

A HISTORICAL PERSPECTIVE OF LATEX ALLERGY STUDIES

Samuel M Risenga, BSc, MBChB, DCH, DipAllergology(SA), MMed(Paed), FAAAAI, CertPulmonology (Paed)

Associate Professor and Head of Clinical Department, Department of Pulmonology and Allergy, Pietersburg Hospital and University of Limpopo



Prof Samuel Risenga

Correspondence:

Samuel Risenga, email: sam.risenga@gmail.com

INTRODUCTION AND HISTORICAL PERSPECTIVES

Latex gloves are made from natural rubber latex (NRL) manufactured after drawing the raw material from the rubber tree. The gloves are widely used in health and environmental care because of their durability, comfort and tactile properties. They are ideal for providing barrier protection against potentially infectious materials. More than 99% of devices used for commercial purposes are from one species of the rubber tree *Hevea brasiliensis*.¹ There are about 250 different proteins found in NRL with about 5% or 11 of these proteins having been identified as allergens that can induce hypersensitivity reactions.^{1,2} Both residual proteins and chemical compounds used in the production of latex gloves and devices are capable of causing the development of reactions. An average of 50% of medical devices contain latex,² and this is worth noting when dealing with latex allergic patients.

Although latex gloves have been used since the 19th century for protection of patients from the transmission of infectious diseases,^{2,3} the use of latex gloves increased in frequency by the end of the 1980s as a result of, amongst other things, the emergence of the HIV virus and proposed universal precautions of 1987 and 1989 by the Centres for Disease Control.^{2,3}

The first two cases of type-1 hypersensitivity to NRL were recorded in German literature in 1927, with the first one involving urticaria and laryngeal oedema after dental exposure to NRL and the second one involving asthma.³ Most studies of immediate hypersensitivity reactions to latex followed from 1979 onwards.¹ The first South African case was diagnosed in 1993 at Groote Schuur Hospital in Cape Town, South Africa in a nursing sister.⁴ Reactions to latex may present as follows:

- Irritant contact dermatitis, which is a non-allergic skin and inflammatory reaction due to chemical compounds or the products' mechanical action.

- Allergic contact dermatitis which is a type IV delayed hypersensitivity reaction as a result of chemical compounds such as carbamates, thiourams and benzothiazoles.
- Type I hypersensitivity which is IgE mediated. It is a systemic response to residual latex proteins. This is the only reaction classified as latex allergy.² Patients with this type of hypersensitivity might present with severe anaphylactic reactions which can be fatal.

In terms of the Compensation of Occupational Injuries and Disease Act No. 130 of 1993, latex allergy in healthcare workers (HCW) in South Africa is a compensable disease.⁵

This article will look at comparative latex prevalence studies in South Africa and abroad done in the past two decades, and are divided into occupationally exposed, surgical and children with congenital malformation groups.

LATEX PREVALENCE STUDIES IN OCCUPATIONALLY EXPOSED GROUPS

These studies were all conducted on healthcare workers (HCW) based in hospital settings. The major source of workplace exposure to latex is powdered NRL which is used for protection against infection by HCWs. Sensitisation may occur due to contact with gloves or inhalation of latex protein carried in glove powder.

The prevalence of latex sensitisation in the four South African studies that were compared, was very similar, ranging from 7-9.2%. These studies were done between 2001 and 2013.

In the Potter et al. study the prevalence rate was 9.2%,⁶ with the highest prevalence found in nurses in the labour ward and operating theatres, followed by doctors and laboratory staff. The study further showed that latex avoidance caused an overall reduction in symptoms. The study by Brathwaite et al. found a prevalence rate of 7%,⁷ with the highest prevalence amongst laboratory and operating theatre staff

at Red Cross Children's Hospital (RCCH). Risenga et al. found a prevalence rate of 8.3%,⁴ with the highest prevalence in the labour ward, outpatients department and intensive care unit. The study by Phaswana et al. was the first in South Africa to document the prevalence of latex sensitisation in HCWs using hypoallergenic lightly powdered gloves.⁵ Latex prevalence in this study was 7.1%, similar to the RCCH study, despite the use of hypoallergenic gloves. This study showed that even in the presence of powder-free hypoallergenic glove use, there is still a risk of latex sensitisation. These four South African latex prevalence studies show a similar latex sensitisation trend among HCW's, despite the fact that the first two were published in 2001 and the last two in 2013 and from three different provinces.

