(2) We understand that the word "substantial" was inserted before "personal injury or illness" to convey the intent that cautionary labeling be not required to guard against wholly insignificant or negligible illness or injury—such as the very temproary indisposition which a child might suffer from ingesting a piece of the standard type of toilet soap—while on the other hand not limiting the requirement of cautionary labeling to cases where the illness or injury would be severe or serious. We recognize that, if labeling were required to caution against the risk of even the most trifling indisposition, there would scarcely be any substance which would not have to bear cautionary labeling, so that label warnings would tend to be more and more disregarded by consumers, and we believe that even without any qualifying term the bill would be interpreted so as to rule out that which is wholly negligible or insignificant. On the other hand, if a qualifying term as susceptible to misinterpretation as the word "substantial" is used, we believe it important that there be clear legislative history clarifying the legislative intent along the above-indicated lines.

(3) Further, the definition should be amended so as to apply to a substance which could cause the requisite injury or illness "during, or as the proximate result of" any customary or reasonably foreseeable handling or use.

(*b*) *Declaratory regulations as to coverage.*—It is apparent that, even with the above-suggested clarifications, the application of the second part (i.e., the so-called "if" clause) of the basic definition of "hazardous substance" in the bill is so largely dependent on judgmental factors—e.g., what is "reasonably foreseeable"—that it will lead to considerable uncertainty and much costly litigation, with different courts and juries reaching different results, unless some mechanism for authoritatively resolving this uncertainty short of litigation is devised. We realize that, on the one hand, in view of the broad sweep of the bill, and because of the constant development of new useful but hazardous substances suitable for household use, the inclusion of a statutory list of covered substances (in analogy to the list in the Federal Caustic Poison Act) or the limitation of coverage to substances listed by regulation would not be feasible. And while, on the other hand, we would prefer elimination of the "if" clause altogether from the point of facility of enforcement, we recognize that the inclusion of some such clause can be justified.

It is feasible, however, and we strongly urge, that the committee include in the bill provisions deeming a substance to be hazardous where the Secretary by regulation declares it to be such upon the basis of a finding that it meets the requirements of the bill's basic definition of "hazardous substance." The Secretary should be authorized to take such action whenever in his judgment this will promote the objectives of the bill by avoiding or resolving uncertainty. (The failure of the Secretary to take such action, of course, should not absolve anyone from the consequence of noncompliance with the labeling requirements of the bill in the case of a substance which is "hazardous" under the basic definition.) We would not object to making the issuance, amendment, or repeal of these declaratory regulations subject to procedural safeguards (with opportunity for administrative hearing, and for judicial review on the basis of the hearing record) such as those contained in section 701 (e)-(g) of the Federal Food, Drug, and Cosmetic Act.

(c) *Exemption of food, drugs, and cosmetics.*—As above indicated, the bill excludes from coverage foods, drugs, and cosmetics subject to the Federal Food, Drug, and Cosmetic Act. On the other hand, the Federal Caustic Poison Act, which the bill would repeal, applies the labeling requirements of that act to substances covered by it in addition to the requirements of such other laws. The virtue of the latter approach is to avoid any gaps in protection. For example, except with respect to drugs and devices, we doubt that in general we could, under the Federal Food, Drug, and Cosmetic Act, require the necessary warning labels in the case of foods or cosmetics which, because of the way they are packaged or otherwise, are capable of causing injury if not carefully handled. (This situation is to be distinguished from the outlawing of containers under that act where the container consists in whole or part of a poisonous or deleterious substance which may render the contents injurious to health.) Even with respect to drugs, the provisions of the act (sec. 502(f)) on which we base our regulations as to certain incidental hazards, such as our proposed labeling requirements in the case of drugs in self-pressurized containers, would benefit from being clarified and made more explicit.

We understand that the industries concerned would strongly object to the deletion of the food, drug, and cosmetic exemption from the bill, on the grounds that consumer protection with respect to these articles should be dealt with in a single act,—i.e., the Federal Food, Drug, and Cosmetic Act,—that inclusion of these articles in a Federal Hazardous Substances Labeling Act, which is the proposed short title of the bill, would give a false impression to the public as to the safety of these articles, and that the labeling requirements of the bill are, largely, ill suited to any hazards involved in these articles.

Our basic concern is to close any gap in our authority to afford needed consumer protection with respect to these articles at least comparable to the protection which would be afforded by the bill for substances which it does now cover. So long as this is done, we do not insist on one approach over another. Hence, we urge that, if the present exemption of foods, drugs, and cosmetics is retained for the proposed Federal Hazardous Substances Labeling Act, appropriate corresponding amendments to the Federal Food, Drug, and Cosmetic Act be inserted in the bill as a separate title II. (This would require designation of the present sections of the bill—except section 13 (time of taking effect), section 14 (application to existing law), and section 15 (repeal of Federal Caustic Poison Act)—as title I, and changing the word "act" on page 1, line 4, to "title." Sections 13–15 of the bill, appropriately renumbered and with the modifications suggested in this report, should become title III.)

We are developing draft language for the above-suggested title II of the bill. As respects food, the proposed amendments will provide for cautionary labeling only when the food is packaged in self-pressurized containers. While cautionary labeling might also be called for in the case of certain other foods, such as concentrates, we have not explored the need for such food labeling sufficiently to go beyond the case of self-pressurized containers at this time.

It should be understood that our recommendation for cautionary labeling requirements in the case of cosmetics should not be construed as in any way prejudicing consideration of bills for pretesting of cosmetics. On those proposals (other than proposals on color additives), we intend to submit our views at a later stage.

(*d*) *Authority to establish exemptions administratively.*—We believe that the Secretary should be authorized to exempt a substance where he finds that adequate safety requirements have been established by or under some other Federal law.

(*e*) *Toxic substances.*—(1) In general: Under section 2(g) of the bill, the term "toxic" is defined to apply to "any substance which has the inherent capacity to produce bodily injury to man through ingestion, inhalation, or absorption through the skin." For the reasons stated in the enclosed staff memorandum, we believe that the word "inherent" is an unnecessary and confusing limitation and should be eliminated.

(2) Radioactive substances: The above-mentioned definition of "toxic" would seem to cover substances emitting ionizing radiation. The extent to which radioactive materials should be covered under the bill is under discussion with other interested agencies and we shall submit our suggestions on this matter shortly.

(*f*) *Strong sensitizer.*—The bill (sec. 2(k)) provides that, before designating a substance as a strong sensitizer, "the Secretary shall find that the frequency of occurrence and severity of the reaction indicate a significant potential for causing hypersensitivity." We agree that both the frequency and the severity of the reaction should be considered, but, contrary to what we believe was intended, the language used is open to the contention that the reaction must be both frequent and severe. We believe, rather, that, in determining whether to designate a substance as a strong sensitizer, the weight to be given to frequency of occurrence should decline as the severity of the reactions increases, and vice versa. To clarify the matter, we recommend changing the above-quoted phrase to read, "the Secretary upon consideration of the frequency of occurrence and severity of the reaction, shall find that the substance has a significant potential for causing hypersensitivity."

(*g*) *Flammability.*—The bill defines the term "flammable" as applying to any substance which has a flash point of 20–80° F., and the term "extremely flammable" as applying to any substance which has a flash point at or below 20° F., as determined in both cases by the Tagliabue Open Cup Tester; except that the flammability of the contents of self-pressurized containers shall be determined by methods generally applicable to such containers and established by regulations.

We believe that we should be authorized to determine the flammability of solids, such as pastes, by equipment more suitable than the Tagliabue Open Cup Tester. We, therefore, suggest amending these provisions so as to authorize the Secretary to determine the flammability of solids, as well as the flammability of the contents of self-pressurized containers, by methods found generally applicable thereto and established by regulations. It should be made clear, moreover, that such regulations, with respect to solids and the contents of self-pressurized containers, should establish criteria for distinguishing between what is "flammable" and what is "extremely flammable." The difference in result is that in the case of extremely flammable substances the warning label would have to bear the signal word "Danger."

Suggested language for carrying out these suggestions is included in the enclosed memorandum.

3. Labeling requirements

Like the coverage provisions of the bill, these are key provisions and should be carefully considered to make them adequate for consumer protection, insofar as such protection can reasonably be achieved by cautionary labeling.

(*a*) *Exemptions.*—In lieu of the above-mentioned provisos relating to partial exemption of substances presenting only minor hazards or packaged in small packages (p. 7, lines 20–25; p. 8, lines 1 and 2, of the bill), we believe that the Secretary should be authorized to exempt hazardous substances from the requirements of the bill to such extent as he finds consistent with adequate protection of the public health, where he finds that, because of the size of the package or the minor hazard involved, or for other good and sufficient reasons, full compliance is impracticable or is not necessary for adequate protection of the public health.

(*b*) *Additional requirements or variations.*—On the other hand, this Department should, we think, be authorized to establish such additional labeling requirements, or require such variations in labeling, as may be necessary for the protection of the public health in view of the special hazard involved in the case of a particular substance.

(*c*) *Improvements in specific statutory labeling requirements.*—Certain specific label requirements set forth in the bill should, we think, be improved. Our suggestions to accomplish these improvements are set forth in the enclosed memorandum in view of their detailed and technical nature, but this should not be understood as intended to derogate from their importance for consumer protection and for effective enforcement.

4. Prohibited acts

In certain respects, the section which sets forth the acts prohibited (sec. 3), and to which the penalty and injunction sections will be keyed, should be revised by supplying certain omissions and embodying certain other needed improvements, as suggested in the enclosed memorandum.

5. Effective date

In view of the sizable task of preparing necessary implementing regulations, including exemptions and variations from the requirements of the bill in appropriate cases, we recommend that the Secretary be empowered to extend the 6-month deferred-enforcement date of the bill for an additional period not exceeding 18 months after the month of enactment. Also, we would suggest that the first 6-month period begin to run at the beginning of the first full calendar month after enactment of the bill, rather than on the day after enactment.

We recommend that the bill, modified as suggested above and in the enclosed memorandum, and with certain additional technical corrections, be enacted by the Congress. (We should be glad, if your committee so desires, to furnish technical assistance in connection with the revision of this bill.)

The Bureau of the Budget advises that it perceives no objection to the submission of this report to your committee.

Sincerely yours,

ARTHUR S. FLEMMING, *Secretary.*

MEMORANDUM TO ACCOMPANY REPORT OF DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE ON HAZARDOUS SUBSTANCES BILL

1. Factory inspection

To carry out the recommendations in the Secretary's letter, it is suggested that section 8(b) of the bill, entitled "Examinations and investigations," be amended to read as follows:

"(*b*) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (1) to enter, at reasonable times, any factory, warehouse, or establishment in which hazardous substances are manufactured, processed, packed, or held for introduction into interstate commerce or are after such introduction, or to enter any vehicle being used to transport or hold such hazardous substances in interstate commerce; (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle, and all pertinent equipment, finished and unfinished materials, and labeling therein; and (3) to obtain samples of such materials or packages thereof or of such labeling. A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness."

2. Toxic, including radioactive, substances

(*a*) Strike the word "inherent" from the definition of "toxic substance." We understand that the word "inherent" was originally inserted in the prototype draft of this bill in an attempt to relate the term "toxic" to substances which are toxic in a pharmacological sense and to exclude such items as knives, etc. This function is now adequately performed by other limiting language in the definition, whereas the word "inherent" may give rise to controversy.

(*b*) On the problem of radioactive substances, recommendations will be submitted shortly.

3. Improvements in specific statutory labeling requirements

(*a*) *Name of substance.*—Change clause (B), on page 5, lines 19–22, of the bill, to read: "(B) the common or usual name or the chemical name (if there be no common or usual name) of the hazardous substance or of each component which contributes substantially to the hazard, unless the Secretary by regulation permits or requires the use of the recognized generic name;".

This revision will require the label to describe the substance by the name which will be most useful to physicians or others attending a person injured by a substance. (Under the bill as introduced, the manufacturer, producer, or distributor could choose between the common or usual name, the chemical name, and the generic name.) It should be understood that components of a mixture must be named if they contribute substantially to the hazard. By "substantially" is meant such a contribution to the hazard as is significant enough to make it useful to an attending physician to know the name of the component.

(*b*) Clause (G) of the label requirements of the bill (p. 7, lines 7–9) would require "instructions, when necessary, for the first-aid treat-

ment in case of contact or exposure, if the substance is hazardous through contact or exposure". We understand that the "if" clause may be intended to exclude cases of hazard through ingestion of a substance. Any statutory hazard selection for determining whether first-aid instructions should be on the label is inconsistent with the purposes of the bill. Likewise, when such instructions could be helpful, they should not be dispensed with on the theory that they are not "necessary." The clause should therefore be amended to read in its entirety, simply: "instructions, when necessary or appropriate, for first-aid treatment;".

4. Prohibited acts

(*a*) Section 9 of the bill makes unlawful the failure to afford access to, and permission to copy, certain records to the Department's officers. Such failure should also be listed as a prohibited act in section 3.

(*b*) The manufacture, within any territory, of a misbranded package of a hazardous substance should, we believe, be made a prohibited act, as proposed in S. 1900, 85th Congress.

(*c*) Paragraph (f) of the list of prohibited acts (p. 9, lines 9–12), relating to use of a food, drug, or cosmetic container as a container for a hazardous substance, should be rephrased to read substantially as follows:

"(f) The introduction or delivery for introduction into interstate commerce, or the receipt in interstate commerce and subsequent delivery or proffered delivery for pay or otherwise, of a hazardous substance in a reused food, drug, or cosmetic container or in a container which, through not a reused container, is identifiable as a food, drug, or cosmetic container by its labeling or by its characteristic shape, impression, or closure. The reuse of a food, drug, or cosmetic container as a container for a hazardous substance shall be deemed to be an act which results in the hazardous substance's being in a misbranded package. As used in this paragraph, the terms 'food,' 'drug,' and 'cosmetic' shall have the same meanings as in the Federal Food, Drug, and Cosmetic Act."

(*d*) Insert, as a prohibited act, a provision prohibiting unauthorized disclosure of trade secrets obtained under the act, along the lines of section 301(j) of the Federal Food, Drug, and Cosmetic Act.

5. "Label"

In the definition of "label" (p. 5), strike out "or attached to" in line 2 and "package or" in line 3, thus bringing the definition into correspondence with the corresponding definition in the Federal Food, Drug, and Cosmetic Act.

6. Flammability

In order to carry out the recommendations of the Secretary concerning the definitions of "flammable" and "extremely flammable," it is suggested that section 2(1) of the bill be revised to read as follows:

"(1) The term 'extremely flammable' shall apply to any substance which has a flash point at or below twenty degrees Fahrenheit as determined by the Tagliabue open cup tester, and the term 'flammable' shall apply to any substance which has a flash point of above twenty degrees to and including eighty degrees Fahrenheit, as determined by the Tagliabue open cup tester; except that the flammability of solids,

and of the contents of self-pressurized containers shall be determined by methods found by the Secretary to be generally applicable to such materials or containers, respectively, and established by regulations issued by him, which regulations shall also define the terms 'flammable' and 'extremely flammable' in accord with such methods."

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,

February 24, 1960.

HON. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate, Washington, D.C.

DEAR MR. CHAIRMAN: As you know, there is pending before your committee a bill (S. 1283) to regulate the interstate distribution and sale of hazardous substances intended or suitable for household use. As you will recall, I have reported favorably on this legislation and have recommended its passage with certain modifications which I believe are necessary in order to accomplish the full objectives of the bill. A subcommittee of your committee has held a hearing on the bill.

The reason for writing you at this time is to reaffirm the Department's interest in this legislation and to request that every effort be made to complete action on it at this session of the Congress. The Department will cooperate in this effort in every way possible.

There is wide agreement that present legislation in this field—the Federal Caustic Poison Act of 1927—has been greatly outmoded by the rapid increase in the number of chemical compounds available for household use. The 1927 act has helped to save many lives, but it is not applicable to many poisons and other hazardous substances and devices that are being used in homes today in ever increasing numbers. In fact, the chemical age has developed very largely since this problem of labeling was last dealt with by the Congress more than 30 years ago.

The proposed legislation would supersede the Federal Caustic Poison Act. It would require appropriate labeling on packages of toxic, corrosive, flammable, and other hazardous substances which are intended for or are suitable for household use.

A number of ordinary household materials, when swallowed, are poisonous and can cause death. Frequently—and often because parents are not aware of their danger—they are placed within easy reach of small children. These include paint and paint thinners and removers, cleaning agents, furniture waxes, and polishes, bleaches, detergents, lighter fluids, and, of course, drugs, and sometimes cosmetics. The very color and design of attractive modern packaging can offer a special attraction to small children and make the harmful substances the packages contain interesting—and often fatal—subjects for childish investigation.

The need for legislation requiring proper labeling of these materials is amply demonstrated. Behind the infant mortality statistics are many instances of accidental poisonings which could have been avoided

had the parents been properly warned and had information for proper emergency treatment been readily available.

For example, there is no Federal legislation requiring that furniture polish containing a petroleum product be labeled as hazardous if swallowed. I cite this because such a product was involved in a near-fatal poisoning of a 1-year-old child in a case that came to the attention of the Public Health Service's National Clearinghouse for Poison Control Centers. When the child's mother saw the child swallowing the polish, she innocently undertook a simple home treatment which is effective in many instances but in this case was exactly wrong and nearly caused the child's death.

As in the case of furniture polish, there is no Federal labeling requirement that household drycleaning preparations be labeled as poisonous, although many of these preparations contain carbon tetrachloride, a potent liver poison that has caused serious injury and death when used without adequate ventilation.

Such an accident happened in February 1959 when a 3½-year-old child was seriously injured from inhaling carbon tetrachloride while his mother was cleaning a rug.

Even when accidental injury occurs in a community that is ideally equipped to handle such cases, the present resources are not always adequate. When a 2-year-old child swallowed a dishwasher detergent, the head of the city's poison control center was called almost immediately. Moreover, he found the product listed in his poison reference guidebook.

However, although the guidebook contained information on the identity of the harmful ingredient, the physician needed more information about treatment than he could obtain from the text. Probably the child's life was saved only because the doctor knew about the PHS Clearinghouse and because the Clearinghouse was able to phone more recent information to him.

While I am well aware that precautionary labeling will not of itself prevent all accidental poisonings and other tragedies in the home resulting from the improper use of household chemicals and other hazardous substances, nevertheless such a step would constitute an important contribution toward that goal. I am sure that when, through proper labeling, parents are alerted to the danger to their children they will be much more likely to take precautions to keep harmful substances beyond their children's reach. And in cases when children do swallow the substances, the treatment or antidote, when first-aid treatment is appropriate, would be right there on the label so that immediate and effective action may be taken.

