RELEVANCE OF A POSITIVE LATEX SPECIFIC IgE RESULT IN A NON MEDICAL OCCUPATIONAL SETTING

By

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Table of Contents

DECLARATION

I, Didintle C Motsepe, hereby declare that the work on which this thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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DEDICATIONS

I would like to dedicate this thesis to my wonderful husband, father and best friend. You are my strength and inspiration. Your love, wisdom and encouragement help me realize anything is possible. I shall always love you.

To my daughter, Bontle and son, Obie thank you. Your unconditional love and understanding help me remember what is truly impotant. You brighten my days and fill my life with happiness and love.

To my parents who have given me love and support for my entire life. Mama and Papa, I love you very much.

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Summary

Background: In 2007, three patients from Impregnated Web Technology (IWT) factory were referred to Groote Schuur occupational clinic with contact dermatitis. The IWT factory manufactures sanding and grinding discs, traditionally a low latex exposure industry. Workers at this factory were introduced to latex gloves in 2004 to protect their hands for various reasons. One of the patient was referred with raised latex specific IgE. Our preliminary diagnosis was irritant contact dermatitis. The dermatitis cleared after avoiding latex gloves. The other two were referred with negative latex specific IgE. One was subsequently diagnosed of fiberglass dermatitis confirmed with histology and the other with urticaria based on the history. Because of the perception that skin problems equate to latex allergy we decided to study the relevance of a positive latex specific IgE in a non-medical setting.

Objective: The objective of this study is to determine the prevalence and relevance of latex sensitization at this traditionally a low latex exposure factory. It also aimed to increase awareness of latex exposure and provide recommendations for preventing and managing latex allergies.

Methods: A cross sectional study of the workers on duty was conducted at the IWT factory over 2 days. There were no exclusion criteria. Ethics approval was obtained. Workers who volunteered were asked to sign informed consent and answer 3 questionnaires. Questioned asked were related to glove use at work and at home. They were also examined by the investigator and had a blood sample taken for total IgE and latex specific IgE measurement.

Results: There were 160 workers on the factory floor over the study period. Only 81 workers volunteered giving a response rate of 51%. The point prevalence of latex sensitization was 16%(13/81). There was a significant relationship between workers who had skin signs and wore glove, however there was no association between glove usage and total and latex specific IgE. A

raised latex specific IgE was associated with permanent employment.

Conclusion: The prevalence of elevated latex specific IgE amongst workers at IWT factory was high, in the range of that reported of medical personnel, suggesting a source of latex exposure in the work place. The reasons for glove use amongst the workers revealed an appropriate use of natural rubber latex gloves with unnecessary latex exposure. Although we could not link the high prevalence of latex specific IgE to the use of gloves, subgroup analysis with larger numbers of workers may expose an association suggested by a higher prevalence in permanent workers. We suggest the use of more appropriate gloves selected for the protection needed. A latex specific IgE test should be performed only for workers with strong suspicion of latex sensitization, not simply skin signs and symptoms.

CHAPTER 1

INTRODUCTION

1.1 Background:

In 2007 while I was on rotation in the Occupational Health Clinic, three patients from the Cape Town Impregnated Web Technology (IWT) factory were referred to the Groote Schuur Hospital clinic with suspected contact dermatitis thought to be due to the use of latex gloves at their workplace.

Figure 1.1a Press machine operator in the dry coat department

The first patient reported to have developed an itchy rash on the upper limbs, flexural areas and neck since August 2006. The rash subsided when applying topical steroids and also during periods of being off from

work i.e. on leave. He associated the rash with wearing latex gloves. He had no history of atopy. He had worked as a press machine operator in the dry coat section since July 2006 (Figure 1.1a).

He was exposed to fibre glass dust and wore latex gloves during working hours. He changed gloves 3x in a day. He was referred with a moderate positive specific IgE latex result (1.53kU/L). On examination he presented with post-inflammatory hyperpigmentation on the wrists, forearms and neck area. A patch test using 45 commercial allergens most commonly implicated in allergic contact dermatitis was negative. Our preliminary diagnosis based on history and clinical examination was irritant contact dermatitis. An extended patch testing with products from work was not performed to fully exclude allergic contact dermatitis.

The second patient presented with generalised excoriated papules and mild eczematous plaques on the flexural areas with lichenification on the neck area (Figure 1.1b).

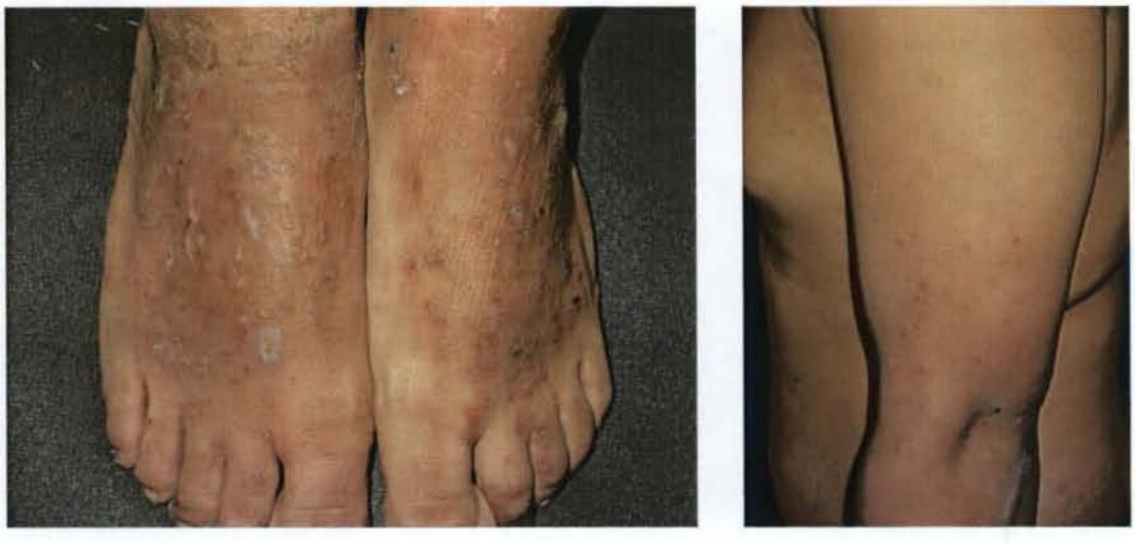


Figure 1.1b Excoriated papules and mild eczematous plaques and lichenification suggestive of fibre glass dermatitis

He worked in a waste recycling department where he immersed nylon bags filled with used fibre glass coated with resin in tanks of methanol. He wore double latex gloves and changed them approximately 5x during working hours as they got torn. He also wore protective cotton overall and boots, as there was a lot of fibre glass dust in the working area. He started experiencing the itchy rash all over the body a month after starting to recycle fibre glass materials. He denied having skin problems before. Because his clinical presentation was classic of fibre glass dermatitis a skin biopsy was done which confirmed the diagnosis (Figure 1.1c). He was referred with a negative specific IgE latex result. A patch test using 45 commercial allergens most commonly implicated in allergic contact dermatitis was negative.

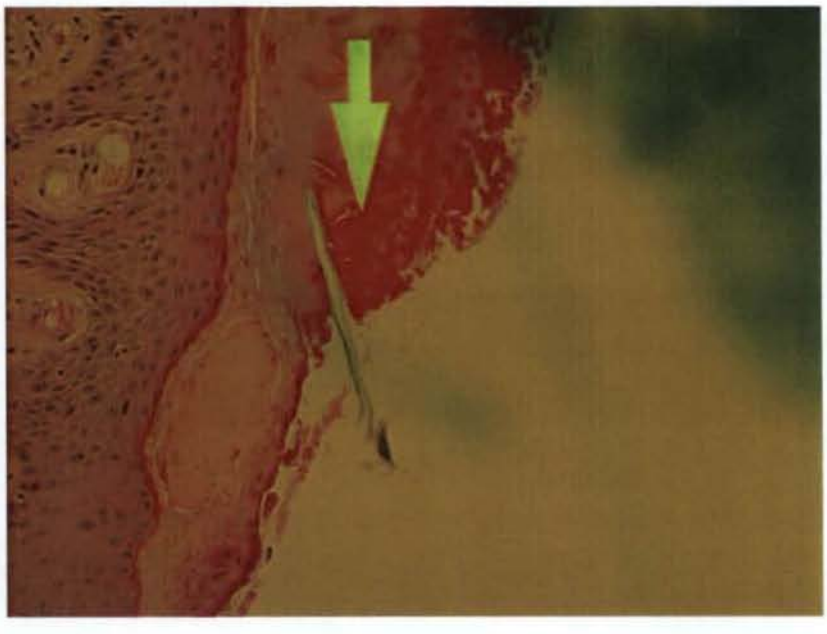


Figure 1.1c Histology: Fibre glass (arrow) embedded in the skin

The third patient had a 5-year history of a red itchy rash with associated allergic rhinitis and conjunctivitis, which became worse whenever exposed to powdered latex gloves or dusty work areas. The dermatitis subsequently improved on cessation of exposure to both latex gloves and dust. She had no active rash at the time of presentation to our clinic, but the lack of post inflammatory changes and the history strongly supported

a diagnosis of urticaria. She was referred with a negative specific IgE latex result.

All of the above patients had latex exposure and presented with dermatitis which the referring doctor attributed to latex exposure in gloves yet only one patient had a positive specific IgE latex test. The question was raised of the relevance of a single test result in a low latex prevalence, non-medical setting and the contribution of personal protective equipment (PPE) to this finding.

Gloves are a frequent cause of occupational contact dermatitis, especially in health care workers. Many studies of latex allergies in health workers have been reported (Maibach et al., 2000) but few on non-health workers.

The purpose of this study is to obtain information about latex allergies and the relevance of laboratory tests in workplaces other than a medical setting.

1.2 Justification:

Latex products can cause contact dermatitis, urticaria and anaphylaxis; even aerosolized latex particles or their absorption onto powder can precipitate significant allergic symptoms in sensitized person (Reddy, 1998).

Allergic reactions to NRL consist of immediate-type I hypersensitivity reaction and delayed-type IV hypersensitivity reaction. Delayed-type IV hypersensitivity is an eczematous cell mediated immune reaction in the skin that results from hypersensitivity to one of the numerous chemicals added during the processing of NRL (Wyss et al., 1993). Immediate-type I hypersensitivity reactions manifest as urticaria and occur within minutes of exposure to NRL products and are mediated by specific IgE to various latex proteins. Contact urticaria may develop

locally in skin exposed to latex or become generalised (Fuchs and Wahl, 1992).

Delayed-type IV reactions and immediate-type I reactions can also occur concurrently (Fuchs and Wahl, 1992) or in association with nonimmune irritant dermatitis.

Persons at high risk of sensitization include those with prolonged cumulative exposure to latex or those with significant barrier dysfunction of the skin. Once individuals have become sensitized, they may experience allergic symptoms when exposed to any product containing latex (Reddy, 1998).

Personal protective equipment commonly contains some rubber component. This has become particularly important with the general introduction of personal protective equipment into the work place as skin exposure is increasingly being recognized as a major route of substance absorption.

Specific IgE latex testing was done in most patients who had presented with any rash at this industry because it has high profile in occupational heath teaching and is easy and accessible, as opposed to skin prick testing which needed experienced, qualified personnel with emergency equipments.

This study was designed to investigate the relevance of raised specific IgE latex in historically low latex exposure occupations and to evaluate the contribution of PPE.

The outcomes of this study will be used to educate policy makers, the workforce and management.

The study will be educational, raising awareness of latex allergies within the workplace environment so workers understand the risks associated with latex exposure. In addition, education serves to help people

understand the symptoms and know how to recognize whether they are victims of latex sensitivity.

1.3 Aims and objectives of this study:

- To establish the prevalence of latex sensitivity in an occupational setting other than health care
- To determine the relevance of the appropriate use of the latex specific IgE tests in an occupational setting other than health care
- To increase awareness among those at increased risk of sensitization
- To provide pragmatic recommendations for preventing and managing latex allergies in the workplace

CHAPTER 2

LITERATURE REVIEW

Since 1979, there have been an increasing number of reports in the medical literature of immunoglobulin E (IgE) mediated allergic reactions to latex-containing products. The first reports of sensitivity to natural rubber latex (NRL) were delayed type IV, cutaneous reactions. The most common antigens causing type IV reactions were identified as dyes, accelerants and antioxidants used in the manufacturing process. (Weiss, 2007). In 1979 Nutter reported urticaria to natural rubber latex and suspected that the latex resin was the cause of the type I hypersensitivity.

Concerns about latex allergy increased greatly in 1988 when several deaths occurred during barium enema administration due to exposure to latex in enema cuffs. The Food and Drug Administration (FDA) issued an alert to all health care workers and set up a problem-reporting program. In the period from October 1988 through September 1992, 1118 adverse reactions to latex were reported, including 15 deaths from enema cuff exposure. (FDA statistics, 1992).

2.1 Latex

2.1.1 Definitions

To avoid confusion clear definitions of the terms latex, natural rubber latex and rubber are needed because, depending on the context, they can have multiple meanings.

