In support of the Petition, its proponent relies upon research conducted in connection with the federal Food and Drug Administration ("FDA") final rule regulating NRL-containing medical devices, 21 C.F.R. § 801.437; a July, 1998 Journal of the American Academy of Dermatology article (the "JAAD Article"); and a handful of CPSC incident reports. None of these items justifies the proposed rulemaking requested in the Petition.

The CPSC should deny the action requested by the Petition because insufficient basis exists to regulate NRL as a strong sensitizer and because the actions requested are too over reaching and are practically infeasible to implement.

Insufficient Basis Exists to Regulate NRL as a Strong Sensitizer

The Act defines the term, "strong sensitizer," as

> a substance which will cause on normal living tissue through an allergic or photodynamic process a hypersensitivity which becomes evident on reapplication of the same substance and which is designated as such by the [CPSC].

15 U.S.C. § 1261(k). CPSC regulations supplement this statutory definition and similarly require a substance to trigger, on normal living tissue, an allergic or other hypersensitivity upon exposure. See 16 C.F.R. § 1500.3(5)(i) ("a sensitizer is a substance that will induce an immunologically-mediated (allergic) response, including allergic photosensitivity" in "normal living tissue"); id. at § 1500.3(5)(v) ("the allergic hypersensitivity reaction occurs in normal living tissues, including the skin and other organ systems . . . following sensitization by contact, ingestion, or inhalation").

"Strong sensitizers" are among the CPSC's list of "hazardous substances" which are subject to regulation under the Act. 15 U.S.C. § 1261(f)(1)(A).

In order to declare a substance a "strong sensitizer," the CPSC must consider the frequency of occurrence and severity of the reaction, and must make a finding that the substance has a significant potential for causing hypersensitivity on normal tissue. 15 U.S.C. § 1261(k) ("Before designating any substance as a strong sensitizer, the [CPSC], upon consideration of the frequency of occurrence and severity of the reaction, shall find that the substance has a significant potential for causing hypersensitivity). See also, 16 C.F.R. § 1500.3(5) ("significant potential for causing hypersensitivity" is a relative determination that must be made separately for each substance").

CPSC regulations require this finding to be based upon, among other things, chemical or functional properties of the substance, documented medical evidence of allergic reactions obtained from epidemiological surveys or individual case reports, controlled in vitro or in vivo experimental assays, or susceptibility profiles in normal or allergic subjects. Id. None of the information submitted in support of the Petition meets these kinds of medical and scientific standards. Moreover, none of the information is sufficient to indicate that NRL has a significant potential for causing hypersensitivity.

The Petition Cites No Appropriate Scientific or Medical Evidence Upon Which to Make a Finding that NRL is a Strong Sensitizer.

The eleven case incident reports are individual accounts of complaints relating to products containing, in part, components that may (or may not) have contained NRL. With one exception, none of the reports identifies the latex component as NRL, as opposed to a synthetic product, for example.

Moreover, none of the reports offers any support for the notion that the latex component, as opposed to another substance used in the product, was responsible for the reaction alleged in the report. Indeed, even if the latex product involved was NRL, it is possible that another constituent of the product could have caused the reaction, either alone, or acting in combination with the latex component. It is well established that accelerators and product additives (e.g., constituents such as powder in latex gloves) are responsible for a significant majority of reported "latex" reactions.

Additionally, none of the incident reports reflects that the victims' skin would have been considered "normal tissue" as opposed to tissue that is particularly susceptible to reaction. A finding of regular susceptibility to "normal skin tissue" is a prerequisite to a determination that a substance is a strong sensitizer.

Moreover, the information relating to the FDA's study was limited to the use of NRL in medical devices for surgery and other medical applications. The FDA regulation was precipitated in part by the elevated levels of latex sensitivity manifested by latex glove-related exposures, particularly in the medical arena. Studies have shown a higher incidence of sensitization among health care professionals, those persons who undergo numerous surgeries, and those persons with mucous membrane exposure to NRL (e.g., as during obstetric and gynecologic procedures) This population, however, is already adequately protected by the FDA's labeling requirements for medical devices. See 21 C.F.R. § 801.437. The Petition seeks regulation of NRL well beyond the limits of the FDA's regulation and the limited population that its studies demonstrated was necessary to protect. None of the FDA data is thus relevant to the relief sought by the petitioner in this matter.

The JAAD Article similarly offers no medical or scientific support for the actions requested by the petitioner. This article is a broad overview of latex allergy in general. It references, in summary fashion, various research projects conducted over the years on latex sensitivity. The vast majority of these projects concerned healthcare workers and exposure scenarios in medical settings (e.g., sensitivity among allergy clinic patients, preoperative patients, blood donors). These populations are already protected by the FDA medical devices regulation. Thus, neither the JAAD Article itself, nor any of the studies referenced therein, is germane to the actions requested by petitioner

Absent any scientific or medical support of the type required by CPSC regulations to justify a "strong sensitizer" classification, the Commission must deny the relief sought in the Petition.

The Petition Cites No Evidence that NRL Has a Significant Potential for Causing Hypersensitivity that Affects a Significant Portion of the Population.

A strong sensitizer must have a significant potential for causing hypersensitivity. 15 C.F.R. § 1500.3(5)(iv) Moreover, "[a] strong sensitizer must be a substance which affects a significant portion of the population . . ." CPSC Advisory Opinion no. 12 (07/26/73). None of the information cited by the petitioner is sufficient to indicate that NRL has a significant potential for causing hypersensitivity. Indeed, both the FDA data and the JAAD Article indicate that NRL reactions occur in very small percentage of the country's population. See, e.g., JAAD Article at 7 ("prevalence of latex sensitivity in the general population is probably less than 2%.").

The lack of significant potential for causing hypersensitivity is borne out by Textile Rubber's own experience over the past four and a half decades in the NRL industry. Indeed, the Company has never received one comment or complaint from any of its manufacturers, distributors or other customers about NRL causing an allergic reaction. Moreover, the Company has polled most of its principal customers and manufacturing mills and has not learned of any grievances or other comments concerning any type of medical reaction associated with NRL. Given the volume of products produced by Textile Rubbers'

customers, the lack of such comments or complaints is significant.

As referenced in the Carpet and Rug Institute's article in "Industry Review 1998," an except of which is enclosed, during 1998 alone, 99,686,000 square yards of tufted, washable scatter rugs, bathmat and sets were produced. A typical bathmat 18"x36" is ½ square yard in size. This means that approximately 199,000,000 washable rugs were produced in 1998, containing 49,000,000 dry pounds of NRL. Industry data from 1991-1997, indicates that 1,080,000,000 rugs containing 200,000,000 dry pounds of NRL were produced.

Eleven individual and unsubstantiated incident reports attributing allergic reactions to NRL-containing consumer products, even when compared only with the number of NRL-containing bathmats produced and sold in the United States over the past decade, clearly does not represent a "significant" potential for causing hypersensitivity. As such, regulation of NRL as a strong sensitizer is neither warranted nor permissible pursuant to the Act or the CPSC's regulations. Accordingly, the Commission should deny the proposed rulemaking

The Actions Requested are Too Over Reaching and are Practically Infeasible to Implement.

A declaration that NRL is a strong sensitizer would require manufacturers of NRL-containing products such as Textile Rubber to comply with the labeling provisions of Section 2(p)(1) of the Act and the regulations set forth at 16 C.F.R. § 1500.121. These provisions would require NRL-containing products to include a wide range of statements concerning the products' manufacture, packaging, and distribution, and information concerning the potential hazards associate with such products' use The increased production costs and enormous regulatory compliance burdens to the NRL industry are simply not justified by the extremely limited benefit such a designation would offer.

Indeed, the Petition seeks far more than a content disclosure indicating that NRL is used in a product. It would include NRL with the five other listed strong sensitizers, each of which is significantly more dangerous and affects a vastly wider population than NRL. If listed as strong sensitizer and thus a hazardous substance under the Act, NRL could additionally be subject to classification as a "banned hazardous substance," and its use altogether prohibited. Such a result would be particularly unjustified, especially in light of NRL's beneficial qualities. NRL's unique qualities of elasticity, strength, and softness are not matched by any synthetic rubber latex manufactured today. These unique properties make NRL the polymer of choice in a host of industries and products. The beneficial use of NRL by Textile Rubber's manufacturing customers alone in no-slip rugs, safety shower mats and the like clearly demonstrates the need to keep NRL on the market and free from unnecessary and burdensome regulation.

Finally, over 40,000 products in the American marketplace are made with NRL, from pencil erasers to tires to baby pacifiers. The manufacture of each of these products varies tremendously, including with respect to the nature and amount of chemicals and other additives used in addition to raw NRL. Such a variation necessarily impacts the potential for latex allergy reactions. A blanket classification of NRL as a strong sensitizer would, without basis, ignore such considerations and would be far too drastic a measure to protect the extremely small number of individuals who are particularly susceptible to NRL allergies. Unlike the FDA regulation, which is narrowly tailored to medical devices, and which prescribes very limited labeling requirements, the regulation proposed by the Petition would simply be too broad and unwieldy.

In addition to the foregoing comments, Textile Rubber adopts the comments in opposition to the Petition submitted by Centrotrade Rubber USA, Inc., Guthrie Latex, Inc. and Lewis & Peat Rubber, LP. Textile Rubber additionally reserves the right to submit additional comments in opposition to the Petition and any proposed rule or other action by the CPSC in connection with these issues as necessary or

appropriate.

Thank you for the opportunity to submit these comments. While Textile Rubber is sympathetic to those individuals with latex sensitivities, the Company does not believe the solution to their problem is dependent upon CPSC regulation, particularly regulation as advocated in the Petition. As such, we urge the Commission to deny the Petition.

Very truly yours,

TEXTILE RUBBER & CHEMICAL CO.

Ray N. Taylor
Executive Vice President

Enclosure

Table 2. Shipments of Carpet and Rugs: 1998 and 1997
[Quantity in thousands of square yards. Value in thousands of dollars]

Product Code	Product description	1998 Quantity	1998 Value	1997 Quantity	1997 Value
	Total	1,832,500	10,853,016	1,695,804	10,263,916
3141101000	Woven carpet and rugs	36,656	437,822	26,954	346,687
	By fiber of face yarn:				
3141101002	Cotton	(D)	(D)	(D)	(D)
3141101004	Manmade	31,233	295,690	22,726	233,248
3141101006	Wool	(D)	(D)	(D)	(D)
3141101008	Other	(D)	(D)	(D)	(D)
3141103110	Tufted carpet and rugs	1,647,092	9,976,133	1,533,252	9,494,106
	By type:				
* 3141103112	Washable scatter rugs, bathmats, and sets (rugs 6' x 9' and smaller)	99,686	769,711	92,015	721,845
3141103114	Hard-backed non-washable accent/area rugs (6' x 9' and smaller)	23,312	134,888	20,373	117,614
3141103116	Room size rugs over 6' x 9'	3,914	57,832	3,686	53,273
3141103118	Roll goods 6' and larger, excluding artificial grass	1,431,216	8,528,670	1,308,707	8,080,546
314110311A	Tufted artificial grass for nonathletic surface	33,013	68,046	26,631	r/ 60,005
314110311C	Automobile and aircraft carpeting	55,951	416,986	81,840	460,823
	By fiber of face yarn:				
314110311E	Nylon	1,007,756	6,791,882	998,260	6,855,674
314110311G	Polyester	131,595	708,296	74,723	415,422
314110311J	Polypropylene	388,285	1,752,755	353,368	1,586,411
314110311L	All other	119,456	723,200	106,901	636,599
	Other carpet and rugs	148,752	439,061	135,598	423,123
3141105002	Knitted	(D)	(D)	(D)	(D)
3141105004	Needle punched	129,910	265,634	118,779	251,475
3141105006	Felt	(D)	(D)	(D)	(D)
3141105008	Braided, hooked, and other carpet and rugs n.e.c	15,265	142,235	13,889	135,050

(D) Withheld to avoid disclosing data for individual companies
n.e.c. Not elsewhere classified
r/ Revised by 5 percent or more from previously published data

Attachment to Comments of Textile Rubber & Chemical Co.
Petition HP 00-2

KINNEY, KEMP, SPONCLER, JOINER & THARPE
ATTORNEYS AT LAW
A PARTNERSHIP INCLUDING A PROFESSIONAL CORPORATION
225 WEST KING STREET
P O BOX 398
DALTON, GEORGIA 30722-0398

FAX COVER SHEET

DATE: 6/21/00

TO: Office of the Secretary
Consumer Product Safety Comm

FAX 301-504-0127
TEL

FROM:
Henry C. Tharpe, Jr.
E-mail: hctharpe@kinneyandkemp.com
FAX (706) 275-6566
TEL (706) 278-5211

SUBJECT:
Petition HP00-2, Petition on Natural Rubber Latex

PAGES
7, including this cover sheet.

CLIENT/MATTER NO. 10385.04901

REMARKS

Attached are the comments of Textile Rubber & Chemical Co. to the above petition.

letter 73

AMERICAN APPAREL MANUFACTURERS ASSOCIATION

American Apparel Manufacturers Association
Comments To The Consumer Product Safety Commission
On The Petition To Declare
Natural Rubber Latex And Products Containing Natural Rubber Latex A Strong Sensitizer

Petition HP 00-2, Petition on Natural Rubber Latex

21 June 2000

The American Apparel Manufacturers Association ("AAMA") is pleased to submit comments on the petition asking the Consumer Product Safety Commission ("CPSC") to declare natural rubber latex ("NRL") and products containing NRL "strong sensitizers" under the Federal Hazardous Substance Act. (*65 F R. 15133, March 21, 2000*). AAMA is the national trade association of the domestic apparel industry. Its members produce about 85 percent of the clothing sold at wholesale in the U.S. and have operations in almost every state.

AAMA believes that there is no objective evidence or data to support a conclusion or proposed rulemaking that wearing apparel products containing NRL should be declared strong sensitizers. Three points can be made regarding the question of NRL use in apparel and its relation to said petition These are:

1.) There is no objective evidence supporting a conclusion that wearing apparel containing NRL is hazardous to consumers. AAMA is not aware of any objective evidence of widespread or serious reactions or sensitization from the use of apparel containing NRL. A wide variety of apparel containing differing types and amounts of NRL has been safely used by hundreds of millions of people for decades and continues to be so used.

2.) The vast majority of apparel containing NRL uses it in very low percentages. Where NRL is used, it is typically covered by some other material, usually textiles, and therefore direct dermal contact is minimized or eliminated altogether. Use of NRL in apparel products is low because many synthetic elastic products exist to replace it – these products are often more appealing and comfortable for the consumer, and therefore more popular with manufacturers. Because of the minute quantities used, no data currently exists on exactly how much NRL is used in garments today.

3.) The Textile Fiber Products Identification Act, 15 U.S.C. §70b(b) currently provides labeling rules for NRL and other fibers. When used in larger concentrations, all fibers, including rubber, must be disclosed on the fiber content label.

Consequently AAMA firmly believes that there is no basis for including apparel products in any proposed rulemaking regarding NRL.

2500 Wilson Boulevard • Suite 301 • Arlington, Virginia 22201 • 703/524-1864 • FAX 703/522-6741
Toll Free 1-800-520-AAMA (2262) • www.americanapparel.org

AAMA
2500 Wilson Boulevard - Suite 301
Arlington, VA 22201
Tel: (703)524-1864
Fax: (703)522-6741

PLEASE DELIVER THE FOLLOWING 2 PAGE(S), INCLUDING COVER PAGE TO:

Name: Office of the Secretary

Firm/Company: Consumer Product Safety Commission

Date: June 2', 2000

Telecopier Number: 301/504-0127

Client Number.

FROM: Rachel Subler

IF YOU DO NOT RECEIVE THE TOTAL NUMBER OF PAGES INDICATED ABOVE, PLEASE CALL OUR PRODUCTION DEPARTMENT AS SOON AS POSSIBLE AT THE ABOVE-REFERENCED TELEPHONE NUMBER. THANK YOU.

COMMENTS:

Petition HP 00-2, Petition on Natural Rubber Latex

Joan N. Martellotto, PhD, RN
1011 Delles Road
Wheaton, Illinois 60187
Phone 630-665-2277 Fax 630-665-2679
E-mail jmartell@ameritech.net

June 21, 2000

Ms. Rockelle Hammond
Office of the Secretary
Consumer Product Safety Commission
Washington, DC 20207

Re: Petition Requesting Rule Declaring Natural Rubber Latex a Strong Sensitizer

Dear Ms. Hammond:

I am writing to support the petition to declare natural rubber latex (NRL) a strong sensitizer under the Federal Hazardous Substances Act and to require labeling of products containing NRL.

Allergy to natural rubber latex is an important and untreatable medical problem that causes severe allergic reactions, chronic lung disease, disability, and death. Populations particularly affected are health care personnel and other workers who wear latex gloves, children who undergo multiple surgical procedures to correct congenital anomalies, those who use natural rubber nipples and pacifiers, and individuals who have food allergies that immunologically cross-react with latex. Additionally, approximately 1% of the general population has latex allergy, and a greater percentage shows serologic evidence of latex antibodies although they may not have developed symptoms. Common routes of latex exposure include skin contact, inhalation, surgical inoculation, parenteral injection, and ingestion.

Avoidance of natural rubber latex is the only effective treatment for latex allergy. Recently, the Food and Drug Administration required manufacturers to label medical devices containing natural rubber latex. However, no such mandate exists for labeling latex-containing consumer items, and patients and their care givers are having great difficulty identifying these products short of having allergic reactions, which sometimes are life-threatening.

My doctoral research concerning the experience and quality of life of latex-allergic health care workers, revealed that patients have serious difficulties with most aspects of everyday life because of the ubiquitous presence of natural rubber latex in unlabeled consumer products. Therefore, I am mailing a copy of my dissertation to you to support the petition to require labeling latex-containing consumer items.

Sincerely,

Joan N. Martellotto, PhD, RN

Stevenson, Todd A.

letter 75

From: Judith Herkimer [jherkimer@snet.net]
Sent: Wednesday, June 21, 2000 4:55 PM
To: cpsc-os@cpsc gov
Subject: Petition HP 00-2, Petition on Natural Rubber Lates

Dear Sir/Madam:
I am a Registered Nurse 100% disabled due to occupationally acquired severe Natural Rubber Latex (NRL) allergy and asthma.

I am homebound due to the prevalence of NRL found throughout the community. If consumer products were labeled as containing NRL, me and others like me would have a greater degree of freedom, safety, and peace of mind when venturing out of our homes. The simple act of purchasing items (which most take for granted) can prove lethal to NRL allergy sufferers. Even being in an area where inflated latex balloons are or have been can create a medical emergency. Going to a restaurant is no longer possible due to the difficulty in determining if the food has been handled at any point with latex gloved hands.

It is long past due in recognizing how serious a hazard NRL is. Consumers need to be informed and be made more aware of its danger as a serious sensitizer. NRL allergy individuals are deserving of consumer products that are clearly labeled in order to maintain their safety.

Please give your support to Petition HP 00-2.

My gratitude is extended for allowing this public comment period.

Respectfully Submitted,
Judith A. Herkimer, RN
32 Warren Hill Road
Cornwall Bridge, CT 06754
860-672-6867 phone/fax

Late
76

Stevenson, Todd A.

From: Leslie Gahagan [leslieg@tcbi com]
Sent: Wednesday, June 21, 2000 9.54 AM
To: cpsc-os@cpsc.gov
Subject: Petition HP 00-2, Petition on Natural Rubber Latex

I would like to publicly announce that I support the petition HP 00-2 to declare natural latex a strong sensitizer. The labeling of the substance can be a lifesaver for many with natural rubber latex allergy, including my 7 year-old daughter.

No one can possibly know how frightening it is to attempt to purchase any product (including shoes, clothing, food, medical supplies, even a bandage to cover those common childhood scrapes) when you have a child with a latex allergy. Every pair of shorts or pants has to be checked thoroughly to make sure the elastic is covered and no loose strands are sticking out anywhere. Sometimes spending days calling and emailing manufacturers gets some results, but more often than not it is bad news: yes, there is some amount of latex in our product.

I am currently in the process of choosing carpeting and linoleum for our home, but I hesitate to start because I know there will be store managers and manufacturers who will either not know whether a carpet backing or linoleum glue contains latex or will just deny me the information. Of course, they will not get my business, but then I must start out all over again, hoping the manufacturer who finally does tell me their product contains no natural latex is being honest. Otherwise, our home will be toxic to my daughter, who has had a serious anaphylactic reaction to something as simple as foam rubber.

Thank goodness for our local Wal-Mart store manager who gladly banned inflated latex balloons from her store per my request. Of course, my request was more like a show-and-tell plea after my daughter, Zoe, had a bad coughing/wheezing spell and vomited all over herself just walking past a baby product display complete with latex balloons. I would think that if Wal-Mart can listen, the government surely can as well.

Please consider declaring natural latex a strong sensitizer and label products which contain it! We parents and individuals with latex allergy just cannot know every latex-containing product by smelling, touching, and guessing. It's much too risky!