This is a major problem. The Public Health Service estimates that every year 600,000 children swallow household aids left within their reach, and that about 500 children die each year as a result of such accidents.

I hope that your committee will be able to take favorable action on the pending legislation at an early date.

Sincerely yours,

ARTHUR S. FLEMMING, *Secretary.*

DEPARTMENT OF THE INTERIOR,
OFFICE OF THE SECRETARY,
Washington, D.C., March 17, 1959.

Hon. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate, Washington, D.C.

DEAR SENATOR MAGNUSON: This is in response to your request for a report on S. 1283, a bill to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use.

The bill does not appear to relate to any matter within the jurisdiction of this Department or to affect any matter upon which the Department would be in a position to give helpful information or advice. Accordingly, this Department has no comment to offer with respect to the merit of the purpose or provisions of the bill.

We greatly appreciate your bringing this matter to our attention, and welcome the opportunity to submit recommendations on any measure where the activities of the Department may possibly be involved, or where its experience may possibly be of value.

Sincerely yours,

D. OTIS BEASLEY,
Administrative Assistant, Secretary of the Interior.

AUGUST 10, 1959.

Hon. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate, Washington, D.C.

DEAR CHAIRMAN MAGNUSON: Your letter of March 9, 1959, addressed to the Chairman of the Commission, and requesting comments on a bill S. 1283, introduced by you for yourself and Senator Bush, to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use, has been referred to our committee on legislation. After consideration by that committee, I am authorized to submit the following comments in its behalf.

The proposed legislation would be known as the Federal Hazardous Substance Labeling Act, and would be administered by the Secretary of the Department of Health, Education, and Welfare. The Federal Caustic Poison Act would be repealed 6 months after the date of the bill's enactment into law.

Section 14 of the bill states that nothing contained in the proposed legislation would be construed to modify or affect the provisions of certain existing legislation, including chapter 39, title 18 of the United States Code (18 U.S.C. 831 et seq.) under which this Commission has the duty of formulating regulations for the safe transportation within the limits of the jurisdiction of the United States of explosives and other dangerous articles, including flammable liquids, flammable solids, oxidizing materials, corrosive liquids, compressed gases, and poisonous substances, by common carriers engaged in the transportation of these commodities in interstate or foreign commerce by land. Shippers of such commodities moving by land or water in interstate or foreign commerce are also bound by these regulations.

At the outset we wish to point out that contract carriers, and private carriers of property, by motor vhicle, are not covered under the statutes cited. Nevertheless these classes of carriers are regulated in a similar manner under sections 204(a)(2) and 204(a)(3) of the Interstate Commerce Act. For purposes of consistency section 14 of the proposal should be amended accordingly. We suggest the following language in lieu of that presently used at lines 18, 19, and 20 of page 19 of the bill immediately following the word "Code" at line 18 and preceding the word "or" at line 20 for your consideration:

"* * * as amended, or any regulations promulgated thereunder, or under sections 204(a)(2) and 204(a)(3) of the Interstate Commerce Act, as amended (49 Stat. 546; 54 Stat. 922; 49 U.S.C. 304(a)(2), 304(a)(3)), relating to the transportation of explosives and other dangerous articles; * * *.

The bill defines a number of key terms, including "hazardous substance," and "misbranded package." Under section 3 of the proposal the following acts would be prohibited: (*a*) introduction or delivery for introduction into interstate commerce of any misbranded package of a hazardous substance; (*b*) tampering with the label of such a substance in a manner which would result in a misbranded package, while it is in interstate commerce or held for sale after shipment in interstate commerce; (*c*) receipt of any such misbranded package of a hazardous substance and the delivery or proffered delivery thereof for pay or otherwise; (*d*) knowingly giving of a false guarantee or undertaking obtained from the person from whom the hazardous substance was received, to the effect that the substance is not in misbranded packages; (*e*) refusing to permit entry or inspection of any place where hazardous substances are held for introduction into interstate commerce or are held after such introduction, or of any vehicle being used to transport or hold such hazardous substances in interstate commerce, or refusing to permit inspection and sampling, in accordance with the terms of the proposal, of finished hazardous substances in retail packages and labeling thereon in such place or vehicle, by authorized persons; and (*f*) reuse of food, drug, or cosmetic containers still bearing original lables or identifiable as such by characteristic shape, impression, or closures as containers for hazardous substances.

Penalties would be provided in the form of fines and/or imprisonment for violations of the proposed measure. The receipt delivery, or proffered delivery of a hazardous substance mentioned in (*c*) above, if in good faith, would not be a violation of the proposal unless the person so receiving, delivering, or proffering for delivery refused to furnish certain information regarding its origin. As to (*a*) above it would be a defense to establish a guarantee or undertaking signed by, and containing the name and address of, the person residing in the United States from whom the hazardous substance was received in good faith, to the effect that such substance is not in misbranded packages. Nor would it be a violation of (*a*) and (*c*) above where there is involved any hazardous substance shipped, or delivered for shipment for export, to any foreign country, in a package marked for export and branded in accordance with the specifications of the foreign purchaser and the laws of the foreign country.

Section 3(e) of the bill probably should be modified to allow for shipments which, for reasons of security, may not be open to the inspection contemplated by the proposal.

Section 5 of the bill, among other provisions, would permit the bringing of a libel proceeding against any hazardous substance in a misbranded package while it is in interstate commerce, its seizure, and the condemnation thereof in the district court of the United States having jurisdiction of the matter.

Under section 5(a) of the bill shipments of hazardous substances destined for export to foreign countries would not be subject to the proposed legislation so long as the comparable regulations of the foreign country concerned are complied with. If that country did not have any such requirements an unmarked shipment would apparently be legal, but the hazard to carrier employees and others coming in contact with the shipment would be the same.

Section 8 of the proposed measure provides, among other things, that officers or employees designated by the Secretary of the Department of Health, Education, and Welfare, upon proper identification and written notice, would be authorized (1) to enter, at reasonable times, any place where hazardous substances are held for, or after introduction into, interstate commerce, or to enter any vehicle being used to transport or hold such substances in interstate commerce; and (2) to inspect and sample, at reasonable times, and within reasonable limits and manner, finished hazardous substances in retail packages and the labeling thereon in any such place or vehicle. A separate notice would be necessary for each inspection, but a notice would not be required for each entry made during the period covered by the inspection.

The examination, inspection, and investigation procedures which would be authorized by this section of the bill are, in our opinion, broader than necessary to accomplish the purposes of the proposal. Specifically, the inspection of vehicles while holding or transporting hazardous substances would appear to impede and delay unnecessarily the operations of the affected carrier, in view of the provision made for inspection in places other than the vehicles. It will be noted that the Federal Caustic Poison Act exempts from its provisions common carriers operating in the ordinary course of business.

Under section 9 of the bill interstate carriers and certain other persons would be obliged to permit authorized inspectors to have access to and copy all records showing the movement in interstate commerce of any hazardous substance, or the holding thereof during or after such movement, and the quantity, shipper, and consignee involved. When a request by an inspector is accompanied by a written statement specifying the nature or kind of such hazardous substance, it would be unlawful for any carrier or person to fail to permit access to or the copying of the record in question. This section contains a proviso that evidence obtained thereunder shall not be used in a criminal prosecution of the person from whom it is obtained.

This Commission's representatives have authority to inspect and copy any and all accounts, books, records, memorandums, correspondence, and other documents of carriers subject to its jurisdiction (secs. 20(5), 220(d), 313(f), and 412(d) of the Interstate Commerce Act). However, in each instance an accompanying provision prohibits such representatives from knowingly and willfully divulging, except under certain conditions, any fact or information which may come to their knowledge during the course of any such examination or inspection (secs. 20(7)(f), 222(d), 317(c), and 421(c) of the act).

We believe similar protection against unauthorized disclosures should be incorporated in the proposal if it is enacted into law.

The bill appears to have as its primary purpose the protection of household consumers of hazardous substances in retail-size packages and containers. If this is true, it seems that more definitive terms should be used in order to clarify any areas of doubt which might otherwise obtain.

The Federal Caustic Poison Act (44 Stat. 1406 et seq.; 15 U.S.C. 401 et seq.), which would be repealed by the proposed law, makes clear in its definition of the term "misbranded parcel, package, or container" that it refers to retail parcels, packages, or containers. Section 8(b)(2) of the bill refers to retail packages, but other sections of the bill, notably section 2(2)(o) defining the term "misbranded package," appear susceptible of a broader construction.

In the event the bill is meant to apply not only to retail packages and containers but to the outer or shipping container, then it appears that considerable confusion might result from (1) the addition of the proposed legislation to this Commission's regulations, and (2) variances in definitions and coverage. For example:

1. The definition of the term "toxic" (sec. 2(g) of the bill) is rather broad. This Commission's regulations (49 CFR 73.325) use the term "poisonous articles" and divide them into four classes according to degree of hazard in transportation, i.e., (1) extremely dangerous poison, (2) less dangerous poison, (3) tear gases or irritating substances, and (4) radioactive materials.

2. The definition of the term "highly toxic" (sec. 2(h)(1) of the bill) follows the wording and description of "less dangerous poisons" as defined in this Commission's regulations (49 CFR 73.343), except that the fatality rate for the same number of rats is 48 hours in the bill rather than 14 days as specified in our regulation. Radioactive materials would not appear to be covered by the bill.

3. The definition of the term "corrosive" (sec. 2(h)(2) of the bill) appears to be unnecessarily broader than the definition of the term in the Commission's regulations (49 CFR 73.240).

4. The Commission's regulations do not extend to "irritants" and "strong sensitizers" as those terms are used in sections 2(j) and 2(k) of the bill.

5. The definitions of the terms "extremely flammable" and "flammable" (sec. 2(l) of the bill), as well as being applicable to liquids, appear to embrace materials in other than a liquid state, particularly gases. The Commission's regulations at 49 CFR 73.115 and 73.119 cover flammable liquids and gases of many types and under a variety of conditions.

Section 2(m) of the bill is concerned principally with the labeling of the immediate package or container of the substance involved. In the event there is an outside container or wrapper, the required information must appear thereon, unless it is easily legible through the outside container or wrapper. Any accompanying literature containing directions for use must also contain the required information.

While this language logically appears to be referring to packages or containers of a size suitable for household use, it is also capable of being construed broadly, perhaps to apply to outside shipping containers. Any such construction would lead to confusion and some duplication of effort, especially since the size or type of labels to be used is not

specified. Labels required under this Commission's regulations are of designated sizes, colors, and wording. (See 49 CFR 73.403 through 73.411.) It should also be noted that section 73.404(c) prohibits the use of labels which by their size, shape, and color may be readily confused with standard Commission labels. The chemical industry now applies additional warning labels to packages of many dangerous materials, and the Federal Insecticide, Fungicide, and Rodenticide Act imposes a label requirement upon shipments of so-called economic poisons.

The importance of clarifying the proposal with respect to the type of package or container envisioned is further pointed up by the fact that the term "immediate package or container" could be construed to apply to such immediate containers as tank cars, cargo tanks, portable tanks, drums, carboys, and so forth. Box cars, tank cars, motor vehicles, and tank trucks are now required under this Commission's regulations to be either placarded or marked when they are used for transporting dangerous substances in interstate or foreign commerce. The application of a small label to such vehicles should, if it will serve a useful purpose, be done in some specific manner and at specific locations, since a small label might go unnoticed or be placed where it would provide little warning to those who might come in contact with the lading.

It should be borne in mind that this Commission's regulations in this respect (49 CFR 71–90) have been adopted by the Canadian authorities, several individual States in connection with interstate transportation, the U.S. Coast Guard, and the Federal Aviation Agency. If the proposal is enacted into law, shippers and carriers would be forced to compare its provisions with the regulations of this Commission so as to determine where our regulations end and those promulgated under the new law begins. This would appear to unduly complicate their operations.

For the reasons shown we do not favor enactment of the proposed legislation in its present form.

Respectfully submitted.

COMMITTEE ON LEGISLATION,
KENNETH H. TUGGLE, *Chairman.*
ANTHONY ARPAIA.
HOWARD FREAS.

INTERSTATE COMMERCE COMMISSION,
OFFICE OF THE CHAIRMAN,
Washington, D.C., January 13, 1960.

HON. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate, Washington, D.C.

DEAR CHAIRMAN MAGNUSON: Your letter of January 6, 1960, addressed to the Chairman of the Commission, and requesting comments on certain amendments proposed by the chemical industry to S. 1283, a bill to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use, has been referred to our Committee on Legislation. After consider-

ation by that Committee, I am authorized to submit the following comments in its behalf:

The amendments proposed by the chemical industry, as set forth in the enclosure transmitted with your letter, are designed to meet the objections set forth in our report of August 10, 1959, on S. 1283. These proposed amendments appear to correct the deficiencies which we felt existed in this measure, as introduced, with one exception. As stated on page 7 of our August 10 report, representatives of this Commission have authority to inspect and copy any and all accounts, books, records, memorandums, correspondence, and other documents of carriers subject to its jurisdiction (secs. 20(5), 220(d), 313(f), and 412(d) of the Interstate Commerce Act). Such representatives are prohibited, however, from knowingly and willfully divulging, except under certain conditions, any fact or information which may come to their knowledge during the course of any such examination or inspection. We are still of the view that similar protection against unauthorized disclosures which could result from authority granted under section 9 of S. 1283 should be incorporated in the bill before it is enacted into law. We suggest that section 222(d) of the Interstate Commerce Act might be used as a guide to the accomplishment of this purpose.

If an amendment along the lines suggested with reference to section 222(d) is added to those proposed by the chemical industry we would have no objection to the enactment of S. 1283.

Respectfully submitted.

COMMITTEE ON LEGISLATION,
JOHN H. WINCHELL, *Chairman.*
HOWARD FREAS.
EVERETT HUTCHINSON.

PANAMA CANAL COMPANY,
Washington, D.C., August 11, 1959.

Hon. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate.

DEAR SENATOR MAGNUSON: This is in response to your request for comments of this agency on S. 1283, a bill to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use.

Section 2(a) of the bill defines the term "territory" as used in the bill as any territory or possession of the United States, including the District of Columbia and Puerto Rico, "but excluding the Canal Zone." This section renders the provisions of the bill inapplicable to the Canal Zone and inasmuch as no substances of the type covered by the bill are manufactured there, no reason appears for requesting amendment of the bill to make it applicable in the Canal Zone.

The Bureau of the Budget has advised that it has no objection to the submission of this report to your committee.

Sincerely,

MERRILL WHITMAN, *Secretary.*

69002°— 60 S. Rept., 86-2, vol. 2——6

OFFICE OF THE POSTMASTER GENERAL,
Washington, D.C., August 11, 1959.

Hon. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate, Washington, D.C.

DEAR MR. CHAIRMAN: Reference is made to your request for a report on S. 1283, a bill to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use.

This measure, among other things, proposes to prohibit the introduction or delivery for introduction into interstate commerce of any misbranded package of a hazardous substance. It would also provide penalties for violations.

Section 14 of the bill among other things, provides that the measure would not affect the present law (18 U.S.C. 1716) or any regulations promulgated thereunder (relating to mailing of dangerous substances).

Since section 1715 of title 18 relates exclusively to concealable firearms rather than hazardous material it is believed that the reference to 1715 in line 20, page 19 of the bill, should be deleted.

This Department has no other comments or recommendations to submit as to the enactment of S. 1283.

The Bureau of the Budget has advised that there is no objection to the submission of this report to the committee.

Sincerely yours,

E. O. SESSIONS,
Deputy Postmaster General.

STATE DEPARTMENT,
August 12, 1959.

Hon. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce, U. S. Senate.

DEAR SENATOR MAGNUSON: In your letter of March 9, 1959, acknowledged on March 11, 1959, you requested the views of the Department of State on S. 1283, a bill to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use.

The purpose of this legislation is apparently to protect human life and health by bringing obsolete legislation on hazardous substances up to date. The Department of State has studied it from the viewpoint of foreign policy implications and has no objection to its enactment. The proposed legislation does not discriminate between foreign and domestically produced products, nor is it in conflict with our international obligations.

The Department has no comment on the standards defined in the bill which pertain to hazardous substances, as this is the concern of other agencies.

The Department also has no comment on the administration of the import provisions of the bill, which is primarily the concern of the

Department of Health, Education, and Welfare, and the Department of the Treasury.

The Department has been informed by the Bureau of the Budget that there is no objection to the submission of this report.

Sincerely yours,

WILLIAM B. MACOMBER, Jr.,
Assistant Secretary
(For the Acting Secretary of State).

OFFICE OF THE SECRETARY OF THE TREASURY,
Washington, August 12, 1959.

Hon. WARREN G. MAGNUSON,
Chairman, Committee on Interstate and Foreign Commerce,
U.S. Senate, Washington, D.C.

MY DEAR MR. CHAIRMAN: Reference is made to your letter of March 9, 1959, requesting the views of this Department on S. 1283 to regulate the interstate distribution and sale of packages of hazardous substances intended or suitable for household use.

The proposed legislation would prohibit the introduction into interstate commerce of any misbranded package of a hazardous article which includes articles that are toxic, corrosive, flammable, and the like and would vest primary enforcement authority in the Secretary of Health, Education, and Welfare. It would authorize the issuance of joint regulations relating to imports of such articles by the Secretary of the Treasury and the Secretary of Health, Education, and Welfare.

Since the administration of the proposed bill will, if enacted into law, be vested primarily in the Department of Health, Education, and Welfare, the Treasury Department does not wish to make any recommendation on its merits. In the event the bill is enacted into law, additional work will be required of certain Bureau of Customs employees. However, a survey has not been made to ascertain the probable amount of such work.

The Department has been advised by the Bureau of the Budget that there is no objection to the submission of this report to your committee.

Very truly yours,

A. GILMORE FLUES,
Acting Secretary of the Treasury.

10. CHANGES IN EXISTING LAW

In compliance with subsection (4) of rule XXIX of the Standing Rules of the Senate, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets):

CHAPTER 11. CAUSTIC POISONS (15 USC 401 ET. SEQ.)