- **Latex** refers to the milky sap produced from the rubber tree, *Hevea brasiliensis*. The latex fluid consists of about 34% rubber polymer (poly-isoprene), 2% proteins, 1.6% resins, 1.4% sugar, 0.6% ash, 0.4% fatty acids and 60% water (Mellstrom, 1994).

- **Natural rubber latex** refers to the rubber products manufactured

using the milky sap (latex) of the rubber tree *Hevea brasiliens*is (Brehler & Kutting, 2001).

- **Synthetic rubber** is produced by polymerisation of synthetic monomers of isoprene to poly-isoprene. It does not have the sensitizing properties of latex (Brehler & Kutting, 2001).

- **Latex rubber** is used to refer to NRL and synthetic rubber (Brehler & Kutting, 2001)

2.1.2 Natural rubber latex (NRL) manufacture

Natural rubber latex is the product manufactured from the milky fluid derived from a member of the Euphorbiaceae, the rubber tree *Hevea brasiliensis* (Willd. ex Adr. de Juss.) Müell. Arg. (Cuco et al., 1998). *Hevea brasiliensis* was originally discovered in the tropical evergreen rainforest of the Amazon Basin in Brazilia.

Although the same process is followed for the manufacture of many natural rubber latex products I will focus on glove manufacture as this form of PPE has probably contributed to most cases of sensitisation in a work environment.

The latex glove manufacturing process is a complex multi-stage process, during which the raw material undergoes many physical and chemical treatments. The milky fluid, tapped from *Hevea brailiensis* rubber trees is added to a stabilizer, ammonia to prevent it from coagulating. (Cohen et al., 1998). It is then centrifuged to remove some of the water. Centrifugation concentrates the rubber content up to about 60%, and simultaneously reduces the protein content. At no stage in the process is the latex heated. This means most of the proteins remain unchanged in the latex.

At this stage, chemicals are added, including accelerators such as thiurams, mercaptobenzothiazole (MBT), carbamates and thioureas, and

antioxidants. Antioxidants are added to decrease the rate of rubber degradation. Accelerators, chemicals used to speed up the transition from a solution into a usable solid film such as a glove, are well documented Type IV allergens.

This latex concentrate, containing various additives, is used in the dipping process when making gloves, condoms, catheters, and toy balloons. A metal form is dipped into the latex concentrate mixture and then retracted and the excess latex mixture is allowed to drip off to form a uniform film over the form.

Vulcanization is the process whereby the rubber form and added sulfur, peroxide or bisphenol vulcanisers are heated to improve resilience and elasticity and to prevent the perishing of the final rubber product.

Dipped rubber products contain higher levels of Hevea latex proteins, responsible for the majority of allergic reactions. To reduce the latex proteins, dipped rubber products are put through a leaching line comprising a bath or spray of water to remove residual chemicals and proteins from the glove substance. This step is crucial to minimize the occurence of latex sensitivity. The effectiveness of the process is dependent on the temperature of the water, the duration of the process, and the number and rate of water exchanges.

Powder is then applied to NRL gloves to prevent stickiness and to give the gloves a smooth feel. (Beezhold et al., 1992). Powder acts as a carrier for latex proteins and may potentially have adjuvant effects (Ruhl et al., 1994). Before 1940 mineral talc was used inside gloves as a drying agent. It was then replaced with cornstarch because the mineral talc binds more firmly to latex molecules and caused more severe reaction in latex-sensitive individuals (Crippa et al., 1997).

2.2 Natural rubber latex reactions

Adverse reactions to natural rubber latex have been recognized for many

years (Kateralis et al., 1996). Clinical reactions to contact with NRL can be divided into nonimmunological and immunological reactions. Nonimmunological reactions manifests as irritant eczema or urticaria in areas of contact. Immunological skin reactions include delayed-type allergic contact eczema and immediate type I IgE mediated urticaria.

Irritant dermatitis is a common nonimmune disease that may present as an eczematous rash and may occur on body areas occluded with NRL on any occlusive PPE. This reaction develops due to cumulative exposures to chemical irritants such as sanitizers and cleaners; physical irritants such as repeated washing of hands and/or occlusion in gloves or mechanical irritants such as scourers and abraders. It is due to repeated damage to the skin barrier and is often not clinically evident. Clinical changes occur when damage reaches a threshold that results in disease (Packham, 1998).

There are 2 groups of substances that cause hypersensitvity: added chemicals such as antioxidants, accelerators, vulcanizers and dyes and natural protein contaminants (Binkley et al., 2003). The added chemicals cause type IV reactions, and the natural proteins cause type I immunoglobulin E (IgE) - mediated reactions in susceptible individuals (Reddy, 1998). Simultaneous type I and type IV allergy to NRL gloves may also occur (Turjanmaa, 1994 &1997).

Type IV delayed hypersensitivity causes allergic contact dermatitis and develops due to the addition of chemical haptens to latex resin during processing, harvesting, and manufacturing of products. These include emulsifiers (e.g. phenol formaldehyde resins), accelerators (e.g. thiurams, thiazoles, mercaptans and carbamates), and stabilizers (e.g. epoxy resin). The rash develops within 24-48 hours after low-level exposure contact in a sensitized person and takes the form of eczema at sites of contact with or without spread all over the body (auto-eczematous Id reaction). The symptom of itch can occur much sooner in exposed sensitized individuals (Packham, 1998).

Type I immediate hypersensitivity is an immunoglobulin E (IgE) antibody reaction to latex protein. The reaction causes urticaria, rhinitis, asthma, anaphylaxis, bronchospasm and conjunctivitis. Even low-level exposure can trigger these reactions in sensitive people. It is essential to recognize the type I reactions immediately as anaphylaxis is life threatening (Packham, 998).

Immediate-type reactions have been classified as the **contact urticaria syndrome** defined by Maibach and Johnson in 1975. The contact urticaria syndrome can be described in 2 broad categories; nonimmunologic contact urticaria and immunologic contact urticaria.

Nonimmunologic contact urticaria is the most frequent immediate contact reaction and occurs without prior sensitization in most individuals who are exposed. Immunological contact urticaria is a type 1 hypersensitivity reaction mediated by IgE antibodies specific to the eliciting substance.

The severity of clinical reactions can be classified according to the system of von Krogh and Maibach:
Stage 1 of contact urticaria syndrome indicates localized urticaria;
Stage 2 denotes generalized urticaria with or without angioedema;
Stage 3 includes bronchial asthma, rhinoconjunctivitis, orolaryngeal, and gastrointestinal symptoms;
Stage 4 is anaphylactic shock.

The **latex-fruit syndrome** is due to cross-reactivity between latex proteins and proteins present in certain foods. Fruits involved in this syndrome include banana, pineapple, avocado, chestnut, kiwi fruit, mango, passion fruit and strawberry. The Asthma and Allergy Foundation of America estimates that nearly 6 percent of the United States population have some type of food allergy and up to 4 percent have an allergy to latex (Brehler et al., 1997).

Protein contact dermatitis was first described by Hjorth and Roed-Petersen in 1976. They showed that not only haptens but also proteins can induce acute dermatitis but via a type 1 hypersensitivity mechanism. High molecular weight proteins bypass the normal skin barrier in damaged epidermis and lead to sensitization (Ilieve & Wuthrich, 1998). The clinical presentation is that of a chronic dermatitis, and it is often difficult to differentiate from irritant and allergic contact dermatitis and other eczematous dermatoses. One distinguishing clinical feature is that acute flares of pruritus, urticaria, edema, or vesiculation are noted minutes after contact with the offending allergen. Some authors have classified protein contact dermatitis as part of the contact urticaria syndrome because of the immediate wheal and flare response (Levin & Warshaw, 2008). The patch tests to the protein allergen causing protein contact dermatitis are described as being typically negative. Some authors suggest that the patch tests are negative because large molecules cannot penetrate the normal skin barrier unless it is damaged (Ilieve & Wuthrich, 1998).

The skin changes seen with these reactions are commonly eczema (acute, chronic or a combination of both) and urticaria, but it is increasingly recognized that a much wider clinical disease spectrum can occur. In order to make the correct diagnosis one must be able to recognize and diagnose the skin condition correctly. Eczema and urticaria are discussed below.

2.3 Clinical appearances

Eczema

The term eczema and dermatitis are interchangeable, covering a wide variety of conditions from a child with atopic eczema to the adult with a contact dermatitis. Eczema is an inflammatory condition of the skin and can be classified into acute and chronic eczema (Hunter et al., 2003).

Acute eczema presents with vesicular lesions and variable degrees of erythema, exudates, crusting and peeling Figure 2.3a

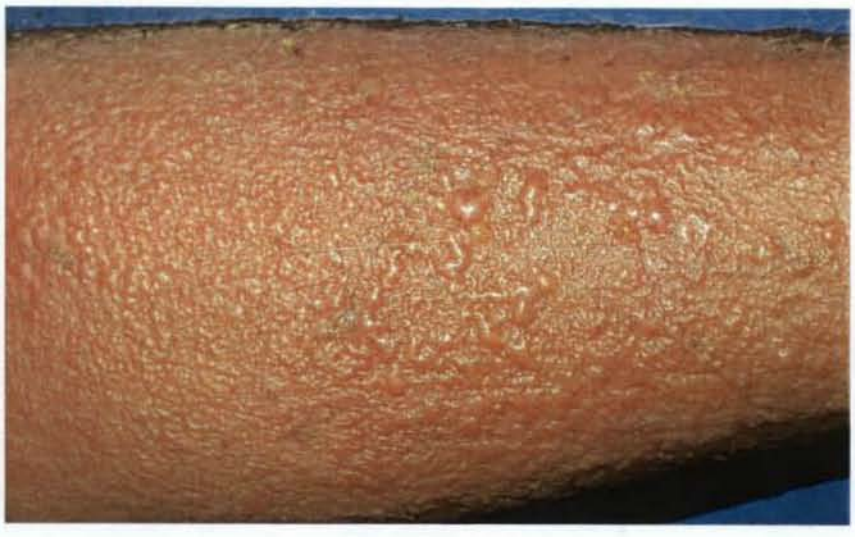


Figure 2.3a Acute eczema

Chronic eczema will show signs of chronic irritation/scratching. This is recognized as thickened, scaly dry skin with increased skin markings (lichenification), and variable excoriations, fissures and associated acute features. Figure 2.3b (Hunter et al., 2003).

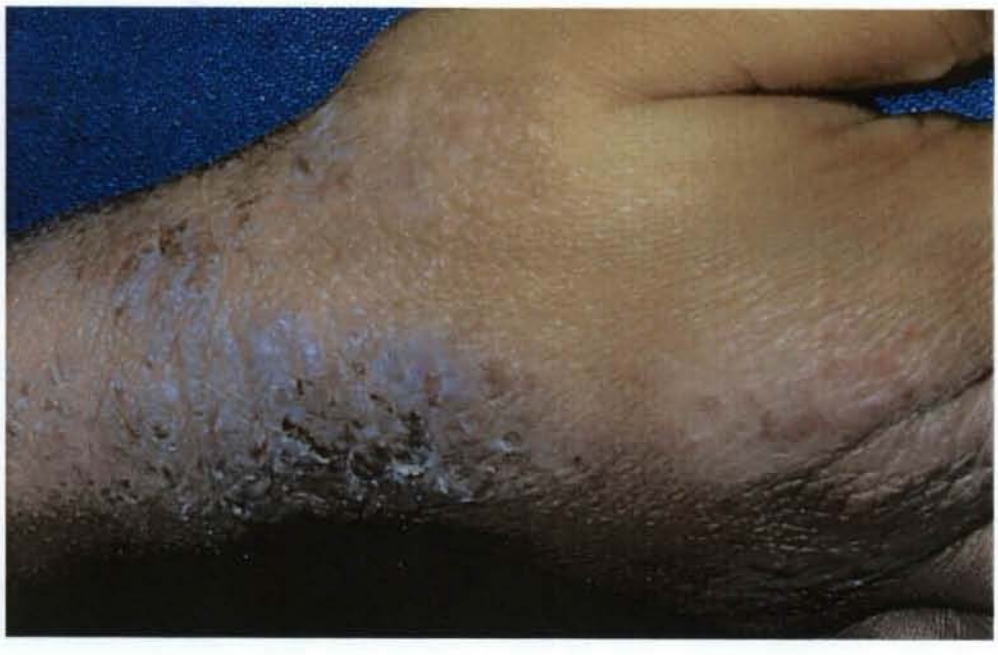


Figure 2.3b Chronic eczema

Urticaria

Contact urticaria presents as swelling (wheal) and erythema (flare) Figure 2.3c (Contact urticaria). Lesions are transient and migratory disappearing within 24 hours of onset leaving no postinflammatory change. Therefore the skin may appear healthy, depending on when the patient presents (Hunter et al., 2003).