Leslie D. Gahagan
110 Amherst Avenue, Apt. D101
Sheboygan Falls, WI 53085

(920) 467-9025
dis_advocate@yahoo.com
For more information on my daughter's latex allergy, see
http://www.geocities.com/dis_advocate/latex.htm
My Home Page: http://www.geocities.com/dis_advocate
Check out my brother's band: http://www.bandclearer.com

The Hosiery Association
Serving the Industry since 1905

3623 Latrobe Drive • Suite 130 • Charlotte-NC 28211-2117 USA
tel 704 365 0913 • fax 704 362 2056
internet www.hosieryassociation.com • e-mail hosierytha@aol.com

(formerly the National Association of Hosiery Manufacturers)

June 20, 2000

Office of the Secretary
Consumer Product Safety Commission
Room 502
4330 East-West Highway
Bethesda, MD 20814

Ref Petition to Declare Natural Rubber Latex a Strong Sensitizer
65 Federal Register 15133 (March 21, 2000)

The Hosiery Association (THA) is the trade association representing companies in the United States that make all types of men's, women's and children's hosiery Our members produce and market approximately 90% of all the hosiery sold in this country We are pleased to have the opportunity to submit comments on the petition requesting the Consumer Product Safety Commission (CPSC) to declare natural rubber latex (NRL) and products containing NRL as strong sensitizers under the Federal Hazardous Substance Act While we support and join the comments of the Rubber Manufacturers Association (RMA) and the American Apparel Manufacturers Association (AAMA), we will focus our comments on the specific issue of the use of NRL in hosiery and socks

Survey data shows that approximately 55% of the hosiery companies participating in a recent survey use some type of rubber yarn in their products Whether natural or synthetic rubber, almost 100% of these yarns were covered with another textile fiber, versus bare or uncovered Natural rubber is often the preferred product used in socks to hold the top up It is the preferred fiber because some consumers have complained that synthetic covered yarn does not last, and natural rubber yarn is relatively available at reasonable prices Therefore, it is a consumer preferred product based on both quality and price

Looking at the type of rubber yarn used, 53% was natural rubber, with 20% synthetic, while 27% of respondents indicated they use both natural and synthetic

Looking just at natural rubber, 90% of respondents indicated it was dry processed (vulcanized) It is our understanding that the dry processed natural rubber yarns are not under consideration in this petition, as it pertains primarily to dipped processed natural rubber yarns Since

these only account for 10% or less of the natural rubber yarns used, segregating these yarns and the products that contain them, through the manufacturing process so they could carry a different consumer label, would be extremely difficult and costly We saw no objective scientific evidence in the petition that would support the need for substantially adding-to the consumer price of products like hosiery and socks containing utilitarian yarn characteristics that consumers desire Also, our survey indicated that almost 100% of all natural rubber yarns used were covered and therefore, significant or prolonged dermal contact was very low

The petition also failed to establish evidence of widespread or serious reaction or sensitizations from the use of apparel or hosiery containing NRL This fact is born out by our industry survey data Only 19% of our companies indicated that they had ever received any consumer complaints of allergic reactions to any of their products containing rubber yarn, whether natural or synthetic This covered a time span of 10-25 years The average time span reported was 18 years and the average number of complaints received during this 18-year period of time was 4 5 complaints

We would also like to remind the CPSC that consumer labeling of yarn and fiber content is already required under the Textile Fiber Products Identification Act, 15 U S C 70b (b) Any fiber or yarn present in an amount of 5% or more by weight must be clearly identified by its generic name, including rubber Fibers present in less than 5% of the weight may be disclosed by generic name, and many hosiery companies do disclose the presence of these fibers for competitive reasons, since they impart specific utilitarian aspects, and therefore, desirability for the product

While we are sympathetic to human sensitivities, we must be mindful that someone in the population is sensitive to virtually any natural or synthetic substance Unnecessary over-labeling adds to consumer costs and further pushes manufacturing and sourcing to foreign countries where our oversight and control is limited We must always carefully balance the cost of regulations to the benefits derived, and ensure that rulemaking activity is based on sound scientific data and reasonable supporting evidence We do not feel the petition to declare natural rubber latex and products containing NRL a strong sensitizer meets the criteria for initiating rulemaking on this issue

Regards,

Sid Smith
President and
Chief Executive Officer
The Hosiery Association

78

LOCKER GREENBERG & BRAININ, P C
ATTORNEYS AT LAW

AARON LOCKER
THEODORE M GREENBERG
FREDERICK B LOCKER
JEFFREY M LOCKER

DAVID N BRAININ
OF COUNSEL

420 FIFTH AVENUE, NEW YORK N Y 10018
(212) 391-5200
TELECOPIER (212) 391 2035

June 21, 2000

Ms. Sayde Dunn
Office of the Secretary
U S Consumer Product Safety Commission
4330 East West Highway
Bethesda, Maryland 20814

Re: Petition to Ban Natural Rubber Latex
(65 Fed. Reg 15133 [2000])

Dear Ms Dunn:

We represent the Juvenile Products Manufacturers Association, Inc. ("JPMA"), a not-for-profit trade association comprised of more than 300 manufacturers of juvenile products, which are sold nationally throughout the United States. In 1999, the industry had sales of approximately $4 billion Some members of JPMA manufacture pacifiers which include nipples made of natural rubber latex and some members distribute baby bottles which contain nipples made of natural rubber latex

JPMA is opposed to the Petition and respectfully requests that it be denied in all respects for the following reasons

1 No Adequate Substitute for NRL in Nipples for Baby Bottles and Pacifiers A rule banning natural rubber latex (NRL) or declaring it a hazardous substance would eliminate the use of NRL in pacifiers and baby bottles At the present time, there is no other substance which industry could use to replace NRL in these products Nipples made of polyvinyl chloride are under attack by various consumer organizations, including Greenpeace and the National Environmental Trust, who have petitioned the U.S. Consumer Product Safety Commission ("CPSC" or "Commission") for a ban on PVC in children's products. Silicon, the only other alternative product, has not proved to be as resistant to aging or tension as NRL. The elimination of NRL as a material for nipples could effectively eliminate pacifiers and baby nipples

2. NRL Should Not Be Declared a Strong Sensitizer For reasons which are apparent from the Petition in this proceeding, NRL does not meet the requirements for declaring a product a strong sensitizer Precautionary labeling under the Federal Hazardous Substances Act (FHSA) was never intended to label the infinite variety of household products which may present a slight or casual risk of injury (S Rep No 1158 at 11 (1960)) In order to be classified as a hazardous substance under the FHSA, the Commission must, by rule, show that (a) the product is toxic, corrosive, an irritant, a strong sensitizer, flammable or combustible; or generate pressure through decomposition, heat or other means; and (b) the product can cause substantial personal injury or substantial illness during or resulting from customary or reasonably foreseeable handling or use. (15 U.S C. §1261(f)(1)(A)).

The FHSA defines a strong sensitizer as a substance that can cause hypersensitivity on normal living tissue through an allergic or photo-dynamic process in which hypersensitivity becomes evident on re-application (15 U S C §1261(k)). To determine whether a substance causes hypersensitivity, the CPSC will on a case-by-case basis consider factors such as the substance's chemical or functional properties, documented medical evidence of allergic reactions, and/or susceptibility profiles. (16 C F R. §1500 3(e)(5)(iv) (2000))

Only five substances have ever been the subject of regulation declaring them as strong sensitizers (1) paraphenylenediamine (and products containing it); (2) powdered orris root (and products containing it), (3) certain epoxy resins systems, (4) formaldehyde (and products containing 1% or more of formaldehyde); and (5) oil of bergamot (and products containing 2% or more of oil of bergamot) (16 C F R §1500 13). Importantly, this list was part of the original promulgation of implementing regulations under the FHSA in 1961 and nothing has been added to this list since that time. Unlike the characterized substances that have been codified as strong sensitizers, NRL, even under the facts set forth in the Petition, has a remote and statistically insignificant likelihood of producing an allergic reaction

3. NRL Does not Affect a Significant Portion of the Population with a severe Adverse Reaction The CPSC has held that a strong sensitizer is a substance that affects a significant portion of the population and which may cause a severe adverse reaction. See Advisory Opinion #12, July 26, 1973 In that opinion, the CPSC relied on the intention of Congress in enacting the FHSA and acknowledged " that some portion of the population is sensitive in one way or another to almost every article that enters the household . " The Commission noted in the Opinion that Congress did not intend that precautionary labeling be required on all such products. The definition of "hazardous substance" under the FHSA was not

intended to include substances where the hazard is minor, comparing the risk or chance of injury against the degree of injury probable or possible.

4 NEISS Incident Data Does Not Support a Ban We have received and reviewed the incident data in the NEISS system from its inception to date JPMA has not found a single instance of a recorded allergic reaction since 1980, the date when NEISS began collecting statistics of injuries associated with consumer products. Statistically, there are no injuries or severe allergic reactions reported in the NEISS system which would support a rule declaring NRL a strong sensitizer and a banned hazardous substance in articles intended for use by children

For all the foregoing reasons, JPMA respectfully urges the Commission to deny the Petition

Very truly yours,

Frederick B Locker

FBL.dd

F:\APPS\WPFILES\LEGISLAT\Petition to Ban Natural Rubber Latex JPMA.wpd

LOCKER GREENBERG & BRAININ, P C.
ATTORNEYS AT LAW

AARON LOCKER
THEODORE M GREENBERG
FREDERICK B LOCKER
JEFFREY M LOCKER

DAVID N BRAININ
OF COUNSEL

420 FIFTH AVENUE NEW YORK N Y 10018
(212) 391-5200
TELECOPIER (212) 391-2035

June 21, 2000

Ms. Sayde Dunn
Office of the Secretary
U S. Consumer Product Safety Commission
4330 East West Highway
Bethesda, Maryland 20814

Re. Petition to Ban Natural Rubber Latex
(65 Fed. Reg. 15133 [2000])

Dear Ms Dunn·

We represent the Toy Manufacturers of America, Inc. ("TMA"), a not-for-profit trade association composed of three hundred (300) manufacturers whose aggregate sales at the retail level exceed $23 billion annually. The members of TMA are international in character and their sales are made extensively throughout the United States, the European Union and the rest of the world Some members of TMA manufacture pacifiers which include nipples made of natural rubber latex and some members distribute baby bottles which contain nipples made of natural rubber latex

TMA is opposed to the Petition and respectfully requests that it be denied in all respects, for the following reasons

1. No Adequate Substitute for NRL in Nipples for Baby Bottles and Pacifiers A rule banning natural rubber latex (NRL) or declaring it a hazardous substance would eliminate the use of NRL in pacifiers and baby bottles At the present time, there is no other substance which industry could use to replace NRL in these products Nipples made of polyvinyl chloride are under attack by various consumer organizations, including Greenpeace and the National Environmental Trust, who have petitioned the U S Consumer Product Safety Commission ("CPSC" or "Commission") for a ban on PVC in children's products. Silicon, the only other

alternative product, has not proved to be as resistant to aging or tension as NRL The elimination of NRL as a material for nipples could effectively eliminate pacifiers and baby nipples.

2 NRL Should Not Be Declared a Strong Sensitizer For reasons which are apparent from the Petition in this proceeding, NRL does not meet the requirements for declaring a product a strong sensitizer Precautionary labeling under the Federal Hazardous Substances Act (FHSA) was never intended to label the infinite variety of household products which may present a slight or casual risk of injury (S. Rep. No. 1158 at 11 (1960)) In order to be classified as a hazardous substance under the FHSA, the Commission must, by rule, show that (a) the product is toxic; corrosive, an irritant; a strong sensitizer; flammable or combustible; or generate pressure through decomposition, heat or other means; and (b) the product can cause substantial personal injury or substantial illness during or resulting from customary or reasonably foreseeable handling or use (15 U S C §1261(f)(1)(A)).

The FHSA defines a strong sensitizer as a substance that can cause hypersensitivity on normal living tissue through an allergic or photo-dynamic process in which hypersensitivity becomes evident on re-application. (15 U S C. §1261(k)). To determine whether a substance causes hypersensitivity, the CPSC will on a case-by-case basis consider factors such as the substance's chemical or functional properties, documented medical evidence of allergic reactions, and/or susceptibility profiles. (16 C F R. §1500 3(e)(5)(iv) (2000))

Only five substances have ever been the subject of regulation declaring them as strong sensitizers· (1) paraphenylenediamine (and products containing it), (2) powdered orris root (and products containing it), (3) certain epoxy resins systems, (4) formaldehyde (and products containing 1% or more of formaldehyde); and (5) oil of bergamot (and products containing 2% or more of oil of bergamot) (16 C F R. §1500 13). Importantly, this list was part of the original promulgation of implementing regulations under the FHSA in 1961 and nothing has been added to this list since that time Unlike the characterized substances that have been codified as strong sensitizers, NRL, even under the facts set forth in the Petition, has a remote and statistically insignificant likelihood of producing an allergic reaction.

3 NRL Does not Affect a Significant Portion of the Population with a Severe Adverse Reaction. The CPSC has held that a strong sensitizer is a substance that affects a significant portion of the population and which may cause a severe adverse reaction See Advisory Opinion #12, July 26, 1973 In that opinion, the CPSC relied on the intention of Congress in enacting the FHSA and acknowledged " that some portion of the population is

sensitive in one way or another to almost every article that enters the household " The Commission noted in the Opinion that Congress did not intend that precautionary labeling be required on all such products. The definition of "hazardous substance" under the FHSA was not intended to include substances where the hazard is minor, comparing the risk or chance of injury against the degree of injury probable or possible.

4 NEISS Incident Data Does Not Support a Ban. We have received and reviewed the incident data in the NEISS system from its inception to date TMA has not found a single instance of a recorded allergic reaction since 1980, the date when NEISS began collecting statistics of injuries associated with consumer products Statistically, there are no injuries or severe allergic reactions reported in the NEISS system which would support a rule declaring NRL a strong sensitizer and a banned hazardous substance in articles intended for use by children.

For all the foregoing reasons, TMA respectfully urges the Commission to deny the Petition.

Very truly yours,

Aaron Locker

AL jv

F \APPS\WPFILES\LEGISLAT\Petition to Ban Natural Rubber Latex- TMA.wpd

Stevenson, Todd A.

80

From: Meeropol, Elli [emeeropol@shrinenet org]
Sent. Thursday, June 22, 2000 4 30 PM
To. 'cpsc-os@cpsc gov'
Cc· 'DebiAdkins<debilan1@cs com>'
Subject: Petition HP 00-2, Natural Rubber Latex as a strong sensitizer

Comments on Petition HP 00-2, Petition on Natural Rubber Latex

June 21, 2000

I am a pediatric nurse practitioner on medical staff in a children's hospital Many of my patients have symptomatic allergic reactions to natural latex rubber

For the past ten years, we have worked hard to educate patients, families
and other healthcare providers about this condition in order to prevent potentially life-threatening reactions Progress has been made in avoidance
of latex in the healthcare environment, particularly since the labeling recommendations effectively last year

However, there are still many problems with inadvertent latex exposures in
the home, school and community These reactions often occur in response to
items with hidden or unknown latex content Items that have caused reactions
in my patients include Koosh balls, pencil erasers, elastic on pajamas, rubber tubing in the high school science lab, swimming goggles and balloons
In addition, one child had a severe reaction in a fast food restaurant when
he ate food prepared by a person wearing latex gloves

I strongly support the petition from Ms Adkins and respectfully request that
the Commission declare natural rubber latex (NRL) and products containing
NRL to be strong sensitisers under the Federal Hazardous Substances Act Labeling of consumer products will greatly assist my patients and their families in identifying which items to avoid to keep safe

Thank you very much for addressing this important issue,

Ellen Meeropol MS, RN, CS, PNP
Shriners Hospital for Children
Springfield, Massachusetts

Late 81

Stevenson, Todd A.

From: SandraWte@aol com
Sent: Thursday, June 22, 2000 3 31 PM
To: cpsc-os@cpsc gov
Subject: Petition HP00-2 Petition on Natural Rubber Latex

Dear CPSC,
I am the parent of a child (age 7) who has a severe Type 1 latex allergy as a result of having had multiple surgeries as an infant and toddler It had been very difficult to obtain information on what products are safe for him and what contain natural rubber latex I have spent countless hours on the phone with customer service representatives trying to learn about specific products There is a great deal of confusion about natural rubber latex and "rubber" or "latex" The passage of this petition would be of immense help to all the people who already have this difficult allergy
It is heart breaking as a parent to have to take away a toy because, despite one's best efforts, it causes an allergic reaction Unfortunately, many products used by children contain natural rubber latex The children who have this allergy in most cases have already been through a lot with their medical problems If products that contained natural rubber latex were labeled it would make the lives of these children and those of their parents much easier
Thank you for your consideration

Sandra T

Whitehouse,
Ph D

The Carpet and Rug Institute
310 Holiday Avenue, P O Box 2048, Dalton, Georgia 30722
Phone (706) 278-3176 Fax (706) 278-8835

82 Comments

June 22, 2000

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

By email. cpsc-os@cpsc.gov

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

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 the Carpet and Rug Institute's comments concerning the Petition

The Carpet and Rug Institute (CRI) is the national trade association representing the carpet and rug industry Headquartered in Dalton, Georgia, the Institute's membership consists of manufacturers representing 92% of all carpet and rugs produced in the United States, and suppliers of raw materials and services to the industry There is continued coordination with other segments of the industry, such as distributors, retailers, and installers

The preponderance of broadloom carpet produced in the U S A contains a backing material composed of Styrene Butadiene synthetic latex material As referenced in the Carpet and Rug Institute's article in "Industry Review 1998," 99,686,000 square yards of tufted, washable scatter rugs, bathmats and sets were produced. A typical bathmat 18"x36" is ½ square yard in size which means that approximately 199,000,000 washable rugs were produced in 1998, with the potential of containing 49,000,000 dry pounds of NRL.

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 in accordance with 15 U S C § 1261(p)(1) and 16 C F R. § 1500 121

In support of the Petition, its proponent relies upon research conducted in connection with the federal Food and Drug Administration ("FDA") final rule regulating NRL-containing medical devices, 21 C F R § 801 437, a July, 1998 Journal of the American Academy of Dermatology article (the "JAAD Article")' and some of CPSC incident reports. None of these items justifies the proposed rulemaking requested in the Petition relative to the lack of evidence of a problem in the application and use of NRL on rugs and bathmats.

Is NRL a "strong sensitizer?

In order to declare a substance a "strong sensitizer," the CPSC must consider the frequency of occurrence and severity of the reaction, and must make a finding that the substance has a significant potential for causing hypersensitivity on normal tissue. 15 U S C § 1261(k), also, 16 C F R § 1500 3(5)

CPSC regulations require this finding to be based upon, among other things, chemical or functional properties of the substance, documented medical evidence of allergic reactions obtained from epidemiological surveys or individual case reports, controlled in vitro or in vivo experimental assays, or susceptibility profiles in normal or allergic subjects The information submitted in support of the Petition does not meet these kinds of medical and scientific standards.

The information relating to the FDA's study was limited to the use of NRL in medical devices for surgery and other medical applications The FDA regulation was precipitated in part by the elevated levels of latex sensitivity manifested by latex glove-related exposures, particularly in the medical arena. Studies have shown a higher incidence of sensitization among health care professionals, those persons who undergo numerous surgeries, and those persons with mucous membrane exposure to NRL This population, however, is already adequately protected by the FDA's labeling requirements for medical devices See 21 C F R § 801 437 The Petition seeks an inappropriate regulation of NRL well beyond the limits of the FDA's regulation and the limited population that its studies demonstrated was necessary to protect

The JAAD Article similarly offers no medical or scientific support for the actions requested by the petitioner This article is a broad overview of latex allergy in general It references, in summary fashion, various research projects conducted over the years on latex sensitivity The vast majority of these projects concerned healthcare workers and exposure scenarios in medical settings (e g., sensitivity

among allergy clinic patients, preoperative patients, blood donors). These populations are already protected by the FDA medical devices regulations

Thank you for the opportunity to submit these comments. The Carpet and Rug Institute does not believe the solution to the reported problem is dependent upon CPSC regulation, particularly regulation as advocated in the Petition. The actions requested are not justified, too complicated, and unrealistic to implement.

Sincerely,

E. Ken McIntosh
Technical Director

EKM:ld

Enclosure

84

Gerber

GERBER PRODUCTS COMPANY 560 MORRIS AVENUE SUMMIT NJ 07901

2000 JUL -5 A 10 59

June 29, 2000

Ms Sadye E. Dunn
Office of the Secretary
Consumer Product Safety Commission
4330 East-West Highway
Room 502
Bethesda, Maryland 20814

Re: **Gerber Products Company Comments on Petition HP 00-2: Petition on Natural Rubber Latex ("NRL")**

Dear Ms Dunn

Gerber Products Company ("Gerber") hereby submits comments to the Consumer Product Safety Commission ("CPSC") on the above-referenced Petition filed by Ms Debbie Adkins which was referenced in the Federal Register on March 21, 2000 and May 24, 2000 Ms Adkins' Petition requests that the CPSC take two actions: 1) designate natural rubber latex ("NRL") as a "strong sensitizer" in accordance with the Federal Hazardous Substances Act ("FHSA") and 2) apply FHSA requirements to label or ban products containing NRL. Based on the support cited within the Petition, the pertinent provisions of the FHSA, criteria specified in FHSA regulations, scientific research articles and our experience with NRL, Gerber respectfully submits that this Petition should be denied

Gerber Products Company was established in 1928 and is a worldwide leader in the development, manufacture and marketing of food and care products for children from birth through age three Gerber's overall sales total in the United States is approximately $1 2 Billion Gerber is a subsidiary of Novartis AG Since 1960, Gerber has produced and marketed baby care products worldwide. Our baby care line consists of more than 300 Gerber items as well as NUK®, Looney Tunes™ and Suzy Zoo® branded products. Gerber's line of baby care products features bottle feeding systems, eating/feeding utensils, breastfeeding accessories, safety items, playthings, as well as pacifiers and nipples

made of latex The Gerber baby care business accounts for more than $100 Million in annual sales.

