Allergic contact hand dermatitis due to constituents of nitrile gloves

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ABSTRACT

Purpose: This report of a case of allergic contact hand dermatitis due to constituents of nitrile gloves is to bring to the attention of practitioners four important practice points: 1) allergic contact dermatitis may occur due to exposure to chemicals in nitrile gloves; 2) skin patch testing is used to identify the causative allergens; 3) targeted allergens may be necessary in addition to the baseline European standard series if the standard series is unhelpful; and 4) there are potential interventions to manage nitrile glove dermatitis.

Findings: A laboratory analyst had occupational exposure to several allergens and had worn latex gloves. She was exposed to laboratory chemicals and powdered ore dust, containing precious metals. She developed hand dermatitis and was relocated to administrative duties not requiring glove use. Her dermatitis cleared but recurred when she returned to the laboratory and started using nitrile gloves. On history, nitrile gloves and platinum group metal ore dust were consistently associated with her hand dermatitis, but laboratory chemicals were not. Latex-specific immunoglobulin E (IgE) was negative, as were skin patch tests for 13 allergens in the metal series, including salts of platinum group metals. She had positive allergic reactions to cobalt chloride, formaldehyde, nickel sulphate, and quaternium 15 in the European standard series patch tests. She did not react to the rubber chemicals in the European standard series, including thiuram mix. The patient was then tested with the rubber additives series because of the glove-relatedness of her hand dermatitis. She had positive reactions to three thiuram compounds used as accelerators in rubber gloves. The patient went on vacation during which time her dermatitis improved. She was relocated to a position without glove use or ore contact and her dermatitis did not recur.

Conclusions: An analytic laboratory worker developed hand allergic contact dermatitis due to nitrile glove constituents. The diagnosis is supported by the improvement in her dermatitis after cessation of glove use, negative metal series patch tests, and positive patch tests to accelerators found in rubber gloves. Nevertheless, a contribution to the dermatitis by metals in the platinum group metal ore dust cannot be excluded.

Recommendations: Nitrile glove constituents should be considered in wearers who develop hand dermatitis. Skin patch testing is recommended to investigate putative agents. Specific patch test series for more targeted testing may be required.

INTRODUCTION

Nitrile, also called nitrile butadiene, is a synthetic rubber produced from a copolymer of acrylonitrile and butadiene.[1] Nitrile gloves contain this rubber but also other constituents such as accelerators. Accelerators are chemicals used to speed up the process of vulcanisation – chemical crosslinking to give rubber its useful characteristics, such as strength and retraction to its original shape after stretching – at a lower temperature and with greater efficiency. Commonly used classes of accelerators in rubber gloves are thiurams, dithiocarbamates, thiazoles, guanidines, and thiourea. Each class contains several individual chemicals.[2,3]

Nitrile gloves have replaced latex gloves in many workplaces because of latex allergy concerns.[4] Hand protection is required in many occupations; consequently, nitrile glove use is widespread, as shown in Box 1.

Given the multiple uses of these gloves, the global market is large, estimated at US$ 6.55 billion in 2022.[5] We could not find data on the number of people using nitrile gloves in South Africa or southern Africa, but it is reasonable to expect that it is many thousands due to the size of the workforces in the occupations listed in Box 1.

Despite the preference for nitrile gloves in some settings, they have also been shown to cause allergic contact dermatitis (ACD) [2,3] through a type IV cell-mediated immune response. Hypersensitivity due to the actual nitrile rubber in gloves is rare,[6] but the accelerators used in regular nitrile gloves are common causes of sensitisation. [2,3]

Box 1. Some occupations in which nitrile gloves are used

- Automotive workers
- Cleaners
- Food handlers
- Gardeners
- Hair salon workers (stylists, washers, etc.)
- Healthcare workers (doctors, nurses, dentists, phlebotomists, students, etc.)
- Housekeepers
- Laboratory workers (technicians, technologists, scientists)
- Tattoo artists
- Veterinary care workers

Skin patch tests are used to identify compounds causing ACD. Patch testing involves the application against the skin – usually on the upper back – of suspect allergens in chambers held against the skin by hypoallergenic tape (Figure 1). An occlusion time (contact with the skin) of two days is recommended before removing the chambers.[7] Reading the skin reactions to identify allergic responses is done some days after initial application; the exact number varies but the European Society of Contact Dermatitis recommends readings at day 2 (i.e. after removal of patches), day 3, or day 4, and when indicated around day 7.[7] Reading on day 7 is only necessary for some allergens, e.g. corticosteroids and aminoglycoside antibiotics, and when earlier readings are negative. There are standard commercially available series of compounds that are used in patch testing.

