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Review

Current prevalence rate of latex allergy: Why it remains a problem?

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Abstract: Objectives: This article aims to review the current prevalence rate of latex allergy among healthcare workers, susceptible patients, and the general public, and to investigate why latex is still a ubiquitous occupational health hazard. **Methods:** Scientific publications on PubMed, particularly those published within the last five years, and current regulations from agencies such as Food and Drug Administration (FDA) were reviewed. Consumer and commercial products that may contain latex were also surveyed. **Results:** Approximately 12 million tons of natural rubber latex is produced annually and is widely used to manufacture millions of consumer and commercial products. Only limited number of latex-derived products have been approved and regulated by government agencies, such as FDA, whereas the majority of finished products do not label whether they contain latex. Owing to millions of unidentifiable products containing latex and many routes for exposure to latex, preventing contact with latex allergens and reducing the prevalence of latex allergy are more difficult than expected. Reported data suggest that the average prevalence of latex allergy worldwide remains 9.7%, 7.2%, and 4.3% among healthcare workers, susceptible patients, and general population, respectively. **Conclusions:** Latex-derived products are ubiquitous, and latex allergy remains a highly prevalent health risk in many occupations and to the general population. Developing alternative materials and increasing the ability to identify and label latex-derived products will be practicable approaches to effectively control the health risks associated with latex.

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Introduction

Natural rubber latex is one of the most important industrial raw materials. Currently over 12 million tons of natural rubber is produced annually[1)], which is used in many industries to manufacture millions of consumer and commercial products such as gloves, tires, condoms, balloons, rubber boots, mattresses, swim caps, catheters, and vial stoppers[2,3)]. However, natural rubber latex contains fifteen proven allergenic proteins (Hev b1 to Hev b15), which can elicit a hypersensitive immune response in the latex-responsive population and may lead to death if severe (anaphylaxis). The outbreak of latex allergy in the late 1980s and 1990s among healthcare workers[4-7)] has drawn great attention from biomedical researchers, clinicians, and occupation safety regulatory agencies, and thus far, millions of affected individuals have been identified. Data published in the early 21st century have shown that approximately 10%-17% healthcare workers[8-11)] and as much as 73% patients with spina bifida[8,11,12)] have been diagnosed with latex allergy. This article aims to evaluate the current prevalence rate of latex allergy among healthcare workers, susceptible patients, and general population, on the basis of publications and data from the last five years. As latex allergy is a hypersensitive allergic reaction occurring when people come in contact with latex allergic proteins, we also strive to identify latex-containing products and understand the possible sources of latex allergen exposure. Because latex allergy affects not only workers in occupations such as healthcare and those where latex gloves are frequently used but also the general population without occupational exposure to latex products, we also investigated the possible exposure routes to latex allergens.

Table 1. The latest reported prevalence of latex sensitization and allergy among healthcare workers (HCWs)

Latex allergy	Latex sensitization	Population (number of study subjects)	Country	Year reported	Ref
4%		HCW students (619)	Italy	2015	35
13.3%		HCWs (4,529)	Thailand	2014	36
4.2%		HCWs (1,115)	Turkey	2014	6
8.8%		Nurses (8,485)	China	2013	37
9.8%	14.1%	HCWs (178)	Netherlands	2013	25
5.9%	7.1%	HCWs (337)	South Africa	2013	5
8.3%		HCWs (144)	South Africa	2013	38
18%		Nurses (899)	Thailand	2013	39
	22.4%	HCWs (295)	Brazil	2012	40
5%		HCWs (804)	USA	2012	41
5.0%	14.2%	Dental students (617)	Bangkok	2011	22
5.9%		HCWs (620)	Spain	2011	31
16%		Dentists (163)	India	2010	42
16.3%		HCWs (324)	Sri Lanka	2010	43
17.9%		HCWs (104)	Iran	2009	44
		Summary			
9.7%	12.4%	N=19,233			

The Current Prevalence Rate of Latex Allergy

I) Healthcare workers

It has been well known that healthcare workers (such as physicians, dentists, nurses, clinical laboratory workers, sonographer, and practicing midwife) are the most affected occupational group for latex allergy due to their frequent use of latex gloves to prevent transmittable infections since 1980s[5-7]. With the introduction of powder-free low-protein (PFLP) latex gloves and synthetic gloves (latex-free), occupational hazards due to latex among healthcare workers seem to have been effectively halted. However, the risk remains, particularly in those countries that are short of appropriate resources or with risk of possibly further exposure to other latex-containing products. Table 1 summarizes recent studies on the prevalence of latex sensitization and allergy among healthcare workers. Although both latex sensitization and latex allergy are IgE-mediated hypersensitivities in response to natural rubber latex allergen exposure, latex sensitization is asymptomatic. If latex exposure continues, latex sensitization can deteriorate and become latex allergy, which presents with clinical manifestations such as itchy skin, itchy nose, urticarial, angioedema, swellings, cough, asthma, and anaphylactic reactions[5,13,14]. Based on these data, the current prevalence of latex allergy and sensitization among healthcare workers worldwide are 9.7% and 12.4%, respectively.