Three studies were conducted overseas and had similar latex sensitivity prevalence of 4.75%, 4% and 5.9%, respectively. Jones et al. showed that exposure to powder-free latex gloves in dental students was not associated with subsequent sensitisation over a 5-year period in a population with a high incidence of atopy.⁸ The study by Buss et al. found the major latex symptoms to be contact dermatitis, asthma and allergic rhinitis. The study also found no clear evidence for a relationship between skin prick test (SPT) and specific latex IgE, with SPT showing a higher sensitivity and specificity.⁹ The prevalence of latex allergy in primary healthcare workers of 5.9%¹⁰ in the study by Galindo et al. was similar to the other studies conducted

in hospital HCW's. A study by Vandenplas et al. showed that reduction of exposure to latex and avoidance of latex had similar outcomes in terms of improvement of asthma and rhinitis symptoms, as well as a decrease in the level of non-specific bronchial hyperresponsiveness.¹ Table I lists the latex prevalence studies in occupationally exposed groups.

LATEX PREVALENCE STUDIES IN SURGICAL PATIENTS AND CHILDREN WITH CONGENITAL MALFORMATIONS

These studies assess the prevalence of latex sensitisation and allergy in patients undergoing surgical and obstetrics procedures, children with congenital central nervous system malformations and anaesthesiology patients. This is a group which has a higher latex allergy prevalence due to repeated exposure to latex in gloves, airway masks, endotracheal tubes and urinary catheters.

A study by Rueff et al. done on adults with multiple operative procedures found that frequent invasive procedures were associated with latex allergy, but not with latex sensitisation. This study had a prevalence of latex sensitisation of 9.5% and 1.2% with NRL allergy. They concluded that repeated operative procedures were a risk factor for latex allergy, but not sensitisation.¹²

Hilgert et al. found 20.9% of their ear, nose and throat

Table I: Examples of Latex prevalence studies in occupationally exposed groups

Study (year, country)	Group studied	Method used to determine latex sensitization	Latex prevalence
1. Potter PC et al. (2001), South Africa	Healthcare workers in hospitals	ImmunoCAP and skin prick tests	9.2% of 1 968
2. Brathwaite N et al. (2001), South Africa	Healthcare workers in hospitals	ImmunoCAP and skin prick tests	7% of 142
3. Risenga SM et al. (2013), South Africa	Healthcare workers in hospitals	ImmunoCAP and skin prick tests	8.3% of 144
4. Phaswana SM et al. (2013), South Africa	Healthcare workers in hospitals	ImmunoCAP and skin prick tests	7.1% of 337
5. Jones KP, et al. (2002), Wales	Dental students	Skin prick test	4.75% of 63
6. Buss ZS, et al. (2007), Brazil	Healthcare workers in hospitals	ImmunoCAP and skin prick tests	4% of 140
7. Galindo MJ et al. (2011), Spain	Healthcare workers in primary healthcare facilities	ImmunoCAP and skin prick tests	5.9% of 620

(ENT) surgery patients to be sensitised to NRL as compared to 11.3% of their abdominal surgery patients.¹³ There was also a clear association between the numbers of previous surgical procedures and NRL sensitisation. There was however an inverse correlation between these parameters in ENT patients.¹³

Draisci et al. compared healthy women with a singleton pregnancy scheduled for caesarean section delivery and healthy nulliparous women with childbirth potential undergoing gynaecological surgery. Obstetrics patients had a high sensitisation of 5.1% compared to 1.7% of gynaecology surgery patients. Only two obstetrics patients developed anaphylaxis after starting the procedure and receiving an oxytocin infusion. They were successfully resuscitated.¹⁴

The study by Shi Chia Yeh et al. looked at the prevalence of sensitivity signals to latex in meningomyelocele patients undergoing multiple surgical procedures. Of the 69 patients in the study, the observed prevalence of clinical allergy signals was 23.2%.¹⁵ Two of the patients had intraoperative clinical manifestations such as rash, bronchospasm and anaphylactic shock.¹⁵

In a study by Chua et al. the prevalence of latex sensitisation was 46% of 35 subjects with spina bifida, with 31% of the patients presenting with clinical manifestations.¹⁶