Gerber is a leading manufacturer of baby pacifiers and nipples Current federal safety regulations require baby products to be produced with high endurance properties and NRL allows Gerber to meet, and in many cases exceed, these standards Over the last seven years, Gerber has produced approximately 140 million latex pacifiers and nipples Gerber has had the number one selling pacifier brand in the United States for the past 10 years

Listening and responding to consumers over the years has helped Gerber maintain the tradition of being the leader in infant care and nutrition in the United States Gerber maintains a toll free 1-800 line for consumers to call with questions. The consumer response "hotline" is available 24 hours a day, 7 days per week Operators are available to assist consumers in a number of languages Gerber receives over 675,000 calls annually. Our telephone records indicate that Gerber has not received any reports of serious illness or injury from the use of any Gerber pacifiers or nipples based on the fact that they contain latex In the past 3-1/2 years, Gerber has received only 35 calls concerning latex in pacifiers or nipples Approximately 20 of those calls concerned apparent minor allergic reactions to latex In comparison, over the past 3-1/2 years, Gerber has received an almost equal number of calls (24 calls) concerning apparent minor allergic reactions to non-latex products Our successful safety record reflects the effort expended by Gerber to produce a safe product

The Petition and its Support

Ms Adkins' Petition appears to request two actions 1) designate NRL as a "strong sensitizer" in accordance with the FHSA, and 2) apply FHSA requirements to label or ban products containing NRL.

As support for her Petition, Ms. Adkins cites research used by FDA to address latex allergies in the health care (medical device) context, and one dermatology journal article from the *Journal of the American Academy of Dermatology* (hereinafter referred to as the "*Journal* article") [1] Ms. Adkins also includes eleven CPSC Incident Reports These reports involve various medical devices and other products unrelated to Gerber

[1] See Volume 39-1, July 1998

This modest array of information is insufficient support for listing NRL as a strong sensitizer

The cited FDA material does not establish any basis to regulate NRL outside of the medical device context Because the FDA regulations differ from those found in FHSA, it is inappropriate to state that because FDA has taken action in the medical device field, the CPSC should take action in the consumer product arena The FDA regulations apply to medical devices, including latex gloves, and were developed *specifically* to address the high occurrence of NRL allergies in the health care industry.[2] The high-risk health care environment is unique and not representative of the general population. This fact is supported by government findings,[3] and scientific research as presented in many journal articles, including the *Journal* article attached to Ms Adkins' Petition [4]

Ms Adkins also includes eleven CPSC Incident Reports with her petition as support for her position Of these eleven incident reports, two reports highlight the unfortunate and tragic fatality of individuals likely to have developed their allergy to latex in a health care environment In addition, of the eleven incidents cited, several appear to be from the same individual. This limited number of reports does not support the assertion that this condition affects a sizable portion of the general population

Requirements of FHSA and Regulations

The definition of a "strong sensitizer" is set forth in both the FHSA,[5] and the regulations promulgated thereunder [6] The statutory definition of a "strong sensitizer" is "a substance which will cause on normal living tissue through an allergic . process a hypersensitivity

[2] FDA Talk Paper (September 30,1997)
[3] See FDA Final Rule on Medical Devices, 62 Fed Reg 51021-51030 (Sept 30, 1997), and OSHA Technical Information Bulletin on Potential for Allergy to Natural Latex Gloves and other Natural Rubber Products, April 12, 1999 (addressing latex allergies in the workplace)
[4] See *Journal* article at 2, 6-8
[5] 15 U S C A §1261(k) (1998)
[6] 16 C F R 1500 3(c)(5) (1997) The list of "strong sensitizers" has, from its inception in the early 1960's, only contained the following five chemicals (a) Paraphenylenediamine and products containing it, (b) Powdered orris root and products containing it, (c) Epoxy resins systems containing in any concentration, ethylenediamine, diethylenetriamine, and diglycidyl ethers of molecular weight of less than 200, (d) Formaldehyde and products containing 1 percent or more of formaldehyde, (e) Oil of bergamot and products containing 2 percent or more of oil of bergamot (16 C F R 1500 13 (1999))

which becomes evident on reapplication of the same substance and which is designated as such by the Commission." Before making its determination regarding a substance, the Commission is directed by the statute to consider "the frequency of occurrence and severity of the reaction" and "shall find that the substance has a significant potential for causing hypersensitivity "

Once a product is declared a "strong sensitizer," it must then be deemed a "hazardous substance" in order to require the product to be labeled. The term "hazardous substance" under FHSA means it causes "substantial personal injury or substantial illness during or as a proximate result of any customary or reasonably foreseeable handling or use, including reasonably foreseeable ingestion by children "[7]

In addition, in summarizing the FHSA definition of "strong sensitizer," both Congress and CPSC have noted that "some portion of the population is sensitive in one way or another to almost every article that enters the household" and that in enacting the FHSA, Congress "did not intend that precautionary labeling would be required on all such products "[8] Both Congress and CPSC noted that "a strong sensitizer must be a substance which affects a significant portion of the population and which may cause a strong or severe reaction."[9]

Based on the above, it is clear that the factors to be considered in determining whether a substance is a strong sensitizer are (1) frequency of occurrence, and (2) severity of reaction Natural rubber latex in the consumer product arena, specifically baby pacifiers and nipples, does not meet the above definition for strong sensitizer The following comments address these two factors in detail.

NRL Is Not a Strong Sensitizer

Frequency of Allergic Reaction in the General Population

To our knowledge no data has been presented in the Petition or otherwise which supports the conclusion that the frequency of an allergic reaction to NRL in the general population is significant. The *Journal* article cited as support for the Petition listed approximately 50 products that are commonly produced with NRL. Over two-thirds of the products

[7] 16 C F R 1500 3(b)(4)(i)(A) (1999)
[8] CPSC Advisory Opinion No 12, p 2 (7/26/73)
[9] Id

listed are medical products, most of which are regulated under the FDA medical device rules In fact, the *Journal* article supports the conclusion that the health care industry is the primary area of concern with regard to latex allergies [10] Regardless, the common household products listed include adhesives, toys, rubber bands, shoes, underwear elastic, shower curtains, pacifiers, nipples, clothing (stretch textiles), and raincoats In fact, it is estimated that 40,000 products that are commonly used by consumers on a daily basis contain NRL If the frequency of allergic reaction to consumer products in the general population were significant, then the fact that NRL-containing products are so pervasive would likely produce a high, possibly even alarming, frequency of allergic reactions

The facts support that the latex-sensitive population within the general population is about 1-6 percent. [11] Some experts opine that a 1-2 percent figure is more appropriate. *In fact, the FDA has stated that "the risk of allergic reaction to latex is estimated to be less than 1 percent."*[12]

With regard to NRL sensitivity within the general population, the Gerber data presented above provides real world support By extrapolating the available data, one can estimate that Gerber receives a call concerning latex in its products on average one time for every 1.7 million products sold. Note that only about two-thirds of the calls involved complaints and none of the complaints specified a serious illness, injury or death.

The available data supports the conclusion that allergic reactions to NRL are neither frequent nor significant in the general population Based on this fact alone, it is inappropriate to list NRL as a strong sensitizer

Severity of Allergic Reaction

The FHSA regulations direct CPSC to consider all relevant data to establish that the substance to be listed as a "strong sensitizer" causes a strong or severe reaction.

---

[10] See *Journal* article at 2, 6-8

[11] See for example the OSHA Technical Information Bulletin on Potential for Allergy to Natural Latex Gloves and other Natural Rubber Products, April 12, 1999, p 3 Common allergies, such as those to pet fur/dander and grass, are said to occur in about 1-6% of the population

[12] FDA Talk Paper (September 30, 1997), p 2

Research and government findings support the fact that mild to moderate reactions, such as rash or localized redness, are the common reactions to NRL. While there can potentially be fatal reactions, they are extremely rare [13] The CPSC consumer complaint log also supports the fact that extreme reactions are rare. The consumer complaint log only has two serious complaints, which, as mentioned before, are linked to the high-risk health care environment

Finally, based on the years of consumer data gathered by Gerber and set forth above, severe reactions to baby pacifiers or nipples are *unrecorded* and minor reactions occur at a rate of about 1 in every 1 7 million products sold Statistically speaking, the likelihood of a severe allergic reaction from exposure to NRL appears extremely low, approaching non-existent in the context of consumer products, especially baby care products such as pacifiers and nipples

Conclusion

The above information supports the conclusion that NRL is not a strong sensitizer. First, neither the *Journal* article nor the FDA provides sufficient information to support the conclusion, or warrant the further investigation of NRL as a strong sensitizer Second, research and government reports contradict the allegations found in the Petition and firmly establish that NRL does not meet the necessary criteria to be listed as a strong sensitizer Finally, Gerber's internal consumer response documentation supports the conclusion that the frequency of occurrence and severity of reaction are insufficient to support the listing of NRL as a strong sensitizer

Should the CPSC grant Ms. Adkins' Petition, it would begin an unwarranted process that could remove safe products from the market If NRL was designated a strong sensitizer, CPSC would then be required to review each of the 40,000 products that contain NRL and determine which products must be labeled, exempted or banned.[14]

---

[13] See for example, OSHA Technical Information Bulletin on Potential for Allergy to Natural Latex Gloves and other Natural Rubber Products, April 12, 1999, p 3

[14] 16 C F R 1500 3(b)(15)(i) (1999) Based on the structure of the FHSA, the CPSC in many cases would not be able to merely label the many consumer products containing NRL as requested In fact, the CPSC may have to ban many common consumer products because by listing NRL as a strong sensitizer, these products will be in a class of products that are then systematically banned as a hazardous substance because of their use by or contact with children

Gerber is empathetic to those with latex allergies However, based on the evidence presented, Gerber requests that the Commission deny Petition HP 00-2 and cease further investigation into regulating consumer products containing NRL We sincerely hope that our comments are helpful to the CPSC and we are available should the CPSC have further questions.

Respectfully Submitted,

Judith A Weinstein

Judith A Weinstein, Esq
Associate General Counsel

Attachments

Cc Frank Palantoni, CEO and President
Jan Relford, Vice President, Research & Development
David Yates, Vice President, Marketing
Christopher G. FitzPatrick, Vice President & General Counsel
Brett Merrell, General Manager Baby Care

CPSC Advisory Opinion
1973

12.

July 26, 1973

Honorable Sam J. Ervin, Jr.
United States Senate
Washington, D.C. 20510

Dear Senator Ervin:

The Congressional Liaison Office of the Department of Health, Education, and Welfare has directed your June 18 referral of Mrs. Willie Edmondson's letter to this agency for consideration. Mrs. Edmondson is concerned that such chemicals as formaldehyde, dieldrin, aldrin, and lindane are being used to treat permanent press clothing.

We have no information on dieldrin, aldrin, and lindane in permanent press fabrics or clothing. Since these chemicals are pesticides as defined by the Federal Insecticide, Fungicide and Rodenticide Act, they are not subject to the jurisdiction of the Consumer Product Safety Commission. We are therefore forwarding a copy of your correspondence to the Environmental Protection Agency for their consideration. Formaldehyde, however, is subject to the Federal Hazardous Substances Act, which is administered by the Commission. Under the provisions of this Act, household substances containing 1 percent or more of formaldehyde have been found to have significant potential for causing hypersensitivity and are thus designated as strong sensitizers.

An excess of formaldehyde is sometimes used in the polymerization of resins in permanent press fabrics or may be liberated from an incomplete polymerization process. However, such fabrics do not contain 1 percent or more of formaldehyde. Most cases of skin rash appear to be due to the unusual sensitivity of a few individuals to this chemical and to the slight excess or incomplete polymerization described above. One or two washings usually remove the source of irritation since formaldehyde is water soluble.

We have previously considered the status of permanent press clothing under the Act and have concluded that is not in the strong sensitizer category. In reaching this conclusion, it was

14

acknowledged that some portion of the population is sensitive in one way or another to almost every article that enters the household, including foods and household soaps. Congress, in enacting the Federal Hazardous Substances Act, did not intend that precautionary labeling would be required on all such products (Senate Report 1158, 86 Congress 2nd Session, p. 11). A strong sensitizer must be a substance which affects a significant portion of the population and which may cause a strong or severe reaction.' This is not the case with permanent press clothing.

We hope these comments are helpful. If you have any further questions, please let us know.

Sincerely yours,

Richard O. Simpson
Chairman

cc: Environmental Protection Agency
Pesticides Regulation Division
South Agricultural Building
Washington, D. C. 20250

bcc: R. O. Simpson
S. M. Hart (w/cy inc.)
J. W. Locke (w/cy inc.)
E. R. Finch
R. G. Poth
M. A. Brown

Prepared by: RGPoth:cvi 7/5/73
Revised by: JWLocke 7/5/73
Revised by: MABrown/PWHallman:mli:7/23/73

Journal Article

JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY

July 1998 • Volume 39 • Number 1

Latex allergy

Erin M. Warshaw, MD [MEDLINE LOOKUP]
Minneapolis, Minnesota

Sections

- Abstract
- History of Rubber Production
- History of Rubber Allergy
- Nomenclature
- Biology of Natural Rubber
- Natural Latex Glove Production
- Immediate, IgE-mediated Reactions to Latex
- Mechanism of Immediate Reactions
- Potential Role of Endotoxin
- Delayed-Type Hypersensitivity to Latex
- Prevalence of Latex Allergy
- Why Increase?
- Diagnosis
- SPT
- Differential Diagnosis
- Variables in Antigen Determination
- Antigen Identification
- Latex Allergens in Air Pollution
- Cross-Reactions
- Predicting Anaphylactic Reactions
- Precautions
- Surgery For Latex-Sensitive Persons
- Latex Substitutes
- Latex Product Labeling
- Efforts to Decrease Allergen Content
- Alternative Sources of Natural Rubber
- Management
- Future Issues
- Summary
- References
- Publishing and Reprint Information
- Articles with References to this Article

Abstract TOP

Coined the next major health concern of the decade, allergy to natural rubber latex affects people routinely exposed to rubber products Groups at highest risk include health care workers, rubber industry workers, and persons who have undergone multiple surgical procedures especially those with spina bifida Allergy to latex is a type I, immediate, IgE-mediated reaction, which can lead to anaphylaxis and death Much of latex research is published in allergy journals Dermatologists may not be aware of the prevalence, symptoms, risks, diagnosis, and treatment of latex allergy These topics are the subject of this review Research concerning antigenic proteins, as well as sources of latex alternatives, is also summarized (J Am Acad Dermatol 1998,39 1-24)
Learning objective At the completion of this learning activity, participants should have a clear understanding of the history, biology, epidemiology, mechanism, clinical characteristics, diagnostic work-up, and treatment of latex allergy Readers should also have a greater

understanding of multiple potential allergenic latex proteins and their importance in preventing future latex-sensitization

HISTORY OF RUBBER PRODUCTION

Pre-Columbian sketches depicting natural rubber religious offerings are probably the earliest documentation of the use of natural rubber latex (NRL) The first European explorers to visit Central America in the 15th century saw local people fashioning rubber shoes, balls, and bottles Samples of these products were sent to Spain by the conquistadors Rubber became an industrial product in Europe during the late 1700s after MacIntosh developed a waterproofing process [1]

Unfortunately, early rubber products became brittle under cold conditions as well as sticky with age These problems were solved in 1839 when Goodyear accidentally discovered vulcanization, a process that utilizes sulfur to stabilize the elastic properties of rubber Dunlop invented the inner tube and hollow tire in 1888,[1] and the first pair of rubber gloves was made by the Goodyear Rubber Company in 1890 at the request of William Stuart Halstead of breast surgery fame [2] In 1850, Wickham, a British rubber planter in Brazil, introduced rubber seed into Asia, now the major supplier of raw latex [3]

HISTORY OF RUBBER ALLERGY

TOP

Two types of allergic reactions to rubber products are now known type I (immediate-type) and type IV (delayed-type hypersensitivity [DTH]) (Table I).

Table I. Allergic reactions to natural rubber latex

Reaction	Mechanism	Antigens	Diagnosis
Immediate, type I	IgE	Small latex proteins	SPT, RAST, etc
Delayed, type IV	Cell-mediated	Manufacturing additives	Patch testing

RAST, Radioallergosorbent test, *SPT*, skin prick test

The first case of an immediate reaction to NRL was reported in 1927 by Stern[4] who described severe generalized urticaria caused by a rubber dental prosthesis Almost half a century later Nutter[5] reported the first glove-related case of an immediate-type reaction, contact urticaria Soon after, several researchers[6-10] established a link between NRL glove–induced symptoms and IgE mechanisms

Immediate reactions may be life-threatening By November 1992, more than 1000 reports had been received by the Food and Drug Administration (FDA) describing severe systemic allergic reactions to NRL medical devices The majority were related to latex gloves and barium enema catheter tips [11] The latter caused 15 deaths, prompting the FDA to recall a particular brand of barium enema catheter tip[12] and to publish a bulletin identifying the risk of anaphylaxis associated with NRL devices [13]

NOMENCLATURE

TOP

Natural latex refers to the milky fluid produced by the *Hevea brasiliensis* tree NRL refers to products, such as gloves, balloons, and condoms, which are made from water-based natural latex emulsions Dry rubber latex refers to products made from processed, dried, or milled sheets of latex rubber (Table II) [14]

Table II. Common natural rubber latex and dry rubber latex products*

General medical
- Gloves
- Elastic bandage
- Esophageal dilator
- Face mask with elastic band
- Hemodialyzer
- Enema retention cuff
- Syringe stopper
- Medication stopper
- Feeding tube
- Tourniquet
- Hot water bottle
- Rubber sheet, pillow

- Wheelchair tire
- Blood pressure cuff
- Electrode pad
- Intravenous tubing
- Catheter
- Stethoscope tubing
- Elastic support stockings

Obstetric/gynecologic
- Cervical cap
- Cervical dilator
- Diaphragm
- Condom

Dental
- Dental dam
- Bite block

Surgical/urologic
- Implants
- Urine bag and strap

Anesthesia
- Endotracheal tube
- Induction mask
- Teeth protector
- Breathing circuit
- Ventilator tubing
- Ventilator bellows

Household products
- Gloves
- Adhesive
- Rubber toys
- Balloons
- Rubber bands
- Shoes
- Carpet backing
- Underwear elastic
- Baby bottle nipple
- Pacifier
- Raincoat
- Swim goggles
- Swim cap
- Stamps
- Shower curtain
- Window insulation
- Air mattress
- Stretch textiles
- Whoopee cushion

*Adapted from Hamann CP Am J Contact Dermatitis 1993,4 4-21

Most immediate-type reactions result from exposure to NRL products

BIOLOGY OF NATURAL RUBBER

TOP

Latex is actually the cytoplasm of *H brasiliensis* lactiferous cells The nuclei and mitochondria are not expelled during collection, thereby enabling cell regeneration Latex consists of four major components rubber particles, lutoids, Frey Wyssling particles, and cytosol

Rubber particles are the most numerous organelles in lactiferous cells and consist of spherical droplets of *cis*-1,4 polyisoprene chains enclosed in a fine phospholipoprotein envelope [15] Two proteins important in *cis*-1,4-polyisoprene synthesis were identified and sequenced in 1989 The first, *cis*-prenyl transferase (38 kd), is a hydrophobic membrane-bound enzyme, which catalyzes the addition of isoprene units resulting in a polyisoprene chain several thousand isoprene units in length [16,17] The second, rubber elongation factor, is a 14 6 kd stabilizing cofactor necessary for efficient function of *cis*-prenyl transferase [18]

Lutoids are small vacuoles that comprise 10% to 20% of latex volume and are important for latex coagulation Hevein (5 kd) and prohevein (20 kd) are major lutoid body proteins [15] Hevein makes up 70% of lutoid proteins and has considerable structural homology with many plant agglutinins (lectins) such as those found in wheat, barley, rice, and potatoes [19] Hevamines (29 kd) are lysozymes that demonstrate homology with lysozymes in other plants such as ficus and papaw [20]

Frey Wyssling particles comprise 2% to 3% of latex volume, their biologic role has not been clearly defined The remaining cytosol forms 40% to 50% of latex volume and contains soluble carbohydrates, organic acids, amino acids, nucleotides, and proteins important in isoprene synthesis [15]

NATURAL LATEX GLOVE PRODUCTION

TOP

Many immediate-type I allergic reactions result from contact with NRL gloves The process of glove production is important for understanding latex allergy and will be briefly reviewed The steps in NRL production include collection, centrifugation, compounding, coagulation oven curing, vulcanization, and powder application [14]

As reviewed by Hamann,[14] *H brasiliensis* trees take 6 to 8 years to reach harvesting maturity, and an average tree yields enough latex to make approximately 10 pairs of gloves per week (1500 pairs per acre) Latex is harvested by cutting a spiral groove into the bark of the tree, a process termed tapping The milky contents of the exposed articulated lactiferous cells drain into a cup at the base of the tree Latex coagulates on the tapping cut and seals the wound The lactiferous system then regenerates lost cell material before the next tapping, typically 2 to 3 days later Autocoagulation, deterioration, and bacterial contamination occur rapidly in fresh latex unless preservatives and anticoagulants, such as ammonia, are immediately added Anticoagulants convert the emulsion into approximately 60% liquid and 40% solid phases Centrifugation removes liquid and concentrates solids [14]