II) Susceptible patients

Epidemiologic studies have also revealed that patients, particularly those undergoing surgical procedures (such as spina bifida, cesarean delivery, and bladder exstrophy), under anesthesia, or with catheterization (such as urological abnormalities, cloacal anomalies, and diabetes with insulin injections)[15-17], have higher chance to be exposed to latex allergens and therefore have higher risk to develop latex allergy. For example, reviewing 8 studies published between 1966 and 2011 suggested that the average time for presenting allergic reaction was 59.8 minutes after anesthetic induction[17]. Table 2 summarizes recent studies on the prevalence of latex sensitization and allergy among patients who have high chance of exposure to latex during medical care. Based on these studies, the current prevalence of latex allergy and sensitization among patients are 7.2% and 30.4%, respectively.

III) Other occupations

In addition to healthcare workers and their patients, other occupational workers including rubber industry workers, researchers who work in biology or chemistry laboratories, housekeeping personnel, gardeners, hairdressers, and food handlers, are also at high risk for latex allergy[18,19]. Sensitization or allergy to latex and latex-containing products may pose life-threatening risks for astronauts because of limited access to medical resources during their space travel. However, few studies have been performed among these occupational groups. Attention is needed to monitor their occupational exposure to latex

Table 2. The latest reported prevalence of latex sensitization and allergy among patients with high risk of latex exposure.

Latex allergy	Latex sensitization	Population (number of study subjects)	Country	Year reported	Ref
4%		Children with allergic diseases (400)	Egypt	2014	33
11.4%		Elderly patients (88)	Italy	2014	45
3.4%		Hemodialysis patients (205)	Turkey	2013	46
20%	25%	Myelomeningocele patients (55)	Brazil	2013	15
46%		Spina bifida patients (35)	Singapore	2013	34
5.1%		Caesarean section (294)	Italy	2011	47
	47.9%	Spina bifida patients (96)	Germany	2011	48
	37%	Spina bifida patients (87)	Germany	2010	49
16%		Spina bifida patients (88)	Turkey	2010	50
1%	10.4%	Spina bifida patients (96)	Turkey	2010	13
8.2%	30.6%	Myelomeningocele patients (73)	Iran	2009	51
		Summary			
7.2%	30.4%	N=1,515			

Table 3. The prevalence of latex sensitization and allergy among general public and those without occupational exposure to latex.

Latex allergy	Latex sensitization	Population (number of study subjects)	Country	Year reported	Ref
3.3%		Dental visitors (1,798)	USA	2013	52
1.8%	3.1%	HCWs unexposed to latex gloves (164)	South Africa	2013	5
	0.8%	Spina bifida children under latex-free conditions (120)	Germany	2010	49
6.4%		Volunteers (1,099)	Australia	2004	53
2.1%		Volunteers (952)	Turkey	2003	54
6.4%		Volunteers (1,000)	USA	1996	55
		Summary			
4.3%	2.1%	N=5,133			

and to prevent latex allergy health risks.

IV) The general public

It is worth noting that latex allergy does not exist exclusively among the aforementioned occupational groups. Reports have suggested that general populations who have not had occupational contact with latex products can also develop latex sensitization and latex allergy (Table 3). Data analysis from limited studies suggests that the average latex allergy prevalence among the general population worldwide is 4.3%.

Latex-derived Products: What We Know and What We Do not Know About

Although public attention has been directed to the possible health risks of latex allergen exposure and the development of countermeasures including latex-free alternative products, recent reports indicate that the prevalence of latex allergy remains 9.7%, 7.2%, and 4.3% among healthcare workers, susceptible patients, and general population, respectively (Table 1-3). As latex allergy is a hypersensitive immune response when an individual comes in contact with latex allergic proteins, understanding the sources of latex allergen exposure will help prevent allergy development and minimize the health risks. According to the International Rubber Study Group, global natural rubber production continued to annually increase from 2000 to 2014, and approximately 12.1 million tons of natural rubber was produced in 2014 (Fig. 1)[1]. Owing to its great elasticity, latex has been processed to produce many products, such as gloves, tires, condoms, balloons, rubber boots, mattresses, swim caps, catheters, and vial stoppers.