[SEC. 401. Citation.
[This chapter may be cited as the "Federal Caustic Poison Act." Mar. 4, 1927, ch. 489, sec. 1, 44 Stat. 1406.]
[SEC. 402. Definitions. * * *]
[SEC. 403. Prohibition against misbranded shipments. * * *]
[SEC. 404. Libel for condemnation proceedings. * * *]
[SEC. 405. Exclusion of misbranded imports. * * *]
[SEC. 406. Removal of labels. * * *]
[SEC. 407. Penalties. * * *]
[SEC. 408. Institution of libel for condemnation and criminal proceedings. * * *]
[SEC. 409. Enforcement of chapter. * * *]
[SEC. 410. Separability clause. * * *]
[SEC. 411. Application to existing law. * * *]

With respect to the time of repeal of the Federal Caustic Poison Act of 1927, section 18 of S. 1283 is important, and accordingly is reprinted below:

REPEAL OF FEDERAL CAUSTIC POISON ACT

SEC. 18. The Federal Caustic Poison Act (44 Stat. 1406) is repealed effective at the close of the sixth calendar month after the month of enactment of this Act. Provided, That, if the Secretary, pursuant to section 16(5) of this Act, prescribes an additional period or periods during which violations of this Act shall not be enforceable and if such additional period or periods are applicable to violations of this Act involving one or more substances defined as "dangerous caustic or corrosive substances" by the Federal Caustic Poison Act, that Act shall, with respect to such substance or substances, remains in full force and effect during such additional period or periods: Provided further, That, with respect to violations, liabilities incurred or appeals taken prior to the close of said sixth month or, if applicable, prior to the expiration of the additional period or periods referred to in the preceding proviso, all provisions of the Federal Caustic Poison Act shall be deemed to remain in full force for the purpose of sustaining any proper suit, action, or other proceeding with respect to any such violations, liabilities, and appeals.

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Clinical and Experimental Allergy, 1999, Volume 29, pages 1572–1578

The prevalence of immunoglobulin E antibodies to the proteins of rubber (*Hevea brasiliensis*) latex and grass (*Phleum pratense*) pollen in sera of British blood donors

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Summary

Background Although there have been many studies of the prevalence of latex allergy in populations deemed to be at risk, little is known of the potential allergic susceptibility to latex products prevailing in the general population.

Objective To assess the possible prevalence of allergy to latex goods in a population of blood donors by measurement of specific antilatex immunoglobulin (Ig) E in blood, to relate this to prevalence of antigrass IgE in the blood donations, and to assess the prevalence of antibodies to grass, house dust mite and cat allergens in those donors having antilatex IgE antibodies.

Methods Sera from two groups of donations obtained in the English West Midlands were assayed. A group of 2000 donations obtained in midwinter was assayed for antilatex and antigrass pollen IgE. A group of 5000 midsummer donations was assayed for total IgE, and antilatex IgE and the sera giving a positive reaction, assayed for antigrass pollen, antihouse dust mite and anticat IgE. The nature of the principal latex and grass pollen polypepudes reacting with IgE in the sera was assessed by immunoblotting.

Results Anti-latex IgE was detected in approximately 4% of the winter and 7% of the summer donations. The prevalence of antigrass IgE in the winter donations was approximately 20% and amongst the latex-positive sera approximately 84% contained antigrass IgE. Of the summer donations of latex-positive sera, 96% contained antigrass, 48.6% antimite IgE and 34% anticat IgE. The prevalence of both antilatex and antigrass IgE was age and sex related. Inhibition studies indicated cross-reactivity of IgE with latex and grass pollen proteins.

Conclusions Whilst 4–7% of the population may have serum IgE reacting with latex, the levels are low compared with those reacting with the aeroallergens studied. The apparent cross-reactivity of some serum IgE with both latex and grass pollen taken with other evidence suggests that, in some individuals, allergy to latex may arise from an initial sensitization by grass pollen.

Keywords: blood donors, cat, English West Midlands, grass pollen, house dust mite, latex allergy, serum IgE

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Introduction

Although type I allergy to natural rubber latex goods has been recognized relatively recently [1], a considerable literature describing the prevalence of the sensitivity amongst workers exposed to latex articles during their occupations has emerged [2,3]. From both a public health and a commercial viewpoint it would be useful to have an assessment of the proportion of the general population that might be at risk. An objective and reliable procedure is difficult to set in motion. Questionnaires are somewhat unreliable, skin prick testing of a sample of the general

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population is not very feasible, the correlation of specific immunoglobulin (Ig) E assays of blood serum with a type I allergy is not absolute and a completely random selection of the population is difficult to achieve. With these caveats in mind the simplest procedure for obtaining an approximate picture of the situation is to assay for antilatex IgE in a large number of blood donations. A preliminary series of assays of 1436 British blood donations indicated an overall prevalence of 7.9% containing antilatex IgE [4]. Similar results have been reported by Ownby *et al.* [5,6] who found a prevalence of 6.4% in 1000 donations from the southeast Michigan region of USA. In view of the relatively few reports of the condition in the UK subsequent to the original description [1], it seemed desirable to extend our earlier work with a view to establishing the groups, in respect of age and sex, most likely to be at risk. Furthermore it was thought useful to carry out a simultaneous series of assays of IgE antibodies to allergens to which the sensitivity of the general population was well documented. The donations were therefore assayed for IgE specific for both natural rubber *Hevea brasiliensis* latex and timothy grass *Phleum pratense* pollen antigens and an attempt was made to characterize the antigens with which IgE most frequently reacted.

Materials and methods

Blood donations

The remains of blood test samples of 2035 donations taken by the W. Midlands Centre of the UK National Blood Service during the winter (January) and 5007 similar samples taken during the summer (July and August) were centrifuged and the serum stored at −20° prior to assay for IgE. The midwinter donations were all tested for antilatex and antigrass IgE, all the summer donations were tested for antilatex IgE and the positive sera were tested for antigrass, antihouse dust mite and antical IgE, a sample of the latex-negative sera from the summer donations was also tested for antigrass IgE. The total IgE of all the summer donations was measured.

IgE assay

The allergen-specific IgE of the serum samples was measured by the AlaSTAT® Microplate Immunoassay (Diagnostic Products Corp., Los Angeles, CA, USA) as recommended by the manufacturer [7]. This assay, which was, at the time, the only procedure for the assay of latex-specific serum IgE, approved by the US Food and Drugs Administration [8], is a fluid phase determination in which allergens, covalently linked to a biotinylated water soluble polymer, bind to serum antibodies. On the addition of streptavidin which binds to the biotin groups, the biotinylated antigen–antibody complex becomes attached to biotinylated serum albumen coating the walls of a microtitre plate. The bound IgE is estimated colourimetrically after the further addition of enzyme-labelled IgE. The results, calibrated against values obtained for total serum IgE, are scored in classes 0–VI where the class number is a semiquantitative index of the amount of allergen-specific IgE, class 0 being 0–0.34, class I 0.35–1.49, class II 1.5–2.99, class III 3.0–14.9, class IV 15–49.9, class V 50–100, class VI > 100 IU/mL (1 IU = 2.4 ng IgE).

Inhibition of the assay for latex-specific IgE by timothy grass pollen extract (Allergon, Vällinge, Sweden) was estimated by pre-incubating duplicate identical samples of serum, each with 10 μL grass pollen extract (containing, respectively, 10 and 100 μg pollen protein in phosphate-buffered saline) for 30 min prior to assay for latex-specific IgE as above. Comparison with the uninhibited specific IgE assay, containing 10 μL phosphate-buffered saline as control, gave the degree of inhibition. The number of samples of an individual serum assayed for grass inhibition was restricted by the volume available.

Polypeptide binding

Proteins of fresh latex and grass pollen were separated by SDS polyacrylamide gel electrophoresis (SDS-PAGE) according to Laemmli [9] and were electroblotted on to nitrocellulose membranes by the procedure of Towbin *et al.* [10]. After blocking with 5% reconstituted low fat milk, the membranes were incubated overnight with the AlaSTAT-positive donor sera diluted 1 : 5 with TRIS-buffered saline (pH 7.4). IgE binding was detected by incubation with biotin-labelled mouse antihuman IgE followed by avidin-labelled alkaline phosphatase. Incubation with the substrate 5-bromo 4-chloro 3-indolylphosphate revealed the zones of IgE binding.

Results

Antilatex and antigrass IgE in winter donations

Table 1 shows the concentrations of antilatex and antigrass-specific IgE found in the sera from a group of 2035 blood donations obtained in the winter sorted according to donor age and sex. Although the overall prevalence in the entire group containing antilatex IgE was 4%, the prevalence in the different age groups differed considerably from this value, that in sera from males aged 30–34 being the greatest at 8.2%. As expected, the overall prevalence of detectable antigrass-specific IgE in the group was much higher at 19.5%. Again there was considerable variation between the sex and age groups, the highest value, 36.5% prevailing in the 20–24-year-old male cohort, sera from young women

Table 1. Latex- and grass-specific IgE levels in winter blood donations

Age group	Donors (n) (F/M)	Antilatex IgE % +ve sera						Antigrass IgE % +ve sera					
		All classes			>class I			All classes			>class I		
		F	M	Total	F	M	Total	F	M	Total	F	M	Total
18–9	17/13	5.9	7.7	6.6	5.8	7.6	6.6	23.5	30.8	26.6	23.5	23.1	23.3
20–4	78/63	2.6	6.3	4.2	2.5	4.8	3.5	26.9	36.5	31.2	24.3	34.9	29 1
25–9	73/114	4.1	7.0	4.8	1.3	5.2	3.7	23.3	30.7	27.8	17.8	28.0	24 1
30–4	86/147	4.7	8.2	6.8	3.4	6.1	5.1	24.4	28.6	27.0	23.3	25.2	24 0
35–9	122/175	4.9	6.3	5.7	2.4	0.6	1.3	19.7	24.0	22.2	16.3	21.7	17.6
40–4	137/192	2.2	4.2	1.3	0.7	1.5	1.2	16.8	22.4	20.1	13.8	20.8	17.9
45–9	146/209	2.7	1.4	2.0	0.7	1.0	0.8	8.9	14.4	12.1	8.9	12.4	10.9
50–4	91/137	1.1	2.9	1.8	1.1	2.2	1.8	7.7	19.0	14.5	6.6	17.5	13 2
55–9	55/83	3.6	3.6	3.6	3.6	2.4	2.9	12.7	10.8	11.5	10.9	10.8	10 9
60+	44/53	2.3	0.0	1.0	2.2	0.0	1.0	11.4	5.7	8.2	9.1	5.6	7 2
Total	849/1186	3.2	4.6	4.0	1.8	2.5	2.3	16.7	21.7	19.6	14.6	19.7	17 5

also showed a high prevalence reaching 26.9% in the 20–24-year-old age group. The overall prevalence of antilatex IgE-positive sera was 4.6% in donations from males and 3.3% in those from females.

Of the sera in these winter donations containing antilatex IgE, 84% also contained antigrass-specific IgE. Only 19.9% of those sera containing antigrass IgE also contained antilatex IgE. In Table 2, the results obtained with sera containing both antilatex and antigrass IgE have been sorted according to the classes into which the concentrations of each antibody fell. It is seen that all of the sera containing antilatex IgE at the class III level also contained antigrass IgE, and 71.4% of those containing this activity at the class I level also contained some antigrass IgE. High levels of antigrass IgE were associated with the higher prevalence of antilatex IgE, thus 35.7% of the sera having antigrass IgE at the class VI level contained antilatex IgE but only 16.7% of those reacting to grass pollen at the class I level had detectable antilatex activity.

Relation of antilatex IgE to anti-aeroallergen IgE in summer donations

In view of the high prevalence of antigrass IgE in the winter blood donations containing antilatex IgE, antigrass IgE was assayed in those members of a series of summer donations found to contain antilatex IgE; these donations were also assayed for two other common aeroallergens, house dust mite (*Dermatophagoides pteronyssinus*) and cat (*Felis domesticus*).

Table 3 shows the distribution of antilatex IgE-positive sera amongst the 5007 summer donations, sorted according to age and sex. The overall prevalence of IgE-positive sera was 7.3% and again the prevalence in donations from

Table 2. Relation between antilatex and antigrass IgE levels in winter blood donations

Antilatex IgE classes	Total sera	Numbers of sera Antigrass IgE classes							% grass +ve
		0	I	II	III	IV	V	VI	
0	1954	1615	35	103	111	38	16	36	17.3
I	35	10	5	3	3	6	3	5	71.4
II	40	3	2	15	2	3	1	14	92.5
III	6	0	0	2	2	1	0	1	100.0

Table 3. Total and specific IgE levels in summer blood donations

	Donors (n)			Total IgE*			% latex + ve sera in age groups: All classes			% latex + ve sera in age groups: > class I		
Age	M	F	Total	M	F	All	M	F	Total	M	F	Total
18–9	31	27	58	53.0	30.8	40.9	9.7	7.4	8.6	6.5	3.7	5.2
20–4	178	219	397	62.0	30.2	42.0	13.5	11	12.1	7.9	7.3	7.6
25–9	305	244	549	41.0	34.4	37.9	14.1	10.7	12.6	7.5	7.8	7.7
30–4	387	286	673	50.0	23.1	41.5	13.4	9.8	11.9	8.3	8.0	8.2
35–9	427	294	721	44.0	32.4	39.0	8.9	5.8	7.6	5.6	3.4	4.7
40–4	406	312	718	40.0	28.4	34.6	7.9	4.8	6.5	4.7	2.6	3.8
45–9	459	369	828	36.0	26.0	31.2	5.4	2.2	4.0	3.3	1.1	2.3
50–4	314	213	527	38.0	23.0	31.5	3.8	1.4	2.8	1.6	0.5	1.1
55–9	198	132	330	38.0	26.5	32.9	2.0	3.8	2.7	1.0	2.3	1.5
60+	142	64	206	40.0	31.0	36.6	3.5	3.1	3.4	3.5	0.0	2.4
Total	2847	2160	5007	42.2	29.5	36.2	8.4	6.0	7.3	5.0	3.9	4.5

*Total IgE expressed as geometric mean of kU/gE/L for both latex-positive and -negative sera.

males (8.4%) was higher than that in those from females (6.0%).

The results of testing 350 of the 368 antilatex IgE-positive sera for antigrass, antimite and anticat IgE are shown in Table 4. Whilst 96% of the sera contained antigrass IgE, 48.6% contained antimite IgE and only 34% contained anticat IgE. Twenty-four of the 25 sera containing antilatex IgE at the class III level also contained antigrass IgE but only 16 of the group also had antimite IgE and 14 had anticat IgE. Overall 28% of the latex-positive sera reacted with all three aeroallergens.

When 380 of the summer donations not testing positive for antilatex IgE were assayed for antigrass IgE, 88 (23.2%) were positive. If it is assumed that 7.3% of all the donations had antilatex IgE then 380 represents the latex-negative portion of a total of 410 donations. When allowance was made for the observation that, in the summer donations, 96.4% of the latex-positive samples were also grass-positive, the total prevalence of antigrass IgE in a sample of 410 members of the summer group was calculated to be 28.5%.

Table 4. % latex-positive sera containing antigrass, mite and cat specific IgE

		% positive sera		
Antilatex IgE class	No. in class	Antigrass IgE	Antimite IgE	Anticat IgE
I	136	94.1	47.8	32.4
II	188	97.3	47.3	32.4
III	25	96.0	64.0	56.0
IV	1	100.0	0.0	0.0
Total	350	96.0	48.6	34.0

Relation of presence of allergen-specific IgE to total serum IgE levels in summer donations

The total serum IgE was measured in all the 5007 summer donations. The geometric mean was 36.2 kU/L, the value for males (42.2) being higher than that for females (29.5). From the age grouping shown in Table 3 it is seen that there is no clear correlation with age for total serum IgE. In addition to the 350 latex IgE-positive donations of Table 4, a further 348 latex IgE-negative donations were assayed for antigrass, antimite and anticat IgE. The sera were grouped according to the number of aeroallergens with which the IgE reacted. The geometric mean of the total IgE was found to be proportional to the number of allergens bound. Thus the geometric mean of the total IgE for 98 sera binding five allergens was 457.6, that for 101 sera binding three was 205.8, for 178 sera binding two was 109.2 and for 91 sera binding one was 41.8.

Age and sex relatedness of serum-specific IgE levels

It is clear from Tables 1 and 3 that the prevalence of serum-specific IgE is higher in the younger age groups. The highest prevalence of antigrass and antilatex IgE in the winter donations was found in the 20–4-year-old male and female cohort.

Application of the χ^2 test to the data in Tables 1 and 3 confirmed that the prevalence of serum-specific IgE antibodies to both grass and latex was age and sex related. Thus for the age relatedness of antilatex and antigrass IgE in the winter donations, the values were $P=0.1$ and 0.005, respectively; the summer donations gave a value of $P<0.001$ for antilatex IgE. For sex relatedness, the winter donations gave values of $P=0.3$ and $P=0.05$ for antilatex and antigrass IgE, respectively, and the summer donations gave a value of $P=0.01$ for antilatex IgE.

Latex and grass pollen polypeptide specificity of donor sera IgE in both series of donations

The approximate molecular weights of latex polypeptides reacting with the antilatex IgE of donor sera in 50 immunoblots are listed in Table 5. The most frequently bound polypeptides had molecular weights in the range 32 and 39 kDa with which 58 and 66% of the sera reacted, respectively, whilst 38% reacted with a polypeptide molecular weight 19 kDa. This latter polypeptide could be the latex allergen prohevein.

Table 5 also shows the molecular weights of grass pollen polypeptides giving positive immunoblots with 68 of the donor sera. The two principal antigens had molecular weights of 27 kDa (58.8% reacting) and 36 kDa (50.0% reacting), respectively, other significant antigens had molecular weights of 30 kDa (39.7% reacting) and 46 kDa (33.8% reacting).

Table 5. Reactions of donor sera IgE with latex and grass antigens

Latex polypeptides		Grass polypeptides	
M_W (kDa)	% sera reacting	M_W (kDa)	% sera reacting
97	2.0	80	8.8
83	2.0	75	4.4
70	4.0	70	10.2
66	6.0	58	7.3
59	44.0	54	14.7
48	54.0	46	33.8
42	8.0	40	10.2
39	66.0	36	50.0
36	14.0	30	39.7
32	58.0	27	58.8
30	54.0	24	29.4
27	18.0	20	29.4
24	8.0	15	16.1
21	4.0	12	20.5
19	38.0		
16	12.0		
14	34.0		

The results were obtained from immunoblots of 50 latex-positive sera and 68 grass-positive sera.

Cross-reactivity of donor sera IgE

The possibility that the high frequency of co-occurrence of antilatex with antigrass-specific IgE was attributable to cross-reactivities of IgE species was investigated by measuring the inhibition of IgE antilatex activity resulting from pre-incubation with a grass pollen extract. When those sera of the summer donations found to contain antilatex IgE at the class III level were pre-incubated with pollen protein at an effective concentration of 0.017% a minimum of 50% inhibition of the IgE antilatex activity was produced in 57% of the sera. A 10-fold increase in the pollen protein concentration in the pre-incubation mix produced at least a 50% inhibition in 91% of the sera.