Peer et al. evaluated a prospectively administered written questionnaire on latex allergy to reduce the incidence of latex anaphylaxis during elective caesarean section (CS) delivery. They used a nine-item written questionnaire and compared it to a historical verbal inquiry on latex allergy. Their questionnaire identified suspected latex sensitivity in 14.6% of 453 women compared to 2.6% of 460 women identified by the standard verbal inquiry. The patients who were suspected of latex sensitisation underwent a latex-free CS. The incidence of anaphylaxis was significantly lower during the questionnaire period (0.6% of 516) than during the historical period (2.4% of 460).¹⁷

A study done at the Red Cross Children's Hospital in Cape Town, South Africa found a low prevalence of latex sensitisation of 16.7% in spina bifida children aged between 6 months and 18 years¹⁸ as compared to the USA and European countries.¹⁸ Table II gives a summary of the latex prevalence studies in patients exposed to latex through operative procedures.

Table II: Latex prevalence studies in patients exposed to latex through operative procedures

Study (year, country)	Group studied	Method used to determine latex sensitization	Latex prevalence
1. Rueff F et al. (2001), Germany	Surgical and urological procedures	Skin prick test and ImmunoCAP	9.5% of 325
2. Hilgert E et al. (2007), Germany	Abdominal and urological surgery	Skin prick test and ImmunoCAP	20% of 206 ENT surgery patients and 11.2% of 204 abdominal surgery patients
3. Draisci G et al. (2011), Italy	Obstetrics and gynaecology	Skin prick test and ImmunoCAP	5.1% of 294 obstetrics patients and 1.7% of 294 gynaecology patients
4. Shi Chia Yeh W et al. (2012), Brazil	Meningomyelocele patients	ImmunoCAP	23.2% of 69
5. Chua X et al. (2013), Singapore	Spina bifida patients	Skin prick test	46% of 35 subjects
6. Johar A et al. (2005), South Africa	Spina bifida patients	Skin prick test, ImmunoCAP, ELISA and Western blot	16.7% of 24
7. Peer L et al. (2014), Israel	Obstetrics patients	Questionnaire	14.6% of 453 of questionnaire group and 2.6% of verbal group

DISCUSSION

The overall prevalence of latex allergy amongst occupationally exposed groups in the South African studies was between 7 and 9.2%. This was similar in studies done a decade apart, and was unchanged even when healthcare workers used hypoallergenic latex gloves. This may however be attributable to the HCWs being sensitised before their hospital implemented a hypoallergenic latex glove policy.⁵ The South African studies showed a higher prevalence of latex allergy than the international studies. This could be a result of low-protein, non-powdered latex gloves being used in the overseas hospitals.

Latex prevalence in studies of surgical patients and children with congenital malformations was higher than in HCWs, except in the study by Draisci et al. in which the prevalence was 5.1% for obstetrics patients and 1.7% for gynaecology patients. In Peer's questionnaire-based study the prevalence rate was 14.6%, also in obstetric patients. In patients with meningomyelocoele and spina bifida the prevalence was the highest at 23.2% and 46%, respectively. This is supported by epidemiological data which put the prevalence of latex allergy in spina bifida patients at 16.7-70%.^{1,13,16,19} Latex sensitisation has also been shown to be more common in women, especially patients in obstetrics.¹⁴

The high prevalence of latex sensitisation and allergy poses a problem, especially in patients that need to be operated upon. The most serious problem is that of a perioperative hypersensitivity reaction, including anaphylaxis. Latex allergy is the second most common cause of anaphylaxis, second only to muscle relaxants during general anaesthesia.^{14,17,19,20,21,22} It is therefore important for the anaesthetists and surgeons to be aware of the importance of diagnosing latex allergy and being aware of the importance of latex as a cause of perioperative anaphylaxis. It is important to identify patients that have latex allergy by obtaining a good clinical history and using screening questionnaires,¹⁷ as well as determining the serum tryptase and histamine early during the perioperative period to make a diagnosis.²¹ It is also advisable to put in practice measures of primary prevention of NRL allergy for all patients. Perioperative latex allergy investigations are needed to avoid complications.