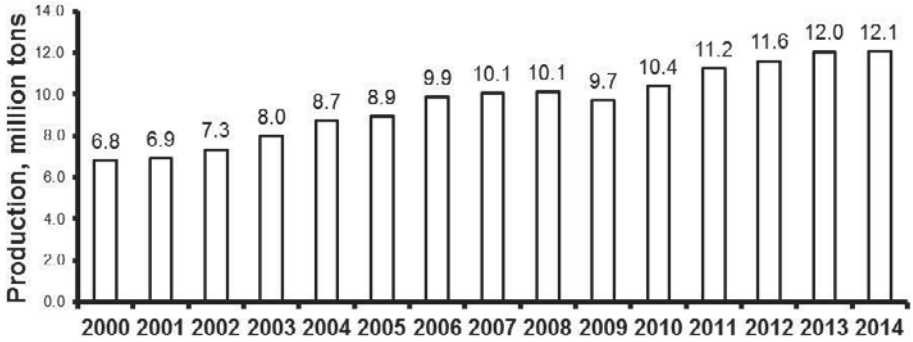

Fig. 1. Global production of natural rubber latex during 2000-2014. Data source: International Rubber Study Group.

I) Application of latex in medical and food industries

With the advent of technical abilities to produce suitable and flexible natural rubber latex materials for commercial application, latex has been used to manufacture medical gloves for over 100 years. To prevent medical workers from dermatitis due to contact with chemicals, Dr. William Halsted, an American surgeon at Johns Hopkins Hospital, invented latex surgical gloves[2]. In the 1980 s, healthcare workers dramatically increased the use of latex gloves because of concerns of infectious agents (such as HIV and Hepatitis B viruses)[4]. When compared with synthetic gloves (nitrile and vinyl), latex gloves appear to be stronger, more flexible, and protective[20], and hence are better acceptable by workers.

Today, rubber latex is present in many food and medical products. The U.S. Food and Drug Administration (FDA) has approved the application of natural rubber latex in food additives (such as chewing gum), food packaging (such as adhesives, pressure-sensitive adhesives, resinous and polymeric coatings, and antioxidants and/or stabilizers for polymers), and medical devices (such as dental, gastroenterology-urology, plastic surgery, obstetrical, and gynecological devices). Table 4 lists the regulations passed by FDA to allow the usage of natural rubber latex in food and medical industries as of September 1, 2014.

II) Application of latex in consumer and commercial products

Today, latex-derived products exist everywhere and have become a part of our daily life. From your home, school, and office to your daily personal care and sport activities (Table 5), the chance of you coming in contact with products totally devoid of latex are limited. In a bill introduced in the House of Representatives (H.CON. RES.387; July 27, 2000), it stated that "latex exposure is ubiquitous and over 40,000 consumer products contain natural rubber latex"[3]. Searching "rubber latex" as keyword in www.walmart.com and www.amazon.com, we also found 136,032 and 73,875 results (as of August 26, 2015), respectively. Therefore, it will be extremely challenging for us able to live in a completely latex-free environment. Table 5 lists products that we use daily and may contain natural rubber latex.

How Do We Get Exposed to Latex Allergens?

Because latex allergy affects not only workers in occupations such as healthcare and those that frequently use latex gloves but also the general population without occupational exposure to latex products, it is important to understand the possible exposure routes of latex allergens.

I) Direct skin contact

Direct skin contact with latex-derived products is the primary route for developing a latex allergy. Studies on healthcare workers have suggested that latex sensitivity appears to build up and increase with exposure time[21,22]. In addition to latex-containing gloves and medical devices that have attracted significant attention, thousands and thousands of products may also contain natural rubber latex (Table 4, 5) that is either present in the product itself or the packaging or is introduced during the manufacturing process or storage. Therefore, the chance for our skin directly coming in contact with latex allergens is almost everywhere.