Immunoblots of sera containing IgE antibodies to both latex and grass pollen proteins showed inhibition of both antigrass and antilatex activity on pre-incubation with either allergens source. Figure 1 shows an example of several such experiments, in this case a striking inhibition of the reaction with a 36-kDa latex protein was obtained after pre-incubation with the grass pollen extract.

The cross-reactivity of antigrass pollen antibodies with

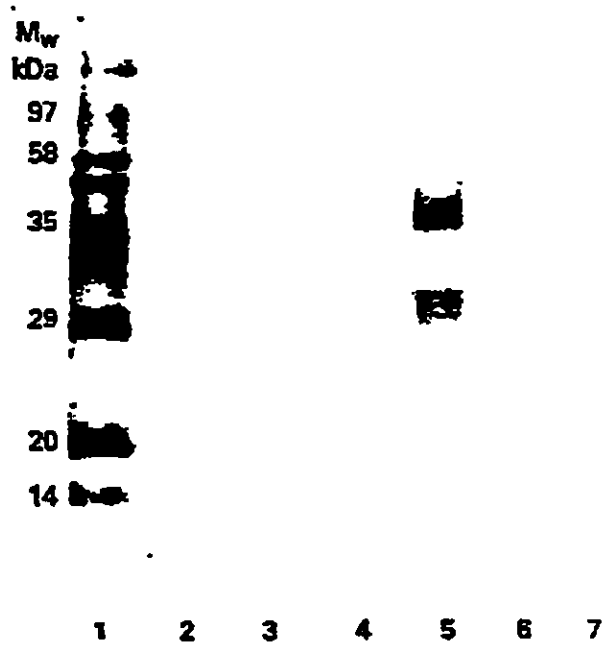

Fig. 1. Immunoblots of grass and latex proteins reacting with uninhibited and inhibited IgE from a donor serum. Tracks: (1) M_W markers, (2) grass vs latex-inhibited serum, (3) latex vs latex-inhibited serum, (4) grass vs uninhibited serum, (5) latex vs uninhibited serum, (6) latex vs grass-inhibited serum, and (7) grass vs grass-inhibited serum.

latex polypeptides was not confined to the IgE fraction. When immunoblots of SDS-PAGE separations of latex and grass pollen polypeptides using sera containing antigrass IgE but no detectable antilatex IgE were analysed using a specific antihuman IgG to detect IgG binding, not only were these sera found to contain, as might be expected, IgG antibodies reacting with grass pollen but, also IgG antibodies reacting with latex antigens.

Discussion

The prevalence of antilatex IgE in the two groups of 2000 winter donations (4.0%) is somewhat lower and that in the 5000 summer donations (7.4%) rather higher than the 6.0% found by Ownby *et al.* [6] for a series of 1000 US blood donations assayed by the same method. The difference between the prevalences in the winter and summer donations is difficult to understand. The prevalence of antigrass IgE in the 2000 members of the winter group (19.6%) is also lower than that estimated for a sample of 410 members of the summer group (28.5%). However, the proportion of these grass-positive sera which would be expected to also be latex-positive is insufficient to account for the observed difference in the prevalence of antilatex IgE in the two groups.

As might be expected the greatest prevalence of antilatex and antigrass IgE-positive sera was found with the younger donors, the χ^2 test showing a strong positive age correlation. Less expected was the sex correlation of both antibody levels and the higher prevalence of detectable specific IgE in donations from males.

Two recent investigations concerned the possible prevalence of latex sensitivity: one in the general population and the other amongst children. In a study reported from France [11] involving 258 subjects aged from 20 to 40 years visiting a health care centre for a check-up who, it was claimed, were representative of the general population, 6.1% were said to be sensitized to latex but only 3.4% had a positive RAST (classes 1 and 2); 3.1% gave a positive skin prick test but all of these had a negative RAST for antilatex IgE. A study of 1175 elementary school children in Italy [12] revealed that only eight gave a positive skin prick test to latex; whilst all of these children also gave a positive skin prick test to one or more aeroallergens, food allergens or both, none of them had a history of latex symptoms.

The 19.6% prevalence of serum antigrass IgE found for the winter donations in this study compares with a prevalence of 15.2% reported by Kerkof *et al.* [13] for 2496 randomly selected members of the general population of Holland assayed by the Pharmacia CAP procedure. On the other hand a similar study [14] of 882 members of the general population drawn from the East Anglia region of the UK revealed a prevalence of 34.5% of male and 22.5% of female subjects having detectable antigrass IgE. The levels of antigrass IgE in both reports were age and sex related. Answers to a questionnaire in the East Anglian study indicated a 30% prevalence of hay fever symptoms in the group assayed for antigrass IgE. The median value of the prevalence of antigrass IgE in the European Community Respiratory Health Survey [15] was 18%.

The likelihood that the high proportion of sera containing antilatex IgE also containing antigrass IgE could be attributed to a cross-reactivity was indicated by the inhibition studies, both of total specific IgE assays and of reactions with individual allergens in immunoblots. Fuchs *et al.* [16] have reported 90–100% inhibition of the Pharmacia CAP assay for latex-specific IgE by a grass extract in six out of nine sera of latex-sensitive patients. These workers found that immunoblots of sera from six such patients showed complete inhibition of binding to antigens of molecular weight 30–90 kDa by four sera when pre-incubated with a grass extract.

The small proportion of sera in this study found to contain both antilatex and antimite or anticat allergen IgE may be ascribed to atopy in these donors, certainly the sera which reacted with all four allergens studied may be attributed to atopic donors.

The geometric mean of the total serum IgE levels found in the summer donations is close to that obtained by Nye *et al.* in 1975 [17] for a group of 47 males and 55 females aged from 18 to 23 years and to those found in samples of the general population aged between 20 and 44 years [15]. The observation that the geometric mean of the total IgE was higher in males than in females is in accord with the original report of Merrett *et al.* [18] on a group of 136 men and 272 women aged 70–79 living in Wales and also that of Burney *et al.* in the European Community Respiratory Health Survey [15].

The principal latex allergens have molecular weights in the 30–40 kDa range and those of the grass pollen from 27 to 36 kDa. The relatively high proportion of donor sera reacting with latex polypeptides of molecular weight 30, 32 and 39 kDa is of interest in respect to the recent findings of Yagami *et al.* [19]. These workers have shown a purified latex chitinase molecular weight 29.5 kDa and 1.3 glucanase enzymes having polypeptides molecular weight 35.1, 36.7 and 38 kDa to be allergenic.

Earlier studies [20] have shown that, for a group of 43 latex-sensitive patients, the allergens of fresh latex were more potent than those of preserved high ammonia latex. Taking this observation together with the apparent cross-reactivity of donor antilatex IgE with grass pollen it is suggested that the primary cause of sensitization in some latex-sensitive individuals may be the conformational epitopes of some grass pollen proteins and that subsequent sensitivity to latex goods may arise from the reaction with

similar conformational epitopes of latex proteins surviving after storage and manufacture.

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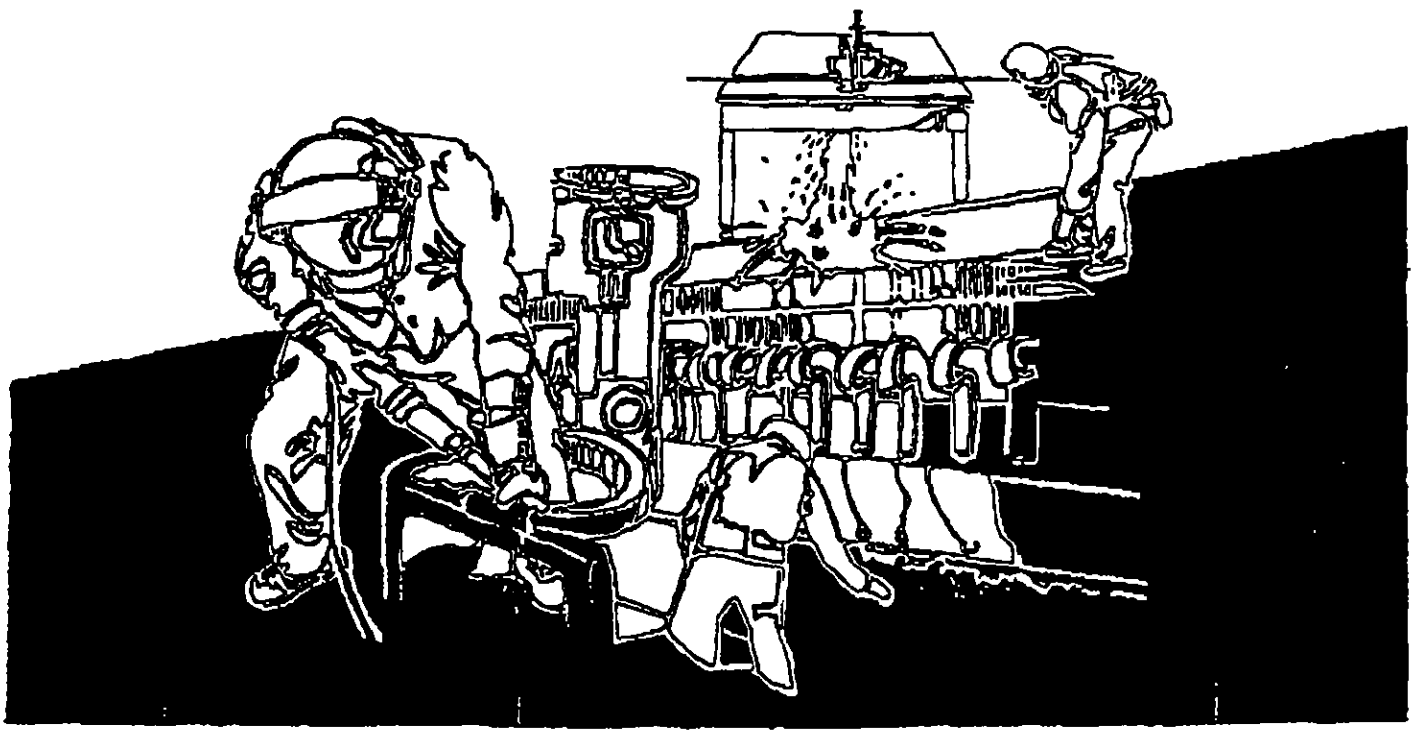
NIOSH HEALTH HAZARD EVALUATION REPORT

HETA 98-0096-2737
Exempla St. Joseph Hospital
Denver, Colorado

Elena H. Page, M.D., M.P.H.
Eric J. Esswein, C.I.H., M.S.P.H.



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

PREFACE

The Hazard Evaluations and Technical Assistance Branch of NIOSH conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The Hazard Evaluations and Technical Assistance Branch also provides, upon request, technical and consultative assistance to Federal, State, and local agencies, labor, industry, and other groups or individuals to control occupational health hazards and to prevent related trauma and disease. Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

ACKNOWLEDGMENTS AND AVAILABILITY OF REPORT

This report was prepared by Elena H. Page, M.D., M.P.H. and Eric J. Esswein, C.I.H., M.S.P.H., of the Hazard Evaluations and Technical Assistance Branch, Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS). Field assistance was provided by Boris Lushniak, M.D., M.P.H., Sue Ting, M.D., M.P.H., Helga Daftarian, D.O., M.P.H., Joel McCullough, M.D., M.P.H., M.S., Yvonne Boudreau M.D., M.P.H., Marian Coleman, B.J. Haussler, Jenise Brassell, Barbara MacKenzie, Deborah Sammons, Elaine Moore, and Joyce Woody. Analytical support was provided by Mark Swanson of the Mayo Clinic, Rochester, Minnesota, and Daniel M. Lewis, Ph.D. and Toni Bledsoe of the Health Effects Laboratory Division. Martin R. Petersen, Ph.D. provided statistical support. Desktop publishing was performed by Elaine Moore. Review and preparation for printing was performed by Penny Arthur.

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Health Hazard Evaluation Report 98-0096-2737
Exempla St. Joseph Hospital
Denver, Colorado

Elena H. Page, M.D., M.P.H.
Eric J. Esswein, C.I.H., M.S.P.H.

SUMMARY

On January 23, 1998, the National Institute for Occupational Safety and Health (NIOSH) received a confidential employee request for a health hazard evaluation (HHE) at Exempla Health Care Facility/St. Joseph's Hospital in Denver, Colorado. The request stated that hospital employees experienced facial flushing, rhinitis, sneezing, itching and watery eyes, and fainting while at work. According to the request, the exposure thought to cause the employees' health problems was latex protein from powdered natural rubber latex (NRL) gloves.

The NIOSH investigation consisted of concurrent medical and industrial hygiene evaluations during the weeks of July 13–16, 1998, and August 3–6, 1998. Additional medical evaluations were completed November 9–13, 1998. The medical evaluation included a self-administered questionnaire and blood tests for total IgE and latex-specific IgE. The industrial hygiene evaluation consisted of air, surface, and bulk dust sampling to evaluate the presence of latex proteins within the hospital environment.

The overall prevalence of latex sensitization (defined by the presence of latex-specific IgE) was 6.2% (33/531). There was no statistically significant difference in the prevalence of latex sensitization between employees who wear latex gloves (6.1% or 16/248) and those who do not wear latex gloves (6.3% or 16/239) (p=0.9). There was also no statistically significant difference in the prevalence of latex sensitization between employees who reported current latex glove use or having worn at least one pair of latex gloves per day at another job or in training (i.e., ever having occupational latex glove use), with a prevalence of 6.3%, and those who reported never having occupational latex glove use, with a prevalence of 5.1% (p=0.6). Reporting of work-related hand dermatitis was more common among those who currently wore latex gloves (23.4%) than among those who did not (4.9%) ($p < 0.01$), as were rhinoconjunctivitis (16.3% and 7.9%, respectively, $p < 0.01$) and hand urticaria (9.9% and 2.1%, respectively, $p < 0.01$). There was no significant difference by latex glove use in the reporting of work-related asthma or general urticaria. There was no statistically significant association between any of these symptom complexes and latex sensitization, although hand urticaria and hand dermatitis were more prevalent in those who were sensitized.

Atopy (history of allergic rhinitis, asthma, or atopic dermatitis) was significantly associated with latex sensitization; 81.3% of those with latex sensitization were atopic, compared to 59.5% of those who were not sensitized (p=0.02). Twenty-four percent of those with latex sensitization reported no Type I allergic symptoms, i.e., urticaria, rhinoconjunctivitis, or asthma, either at work or home, while 62% reported no work-related Type I symptoms.

A total of 23 area air samples for NRL allergen were collected in clinical (16) and non-clinical (7) areas of the hospital. Five of the seven samples collected in the non-clinical areas had no detectable NRL protein. One sample,

collected in inpatient admitting, had a concentration between the limit of detection (LOD) and the limit of quantitation (LOQ), that is, a trace concentration One sample, collected in the medical records area, had a quantifiable concentration, 0 26 nanograms per cubic meter (ng/m^3) Sixteen air samples were collected in clinical areas of the hospital Nine of 16 samples (from a variety of clinical areas) had NRL protein concentrations ranging from 0 41 to 3 33 ng/m^3 Four samples contained trace concentrations, and three samples had no detectable NRL protein.

Nineteen surface dust samples were collected from ceiling tiles and air handling unit (AHU) plenums Ten samples were collected from clinical areas and nine from non-clinical areas In the non-clinical areas, no NRL was detected in seven of the samples, one had a trace amount, and one sample from an AHU serving the inpatient admitting had 368 nanograms of NRL per 100 square centimeters (ng/100 cm^2) In the clinical areas, 7 of 10 surface dust samples had no detectable NRL protein One sample collected from the back of a ceiling tile in the labor and delivery (L&D) suite 242 had 118 ng/100 cm^2, and two surface samples collected inside AHUs contained 1,022 and 3,952 ng/100 cm^2

Two filter dust samples were collected from AHUs serving non-clinical areas of the hospital, neither had detectable NRL protein Five samples of filter dust collected from AHUs serving clinical areas of the hospital had NRL protein concentrations ranging from 4,433 ng/gram of dust (ng/gm), from an AHU which serves the emergency department (ED), to 83,682 ng/gm, from an AHU which served the labor and delivery areas

We found that levels of airborne, surface, and filter dust latex proteins were higher in the work areas of the employees who were not sensitized to latex than those who were sensitized.

We found that neither current nor past occupational use of latex gloves was associated with latex sensitization in this study population Latex glove use, however, was associated with reporting of work-related rhinoconjunctivitis, hand urticaria, and hand dermatitis. Airborne natural rubber latex protein levels were very low, but there was a significant amount of latex protein on filters in the ventilation system Exposure to filter dust could present risks to individuals who change AHU filters (e.g , maintenance workers), or to other workers if NRL proteins were to be released into the hospital environment Recommendations include the use of nonlatex gloves for those who do not encounter infectious materials, and the use of low-protein, powder-free latex gloves for those who do encounter infectious materials; education for employees about latex allergy; and re-assessment of prevention strategies if a worker is diagnosed with latex allergy.

Keywords: SIC 8062 (General medical and surgical hospitals) natural rubber latex, hospital, allergy

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INTRODUCTION

On January 23, 1998, the National Institute for Occupational Safety and Health (NIOSH) received a confidential employee request for a health hazard evaluation (HHE) at Exempla Health Care Facility/St Joseph's Hospital in Denver, Colorado. The request stated that hospital employees experienced facial flushing, rhinitis, sneezing, itching and watery eyes, and fainting while at work. According to the request, the exposure thought to cause the employees' health problems was latex protein from powdered natural rubber latex (NRL) gloves.

The NIOSH investigation consisted of concurrent medical and industrial hygiene evaluations during the weeks of July 13–16, 1998, and August 3–6, 1998. Additional medical evaluations were completed November 9–13, 1998. The medical evaluation included a self-administered questionnaire, serum tests for total IgE and latex-specific IgE, and skin patch testing for rubber additives. The industrial hygiene evaluation consisted of air, surface, and bulk dust sampling to evaluate the presence of latex proteins within the hospital environment.

Participants were notified by letter of their own test results during November and December of 1998. Management and employees were notified of preliminary findings and recommendations on February 26, 1999.

BACKGROUND

NRL is contained in the milky fluid from the *Hevea brasiliensis* tree. It contains a variety of proteins capable of inducing an allergic reaction. Routes of exposure include dermal, mucosal, percutaneous, and inhalation. Latex proteins are reported to be adsorbed onto cornstarch particles.[1] United States Pharmacopoeia (USP) absorbable dusting powder (cornstarch) is used to powder sterile and non-sterile NRL gloves to aid in glove donning. NRL proteins alone or glove powder containing NRL proteins can become airborne and represent a health hazard for health care workers. Glove powder present in environmental dusts also can pose a hazard.