The European standard series (ESS) is the most used baseline series and covers more than 30 common skin allergens or groups of allergens, including group mixes of rubber accelerators. There are specific series available commercially for more targeted testing based on the patient's exposure. The rubber additives series made by Chemotechnique Diagnostics is an example. This series includes 27 different allergens, including accelerators, stabilisers, antioxidants, and preservatives (biocides). It is recommended that the individual rubber additives be tested if glove allergy is suspected, in addition to the baseline series, to avoid false negative reactions. In addition, patch testing using the patients' own protective gloves may be required – pieces of the protective glove are moistened with water, applied under a tape, and left on for a week.[2]

We report a case of allergic hand dermatitis due to accelerators in nitrile gloves. The purpose of this report is to bring to the attention of practitioners four important practice points:

1. ACD may occur due to exposure to chemicals in nitrile gloves;
2. Skin patch testing is used to identify one or more of the causative allergens;
3. There is a need to use more targeted allergens in addition to the ESS if the patch test results with the latter are unhelpful; and
4. Potential interventions to manage glove-induced allergy include use of accelerator-free or low allergenic accelerator gloves.

The patient gave written consent for the use of her clinical information and pictures shown in this report. Ethical approval was obtained from the Human Research Ethics Committee (Medical), University of the Witwatersrand (clearance certificate no. M2211128).

CASE DESCRIPTION

The patient was a 38-year-old female laboratory analyst evaluated at the National Institute for Occupational Health (NIOH) Dermatology Clinic in Johannesburg in 2022. She had a strong family history of atopic disease. Occupational laboratory exposures reported by the patient were mainly fine dust from platinum group metal (PGM) ore, acetone, borax, hydrogen peroxide, and several acids. She changed her nitrile gloves three to four times a shift and was careful to avoid contaminating her hands with dust or chemicals during glove changes.

Her main complaint was hand dermatitis that started in 2014. At that time, she was working as an analyst in laboratories and wore latex gloves. There was no record of a positive test of latex sensitisation and the diagnosis is thus uncertain. She was relocated to mostly administrative work, partly due to suspected latex allergy. During her absence from the laboratories, she did not wear gloves or work with laboratory materials. Her dermatitis cleared and she stopped treatment. In 2021 she returned to laboratory work and wore nitrile gloves and worked with PGM ore dust. Her hand dermatitis recurred in September 2021 (Figure 2) and treatment, including oral prednisone, was reinitiated.

RESULTS

Skin prick tests and latex IgE

Skin prick tests (SPTs) were done at the NIOH with 10 common aeroallergens. The patient had positive reactions (≥ 3 mm larger than the negative control) to house dust mite, cockroach group mix, Bermuda grass, and London plane tree – findings consistent with atopy. She had negative SPTs to nickel chloride and sodium hexachloroplatinate. Latex-specific IgE was negative at 0.00 kU/L. Latex sensitisation was not pursued as the patient did not wear latex gloves or report symptoms associated with latex.

Skin patch tests

Skin patch test chambers were prepared by the NIOH Immunology and Microbiology Section from commercial patch tests series allergens (Chemotechnique MB Diagnostics, Sweden). Skin patch tests were negative for 13 allergens in the metal series, including salts of five PGMs, viz. iridium, palladium, platinum, rhodium, and ruthenium. The patient had positive allergic reactions to cobalt chloride, formaldehyde, nickel sulphate, and quaternium 15 in the ESS, but negative reactions to the rubber chemicals, including thiuram mix (Figure 3).

Because the patient reported a strong association between glove wearing and her dermatitis, a decision was made also to test her reactions to the specific rubber additives series. She had 1+ positive allergic reactions to tetramethylthiuram disulphide, tetramethylthiuram monosulphide, and tetraethylthiuram disulphide, and 2+ positive allergic reactions to methenamine (hexamethylenetetramine) (Figure 4).

