex allergy in operating room nurses. Ann Allergy Asthma Immunol 1998;80:252-6.
34. Miller A, Wiedbruuk D, Laurer CB. Prevalence of latex allergy in newly hired house staff. J Allergy Clin Immunol 1998;101(suppl):S204-5.
35. Page EH, Esswein EJ, Petersen MR, Lewis DM, Bledsoe TA. Natural rubber latex: glove use, sensitization, and airborne and latent dust concentrations at a Denver hospital. J Occup Environ Med 2000;42:613-20.
36. Palczynski C, Walusiak J, Hanke W, Gorski P. Latex allergy in Polish nurses. Am J Ind Med 1999;35:413-9.
37. Safadi GS, Corey EC, Taylor JS, Wagner WO. Latex hypersensitivity in emergency medical service providers. Ann Allergy Asthma Immunol 1996;77:39-42.
38. Safadi GS. Latex hypersensitivity: its prevalence among dental professionals. J Am Dent Assoc 1996;127:83-8.
39. Schopf P, Rueff F, Przybilla B. Natural rubber latex (NRL) allergy-a dissimulated disease. J Allergy Clin Immunol 1998;101(suppl):S158.
40. Sinha A, Harrison PV. Latex glove allergy among hospital employees: a study in the north-west of England. Occup Med 1998;48:405-10.
41. Smedley J, Bendall H, Coggon D. Prevalence and risk factors for latex allergy: a cross sectional study in a United Kingdom hospital. Occup Environ Med 1999;56:833-6.
42. Sussman GL, Lem D, Liss G, Beezhold D. Latex allergy in housekeeping personnel. Ann Allergy Asthma Immunol 1995;74:415-8.
43. Sussman GL. Incidence of latex sensitization among latex glove users. J Allergy Clin Immunol 1998;101:171-8.
44. Tarlo SM. Latex sensitivity in dental students and staff: a cross-sectional study. J Allergy Clin Immunol 1997;99:396-401.
45. Vandenplas O, Delwiche JP, Evrard G, Aimont P. Prevalence of occupational asthma due to latex among hospital personnel. Am J Resp Crit Care Med 1995;151:54-60.
46. Watts DN, Jacobs RR, Forrester BG, Bartolucci A. An evaluation of the prevalence of latex sensitivity among atopic and non-atopic intensive care workers. Am J Ind Med 1999;34:359-63.
47. Wrangsjo K, Osterman K, Van Hage-Hamsten M. Glove-related skin symptoms among operating theatre and dental care unit personnel (II): clinical examination, tests and laboratory findings indicating latex allergy. Contact Dermatitis 1994;30:139-43.
48. Wrangsjo K, Osterman K. Glove-related skin symptoms among operating theatre and dental care unit personnel. Contact Dermatitis 1994;30:102-7.
49. Yassin MS, Lierl MB, Fischer TJ, O'Brien K. Latex allergy in hospital employees. Ann Allergy 1994;72:246-9.
50. Cherry N, Meyer JD, Adisesh A, Brooke R. Surveillance of occupational skin disease: EPIDERM and OPRA. Br J Dermatol 2000;142:1128-34.
51. Page EH, Esswein EJ. NIOSH health hazard evaluation report: HETA 98-0096-2737 Exempla St. Joseph Hospital (including survey questionnaire). Cincinnati (OH): National Institute for Occupational Safety and Health; 1998. p. 1-25.