There are three main types of reactions to latex-containing objects: irritant contact dermatitis, allergic contact dermatitis, and immediate hypersensitivity.[2] Irritant contact dermatitis is the most common reaction in latex glove wearers. It is not an immune-mediated reaction and can occur with occlusive gloves of any material. It typically presents over time as dry, cracked, red, and itchy skin. It can be caused by moisture and friction under the gloves, frequent hand washing, and dermal exposure to soaps and other chemicals.

Allergic contact dermatitis is a Type IV, delayed hypersensitivity reaction. It is T-cell mediated. Allergic contact dermatitis related to exposure to chemicals used in manufacturing latex gloves has been recognized for years. Accelerators and antioxidants, including thiurams, carbamates, thiourea derivatives, benzothiazole derivatives, and amine derivatives, are the main allergens in rubber products that can induce allergic contact dermatitis.[3,4] Allergic contact dermatitis is diagnosed by skin patch testing. Several cases have recently been reported of allergic contact dermatitis due to NRL itself, not the additives.[5,6,7] One study reports that 6% of glove users with hand dermatitis had positive patch tests to natural rubber latex, often in the absence of contact urticaria.[6] Another study reported positive patch test reactions to latex in 1.2% of contact dermatitis patients.[7]

Sensitization is the development of antigen-specific antibodies. This occurs after an initial exposure to the offending antigen. Subsequent re-exposure to the same antigen results in production of antigen-specific antibodies.[8] It is common to be sensitized to a substance but not have clinical symptoms of allergy. For example, about 60% of positive skin prick test results do not reflect symptomatic food allergy.[10] One-third[11] to

one-half[12] of patients with positive skin prick test results to latex are asymptomatic. Immediate hypersensitivity is a Type I, IgE-mediated reaction. It was first reported in the English literature in 1979, when Nutter described a case of contact urticaria in a housewife who wore rubber gloves.[13] Type I hypersensitivity reactions may manifest as urticaria, asthma, allergic rhinoconjunctivitis, and anaphylaxis.[14] Persons thought to be at risk of developing latex allergy include health care workers, latex product manufacturing workers, children with spina bifida, and persons who have had multiple surgeries. Atopy (history of allergic rhinitis, asthma, or atopic dermatitis) is also a risk factor, as is allergy to cross-reacting foods, such as banana, kiwi, avocado, and chestnut.[14] The estimated prevalence of sensitization to latex, manifested by either a positive skin prick test or the presence of antibodies to latex in serum, among health care workers ranges from 2.9% to 22%,[15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30] with most studies reporting prevalence rates in the range of 5-15%. The prevalence of latex-specific IgE is reported to be from 6.4%[31] to 7.7%[32] in blood donors, and ranges from 0.12% to 20% in a variety of occupationally unexposed populations, such as adults attending health screening or allergy clinics, children admitted for allergy testing, or in the general population.[30,33,34,35,36,37,38,39,40]

Diagnosis of Type I allergic conditions is most commonly accomplished with skin prick testing (SPT) with specific antigens.[9] However, no SPT eluate has been approved by the Food and Drug Administration (FDA) for use in the United States. While SPT is traditionally considered more sensitive, the radioallergosorbent test (RAST) has been shown to be highly sensitive (94%) and specific (96%).[41] Four serum tests for the detection of latex-specific IgE have been approved and are currently in use. These are the Pharmacia CAP™, Immunolite™, HY-TEC™, and the Alastat™.[14] The Pharmacia CAP demonstrated a sensitivity of 97% and a specificity of 83%, compared to clinical history, while SPT demonstrated a sensitivity of 97% and a specificity of 100%.[42] Another study found the sensitivity and specificity of the CAP to be 100% compared to clinical history and a positive SPT to define latex allergy.[43] The Alastat was found in one study to have a specificity of only 33%,[42] but, another study found it to have a sensitivity of 63.6% and specificity of 98.4% with reference to SPT.[16]

METHODS

The purpose of this study was to compare the prevalence of latex sensitization (presence of latex-specific IgE) between employees who wear latex gloves and those who do not wear latex gloves, determine occupational and non-occupational risk factors for sensitization, and whether work-related symptoms (asthma, rhinoconjunctivitis, urticaria, and hand dermatitis) were associated with being sensitized to latex or wearing latex gloves, and determine the proportion of irritant and allergic contact dermatitis among those with self-reported dermatitis.

Medical

Study Population

Two groups of employees, those who wear latex gloves on a regular basis, and those who do not wear latex gloves were selected to participate in this study. The no-latex-gloves group consisted of employees in human resources, finance, marketing, library, admitting, business office, audiovisual, facilities maintenance, medical records, volunteer office, payroll and reimbursement, quality assurance, pastoral care, the Sisters of Charity, medical education, patient and family counseling, material management, information services, and the nursing staff office. Housekeeping and food service employees were not included because these employees wear latex gloves on a regular basis.

Three clinical areas were selected to represent the latex glove using group. These were selected based on number of employees, glove use as reported by central supply, and convenience of access to employees to accomplish the evaluation. This group

included labor and delivery (L&D), the emergency department (ED), and the laboratory service. L&D used 189,384 pairs of gloves in 1997 (98,184 powdered latex, 55,800 powder-free latex, and 35,400 nonlatex) The ED used 429,600 pairs of gloves (213,600 powdered latex, 205,200 powder-free latex, and 10,800 nonlatex), and the lab used 114,870 pairs of gloves (4,320 powdered latex, 109,250 powder-free latex, and 1,300 nonlatex).

Only those employees who were present at work at the time of our visit were included in the denominator for the purpose of calculating participation rates Those on vacation, sick leave, or not scheduled to work were not considered eligible for the study.

Questionnaire

Questionnaires were self-administered under the supervision of a NIOSH employee and consisted of questions concerning demographics (age, race, gender, job title, years worked, etc.) and information about personal history of allergic disorders, surgical procedures, latex allergy, and smoking, as well as about glove use, symptoms, and possible symptom triggers. Before the participant left, the questionnaire was reviewed for completeness by a NIOSH employee.

For analysis, latex glove exposure was determined by two questions: "Do you usually wear gloves when working in your current position?" and "What type of gloves do you wear most often?" Persons answering the first question affirmatively and specifying that they wore either powdered or non-powdered latex gloves were categorized as wearing latex gloves, while those answering the first question negatively, or in the affirmative but specifying nonlatex gloves, were classified as not using latex gloves.

Latex sensitization was defined as the presence of detectable levels of latex-specific IgE, i.e., levels $\geq$ 0.35 kiloUnits of allergen-specific antibodies per liter of serum (kU_A/L). Work-related symptoms were defined as either those present at work but not at home, or those present both at work and at home that improved away from work. Asthma was defined as the presence of wheezing, or any two of the following three symptoms cough, shortness of breath, and chest tightness Rhinoconjunctivitis was defined as the presence of two of three of the following: itchy, runny nose (with or without sneezing), stuffy nose, and itchy, watery eyes. Hand dermatitis was defined as the presence of dermatitis, eczema, or other red, inflamed rash on the hands, while urticaria was defined as red, raised, itchy swellings (called hives, wheals, or urticaria), either on the hands or elsewhere Participants were asked if they had any of these symptoms or diagnoses in the preceding 12 months. Atopy was defined as having a history of hay fever or other allergies (not including allergies to medications), eczema or atopic dermatitis, or asthma.

Antibody Testing

Blood was drawn by NIOSH phlebotomists using Becton-Dickenson serum-separating tubes. The blood was allowed to clot and then centrifuged for 10 minutes Serum was poured into transfer tubes and frozen. Specimens were shipped on dry ice to the NIOSH Health Effects Laboratory Division in Morgantown, West Virginia, where it was analyzed for latex-specific IgE and total IgE utilizing the Pharmacia CAP test. A negative latex-specific IgE is <0.35 kU_A/L (no detectable antibodies) and positive is $\geq$ 0.35 kU_A/L (presence of detectable antibodies).

Patch Testing

Skin patch testing was offered to a sample of employees from the laboratory service who reported hand dermatitis in the preceding 12 months. The lab was selected for patch testing because of the high reported prevalence of hand dermatitis and because of convenience. Employees in L&D and ED tend to work irregular schedules, such as three on, four off, while many lab employees work Monday – Friday. The True Test™ allergen patch test set was used. It

consists of 23 substances and one negative control. They were applied on Monday, removed and read on Wednesday, and final readings were done on either Thursday or Friday. All were read by a NIOSH board-certified dermatologist. Readings of 2+ or higher were considered positive, 1+ was equivocal, and 0 was no reaction.

Industrial Hygiene Methods

To evaluate the presence of airborne or occult NRL latex proteins at Exempla St Joseph Hospital, three types of samples were collected, air samples, surface dust samples (from the back surfaces of ceiling tiles and inside air handling units), and dust accumulated on air filters in the hospital's air handling units To evaluate concentrations of airborne NRL proteins, 23 area air samples were collected using high-volume samplers, with an average sample time of 8 hours, 17 minutes The samplers were calibrated and it was determined that one operated at 5 7 liters per second (L/sec), the other at 6.1L/sec To confirm sampler flow rates, the samplers were calibrated (with new filters in-line) using a recently calibrated TSI VeliCicalc® Plus Model 8360 thermoanemometer. The 8360 was first programmed to measure air flow in a 3" (7.6 cm) round duct in units of liters per second To calibrate the samplers a 61 centimeter (cm.) length of schedule 40 PVC pipe (7.6 cm in diameter) was connected to a flange on top of the sampler using a standard circular PVC connector sleeve. A small amount of vacuum grease was used to insure a good seal between the PVC pipe and the sampler head The pipe was attached to the sampler only temporarily for use as an extended intake plenum so that air flow calibration could be conducted. Two 1.3 cm ports had been drilled into the plenum at 90 degrees to insert the probe of the 8360 to measure airflow. To insure smooth flow in the duct, the ports were located 2.5 duct diameters from the end of the plenum and 5.5 duct diameters from the filter. The tip of the VeliCicalc® Plus was inserted in each port and five flow measurements were made across the diameter of the plenum. Ten flow measurements were taken in total and the results averaged to determine nominal flow rates in liters per second NRL allergen was collected using bilaminate [glass fiber and polytetrafluroethylene (PTFE)] membrane filters Samplers were located at a height of 52" (approximate seated breathing zone height).

Surface dust was collected using micro-vacuuming techniques according to the American Society for Testing and Materials (ASTM) method D 5755-95[44] with several modifications The area to be sampled was masked using 100 square centimeter (cm^2) disposable clear plastic masking templates to demarcate an area on the back of a ceiling tile. Dust was collected using 37-millimeter sampling cassettes connected in line with Tygon® tubing to a high-volume sampling pump. The sampling train was calibrated to 28.3 liters per minute (L/min). A 1.5 inch piece of Tygon tubing was connected to the face of the cassette to act as a nozzle. The nozzle was cut to a 45° angle. As per the ASTM method, surface dust was collected by micro-vacuuming within the area of the masking template up, then down, then back and forth, for a period of two minutes, or as the method states, until no visible dust remains on the surface of the sampling area. After the surface dust sample was collected, the cassette was inverted and the pump was shut off The nozzle was capped with a plug, and the sampler was packaged to prevent separation of the nozzle from the cassette and sealed upright in a plastic bag. For ceiling tiles, a tile adjacent to a return air grille in the room or area where air sampling was conducted was chosen Samples were collected from sheet metal surfaces in air handling units (AHUs) using the same sample collection technique for ceiling tiles. Filter dust was collected by micro-vacuuming back and forth, then up and down, on approximately 100 cm^2 areas of AHUs prefilters. In some locations, where vacuum collection of a surface sample was not possible, a surface wipe sample was collected by wiping a 100 cm^2 area. All samples were sent to the Mayo Clinic, Rochester, Minnesota, for analysis by an inhibition assay using IgE antibodies from latex sensitive individuals [45]

Statistical Analysis

Statistical analysis was done using SAS software (SAS Institute, Cary, North Carolina) Univariate associations between categorical outcome and exposure variables were assessed with contingency tables using Chi square or Fisher's exact test (two-tailed). Univariate associations between categorical outcome and continuous exposure variables were evaluated comparing group means using the *t* test, or for nonparametric data using the Mann-Whitney test. A p value of <0.05 was considered statistically significant Univariate logistic regression was also used to evaluate associations between exposure and outcome variables. Odds ratios (OR) were used as a measure of association. An OR less than 1 means there is reduced risk; an OR greater than 1 means there is increased risk. Along with the OR, we calculated its confidence interval (CI). A CI excluding 1 means we have convincing evidence of an association with the disease. All participants were included in the analyses unless specific necessary data were missing; therefore, the denominators vary for some analyses. Values for sampling results that were below the limit of detection (LOD) were estimated by dividing the LOD by the square root of two [46] Geometric means were calculated for area air samples, surface samples, and filter samples by department.

EVALUATION CRITERIA

Because of the wide range in dose-response for allergens in general, it is difficult to determine a safe threshold concentration for which sensitized individuals would not experience reactions, or unsensitized individuals would not experience allergic sensitization with exposure to NRL allergens. Neither NIOSH, nor the Occupational Safety and Health Administration (OSHA), nor the American Conference of Governmental Industrial Hygienists (ACGIH) has established numerical exposure limits for latex exposures. However, individual studies have suggested exposure limits. This information is provided only for comparison purposes, and is meant to be neither an endorsement nor a confirmation One researcher suggested that air concentrations of total latex protein less than 10 ng/m^3 pose a "low" risk of latex sensitization.[47] Another researcher from Germany suggested 0.6 ng/m^3 of total latex protein as an exposure limit to minimize the risk of allergic reactions in sensitized health care workers.[48]

RESULTS

Medical

Overall participation in the medical evaluation was 83.1% (532/640). Participation rates by department are listed in Tables 1 and 2. The latex glove users and non-users were very similar demographically (Table 3), except that the latex glove non-users were older by an average of 4 6 years. There was also a significant difference in the number of hours worked weekly, with the latex glove non-users working more hours than the latex glove users (Table 3). There was no difference in the length of time working in either the current department (p=0 9) or in the hospital (p=0.4)

The overall prevalence of latex sensitization (defined by the presence of latex-specific IgE) was 6.2% (33/531). There was no statistically significant difference in the prevalence of latex sensitization between employees who wear latex gloves (6.1% or 16/264) and those who do not wear latex gloves (6.3% or 16/255) (p=0.9). There was also no statistically significant difference in the prevalence of latex sensitization between employees who reported current latex glove use or having worn at least one pair of latex gloves per day at another job or in training (i.e., ever having occupational latex glove use), with a prevalence of 6.3%, and those who reported never having occupational latex glove use, with a prevalence of 5.1% (p=0.6).

Reporting of work-related hand dermatitis was more common among latex glove users (23.4%) than in the non-users (4 9%), as were rhinoconjunctivitis

(16 3% and 7 9%, respectively) and hand urticaria (9.9% and 2.1%, respectively), ($p < 0.01$ for each association) There was no significant difference in the reporting of work-related asthma or general urticaria (Table 4) Employees who reported rhinoconjunctivitis, hand or general urticaria, and hand dermatitis reported a significantly higher median number of gloves used per day and median number of pair-hours, a variable calculated by multiplying the number of gloves worn daily by the average duration of wear of each pair (Tables 5 and 6) There was no difference between those who were sensitized and those who were not sensitized in median number of gloves used per day(1.5 vs 1 0, respectively, $p=0.8$) or median number of pair-hours (0.4 and 0.3, respectively, $p=0.7$). There was evidence of a dose-response relationship between increasing levels of glove use and all health effects except asthma (Table 7). There was no significant association between work-related asthma, rhinoconjunctivitis, general or hand urticaria, or hand dermatitis and latex sensitization, although prevalence of hand urticaria and hand dermatitis was higher in those who were sensitized (Table 8) Twenty-four percent of those with latex sensitization reported no Type I (immediate hypersensitivity) allergic health effects either at work or home, while 62.1% reported no work-related Type I symptoms.

The prevalence of atopy was similar in both groups, 60.2% in the latex glove non-users and 61.1% in the latex glove users. The mean total IgE level in atopics was 96.6 kU/L, compared to 58 1 kU/L in nonatopics ($p=0.06$). Atopy was significantly associated with latex sensitization, with 81.3% of those with latex sensitization being atopic, compared to 59.5% of those who were not sensitized ($p<0.05$).

Reported respiratory and dermatologic allergic reactions related to avocados, kiwis, peaches, chestnuts, or bananas were not significantly associated with latex sensitization ($p=1.0$). The number of surgeries ranged from 0-30 and was not significantly associated with latex sensitization ($p=0.3$). There was no association between sensitization and the number of gloves worn daily (e g., those who wore more than 18 pairs of latex gloves daily were as likely as those who wore no latex gloves to be sensitized [OR=0 9, 95% CI=0.3-2.3]). Similarly, those who reported more than 7 pair-hours of latex glove use daily were not more likely to be sensitized than those who reported 0 pair-hours (OR=0.8, 95% CI=0.3-2.2) There was no significant difference in the prevalence of sensitization between those who wore powdered latex gloves and those who wore powder-free latex gloves (4 7% vs. 7 0%, $p=0.4$)

Males were significantly more likely to have latex sensitization (12.1% vs 4.1% [$p < 0.01$]). Gender, however, was not related to atopy. Females predominated in all job categories except facilities maintenance worker, physician, and physician's assistant, but sensitization was not associated with job category. Office workers (administrative and clerical, managers, and telephone operators) had a sensitization rate of 6 3%, facilities workers, housekeepers, and other 11.4%; medical technologists and phlebotomists 5.3%; nurses and nurses assistants 3 0%, and physicians assistants and physicians 5.9% ($p=0.3$). Categories had to be combined into these 5 groups due to small expected numbers in certain cells.

Age and race were not significantly associated with latex sensitization ($p=0.07$ for both). Hours worked per week were not associated with latex sensitization ($p=0.3$). There was no difference in the length of time working in either the current department ($p=0.6$) or in the hospital ($p=0.7$) between the sensitized and the nonsensitized

Six persons reported being diagnosed with latex allergy by a physician, five by history and physical exam alone, and one by a glove use test. None had skin prick testing or serum antibody testing performed by their physician. Only one of the six had latex-specific IgE in this study This individual reported work-related hand urticaria and eczema. Of the other five, one reported work-related asthma,

two rhinoconjunctivitis, one hand urticaria, two generalized urticaria, and three hand dermatitis.

