Invited Commentary: Assessing Latex Sensitization Using Data from NHANES III

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Natural latex rubber is a substance commonly used for making gloves to protect health care workers from infections and other hazards. While gloves mediate one extremely high risk by creating a barrier between health care workers and infectious agents, some argue that the occurrence of sensitization and allergic response from the use of these gloves has created an important occupational health concern (1). Consequences of this sensitization and allergic response, in addition to the direct health risks, include job reassignment and disability and may result in compensation claims. It is from this context that Garabrant et al. (2), in their article in this issue of the Journal, assess whether latex sensitization (or allergic response) is more common among health care workers than among the general population by using the National Health and Nutrition Examination Survey (NHANES III) data (3). Specifically, they question whether or not this sensitization likely comes from latex glove use. In this commentary, we address two issues. First, methodologically, we briefly discuss the usefulness of large, publicly available databases for clarifying known public health concerns. Second, specific to their study, we evaluate whether Garabrant et al. provide useful and convincing evidence on the status of the latex issue.

USING LARGE, PUBLICLY AVAILABLE DATABASES FOR PUBLIC HEALTH RESEARCH

With the continuing revolution in computer technology, the availability and use of important public health databases is expanding exponentially. From vital statistics to survey results to demographic and environmental quality data, sources that were proprietary, obscure, or available only in hard copy are now accessible online (e.g., the Environmental Protection Agency’s Toxics Release Inventory (4), CDC WONDER (5), the US Census (6)), on CD-ROM (e.g., the Surveillance Epidemiology, and End Results program (7) and NHANES III (3)) and through access-controlled computerized searches (e.g., the National Death Index (8)). In addition, the extent and the quality of the data continue to improve, for example, with the National Death Index, including a nosologist’s coding of cause-of-death information in addition to date and location of death in its National Death Index Plus service (9) or the National Center for Health Statistics providing both statistically smoothed maps of mortality across the United States and age-adjusted cause-of-death data files for each health service area in the United States (10). The potential offered for quick, inexpensive, but powerful, studies using these simple data sources is extraordinary, as is the potential for difficulties in analysis and interpretation. We strongly support the use of these data, but urge researchers to state explicitly the strengths, weaknesses (e.g., internal consistency), and generalizability (e.g., external validity) of their analyses.

The utility of these data for exploratory analyses has been demonstrated in many studies. For example, some have developed environmental exposure databases to be evaluated with respect to disease or mortality registries (11–14). Others have used such data for surveillance (15), looking for outbreaks or trends or comparing data patterns across population strata. Many other applications exist as well.

The issue that is more controversial is the utility of these data to address an existing public health concern, including investigation of etiology, instead of undertaking a study that includes original data collection. One problem with using extant data is that, although a research question may have broad societal implications, the results may be relevant only to the population under study. There is a series of questions that one should consider when making a decision about the utility of the results and their relevance for generalization. First, one must assess whether the appropriate exposure and outcome of concern have been captured in a single database or in complementary databases. Second, one must evaluate whether the population studied is appropriate and timely to the question. Third, one must determine whether the data have adequate resolution and reliability to answer the specific questions under investigation. Fourth, one must determine whether the data set has adequate information on possible confounding variables and effect modifiers and whether the sample size and prevalences can result in a study of sufficient sensitivity and power. Fifth, one must evaluate whether the results can be generalized beyond the
study population. However, what is most important in any such study is that the investigators address these concerns openly and explicitly so that readers can appreciate the strengths, limitations, and generalizability of the study at least from the investigators perspective.