II) Airborne latex exposure

In addition to direct skin contact with latex-derived products, people can be exposed to latex by other routes, which have been far neglected. For example, airborne latex antigens can be inhaled into the lungs and cause allergic reactions[23,24]. Two main sources of airborne inhalable latex allergens include cornstarch particles that are used in powdered natural rubber latex gloves[23] and tire dusts (especially residents living near a busy road)[24]. To prevent sticking, latex gloves were typically manufactured by adding powdered cornstarch particles. Latex allergic proteins from gloves can attach to the particles of powder, which can become airborne and trigger allergic reactions.

Table 4. FDA-approved products to use natural rubber latex, as of September 1, 2014

CFR Code	Title
Food additives permitted for direct addition to food for human consumption	
21 CFR 172.615	-*Chewing gum base*
Indirect food additives: adhesives and components of coatings	
21 CFR 175.105	-*Adhesives*
21 CFR 175.125	-*Pressure-sensitive adhesives*
21 CFR 175.300	-*Resinous and polymeric coatings*
Indirect food additives: paper and paperboard components	
21 CFR 176.170	-*Components of paper and paperboard in contact with aqueous and fatty foods*
21 CFR 176.180	-Components of paper and paperboard in contact with dry food
Indirect food additives: polymers	
21 CFR 177.2600	-*Rubber articles intended for repeated use*
Indirect food additives: adjuvants, production aids, and sanitizers	
21 CFR 178.2010	-*Antioxidants and/or stabilizers for polymers*
Dental devices	
21 CFR 872.6300	-*Rubber dam and accessories*
Gastroenterology	
21 CFR 876.4560	-Urology devices-*Ribdam*
General and plastic surgery devices	
21 CFR 878.4370	-*Surgical drape and drape accessories*
21 CFR 878.4460	-*Surgeon's glove*
Obstetrical and gynecological devices	
21 CFR 884.5300	-*Condom*

Table 5. Products that may contain natural rubber latex

Catalogue	Products that may contain latex
Household items	Airbeds, toothbrush, rubberized raincoats, elastic (in waist bands, socks, and underwear), rubber boots, plastic bags, things with rubber handles, gloves (cleaning, rubberized gardening, etc.), and many baby toys (rubber toys, bottles and feeding nipples, rubber balls, toy car wheels, water toys, plaster molding kits), etc.
School/office items	Erasers, rubber bands, duct tape, adhesives in self-sealing envelopes, rubber buttons and switches on electronic devices, etc.
Sports	Rubber-studded flooring (swimming pools, gym floors), balls (balloon, tennis, basketball, bowling), swimming items (goggles, nose clips, swimsuits), racquet/bat handles, etc.
Health and personal care	Medical gloves, condoms, diaphragms, catheters, contraceptive sponges, eyelash curler, waterproof mascara, false eyelashes, adhesive bandage, rubber pants, sanitary napkins, crutches, blood-pressure monitoring cuffs, wheel chair cushions and tires, etc.

Introducing powder-free gloves has been shown to result in significant decreases in the latex allergy prevalence and workers' compensation claims[21,25-27].

III) Latex contamination in foods and medicines

It has been reported that latex allergies can be caused by food contaminated by workers wearing latex gloves[3] and medicines/vaccines contaminated by latex-containing vial or medical devices[28-30]. Natural rubber is a widely used material approved by FDA for food additive, packaging, and medical devices (Table 4). The Centers for Disease Control and Prevention has maintained an updated list of vaccine packaging that contains latex, possibly in vial, vial stopper, tip cap, and/or syringe (http://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/latex-table.pdf). Therefore, latex contamination is a "hiding" hazard to those with latex sensitivity.

IV) Cross-reactivity with fruits

Studies have shown that tropical fruits (such as avocado, banana, chestnut, and kiwi) contain proteins having allergenic similarities with latex[31,32]. Patients with allergy to these fruits have high risk of cross-reactivity and develop allergy known as "latex - fruit syndrome" when they come in contact with latex-derived products[32-34]. Approximately 30%-50% of individuals with latex allergy show an associated hypersensitivity to one or more fruits[6,32,34].

Conclusions and Recommendations

Compared with data published in the early 21st century, analysis of current latex allergy prevalence rate suggests that a high prevalence of latex allergy remains among healthcare workers, susceptible patients, and general population worldwide (9.7%, 7.2%, and 4.3%, respectively). Owing to the millions of products containing latex and many routes of exposure to latex, it is not surprising that approximately 4% of the general population worldwide exhibit a latex allergy (Table 3). Preventing contact with latex allergens and reducing the prevalence of latex allergy are more challenging than what we have expected. Developing alternative materials for latex and increasing the ability to identify and label latex-derived products are effective approaches to control the health risks associated with latex.

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