There were 36 persons in the lab who reported hand dermatitis in the last 12 months. Five no longer worked at the hospital when patch testing was done. Of the 31 remaining, 20 had work schedules that would accommodate patch testing, and 17 agreed to participate. One of these was unable to tolerate the testing and removed the patches after several hours. Of the 16 who completed testing, only 1 had a positive reaction to any of the rubber additives. This individual had a 2+ reaction to thiuram mix, and a 1+ reaction to carba mix.

Environmental

Area Air Samples

Seven samples were collected in non-clinical areas of the hospital (Table 9). Five of seven samples had no detectable amounts of NRL allergen, the minimum detectable concentration (MDC) was 0.12 nanograms per cubic meter of air (ng/m^3). One sample, collected in inpatient admitting, had a concentration between the LOD and the limit of quantitation (LOQ), that is, a "trace" concentration. The only sample with quantifiable amounts of NRL allergen was a sample collected in the medical records area which had a concentration of 0.26 ng/m^3.

Sixteen samples (from a variety of clinical areas) had concentrations of NRL that ranged from less than the MDC of 0.24 ng/m^3 to 3.33 ng/m^3. Four samples contained trace concentrations and three samples had no detectable NRL (Table 10). The laboratory reported differences in LODs for the sets of air samples from the non-clinical areas (approximately 20 ng/sample) and the clinical areas (approximately 40 ng/sample). The laboratory reported the reason for these differences was a different amount of phosphate buffer used to extract NRL from the filters in the two sets of samples (total sample extraction volumes of either 250 microliters or 500 microliters, respectively, were used in the analyses). Dilutional differences, related to phosphate buffer extraction volumes, accounted for the doubling differences in analytical LODs which were reported.

Surface Dust Samples

Ten samples were collected in clinical areas and nine samples in non-clinical areas (Tables 9 and 10). In the non-clinical areas, seven of the samples had no detectable NRL antigens, one surface dust sample from the AHU serving the medical records area had a trace concentration, and one sample from AHU serving the inpatient admitting had 368 nanograms per 100 square centimeters (ng/100 cm^2).

In the clinical areas, 7 of the 10 samples had no detectable NRL antigens. One sample, collected from the back of a ceiling tile in L&D suite 242, had 118 ng/100 cm^2 and two surface samples, collected inside AHUs AC-16 and AC-10, contained 1,022 and 3952 ng/100 cm^2.

Filter Dust Samples

Two filter dust samples were collected from AHUs serving non-clinical areas of the hospital, neither had detectable NRL antigens (Table 9). Five samples of filter dust were collected from AHUs serving clinical areas of the hospital (Table 10). Filter dust concentrations of antigens ranged from 4,433 ng/gram of dust (ng/gm) in AC-3, which serves the emergency department, to 83,682 ng/gm in AC-18, which serves the labor and delivery areas.

Geometric mean concentrations of NRL in the air and on surfaces and filters were calculated by department. Individual participants were assigned the geometric mean concentration for their department. Mean concentrations were compared between the sensitized and the nonsensitized. We found levels of airborne, surface, and filter latex proteins were higher in the work areas of the nonsensitized (Table 11).

DISCUSSION

We found that neither current nor past occupational use of latex gloves was associated with latex sensitization in this study population. The prevalence rate of latex sensitization at Exempla St. Joseph Hospital is at the low end of the range reported in the medical literature for other hospitals. While prevalence studies of health care workers found rates of sensitization ranging from 2.9 to 22% (most in the 5–15% range),[15-30] few have compared these rates to those in a similar group without occupational exposure to latex. Thus, it has been difficult to determine the magnitude of the occupational risks faced by health care workers. Two studies of blood donors found the prevalence of latex sensitization to be 6.4%[31] and 7.7%.[32] Other studies of non-occupationally exposed groups, such as adults attending health screening or allergy clinics, children admitted for allergy testing, or the general population, have found rates of 0.12% to 20%.[30,33-40]

There was a significant association between latex glove use and rhinoconjunctivitis, hand urticaria, and hand dermatitis. However, there was no significant difference in the prevalence of these symptoms by sensitization status. There are several potential reasons for this apparent discrepancy. First, the serum test may not be as sensitive as reported, and thus we may have missed cases of sensitization. However, the test sensitivity should not differ between exposure groups, and therefore this is an unlikely explanation. Second, glove use may be a proxy for other exposures in the workplace that cause allergic symptoms. Since there were only 32 sensitized individuals in this study, there may have been insufficient statistical power to detect and association between sensitization and the health effects. Finally, because latex allergy is a high-profile issue among HCWs, symptoms reporting may have been subject to an awareness bias.

Atopy is an established risk factor for latex allergy, and this was supported by our study. While the prevalence of atopy was high in our study, it did not differ between the latex glove users and non-users. Our case definition of atopy was based on self-reported history of hay fever, eczema or atopic dermatitis, or asthma. A study of apprentices entering the fields of animal health, pastry making, and dental hygiene found atopy rates of 54.4%, 58.1%, and 52.5%, respectively.[24] This was determined by the presence of at least one SPT positive to common aeroallergens, a common objective method for determining atopic status. The significant association of latex sensitization with male gender has been reported elsewhere,[31,49] as has the lack of an association with age.[14,18,19,20,22,28,31,36]

Other risk factors for latex sensitization identified in previous studies include allergies to kiwi, avocado, banana, chestnut, and other foods. We did not find an association between them and reported respiratory and dermatologic Type I allergic symptoms, but we did not ask about oral symptoms, which may be more common when the route of exposure is ingestion. Having multiple surgical procedures has been hypothesized to be a risk factor, especially in children with spina bifida, because of the extensive mucosal exposure to latex gloves. Some studies have found an association with increasing numbers of surgical procedures;[40,50] others have not.[18,24,49,51] In this study, however, the number of surgical procedures was not associated with the presence of latex-specific IgE. The lack of association between sensitization and number of gloves worn daily, duration of time each pair was worn, or pair-hours of glove use per day and sensitization was not unprecedented. Others have documented a lack of association between measures of glove use and sensitization.[15,16,28] However, retrospective self-reports of glove use as a measure of exposure are subject to error. The lack of association with job title/category has also been documented in other studies.[16,18,28]

Results of area air sampling during this investigation reveal that very low levels of airborne NRL proteins were found at the locations sampled. Concentrations ranged from less than 0.12 to 3.33 ng/m^3. Airborne NRL was more commonly present

in clinical areas, where both powdered and powder-free NRL gloves were used, than in non-clinical areas of the hospital, where no gloves were used. NRL was reported at trace to quantifiable levels in 13 of 16 (81%) of samples from clinical areas, compared to 2 of 7 (29%) samples from non-clinical areas. It is difficult to assign any meaning to the finding that the nonsensitized had significantly higher airborne concentrations of NRL proteins in their work areas because the levels were extremely low overall.

One hospital in the U.S. (which had switched to powder free gloves) adopted an in-house guideline of 10 ng/m^3 for total NRL allergen.[52] The 10 ng/m^3 guideline was based on extensive industrial hygiene sampling at the hospital which suggested that 10 ng/m^3 is a concentration seldom exceeded when powder-free gloves were used at the facility. When sampling results exceed 10 ng/m^3 at this hospital, uncontrolled sources of latex allergen, such as NRL in environmental dust, are investigated. Another study, in a hospital laboratory,[53] found that when powdered latex gloves were used, NRL concentrations ranged from 39–311 ng/m^3. In the same laboratory, concentrations of NRL were less than 0.02 ng/m^3 when powder-free gloves were used. A study in a large medical center found concentrations ranging from 0.3 to 1.8 ng/m^3 in areas where powdered gloves were never or seldom used, and from 13 to 208 ng/m^3 in areas where powdered gloves were used frequently.[45]

The hospital's ventilation system does not use ceiling plenums as return pathways for building supply air, and this is reflected in the low to absent amounts of NRL allergen found on the backs of ceiling tiles. Environmental dusts which contain NRL can pose a hazard for health care workers or other employees who might be exposed to NRL-containing environmental dusts if such dusts are disturbed during maintenance activities. NRL allergen was present in all of the filter dust cake collected from AHUs which serve clinical areas. NRL (adsorbed to USP cornstarch) is reported to be present in a variety of particle sizes, and in one study with a mass aerodynamic diameter of greater than 7 micrometers.[45] This information suggests that AHUs properly configured with a minimum of 30–35% efficient pleated panel or pad prefilters and 65% or greater efficient bag or pocket final filters should be effective in removing NRL-containing particles from building return air.

One limitation of this study is the cross-sectional nature of the investigation. It is possible that sensitized workers who were symptomatic left the workplace. Thus, however, did not appear to be a major factor since there was no difference in years worked in the department or in the hospital by either exposure classification or latex sensitization status. In addition, we asked if employees had ever had another job or training position where they wore at least one pair of latex gloves daily, but we were not able to quantify levels of previous exposure. We found no difference in prevalence of sensitization between those who ever had occupational exposure to latex gloves and those who never had. We did not inquire about non-occupational exposures to latex other than surgery, but there is no reason to suspect they would differ between the two occupational/exposure groups. Symptoms and exposure were self-reported. Other potential limitations are that serologic testing may be less sensitive than SPT, but as noted previously, the Pharmacia CAP has been shown to be highly sensitive and specific.

Strengths of this study include the large sample size, the high participation rates, the use of air sampling to quantify area airborne concentrations of latex, and the inclusion of a virtually unexposed comparison group.

CONCLUSIONS

We found that neither current nor past occupational latex glove use was a significant risk factor for the development of latex sensitization. Job category was not associated with sensitization, either. Atopy is an established risk factor for the development of

sensitization to latex, and this was supported by our study. A large percentage of sensitized individuals were asymptomatic. Sensitized individuals were not more likely to experience work-related respiratory allergic symptoms, but they did have higher rates of hand urticaria and hand dermatitis, although the differences were not statistically significant. Airborne, surface, and filter concentrations of latex proteins were higher in the work areas of the nonsensitized employees than in the work areas of the sensitized employees, but levels were very low, even in areas where powdered gloves were used. Use of latex gloves was associated with self-reported work-related hand dermatitis, rhinoconjunctivitis, and hand urticaria, but not with asthma or generalized urticaria. However, use of any type of gloves will increase irritant contact dermatitis.

RECOMMENDATIONS

Because over 6% of the employees in this study are sensitized and thus at risk of adverse reaction to NRL, it is important to reduce exposures in the hospital to a minimum. The following recommendations for preventing latex allergy in the workplace are based on current knowledge and a common-sense approach to minimizing latex-related health problems.[2]

1. Provide workers with nonlatex gloves to use when there is little potential for contact with infectious materials (for example, in the Food Service Industry).

2. Appropriate barrier protection is necessary when handling infectious materials. If latex gloves are chosen, provide reduced protein (<50 micrograms of total water extractable protein per gram as per FDA labeling regulations), powder-free gloves to protect workers from infectious materials while minimizing their exposure to NRL.

3 Ensure that workers use good housekeeping practices to remove latex-containing dust from the workplace:

Identify occupied areas that might become contaminated with latex dust for frequent cleaning (upholstery, carpets, ventilation ducts, and plenums) Use high-efficiency, low-emission vacuum cleaners and bags.

Make sure that workers carefully change ventilation filters and vacuum bags in latex-contaminated areas, and take precautions to avoid dislodging filter dust into the environment

Insure that HVAC maintenance personnel understand that dust laden prefilters and final filters should be handled with care to insure that NRL-containing dust is not accidently released into building supply air during maintenance activities such as filter change-outs Maintenance employees should avoid excessive exposures to dusts which might be generated during filter change-out. If necessary, use a NIOSH approved N-95 filtering facepiece respirator to reduce exposures to dusts from AHU filters.

4 Provide workers with education programs and training materials about latex allergy

5. Periodically screen high-risk workers for latex allergy symptoms. Detecting symptoms early and removing symptomatic workers from latex exposure are essential for preventing long-term health effects. Medical removal should not be a substitute for other more effective means of protecting workers (reducing or eliminating exposure). In cases where medical removal is necessary, the wages and benefits of the worker should be protected.

6 Evaluate current prevention strategies whenever a worker is diagnosed with latex allergy.

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Table 1. Participation Rates in Non-clinical Areas

Department	Participation Rate (%)
Outpatient/Emergency Department Admitting	9/10 (90%)
Inpatient Admitting	6/9 (67%)
Material Management	23/32 (72%)
Information Services	18/21 (86%)
Medical Records	24/31 (77%)
Environment of Care	40/47 (85%)
Medical Education	4/5 (80%)
Pastoral Care	7/7 (100%)
Library	2/3 (67%)
Human Resources	9/14 (64%)
Business Office	14/19 (74%)
Nursing Staff Office	14/15 (93%)
Volunteer Office	1/1 (100%)
Marketing	6/8 (75%)
Patient and Family Counseling	9/12 (75%)
Payroll and Reimbursement	4/7 (57%)
Quality Assurance	9/9 (100%)
Finance	19/24 (79%)
Audiovisual	2/2 (100%)
Sisters of Charity	6/7 (86%)
Total	228/285 (80%)

Table 2. Participation Rates in Clinical Areas

Department	Participation Rate (%)
Emergency Department	138/166 (83%)
Laboratory	98/106 (93%)
Labor and Delivery	68/83 (82%)
Total	304/355 (86%)

Table 3. Demographics and Selected Characteristics by Exposure Group

	No Latex Gloves n=239	Latex Gloves n=248
Mean Age (Years)	44	39*
Gender		
Male	25%	26%
Female	75%	74%
Race		
White	79%	83%
Black	7%	6%
Hispanic	11%	7%
American Indian or Alaskan native	0%	1%
Asian or Pacific islander	3%	3%
Other	1%	1%
History of Atopy	60%	61%
Smoking Status		
Current	17%	15%
Former	27%	24%
Never	56%	61%
Years Worked in Current Department		
<1	22%	23%
1–5	34%	31%
6–10	18%	22%
11–20	19%	17%
>20	7%	8%
Average Number of Hours Worked Per Week		
1–40	55%	78%*
40+	45%	22%*

*$p < 0.05$

Table 4. Prevalence (%) of Work-related Health Effects# by Latex Glove Use

	No Latex Gloves	Latex Gloves
Asthma	4/246 (2%)	2/260 (1%)
Rhinoconjunctivitis	19/240 (8%)	42/257 (16%)*
Hand Urticaria	5/243 (2%)	26/262 (10%)*
General Urticaria	5/241 (2%)	13/262 (5%)
Hand Dermatitis	12/243 (5%)	61/260 (24%)*

defined as either present at work, but not at home, or present both at work and at home, but improved while away from work

* $p < 0.01$

Table 5. Median Number of Gloves Used Per Day by Work-related Health Effect

Health Effect	Present			Absent		
	n	Median	Range	n	Median	Range
Asthma	6	0	0-160	498	2	0-160
Rhinoconjunctivitis	61	10	0-50	434	0*	0-160
Hand Urticaria	31	20	0-75	472	0*	0-160
General Urticaria	18	19	0-75	483	1*	0-160
Hand Dermatitis	73	15	0-160	428	0*	0-100

* $p < 0.05$

Table 6. Median Daily Pair–Hours of Glove Use by Work-related Health Effect

Health Effect	Present			Absent		
	n	Median	Range	n	Median	Range
Asthma	6	0	0-8	497	0.5	0-193
Rhinoconjunctivitis	61	3.8	0-50	433	0*	0-193
Hand Urticaria	31	6.3	0-50	471	0*	0-193
General Urticaria	18	4.6	0-50	482	0.5*	0-193
Hand Dermatitis	72	5.6	0-53	428	0*	0-193

* $p < 0.05$

Table 7. Prevalence (%) of Work–related Health Effects by Level of Daily Glove Use

	Rhinoconjunctivitis* n (%)	Hand Urticaria* n (%)	General Urticaria* n (%)	Hand Dermatitis* n (%)	Asthma n (%)
0 pairs of gloves	19 (8)	5 (2)	5 (2)	12 (5)	4 (2)
1–9 pairs	9 (12)	5 (6)	0 (0)	17 (21).	1 (1)
10–18 pairs	12 (16)	3 (4)	4 (5)	11 (15)	1 (1)
19+ pairs	21 (22)	18 (18)	9 (9)	31 (31)	0 (0)

* $p<0.05$

Table 8. Prevalence (%) of Work-related Health Effects by Latex-specific Antibody Status

	Negative Latex-specific IgE (<0.35 kU_A/L)	Positive Latex-specific IgE (≥0.35 kU_A/L)
Asthma	6/479 (1%)	0/32 (0%)
Rhinoconjunctivitis	59/471 (13%)	3/31 (10%)
Hand Urticaria	27/479 (6%)	4/31 (13%)
General Urticaria	18/477 (4%)	0/31 (0%)
Hand Dermatitis	67/477 (14%)	8/31 (26%)

Table 9. Environmental Sampling in Non-clinical Areas

Sample Type	Location and Sampling information	Area Latex (ng/m³)	Surface µg/100cm²	Filter dust	Glove usage
Area	Medical Education - AHU 4	< LOD			no gloves
Ceiling tile	100 cm², centered on back surface		< LOD		
Filter dust	30% pleated pre, 75% mini pleat final filters			< LOD	
AHU	RA duct near access panel		< LOD		
Area	Outpatient registration - AHU 2 Russell	< LOD			no gloves
Ceiling tile	100 cm², centered on back surface		< LOD		
Filter dust	from AHU 2 Russell			< LOD	
AHU	from AHU 2 Russell, before final filters		< LOD		
Area	Medical records - AC 8	0.26			no gloves
Ceiling tile	100 cm², centered on back surface		< LOD		
Filter dust	no sample, 30% pre 90% final filters				
AHU	AC-8 between pre and final filters		Trace		
Area	Inpatient admitting - AHU DD1 A&B	Trace			no gloves
Ceiling tile	100 cm², centered on back surface		< LOD		
Filter dust	no sample, 10% pre, 65% final bag filters				
AHU	100 cm² downstream of RA fan on AHU DD1 A&B		368		
Area	Facilities Management - AHU DD1 A&B	< LOD			no gloves
Ceiling tile	100 cm², centered on back surface		< LOD		
Filter dust	no sample, 10% pre, 65% final bag filters				
AHU	see sample above for inpatient admitting				

Table 9 *(continued)*

Area	Mullen Bldg, 3rd Fl FCU above Os	< LOD	no gloves
Ceiling tile	no sample, hard ceiling		
Filter dust	no sample		
AHU	100 cm², center, back surface of access panel		
Area	I-70 Executive Center	< LOD	no gloves
Ceiling tile	no sample		
Filter dust	no sample		
AHU	no sample		

Notes:

LOD	=	limit of detection
MDC	=	minimum detectable concentration (0.12 ng/m³), based on a sample volume of 165,402 Liters
AHU	=	air handling unit
FCU	=	fan coil unit
AHU interior	=	inside AHU or duct plenum
Ceiling tile	=	back side of tile, 100cm² surface area
Area sample	=	on cart 52" above floor in occupied/patient care areas
Trace	=	concentration at the LOD for analytical method
< LOD	=	latex reported not detected (ND) on analytical report
ng/m³	=	nanograms per cubic meter of air
ng/100cm²	=	nanograms per 100 square centimeters

air samples: LOD = approximately 20 nanograms (ng)/sample
surface samples: LOD = approximately 100 ng/sample

Table 10. Environmental Sampling in Clinical Areas

Sample Type	Hospital Location, Air Handler	[illegible] ng/m³	Surface ng/100 cm²	[illegible] ng/g	Glove[illegible]
Area	ED zone 1, Rm 6, AC 3 and AHU 1 Russell	0.62			P, PF
Ceiling tile	no sample				
Filter dust	filter type 30% pre filters, 90% final filters			13,196	
AHU	100 cm² floor of AHU plenum		< LOD		
Area	ED zone 2, bed 16 - AC 3	2.00			P, PF
Ceiling tile	100 cm² ceiling tile near bed 16		< LOD		
Filter dust	filter type 35% pre filters, 90% final filters			4,433	
AHU	100 cm² duct of AC-3 AHU		< LOD		
Area	ED zone 2, Rm. 12 - AC 3 and AHU 1 Russell	< LOD			PF
Ceiling tile	see above sample				
Filter dust	see sample for ED zone 1				
AHU	see sample above				
Area	ED zone 3, bed 35 - AHU 1 Russell	0.41			P, PF
Ceiling tile	CT near bed 35		< LOD		
Filter dust	filter type 10% pre filter and 65% final filters			15,196	
AHU	100 cm² floor of AHU plenum		< LOD		
Area	ED zone 4, room 57, AC 3, AHU 1 Russell	Tr			P, PF
Ceiling tile	no sample				
Filter dust	see sample above				
AHU	see sample above				
Area	Immediate Resp. Lab - dedicated single AHU	Tr			P, PF
Ceiling tile	CT near hematology area		< LOD		
Filter dust	filter type 30% pocket pad filter			16,214	

Table 10. ***(continued)***

Sample	Description	Results	Surface	Filter dust	Status
		ng/m³	ng/100cm²	ng/sample	
AHU					
Area	Immediate Resp. Lab - dedicated single AHU	< LOD			P, PF
Ceiling tile	see above sample				
Filter dust	see IRL sample above				
AHU					
Area	Immediate Resp. Lab - dedicated single AHU	1.1			P, PF
Ceiling tile	CT in lab area		<LOD		
Filter dust	see IRL sample above				
AHU					
Area	L&D Del. Rm 244 - AHU AC 18	2.90			P, PF
Ceiling tile	no sample				
Filter dust	filter type 10% pad pre 65% final bag filter			83682	
AHU					
Area	L&D Del. Rm 247 - AHU AC 16	1.1			P, PF
Ceiling tile	no sample				
Filter dust	see L&D Rm. 244 sample above				
AHU					
Area	L&D Suite 242 - AHU AC 16	3.33			P, PF
Ceiling tile	100 cm² ceiling tile, room 242		118		
Filter dust	see sample above				
AHU interior	100 cm² MA plenum before pre filters		1,022		
	see above, prefilter AC-18				
Area	L&D Del. Rm 3 - AHU AC 16	1.10			P, PF
Ceiling tile	solid ceiling, no sample				
Filter dust	see L&D suite 244 sample above				

Table 10. *(continued)*

Location	Hospital Section - Use Activities	Level ng/m²	Surface Dust Level ng/100cm²	Bulk Dust Level ng/gm	Comments
Area 1	Microbiology Laboratory - AC- 10	< LOD			P, PF
Area 2	Microbiology Laboratory	0.57			
Ceiling tile	solid ceiling, no sample				
Filter dust	filter type 10% pad pre filter, 65% pocket filter			4473	
Area 1	Typing- cross match lab - AHU AC 10	0.49			P, PF
Area 2	Typing- cross match lab	0.39			
Ceiling tile	100 cm² floor of AHU		3,952		
Filter dust	see micro. lab filter dust sample above				

Notes:

LOD	=	**limit of detection**
LOQ	=	**limit of quantitation**
MDC	=	**Minimum detectable concentration (0.24 ng/m³), based on a sample volume of 165,402 Liters**
MA	=	**make-up air (supply air to building)**
AHU	=	**air handling unit**
FCU	=	**fan coil unit**
AHU interior	=	**inside AHU or duct plenum**
ED	=	**Emergency Department**
L&D	=	**Labor and Delivery**
Ceiling tile	=	**sample collected on back side of tile, 100cm² surface area**
Area sample	=	**sampler placed on cart 52" above floor in occupied or work areas**
Trace	=	**concentration at LOD for analytical method**
< LOD	=	**latex reported not detected (ND) on analytical report**
ng/m³	=	**nanograms per cubic meter of air**
ng/100cm²	=	**nanograms per 100 square centimeters**
ng/gm	=	**nanograms per gram**

air samples: LOD = approximately 40 nanograms (ng)/sample
filter dust: LOD = 500 ng/gram of dust
surface samples: LOD = 100 ng/sample

Table 11. Geometric Mean Levels of Environmental NRL Proteins by Sensitization Status

Geometric Mean	Sensitized	Not Sensitized
Airborne Latex	0.34 ng/m^3 (n=23)	0.47 ng/m^3* (n=393)
Surface Latex	124 9 ng/100 cm^2 (n=22)	172.2 ng/100 cm^2 (n=375)
Filter Latex	14,307 6 ng/gm dust (n=14)	25,279 2 ng/gm dust (n=299)

* $p<0.05$

National Institute for Occupational Safety and Health (NIOSH) Study of Latex Allergy in Hospital Employees Summary of Findings

What NIOSH Did

- Sampled air, surfaces, and air handling unit filters for latex proteins, in clinical and nonclinical areas
- Administered questionnaires to employees and tested their blood for antibodies to latex (latex sensitization)

What NIOSH Found

- Latex proteins were more commonly found in clinical areas, but airborne latex levels were very low in all areas
- Neither current nor past use of latex gloves was associated with latex sensitization (the presence of antibodies to latex in worker's blood)
- A personal history of allergies was related to latex sensitization
- Itchy, runny and stuffy noses; itchy, watery eyes; and hives were more common among workers who used latex gloves, but these effects were not correlated with latex sensitization

What Exempla St. Joseph Hospital Managers Can Do

- Provide nonlatex gloves to workers with low potential for contact with infectious material, for example, food service employees
- If latex gloves are provided for employees who handle infectious material, they should be low-protein and powder-free
- Ensure workers use good housekeeping practices to remove latex-containing dust from the workplace
- Provide educational programs and materials about latex allergy to workers
- Periodically screen workers for latex allergy symptoms

What Exempla St. Joseph Hospital Employees Can Do

- Use nonlatex gloves when there is little potential for contact with infectious material, such as in food service or routine housekeeping duties
- If you use latex gloves, use low-protein, powder-free gloves
- Use good housekeeping practices to remove latex-containing dust from the workplace
- Use latex allergy educational programs and materials provided by your employer
- If you develop symptoms of latex allergy avoid direct contact with latex-containing objects until you see a doctor who knows about the problem

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NIOSH National Institute for Occupational Safety and Health

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Prevalence of IgE-mediated allergy to latex in hospital nursing staff

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Abstract

Background: IgE-mediated hypersensitivity to latex proteins has become a significant clinical problem over the last decade. Nursing and medical staff are at risk because of their occupational exposure to latex.

Aims: To determine the prevalence of type I hypersensitivity to latex allergens in the nursing staff of an Australian hospital.

Methods: A questionnaire which asked about symptoms associated with the use of latex gloves was completed by 140 nurses working in the Alfred Hospital (72 in general medical wards, 68 in intensive care units). Skin prick tests with eluates of five different types of latex glove as well as common aeroallergens (rye pollen and house dust mite) and banana extract were performed.

Results: Thirty-one nurses (22%) were skin prick test positive to at least one of the five latex glove eluates. All of these nurses were atopic, having positive skin prick tests to rye pollen or house dust mite. Symptoms of local dryness, itch and erythema associated with glove use were reported by more than half the study group, but not more frequently by those who were skin prick test positive to latex. Urticaria associated with glove use was reported more frequently by those with positive latex skin prick tests (13% vs 4%, $p=0.05$). Eighty-seven per cent of the nurses who were latex skin test positive were also positive to banana extract.

Conclusions: IgE-mediated hypersensitivity to latex is common in nurses working in an Australian hospital. Glove associated symptoms were frequently reported, but in most cases the symptoms were more typical of irritant or contact dermatitis rather than type I hypersensitivity reactions. However, the extent of subclinical sensitisation to latex found in this study suggests that symptomatic latex allergy is likely to emerge as an increasing problem for nursing staff in this country. (Aust NZ J Med 1997; 27: 165-169.)

Key words: IgE-mediated hypersensitivity, latex allergens, nursing staff.

INTRODUCTION

Latex gloves have been recognised as a cause of contact dermatitis for many years.[1] The inflammatory response is a consequence of cell mediated hypersensitivity to chemical accelerators used in the manufacture of latex products. However, recognition of IgE-mediated hypersensitivity reactions to protein allergens within latex is a much more recent phenomenon. Contact urticaria while using latex gloves was first described in 1979,[2] and two cases of intraoperative anaphylaxis resulting from latex hypersensitivity were reported

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in 1984.[3] The number of cases of latex allergy published in the literature has increased exponentially over the last decade, reflecting the greatly increased use of latex gloves by health care workers since the adoption of universal precautions.[4] Studies performed in several different countries have found that between 5.5 and 17% of exposed health care workers have been sensitised to latex allergens.[5-7]

The manifestations of latex allergy include urticaria, rhinitis, conjunctivitis, bronchospasm and anaphylaxis.[8] Cornstarch powder applied to gloves can adsorb latex proteins, which become airborne when the glove is used.[9] Significant levels of latex allergens have been detected in air samples from operating theatres and hospital laboratories.[10] Given these findings and the ubiquitous presence of latex products within hospitals, it is difficult for the highly sensitised hospital personnel to avoid contact with latex allergens. Accordingly, latex allergy may have profound career implications for a health care worker.

A recently published study reported a 9% prevalence of symptoms suggestive of latex hypersensitivity in dental workers at a large dental facility in western Sydney.[11] However, the prevalence of latex hypersensitivity among nurses working in an Australian hospital has not been reported previously. The objectives of this study were to determine the skin prick test reactivity to latex allergens in nurses and to relate these results to the symptoms which nurses attributed to glove use.

Subjects

One hundred and forty nurses employed at the Alfred Hospital (Melbourne, Victoria) were evaluated for latex allergy. Seventy-two nurses were working on general medical wards and 68 in the intensive care unit. All but four were in full time employment (working more than 30 hours a week). The protocol was reviewed and approved by the hospital's Ethics Committee and signed consent was obtained from all participants.

METHODS AND MATERIALS

The nurses were requested to complete a questionnaire which asked the average number of hours worked each week, the number of hours spent gloved each day and number of glove changes over a shift, symptoms attributed to glove use and probed a history of allergic diseases including food and drug allergies.

Skin prick tests were then performed with extracts of rye pollen, house dust mite (*Dermatophagoides pteronyssinus*, 10,000 AU/mL), banana (1:10 wt:vol) (Hollister-Stier Laboratories), and eluates of five different brands of latex gloves. The latex glove eluates were prepared by soaking 1 g of glove cut into small pieces in a 5 mL volume of normal saline for 15 minutes and then pouring off the eluate.[12] The gloves used were Gammex and Conform (Ansell International), Triflex (Baxter Healthcare), Duotex (Smith and Nephew) and Profeel (Wembley Rubber Company). Banana extract was chosen because a cross reactivity between latex and banana (and a number of other fruits) has been reported by others.[13,14] Normal saline was used as a negative control and histamine phosphate (10 mg/mL) as a positive control. The skin prick tests were examined after 15 minutes, and the maximum diameter of the wheals were recorded by a single observer. Wheals 3 mm larger than the negative control were considered positive.

Frequency data were compared by Chi-square analysis and non-paired *t*-tests were used to compare other values. The data are expressed as means ±standard error of the means.

TABLE 1
Skin Prick Test Results

	Latex skin prick positive *n*=31		Latex skin prick negative *n*=109	
	Skin prick positive (%)	Mean wheal diameter (mm)	Skin prick positive (%)	Mean wheal diameter (mm)
Rye	84	8.3±0.6	28	7.1±0.8
House dust mite (Der p I)	97	8.9±0.6	41	5.6±0.3
Banana	87	3.9±0.2	9	3.8±0.2
Gammex	74	3.6±0.2	-	-
Conform	71	4.0±0.2	-	-
Triflex	74	4.2±0.2	-	-
Duotex	68	4.2±0.4	-	-
Profeel	48	3.9±0.2	-	-
Histamine	100	5.2±0.1	100	5.5±0.1

RESULTS

Thirty-one (22%) of the 140 nurses tested were skin prick positive to at least one of the five latex glove eluates. There were no significant differences between the latex skin prick positive and latex skin prick negative groups in regard to age, sex distribution, years working as a nurse, hours worked each week, hours gloved each day and number of glove changes each day. A history of atopic illnesses was strongly associated with latex prick test positive results; 56% of the latex

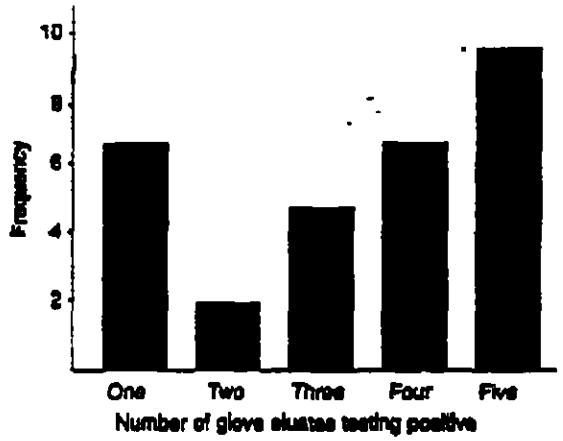

Figure 1: The number of types of glove eluates which were skin prick positive in each subject as frequency.

positive subjects had a history of rhinitis and 28% a history of asthma, whereas none of the latex negative subjects had a history of these two conditions ($p<0.0001$). Four of the latex positive group had a history of drug allergy and one had allergic symptoms after eating bananas.

Latex positive skin prick tests were strongly associated with atopy (which was defined for the purpose of this study as a positive skin prick test to rye pollen or Der p I) (Table 1). All of the nurses who were latex positive were atopic. Of the nurses who were latex skin prick test positive, only one third had wheals >3 mm diameter with all five glove types tested (Figure 1). The mean wheal diameter elicited by the latex glove eluates was less than the histamine control (4.0±0.1 mm vs 5.2±0.1 mm, $p<0.0001$).

A comparison of the latex exposure and latex skin prick test results is made between intensive care and medical ward nurses in Table 2.

Most of the nurses associated some symptoms with glove use (Table 3). The most commonly reported symptoms were dryness, erythema and itch affecting the skin of the hands. Except for

TABLE 2
Characteristics of Intensive Care Compared with General Medical Ward Nurses

	Intensive care n=68	Medical wards n=72	Significance
Latex skin prick positive	19 (28%)	12 (17%)	$p<0.11$
Age (years)	30±1	28±1	$p<0.0001$
Years as a nurse	10±1	4±1	$p<0.0001$
Hours worked each week	38±1	36±1	ns
Hours gloved	3.1±0.2	2.2±0.1	$p<0.0001$
Glove changes each shift	17±1	9±1	$p<0.0001$

TABLE 3
Symptoms Associated with Latex Glove Usage

	Latex skin prick test positive	Latex skin prick test negative
Skin dryness	26 (84%)	80 (73%)
Itch	18 (58%)	52 (48%)
Skin erythema	17 (55%)	48 (44%)
Urticaria	4 (13%)*	4 (4%)*
Eczema	10 (32%)	29 (27%)
Eye symptoms	4 (13%)	6 (6%)
Nasal symptoms	5 (16%)	10 (9%)
Dyspnoea	1 (3%)	0 (0%)
Asthma	0 (0%)	0 (0%)
Rapid onset†	23	65
Delayed onset†	7	5

The nurses were asked to estimate the time delay between putting on gloves and onset of each symptom. If the first symptom began less than one hour after putting on the gloves, the subject has been classified as a rapid responder

*$p<0.05$ (comparing latex skin prick test positive and negative nurses for this symptom).

†The delay of onset of symptoms was answered by 30 of the nurses who were latex skin prick test positive and 70 nurses who were skin prick test negative.

urticaria, no symptom was reported more frequently in the latex skin prick positive group than in the skin prick negative group. In the majority of subjects, the first symptom associated with glove use occurred within an hour of putting the gloves on.

Twenty-seven of 31 latex skin prick positive subjects (87%) were skin prick positive to banana allergen. Only 10 (9%) of the latex skin prick negative group tested positive to banana extract ($p<0.0001$).

DISCUSSION

These results show that hypersensitivity to latex allergens is common among nurses working in our institution. The proportion who were latex skin prick positive (22%) was higher than in series reported from hospitals in Europe and North America.[1-7] Two possible explanations for the high observed prevalence are 1) the nature of the study group and 2) the method of testing for latex specific IgE. The prevalence of atopy was high in this group of Australian nurses; fifty-eight per cent of the study group were atopic and atopy has consistently been reported to be strongly associated with latex allergy.[15] Skin prick testing is more sensitive than radioallergosorbent (RAST) tests,[16] and eluates from several different gloves were used. As only one third of the latex positive patients developed wheals with all five gloves, testing with a smaller number of gloves eluates would have reduced the number of positive results.

The variability in skin prick test responsiveness between the different brands of gloves suggests either qualitative or quantitative differences in the allergenic proteins present in the gloves. Up to 500 fold differences in the quantity of latex allergen have been found between gloves of different manufacturers.[1] In this study, there were no significant differences in the percentages of positive skin prick tests produced by eluates of the different brands. The Ansell gloves, which are regarded to be a low allergen brand, caused as many positive reactions as any of the other brands. This may be a consequence of the almost exclusive use of gloves of *this* brand within the hospital, resulting in the personnel being exposed to the full range of allergens contained within it.