In the case of latex sensitivity and allergy among health care workers, we see a number of pluses and minuses with the use of the NHANES III data. For example, while the NHANES III data contain information on both exposure and outcome, neither is the ideal measure for comprehensive assessment of this issue. For outcomes, adverse reactions to latex use include nonallergic irritant contact dermatitis, allergic contact dermatitis (type IV delayed hypersensitivity), and allergic reaction (type I or immediate hypersensitivity); yet, NHANES III reports only on the most severe of these, the sensitization and possible allergic reaction (immunoglobulin E (IgE) level in a single blood sample). Less severe adverse effects than immediate allergic response are also of concern and may be a substantial occupational health issue, and statistical analyses of such outcomes may be more informative because of the greater statistical power due to higher prevalences.

A second concern with using the NHANES III data to assess latex sensitivity is that the methodology used, the AlaSTAT EIA (enzymometric immunoassay) (Diagnostic Products Corporation, Los Angeles, California) (16) has moderate misclassification rates. According to the manufacturer, the clinical specificity is 80.6 percent (95 percent CI: 61.9 percent, 91.9 percent), or a moderate rate of false positives (17).

For exposure, NHANES III reports only current and longest-held occupations rather than a complete job history, along with self-reports of whether gloves are worn in occupations. Further, responses on some questions, such as glove use, are rather sparse. There are no quantitative data on frequency or length of time that gloves were used, on whether glove use was avoided due to mild sensitivity or concern, what the prevalence of glove use is within an occupation, what the glove is made of (e.g., latex or not), how frequent glove changes were (which results in airborne latex particles), or whether the glove was powdered. The cornstarch powder used on gloves is another potential source of allergic response. There is no consideration of the accuracy of the occupational coding, and researchers are limited to 40 broad categories, each of which includes a variety of different jobs and exposures. All of these concerns can lead to substantial misclassification. Therefore, while both exposure and outcome are available in the database, their appropriateness, resolution, and reliability are open to question and should be justified. Depending on the level of resolution desired, they may be adequate. One also must consider the possibility of confounding and effect modification. As noted by Garabrant et al. (2), there are no data on nonoccupational exposures to latex. The only risk factors considered were demographic and allergic conditions.

The population studied in NHANES III represents a weighted, random sample of the civil, noninstitutionalized population of the United States aged 2 months and older from 1988 to 1991. To estimate the prevalence of latex sensitization in these data, the Centers for Disease Control and Prevention utilized stored sera to assess IgE-specific latex sensitivity in a subpopulation of this study (a sample of those of aged 17–60 years) (16). The data resulting from these tests were analyzed by Sosovec et al. (18) as well as Garabrant et al. (2). There is one striking characteristic of these data that raises concern for these particular studies. Garabrant et al. (2) and others (1) report that the prevalence of latex sensitization in the general population in the United States and internationally ranges from 0 to 12 percent. Yet, in NHANES III, the prevalence in all nonhealth care workers is more than 18 percent, and in nonhealth care workers who use gloves, it is more than 20 percent. No explanation is given for this discrepancy between NHANES III and previous studies, raising issues of validity and generalizability (1). This elevated prevalence could be due, in part, to the low specificity of the AlaSTAT test used (19), particularly if other tests, such as the skin prick test, were used in estimating the prevalence in other populations. In short, while innovative in its approach, the population sample and limitations of the database may preclude development of useful inferences or generalizations.

RESULTS OF GARABRANT ET AL. (2)

The specific analyses undertaken by Garabrant et al. (2) assess whether the prevalence of latex sensitization (elevated latex-specific blood IgE level) is higher in health care workers than in other workers or the general population and consider risk factors for elevated IgE levels. The results Garabrant et al. (2) report show a 50 percent greater risk of latex sensitization among those whose longest job was in health care and a 17 percent greater risk of those currently in health care. Those currently in health care who reported no glove use showed a 130 percent greater risk if they did not have atopy and a 2,700 percent greater risk if they did have atopy. Finally, Garabrant et al. reported that unadjusted latex sensitivity is more common, on average, in occupations in which gloves are used frequently, including health care. They interpret these results as showing a possible association between work in health care and latex sensitization, although not necessarily due to glove use.