Approximately 5% of finished glove weight represents chemicals added during compounding These chemicals are responsible for type IV DTH reactions and include accelerators, antioxidants, antiozonants, emulsifiers, stabilizers, extenders, colorants, retarders, stiffeners, biocides, UV light absorbers, and fragrances Accelerators primarily control the rate, uniformity, and completeness of vulcanization, the most common include thiurams, carbamates, and mercaptobenzothiazoles Anti-oxidants and antiozonants stabilize unsaturated isoprene bonds and prevent deterioration [14]

Glove-shaped glass or porcelain formers are then dipped into the emulsion of compounded latex Some formers are pretreated with coagulants such as calcium nitrate and/or releasing agents such as cornstarch powder Formers are then pulled into a coagulation oven After emerging from the oven, gloves are dipped into a water bath to leach excess chemicals and water-soluble proteins The amount of time spent in leaching tanks and rate of water exchange are crucial variables that influence degree of protein removal [14]

Vulcanization creates disulfide bonds that cross-link *cis*-1,4 polyisoprene chains to each other, the completeness and speed of this process depend on choice and concentration of accelerators added earlier during compounding After vulcanization, cornstarch powder may be applied in a wet emulsion dip or as a dry aerosolized powder Gloves are then removed from formers An extra wash with chlorine yields powder-free gloves, although this additional wash reduces the amount of water-soluble proteins, it also accelerates glove deterioration [14]

IMMEDIATE, IGE-MEDIATED REACTIONS TO LATEX

TOP

The contact urticaria syndrome, as defined in 1975 by Maibach and Johnson,[21] includes localized urticaria (stage 1), angioedema (stage 2), asthma (stage 3), and anaphylaxis (stage 4) Typical reactions occur within an hour of exposure as a result of IgE-mediated hypersensitivity to NRL proteins Clinical manifestations depend on exposure route as summarized in Table III [22]

Table III. Immediate type I hypersensitivity reactions*

Route	Clinical manifestations
Cutaneous	Urticaria
	Dermatitis
	Pruritus
Airborne	Rhinitis
	Conjunctivitis
	Asthma
Mucosal	Anaphylaxis
	Tachycardia
	Angioedema
	Nausea
	Vomiting

Abdominal cramps
Hypotension

*Adapted from Sussman GL. Allergy Proc 1992,13 67-9

Immediate itching and urticarial wheals are the most common manifestations of allergy to NRL gloves

Glove-induced asthma was first reported by Seaton, Cherrie, and Turnbull[23] who postulated terpene vapor as the offending agent In vitro and in vivo experiments have now produced convincing evidence that NRL proteins bind to cornstarch glove powder[10] and induce respiratory tract reactions through IgE-mediated mechanisms [24-27] Both maize allergens in cornstarch powder[28,29] and ethylene oxide[30] used for sterilization have been suggested as etiologic agents, but have not been proven to induce asthma during specific inhalation challenge tests [31]

Latex causes at least 10% of all intraoperative anaphylactic reactions [32,33] Anaphylaxis has been reported from contact with baby bottle nipples,[34] baby pacifiers,[35] rubber vaginal vibrators,[36] Foley catheters,[37] condoms,[38-40] latex balloon tip catheters,[41,42] balloons,[43] dental cofferdams,[44] endotracheal tubing,[45] electrocardiographic pads,[45] squash balls,[46] air expelled from a whoopee cushion,[47] and food prepared with latex gloves [48]

Hands most commonly come into contact with NRL products, but there are relatively few cases[49] of serious allergic reactions resulting from this exposure because an intact epidermis helps prevent absorption of allergenic proteins Anaphylaxis to latex, therefore, occurs primarily when NRL products contact abraded mucosa[50] such as occurs during obstetric/gynecologic procedures,[44,47,51] rectal manometry,[52] and surgery [53]

MECHANISM OF IMMEDIATE REACTIONS

TOP

Reactions to latex probably follow the typical sequence of events seen in other immediate reactions [14] Briefly, first exposure to NRL may induce sensitization This occurs when a new antigen, through a series of steps, induces plasma cells to produce NRL-specific IgE or IgG4 antibodies that bind to high-affinity surface receptors on mast cells On reexposure, elicitation of an allergic reaction occurs when these bound antibodies are cross-linked by NRL antigens Mediators such as histamine and arachidonic acid metabolites are immediately released from mast cells, causing increased vascular permeability, vasodilatation, and bronchoconstriction expressed as urticaria, hypotension, and asthma [54] Type I, late-phase reactions are mediated by low-affinity receptors and occur 6 to 12 hours after exposure [55]

POTENTIAL ROLE OF ENDOTOXIN

TOP

Mechanisms other than those in immediate-type hypersensitivity may play a role in latex protein reactions Endotoxin is a potent proinflammatory agent produced by gram-negative bacteria It has been linked to irritation of skin,[56] eyes, and lungs [57,58] Clinical symptoms range from skin erythema and respiratory distress to fever, malaise, and shock Williams and Halsey[59] found that endotoxin was a highly significant contaminant of some latex gloves The highest levels of endotoxin were found in powdered examination gloves caused by heavy bacterial contamination of cornstarch slurries used during manufacturing These researchers found that endotoxin was not physically associated with powder (as are latex proteins) but instead was released in association with tiny respirable particles [60] These findings suggest that endotoxin may be responsible not only for skin irritation, but also for enhancement of allergic reactions to NRL products, especially powdered gloves

DELAYED-TYPE HYPERSENSITIVITY TO LATEX

TOP

Many allergic reactions to rubber are DTH reactions to chemicals added to NRL during manufacturing These DTH reactions and allergens are not the subject of this review, and readers are referred elsewhere[61-64] for such information There are few reported cases of DTH to raw latex without added chemicals [65,66] Wilkinson and Beck[67] patch-tested 822 patients to ammoniated latex applied in Finn Chambers Ten patients had positive patch tests to latex, half of these were also prick test positive to latex These rare DTH reactions to latex should be interpreted cautiously because chemicals such as 1,2-benzisothiazolin-3-one, a recognized cause of DTH allergic contact dermatitis, may be added to raw latex in the country of origin [65] Patch testing with glove pieces should also be interpreted with caution because ingredients of glove powder, such as epichlorhydrin and sorbic acid, may cause DTH [68]

PREVALENCE OF LATEX ALLERGY

TOP

General population

Prevalence of latex sensitivity in the general population is probably less than 2% (Table IV)

Table IV. Latex sensitivity in the general population

Author(s)	Population	Sample size	Test	% Positive
Turjanmaa[69]	Consecutive allergy clinic patients	130	Scratch	0 8
Moneret-Vautrin et al [70]	Allergy clinic patients without risk factors	272	SPT	0 4
Turjanmaa[34]	Consecutive preoperative patients	800	SPT	0 13
Porn et al [71]	Patients seen for annual check-up	365	SPT/RAST	2 3
Ownby et al [72]	Blood donors	1000	RAST	6 5
Merrett et al [73]	Blood donors	1436	RAST	7 9

RAST, Radioallergosorbent test, *SPT,* skin prick test

[34,69-71] Studies analyzing serum samples from blood donors[72,73] indicate higher rates of sensitization probably because health care workers, known to be at risk for latex allergy, are more likely to donate blood

Importantly, not all persons who show evidence of sensitivity by testing have or will have clinical symptoms Study design obviously affects reported prevalence rates, people without symptoms are less likely to answer questionnaires and undergo testing [74]

Atopic patients

Predisposing risk factors for the development of latex allergy are summarized in Table V

Table V. Risk factors for development of latex allergy*

Occupational exposure to latex
Health care workers
Rubber industry employees
Janitorial workers
Food handlers
Multiple surgical procedures
Patients with spina bifida
Patients with congenital abnormalities
Frequent mucosal exposure to NRL products
Dental
Contraceptive
Daily urinary catheterization
Manual fecal disimpaction
Preexisting hand eczema
Atopy
Female gender
Fruit allergy

*Adapted from Barton EC Nurse Pract 1993,18 54-8

Studies of atopic persons indicate latex sensitivity rates of 3% to 9%, whereas rates in atopic children without other risk factors are 2% to 4% [70 71,75] This lower rate in atopic children compared with atopic adults probably stems from less exposure to NRL products with high allergen content such as gloves

Spina bifida

The first cases of latex-induced anaphylactic shock during surgery in children with spina bifida were reported in 1989 and 1990[30,77], many more followed [53 78,79] In 1991, the Centers for Disease Control (CDC) alerted the medical community to this high-risk group [80] Currently 8 of 10 anaphylactic reactions occurring during surgery in all children are due to latex allergy The risk of anaphylaxis to latex in children with spina bifida has been estimated to be 500 times greater than the general population, probably because of the need for multiple surgeries [81,82] Most studies have found latex-sensitivity rates of 30% to 51%,[70 83-89] although a recent study demonstrated a rate of 65% [90] Lower sensitivity rates have been reported from mostly questionnaire studies [91-94] Of course, not all of these children have clinical symptoms

Occupational

As summarized in Table VI,[95-115] most studies estimate latex sensitivity in health care workers without symptoms to be 2% to 17%

Table VI. Occupational prevalence of latex sensitivity

Author(s)	Population	Sample size	Test	% Positive
Berky, Luciano, James[95]	Dental workers	1043	Questionnaire	14
Rankin, Jones, Rees[96]	Dental school staff	526	Questionnaire	15
Tipirneni et al [97]	HCWs	1526	Questionnaire	33
Katelaris, Widmer, Lazarus[98]	Dental school staff	177	Questionnaire	33
Kujala and Reijula[99]	HCWs	534	Questionnaire	44
Turjanmaa[69]	Hospital employees	512	Scratch	3
	OR nurses	71	Scratch	6
	OR doctors	54	Scratch	7
Salkie and Chir[100]	Laboratory technologists	230	RAST	1
Akasawa et al [76]	HCWs	601	RAST	2
Wrangsjo et al [101,102]	HCWs	202	SPT/RAST	4
Kaczmarek et al.[103]	HCWs	504	RAST	6
Eriksen et al [104]	HCWs	200	RAST/LHRT	17
Harfi et al [105]	HCWs	128	RAST	21
			SPT	19
Caprles-Hulett et al [91]	1st yr dental students	43	SPT	0
	OR HCWs	80	SPT	3
Beaudouin et al [106]	Hospital employees	907	SPT	3
Arellano, Bradley, Sussman[75]	Anesthesiologists	101	SPT	10
Lagier et al [107]	OR nurses	197	SPT	11
Sussman and Liss[108]	HCWs	1351	SPT	12
Yassin et al [109]	HCWs	224	SPT	17
Charous[110]	Symptomatic HCWs	39	RAST	49
Jones et al [111]	Symptomatic HCWs	41	SPT	68
Bubak et al [112]	Symptomatic HCWs	49	SPT	69
van der Walle and Brunsveld[113]	Hairdressers with rubber glove exposure	48	Scratch	10
Tarlo et al [114]	Glove factory workers	81	SPT	11
Moneret-Vautrin et al [70]	Occupational exposure	31	SPT	29
Heese et al [115]	Occupational exposure	39	SPT/RAST/Use	33

HCWs, Health care workers, *LHRT*, leukocyte histamine release test, *OR*, operating room, *RAST*, radioallergosorbent test, *SPT*, skin prick test

Similar rates of sensitization are found in other workers who are regularly exposed to NRL gloves, such as glove factory workers (11%)[114] and hairdressers (10%) [113] When health care workers with symptoms are tested, up to 69% show evidence of sensitivity [112]

In addition to contact urticaria, persons occupationally exposed to powdered NRL gloves are at higher risk for the development of rhinoconjunctivitis and asthma There have been numerous reports of health care workers disabled in the workplace from respiratory symptoms, which were subsequently linked to aerosolized latex proteins [116-118] A large study of occupational asthma confirmed by skin prick tests (SPTs), as well as inhalation challenge tests, indicated a prevalence of 2 5% [119] Smaller and less well-designed studies have shown prevalences as high as 38% [27,99,103,114,120]

Other risk factors

Presence of multiple risk factors increases the incidence of latex sensitivity More than half of latex-sensitive health care workers in one study reported a history of hand dermatitis before the development of contact urticaria and systemic reactions More than three fourths of Taylor and Praditsuwan's series[121] of predominantly female, occupationally exposed, latex-allergic persons had current or prior hand eczema Arellano, Bradley, and Sussman[75] found that atopic physicians were 19 times more likely to be SPT positive to latex than nonatopic physicians and nine times more likely to be SPT positive than atopic control subjects who were not occupationally exposed [75] Moneret-Vautrin et al [70] investigated risk factors of atopy and exposure in 569 subjects and found that these factors were not just additive,

but synergistic Latex SPT positivity was 0 4% for neither risk factor, 6 9% for exposure alone, and 9 4% for atopy alone Atopy and exposure together, however, increased the positivity rate to 36%

Female gender increases the incidence of latex sensitivity Tomazic et al [50] found a female predominance of 3 1 in a review of 145 cases of latex-induced systemic allergic reactions This female predominance may be attributable to the fact that more women are employed in high-risk professions Other factors, however, may also play a role For example, it is known that female hormones enhance histamine release [122,123]

Although attention to high-risk groups may help screen persons for latex sensitivity, it is important to remember to ask all patients about sensitivity Diaz et al [124] described three women without risk factors in whom anaphylaxis developed from latex gloves worn by obstetricians during the delivery of their children

WHY INCREASE?

TOP

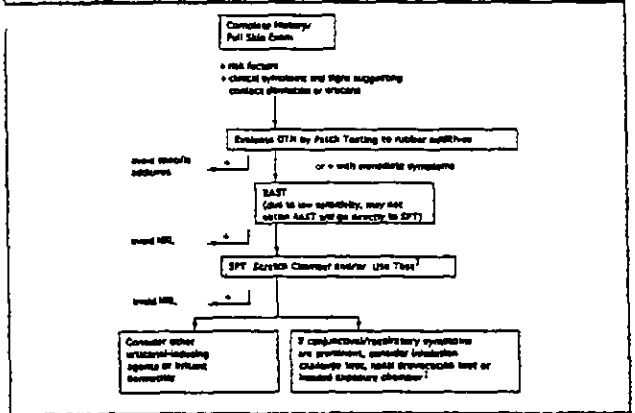
The CDC published a report on Aug 21, 1987 that came to be known as "universal precautions " It emphasized the need for all health care workers to routinely use appropriate barrier precautions, such as gloves, when contacting body fluids To meet this demand, new inexperienced glove manufacturers produced poorly compounded, inadequately leached products These gloves contained unprecedented concentrations of protein allergens, which sensitized thousands Annual glove imports rose dramatically from less than 1 billion gloves to about 11 billion by 1992. During the late 1980s, a glove glut ensued, prices plummeted, and many new manufacturers folded However, a newly sensitized population continued to have problems, even with previously used, high-quality products [125] Today, despite pleas from the FDA to manufacturers for tighter regulations, allergen levels in gloves can vary 40-fold from batch to batch [126]

DIAGNOSIS

TOP

Fig 1 outlines a reasonable approach to diagnosing latex allergy

Fig 1. Diagnosis of latex allergy *Dagger,* Epinephrine and resuscitation equipment are recommended if these diagnostic tests are performed *DTH,* Delayed-type hypersensitivity, *NRL,* natural rubber latex, *RAST,* radioallergosorbent test, *SPT,* skin prick test (Modified from Hamann CP Am J Contact Dermatitis 1993,4 4-21)



Click on Image to view full size

As with any diagnosis, a detailed history and thorough clinical examination are essential Evidence of risk factors and history of immediate symptoms should prompt an evaluation DTH to rubber additives and immediate reactions to latex proteins may coexist, therefore both patch testing and evaluation for latex antibodies may be necessary [121] A clinical examination showing patchy or diffuse eczema or urticaria (or both) on an exposed body part is classic Hands can transfer allergens to other body parts, especially the face, resulting in unusual presentations

As summarized in Table VII, multiple tests have been developed to detect latex allergy

Table VII. Diagnostic tests

Research	Clinical
Cytometric assay	SPT
Radioimmunoassay	RAST
Basophil histamine release test	Latex allergosorbent test
	Use test
Flow cytometry	Rub test
Immunoblots	Scratch chamber test
ELISA	Intradermal test
	Inhalation tests
Cross and rocket immunoelectrophoresis	Open and closed patch tests
Reverse enzyme immunoassay	Latex-specific antibody assays

ELISA, Enzyme-linked immunosorbent assay

Most experts feel that SPT with diluted latex antigen extracts is the most sensitive and, therefore, the standard for detecting latex allergy Unfortunately, although commercial, unstandardized extracts are available in Europe (Stallergenes) and Canada (Bencard), the FDA has yet to approve a skin testing latex extract for use in the United States [127] As a result, clinicians often resort to skin testing with office-made extracts

SPT

TOP

Glove brands vary greatly in allergenicity, Turjanmaa et al [128] found that prick test positivity of solutions made from 19 brands of NRL gloves among 40 sensitive persons varied from 8% to 87%, and relative concentrations of total protein in gloves ranged 3000-fold Therefore a known allergenic brand should be chosen to make prick solutions, and ideally concomitant testing of three different brands is recommended [74]

Most investigators prepare prick solutions by stirring twenty 1 cm^2 (1 gm) glove squares in 5 ml of sterile saline for 15 minutes Glove pieces are then removed and the solution is stored in a sterile bottle No preservatives are needed if the test material is refrigerated and replaced monthly [74] The stock solution may be diluted in saline 1 1,000,000, if no reaction is noted at 15 minutes, then subsequent increasing concentrations (e g , 1 100,000, 1 10,000) are tested [87] Histamine dihydrochloride (10 mg/ml) and saline are used as positive and negative controls, respectively [74]

Testing is done by placing a drop of diluted antigen solution on the skin and gently pricking the skin with a lancet The remaining solution is gently wiped away with blotting paper Fifteen minutes after application, the wheal is measured by adding the two largest perpendicular axes and dividing the sum by two A positive reaction is defined as a number equal to or greater than half the value of the histamine control The risk of sensitization after skin prick testing is unclear [74]

Although anaphylactic risk during prick testing is minimized by initially using very diluted solutions, physicians should be prepared with resuscitation equipment and epinephrine [129,130] As summarized in Table VIII,[131-136] most studies indicate SPT sensitivity and specificity rates of at least 90%

Table VIII. Sensitivity and specificity of diagnostic tests

		Skin prick test		RAST		Other tests
Author(s)	Sample size	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)
Rueff, Thomas, Przybilla[131]	63	NRL solution 91	92-95	89	87	NR
		NRL sap 100	74			
Turjanmaa, Reunala, Rasanen[132]	15	NRL solution 100	NR	53	NR	Scratch 86
		NRL sap 80				Use test 92
Ebo et al [133]	83	95	100	ImmunoCap 97	83	NR
					33	
Kadambi, Field, Charous[134]	33	NR	NR	54	NR	SPT/Use test 78
Blanco et al [135]	50	NRL extract 98	Both extracts 96-100	ImmunoCap 86	80	NR
		Glove extract 72-96		AlaSTAT 84	80	
Pecquet, Leynadier, Dry[33]	17	NR	NR	76	NR	NR
Turjanmaa et al [136]	15	NR	NR	60	NR	BHRT 93

Beaudouin et al [106]	907	100	99	NR	NR	NR

AlaSTAT, RAST produced by Diagnostic Products Corporation, *BHRT*, Basophil histamine release test, *ImmunoCap*, RAST produced by Upjohn-Pharmacia, *NR*, not reported

Radioallergosorbent test

A radioallergosorbent test (RAST) is an in vitro test in which solid phase allergen is incubated with serum to induce specific antigen-antibody reactions. Radiolabeled anti-IgE antibodies are mixed with solid-phase allergen-antibody complexes, and bound radioactivity is measured [137]

At least two RASTs are available in the United States, AlaSTAT by Diagnostic Products Corporation and ImmunoCap by Upjohn-Pharmacia As summarized in Table VIII■ , although specificities range from 80% to 87%, sensitivities are low (50% to 90%), making these poor screening tests A negative RAST does not exclude latex sensitivity Latex-sensitive persons with documented positive RASTs who avoid latex products for several years have subsequently developed negative RASTs [43] Presumably, in the absence of allergen exposure, specific IgE concentration decreases over time Nonetheless, because it is easy to perform and carries no risk of anaphylaxis, RASTs remain a diagnostic option,[138] and there is evidence that sensitivities of latex RASTs are improving Jaeger et al [27] found a correlation of 82% between IgE RAST and latex SPT The latex allergosorbent test (LAST) is similar to RAST, but avoids radioisotopes It can be performed in less than 6 hours and correlates well with latex RASTs [139]

Use test

A use test involves applying a latex glove directly to a wet hand; a vinyl glove serves as a control First, one wet finger is exposed to a glove finger for 15 minutes A positive test is defined as two to five urticarial wheals If no reaction is observed, the entire glove is applied to a wet hand for an additional 15 minutes If no wheals are noted, exposure can be lengthened to several days This test carries a risk of anaphylaxis [74,140]

Rub test

The rub test is a modification of the use test in which latex fluid, a glove piece, and/or glove powder are repeatedly rubbed into the volar aspect of the forearm A positive reaction is defined as one or more wheals This test also carries a risk of anaphylaxis [141]

Scratch chamber test

\ scratch chamber test is performed by using a lancet to create a 6 mm scratch on the volar aspect of the forearm A small piece of latex glove moistened with saline is placed in a Finn Chamber and applied over the scratch for 15 to 20 minutes A positive reaction is defined as in prick testing This test carries a risk of anaphylaxis, and false-positive reactions are well documented [69]