The majority of nurses associated a number of symptoms suggestive of local irritation (dryness, erythema and itch) with glove use. With the exception of urticaria, there was no difference in the frequency of reporting of glove associated symptoms between those nurses who were latex skin prick positive and those who were not. This result suggests that in many cases latex hypersensitivity was either asymptomatic, or the symptoms caused by it were obscured by the high frequency of non-specific symptoms reported. It is likely that many of the non-specific symptoms were caused by irritant contact dermatitis resulting from regular hand washing and the skin's moist environment within a latex glove. Other cases of local irritation may represent allergic contact dermatitis. Allergic contact dermatitis has been shown to be associated with a high prevalence of immediate hypersensitivity to latex allergens.[3] The dry, fissured skin of allergic contact dermatitis is likely to promote greater contact between latex protein allergens and antigen presenting cells within the dermis.

Eighty-seven per cent of nurses who were skin prick positive to latex were also positive to banana eluate, which suggests a strong biochemical cross-reactivity between these two allergens. Latex allergy has been associated with allergy to a number of fruits such as banana, avocado, chestnut, kiwifruit and others.[4] Between 28 and 50% of latex allergic subjects have been reported to have banana allergy.[3,5,6] A recent immunoblot inhibition study has demonstrated that more than ten allergens are involved in the cross-reactivity between latex and banana.[6] In our study, only one of the 27 nurses who were skin prick positive to banana reported allergic symptoms after eating bananas. A similarly high rate of asymptomatic hypersensitivity to food extracts in latex allergic subjects has recently been reported.[7]

The results of this study demonstrate that a large number of the nurses working in our hospital are sensitised to latex allergens. Presumably this is a result of workplace exposure, both from the wearing of latex gloves and the inhalation of latex proteins carried in cornstarch powder. The reports published to date on the prevalence of latex allergy have been confined to single time point studies and so the natural history of latex allergy remains undefined in the absence of longitudinal studies. Such studies are urgently needed so that appropriate advice can be given to nursing or other medical professionals who are found to be sensitised to latex allergens.

There are several measures which can be taken to reduce the impact which latex allergy may have on health care professionals in Australia. Greater awareness of the problem should lead to more frequent recognition of type I hypersensitivity to latex. The diagnosis of this condition has been facilitated by the recent commercial development of a standardised latex allergen. Unfortunately this allergen is not yet widely available in Australia. Once the diagnosis of latex hypersensitivity has been established, the optimal management would include the avoidance of all latex containing products. As this is virtually impossible in the hospital environment, this may require some health care workers who have had life threatening allergic reactions to seek alternative employment. In those with less severe symptoms, or who have asymptomatic hypersensitivity, reducing allergen exposure by using low allergen gloves or gloves made of latex alternatives such as neoprene and fastidious hand care to reduce irritant dermatitis, may suffice.

The high prevalence of latex hypersensitivity found in this study would suggest that latex allergy is likely to become an increasing problem for Australian health professionals. ■

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The prevalence of anti-latex IgE antibodies in 1000 volunteer blood donors

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Background: *Latex allergy has been recognized as a medical problem with increasing frequency since the mid 1980s. Although certain groups of individuals, such as health care workers, have been recognized as having increased risk for latex allergy, little is known about the prevalence of latex allergy in the general population.*
Methods: *To estimate the prevalence of latex allergy among healthy adults, we measured anti-latex IgE antibodies in residual serum samples from 1000 volunteer Red Cross blood donors. The 1000 samples were from a sample of blood units collected from workplace mobile sites throughout Southeastern Michigan. Samples collected from mobile sites operating at health care institutions were excluded to minimize sampling of health care workers. Anti-latex IgE antibodies were measured by using the AlaSTAT assay (Diagnostic Products Corp, Los Angeles, Calif.) according to the manufacturer's directions. Samples with anti-latex IgE concentrations of 0.35 IU/ml or greater were classified as positive and samples with IgE concentrations of 1.50 IU/ml or greater were classified as strongly positive. All positive samples were assayed a second time to confirm the result. All positive samples were also measured with the CAP assay (Pharmacia Diagnostics, Dublin, Ohio).*
Results: *The samples tested were from donors with a mean age of 37.8 years, and 47% were women. Sixty-four (6.4%, 95% confidence interval = 4.9-8.1%) of the samples were confirmed as repeatedly positive for anti-latex IgE, and 23 of the 64 positive samples were strongly positive (2.3% of the 1000). Sixty-one percent of the samples positive as determined by the AlaSTAT assay were also positive as determined by the CAP assay. Samples from male donors were more likely to be positive than those from female donors (8.7% vs 4.1%, p = 0.003). Prevalence of positive samples was not related to age or race.*
Conclusions: *We conclude that the prevalence of detectable anti-latex IgE antibodies, in a large and relatively unselected adult population, is higher than previous estimates have suggested. Although the clinical significance of these observations needs further evaluation, the data suggest that latex allergy is not confined to individuals in previously recognized high-risk groups. (J Allergy Clin Immunol 1996;97:1188-92.)*

Key words: *Latex allergy, anti-latex IgE antibodies, prevalence, volunteer blood donors*

During the last decade, latex allergy has been increasingly recognized as a potential medical problem. Allergic reactions to latex have ranged from mild local urticaria to fatal anaphylaxis.[1-3] Because latex allergy has only recently been recognized, limited data are available concerning the extent of this problem. Several studies have shown that certain groups of individuals, with frequent exposure to latex, have a relatively high prevalence of latex allergy including children with spina bifida, health care workers, and rubber plant workers.[4-9]

Few studies have been done on the prevalence of latex allergy in individuals outside of recognized risk groups. Some have estimated the prevalence of latex allergy in the general population as less than one per thousand, and at least one study from Finland substantiates this estimate.[10, 11] However, a few small studies of relatively unselected children suggest that the prevalence may be higher.[12, 13] Our own experience with latex-induced reactions during barium enema examinations (six reactions of

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5554 procedures) suggested that the prevalence of clinically significant latex sensitivity in the population of southeastern Michigan could be as high as one per thousand.[1] If the estimate of one severe latex-induced reaction per thousand population were accurate, the prevalence of any latex sensitivity in the general population would be expected to be substantially greater than one per thousand.

It is difficult to obtain a large study population of individuals who are representative of the general population of a region. We believed that the study population that would best represent the general population of healthy adults in Southeastern Michigan was a sample of volunteer Red Cross blood donors.

METHODS

Serum samples

Samples were collected from residual serum tubes of 1000 blood donations over a 3-week period. All donations were from workplace mobile collection sites, excluding sites at health care institutions. To obtain a sample broadly representative of the population, no more than 30 samples per day were accepted from a single mobile unit. All donors were informed that a sample of the donated blood might be used for additional tests or to evaluate experimental blood tests, unless they objected. Strict confidentiality was maintained by identifying samples only by code numbers, which were matched with limited demographic data for analysis. It was not possible to ask the blood donors any questions about their personal allergic histories or potential risk factors for latex allergy.

In vitro assays

The AlaSTAT assay (Diagnostic Products Corp., Los Angeles, Calif.) was used for measuring anti-latex IgE antibodies according to the manufacturer's instructions. Previous experience with this assay suggested that it offered maximal sensitivity with good specificity.[14] Briefly, 50 μl aliquots of serum from each donor was added to duplicate assay tubes along with the liquid latex matrix. After a 1-hour incubation, the anti-ligand solution was added. This solution contains avidin, which binds the biotin on the liquid latex matrix to the biotin-coated walls of the assay tubes. The tubes were then washed three times to remove all unbound serum proteins. IgE that bound to the liquid matrix was detected by the addition of an enzyme-labeled anti-human IgE, followed by washing and the addition of a chromogenic substrate. The amount of IgE bound in the tube was determined by extrapolation from a standard curve. Samples with IgE concentrations of 0.35 IU/ml or greater were graded as positive. We arbitrarily chose to grade samples with concentrations of 1.50 IU/ml or greater as strongly positive. All positive samples were assayed a second time in another AlaSTAT assay to verify the positive result, and only samples positive in both assays were considered as positive in the analysis.

Because of the limited experience with in vitro tests for anti-latex IgE antibodies, we also re-assayed all positive samples, with sufficient serum, in the CAP assay (Pharmacia Diagnostics, Dublin, Ohio). The CAP assay was performed according to the manufacturer's instructions. Samples with IgE concentrations of 0.35 kU/L or greater were graded as positive. The CAP assay was chosen as a secondary comparison method because many investigators have found that the CAP assay has performed well with other allergens.[12, 16] It was not possible to evaluate all 1000 samples in the CAP assay.

Both the AlaSTAT and CAP results can be converted into class scores on the basis of reference curves. The criteria for the AlaSTAT classes are: 0, 0.00 to 0.29; 0/I, 0.30 to 0.34; I, 0.35 to 1.49; II, 1.50 to 2.99; III, 3.00 to 14.9; and IV, ≥15.0 IU/ml. The criteria for the CAP classes with traditional scoring are: 0, <0.35; I, 0.35 to 0.7; II, 0.7 to 3.5; III, 3.5 to 17.5; IV, 17.5 to 50; V, 50 to 100; and VI, >100 kU/L. The nominal criterion for classifying a sample as positive is the same, 0.35 U/ml or greater, in both assays, but the criteria for the classes are otherwise different.

TABLE I. Comparison of the AlaSTAT and CAP class scores in the 64 sera positive in the AlaSTAT assay

	CAP class				
	0	I	II	III	Total
AlaSTAT class					
0	0	0	0	0	0
I	25	10	5	1	41
II	3	4	6	0	13
III	3	0	5	2	10
Total	31	14	16	3	64

RESULTS

The 1000 samples tested came from donors with a mean age of 37.8 years (range, 17 to 66 years). Four hundred seventy (47%) of the donors were women; and 879 of the donors described themselves as white, 80 as black, and 41 as belonging to other racial groups. These proportions are similar to those of all blood donors in southeastern Michigan. No information concerning the occupations or personal allergy histories of the donors was obtained.

We first compared the results of the AlaSTAT and CAP assays in the 64 sera that were repeatedly positive according to the AlaSTAT. The results are shown in Table I. Overall, 39 (61%) of the 64 AlaSTAT-positive samples were also positive in

TABLE II. Distribution of positive test results for anti-latex IgE among 1000 study subjects by sex, age, and race

	AlaSTAT				
	Negative	Positive	Total (%)	p Value*	1990 Census (%)†
Sex					
Male	485	45	530 (53)		47.0
Female	451	19	470 (47)	0.014	53.0
Age					
<45 yr	665	41	706 (70.6)		
≥45 yr	271	23	294 (29.4)	0.14	
Race					
White	829	50	879 (87.9)		77.0
Black	70	10	80 (8.0)		20.6
Other	37	4	41 (4.1)	0.039	2.6

*p Values were determined by using the chi square statistic.

†Data from Census of Population and Housing 1990: Summary Tape File 1 on CD-ROM (Michigan), prepared by the Bureau of the Census. Washington, DC, 1991.

the CAP assay. The major differences in the results of the two assays are the 31 sera that were positive in the AlaSTAT and negative in the CAP, including six sera that were class II or III according to the AlaSTAT assay but negative according to the CAP assay. However, if the 23 sera with class II or III AlaSTAT results are considered, 17 of the 23 (74%) are positive according to the CAP assay.

The prevalence of anti-latex IgE antibodies according to the AlaSTAT assay was 64 of 1000 or 6.4% (95% confidence interval = 4.9-8.1%). Twenty-three of the 64 samples were strongly positive (IgE ≥1.50 IU/ml). As shown in Table II, positive samples were significantly more frequent in men than in women and in blacks compared with whites or others. Age did not appear to influence the prevalence of seropositivity. The composition of the entire five-county population, from which the studied blood samples were drawn, is also shown in Table II. The male-to-female ratio in the blood donors is the opposite of the ratio in the population, and whites are overrepresented among the blood donors.

DISCUSSION

We have found a 6.4% prevalence of seropositivity for anti-latex IgE antibodies in 1000 Red Cross volunteer blood donors from whom serum samples were obtained during 1993 in Southeastern Michigan. Units collected at health care institution sites were excluded to minimize the possibility of obtaining a spuriously high prevalence estimate because of the inclusion of a large number of health care workers. Because it was not possible to directly question the blood donors, we cannot exclude the possibility that some of them may have been occupationally exposed to latex, either as health-care workers or in other occupations. The overall prevalence of seropositivity for anti-latex IgE antibodies remains high, even if the only samples considered positive are those that were strongly positive (2.3%) or those that were positive according to both the AlaSTAT and CAP assays (3.9%). The prevalence of 6.4% is consistent with our previous experience of approximately one latex-induced reaction per 1000 patients during barium enema examinations.[1] In comparison with the 6.4% prevalence in this population of blood donors, we found an 8.8% prevalence of anti-latex antibodies, by using the same AlaSTAT assay and criteria for a positive test result, in a population of 741 inpatient registered nurses.[17]

The major strengths of this study are the large number of serum samples drawn from a population of relatively healthy adults and the objective measurement of anti-latex IgE antibodies. Some studies have relied on history of symptoms associated with latex exposure, which is an unreliable method of determining sensitivity.[3,6,7]

Concerns about confidentiality made it impossible to obtain any information directly from the donors about possible risk factors for latex allergy or clinical reactivity to latex. Lacking this information, we were not able to evaluate questions about specific risks for latex sensitivity. We speculate that blood donors, and others without recognized oc-

cupational exposure to latex, may become sensitized by latex contact with household rubber products or by contact with latex during routine medical care.

The 6.4% prevalence of detectable anti-latex IgE antibodies may initially appear to be unreasonably high, but this prevalence is low compared with the prevalence of anti-Hymenoptera venom IgE found in population surveys. Stuckey et al.[18] used the Pharmacia RAST to measure anti-honeybee IgE in 3439 subjects and found a RAST score of 2 or greater in 542 (15.8%) of the subjects. Of the 542 positive RAST test results, 450 (83%) occurred in individuals who did not have histories of adverse sting reactions.[18] Similar data were obtained by Golden et al.[19] in a study of a stratified sample of 320 employees representative of 2097 electric plant employees. Seventeen percent of workers had positive skin test results and 24% had positive in vitro test results in response to either or both honeybee and yellow jacket venoms. Only 3.3% of the workers had a history of systemic reactions after insect stings. These studies demonstrate that the prevalence of venom-specific IgE in unselected adults is relatively high, even though reported episodes of anaphylaxis are infrequent. Compared with these studies of the prevalence of venom-specific IgE, the 6.4% prevalence of anti-latex IgE antibodies found in our study is modest and consistent with the relatively infrequent reports of systemic reactions associated with latex exposure.

Another concern about the results of our study is whether the AlaSTAT assay is specific for anti-latex IgE. The small quantities of serum available precluded performing inhibition assays with the positive sera; however, we have performed multiple inhibition assays in the past, and we have always been able to inhibit positive AlaSTAT test results with latex extracts.[12-14] We also believe that the positive AlaSTAT test results accurately indicated the presence of anti-latex IgE antibodies because the CAP assay produced similar positive results in 61% of the AlaSTAT-positive sera. The discrepancy between the AlaSTAT positive results and negative CAP results in 31 sera may be due to several factors. We have observed similar discrepancies between AlaSTAT and CAP results with sera from individuals with histories highly suggestive of latex allergy, and we believe that the criteria for a positive CAP result may be unduly conservative, even though the criteria for a positive test result in both assays is 0.35 IU/ml specific IgE. Another possible explanation is that the relative concentrations of various latex proteins differ between the solid phases of the two assays. Differences in solid-phase latex protein concentrations are likely to affect the detection of anti-latex IgE antibodies. The two assays may also differ in the detection of IgE cross-reactivity between latex and other allergens. Because we did not test all samples in the CAP assay and we did not obtain histories or skin test data on the blood donors, we cannot comment on the relative diagnostic value of either test.

The most important feature of this study is that it provides a baseline estimate of latex sensitization in a relatively unselected adult population. Because latex allergy has only recently been commonly recognized and because latex use and manufacturing are rapidly changing, it will be valuable to resurvey similar populations in the future to determine whether the prevalence of latex sensitization in the adult population of the United States changes with time. It is also useful to have a baseline estimate of latex allergy in a general population to compare against estimates of the prevalence of latex sensitization in high-risk populations. Without an estimate of allergy in the general population, it is impossible to accurately estimate the magnitude of increased risk associated with belonging to the high-risk population.

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June 21, 2000

Office of the Secretary
Consumer Product Safety Commission
Washington, D.C. 20207

Re: Petition HP 00-2, Petition on Natural Rubber Latex

Dear Sir or Madam:

Textile Rubber & Chemical Company ("Textile Rubber") is a multinational research and manufacturing operation headquartered in Dalton, Georgia. Since 1953, Textile Rubber has been a leading processor and distributor of natural rubber latex ("NRL") and latex compounds for a variety of commercial and industrial uses. Among other applications, its products are used in scatter rug and bathroom carpet backing and in non-slip padding for bathtubs and showers. The Company additionally produces a wide range of specialty latex compounds for the manufacturing sector. In business for over forty-five years, the Company's latex division is today one of the world's largest suppliers of NRL to the floor covering and textile industries.

Given Textile Rubber's operations, the Company read with significant interest the recent NRL-related citizen petition (the "Petition") filed by Deborah M. Adkins with the Consumer Product Safety Commission (the "CPSC"). Pursuant to the CPSC's invitations referenced in the Tuesday, March 21, 2000, and Wednesday, May 24, 2000, editions of the Federal Register, 64 Fed. Reg. 15133 and 65 Fed. Reg. 33525, please accept this correspondence as Textile Rubber's comments concerning the Petition. As outlined below, Textile Rubber strongly opposes the actions requested by the Petition.

Actions Requested by the Petition

The Petition requests the CPSC to add NRL to the list of "strong sensitizers" found at 16 C.F.R. § 1500.13, thereby subjecting NRL and products containing it to regulation as a "hazardous substance" under the federal Hazardous Substances Act, 15 U.S.C. § 1261, et seq. (the "Act"). Among other things, this would require NRL and products containing it to carry certain warning labels pursuant to 15 U.S.C. § 1261(p)(1) and 16 C.F.R. § 1500.121.

Although somewhat unclear, the Petition additionally seems to request that, once the CPSC has designated NRL as a "hazardous substance" by virtue of it being a "strong sensitizer," the CPSC should further classify NRL as a "banned hazardous substance" pursuant to section 2(q)(1) of the Act, 15 U.S.C. § 1261(q)(1). Substances designated as "banned hazardous substances" are subject to a host notification, labeling and other requirements. See, e.g., 15 U.S.C. § 1274. In particular, the Petition seeks to require the labeling of toys and other articles containing NRL that are intended for children's use.