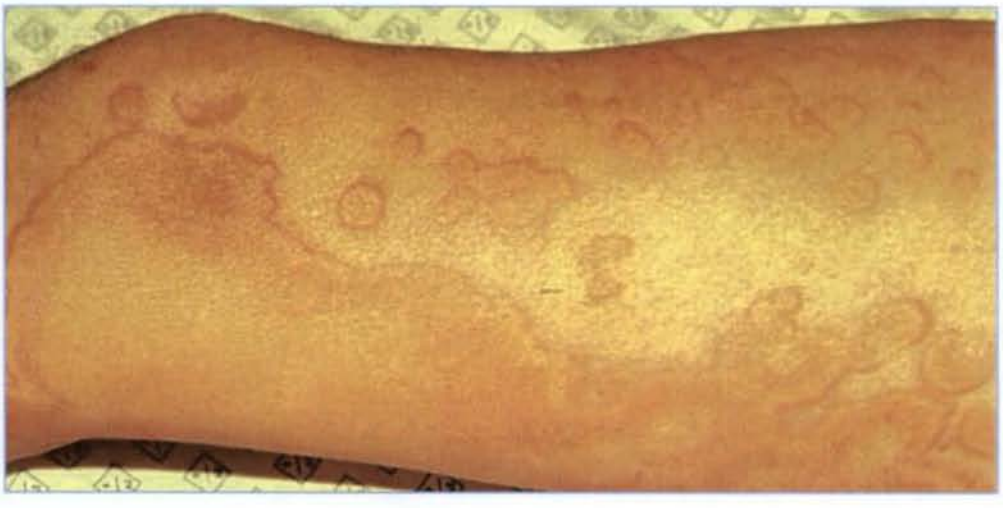


Figure 2.3c Urticaria

2.4 Latex allergy.

Allergy to rubber products is due to the proteins and chemicals and/or residues thereof used in product manufacture. The condition now known as "Latex allergy" is caused by the proteins of the *Hevea brasiliensis* tree present in the products manufactured from latex (Hamilton et al., 2010).

Diagnosis of latex allergy is made by the history and by immunologic testing; a thorough medical history is the cornerstone of diagnosis. The patient should be asked about his or her occupation and whether previous reactions have occurred in an occupational or other setting and,

if so, what type of reactions occurred (Reddy, 1998).

Prevalence estimates of sensitization to both chemicals and protein allergens are highly dependent upon the population studied and the techniques and reagents used to identify cases and the clinical interpretation of relevance (Hamilton et al., 2010; Mari et al., 2007).

Exposure to latex allergens increases the risk of developing allergic symptoms. Exposure to latex allergen usually occurs at mucosal surfaces but can also be from cutaneous and percutaneous transmission and ingestion (Goldsobel., 1993). Aerosol transmission has been ascribed to latex protein allergens adhering to powder (cornstarch, talc) released into the air with the manipulation of powdered rubber gloves. Latex gloves can cause a wheal and flare reaction at the site of contact. Reaction can affect either the person wearing the gloves or the person being touched by the person wearing the gloves or can be caused by airborne natural rubber latex (Reddy, 1998). Furthermore, airborne particles of powder and NRL proteins may remain suspended for up to 5 hours, contaminating the air and the ventilating system (Kelly et al. 1996).

The amount of latex exposure needed to produce sensitization or an allergic reaction is not precisely known. It is thought that repeated exposure to latex together with a genetic predisposition leads to latex sensitization (Carrillo et al., 1995).

Workers with high exposure to latex gloves and glove powder are particularly susceptible to latex allergy. Other persons at high risk of sensitization include those with cumulative, prolonged exposure to latex, such as health care workers, workers in rubber industry and those who have undergone repeated procedures, particularly early in life (especially for spina bifida or urogenital abnormalities) (Reddy, 1998). Other reported occupations with hidden latex exposure are the textile industry and plant handlers.

Universal precautions to prevent the spread of human immunodeficiency virus have increased the frequency of latex exposure (i.e. increased usage of NRL gloves and condoms). Increased demand resulted in lower quality products with more protein contamination. This may account for the epidemic, sharp upsurge in latex allergy in the 1980's (Carrillo et al., 1995; Palosuo et al., 2011).

Occupations in which latex gloves are commonly used include:

- Healthcare workers
- Food handlers/restaurant workers
- Domestic workers
- Hairdressers
- Security personnel
- Construction workers
- Greenhouse workers/gardeners
- Painters
- Funeral home workers
- First-responders such as police officers, ambulance attendants

Risk factors for latex sensitisation and allergy are listed in Table 2.1. (Kean & McNall, 2009)

Table 2.1 Individuals at risk for latex sensitisation

Health care workers
Atopic individuals
Spina bifida patients
People undergoing multiple surgeries during early childhood
People undergoing multiple urinary, rectal or thecal tract procedures
People experiencing other multiple latex-exposing procedures
People with allergies to avocado, banana, chestnut, kiwi, papaya, peach or nectarine
Rubber industry workers

Outside the workplace, latex is widely used in modern homes, leisure facilities and sporting gear. These rarely cause problems, except to very sensitive people. Natural rubber latex is found in many medical devices and other nonmedical products (Table 2.2)

Table 2.2 Products Containing Natural Rubber Latex (Source: Occupational Health Surveillance Update, Jan 1998)

1. Emergency Equipment	**2. Office Supplies**
Blood pressure cuffs	Rubber bands
Stethoscopes	Erasers
Disposable gloves	Adhesive tape
Oral and nasal airways	Glue
Tourniquets	Stamps, envelopes
Intravenous tubing	Mouse pads
Syringes	
Endotracheal tubes	
Electrode pads	
3. Protective Equipment	**4. Hospital Suppliers**
Gloves	Anaesthesia masks
Surgical masks	Catheters
Goggles	Band aids
Respirators	Injection ports
Rubber aprons	Rubber tops of multidose vials
	Dental dams
5. Household Objects	
Automobile tyres	Diaphragms
Motorcycle and bicycle handgrip	Balloons
Carpeting	Bath mats
Swimming goggles	Cosmetics
Racquet handles	Chewing gums

Shoe soles	Foam rubber
Expandable fabrics	Water toys
Dish washing gloves	Shoes
Hot water bottles	Nappies
Condoms	Toothbrush handles
Rubber plants	Rubber boots
Ear phones	Baby bottle nipples
Panty hose	Rubber balls
Camera eyepieces	

2.5 *Hevea* latex allergens

There are at least 13 known *Hevea* latex allergens, Hev b 1 through Hev b 13 included in the latest nomenclature list of the International Nomenclature Committee of Allergens (IUIS). The Hev proteins differ in structure, size, and net charge.

Proteins that have been identified as being involved in the latex-fruit syndrome are class I chitinases from avocado and banana which cross-react with Hev b 6.02 i.e a major IgE allergen for patients who are allergic to NRL. Other important NRL-allergens are Hev b 2 which cross-react with proteins of bell pepper; Hev b 7, a patatin-like protein cross-reacting with its homologous protein in potato and the Hev b 12 which shows cross-reactivity with its counterpart in peach. (Raulf-Heimsoth et al., 2007) Table 2.3 summarises molecular weight, plant family, and known cross-reactivity characteristics of these allergenic proteins.

Table 2.3 *Hevea brasiliensis* latex allergens

IUIS Allergen Nomenclature Subcommittee available from: http//www.allergen.org. (Raulf-Heimsoth et al., 2007; Palosuo et al., 2002).

Table 2.3 *Hevea brasiliensis* latex allergens

Name	Description	MW (kD)	Plant family	Cross reactivity
Hevb1*	Rubber elongation factor	58/14.6	-	Papain, fig
Hev b 2	Beta 1/3 glucanase	34-36	PR-2	-
Hev b 3*	Prenyltransferase	24-27	-	-
Hev b 4	Microhelix	110/115	-	-
Hev b 5*	Acidic protein	16	-	Kiwi
Hev b 6.01	Hevein preprotein (prohevein)	20	PR-3	Avocado, banana, chestnut
Hev b 6.02*	Hevein protein (mature hevein)	4.7	PR-3	Avocado, banana, chestnut
Hev b 6.03	Hevein C-terminal fragment	15.3	PR-3	Avocado, banana, chestnut
Hev b 7	Patatin homologue (Hev b 7.01/7.02)	43-46	-	Potato (patatin-Sol t 1)
Hev b 8	Hevea profilin	14-14.2	Profilin	Pollens, celery
Hev b 9	Hevea enolase	51	-	Molds
Hev b 10	Mn superoxide dismutase	22-26	-	Molds
Hev b 11	Class I chitinase	33	PR-3	Banana, avocado
Hev b 12	Lipid transfer protein	9.4	PR-14	Peach and other stone fruit
Hev b 13	Esterase	42		

IUIS Allergen Nomenclature Subcommittee available from: http//www.allergen.org. (Raulf-Heimsoth et al., 2007; Palosuo et al., 2002).

In the last few years *Hev* proteins have been produced in recombinant form. The development of these recombinant allergens provides reagents that should improve the diagnostic accuracy of tests for latex allergy.

2.6 Laboratory tests

The identification of susceptible individuals may be ascertained with a medical-history questionnare (Toraason et al., 2000). According to a report entitled 'Opinion on Natural Rubber Latex Allergy' adopted by scientific committee on medicinal products and medical devices, it is important to make a distinction between latex sensitisation and latex allergic disease. The diagnosis of latex sensitisation can be made both by *in vivo* skin prick test (SPT) with soluble antigens and/or *in vitro* determination of specific IgE in blood samples. In vitro tests are important to assist or ensure the main allergens in multi-allergen-sensitive patients. For the diagnosis of latex allergic disease challenge (provocation) tests can be used.

2.6.1 Total IgE test

Increased IgE production is one of the hallmarks of atopic disease. Yet, the simple equation " atopy=IgE" is incorrect. Atopy is associated with but not necessarily caused by IgE antibodies and is only one of many conditions associated with increased IgE production (J Ring et al., 1991). Total IgE may be of help in discriminating atopic conditions from other diseases with similar symptoms.

Suggested methods of predicting atopic status have ranged from total IgE values in cord blood and throughout child-hood to neonatal peripheral blood basophil counts (Edenharter et al., 1998; Kjellman et al., 1984; Calbi et al., 1996).

Total IgE should provide a good method for the screening for atopic diseases, although its actual value is controversial because normal values of total IgE do not exclude the existence of atopic disease, and high

values of total IgE are not pathognomonic of atopy by themselves (Ebo et al., 2003; Kerkhof et al., 2003). Patients with a high total IgE have a higher probability of allergic sensitization, but clinical support and specific allergy tests for carefully selected allergens are often warranted.

Serum IgE value above 100 kU/l in an adult patient is strong evidence for the presence of an atopic diathesis while a value below 20 kU/l indicates that the symptoms are due to other conditions (Zetterstrom & Johansson, 1981). Elevated IgE antibody levels can be found in people with parasite infections, hyper-IgE syndrome, cigarette smokers with alcohol consumption and certain cancers (Campos et al., 2005).

In 2004, Sinclair et al found that allergen specific IgE testing in children with low IgE concentrations (10 kU/litre) produces very few positive results in patients with non-specific symptoms. A raised IgE in childhood is a poor predictor (positive predictive value, 50%) of allergic disease (Backer et al., 1992).

In general, total IgE concentrations are a relatively crude method of detecting allergic disorders. Normal values will not exclude the presence of ''allergic disease'', particularly to a single allergen, and raised concentrations can be found in many patients who have no evidence of allergy (Saarinen et al., 1982).

2.6.2 Specific Latex IgE test (RAST, Immuno-CAP) and Skin Prick Test (SPT)

Latex allergy sufferers have raised levels of latex specific IgE. This can be measured *in vitro* by testing the blood using the RadioAllergoSorbent Test (RAST) and/or immuno-CAP and *in vivo* by Skin Prick Test (SPT). *In vitro* tests are less sensitive than the skin prick test, and may miss 10-40% of skin-prick- test-positive patients (De Queiroz et al., 2009).

The presence of allergen-specific IgE does not always correlate with clinical symptoms (Bollinger et al., 2002). The quantitative measurement of specific IgE antibodies in serum to NRL is accepted as

a diagnostic tool for latex allergy. However, the presence of allergen-specific IgE does not always correlate with clinical symptoms (Bollinger et al., 2002). The sensitivity of specific-IgE analysis ranges from 8% to 100% (Blanco et al., 1998) depending on the population studied and allergen used. Ortiz et al found IgE antibodies to NRL proteins in 85.9% of patients allergic to fruits. Only 10.5% of them had clinically relevant latex allergy. This indicates that patients sensitized primarily by food allergens may also react to NRL. The specific latex IgE test can confirm a NRL allergy diagnosis, but it should not be used as a screening tool as demonstrated by the finding that only 50% of a group of individuals identified as latex allergic by the skin-prick test had IgE antibodies to latex (Taylor & Praditsuwan , 1996). Specific latex IgE allergy tests have the advantage though, of not producing anaphylaxis, the patient does not have to stop taking antihistamines before the test, and it can be used even in patients with generalized dermatitis.