Intradermal test

Intradermal testing involves injecting diluted antigenic solutions directly under the skin Reports of anaphylaxis[142,143] advocate against this test, five deaths occurred from intradermal testing in a 42-year study period [130]

Basophil histamine release test

The basophil histamine release test is an in vitro test in which donor-washed leukocytes are incubated with diluted latex antigen Histamine release by basophils is measured directly by fluorometric, enzymatic, or immunologic methods or indirectly by enumerating degranulated basophils. It is a time-consuming and expensive test but carries no risk of anaphylaxis and has a sensitivity rate comparable to SPTs Turjanmaa et al [136] studied 15 patients with latex contact urticaria and found that the basophil histamine release test was positive in 93% compared with a commercial RAST positivity of 60%

Inhalation tests

Several tests detect mucosal sensitivity to latex The workplace challenge test involves measuring spirometry in workplace and nonworkplace environments [120] The inhalation challenge test involves measuring spirometry at 15- to 30-minute intervals while subjects handle latex gloves, vinyl gloves are used as controls [119] The nasal provocation test consists of applying a substance on a cotton swab to the nasal mucosa for 5 minutes Responses are monitored with anterior rhinoscopy, rhinomanometry, and measurement of nasal secretions Sensitivity and specificity of this test have yet to be determined [144] The hooded exposure chamber system produces a precise and reproducible NRL allergen-cornstarch particle cloud of uniform size that simultaneously challenges the eyes, nose, and bronchi [145]

Latex-specific IgG

Latex-specific IgG has been reported as an indicator of latex sensitivity Higgins et al [146] found that control subjects had low levels of latex-specific IgG antibodies, whereas those known to be latex-sensitive demonstrated much higher levels A Japanese study found that latex-specific IgG was at least nine times more common than IgE in atopic children and six times more common in hospital workers [76] Alenius et al [147] found eight latex antigens common to both IgG4 and IgE antibodies, which suggests that IgG4 antibodies may play a role in the pathogenesis of latex allergy

The presence of IgG4 antibodies in the sera of latex-allergic patients may be due to prolonged and intense antigen exposure [148] In vitro

evidence shows that interleukin-4 upregulates both IgE and IgG4 production,[149] and this may explain the concomitant occurrence of IgE and IgG4 antibodies in latex, food,[150] and insect sting allergies [151] The significance of allergen-specific IgG antibodies is controversial and, as the aforementioned studies indicate, not particularly specific

DIFFERENTIAL DIAGNOSIS

TOP

If tests are negative and suspicion for type I allergy remains, evaluation for other types of urticaria should be considered Nonimmunologic urticaria occurs without previous sensitization and can be caused by chemicals that directly induce degranulation of mast cells Sorbic acid, found in some glove powders, can induce nonimmunologic contact urticaria [152]

Immediate-type allergic reactions to rubber additives (which usually cause DTH) have been reported Fuchs and Wahl[153] described two patients with urticarial patch test reactions to tetramethylthiuram disulfide, mercapto mix, and *p*-phenylenediamine mix Helander and Makela[154] reported a kitchen worker with contact urticaria to rubber gloves who had negative immediate and delayed patch tests to standard rubber allergens and gloves. Scratch tests, however, were positive to zinc diethyldithiocarbamate, an accelerator, as well as a glove piece Belsito[39] described three patients with rubber contact urticaria with positive scratch tests to mercaptobenzothiazole, carba mix, and black rubber mix Wrangsjo, Mellstrom, and Axelsson[155] described a RAST-positive and scratch test–positive patient who also had an urticarial response to two accelerators, zinc pentamethylene dithiocarbamate and zinc dibutyl dithiocarbamate The significance of these immediate reactions to rubber additives is uncertain, well-designed large studies are needed to rule out false-positive tests caused by contaminants

Although granulomatous responses to cornstarch are well described,[156,157] there have also been several reported cases of contact urticaria to cornstarch in gloves [28,39,158,159] Most researchers, however, believe this immediate hypersensitivity is due not to cornstarch itself but rather to contamination by latex protein allergens [10] Pure powder supplied by manufacturers, in several cases, did not induce urticarial reactions,[29,112,128] and no maize-specific IgE antibodies were identified Milk allergy may also masquerade as latex allergy because casein may be added to powder during manufacturing [160]

VARIABLES IN ANTIGEN DETERMINATION

TOP

Identification of major latex allergens is important for two major reasons First, diagnostic accuracy will greatly improve, enabling the development of standardized extracts of well-characterized latex allergens Second, once antigens are characterized, their source (biologic vs industry) can be determined and eliminated [161]

Unfortunately, there are multiple variables that make detection and characterization of latex allergens difficult Different proteins are roduced by *H brasiliensis* during different seasons and by different plant hybrids Variations in collection, preservation, and compounding f latex can lead to chemical hydrolysis resulting in different protein profiles Haptenization with various compounding chemicals may alter bioavailability and antigenicity Modifications can also result from different isolation detection methods [162] Finally, nuances of individual immune systems can produce different reaction patterns when challenged with identical proteins

The source of NRL (crude nonammoniated latex [NAL], high or low ammoniated latex [AL], rubber tree leaves, dry rubber, or latex-containing end products such as gloves) used for extraction and testing is still under debate [163,164] Hamilton et al [165] found that glove extracts were more sensitive in detecting latex allergy than NAL or AL Jones, Scheppmann, and Yunginger[166] found that extractable latex allergen levels varied 500-fold among 27 medical latex gloves and 6- to 40-fold in the same brand sampled at different times Turjanmaa and colleagues[128] [167] performed skin tests with extracts from 17 brands of latex surgical gloves and 16 brands of latex condoms and similarly found that allergenicity varied widely Yunginger et al [168] reported a cross-sectional study of 71 glove brands and found that the latex allergen level varied over 3000-fold

Some investigators have suggested that ammoniation of latex can result in formation of new antigens [169] Lu et al [170] investigated this question and found that ammonia treatment alters latex proteins but does not create new antigens with novel epitopes Mäkinen-Kiljunen et al [171] found that AL and NAL shared at least 10 common antigens, but a surgical glove extract had only six of these antigens The surgical glove extract also demonstrated one allergen not found in natural rubber, suggesting that rubber proteins may be altered and/or created during glove manufacturing

Geographic differences can result in different antigenic profiles Kurup et al [172] compared Finns and Americans for reactivity to gloves from their respective countries and to raw latex from Malaysia and India The results showed that persons are more likely to react to extracts made from products distributed in their country of origin As expected, raw latex extracts were more sensitive (29 of 45 subjects [64%]) than glove extracts combined (22 of 45 subjects [49%])

Different patient populations produce antibodies that recognize distinct latex peptides In one study by Alenius et al ,[173] 46 of 57 allergens were identified by patients with spina bifida, 19 of 57 by health care workers, and 8 of 57 by both groups It is unknown whether sensitivity among different risk groups is due to different modes of exposure or if immune responses are modified by medical conditions such as spina bifida

ANTIGEN IDENTIFICATION

TOP

As summarized in Table IX,[143,147,174-183] immunoblotting studies show that IgE from sera of latex-allergic patients binds heterogeneously to many different proteins ranging from 4 to 200 kd

Table IX. Identified latex antigens

Author(s)	Molecular weight of identified antigen(s) (kd)*
Turjanmaa et al.[128]	**2*** **5** **30**
Morales et al.[143]	**10** 24 **35** **1**
Turjanmaa and Reunala[167]	3——10
Turjanmaa et al.[10]	**10**
Alenius et al.[169]	4——14——21——7
Alenius et al.[147]	**14** **21** **29** **53**
Chambeyron et al.[174]	**10** 15 18 20 25 **30** 35 6
Fuchs and Wahl[153]	**28**
Jaeger et al.[27]	**14** 30——45
Slater and Chhabra[175]	**14** **20**
Tomazic et al.[50]	0——20 (AL)
	4——2(
	(N/
Alenius et al.[176]	**14** **20** **27**
Czuppon et al.[177]	**14.6** **58** (tetra of 14
Alenius et al.[173]	**14** **27**
Alenius et al.[178]	**14**——**20**——20
Slater and Trybul[88]	**14.3** **26.7**
Alenius et al.[179]	**20** **30** **36**
Aamir et al.[180]	**14** 24 46
Chiu et al.[181]	**14** 18 23 25 6(
Eriksen et al.[104]	14 21 30——35 44
Nieto et al.[182]	**11 12 13** **27** **32**
Yeang and Ward[183]	22-23

AL Ammoniated latex, *NAL* nonammoniated latex.

*Boldface type indicates major antigen.

Identification of one or two major allergens is a daunting task

Currently, there is no consensus on which proteins are most important Some authors believe that proteins of 14 6 kd (rubber elongation factor, Hev b 1),[175-177,180,184-187] 20 kd,[176] 22 and 23 kd,[183] and 27 kd[88,176,188] are particularly important in spina bifida. Others believe that hevein (4 7 kd)[189] and prohevein (20 kd)[178,179,190] may be important antigens Several other potential antigens have recently been identified with molecular weights of 10,[174] 16,[191-193] 18,[181] 21,[147] 23,[181] 25,[181] 30,[44,194] 36,[188] and 66 kd [181]

LATEX ALLERGENS IN AIR POLLUTION

TOP

Small particles suspended in polluted air are significantly linked to hospital admissions for asthma, particularly in young children [195] Many of these particles originate from abrasion of rubber tires on road surfaces Williams et al [196] analyzed these respirable particles by optical microscopy, chemical solubility tests, and mass spectrometry and found them to be consistent with those observed from latex gloves Antibody inhibition assays demonstrated that six of seven sera samples from latex-sensitive persons were inhibited equally by rubber tire and latex glove extracts Therefore latex antigens from respirable tire fragments may be immunologically active, contributing to asthma and other respiratory problems [196] In a further study by Williams et al ,[197] immunoblots tentatively identified a 50 kd protein in rubber tire fragments Respirable latex allergens may also act as specific adjuvants for IgE responses by enhancing reactions induced by unrelated allergens [198]

CROSS-REACTIONS

TOP

Allergies to multiple foods and plants are associated with allergy to NRL (Table X)[40,199-202] and allergens common to both latex and food have been identified [191,192,203-206]

Table X. Food allergies associated with latex allergy

Avocado*
Banana*
Chestnut*
Kiwi
Passion fruit
Peach
Mango
Pineapple
Fig
Cantaloupe
Apple
Papaya
Pear
Melon
Cherry
Wheat
Turnip
Spinach
Potato
Celery
Tomato

*Highest association

Preincubation with latex extracts has been shown to inhibit binding of food-specific antibodies and vice versa [207,208] Other studies have not supported the association between latex and food allergy [209,210] It may be important to test fresh food extracts because commercial extracts have yielded false-negative tests [211]

It is unclear whether latex sensitization predisposes persons to food allergy or vice versa Eades, Keane, and Cullom[212] studied 11 latex SPT-positive persons and found that food sensitivity appeared concurrently with latex sensitization. It may be that similarity of epitopes in food and latex allergens is responsible for this observation It is possible, therefore, that anaphylaxis in latex-sensitive patients is due to cross-reactivity among food and latex antigens rather than to specific sensitization with latex

Fruit-latex cross-reactivity may be due to ethylene, a gas used to hasten commercial ripening When forced to ripen quickly under high ethylene concentrations, plants produce allergenic wound-repair proteins that are similar to wound-repair proteins made by *H brasiliensis* [213] There are reports of cosensitization to latex and items sterilized by ethylene [30,214]

Reported cross-reactions of latex with inedible plant proteins include reactions to profilin, an allergen present in many plant species,[215] and ficin, a protease found in the sap of the ficus tree, *Ficus glabrata* [216,217] Because ficin is utilized in many pharmaceutical, textile, and cosmetic products, it may be an important cross-reactant and/or cosensitizing agent

PREDICTING ANAPHYLACTIC REACTIONS

TOP

Anaphylactic reactions occur between 1 in 1500 and 1 in 5000 operations, approximately 5% to 10% of patients die as a direct result [218] It is estimated that latex allergy is responsible for at least 10% of all intraoperative anaphylactic reactions [32,33] The rate of anaphylaxis in patients with spina bifida is approximately 13 5% [219] As these numbers demonstrate, we need reliable and accurate predictors of anaphylaxis

Unfortunately, preoperative evaluation has not predicted anaphylaxis [89] Kelly et al [219] authored a large study that specifically addressed historical, lifestyle, and immunologic risk factors for anaphylaxis caused by latex Of 7389 surgical procedures done in children, 11 (10 with spina bifida and one with a congenital urologic abnormality) experienced 12 anaphylactic reactions Risk factors that reached statistical significance included history of anaphylaxis, history of immediate reactions to rubber products, food allergy, and daily rectal disimpaction The most important predictive immunologic evaluation was total IgE level, a nonspecific indicator, latex SPT, enzyme-linked immunosorbent assay, and RAST alone or in combination were not statistically significant [219]

In the same study, univariate analysis determined that the following variables were sensitive but not very specific latex sensitivity, history of asthma, history of immediate reactions to rubber products, food allergy, or rash caused by adhesive tape The most specific, but not very

sensitive, variable was the need for daily rectal disimpaction Anaphylaxis was best predicted by a combination of the following three factors RAST or SPT positivity to latex, history of immediate clinical symptoms to rubber products, and daily rectal disimpaction The authors concluded that although SPT, ELISA, and RAST are helpful for identifying patients who are sensitive to latex, these tests lack specificity for predicting anaphylactic reactions Clinical history in combination with total serum IgE was a more sensitive and specific predictor of patients at risk for anaphylactic reactions [219]

PRECAUTIONS

TOP

Multiple educational resources are available (Tables XI and XII)

Table XI. Latex allergy sources

Organizations

ALERT, Allergy to Latex Education and Resource Team, Asthma/Allergy Center #795, PO Box 1997, Milwaukee, WI 53201 (414-677-9707)

ELASTIC, Education for Latex Allergy Support Team and Information Coalition, 176 Roosevelt Ave , Torrington, CT 06790 (800-482-6869)

Spina Bifida Association of America, 4590 MacArthur Blvd , NW, Suite 250, Washington, DC 20007-4226 (800-621-3141 or 202-944-3285)

Publications

The ABC's of Latex Allergy, patient education pamphlet, Asthma and Allergy Foundation of America, 1125 15th St , NW, Suite 502, Washington, DC 20005 (202-466-7643)

The Alternative Resource Catalog, latex-free products for daily living Nicci D Paris, RN, President, Alternative Resource Catalog, 145 Wetzel Rd , Pittsburgh, PA 15209-1127 (800-618-3129)

Latex Allergy Protect Yourself, Protect Your Patients, American Nurses Association, Workplace Information Series, 600 Maryland Ave , SW, Suite 100W, Washington, DC 20024-2571 (800-274-4ANA)

Natural Rubber-containing Medical Devices, User Labeling, Department of Health and Human Services, Food and Drug Administration, Docket No 96N-0119, 21 CFR Part 8 01, Federal Register, Vol 62, No 189, Sept 30, 1997 For more information contact Donald E Marlowe, Center for Devices and Radiological Health (HFZ-100), ffice of Science and Technology, Food and Drug Administration, 12725 Twinbrook Parkway, Suite 217, Rockville, MD 20852 (301-827-4777)

Guidelines for the Management of Latex Allergies and Safe Latex Use in Health Care Facilities, American College of Allergy, Asthma and Immunology, 85 W Algonquin Rd , Suite 550, Arlington Heights, IL 60005 (847-427-1200)

Latex Allergy News, information-sharing vehicle of ELASTIC, 176 Roosevelt Ave , Torrington, CT 06790 (800-482-6869)

Immunology and Allergy Clinics of North America, February 1995, Vol 15 Guest Editor Jordan N Fink, MD Entire issue devoted to latex allergy

Other

Medic Alert (to obtain allergy alert ID bracelet) 2323 Colorado Ave , Turlock, CA 95382

Med Watch (to report problems with products to the FDA) Food and Drug Administration, Med Watch Office, Room 1765, 5600 Fishers Lane (HF2), Rockville, MD 20857 (800-332-1088)

Table XII. Latex allergy information on the Internet

Organization/Topic	Web site
Latex Allergy Links	*http //www netcom com/~nam1/latex_allergy html*
The LAIR (Latex Allergy Information Resource)	*http //mediswww cwru edu/dept/anesth/lair/lair htm*
Latex Allergy Help	*http://www latexallergyhelp com*
Foundation for Latex Allergy Research and Education (FLARE)	*http://www flare org*
Allergy to Latex Education and Resource Team (ALERT)	*http //www execpc com/~trukaras/ALERT/*
Latex-Allergy Home Page	*http //allergy mcg edu/physicians/ltxhome html*
Federal Register Notice Latex-containing Devices, User Labeling	*http://www fda gov/cdrh/fr6241xf html*
PALS (Physicians Against Latex Sensitization)	*http //www pals net/*
ELASTIC (Education for Latex Allergy/Support Team and Information Coalition)	*http://www netcom com/~ecbdmd/elastic html*
NIOSH (National Institute for Occupational Safety and Health	*http //www cdc gov/niosh/latexall html*

Patients and physicians can take precautions to prevent serious reactions (Tables XIII[220,221] and XIV)

Table XIII. Providing a latex-safe hospital environment for patients allergic to latex*

1 Use nonlatex examination and sterile gloves
2 Remove all latex products from patient's room
Do not inject or withdraw fluid through rubber ports of intravenous lines
4 Substitute polyvinylchloride, silicone, and/or other nonlatex alternatives for medical supplies such as endotracheal tubes, adhesive bandage strips, bulb syringes, airways, ventilator bellows †
5 Shield direct exposure from certain dry-rubber equipment Blood pressure cuffs can be used over clothing Stethoscope tubing can be covered with a stockinette
6 Utilize single-dose ampules for parenteral medication rather than multiple-dose vials

*Modified from Pasquanello CA, Lowe DA, Schwartz RE Pediatrics 1993,91 983-6
†Extensive list in Latex Allergy News 1997, introductory issue 5-9

Table XIV. Precautions for physicians

1 Consider placing information sheets and signs about latex allergy in waiting room
2. Use nonlatex gloves for all mucosal examinations
3 Consider using nonlatex gloves for all contact with patients
4 If latex gloves are to be used, choose powder-free and low allergen gloves to decrease aerosolized antigen in workplace
5 Screen patients for latex allergy at each clinic visit and hospital admission "Latex allergic" label should be designated for all those patients with a clinical history All high-risk patients (myelodys-plasia, multiple congenital anomalies, or history of multiple operations) should be labeled "latex alert"
6 Create awareness within hospital, clinic, and community
7 Urge development of latex-free operating rooms, especially for high-risk patients
8 Report incidents to the FDA (800-638-6725)

Prevention of sensitization is an ideal goal, especially for those at high risk Many hospitals now have latex-free operating rooms used specifically for children with spina bifida and other congenital anomalies Meeropol et al [94] found that 7 of 16 Shriners children's hospitals surveyed had latex-free operating rooms

SURGERY FOR LATEX-SENSITIVE PERSONS

TOP

When surgery is necessary, prophylactic medication (Table XV[222]) is recommended in addition to latex avoidance

Table XV. Preoperative regimens for latex-sensitive persons*

Start 24 hr preoperatively and continue for 24 hr postoperatively	
Diphenhydramine	1 mg/kg q 6 hr IV/PO (max 50 mg)
Alternative	Terfenadine 30-60 mg q 12 hr PO
Methylprednisolone	1 mg/kg q 6 hr IV/PO (max 125 mg)
Alternative	Prednisone 0 5 mg/kg/dose q 12 hr PO
Cimetidine	5 mg/kg/dose q 6 hr IV/PO (max 300 mg)
Alternative	Ranitidine 1-2 mg/kg/day divided q 8 hr IV or 3-4 mg/kg/day divided q 12 hr PO

IV, Intravenous, *max*, maximum, *PO*, orally, *q*, every
*Modified from Meeropol E, Frost J, Pugh L, Roberts J, Ogden JA J Pediatr Orthop 1993,13 1-4, Kelly KJ Immunol Allergy Clin North Am 1995,15 139-57, and Kwittken PL, Becker J, Oyefara B, Danziger R, Pawlowski NA, Sweinberg S Allergy Proc 1992,3 123-7

Although this is beneficial in some cases of latex sensitization,[83,220] allergic reactions still occur [223-225] Although some authorities[83,226] do not advocate switching to latex-free medication vials and syringes, there have been reports of reactions to latex in these sources [227-230] A detailed anesthesia protocol describing equipment, set-up, and management for surgical latex-sensitive patients has been developed at the Cleveland Clinic and is posted on the Internet [231]

LATEX SUBSTITUTES

TOP

For sources of nonlatex surgical and examination gloves, low allergen latex gloves, and DTH allergens in gloves, several excellent references are available.[14,115,232-235] Lists of latex-safe alternatives to many products found in hospital and home environments are also available [221] Five major glove alternatives are briefly discussed below

Polyvinylchloride (vinyl) gloves are probably the least expensive and most widely used nonlatex examination glove alternative Their main

disadvantages are inflexibility and permeability to fluids and infectious agents [236,237] One study found that 63% of vinyl gloves versus 7% of latex gloves leaked after repeatedly attaching and removing a needle from a syringe [238] Vinyl gloves may also contain colorants and formaldehyde, which may produce DTH allergy, accounting for approximately 1% (5 of 542) of occupational allergic glove dermatitis in one series [61]