CONCLUSION

Latex allergy still causes an occupational risk amongst HCWs and patients despite the fact that there is now greater awareness of the condition. The prevalence and incidence has decreased in first world countries, but still

remains a problem in South Africa. The prevalence is highest in spina bifida patients as shown in the studies that are quoted in this article. Latex allergy is a significant cause of anaphylaxis in the USA and as a result they are excluding latex in many of their operating rooms.¹⁷ It is thus important to identify patients who are at greater risk of life-threatening anaphylaxis.

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DECLARATION OF CONFLICT OF INTEREST

The author is a member of the executive committee of the Allergy Society of South Africa.

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Objective: The incumbent will be responsible for supporting the Regulatory Affairs Manager: Registered Products and Compliance and for maintaining the product registration function of the company through effective dealings with customers and the regulatory authority, ensuring compliance with applicable legislation. The incumbent will be required to effectively interact with Regulatory authorities, internal and external customers as well as third parties in order to secure amendment approvals.

MAIN DUTIES

SUPPORT the Regulatory Affairs Manager: Registered Products and Compliance:

- Provide support to the Regulatory Affairs Manager: Registered Products and Compliance in interpreting, implementing and achieving the RA plan.
- Assist in planning resource to ensure that the RA plan is achieved within the timeframe as specified.
- Co-ordinate and participate in RA projects as identified, ensuring that progress runs according to plan.
- Provide support to the Regulatory Affairs Manager: Registered Products and Compliance to ensure that an accurate departmental report is made available to the Head: Group RA on a monthly basis.
- Provide support to the Regulatory Affairs Manager: Registered Products and Compliance to ensure that the department works according to current good regulatory practice and in compliance with current legislation and regulatory guidelines at all times.
- Provide support to the Regulatory Affairs Manager: Registered Products and Compliance to identify all high profile and/or high risk products and ensure that regulatory documentation supporting this is current.

COMPLIANCE:

- Review and approve any relevant documents.
- Liaise with relevant internal and external customers for information or documentation required.
- Ensure input of accurate, relevant information into various RA systems.
- Evaluate data generated for amendments of products.

MAINTENANCE OF DOSSIER REGISTRATION STATUS:

- Compile amendments to the product dossier in compliance to the current guidelines and regulations.
- Identify and obtain any information that is outstanding in order to complete the amendment.
- Respond to Regulatory Authority resolutions by researching and collating data to expedite approval.
- Manage amendments' due dates effectively.
- Screen responses received from MCC.
- Ensure that the required superceding takes place so that the dossier is an accurate reflection of the current status of the product.
- Complete all administrative functions in order to support and accurately reflect the current status of the product details within the dossier.

GENERAL:

- All queries are followed up and strictly within policy framework.
- A professional attitude is displayed when responding to a customer's needs.
- Methods for improving customer services are proposed and developed.
- Internal and external customers are updated as to the progress of their queries.
- Internal and external customers are updated as to the progress of their queries.
- Liaise on a daily basis with internal and external customers.
- Supply relevant regulatory information as a service requirement to our internal and external customers.
- Assist with problem solving to facilitate decision making and guidance.
- Peer review of colleagues' submissions.
- Training of new employees.
- Ongoing training of current employees.
- Updating of workflows and work instructions.
- Follow up with the MCC on the status of outstanding submissions.
- Ensuring escalation of critical issues.

SKILLS:

Planning; Time management; Problem solving; Analytical skills; Service orientation; Interpersonal skills; Report writing skills; Written and Verbal Communication skills; Bilingual (English & Afrikaans) is advantageous.

ATTRIBUTES:

Initiative; Confidentiality; Customer focused; Interpersonal sensitivity; Patience; Attention to detail; Logical thinking; Information seeking; Sense of urgency.

KNOWLEDGE:

MCC and any other relevant regulatory requirements; Principles governing regulatory requirements such as ICH and SUPAC guidelines on stability, validation of various processes, equipment classification; Knowledge of dossier compilation and requirements; Knowledge of how Pharmaceutical Industry operates; Knowledge of the contents of the different Acts and Regulations governing Pharmacy; Knowledge of project management principles.

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Matric / Grade 12; Bachelor of Pharmacy Degree required; Regulatory Affairs training and certification advantageous; Minimum 3 years of experience in the pharmaceutical industry, in the regulatory affairs environment essential; Additionally, 2 to 3 years of experience in the pharmaceutical manufacturing sector, clinical trials sector, or pharmaceutical quality assurance/quality control (QA/QC) sector would be advantageous.

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