Discrimination between the clinically relevant latex allergy and clinically insignificant IgE sensitization still poses a diagnostic challenge (Raulf-Heimsoth et al., 2007). Food and Drug Administration-(FDA) approved *in vitro* tests to measure latex-specific IgE, include Pharmacia CAP, Pharmacia-UpJohn Diagnostics Inc, Kalamazoo,Mich. and AlaSTAT, Diagnostic Products Corporation., Los Angeles, Clif. (FDA Medical Bulletin, 1995). The low specificity of these tests, which have a false-negative rate of at least 20 percent, and thus poor positive predictive value, limit their clinical usefulness.

Current FDA-approved *in vitro* latex IgE assays have lower sensitivity and specificity than the skin-prick test (Ebo et al., 1997) and produce a substantial number (25-28%) of false-negative and false-positive IgE antibody results (Hamilton et al., 1999). For the widely used Pharmacia CAP (Pharmacia AB, Uppsala, Sweden) radio-allergosorbent test method, the sensitivity is reported to range from 50% to 80% (Shah et al., 1998; Ownby & McCullough, 1993). NRL specific IgE has been detected in the serum samples of patients despite negative findings on skin tests and no history of NRL allergy. This is believed to be due to

cross-reacting IgE antibodies binding to plant proteins and NRL. Cross-reactions between proteins in NRL and several foods have been demonstrated, and a "latex-food" syndrome has been postulated (Frankland, 1995; Brehler et al., 1997). Data about the specificity of *in vitro* diagnosis is not available (Brehler, 1998).

Diagnosis of latex allergy is based on a comprehensive medical history and diagnostic tests. Negative serologic testing with a strongly positive history would require skin prick testing to confirm the diagnosis (Latex Allergy, 1998). The skin-prick test is the preferred and most useful test in diagnosing type I latex hypersensitivity (Taylor & Praditsuwan, 1996). Skin prick tests with latex extract depending on the allergens used are sensitive and specific, but it is recommended they be done only in a hospital setting by a specialist (Reddy, 1998). There is a risk of causing anaphylaxis in highly allergic individuals (Kelly et al., 1993).
The skin-prick test is the best predictor of latex allergy with 97% sensitivity and 100% specificity (Ebo et al., 1997), but the U.S. Food and Drug Administration (FDA) has not approved standardized latex solution to be used in the *in vivo* tests. A skin-prick test may show negative findings if the allergen used did not contain the specific latex allergens responsible for the reaction in the individual being tested. Therefore, it is important that testing occur with more than one type of latex product, as well as with raw latex (Hamilton & Adkinson, 1996).

In conclusion, both SPT and/or determination of specific IgE can be used for diagnosis of latex sensitisation. However, these techniques each have their limitations, possibly resulting in non-specific responses. The sensitivity of the SPT is superior to that of the detection of specific IgE to latex. However, there are very few publications dealing adequately with the problem. Sensitivity and specificity can only be determined when the test results are compared to the test results of a challenge using the same complete allergen spectrum to latex (Brockow, 2000; Turjanmaa, 1988).

2.7 Patch tests

Patch testing may help to differentiate between delayed type hypersensitivity contact allergic and irritant dermatitis.

Commercially available allergens are prepared at internationally accepted and tested concentrations below their irritant threshold to ensure maximum detection of sensitized individuals. The allergens are applied in specially designed commercial chambers under occlusion for 48 hours. There after the skin is examined for a response. Readings are done immediately after removing chambers or 1 or 2 days later. Reactions are read according to the International Contact Dermatitis Research Group system.

The rubber accelerators such as thiurams, carbamates and mercaptobenzothiazoles are commercially available contact sensitisers found in most routine patch testing (Nettis et al., 2002).

In many occupational setting commercial allergens do not cover the full range of substance exposure in any work place (Packham, 1998). This means that substances identified from a work place assessment may need to be included. This should only be done by an experienced tester as serious systemic and local complications could be precipitated.

2.8 Published latex allergy in non medical sector

There are limited studies reported on latex allergy in occupations other than in health care settings. Studies that looked at the prevalence of latex allergy among these workers include a study done amongst housekeeping personnel at Toronto medical school (prevalence 8%) (Sussman et al., 1995) and a study in a glove manufacturing plant in Thailand (prevalence 1.7%) (Chaiear et al., 2001). The prevalence of latex allergy was in the reported range for health care workers (prevalence 3 to 22%) (Lagier et al., 1992). Latex hypersensitivity has

also been described in workers wearing natural rubber gloves to protect their hands in the hairdressing industry (prevalence 1 to 22%) (van der Walle & Brunsveld, 1995; Kanerva & Leino, 1999). In a latex-doll manufacturing plant Nicholas et al. studied occupational asthma caused by latex (prevalence 9%) (Nicholas et al., 1994). They concluded that the sanding and grinding of solid latex during the manufacturing process was the probable cause. They further commented that the atopic workers appeared to be more susceptible to developing latex sensitivity. A study done in a textile factory reported the results of a medical and occupational hygiene survey where latex threads (powdered with pure talc to reduce the stickiness of natural rubber) and nylon or polyamide fibers were braided to produce elasticized ribbon for underclothes (prevalence 40%). Their conclusion was in agreement with other reports that clinical manifestations of allergy to latex are IgE-mediated and that atopy is a common feature. They also pointed out that all workplaces where latex is used are risk areas for latex allergy development.

CHAPTER 3

MATERIALS AND METHODS

3.1 Study design

This is cross sectional study of the current 186 temporary and permanent employees at the Impregnated Web Technology (IWT) factory, where discs are manufactured for various usages. Most of these employees wear natural rubber latex gloves for protection. Powdered natural rubber latex gloves were introduced at IWT in 2004 irrespective of the task or need for personal protection equipment (PPE). These were later changed to non-powdered natural rubber gloves on the advice of the occupational doctor in 2007.

3.2 Study site and population

3.2.1 The IWT factory is situated in the industrial area in the suburb, Bellville South, in the Western Cape Province of South Africa.

3.2.2 The company employs 186 workers on the factory floor. These include permanent staff and a contingent of temporary staff, who are trained for specific tasks but are only called in to work to meet production needs. The workers are split between 2 shifts a day, a day shift and a night shift with shift changeover every week. Interviews were structured to include all workers on the floor during the 2 weeks study period of 18 October to 29 October 2010.

The factory manufactures discs used for sanding in the car industry and grinding discs for cutting metal. In the manufacturing process various substances are used. These include fibre glass and phenol resin plus a range of chemicals like ammonium, ethanol and p-phenylenediamine which are all irritants and potential allergens.

The company has three departments relevant to this study:

Abrasive department - where the yarn and rovings (i.e. glass fibre strands) are woven, dyed and impregnated with phenolic resin. Most of the workers in this department wear NRL gloves to protect their hands from being "hurt" and being stained by the dyes. They do not work directly with chemicals or liquids.

The steps in the process of weaving are shown in Figures 3.1, 3.2, 3.3 and 3.4. The woven material is next impregnated with a mixture of phenolic resin and dye. The process of impregnating and dyeing the woven material is shown in Figures 3.5, 3.6 and 3.7.

Figure 3.1 Rolls of fibre glass strands

Figure 3.2 Fibre glass strands connected to the weaving machine

Figure 3.3 Weaving machine

Figure 3.4 Woven rolled material

Figure 3.5 Woven sheet feeding into the dye machine

Figure 3.6 Dye machine and drying ovens

Figure 3.7 Worker checking the material is evenly dyed and not folded

Phenolics department - where they manufacture and recover the phenol resin.

Workers from this manufacturing section wear gloves to protect their hands from chemicals such as methanol and ammonium and the phenol resin *per se*. These workers need to wear protective gloves as they work with irritating substances.

Figure 3.8 Phenol resin tanks

Workers in the recycling section collect the off-cuts from press machine and rejects to recover the phenolic resin for reuse.

Figure 3.9 Collecting off-cut materials for recycling

Figure 3.10 Sorting used materials for recycling

Figure 3.11 Bags of collected materials for recycling

Figure 3.12 Recycling room

Dry coat department – where a press machine is used to cut discs. The completed discs are then sorted and packed. Most of the workers in this area said that they wore gloves to protect their hands from abrasive materials, glass fibre which

sometimes gets in between finger web spaces and that it was their "right" to wear gloves. Most of the workers from this area presented with callouses and fissures on the palms and fingertips despite wearing gloves. They also complained of sweating under the rubber gloves.

Figure 3.13 Press machine for cutting discs

Figure 3.14 Sorting already cut discs

Figure 3.15 Packing discs

3.3 Methodology

3.3.1 Six factory visits were done:

a. The 1st visit was done in 2007 to observe the original referred patient's workplace and identify all possible exposures.
b. The 2nd visit in 2010 was to meet the administrators and unions to discuss how the proposed project will be conducted so as to minimize production disruption but allow private interview time for each worker.
c. Two visits, prior to data collection, were to address the workers as a group and hand out the subject information pamphlets that were done during tea breaks. Workers were advised that they did not have to volunteer.
d. The last two visits were for data collection. This was carried out over 9 hours on consecutive weeks to ensure we included all workers on the production floor in both shifts.

3.3.2 Sampling Methods:

a. The investigator read and explained the consent form (Addendum 1) to each volunteer.
b. Informed consent, stipulating detailed procedures and the patient's rights to refuse to participate was signed by all workers who were present and volunteered to take part on the two interview days.
c. All consent forms were administered and signed by the dermatologist and countersigned by the assisting nurse.
d. Three questionnaires, modified from the Nordic Occupational Skin Questionnaire – NOSQ-2002 for surveying work-related skin diseases on hands and forearms and relevant exposures, were administered by a trained research assistant.
    (i) One medical questionnaire was designed to identify a medical history with particular emphasis on a history and symptoms (rhinitis, conjunctivitis, asthma and itchy rash on either face, hands, forearms and/or wrist) of allergies (Addendum 2).

(ii) One occupational exposure questionnaire was designed to elaborate an occupational history with particular emphasis on glove usage at the workplace. (Addendum 3).
(iii) One non-occupational exposure questionnaire designed to identify non-occupational natural rubber latex exposures (Addendum 4).

The Nordic Occupational Skin questionnaires were preferred to Tuohilampi questionnaires (Finnish Institute of Occupational Health) as their questionnaires are designed for surveying work-related skin diseases and exposures at the workplaces as opposed to questionnaires designed for epidemiological studies of contact dermatitis and atopy.

Questions were designed so that they could be answered with simple answers, either no, yes or not applicable. These responses were scored as 1, 2 and 3 respectively when capturing the data.

For the purpose of data risk analysis, workers were categorised as being at high risk for latex allergy if they met the following criteria based on a positive history suggestive of respiratory (rhinitis, conjuctivitis and asthma) or skin allergy (an itchy rash on either face, hands, wrists and/or forearms) and/or skin signs (combinations of erythema, eczema, fissures and/or postinflammatory hyperpigmentation on examined areas) suggestive of current or past barrier dysfunction.
Workers were regarded as being high risk workers more likely to be susceptible to allergies if they had:

(i) 4 or more of the symptoms of allergy with or without clinical skin signs or
(ii) clinical skin signs with 3 of the symptoms of allergy

e. Data captured by the questionnaire included demographic data (name, sex, age) and occupational data (occupation, duration of employment, temporary or permanent employment and the use of PPE).
f. All participants were examined for any skin signs by the researcher and the findings captured on a specific form. (Addendum 5)
g. 5ml of venous blood was collected from each volunteer into a silicone plug plastic test tube and allowed to clot at room temperature.
h. Blood specimens were then delivered within 8hours to the National Health Laboratory for total serum IgE and latex-specific IgE testing.
i. Total serum IgE and latex-specific IgE were determined according to the manufacturer's specifications using the ImmunoCAP 100 system (Phadia, Uppsala, Sweden).
j. Skin prick test and standard patch test were included in the consent and subject information sheet as optional tests to be done only if required. They were not used as there was enormous pressure on the company to finish a production order before closing for December holidays. The tests were felt to be too time consuming and could be disruptive.

3.3.3 Inclusion and exclusion criteria:

All employees working on the factory floor during the study period irrespective of whether they wore PPE/gloves or not were free to volunteer. All volunteers willing to sign consent were enrolled.
There were no specific exclusion criteria. All workers on chronic medication including oral antihistamine and topical or oral steroids were allowed to take part.

3.4 Statistical Analysis

A database of 102 variables containing demographic details (age, gender), medical questionnaires, occupational history, job status, exposures, non occupational exposures, laboratory measurements (total IgE and specific IgE) and relevant questionnaire scores were used.
All statistical computations including descriptive statistics were carried out using SPSS for Windows (IBM SPSS).

A qualified statistician performed all statistical computations.

As outcome groupings and variables were categorical, the Chi-square test of independence was chosen for statistical analysis.

Because of small variable numbers in the contingency tables, the Fisher's exact test was chosen to compute two-tailed P values.