Polychloroprene (neoprene) gloves may similarly contain allergenic accelerators such as isodiphenylthiourea, carbamates, and mercaptobenzothiazoles Heese et al [141] reported a latex-sensitive person in whom anaphylaxis developed after wearing polychloroprene gloves Prick and patch tests to polychloroprene were negative On inquiry of the manufacturer, it was discovered that an inner coating of NRL (not declared on the glove box label) had been added to minimize costs

Carbamates may be found in both sterile and nonsterile examination gloves made of styrene butadiene block polymers (elastyren) [232] Nonsterile acrylic nitrile butadiene polymer (nitrile) examination gloves can also contain added chemicals such as mercaptobenzothiazoles and dyes (Allerderm product information) Sterile and nonsterile triblock copolymer (polystyrene-b-[ethylene-cobutylene]-b-polystyrene) gloves (Tactylon) were found to be safe in patients with immediate[239] and DTH to-NRL Lahti et al [240] found one positive reaction in 156 persons patch tested to Tactylon

Availability of nonlatex contraceptive products is important because severe reactions have been reported from mucosal exposure to latex condoms [38,40] Condoms made of processed lamb cecum do not protect against transmission of HIV[241] and therefore are not practical for many persons Fisher[242] recommended that NRL-sensitive men wear a lamb cecum condom under an NRL condom and that this layering be reversed if the partner is sensitive to NRL Unfortunately, wearing two condoms has little appeal

Polyurethane male and female condoms are now available [243] Polyurethane condoms prevent not only pregnancy but also transmission of viral diseases such as herpes and HIV [244,245]

It is expected that a new male condom made of Tactylon will also be available soon [246] A clinical trial has already demonstrated that the breakage rate of Tactylon condoms is as low as NRL condoms [247] Tactylon condoms prevented passage of a small bacteriophage (27 nm) as effectively as NRL condoms when tested as a surrogate for HIV (80 to 100 nm) [248] Tactylon condoms have the added benefit of possessing no unsaturated bonds and therefore are unaffected by conditions that cause NRL to deteriorate, such as contact with petrolatum products and ozone [246]

LATEX PRODUCT LABELING

TOP

Manufacturers use various labels to describe NRL products The term *hypoallergenic* refers to reduced DTH allergen content and does not imply latex-free The FDA restricts the use of this label to products that do not induce DTH during a modified Draize test involving 200 humans Hypoallergenic gloves can still contain latex and therefore are not appropriate for persons who are latex-sensitive [168] Such labeling causes confusion, a latex-sensitive nurse developed anaphylaxis to sterile surgical gloves labeled "specially formulated for hands allergic to latex "[249] The manufacturer used this phrase to refer to the removal of antioxidants that cause DTH.[250] Incidences such as this have prompted the FDA to ban the term *hypoallergenic* on labels of products containing NRL. In the same ruling, the FDA also mandated that labels of NRL medical devices must state "Caution This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions", dry natural rubber medical devices must be labeled "This Product Contains Dry Natural Rubber " Similar labeling will be required for nonmedical devices containing NRL that contact humans, such as NRL adhesives used in adhesive bandage strips These rulings go into effect Sept 30, 1998 [251] The FDA, industry, and the European glove standard are also developing regulations for "powder-free" latex medical devices [125,235]

EFFORTS TO DECREASE ALLERGEN CONTENT

TOP

Efforts to minimize and remove allergens causing type I reactions depend on identification of responsible proteins As the role of specific allergens has yet to be clarified, current aims at eliminating allergens have focused on decreasing total amounts of protein produced during manufacturing Ammonia, added to fresh latex during collection, decreases extractable protein levels Centrifugation halves total protein levels, and double centrifugation reduces protein levels by another 25% to 30% During compounding, however, addition of detergents or potassium hydroxide can actually increase levels of extractable proteins Water leaching is critical, 5 minutes of wet gel leaching removes 60% of extractable protein from postvulcanized films and 85% from prevulcanized films As much as 90% of extractable protein can be removed by combining wet gel and dry film leaching [252]

Vulcanization selectively favors build-up of water-soluble proteins on the inside glove surface Perhaps because of this migration phenomenon, postprocessing chlorination appears to be the most effective method of reducing protein content, not only by rendering remaining surface proteins insoluble, but also by leaching additional extractable proteins Chlorination is a necessary step in producing powder-free gloves and may explain why some latex-sensitive persons are able to tolerate powder-free gloves Autoclaving and application of silicone to NRL surfaces can further reduce protein migration [253]

Although these techniques reduce allergen content, benefits must be balanced against both increases in production costs and changes in physical properties of the finished product For example, chlorination has several disadvantages First, it increases a production facility's rejection rate by 7% to 20% Second, it creates a slippery surface disliked by many clinicians Third, it cleaves isoprene chains, which decreases stretch and strength of NRL films and reduces shelf life [246] Experimental types of latex, such as enzymatically treated or pasteurized latex, may play a larger role in preventing latex allergy in the future [252]

ALTERNATIVE SOURCES OF NATURAL RUBBER

TOP

There are several rubber-producing species other than *H brasiliensis* The rubber particles in the common North American desert shrub, guayule *(Parthenium argentatum)*, contain *cis*-isoprene that is virtually identical to *Hevea* rubber [254] Recently, researchers have developed

hypoallergenic rubber from guayule, which was tolerated by persons allergic to *Hevea* latex and demonstrated superior resiliency, strength, and elasticity This technology has been patented, and guayule rubber medical supplies will soon be available [255]

Immediate-type allergy to guayule has not been described, however, rarely DTH may develop [256] Rodriguez, Reynolds, and Thompson[257] isolated the sesquiterpene cinnamic acid ester, guayulin A, from dried guayule leaf extract and determined that it was a potent elicitor of H Other species of *Parthenium* contain sesquiterpene lactones that are cytotoxic and produce allergic skin reactions [258] This DTH ensitization could be a potential problem for persons exposed to guayule rubber products

Ficus elastica, the common ornamental rubber plant, produces relatively low-molecular-weight rubber proteins and is another potential alternative rubber source Carey et al [259] found that seven *H brasiliensis*–sensitive health care workers all had negative SPTs to *F elastica*.

MANAGEMENT

TOP

Avoidance of direct contact with latex products may not be sufficient [260] Swanson et al [261] collected air samples from 11 medical areas where powdered latex gloves were frequently used and found that latex aeroallergen concentrations were up to 115 times greater than in areas where powdered latex gloves were never or seldom used Use of a laminar flow glove changing station in one work area did not reduce latex aeroallergen levels Use of powder-free gloves appears to be more effective in reducing aeroallergen levels, as demonstrated by Tarlo et al [262] who showed that the asthmatic and anaphylactic reactions of a hospital laboratory technician could be controlled by her coworkers' use of powder-free gloves Vandenplas et al [263] similarly found that latex gloves with lower protein and powder contents significantly reduced the risk of development of asthmatic reactions in eight health care workers who showed latex-induced occupational asthma during inhalation challenge tests

Treatment of symptoms with topical steroids and oral antihistamines has been the mainstay of treatment for latex allergy Hyposensitization has not been successful Immunotherapy, although still experimental, holds promise for future therapy Slater et al [264] found vaccines with cloned Hev b 5 DNA sequences inhibited IgE responses to Hev b 5 in mice sensitized to this antigen These results suggest that DNA vaccines with encoded allergens may offer a new mode of allergen immunotherapy for persons with latex allergy

FUTURE ISSUES

TOP

Latex awareness is growing National television has aired exposés such as ABC's *20/20* "Latex Allergies " A recent fictional drama, NBC's *ER*, depicted a medical student having an anaphylactic reaction to latex gloves Many hospitals and organizations such as the National Institute of Occupational Safety and Health and the American Academy of Dermatology have already formed latex task forces These committees not only deliberate on issues regarding education and development of latex-safe areas, but also address potential legal plications The Americans with Disabilities Act and the Federal Rehabilitation Act of 1973 may require accommodation (e g , lowering ergen levels and special protective equipment) of employees with latex allergy [265] Lawyers are already advertising for clients on latex Web sites, and there are at least two class action lawsuits in the United States filed against manufacturers of NRL gloves [266] Bills entirely banning powdered latex gloves in health care facilities have been introduced in Oregon, Minnesota, and New York [267] Implications of these heated legal debates are far-reaching and affect whom, how, and with what tools medicine is practiced

SUMMARY

TOP

Latex allergy affects thousands of people in several major risk groups Although progress has been made during the past decade in identifying responsible antigens, much research is needed to develop safe, accurate, and reliable tests for detecting latex allergy Almost 50% of hospital products contain NRL, eliminating these sources of sensitization and educating those persons at risk without causing irrational public responses are ongoing goals

REFERENCES

TOP

1. de Livonniere H Industrial natural rubber collection and control procedures Clin Rev Allergy 1993,11 309-23
MEDLINE

2. Walls RS Latex allergy a real problem Med J Aust 1996,164 707-8
MEDLINE

3. Hetier JM Natural latex 1991 economic aspects Clin Rev Allergy 1993,11 299-307
MEDLINE

4 Stern G Überempfindlichkeit gegen kautsckuk als ursache von urticaria und quinckeschem ödem Klin Wochenschr 1927,6 1096

5. Nutter AF Contact urticaria to rubber Br J Dermatol 1979,101 597-8
MEDLINE

6. Warpinski JR, Folgert J, Cohen M, Bush RK Allergic reaction to latex a risk factor for unsuspected anaphylaxis Allergy Proc 1991,12 95-102
MEDLINE

7. Kopman A, Hannuksela M Kumin aihenttama kosketusurtokari Duodecim 1983,99 221-4

MEDLINE

8. Frosch PJ, Wahl R, Bahmer FA, Maasch HJ Contact urticaria to rubber gloves is IgE-mediated Contact Dermatitis 1986,14 241-5
MEDLINE

9 Volcheck GW, Li JTC Elevated serum tryptase level in a case of intraoperative anaphylaxis caused by latex allergy Arch Intern Med 1994,154 2243-5
MEDLINE

10. Turjanmaa K, Reunala T, Alenius H, Brummer-Korvenkontio H, Palosuo T Allergens in latex surgical gloves and glove powder Lancet 1990,336 1588
MEDLINE

11. Barton EC Latex allergy recognition and management of a modern problem Nurse Pract 1993;18 54-8
MEDLINE

12. Nightingale SS Severe adverse reactions to barium enema procedures JAMA 1991,264 2863

13. Anonymous Allergic reactions to latex-containing devices FDA Med Bull 1991,21(July) 1-3

14 Hamann CP Natural rubber latex protein sensitivity in review Am J Contact Dermatitis 1993,4 4-21

15. Jacob JL, d'Auzac J, Prevot JC. The composition of natural latex from *Hevea brasiliensis* Clin Rev Allergy 1993,11 325-7
MEDLINE

16. Cornish K The separate roles of plant *cis* and *trans* prenyl transferases in *cis*-1,4-polyisoprene biosynthesis Eur J Biochem 1993 218 267-71
MEDLINE

17 Light DR, Dennis MS Purification of a prenyl transferase that elongates *cis*-polyisoprene rubber from the latex of *Hevea brasiliensis* J Biol Chem 1989,264 18589-97
MEDLINE

18 Dennis MS, Light DR Rubber elongation factor from *Hevea brasiliensis* J Biol Chem 1989,264 18608-17
MEDLINE

19 Lee H, Broekaert WF, Raikhel NV Co- and post-translational processing of the hevein preproprotein latex of the rubber tree *(Hevea braziliensis)* J Biol Chem 1991,266 15944-8
MEDLINE

20 Jekel PA, Hartmann JBH, Beintma JJ The primary structure of hevamine, an enzyme with lysozyme/chitinase activity from *Hevea braziliensis* latex Eur J Biochem 1991,200 123-30
MEDLINE

21. Maibach HI, Johnson HL Contact urticaria syndrome Arch Dermatol 1975,111 726-30
MEDLINE

22. Sussman GL Latex allergy its importance in clinical practice Allergy Proc 1992,13 67-9
MEDLINE

23. Seaton A, Cherrie B, Turnbull J Rubber glove asthma BMJ 1988,296 531-2

24. Lagier F, Badier M, Martigny J, Charpin D, Vervloet D Latex as aeroallergen [letter] Lancet 1990,330 516-7

25. Baur X, Jaeger D Airborne antigens from latex gloves Lancet 1990,335 912
MEDLINE

26 Reed CE, Swanson MC, Yunginger JW, Warner MA, Hunt LW Latex allergens in the air of operating suites Am Rev Respir Dis 1993,147(Suppl 2) A109

27. Jaeger D, Kleinhans D, Czuppon AB, Baur X. Latex specific proteins causing immediate-type cutaneous, nasal, bronchial and systemic reactions J Allergy Clin Immunol 1992,89 759-68
MEDLINE

28. Fisher AA Contact urticaria due to cornstarch surgical glove powder Cutis 1986,38 307-8
MEDLINE

29. van der Meeren HLM, van Erp PEJ Life-threatening contact urticaria from glove powder Contact Dermatitis 1986,14 190-1
MEDLINE

30 Moneret-Vautrin DA, Laxenaire MC, Bavoux F Allergic shock to latex and ethylene oxide during surgery for spina bifida Anesthesiology 1990,73 556-8
MEDLINE

31. Vandenplas O. Occupational asthma caused by natural rubber latex Eur Respir J 1995,8 1957-65
MEDLINE

32. Nguyen DH, Burns MW, Shapiro GG, Mayo ME, Murrey M, Mitchell ME Intraoperative cardiovascular collapse secondary to latex allergy J Urol 1991,146 571-4
MEDLINE

33. Pecquet C, Leynadier F, Dry J Contact urticana and anaphylaxis to natural latex J Am Acad Dermatol 1990,22 631-3
MEDLINE

34. Turjanmaa K. Allergy to natural rubber latex a growing problem Ann Med 1994,26 297-300
MEDLINE

35. Makinen-Kiljunen S, Turjanmaa K, Palosuo T Allergenicity of baby pacifiers and bottle teats made from natural rubber latex [abstract] J Allergy Clin Immunol 1997,99 S156

36. Effendy I, Gieler U, Bischoff R, Happle R Anaphylaxis due to a latex vaginal vibrator Contact Dermatitis 1992,27 318-9
MEDLINE

37. Guimaraens D, Gonzalez MA, Conde-Salazar L Occupational allergic contact dermatitis and anaphylaxis from rubber latex. Contact Dermatitis 1992,26 268-9
MEDLINE

38. Leynadier F, Pecquet C, Dry J Allergie vaginale au latex d'un preservatif masculin Rev Fr Allergol 1989,29 99

39. Belsito DV Contact urticana caused by rubber Dermatol Clin 1990,8 61-6
MEDLINE

40. Pecquet C, Leynadier F IgE mediated allergy to natural rubber latex in 100 patients Clin Rev Allergy 1993,11 381-4
MEDLINE

41. Scriven RJ, Cirocco WC, Golub RW Latex allergy report of an anaphylactic reaction Surgery 1995,117 350-2
MEDLINE

42. Misselbeck WJA, Gray KR, Uphold RE Latex induced anaphylaxis a case report Am J Emerg Med 1994,12 445-7
MEDLINE

43. Axelsson IGK, Eriksson M, Wrangsjo K Anaphylaxis and angioedema due to rubber allergy in children Acta Paediatr Scand 1988,77 314-6
MEDLINE

44. Axelsson IGK, Johansson SGO, Wrangsjo K IgE-mediated anaphylactoid reactions to rubber Allergy 1987,42 46-50
MEDLINE

45. Zenarola P Rubber latex allergy unusual complication during surgery Contact Dermatitis 1989,21 197-8
MEDLINE

46. Beuers U, Baur X, Schrandolph M, Richter WO Anaphylactic shock after a game of squash in an atopic woman with latex allergy Lancet 1990,335 1095
MEDLINE

47. Mansell PI, Reckless JPD, Lovell CR Severe anaphylactic reaction to latex rubber surgical gloves BMJ 1994,308 246-7
MEDLINE

48. Schwartz HJ Latex a potential hidden "food" allergen in fast food restaurants J Allergy Clin Immunol 1995,95 139-40
MEDLINE FULLTEXT

49 Kerner MM, Newman A Diagnosis and management of latex allergy in surgical patients Am J Otolaryngol 1993,6 440-3

50. Tomazic VJ, Withrow TJ, Fisher BR, Dillard SF Latex-associated allergies and anaphylactic reactions Clin Immunol Immunopathol 1992,64 89-97
MEDLINE

51. Turjanmaa K, Reunala T, Tuimala R, Karkkäinen T Allergy to latex gloves unusual complication during delivery BMJ 1988,297 1029
MEDLINE

52. Sondheimer JM, Pearlman DS, Bailey WC Systemic anaphylaxis during rectal manometry with a latex balloon Am J Gastroenterol 1989,84 975-8
MEDLINE

53 Gerber AC, Jorg W, Zbinden S, Seger A, Dangel PH Severe intraoperative anaphylaxis to surgical gloves latex allergy, an unfamiliar condition Anesthesiology 1989,71 800-2
MEDLINE

54. Abbas AK, Lichtman AH, Pober JS Cellular and molecular immunology 2nd ed Philadelphia WB Saunders, 1994 p 279

55. Leynadier F Pathophysiological and clinical aspects of immediate hypersensitivity to latex Clin Rev Allergy 1993,11 371-80
MEDLINE

56. Shumes E, Darby T Contact dermatitis due to endotoxin in irradiated latex gloves Contact Dermatitis 1984,10 240-4
MEDLINE

57. Thelin A, Tegler Ö, Rylander R Lung reactions during poultry handling related to dust and bacterial endotoxin levels Eur J Respir Dis 1984,65 266-71
MEDLINE

58. Smid T, Heederik D, Houba R, Quanjer PH Dust- and endotoxin-related acute lung function changes and work-related symptoms in workers in the animal feed industry Am J Ind Med 1994,25 877-88
MEDLINE

59. Williams PB, Halsey JF Endotoxin as a factor in adverse reactions to latex gloves Ann Allergy Asthma Immunol 1997,79 303-10
MEDLINE

60 Williams PB, Halsey JF Characterization of the bioaerosol from latex gloves contaminated with endotoxin [abstract] J Allergy Clin Immunol 1997,99(Suppl) S266

61 Estlander T, Jolanki R, Kanerva L Dermatitis and urticaria from rubber and plastic gloves Contact Dermatitis 1986,14 20-5
MEDLINE

62. von Hitzenstern J, Heese A, Koch HU, Peters KP, Hornstein OP Frequency, spectrum and occupational relevance of type IV allergies to rubber chemicals Contact Dermatitis 1991,24 244-52.
MEDLINE

63. Conde-Salazar L, del-Rio E, Guimaraens D, Domingo AG Type IV allergy to rubber additives a 10-year study of 686 cases J Am Acad Dermatol 1993,29 176-80
MEDLINE

64 Pecquet C Allergic contact dermatitis to rubber clinical aspects and main allergens Clin Rev Allergy 1993,11 413-9
MEDLINE

65 Wyss M, Elsner P, Wuthrich B, Burg G Allergic contact dermatitis from natural latex without contact urticaria Contact Dermatitis 1993,28 154-6
MEDLINE

66. Lezaun A, Marcos C, Martin JA, Quirce S, Gomez MLD Contact dermatitis from natural latex Contact Dermatitis 1992,27 334-5
MEDLINE

67. Wilkinson SM, Beck MH Allergic contact dermatitis from latex rubber Br J Dermatol 1996,134 910-4
MEDLINE

68. Rietschel RL, Fowler JF Fisher's Contact dermatitis 4th ed Baltimore Williams & Wilkins, 1995 p 642, 676-8

69. Turjanmaa K Incidence of immediate allergy to latex gloves in hospital personnel Contact Dermatitis 1987,17 270-5
MEDLINE

70 Moneret-Vautrin D, Beaudouin E, Widmer S, Mouton C, Kanny G, Prestat F, et al Prospective study of risk factors in natural rubber latex hypersensitivity J Allergy Clin Immunol 1993,92 668-77
MEDLINE

71. Porri F, Lemiere C, Birnbaum J, Guilloux L, Didelot R, Vervloet D, et al Prevalence of latex allergy in atopic and non-atopic subjects from the general population J Allergy Clin Immunol 1995,95 154

72. Ownby DR, Ownby HE, McCullough BA, Shafer AW The prevalence of anti-latex IgE antibodies in 100 volunteer blood donors [abstract] J Allergy Clin Immunol 1994,93 282

73 Merrett TG, Merrett J, Bhambri S, Kekwick R Prevalence of latex specific IgE antibodies in the UK [abstract] J Allergy Clin Immunol 1995,95 154

74. Turjanmaa K Update on occupational natural rubber latex allergy Dermatol Clin 1994,12 561-7
MEDLINE

75 Arellano R, Bradley J, Sussman G Prevalence of latex sensitization among hospital physicians occupationally exposed to latex gloves Anesthesiology 1992,77 905-8
MEDLINE

76 Akasawa A, Matsumoto K, Saito H, Sakaguchi N, Tanaka K, Obata T et al Incidence of latex allergy in atopic children and

hospital workers in Japan Int Arch Allergy Immunol 1993,101 177-81
MEDLINE

77. Slater JE Rubber anaphylaxis N Engl J Med 1989,320 1126-30
MEDLINE

78 Opsomer O, Van Boven M, Pendeville P, Veyckemans F An unusual presentation of latex allergy [letter]. Can J Anaesth 1993,40 1000-6
MEDLINE