There are two important substantive issues that result from this study: 1) the risk attributed to atopy; and 2) the risk attributed to latex glove use. With respect to atopy, as the authors note, their finding is consistent with previous studies: Those with atopy are at increased risk of sensitization and are also likely to have severe allergic response. Further study, especially with clinical data, might be important in understanding the etiology of the sensitization, although it appears that, given the size of the risk, those with atopy should avoid latex exposure based on these data alone.

The issue of glove use is more difficult to resolve. First, the reported risks are consistent with a variety of explanations, including that glove use and risk of glove use are risk factors for latex sensitization. Although the authors discuss some data on glove use and job changes, it is important to note the limitations of those data. Only 3,861 of 20,050 subjects (fewer than 20 percent) reported on glove use in the NHANES III database, only 11,620 of 20,050 subjects
fewer than 60 percent) reported their current occupation, only 349 of 499 persons who reported current occupation as health care worker also reported on glove use, and only 326 of 847 persons who reported their longest-held occupation to be health care worker reported on glove use. These relatively small sample sizes and low reporting proportions raise issues of reliability and the possibility that reporting bias is substantial.

Garabrant et al. (2) argue, on the basis of their data and the work of others, that glove use is not associated with latex sensitization. A possible alternative explanation is that the sensitization may lead workers to change jobs, resulting in misleading results in some of the analyses. This is consistent with the higher risk of sensitization among health care workers who do not use gloves (odds ratio = 2.5) compared with health care workers who do (odds ratio = 1.5). Once sensitized, health care workers who do not wish to switch industries may seek jobs that do not require glove use, resulting in more sensitized health care workers not using gloves. However, the NHANES III data on glove use and occupation are too limited to confirm or refute such speculation.

Finally, we have some concerns about the IgE testing methodology used by NHANES III and the confusion surrounding it in the literature. There are three different AlaSTAT tests that have been used to estimate the prevalence of latex sensitivity and that often are not distinguished in the literature. As noted above, the AlaSTAT EIA test used by NHANES III has an estimated specificity of 80.6 percent (17), which results in a moderate rate of false positives that could lead to overestimates of the prevalence of latex sensitivity (19). At the time of the initial NHANES III IgE analyses in 1994 (i.e., phase I), this was the only test approved by the Food and Drug Administration for the detection of latex-specific IgE in sera (16). The second test, AlaSTAT RIA (Diagnostic Products Corporation) (radioimmunooassay), has a reported specificity of as low as 33 percent (20), which is even more problematic. The third and newest test, the AlaSTAT microplate test (Diagnostic Products Corporation), is far more accurate, with an estimated specificity in excess of 90 percent (21–26). The AlaSTAT microplate test is being used for additional IgE analyses of the NHANES III sera samples (i.e., phase II). Unfortunately, several technical problems have arisen in processing of these samples, delaying release of the data (16) and precluding methodological comparisons for the time being. If one does not know which specific AlaSTAT test has been used on a set of samples, one would not know the accuracy of the test and may misinterpret the data.

SUMMARY

In sum, Garabrant et al. (2) have used an elegant and appropriate research strategy to address an occupational health concern of growing importance, both in terms of social and economic costs. Their results raise some salient issues but, due to limitations of the database used, these issues are not resolved. The study shows that health care workers have a moderately increased risk of having latex sensitization and that health care workers with atopy have a substantially increased risk of latex sensitization. The question of whether this sensitization is due to latex gloves or not can be answered by further study with data more carefully collected to address these issues as well as by increasing our understanding of the mechanism of response and by identifying the specific triggering agent. Further research is also needed to explain why the NHANES III study population has a prevalence of latex sensitization that is one and a half times larger than that of any previous study and whether the study population results can be generalized. In the interim, fortunately, that there are cost-effective alternatives to latex gloves to limit the exposure of health care and other workers. Avoidance of other latex exposures should be considered for those at risk.

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REFERENCES


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