3.5 Ethical Consideration

Informed, written consent was obtained from all the participating individuals. The investigator read and explained the consent with detailed procedures. Participants were informed of their right to stop participating at any time should they wish to or were not satisfied with the procedure. They were also encouraged to ask questions and advice was given regarding their concerns. Disclosure of information was on a voluntary basis and participants had an option of choosing not to have blood taken.

All information was made anonymous and a unique number identified individuals.

Ethical approval was granted for this study by the Health Sciences Faculty Research Ethics Committee (HREC Ref: 125/2008).

Study participants would benefit from being examined and treated. Those with moderate to severe signs were to be referred appropriately for further investigations and management. The results of the blood tests were to be made available to the workers via the occupational health sister to ensure that they were interpreted correctly. These results were to be filed in the health files of each patient.

3.6 Dissemination of findings

The results of the study will be made available to the Division of Dermatology at Groote Schuur Hospital. The results of the blood tests performed on the volunteers will be made available to them through their health care service provider. An anonymous general report with recommendations will be given to the management and made available to the workers. Results of this study will be made available to the wider community as presentations at national and international congresses and publications in local and international journals.

CHAPTER 4

RESULTS

4.1 Demographics

Data for all 81study participants who completed all 3 questionnaires, had a clinical examination and agreed to blood investigations was included in the analysis, excluding 1 blood result missing due to laboratory technical error. On the study days there were 160 workers on the floor, 79 of whom did not volunteer.

Among 81 participants, there were almost the same number of males (40) and females (41), ranging in age from 18 to 52 years (Table 4.1). Permanent workers accounted for 42 (52%) and 31 (38%) were temporary workers with 8 (10%) where data was missing (Table 4.2). The duration of employment ranged from 4 months to 15 years.

Table 4.1 Distribution of males and females in study population and across departments.

Gender	Study Population N (%)	Departments		
		Abrasive	Phenolics	Dry coat
Male	40 (49)	13	7	20
Female	41 (51)	0	0	41
Total	81	13	7	61

Table 4.2 Workers employment classification

Workers status	Frequency	Percent
Permanent workers	42	52
Temporary workers	31	38
Missing	8	10
Total	81	100

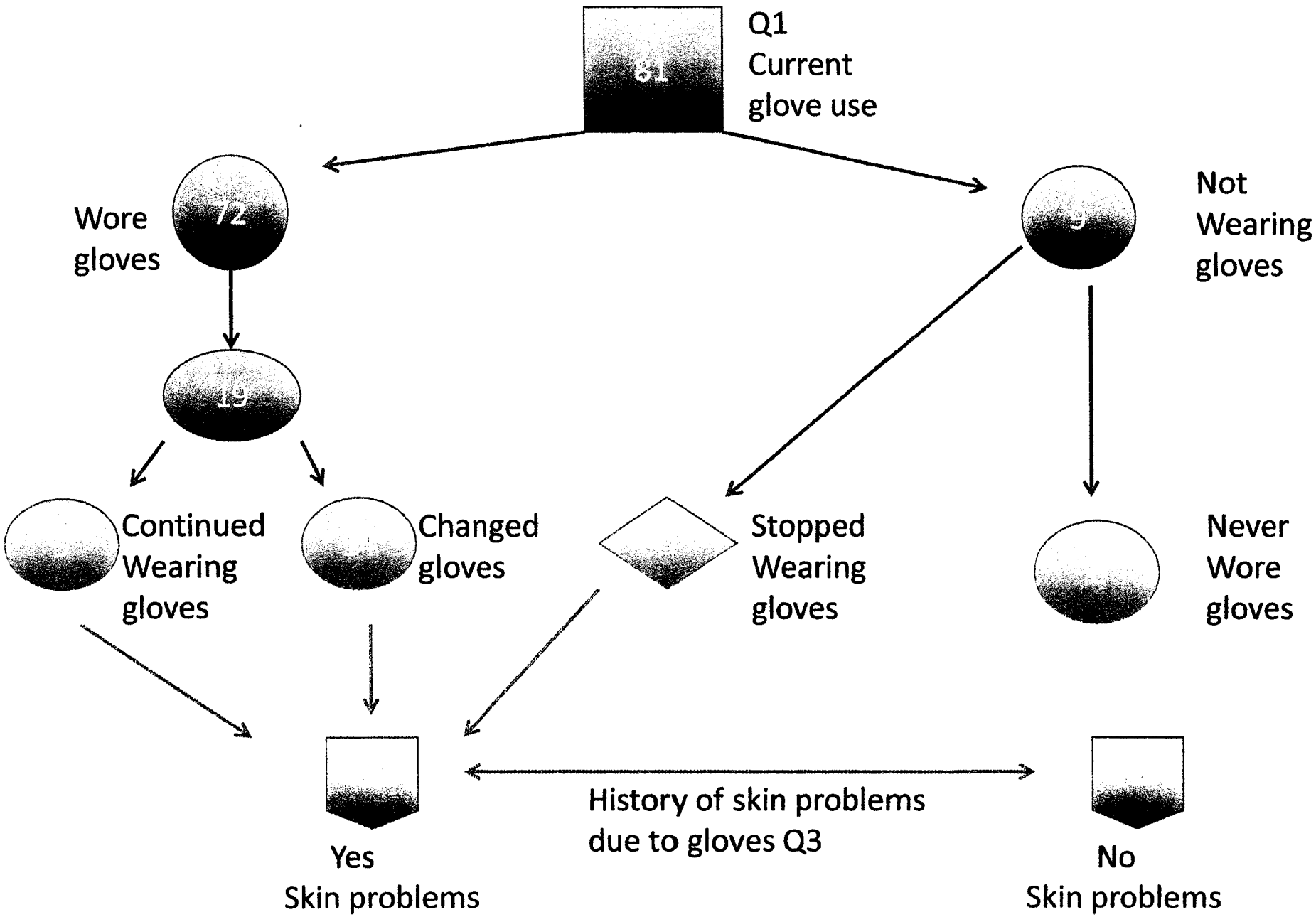
4.2 Workers use of gloves and management of skin problems caused by gloves

Gloves were worn at work by 72 of the 81 workers. Three of the 9 who said they did not wear gloves at work confirmed that they had previously worn NRL gloves but had discontinued using them because of skin symptoms. The remaining 6 said that they had never had a reason to use gloves (Figure 4.1).

A past history of skin symptoms due to the use of NRL gloves (question 3, occupational questionnare) was reported in 22/81 workers. Nineteen of these 22 workers were currently wearing gloves and 3 had stopped wearing them all together (Figure 4.1).

Gloves had been changed to alternate materials (plastic and leather) by 14 of those currently using gloves but 5 continued to use NRL gloves despite having continued skin symptoms (Figure 4.1).

Figure 4.1 Workers' management of skin problems caused by gloves



Nineteen of the 22 workers who had a history of skin symptoms due to the use of NRL gloves at work were currently still using NRL gloves at work, and 3 were not. There was no significant relationship between the current use of gloves and a history of skin symptoms (Fisher's exact test 0.698). Skin symptoms were similarly not shown to correlate with current any NRL gloves use (Fisher's exact test 0.182).

Table 4.3 Relationship between workers who currently wore gloves and had skin symptoms

Glove use	**Skin symptoms**			**Total**	**Fisher's exact test**
	No	**Yes**	**missing**		
No	6	3		9	
Yes,	52	19	1	72	
Total	**58**	**22**	**1**	**81**	**0.698**

4.3 Skin signs recorded on clinical examination

On clinical examination 20/81 workers had skin signs suggesting an inflammatory dermatitis, not urticaria. These included combinations of erythema, eczema, fissures and/or postinflammatory hyperpigmentation on examined areas. One worker had positive dermatographism. The skin findings were recorded predominantly on the hands, face and neck.

Fifteen of these workers with skin signs were currently using gloves at work, and 5 were not. All of these 5 had previously worn NRL gloves but 3 changed to alternative gloves and 2 completely stopped using them (Table 4.4). Skin signs were associated with current gloves use in our study (Fisher's exact test 0.0369).

Table 4.4 Relationship between skin signs and workers who currently wore gloves

Glove use	Skin signs			Fisher's exact test
	No	Yes	Total	
No	4	5	9	
Yes	57	15	72	
Total	**61**	**20**	**81**	**0.0369**

4.4 Workers likely to be at high risk for latex allergy

In total 41 workers met our criteria for being at high risk for latex allergy (Table 4.5). Thirty eight had 4 or more of the symptoms of allergy with or without clinical skin signs and 3 workers had clinical skin signs with 3 of the symptoms of allergy.

Table 4.5 Workers considered high risk for allergies

High risk n (%)	Not at risk n (%)	Total
41(50.6)	40 (49.4)	81

4.5 Prevalence and correlation of total IgE and latex specific IgE for sample population

Total IgE was available for 80/81 workers, 1 result was missing because of a laboratory technical error. The point prevalence of raised total IgE (IgE>100kU/l) was 56% (45/80) (Figure 4.2).

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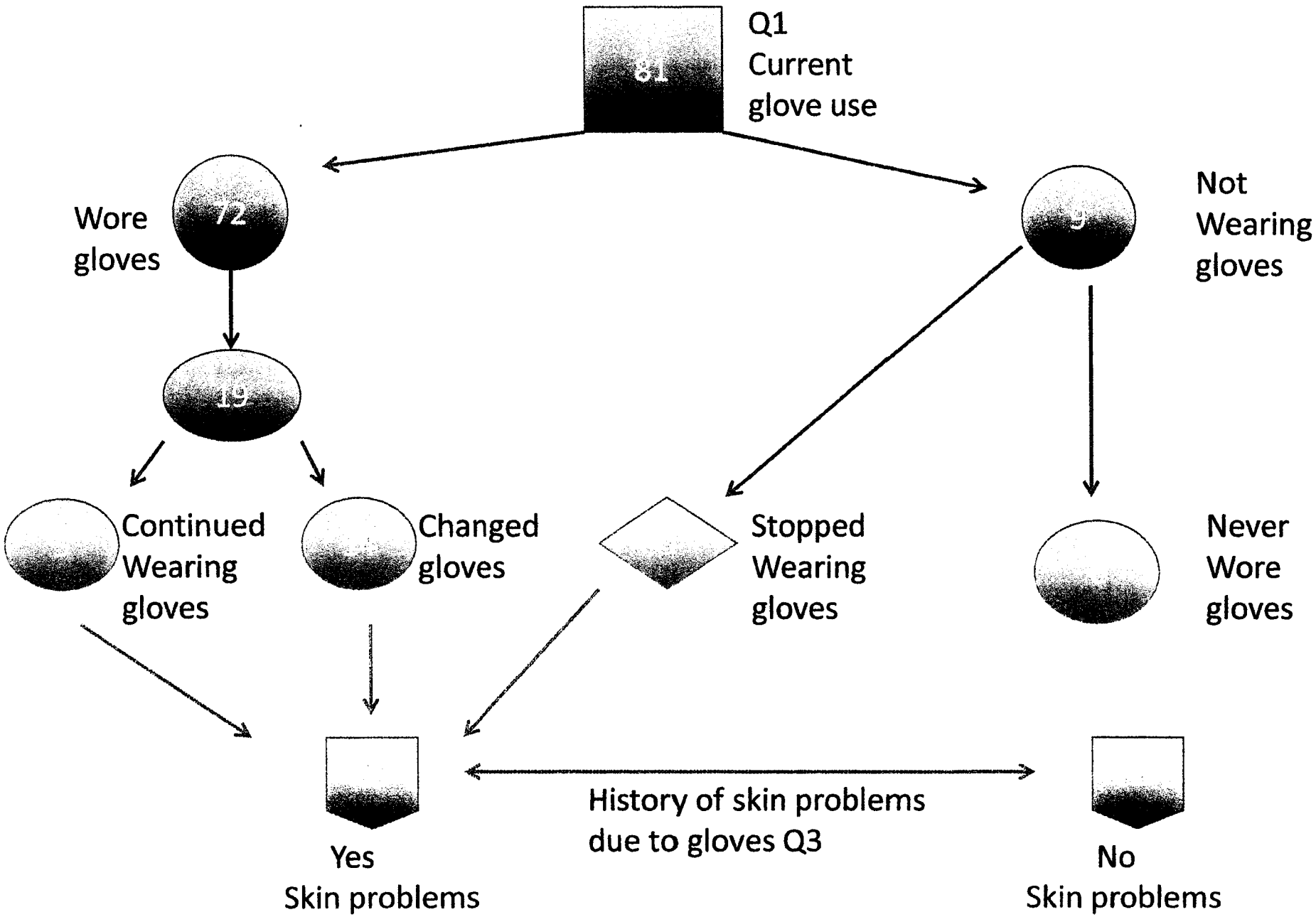

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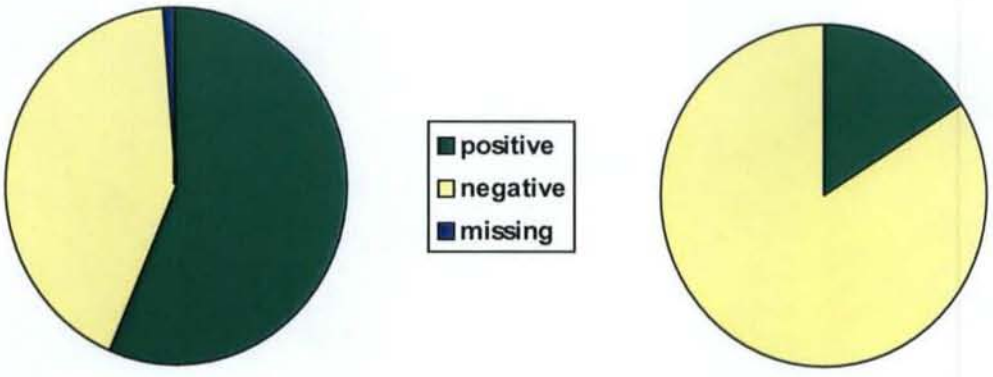
41(50.6)	40 (49.4)	81

4.5 Prevalence and correlation of total IgE and latex specific IgE for sample population

Total IgE was available for 80/81 workers, 1 result was missing because of a laboratory technical error. The point prevalence of raised total IgE (IgE>100kU/l) was 56% (45/80) (Figure 4.2).