79 Sethna NF, Sockin SM, Holzman RS, Slater JE Latex anaphylaxis in a child with a history of multiple anesthetic drug allergies Anesthesiology 1992,77 372-5
MEDLINE

80 Centers for Disease Control [letter] July 1991

81. Setlock MA, Kelly KJ Anaphylaxis on introduction of anesthesia associated with latex allergy [abstract] Anesthesiology 1991,75 3A

82. Kelly KJ, Setlock M, Davis JP Anaphylactic reactions during general anesthesia among pediatric patients MMWR 1991,40 437

83. Tosi LL, Slater JE, Shaer C, Mostello LA Latex allergy in spina bifida patients prevalence and surgical implications J Pediatr Orthop 1993,13 9-12
MEDLINE

84. Slater JE, Shaer C, Mostello LA Rubber-specific IgE in children with spina bifida [abstract] J Allergy Clin Immunol 1990,85 293

85. Beaudouin E, Prestat F, Schmitt M, Kanny G, Laxenaire MC, Moneret-Vautrin DA High risk of sensitization to latex in children with spina bifida Eur J Pediatr Surg 1994,4 90-3
MEDLINE

86. Sandberg ET, Slater JE, Roth DR, Abramson SL Rubber specific IgE in children enrolled in a spina bifida clinic [abstract] J Allergy Clin Immunol 1992,89 223

87. Kelly KJ, Kurup V, Zacharisen M, Resnick A, Fink JN Skin and serologic testing in the diagnosis of latex allergy J Allergy Clin Immunol 1993,91 1140-5
MEDLINE

88. Slater JE, Trybul DE Affinity purification of latex antigens J Allergy Clin Immunol 1994,93 644-9
MEDLINE ABSTRACT FULL TEXT

89. Slater JE, Mostello LA Routine testing for latex allergy in patients with spina bifida is not recommended [letter] Anesthesiology 1991,74 391
MEDLINE

90. Yassin MS, Sanyurah S, Lierl MB, Rischer TJ, Oppenheimer S, Cross J Evaluation of latex allergy in patients with meningomyelocele Ann Allergy 1992,69 207-11
MEDLINE

91 Capriles-Hulett A, Sanchez-Borges M, Scanzoni C, Nunez-Machado J, Capriles-Behrens E Very low prevalence of latex allergy in a tropical environment [abstract] J Allergy Clin Immunol 1997,99(Suppl) S159

92 Meeropol E, Kelleher R, Bell S, Leger R Allergic reactions to rubber in patients with myelodysplasia N Engl J Med 1990,323 1072
MEDLINE

93. Zerin JM, McLaughlin K, Kerchner S Latex allergy in patients with myelomeningocele presenting for imaging studies of the urinary tract Pediatr Radiol 1996,36 450-4

94 Meeropol E, Frost J, Pugh L, Roberts J, Ogden JA Latex allergy in children with myelodysplasia a survey of Shriners hospitals J Pediatr Orthop 1993,13 1-4
MEDLINE

95. Berky T, Luciano J, James D Latex glove allergy JAMA 1992,268 2695-7
MEDLINE

96 Rankin KV, Jones DL, Rees TD Latex glove reactions found in a dental school J Am Dent Assoc 1993,124 67-71
MEDLINE

97. Tipirneni P, Harfi H, Mohammed GH, Lonnevig VG Latex allergy in hospital personnel exposed to rubber materials (gloves) [abstract] J Allergy Clin Immunol 1997,99(Suppl) S160

98. Katelaris CH, Widmer RP, Lazarus RM Prevalence of latex allergy in a dental school Med J Aust 1996,164 711-4
MEDLINE

99. Kujala VM, Reijula KE Glove-induced dermal and respiratory symptoms among health care workers in one Finnish hospital An

J Ind Med 1995,28 89-98
MEDLINE

100. Salkie ML, Chir B The prevalence of atopy and hypersensitivity to latex in medical laboratory technologists Arch Pathol Lab Med 1993,117 897-9
MEDLINE

101. Wrangsjo K, Osterman K, van Hage-Hamsten M Glove-related skin symptoms among operating theatre and dental care unit personnel (I) Interview investigation Contact Dermatitis 1994,30 102-7
MEDLINE

102. Wrangsjo K, Osterman K, van Hage-Hamsten M Glove-related skin symptoms among operating theatre and dental care unit personnel (II) Clinical examination, tests and laboratory findings indicating latex allergy Contact Dermatitis 1994,30 139-43
MEDLINE

103. Kaczmarek RG, Silverman BG, Gross TP, Hamilton RG, Kessler E, Arrowsmith-Lowe JT Prevalence of latex-specific IgE antibodies in hospital personnel Ann Allergy Asthma Immunol 1996,76 51-6
MEDLINE

104. Eriksen P, Nissen D, DuBuske LM, Sheffer A, Skov PS, Cieslewicz G et al Comparison of latex-specific IgE binding of various latex extracts in hospital personnel [abstract] J Allergy Clin Immunol 1997,99(Suppl) S156

105. Harfi H, Tipirneni P, Mohammed GH, Lonnevig VG Latex hypersensitivity prevalence among health care personnel, as measured by skin prick test (SPT), CAP, and challenge [abstract] J Allergy Clin Immunol 1997,99(Suppl) S160

106. Beaudouin E, Pupil P, Jascon F, Laxenaire MC, Moneret-Vautrin DA Allergie professionnelle au latex enquête prospective sur 907 sujets du milieu hospitalier Rev Fr Allergol 1990,30 157-61

107. Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D Prevalence of latex allergy in operating room nurses J Allergy Clin Immunol 1992,90 319-22
MEDLINE

108. Sussman GL, Liss GM Latex allergy epidemiologic study of 1351 hospital workers [abstract]. J Allergy Clin Immunol 1997,99 (Suppl) S344

109. Yassin MS, Lierl MB, Fischer TJ, O'Brien K, Cross J, Steinmetz C Latex allergy in hospital employees Ann Allergy 1994,72 245-9
MEDLINE

110. Charous BL. Occupational latex exposure characteristics of contact and systemic reactions in 47 workers J Allergy Clin Immunol 1994,94 12-8
MEDLINE ABSTRACT FULL TEXT

111. Jones RT, Bubak ME, Grosselin VA, Yunginger JW Relative latex allergen contents of several commercial latex gloves [abstract] J Allergy Clin Immunol 1992,89 225.

112. Bubak ME, Reed CE, Fransway AF, Yunginger JW, Jones RT, Carlson CA, et al Allergic reactions to latex among health-care workers Mayo Clin Proc 1992,67 1075-9
MEDLINE

113. van der Walle HB, Brunsveld VM Latex allergy among hairdressers Contact Dermatitis 1995,32 177-8
MEDLINE

114. Tarlo SM, Wong L, Roos J, Booth N Occupational asthma caused by latex in a surgical glove manufacturing plant. J Allergy Clin Immunol 1990,85 626-31
MEDLINE

115. Heese A, von Hintzenstern J, Peters KP, Koch HU, Hornstein OP Allergic and irritant reactions to rubber gloves in medical health services spectrum, diagnostic approach, and therapy J Am Acad Dermatol 1991,25 831-9
MEDLINE

116. Moneret-Vautrin DA, Debra JC, Kohler C, Stringini R, Kanny G, Guillaumot A, et al Occupational rhinitis and asthma to latex Rhinology 1994,32 198-202.
MEDLINE

117. Rosen A, Isaacson D, Brady M, Corey JP Hypersensitivity to latex in health care workers report of five cases Otolaryngol Head Neck Surg 1993,109 731-4
MEDLINE

118. Hopkins J Rubber latex in the air An occupational and environmental cause of asthma? Food Chem Toxicol 1995,33 895-9
MEDLINE

119. Vandenplas O, Delwiche JP, Evrard G, Aimont P, van der Brempt X, Jamart J, et al Prevalence of occupational asthma due to latex among hospital personnel Am J Respir Crit Care Med 1995,151 54-60
MEDLINE

120. Orfan NA, Reed R, Dykewicz MS, Ganz M, Kolski G Occupational asthma in a latex doll manufacturing plant J Allergy Clin Immunol 1994,94 826-30
MEDLINE ABSTRACT FULL TEXT

121. Taylor JS, Praditsuwan P Latex allergy review of 44 cases including outcome and frequent association with allergic hand eczema Arch Dermatol 1996,132 265-71
MEDLINE

122. Slater J, Kaliner M Effects of sex hormones on basophil histamine release in recurrent idiopathic anaphylaxis J Allergy Clin Immunol 1987,80 285-90
MEDLINE

123. White MV, Slater JE, Kaliner MA Histamine and asthma Am Rev Respir Dis 1987,135,1165-76
MEDLINE

124. Diaz T, Martinez T, Antepara I, Usandizaga JM, Valverde ML, Jaurequi I Latex allergy as a risk during delivery Br J Obstet Gynaecol 1996,103 173-5
MEDLINE

125. Stigi J, Cardamone T, Lowery A U S Department of Health and Human Services, Center for Devices and Radiological Health Regulatory requirements for medical gloves HHS Publication (FDA) 93-4257 May 1993

126. Jones RT, Sheppman DL, Heilman DK, Yunginger JW Prospective study of extractable latex allergen contents of disposable medical gloves Ann Allergy 1994,73 321-5
MEDLINE

127. Hunt LW The epidemiology of latex allergy in health care workers Arch Pathol Lab Med 1993,117 874-5
MEDLINE

128. Turjanmaa K, Laurila K, Mäkinen-Kiljunen S, Reunala T Rubber contact urticaria allergenic properties of 19 brands of latex gloves Contact Dermatitis 1988,19 362-7
MEDLINE

129. Bonnekoh B, Merk HF Safety of latex prick skin testing in allergic patients [letter] JAMA 1992,267 2603
MEDLINE

130. Banov CH Current review of anaphylaxis and its relationship to asthma Allerg Immunol 1991,23 417-20

131. Rueff F, Thomas P, Przybilla B Skin prick tests (SPTs) with natural latex milk (NLM) and a natural latex SPT solution (NLS) [abstract] J Allergy Clin Immunol 1997,99(Suppl) S158

132. Turjanmaa K, Reunala T, Rasanen L Comparison of diagnostic methods in latex surgical glove contact urticaria Contact Dermatitis 1988,19 241-7
MEDLINE

133 Ebo DG, De Clerck LS, Bridts CH, Stevens WJ Comparison of latex-specific IgE, skin testing and lymphocyte transformation (LTT) in latex anaphylaxis [abstract] J Allergy Clin Immunol 1997,99(Suppl) S157

134 Kadambi A, Field S, Charous BL Diagnostic testing in latex allergy [abstract] J Allergy Clin Immunol 197,99(Suppl) S503

135. Blanco C, Castillo R, Quiralte J, Ortega N, Dominguez C, Carrillo T Comparison of skin prick test and specific IgE determination for the diagnosis of latex allergy [abstract] J Allergy Clin Immunol 1997,99(Suppl) S503

136. Turjanmaa K, Rasanen L, Lehto M, Mäkinen-Kiljunen S, Reunala T Basophil histamine release and lymphocyte proliferation tests in latex contact urticaria Allergy 1989,44 181-6
MEDLINE

137. Hozman RS Latex allergy an emerging operating room problem Anesth Analg 1993,76 635-41
MEDLINE

138. DeShazo RD, Lopez M, Salvaggio JE Use and interpretation of diagnostic immunologic laboratory tests JAMA 1987,248 3011-31

139. Gilles JG, Mareschal JC, Saint-Remy JM Latex allergosorbent test (LAST) a new immunoassay for specific IgE with latex particles J Allergy Clin Immunol 1988,82 35-9
MEDLINE

140 Turjanmaa K, Mäkinen-Kiljunen S, Reunala T, Alenius H, Palosuo T Natural rubber latex allergy the European experience Immunol Allergy Clin North Am 1995,15 71-88

141. Heese A, Peters KP, Hornstein OP Anaphylactic reaction to unexpected latex in a polychloroprene glove Contact Dermatitis 1992,27 336-7
MEDLINE

142 Kelly KJ, Kurup VP, Reijula KE, Fink JN The diagnosis of natural rubber latex allergy J Allergy Clin Immunol 1994,93 813-6

MEDLINE FULL TEXT

143. Morales C, Basomba A, Carreira J, Sastre A Anaphylaxis produced by rubber glove contact case reports and immunological identification of the antigens involved Clin Exp Allergy 1989,19 425-30
MEDLINE

144. Kujala V, Pirila T, Nurimake A, Reijula K Latex-induced allergic rhinitis in a laboratory nurse J Laryngol Otol 1995,109 1094-6
MEDLINE

145. Kurtz KM, Schaefer JA, Hamilton RG, Adkinson NF Hooded exposure chamber (HEC) for particulate latex allergen challenge [abstract] J Allergy Clin Immunol 1997,99(Suppl) S158

146. Higgins SM, Fesnic A, Kurup VP, Kelly KJ, Fink JN Latex specific IgE and IgG antibodies in patients with latex sensitivity and age matched controls [abstract] J Allergy Clin Immunol 1994,93 282.

147. Alenius H, Reunala T, Turjanmaa K, Palosuo T Detection of IgG4 and IgE antibodies to rubber proteins by immunoblotting in latex allergy Allergy Proc 1992,13 75-7
MEDLINE

148. Aalberse RC, van der Gaag R, van Leeuwen J Serologic aspects of IgG4 antibodies prolonged immunization results in an IgG4-restricted response. J Immunol 1983,130 722-6
MEDLINE

149. Ishizaka A, Sakiyama Y, Nakanishi M, Tomizawa K, Oshika E, Kojima K, et al The inductive effect of interleukin-4 on IgG4 and IgE synthesis in peripheral blood lymphocytes Clin Exp Immunol 1990,79 392-6
MEDLINE

150. Calkhoven PG, Aalbers M, Koshte VL, Gniffioen RW, van Nierop JC, van der Heide D, et al Relationship between IgG1 and IgG4 antibodies to foods and the development of IgE antibodies to inhalant allergens Clin Exp Allergy 1991,21 91-8
MEDLINE

151. Urbanek R, Forster J, Karitzky D, Ziupa J The prognostic significance of specific IgG antibodies in insect sting allergy Eur J Pediatr 1981,136 31-4
MEDLINE

152. Lahti A Non-immunologic contact urticaria Acta Derm Venereol Suppl (Stockh) 1980,91 1-49

153 Fuchs T, Wahl R Immediate reactions to rubber products Allergy Proc 1992,13 61-6
MEDLINE

154 Helander I, Makela A Contact urticaria to zinc diethyldithiocarbamate (ZDC) Contact Dermatitis 1983,9 327-8
MEDLINE

155. Wrangsjo K, Mellstrom G, Axelsson IG Discomfort from rubber gloves indicating contact urticaria Contact Dermatitis 1986,15 79-84
MEDLINE

156 Soderberg CH Jr, Lou TY, Randal HT Glove starch granulomatous peritonitis Am J Surg 1973,125 455
MEDLINE

157. Saxen L, Saxen F Starch granulomas as a problem in surgical pathology Acta Pathol Microbiol Scand 1970,64 55

158 Fisher AA Contact urticaria and anaphylactoid reaction due to cornstarch surgical glove powder Contact Dermatitis 1987,16 224-35.
MEDLINE

159. Assalve D, Cicioni C, Perno P, Lisi P Contact urticaria and anaphylactoid reaction from cornstarch surgical glove powder Contact Dermatitis 1988,19 61
MEDLINE

160 Mäkinen-Kiljunen S, Reunala T Is cows' milk casein an allergen in latex-rubber gloves? Lancet 1993,342 863-4

161. Ownby DR Is rubber elongation factor the major allergen of latex? J Allergy Clin Immunol 1993,92 633-5
MEDLINE

162. Kelwick RGO The modification of polypeptides in *Hevea brasiliensis* latex resulting from storage and processing Clin Rev Allergy 1993,11 339-53
MEDLINE

163. Alroth M, Reunala T, Alenius H, Makinen-Kiljunen S, Turjanmaa K, Palosuo T Allergens in latex source materials [abstract] J Allergy Clin Immunol 1993,91 242A.

164. Hamilton RG, Charous BL, Yunginger JW Evaluation of crude and end-product latex rubber as allergens for IgE anti-latex assays [abstract] J Allergy Clin Immunol 1993,91 241A

165. Hamilton RG, Charous BL, Adkinson NF, Yunginger JW Serologic methods in the laboratory diagnosis of latex rubber allergy study of nonammoniated, ammoniated latex, and glove (end-product) extracts as allergen reagent sources J Lab Clin Med 1994,123 594-604
MEDLINE

166. Jones RT, Scheppmann DL, Yunginger JW Extractable latex allergen contents of disposable medical gloves [abstract] J Allergy Clin Immunol 1994,93 282.

167 Turjanmaa K, Reunala T Condoms as a source of latex allergen and cause of contact urticaria Contact Dermatitis 1989,20 360-4
MEDLINE

168. Yunginger JW, Jones RT, Fransway AF, Kelso JM, Warner MA, Hunt LW Extractable latex allergens and proteins in disposable medical gloves and other rubber products J Allergy Clin Immunol 1994,93 836-42
MEDLINE ABSTRACT FULL TEXT

169. Alenius H, Turjanmaa K, Palosuo T, Mäkinen-Kiljunen S, Reunala T Surgical latex glove allergy characterization of rubber protein allergens by immunoblotting Int Arch Allergy Appl Immunol 1991,96 376-80
MEDLINE

170 Lu L, Kurup VP, Fink JN, Kelly KJ Comparison of latex antigens from surgical gloves, ammoniated and nonammoniated latex effect of ammonia treatment on natural rubber latex proteins J Lab Clin Med 1995,126 161-8
MEDLINE

171 Mäkinen-Kiljunen S, Turjanmaa K, Palosuo T, Reunala T Characterization of latex antigens and allergens in surgical gloves and natural rubber by immunoelectrophoretic methods J Allergy Clin Immunol 1992,90 230-5
MEDLINE

172. Kurup VP, Kelly KJ, Turjanmaa K, Alenius H, Reunala T, Palosuo T, et al Immunoglobulin E reactivity to latex antigens in the sera of patients from Finland and the United States J Allergy Clin Immunol 1993,91 1128-33
MEDLINE

173. Alenius H, Kurup V, Kelly K, Palosuo T, Turjanmaa K, Fink J Latex allergy frequent occurrence of IgE antibodies to a cluster of 11 latex proteins in patients with spina bifida and histories of anaphylaxis J Lab Clin Med 1994,123 712-20
MEDLINE

174. Chambeyron C, Dry J, Leynadier F, Pecquet C, Thao TX Study of the allergenic fractions of latex Allergy 1992,47 92-7
MEDLINE

175 Slater JE, Chhabra S Latex antigens J Allergy Clin Immunol 1992,89 673-8
MEDLINE

176. Alenius H, Palosuo T, Kelly K, Kurup V, Reunala T, Mäkinen-Kiljunen S, et al IgE reactivity to 14-kD and 27-kD natural rubber proteins in latex-allergic children with spina bifida and other congenital anomalies Int Arch Allergy Immunol 1993,102 61-6
MEDLINE

177 Czuppon AB, Chen Z, Rennert S, Engelke T, Meyer HE, Heber M, et al The rubber elongation factor of rubber trees *(Hevea brasiliensis)* is the major allergen in latex J Allergy Clin Immunol 1993,92 690-7
MEDLINE

178. Alenius H, Turjanmaa K, Makinen-Kiljunen S, Reunala T, Palosuo T IgE immune response to rubber proteins in adult patients with latex allergy J Allergy Clin Immunol 1994,93 859-63
MEDLINE ABSTRACT FULL TEXT

179. Alenius H, Kalkkinen N, Lukka M, Reunala T, Turjanmaa K, Mäkinen-Kiljunen S Prohevein from the rubber tree *(Hevea brasiliensis)* is a major latex allergen Clin Exp Allergy 1995,25 659-65
MEDLINE

180. Aamir R, Safadi GS, Melton AL, Wagner WO, Pien LC, Cornish K, et al Shared IgE-binding sites among separated components of natural rubber latex Int Arch Allergy Immunol 1996,111 48-54
MEDLINE

181. Chiu AM, Murali PS, Fink JN, Kelly KJ, Kurup VP Cellular immune response to purified latex proteins [abstract] J Allergy Clin Immunol 1997,99(Suppl) S343

182. Nieto A, Mazon A, Montor J, Boquete M, Estornell F, Martinez A Pattern of latex sensitization in children with spina bifida [abstract] J Allergy Clin Immunol 1997,99(Suppl) S157

183 Yeang HY, Ward MA Interaction of Hev b 3 with B-serum gives rise to the appearance of multiple immunogens in ammoniated *Hevea* latex [abstract] J Allergy Clin Immunol 1997,99(Suppl) S157

184. Dennis M, Henzel W, Bell J, Kohr W, Light DR Amino acid sequence of rubber elongation factor protein associated rubber particles in *Hevea* latex J Biol Chem 1989,264 18618-26
MEDLINE

185 Attanyaka DP, Kekwick RG, Franklin FC Molecular cloning and nucleotide sequencing of the rubber elongation factor gene from *Hevea brasiliensis* Plant Mol Biol 1991,16 1079-81
MEDLINE

186. Raulf-Heimsoth M, Chen Z, Liebers V, Allmers H, Baur X Lymphocyte proliferation response to extracts from different latex materials and to the purified latex allergen Hev b 1 (rubber elongation factor) J Allergy Clin Immunol 1996,98 640-51
MEDLINE ABSTRACT FULL TEXT