Figure 4.2 Prevalence of total IgE and latex specific IgE



Test	Positive n (%)	Negative n (%)	Missing n (%)	Total
total IgE	45 (56)	35 (43)	1 (1)	81
specific IgE	13 (16)	68 (84)	0	81

Latex specific IgE results were available for all 81 workers. The point prevalence of latex specific IgE was 16% (13/81). The prevalence of latex specific antibodies was significantly less than the prevalence of total IgE. Eleven of those with positive latex specific IgE had raised total IgE and only 1 had a negative total IgE. The remaining one was the one with the missing total IgE data. There was a strong association between the two tests (Pearson chi-square of 0.002).

Table 4.6 Correlation between total and latex specific IgE

Total IgE	Latex specific IgE		Total	Fisher's exact test
	Positive	negative		
Positive	11	34	45	
Negative	1	34	35	
Missing	1	0	1	
Total	13	68	81	**0.0097**

Positive latex specific IgE results, expressed in kilounits per liter were reported in 0-6 classes from undetectable values (<0.10) to extremely high detectable antibody levels (>100). The concentrations of less than 0.35kU/l represented a negative result. The majority of workers (62/81) had antibody levels that were below reliable detectable limits and 6 had very low levels of antibody accounting for the 68 negative group. The 13 positive results were evenly distributed throughout the classes with only 2 having very high level of antibody.

Table 4.7 Class 0-6 latex specific IgE values

Classes	Ranges	values	%
0	Below reliable detectable limits (<0.10)	**62**	**77**
1	Very low levels of antibody (0.10 – 0.35)	**6**	**7**
2	Low levels of antibody (0.35 – 0.7)	4	5
3	Moderate level of antibody (0.70 – 3.5)	3	4
4	High level of antibody (3.5 – 17.5)	4	5
5	Very high levels of antibody (17.5 – 100)	2	3
6	Extremely high levels of antibody (>100)	0	0

4.6 Total IgE, latex specific IgE and current glove use

Of 80 workers, 45 had a positive total IgE. Of these 45 workers who had positive total IgE, 40 wore gloves and 5 did not. Of the 5 who are currently not wearing gloves, 3 had previously worn NRL gloves and 2 had never worn gloves. The association between total IgE and the use of gloves at work was not significant (Fisher's exact test 1.0000) (Table 4.8). We conclude for our population that having positive total IgE does not equate to current glove use amongst these workers (Table 4.8).

Table 4.8 Relationship between total IgE test and current glove use

Glove use	Total IgE		Missing data	Total	Fisher's exact test
	Pos	Neg			
No	5	4		9	
Yes	40	31		71	
Missing data			1	1	
Total	**45**	**35**	**1**	**81**	**1.0000**

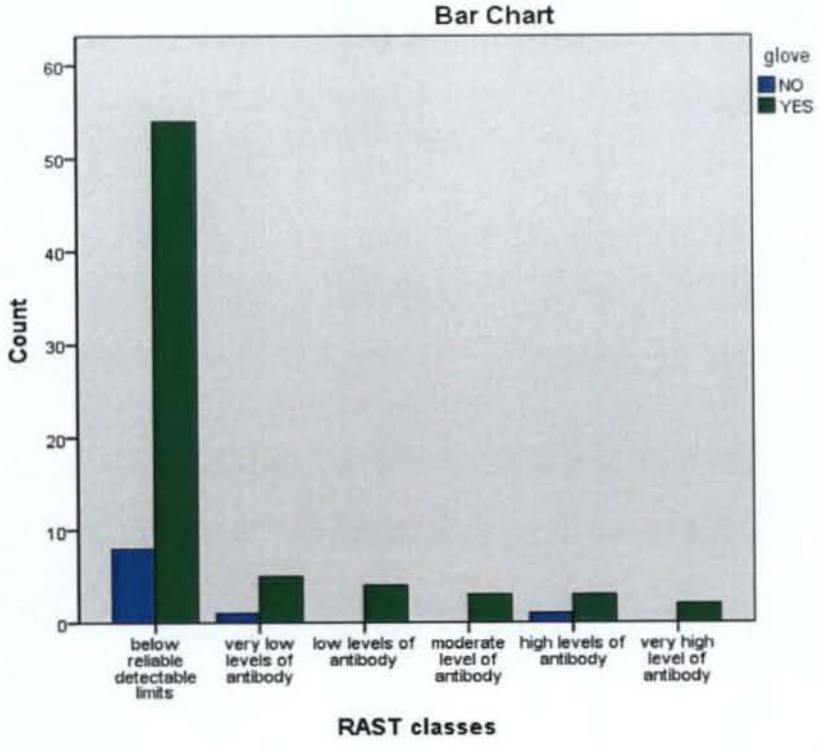
Of the 13 workers with positive specific IgE to latex, 12 currently wore gloves. The remaining one had previously worn gloves but stopped. The Fisher's exact test value of 1.0000 was not significant (Table 4.9). There does not appear to be a direct relationship between the use of gloves and a positive latex specific IgE for our population.

Table 4.9 Relationship between latex specific IgE test and current glove use

Glove use	Latex Specific IgE		Total	Fisher's exact test
	Pos	Neg		
No	1	8	9	
Yes	12	60	72	
Total	**13**	**68**	**81**	**1.0000**

Most of the workers who wore gloves had latex specific IgE readings below reliable detectable limits (Figure 4.3).

Figure 4.3 Workers who wore gloves and their latex specific IgE classes



4.7 Workers status and latex specific IgE

There was a significant relationship between raised latex specific IgE and the workers' employment status (Fisher's exact test 0.0052). Eight workers did not record their status. More permanent workers had raised latex specific IgE.

Table 4.10 Workers status and latex specific IgE

Workers status	Latex specific IgE		Total	Fisher's exact test
	Positive	Negative		
Permanent	12	30	42	
Temporary	1	30	31	
Total	**13**	**60**	**73**	**0.0052**

4.8 Relationship between female and male glove users and latex specific IgE classes

The distribution of raised latex specific IgE classes amongst male and female workers showed little difference. Very high levels of detectable antibodies (class 5) were only seen amongst female glove users (2/8 with raised latex specific IgE) (Table 4.11).

Table 4.11 Female and male glove users and latex specific IgE classes

Latex specific IgE classess	male glove use		female glove use		total
	yes	no	yes	no	
Class 0	**24**	**8**	**30**	**0**	**62**
Class 1	**3**	**0**	**3**	**0**	**6**
Class 2	**1**	**0**	**3**	**0**	**4**
Class 3	**2**	**0**	**1**	**0**	**3**
Class 4	**1**	**1**	**2**	**0**	**4**
Class 5	**0**	**0**	**2**	**0**	**2**
Total	**31**	**9**	**41**	**0**	**81**

4.9 Relationship between high or low risk of allergies with total and latex specific IgE

There was no association between those who we labelled high risk and those labelled not at risk and raised total IgE (Fisher's exact test 0.8219) or latex specific IgE (Fisher's exact test 0.5468) (Table 4.12).

Table 4.12 Relationship between risk for latex allergy, total IgE and latex specific IgE

Test		High risk	Low risk	Total	Fisher's exact test
total IgE	**Positive**	24	21	45	
	Negative	17	18	35	
	Total	**41**	**40**	**80(1)***	**0. 8219**
latex specific IgE	**Positive**	8	5	13	
	Negative	33	35	68	
	Total	**41**	**40**	**81**	**0.5468**

* missing total IgE result

4.10 Relationship between skin symptoms and total and latex specific IgE

There was no association between workers who reported skin symptoms due to glove use with either raised total IgE or latex specific IgE (Table 4.13).

Table 4.13 Relationship between skin symptoms and raised total and latex specific IgE

Test	Skin symptoms		Fisher's exact test
Total IgE	**Yes**	**No**	
Yes	16	29	
No	6	28	
			0.1273
Latex specific IgE	**Yes**	**No**	
Yes	4	9	
No	18	49	
			0.7450

4.11 Relationship between skin findings and total and latex specific IgE

Clinical examination revealed 20/81 workers with skin signs. Of these only 4 had a positive latex specific IgE all of whom had a raised total IgE ranging from 692kU/l – 1484kU/l. There was no relationship between latex specific IgE with skin signs but there was a strong relationship between elevated total IgE and skin signs.

Table 4.14 Skin findings and total and latex specific IgE

Test		**Skin signs**		**Total**	**Fisher's exact test**
Latex specific IgE		**Yes**	**No**		
	Yes	4	9	13	
	No	16	52	68	
	Total	20	61	81	0.7261
Total IgE		**Yes**	**No**		
	Yes	18	27	45	
	No	2	33	35	
	Total	20	60	80 (1)	**0.0004**

CHAPTER 5

DISCUSSION

For years now, latex hypersensitivity has been recognized as a significant medical problem. Studies have been done emphasising occupational medical workers rather than the non-medical sector. Published work focussed on the non medical sector include, studies in a textile factory (Pisati et al., 1998), a latex doll manufacturing plant (Orfan et al., 1994), greenhouse workers (Carillo et al., 1995), housekeeping personnel (Sussman et al., 1995) and hairdressers (van der Walle & Brunsveld, 1995; Kanerva & Laino, 1999).

To our knowledge this is the first study of latex hypersensitivity done in a factory manufacturing sanding and grinding discs, traditionally a low prevalence latex exposure industry. A work place visit confirmed the low natural rubber latex exposure in the actual work process.

In an epidemiological study done in Thailand on workers who were exposed to natural rubber latex during tapping and glove manufacturing the overall response rate was 80%. There were more men than women in the study (Chaiear et al., 2001). In another study done in a latex doll manufacturing plant where they looked at occupational asthma caused by latex, 22 of 25 (88%) workers (17 men and 5 women) participated (Nicholas et al., 1994). In our study, the response rate was 51% representing a sample size of 81 potential participants of the 160 workers on the factory floor on the study days. This is lower than the above reported response rates and although all workers were encouraged to participate those who did not take part gave the following reasons. Some had taken part in an unrelated HIV study done a few months prior to ours. Others were simply not keen to participate. Those who were not keen to take part could represent workers who had no skin problems with wearing gloves or they were not wearing gloves at all.

There was no significant difference in the number of the overall male and female workers who participated in our study in comparison to the studies discussed above which reported males predominantly. In our study males and females were unequally distributed across departments. All 41 female workers who participated were employed in the dry coat department. The 40 participating males were found in all departments but were exclusive to the phenolics (7/40) and abrasive (13/40) departments (Table 4.1).

Most of the workers (52%) were permanent employees and had been working at the factory for more than a year. Temporary workers had been employed for periods ranging between 3 to 10 months. Raised latex specific IgE was detected amongst temporary (1/31) and permanent (12/42) workers. The relationship of latex sensitization and allergy to the duration and extent of exposure has been examined in several studies (Tarlo et al., 1997). Tarlo et al., 1997 reviewed cross-sectional rates of latex sensitization and allergy in University of Toronto Dental School. None of the first- and second-year dental students who were tested were allergic. However, 5% of third-year and 10% of the fourth-year students had become sensitized. According to Pouryaghoub et al atopy, intensity and duration of exposure have been reportedcognized as predisposing factors for latex sensitization.

Other authors report that the time spent in an environment with latex exposure is not a risk factor for latex sensitization. Sensitization may develop at any time after first exposure to latex rubber (Azizah et al., 1996; Weissman et al., 2002). Azizah et al., 1996 found no relation between the duration of time the workers spent in latex glove manufacturing factories and the presence of sensitization to latex as defined by a positive skin prick test to latex. Garabrant and Schweitzer, 2002 reported that length and frequency of exposure to latex gloves is not clearly associated with sensitization.

A number of studies have indicated that many suspected incidences of latex allergy had no allergic basis but were simply related to long-term occlusive glove wearing (Nettis et al., 2002).