187. Chen Z, Czuppon AB, Baur X Analysis of continuous allergenic B-cell epitopes on latex allergen Hev b 1 by ELISA using biotinylated peptides [abstract] J Allergy Clin Immunol 1995,95 154

188. Alenius H, Kalkkinen N, Lukka M, Turjanmaa K, Reunala T, Makinen-Kiljunen S Purification and partial amino acid sequencing of a 27 kD natural rubber allergen recognized by latex allergic children with spina bifida Int Arch Allergy Immunol 1995,106 258-62
MEDLINE

189. Palosuo T, Alenius H, Makinen-Kiljunen S, Reunala T, Turjanmaa K Concentrations of hevein and rubber elongation factor (REF) in relation to total allergen activity in extracts of medical latex gloves [abstract] J Allergy Clin Immunol 1997,99(Suppl) S342

190. Alenius H, Kalkkinen N, Yip E, Hasmin H, Turjanmaa K, Mäkinen-Kiljunen S, et al Significance of rubber elongation factor as a latex allergen Int Arch Allergy Immunol 1996,109 362-8
MEDLINE

191 Akasawa A, Hsieh LS, Martin BM, Liu T, Lin Y A novel acidic allergen, Hev b 5, in latex purification, cloning and characterization J Biol Chem 1996,271 25389-93
MEDLINE

192. Slater JE, Vedvick T, Arthur-Smith A, Trybul DE, Kekwick RGO Identification, cloning, and sequence of a major allergen (Hev b 5) from natural rubber latex *(Hevea brasiliensis)* J Biol Chem 1996,271 25394-9
MEDLINE

193 Hsieh L-S, Martin BM, Doherty AE, Lin Y Determination of major IgE-binding epitopes of a latex acidic allergen, Hev b 5 [abstract] J Allergy Clin Immunol 1997,99(Suppl) S342

194. Carrillo T, Cuevas M, Manoz T, Hinojosa M, Moneo I Contact urticaria and rhinitis from latex surgical gloves Contact Dermatitis 1986,15 69-72
MEDLINE

195. Tseng RY, Li CK, Spinks JA Particulate air pollution and hospitalization for asthma Ann Allergy 1993,68 425-32

196. Williams PB, Buhre MP, Weber RW, Volz MA, Koepke JW, Selner JC Latex allergen in respirable particulate air pollution J Allergy Clin Immunol 1995,95 88-95
MEDLINE ABSTRACT FULL TEXT

197. Williams PB, Akasawa A, Dreskin S, Selner JC Respirable tire fragments contain specific IgE-binding and bridging latex antigens Chest 1996,109 13S
MEDLINE

198. Kurup VP, Kumar A, Choi H, Murali PS, Resnick A, Kelly KJ, et al Latex antigens induce IgE and eosinophils in mice Int Arch Allergy Appl Immunol 1994,103 370-7

199. Sorva R, Mäkinen-Kiljunen S, Suvilehto K, Juntunen-Backman K, Haahtela T Latex allergy in children with no known risk factor for latex sensitization Pediatr Allergy Immunol 1995,6 36-8
MEDLINE

200. Mounedji N, Goacolou I, Matheiier-Fusade P, Levy DA, Leynadier F Sensitivity to pollen and foods in latex-allergic patients [abstract] J Allergy Clin Immunol 1997,99(Suppl) S495

201. Blanco C, Carrillo T, Castillo R, Quiralte J, Cuevas M Latex allergy clinical features and cross-reactivity with fruits Ann Allergy 1994,73 309-14
MEDLINE

202. Beezhold DH, Sussman GL, Liss GM, Chang N-S Latex allergy can induce clinical reactions to specific foods Clin Exp Allergy 1996,26 416-22
MEDLINE

203. Lavaud F, Prevost A, Cossart C, Guerin L, Bernard J, Kochman S Allergy to latex, avocado, pear, and banana evidence for a 30 kD antigen in immunoblotting J Allergy Clin Immunol 1995,95 557-64
MEDLINE ABSTRACT FULL TEXT

204. Mäkinen-Kiljunen S Banana allergy in patients with immediate-type hypersensitivity to natural rubber latex characterization of cross-reacting antibodies and allergens J Allergy Clin Immunol 1994,93 990-6
MEDLINE ABSTRACT FULL TEXT

205 Alenius H, Mikkola J, Turjanmaa K, Reunala T, Palosuo T Chitin-binding proteins in natural rubber latex and in several plants contain cross-reacting IgE-binding epitopes [abstract] J Allergy Clin Immunol 1997,99(Suppl) S503

206. Mikkola J, Alenius H, Turjanmaa K, Palosuo T, Reunala T Molecular identification of cross-reacting allergens in natural rubber latex and banana [abstract] J Allergy Clin Immunol 1997,99(Suppl) S342

207. Rodriguez M, Vega F, Garcia MT, Panizo C, Laffond E, Montalvo A, et al Hypersensitivity to latex, chestnut, and banana Ann Allergy 1993,70 31-4
MEDLINE

208 de Corres LF, Moneo I, Munoz D, Bernaola G, Fernandez E, Audicana M, et al Sensitization from chestnuts and bananas in patients with urticaria and anaphylaxis from contact with latex Ann Allergy 1993,70 35-9
MEDLINE

209. M'Raihi L, Charpin D, Pous A, Bongrand P, Vervloet D Cross reactivity between latex and banana J Allergy Clin Immunol 1991,87 129-30
MEDLINE

210. Kurup VP, Kelly T, Elms N, Kelly K, Fink J Cross-reactivity of food allergens in latex allergy Allergy Proc 1994,15 211-6
MEDLINE

211. Magera BE, Phillips AE, Williams PB Comparison of banana proteins in fresh, frozen, commercial and baby food extracts [abstract]. J Allergy Clin Immunol 1997,99(Suppl) S143

212. Eades JR, Keane BB, Cullom HW Prevalence and temporal relationship of food sensitivity in latex allergic patients [abstract] J Allergy Clin Immunol 1997,99(Suppl) S503

213. Broekaert W, Lee H-I, Kush A, Chua N-H, Raikhel N Wound-induced accumulation of mRNA containing a hevein sequence in laticifers of rubber tree *(Hevea brasiliensis)* Proc Natl Acad Sci U S A 1990,87 7633-7
MEDLINE

214 Moneret-Vautrin DA, Mata E, Gueant JL, Turgeman D, Laxenaire MC High risk of anaphylactic shock during surgery for spina bifida [letter] Lancet 1990,335 865-6
MEDLINE

215. Vallier P, Balland S, Harf R, Valenta R, Deviller P Identification of profilin as an IgE-binding component in latex from *Hevea brasiliensis* clinical implications Clin Exp Allergy 1995,25 332-9
MEDLINE

216. Halsey JF, Williams PB Antigenic determinants in ficin dominate latex-specific IgE responses [abstract] J Allergy Clin Immunol 1997,99(Suppl) S342

217. Axelsson J, Johansson S, Larsson P, Zetterstrom O Characterization of allergenic components in sap extract from the weeping fig *(Ficus benjamina)* Int Arch Allergy Appl Immunol 1990,91 130-5
MEDLINE

218. Swartz J, Braude B, Gilmour R Intraoperative anaphylaxis to latex Can J Anaesth 1990,37 589
MEDLINE

219. Kelly KJ, Pearson ML, Kurup VP, Havens PL, Byrd RS, Setlock ME, et al A cluster of anaphylactic reactions in children with spina bifida during general anesthesia epidemiologic features, risk factors and latex hypersensitivity J Allergy Clin Immunol 1994,94 53-61
MEDLINE ABSTRACT FULL TEXT

220. Pasquanello CA, Lowe DA, Schwartz RE Intraoperative anaphylaxis to latex Pediatrics 1993,91 983-6
MEDLINE

221. Product list Latex Allergy News 1997,introd issue, 5-9

222. Kelly KJ Management of the latex-allergic patient Immunol Allergy Clin North Am 1995,15 139-57

223. Kwittken PL, Becker J, Oyefara B, Danziger R, Pawlowski NA, Sweinberg S Latex hypersensitivity reactions despite prophylaxis Allergy Proc 1992,3 123-7

224. Setlock MA, Cotter TP, Rosner D Latex allergy failure of prophylaxis to prevent severe reaction Anesth Analg 1993,76 650-2
MEDLINE

225. Gold M, Swartz JS, Braude BM, Dolovich J, Shandling B, Gilmour RF Intraoperative anaphylaxis an association with latex sensitivity J Allergy Clin Immunol 1991,87 662-6
MEDLINE

226. Jones JM, Sussman GL, Beezhold DH Latex allergen levels of injectable collagen stored in syringes with rubber plungers Urology 1996,47 898-902
MEDLINE

227. Vassallo SA, Thurston TA, Kim SH, Tradres ID Allergic reaction to latex from stopper of a medication vial Anesth Analg 1995,80 1057-8
MEDLINE

228. Lear JT, English JSC Anaphylaxis after hepatitis B vaccination [letter] Lancet 1995,345 1249
MEDLINE

229. Towse A, O'Brian M, Twarog FJ, Braimon J, Moses AC Local reaction secondary to insulin injection Diabetes Care 1995,18 1195-7
MEDLINE

230. MacCracken J, Stenger P, Jackson T Latex allergy in diabetic patients a call for latex-free insulin tops [letter] Diabetes Care 1996,19 184
MEDLINE

231. Kalhan S Anesthesia protocol for latex allergy Latex allergy Website http //www anes ccf org 8080/pilot/latex

232. Rich P, Belozer ML, Norris P, Storrs FJ Allergic contact dermatitis to two antioxidants in latex gloves 4,4 tho*bis*(6-*tert*-butyl-*meta*-cresol) (Lowinox 44S36) and butylhydroxyanisole J Am Acad Dermatol 1991,24 37-43
MEDLINE

233. Sussman GL, Beezhold DH Allergy to latex rubber Ann Intern Med 199,122 43-6

234 Mellstrom GA, Wahlberg JR, Maibach HI Protective gloves for occupational use Woodbridge (CT) CDC Press, 1994

235. Field EA Hypoallergenic gloves Int Dent J 1995,45 339-46
MEDLINE

236. Leynadier F, Tran Xuan T, Dry J Allergenicity suppression in natural latex surgical gloves Allergy 1991,46 619-23
MEDLINE

237. Kotilainen HR, Brinker JP, Avato JL, Gantz NM Latex and vinyl examination gloves quality control procedures and implications for health care workers Arch Intern Med 1989,149 2749-53
MEDLINE

238. Kornelwicz DM, Laughon BE, Cyr WH, Lytle CD, Larson E Leakage of virus through used vinyl and latex examination gloves J Clin Microbiol 1990,28 787-8
MEDLINE

239. Lahti A, Turjanmaa K Prick and use tests with 6 glove brands in patients with immediate allergy to rubber proteins Contact Dermatitis 1992,26 259-62
MEDLINE

240. Lahti A, Camarasa JG, Ducombs G, Lachapelle JM, Maibach HI, Menne T, et al Patch tests with tactylon in patients with contact allergy to rubber Contact Dermatitis 1992,27 188
MEDLINE

241. Cates W, Stone KM Family planning, sexually transmitted disease, and contraceptive choice a literature update Fam Plann Perspect 1992,24 75-84
MEDLINE

242. Fisher AA Condom conundrums part I Cutis 1991,48 359-60
MEDLINE

243. Fisher AA The new female and male polyurethane condoms Cutis 1995,56 82
MEDLINE

244. Update barrier protection against HIV infection and other sexually transmitted diseases MMWR 1993,42 589-91

245 Trussel J, Sturgen K, Strickler J, Dominik R Comparative contraceptive efficacy of the female condom and other barrier methods Fam Plann Perspect 1994,26 66-72
MEDLINE

246. Hamann CP, Kick SA Update immediate and delayed hypersensitivity to natural rubber latex Cutis 1993,52 307-11
MEDLINE

247. Trussell J, Warner DL, Hatcher R Condom performance during vaginal intercourse comparison of Trojan-enz® and Tactylon® condoms Contraception 1992,45 11-9
MEDLINE

248 Hamann CP, Nelson JR Permeability of latex and thermoplastic elastomer gloves to the bacteriophage pX174 Am J Infect Control 1993,21 289-96.
MEDLINE

249. Wolf BL Anaphylactic reaction to latex gloves [letter] N Engl J Med 1993,329 279-80
MEDLINE

250. Truscott W Anaphylactic reaction to latex gloves [letter reply to Wolf] N Engl J Med 1993 329 280
MEDLINE

251. Natural rubber-containing medical devices user labeling Fed Reg 1997,62 51021-30

252. Pailhones G Reducing proteins in latex gloves the industrial approach Clin Rev Allergy 1993,11 391-402
MEDLINE

253. Subramaniam A Reduction of extractable protein content in latex products Proceedings of the International Latex Conference, Baltimore, Maryland, Nov 5-7, 1993

254. Pan Z, Durst F, Werck-Reichart D, Gardner HW, Camara B, Cornish K, et al The major protein of guayule rubber particles is a cytochrome P450 J Biol Chem 1995,270 8487-94
MEDLINE

255. Latex allergies stretch beyond rubber gloves Environ Health Perspect 1996,104 916

256. Smith LM, Hughes RP Dermatitis caused by Mexican rubber plant Arch Dermatol Syphilol 1938,38 780

257. Rodriguez E, Reynolds GW, Thompson JA Potent contact allergen in the rubber plant guayule *(Parthenium argentatum)* Science 1981,211 1444-5
MEDLINE

258. Warshaw EM, Zug KA Sesquiterpene lactone allergy Am J Contact Dermatitis 1996,7 1-23
MEDLINE

259. Carey AB, Cornish K, Schrank P, Ward B, Simon R Cross-reactivity of alternate plant sources of latex in subjects with systemic IgE-mediated sensitivity to *Hevea brasiliensis* latex Ann Allergy Asthma Immunol 1995,74 317-20
MEDLINE

260. Hunt LW, Boone-Orke JL, Fransway AF, Fremstad CE, Jones RT, Swanson MC A medical-center-wide, multidisciplinary approach to the problem of natural rubber latex allergy J Occup Environ Med 1996,38 765-70
MEDLINE

261 Swanson MC, Bubak ME, Hunt LW, Yunginger JW, Warner MA, Reed CE Quantification of occupational latex aeroallergens in a medical center J Allergy Clin Immunol 1994,94 445-51
MEDLINE ABSTRACT FULL TEXT

262. Tarlo SM, Sussman G, Contala A, Swanson MC Control of airborne latex by use of powder-free latex gloves J Allergy Clin Immunol 1994,93 985-9
MEDLINE ABSTRACT FULL TEXT

263. Vandenplas O, Delwiche JP, Depelchin S, Sibille Y, Vande Weyer R, Delaunois L Latex gloves with a lower protein content reduce bronchial reactions in subjects with occupational asthma caused by latex Am J Respir Crit Care Med 1995,151 887-91
MEDLINE

264. Slater JE, Zhang YJ, Arthur-Smith A, Colberg-Poley A A DNA vaccine inhibits IgE responses to the latex allergen Hev b 5 in mice [abstract] J Allergy Clin Immunol 1997,99(Suppl) S504

265. Veterans Health Administration Medical Service Designated Agency Safety and Health Official's Letter; 1997 June 27, Letter No 00S-97-6

266. Thompson RL Educational challenges of latex protein allergy Immunol Allergy Clin North Am 1995,15 159-74

267 Veach M Latex gloves hand health workers a growing worry Am Med News 1997,40(Oct 13) 1, 30-1

CME examination
Identification No. 898-107
Instructions for Category I CME credit appear in the front advertising section. See last page of Contents for page number.
Questions 1-31. Warshaw EM. J Am Acad Dermatol 1998;39:1-24.

Directions for questions 1-15 Give single best response

1 A mature *Hevea brasiliensis* tree produces sufficient latex to make approximately how many pairs of gloves per week?

a 1
b 10
c 100
d 500
e 1000

2 Accelerators such as thiurams, carbamates, and mercaptobenzothiazoles are important for controlling the rate and completeness of what step in glove production?

a Centrifugation
b Compounding
c Coagulation oven curing
d Vulcanization
e Powder application

3 What process discovered by Goodyear in 1839 creates disulfide bonds that cross-link *cis*-1,4 polyisoprene chains to each other?

a Centrifugation
b Compounding
c Coagulation oven curing
d Vulcanization
e Powder application

4 What are the two crucial variables that influence degree of protein removal during the post–oven leaching bath in glove production?

a Temperature and detergent
b Detergent and time
c Temperature and time
d Detergent and rate of water exchange
e Time and rate of water exchange

5 Clinical manifestations of type I immediate hypersensitivity to latex may include

a urticaria and pruritus
b nausea and vomiting
c rhinitis and conjunctivitis
d *a* and *c* only
e *a*, *b*, and *c*

6 Anaphylaxis caused by latex allergy has been reported after contact with

a squash balls
b food prepared with latex gloves
c air expelled from a whoopee cushion
d *a* and *c* only
e *a*, *b*, and *c*

7 Each of the following statements regarding endotoxin is true *except*

a it can cause irritation of skin, eyes, and lungs
b high levels have been found in containers used for collecting raw latex
c it is produced by gram-negative bacteria
d it is physically associated with tiny respirable particles
e high levels have been found in powdered latex examination gloves

8 The prevalence of latex sensitivity in the general population is approximately

a 0% to 2%
b 3% to 5%
c 9% to 10%
d 13% to 15%
e 18% to 20%

9 Risk factors for development of latex allergy include each of the following *except*

a preexisting hand eczema
b atopy
c fruit allergy
d male gender
e history of multiple surgical procedures

10 The risk of anaphylaxis to latex in children with spina bifida is estimated to be how many times greater than in the general population?

a 10
b 50
c 100
d 500
e 1000

11 Persons in which of the following occupations are at high risk for development of latex allergy?

a Health care
b Hairdressing
c Latex glove manufacturing
d *a* and *c* only
e *a*, *b*, and *c*

12 Formation of a wheal is considered a positive reaction in each of the following tests *except*

a radioallergosorbent test (RAST)
b skin prick test
c use test
d scratch chamber test
e rub test

13 Variables that make detection and characterization of latex allergens difficult include

a haptenization of latex proteins with compounding chemicals
b variations in latex proteins produced by different hybrids of trees
c seasonal variations in latex proteins produced by the same trees
d *a* and *c* only
e *a*, *b*, and *c*

14 Food allergies thought to be important in cross-reacting with latex include each of the following *except*

a avocado
b banana
c chestnut
d fish
e kiwi

15 Each of the following types of gloves is safe for latex-allergic persons *except*

a hypoallergenic
b polyvinylchloride (vinyl)
c polychloroprene (neoprene)
d styrene butadiene block polymers (elastyren)
e nitrile butadiene polymer (nitrile)

Directions for questions 16-25 For each numbered item choose the appropriate lettered item

a True
b False

16 Allergen levels from a specific glove brand are fairly constant when tested at different times
17 Delayed-type hypersensitivity (to rubber additives) and immediate-type hypersensitivity to natural rubber latex products may coexist
18 Latex-specific RAST is considered the standard for detecting latex allergy
19 At least two Food and Drug Administration–approved commercial latex extracts are available for skin prick testing
20 The significance of latex-specific IgG antibodies in diagnosing latex allergy is controversial
21 Antibodies from different high-risk populations (e g , patients with spina bifida and health care workers) may recognize different latex peptides
22 The medical research community has agreed that the 14 6 kd rubber elongation factor is the single most important latex antigen
23 There is no test that reliably and accurately predicts who will have anaphylaxis to latex
24 Avoidance of latex is not necessary if preoperative medication is given to a latex-allergic patient undergoing surgery
25 Powdered latex gloves can cause high aerosolized concentrations of latex allergens, which may cause reactions in latex-sensitive persons who never come into direct contact with the gloves

Directions for questions 26-31 Select the lettered item that is most closely related to each numbered item

a Immediate, type I reaction
b Delayed, type IV reaction

26 Mediated by IgE
27 Cell-mediated
28 Antigens are small latex proteins
29 Antigens are manufacturing additives
30 Diagnosis is made most commonly by patch test
31 Diagnosis is made most commonly by skin prick test, RAST, or use test

Answers to CME examination
Identification No. 898-106

ıne 1998 ıssue of the Journal of the American Academy of Dermatology
.uestions 1-28, Ploysangam T, Breneman DL, Mutasım DF J Am Acad Dermatol 1998,38 877-95

1	d
2	a
3	b
4	d
5	d
6	d
7	c
8	a
9	a
10	b
11	c
12.	d
13	d
14	c
15	a
16	a
17	c
18	b
19	d
20	c
21	c
22	d
23	a
24	a
25	a
26	a
27	c
28	b

Publishing and Reprint Information TOP

- *From Dermatology, University of Minnesota and the Veterans Affairs Medical Center*
- *Reprint requests Ann M Warshaw, MD, Dept 111K Dermatology, VA Medical Center, 1 Veterans Dr , Minneapolis, MN 55417*

- *0190-9622/98/$5 00 + 0 16/2/90031*

Articles with References to this Article TOP

This article is referenced by these articles·

Cow's milk casein, a hidden allergen in natural rubber latex gloves
Journal of Allergy and Clinical Immunology
July 1999 • Volume 104 • Number 1
Leea Ylitalo, MD[a], Soili Mäkinen-Kiljunen, PhD[b], Kristiina Turjanmaa, MD[a d], Timo Palosuo, MD[c], Timo Reunala, MD[a b d]
ABSTRACT FULL TEXT