We noted that those working on a temporary basis showed lower sensitization when compared with permanent workers (Fisher's exact test 0.0052). In our study we did not specifically look at exposure time or duration of employment as study variables. Although it can be assumed that latex exposure occurred in the work place, temporary workers might be less exposed than permanent workers. This suggests that in the workers studied, exposure time might have played a role. Alternately the use of NRL gloves predisposes to skin barrier dysfunction due to their occlusive effects. This increases the risk of exposure to allergen and hence sensitization. Temporary workers, because of less frequent glove use, may have limited risk of barrier dysfunction and hence reduced risk of sensitization. Controversy still exists regarding the exposure response relationships between health care workers and sensitization to NRL (Weissman & Lewis, 2002).

The prevalence of NRL allergy in the general population is unknown but it is estimated to be less than 1% (Turjanmaa et al., 2000). Latex sensitization prevalence amongst healthcare workers ranges from 3% to 22% with variability possibly being partly explained by the use of non-standardised allergen extracts (Lagier et al., 1992). The prevalence of latex allergy at Groote Schuur Hospital was found to be 9.2% among 2316 staff members (Potter et al., 2001) and 16.7% in a cohort of 24 spina bifida children at Red Cross Hospital in South Africa (Johar et al., 2005). A similar range of prevalence of NRL allergy has been reported amongst workers in a latex doll factory 9% (2 of 22) (Orfan et al., 1994), latex glove factory in Thailand (1.7%) (Chaiear et al., 2001), housekeeping personnel (8%) (Sussman et al., 1995) and agricultural workers from a

flower greenhouse (18% of the 418 workers) (Carillo et al., 1995).

The high prevalence of workers with positive latex specific IgE, (16%), in our study suggests a high risk of sensitization in the work place. This was probably due to the introduction of latex gloves as PPE in 2004, prior to our undertaking the study, as the manufacturing process per se does not include significant natural rubber latex exposure.

The use of PPE has become particularly important in the work place as skin exposure is increasingly being recognized as a major route of substance absorption. There were 72 workers who wore gloves to protect themselves from chemicals (49%), from hurting their hands (63%), from dust (9%) and from oil and greases (1%). In the dry coat area, there were 20 males and 41 females who performed the following duties: cutting discs using a press machine and sorting and packing discs. Forklift drivers removed packed boxes. It was noticed that most of the workers in this area wore gloves. They were not involved in wet work or handling of chemicals requiring the use of NRL gloves for PPE. As anticipated, most of the workers from this area showed skin changes consistent with repetitive pressure leading to calluses on their fingers and thenar eminences. Those workers who were not using gloves were noted to have black dye staining of their hands. These workers with stained hands explained that it was difficult to wash off the stain. Similar staining was not evident amongst those who wore gloves, strongly supporting the workers' need to protect themselves. Workers in the dry coat and abrasive areas required gloves mainly for protection from staining and repeated pressure. Leather or cotton gloves would be more appropriate PPE in this area rather than the expensive and inappropriate use of the latex rubber gloves.

The latex specific IgE prevalence in our population was 16%, suggesting that there is significant latex sensitization among

these workers, comparable to medical workers (3-22% dependant on study population and latex allergen used). The reason for this high prevalence was thought to be the use of NRL gloves.

This assumption was not supported by our results, as glove use amongst the 81 workers was not related to raised specific latex IgE. When relating IgE and glove use, we concluded that having elevated total IgE (Fisher's exact test 1.0000) and positive latex specific IgE (Fisher's exact test 1.0000) did not correlate with current NRL glove usage (Table 4.8 and Table 4.9). We have no definite explanation for this high sensitization rate which appears to be work related as permanent workers were more likely to be sensitized than temporary workers (Table 4.10). This could be due to the small sample size.

Nineteen, (86%), of the 22 workers with skin symptoms were currently using gloves and 3/22 (14%) were not (Fisher's exact test 0.6979). These 3 workers had previously used gloves but had stopped. Skin symptoms were not significantly associated with glove use at work (Figure 4.1 and Table 4.3).

Twenty workers were found to have skin signs on examination. Of these, 15 were currently using NRL gloves at work and 5 were not. These 5 workers had all previously worn gloves. Three changed to alternative gloves and 2 had completely stopped using gloves. Skin signs were significantly related to current NRL glove use at work in our study.
A history of skin symptoms thought to be due to the use of gloves at work was reported by 22 (27%) of the 81workers. There were 16 workers who gave a history of skin symptoms and had raised total IgE, but this was not significant when compared with the group as a whole, (Fisher's exact test 0.1273). A history of skin symptoms did not correlate with either raised total IgE or latex specific IgE (Table 4.13). This could be due to irritation caused by the gloves.

In our study, there was no significant relationship between workers with skin signs and raised latex specific IgE (Fisher's exact test 0.7261). On the contrary there was a significant association between workers who had skin signs and raised total IgE (Fisher's exact test 0.0004) (Table 4.14). Only one worker who had raised latex specific IgE did not have raised total IgE. There were in total 45 workers (56%) with raised total IgE.

Atopic individuals appear to be especially at risk for sensitisation to the latex protein because of barrier dysfunction. The use of latex gloves, in contact with damaged skin increases the risk of latex allergy developing (Mellstrom et al., 1994). Suli et al., 2004 reported that the risk of latex IgE sensitisation was four times higher in health care workers reporting atopic manifestations than in health care workers without atopic disorders. In the same study the highest latex-specific IgE levels were found in subjects with personal history of atopy.

There was no difference in the prevalence of raised total or latex specific IgE amongst the high risk and low risks workers (Fisher's exact test 0.5468) (Table 4.12). In our study we did not specifically use internationally standardised criteria for atopy. We specifically chose questionnaires that evaluated skin disease at the work place and not those evaluating atopy *pe se*. Questions suggesting allergic symptoms were combined with signs from clinical examination to define workers at high risk for allergy and a possible atopic diathesis. This discrepancy could explain the lack of the anticipated relationship between raised total IgE and atopy and is a limitation to our study.

History combined with clinical examination is essential in deciding which laboratory tests to perform, as some of these tests are expensive and are not routinely advisable. In the presence of symptoms highly suggestive of latex allergy, a positive latex specific IgE test is supportive evidence for

clinically relevant sensitization (Smedley et al., 1999). This emphasizes that a thorough history is essential.

In Summary:

- The prevalence of latex specific IgE was 16% comparable to the ranges reported for health care workers
- The prevalence of raised total IgE was 50%
- The majority of workers who had raised latex specific IgE had raised total IgE (11/13)
- Permanent workers were more likely to have raised latex specific IgE than temporary workers
- Gloves were used as PPE by 89% of the workers.
- The gloves were inappropriate for the type of work being done and the protection required for the majority of the workers.
- The use of NRL gloves in our study correlated significantly with the presence of skin signs and not symptoms
- The use of NRL glove in this non medical setting did not correlate with raised total IgE or latex specific IgE
- Skin symptoms were not related to NRL glove use at work (current and ever) nor related to a raised total or specific latex IgE
- Skin signs were related to current NRL glove use at work and raised total IgE but not latex specific IgE

- In our study workers defined as at high risk for allergy did not show any significant association with either raised total or latex specific IgE

These findings could be explained by accepting total IgE as a manifestation of atopy and the predisposition to IgE sensitization while skin symptoms and signs are an indication of barrier dysfunction and/or atopy. Importantly, the presence of skin signs and symptoms does not mean that worker has specific latex sensitization.

Future studies are needed to define the source of latex exposure more specifically as glove use amongst various subgroups of workers needs to be done. Inclusion of patch testing will separate contact allergic dermatitis from irritant contact dermatitis neither of which has been explored in our study,

We also suggest that further studies be done with a clear definition of atopy in order to correlate the total IgE and latex specific IgE with the atopic and the non-atopic workers. Further, performing SPT could add more to the study if it is done on workers who have suggestive symptoms and signs but negative latex specific IgE.

5.1 Limitations of the study

One of the limitations to our study was that patch testing was not done to exclude contact allergic dermatits. Workers with skin problems thought to be secondary to latex gloves might be due to rubber chemicals included during the glove manufacturing process. There is now good evidence to support the inclusion of latex rubber for patch testing to identify type IV allergic contact dermatitis in individuals with hand skin problems who use NRL gloves (Wilkinson & Burd, 1998).

Although the Skin Prick Test (SPT) is regarded as the gold standard for diagnosing latex allergy worldwide, the latex-specific IgE determination was preferred to the SPT to obtain quantitative results and also to avoid the possibility of anaphylaxis or in non-medical settings (de Beer & Cilliers, 2004). The aim was to perform SPT on all participants with negative latex-specific IgE in order to pick up false negative. Because of the limited time offered by the company SPT and patch testing was not done.

The response rate to participation for the study (51%) was relatively low compared to the previously mentioned studies, and it is possible that workers with glove problems were more inclined to respond than those without. These could give a positive bias to the study and explain our high sensitization rate.

In our study we elected to use the Nordic occupational skin questionnaire. This questionnaire was designed for surveying work-related skin diseases and exposures at the workplaces as opposed to questionnaires designed for epidemiological studies of contact dermatitis and atopy. Because of this the workers atopic status was not specifically interrogated. The allergic diathesis was defined by a combination of symptoms asked in the questionnaires and clinical findings. Those who had 4 or more of the symptoms of allergy with or without clinical skin

signs, or those who had clinical skins signs with 3 of the symptoms of allergy were regarded as being high-risk workers more likely to be susceptible to allergies. Workers who met the definition of high risk as described above, where then equated to atopic individuals. Further studies should include specific features to allow internationally accepted criteria for the diagnosis of atopy.

We also identified conflicting responses with regards to certain questions. All of the questionnaires were asked in English after consultation with the workers who confirmed that although Afrikaans was their first language they all spoke and understood English. Some of the workers answered positively to rash changes associated to being away from work even though they had previously indicated that they did not have a rash. This could best be explained by the workers interpretation of some of the questions as no attempt was made to give an explanation if the individual was unsure of the meaning. Future questionnaires should be translated into the home language of the workers to prevent misinterpretations.

In depth questions on duration of glove use and other latex exposures in the home and work might have revealed possible exposure that could explain the high sensitization rates. Inclusion of a food and diet questionnaire would also have been helpful in this regard.

Inclusion of all the workers in future studies would give a larger population size and improve statistical analysis especially those related to subgroups that were limited by the small numbers in our study.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

We have demonstrated a high prevalence of latex allergy (16%), in a factory setting, away from the traditionally recognised high-risk occupations such as in the health sector.

This study revealed that raised total IgE and elevated latex specific IgE does not necessarily equate to glove usage. Sixty of the workers who currently wore NRL gloves had latex specific IgE readings below reliable detectable limits and 55% had positive total IgE. Workers reported to have skin problems and those who had skin signs did not show any significant association with latex specific IgE, but there was a strong significant association between skin signs and raised total IgE. This suggests that having skin signs does not necessarily mean latex sensitization and probably reflects irritant dermatitis.

The prevalence of elevated latex specific IgE amongst workers at IWT factory was high, suggesting sensitization to latex. Since latex sensitization carries the risk of serious hypersensitivity reactions, we suggest the use of more appropriate types of gloves in different departments.

We feel that latex specific IgE testing is a good screening test where SPT is contraindicated. It should be performed only on workers with strong suspicion of latex sensitization where there are respiratory symptoms and/or history of urticaria.

6.1 **PPE in the work place**

Trade unions and widely publicised worker rights have correctly increased the awareness of and demand for PPE use. PPE however, should only be used as back up protection when all other attempts to prevent exposure have been explored and instituted. PPE as the first line protection from exposure should

be discouraged, as it will always fail and has inherent associated hazards. Employers and workers thus need to be properly advised about the use, maintenance and care of PPE and the hazards associated with its use.

The first step in choosing PPE should be based on a thorough knowledge of all tasks and exposures in the work place. Once this has been clearly established the appropriate PPE for the task, exposure and protection required can then be decided upon taking into account the worker's medical history. There is seldom a single form of PPE that will meet all the requirements of the various tasks (Mellstrom et al., 1994).

Among the workers studied the wide scale use of natural rubber latex gloves does not appear to have been based on this approach to the choice of PPE. Furthermore the daily use of these gloves could be the cause of irritant contact dermatitis, a consequence of prolonged maceration and occlusion leading to cumulative damage to the barrier function of the skin. This damage would then place the worker at risk of increased allergen exposure and sensitization despite un-powdered gloves being used since 2007.
Although we did not show an association between latex specific IgE and glove use as a whole, subgroup analysis of this association might identify the gloves as the source of the high prevalence of latex specific IgE (16%) amongst the workers.

Most of the workers in the dry coat department needed protection from trauma and skin staining. The work does not involve liquid exposure and alternate glove materials (leather or cotton) would be more appropriate to prevent trauma and dye rubbing off on the skin. A specific task evaluation needs to be done before a formal recommendation can be made.

Most workers in the phenolics department complained of sweating from rubber glove use and/or irritation from fibre glass. Workers dealt with their glove/PPE concerns in several

ways. Some workers stopped wearing gloves at all (Figure 3.11). Others bought gloves made of thicker rubber with cotton lining (Figure 3.10) to protect from the fibre glass and reduce sweating. Other workers continued to use the gloves provided despite the discomfort.

For workers involved in wet work or the handling of chemicals some form of rubber glove would be appropriate. Again natural rubber latex is not necessarily the material of choice as the chemicals or exposures could damage the substance of the glove or the natural rubber latex per se does not offer any barrier to the penetration of the chemicals being used (Mellstrom et al., 1994).

For our workers exposed to phenol, methanol and various dyes each task would need substance exposure evaluation and then the appropriate material chosen for the PPE that should supply suitable back up, splash protection only (Pachkham,. 1998).

6.2 Latex awareness and education (Zak et al., 2000).

If latex exposure is a concern within a work environment, there are several pre-emptive actions one should take:

- Find out if anyone is allergic or sensitive to latex.
- Make everyone aware of the dangers of latex.
- Make allergy-sensitive individuals familiar with the diverse sources of latex.
- Make every effort to reduce latex exposure by engineering alternatives or replacing latex with alternate materials where possible.
- Improve ventilation in areas where latex exposures may occur and change and clean ventilation filters frequently.
- Educate workers about latex allergy and how to recognise symptoms of latex allergy by offering training programmes.

- Conduct regular worksite evaluations to identify areas of potential problems.
- Consider alternate materials to natural rubber latex.

6.3 Alternatives to NRL gloves
(http://www.medicalexamglove.com)

- Low protein non-powdered NRL gloves.
- Synthetic rubber gloves.
- Hypoallergenic gloves do not reduce the risk of latex allergy, but may reduce the risk of contact dermatitis to the additives in latex. Therefore latex allergic staff should not use them.
- Nitrile gloves are latex-free, are less likely to tear with a high resistance to being punctured but cost more than NRL ones. Due to their resilience, nitrile gloves work very well in harsh, high-stress environment.
- Disposable vinyl gloves are the most economical gloves for cost conscious facilities. Made from polyvinyl chloride (PVC), these gloves provide standard barrier protection, are comfortable to wear but tear easily.

6.4 Recommendations for workers needing NRL gloves
(http://www.asosh.org/Programmes/SORDSA/Latex-allergy.htm)

- Use cotton gloves underneath the latex gloves.
- Avoid oil-based hand creams when using latex gloves.
- Wash and dry hands thoroughly after removing latex gloves.
- Avoid touching the mucous membranes during or after contact with a latex product.
- Eliminate unnecessary latex glove use
- Change gloves frequently to minimise sweating due to occlusion

- Limit exposure to irritants such as detergents, alcohol, formaldehyde, and antimicrobial agents that may damage the skin barrier and predispose to latex sensitivity (Thompson, 1997).
- Recognise symptoms of latex allergy and become familiar with preventative strategies.
- Choose gloves needed for PPE appropriately.
- Use gloves that contain reduced latex and powder or those that are powder-free if natural rubber latex cannot be avoided.
- Take advantage of all latex allergy education and training provided by your employer.

6.5 Advice for workers with known latex allergy (http://www.cdc.gov/niosh/latexalt.html)

- Avoid contact with latex products and areas where powder inhalation from latex gloves worn by others may occur.
- Inform management and co-workers of your latex allergy.
- Seek early help from a doctor with experience in latex allergy.
- Carefully follow medical advice for managing allergic reactions to latex when they occur.
- Treat symptoms early to prevent the sensitization to latex becoming too severe.
- Wear a medic alert bracelet.
- Change to working in a latex-free environment if symptoms moderate to severe (SORDSA ALERT, 1998).
- Assess work environment to establish all possible exposures.
- Consider training for redeployment if exposures cannot be contained.

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UNIVERSITY OF CAPE TOWN

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16 April 2008

REC REF: 125/2008

Dr D Motsepe
C/O Prof G Todd
G23, Dermatology Division
Groote Schuur Hospital

Dear Dr Motsepe

PROJECT TITLE: RELEVANCE OF A POSITIVE LATEX (RAST) RESULT IN A NON-MEDICAL OCCUPATIONAL SETTING.

Thank you for submitting your study to the Research Ethics Committee for review.

It is a pleasure to inform you that the Ethics Committee has **formally approved** the above mentioned study.

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the REC.REF in all your correspondence.

Yours Sincerely

PROF M BLOCKMAN
CHAIRPERSON, HSF HUMAN ETHICS

lemjedi

INFORMED CONSENT PARTICIPATION

PROJECT TITLE: Relevance of a positive latex IgE test (RAST) result in a non-medical occupational setting – 2010

RESEARCHER: DR D. MOTSEPE

Contact number : 021-4045269/5273

Has told me what the research project is about and what I will need to do if I agree.

I have received a copy of the study information sheet which I have had explained to me.

The problems that could be caused by the study have been explained to me and I understand what they are.

I have been given a chance to ask questions which have been answered.

I understand that I do not have to take part in this study and I understand that I can stop at any time after signing the consent.

I understand that if I decide to stop, it will not affect my job or treatment required.

I only consent to:

1. Questionnaires
2. Dermatology examination
3. Pictures of my skin/ Test results
4. Total IgE/RAST
5. Skin prick test
6. Patch test

PATIENT:

SIGNED: DATE:

DOCTOR:

SIGNED: DATE:

WITNESS:

SIGNED: DATE:

MEDICAL QUESTIONNARE

1. Have you ever had a skin problem?

Yes ☐

No ☐

2(a)Do you ever sneeze a lot?

Yes ☐

No ☐

2(b) What makes you sneeze

		Yes	No	Don't know
(i)	Pollen	☐	☐	☐
(ii)	Dust	☐	☐	☐
(iii)	Others	☐	☐	☐

3(a) Do your eyes itch a lot?

Yes ☐

No ☐

3(b) If yes.... what could be the cause?

	Yes	No	Don't know
(i) Pollen	☐	☐	☐
(ii)Dust	☐	☐	☐
(iii)Others	☐	☐	☐

4. Do you suffer from dry skin in general?

Yes ☐

No ☐

5(a) Have you ever been told by a doctor that you have an allergy?

Yes ☐

No ☐

5(b) If yes... what is the cause of your allergy?

(i) Allergy to pollens ☐
(ii) Allergy to dust ☐
(iii)Allergy to animals ☐
(iv)Other reasons ☐

6(a) Have you been told by a doctor that you have asthma?

Yes ☐
No ☐

6(b) If yes.... What treatment are you getting?

7(a) Have you ever had an itchy rash on your..... (Tick the correct answer)

.Face ☐
.Hands ☐
.wrists ☐
.forearms ☐

7(b) If yes... What treatment are you using

8. When did you first get this itchy rash?

.below 6 yrs of age ☐

.between 6 and 18 yrs of age ☐

.above 18 yrs of age ☐

9. Is there anyone in your family with the same kind of rash?

Yes ☐

No ☐

10. What makes your rash better?

. Steroid creams/ointments ☐
. moisturisers ☐

. staying away from work

OCCUPATIONAL EXPOSURE QUESTIONNARE

1. Do you use gloves at work place?

   Yes ☐

   No ☐

2. What kind of gloves do you use? (tick the correct answer)
   (i) Rubber ☐
   (ii) Plastics (e.g. vinyl, PVC, polyethene) ☐
   (iii) leather ☐
   (iv) cloth ☐
   (v) cotton gloves underneath rubber or plastic gloves ☐

3. Have gloves caused skin problems?

   Yes ☐

   No ☐

4. Have you changed gloves or stopped using gloves because of skin problems?

   Yes ☐

   No ☐

5. What are you doing or handling in your work at present that requires gloves? (Tick all relevant boxes)

   (i) working on a machinery ☐

   (ii) cleaning machines ☐

   (iii) packing ☐

   (iv) cleaning and sweeping floors ☐

   (v) handling oils ☐

   (vi) wet work ☐

   (vii) others ☐

6. Have you noticed that touching certain materials or chemicals causes you to itch or makes your skin worse/bad?

   Yes ☐

   No ☐

7. Why do you wear gloves? (Tick all relevant boxes)

   (i) to protect you from chemicals ☐

   (ii) to protect you from water ☐

   (iii) to protect you from hurting your hands ☐

   (iv) to protect you from oils and greases ☐

   (v) to protect you from dust ☐

   (vi) because you were told to wear gloves ☐

   (vii) because you feel it is your right to wear gloves as part of personal protection ☐

8. Has the itchy rash affected the everyday work in your occupation in any specific way? Which of the following statements are true?

   (i) in no specific way ☐

   (ii) hands must be protected with gloves ☐

   (iii) I changed jobs because of the itchy rash ☐

   (iv) I have been on sick leave/off work because of itchy rash ☐

   (v) my income has diminished because of the rash ☐

NON-OCCUPATIONAL EXPOSURE QUESTIONNARE

1(a) Have you noticed that contact with certain materials, chemicals or anything else outside your work makes your rash worse?

Yes ☐
No ☐

1(b) If yes.... What are they

2. What do you consider as the most important things outside the workplace that worsen your itchy rash? (Tick only one box)

(a) Personal hygiene e.g.
-soap ☐
-soap liquids ☐
-hair grooming (e.g. dyes etc.) ☐
-creams ☐
- shampoo ☐
-cosmetics ☐

(b) Household cleansing
-detergents
e.g. dishwashing soap, handy andy etc. ☐
-laundry soaps ☐
-fabric softners ☐
-others ☐

(c)Hobbies
-gardening ☐
-machinery maintainance ☐
-household maintainance ☐
-pottery ☐
-painting ☐
-sport ☐
-others ☐

3. How often did you do the following activities during the past 12 months?

	>5x	<5x	Do not know
-gardening	☐	☐	☐
-car or motor repair	☐	☐	☐
- building or renovation	☐	☐	☐
- house work	☐	☐	☐
- others	☐	☐	☐

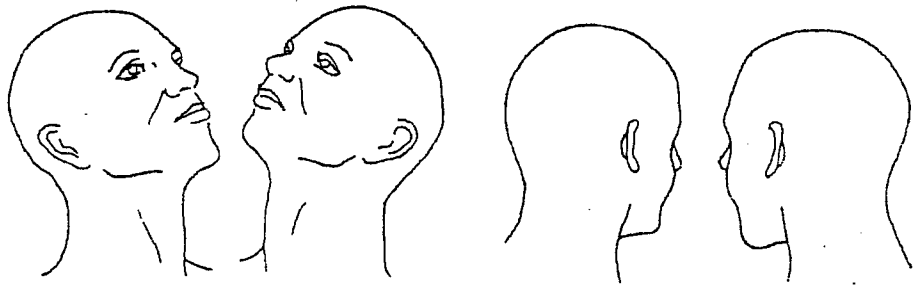
4(a) Does your itchy rash improve when you are away from your normal work place?

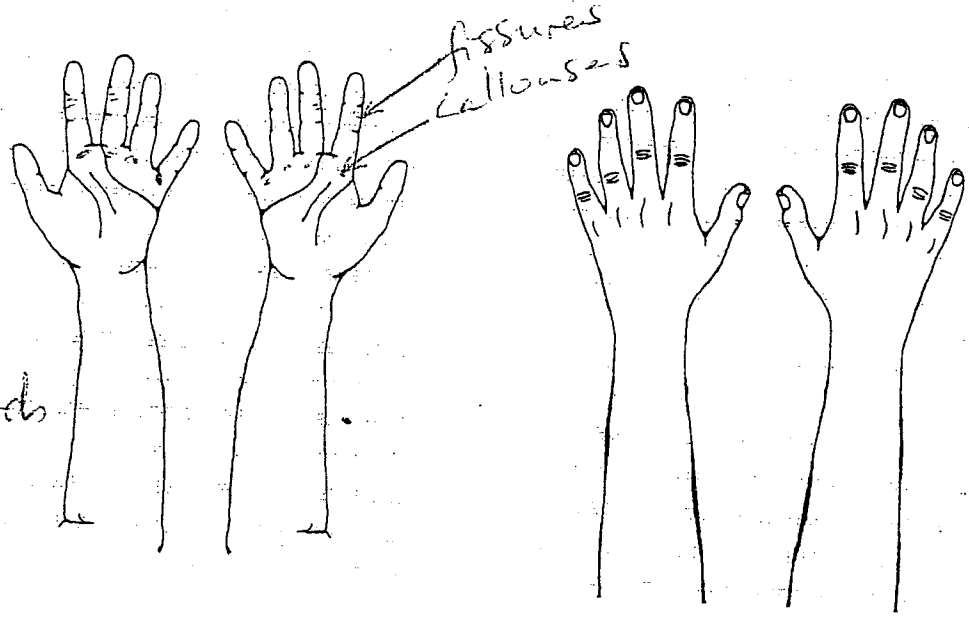
Yes	☐
No	☐

4(b) If yes.... Is it due to

		Yes	No	Do not know
(i)	Not wearing gloves	☐	☐	☐
(ii)	Applying creams more often	☐	☐	☐
(iii)	Not handling chemicals or certain materials	☐	☐	☐
(iv)	Others	☐	☐	☐

N/A





Generally dry hands