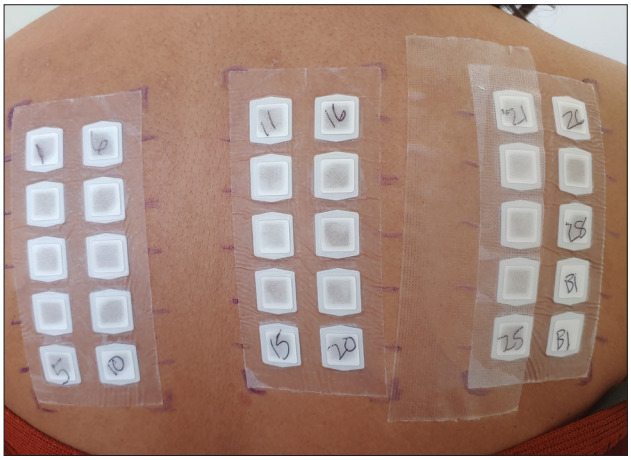

Figure 1. Skin patch tests on the patient's back
Photograph: Anna Fourie

Figure 2. Hand dermatitis during use of nitrile gloves
Photograph: courtesy of patient

NATIONAL INSTITUTE FOR OCCUPATIONAL HEALTH
Division of the National Health Laboratory Service

Patients Name: FM Lab No: IM00100 Date: 15/7/22.

Test done by: ISM Signature: _____

No	European Standard Series	Conc (%)	Results 1 Date: 18/7/22	Results 2 Date: 19/07/22
1	Potassium dichromate	0.5	—	—
2	Neomycin sulphate	20.0	—	—
3	Thiuram mix	1.0	—	—
4	p-Paraphenylene diamine (PPD)	1.0	—	—
5	Cobalt (II) chloride hexahydrate	1.0	1+	1+
6	Caine mix III	10.0	—	—
7	Formaldehyde (aq)	2.0	2+	3+
8	Colophonium	20.0	—	—
9	Propolis	10.0	—	—
10	Balsam of Peru (Myroxylon Pereirae resin)	25.0	—	—
11	N-Isopropyl-N-phenyl-4-phenylenediamine (IPPD)	0.1	—	—
12	Lanolin alcohol (Wool alcohol)	30.0	—	—
13	Mercapto mix	2.0	—	—
14	Epoxy resin – Bisphenol A	1.0	—	—
15	Paraben mix	16.0	—	—
16	4-tert-butyl phenolformaldehyde resin (PTBP)	1.0	—	—
17	Fragrance mix	8.0	—	—
18	Quaternium 15 (Dowicil 200)	1.0	1+	2+
19	Nickel (II) sulphate, $6H_20$	5.0	1+	1+
20	Methylisothiazolinone + methylchloroisothiazolinone	0.02 Aq	—	—
21	Mercaptobenzothiazole (MBT)	2.0	—	—
22	Sesquiterpene lactone mix	0.1	—	—
23	Budesonide	0.01	—	—
24	Tixocortol-21-pivalate	0.1	—	—
25	Methyldibromo glutaronitrile	0.5	—	—
26	Fragrance mix II	14.0	—	—

No	European Standard Series	Conc (%)	Results 1 Date: 18/7/22	Results 2 Date: 19/07/22
27	Lyral (Hydroxyisohexyl 3-cyclohexene carboxaldehyde)	5.0	—	—
28	Methylisothiazolinone	0.2Aq	—	—
29	Textile Dye mix	6.6	—	—
30	2-Hydroxyethyl methacrylate	2.0	—	—
31	Petrolatum	100	NT	NT

Read by: ISM ISM

NT – NOT TESTED

Figure 3. Patient responses to the European standard series skin patch tests 2022

NATIONAL INSTITUTE FOR OCCUPATIONAL HEALTH
Division of the National Health Laboratory Service

Patients Name: FM Lab No IM00100 Date: 6/9/22

Test done by: ISM Signature: _____

No	Rubber Series	Conc (%)	Results 1 Date: 9/9/22 AM	Results 2 Date: 9/9/22 PM
1	Tetramethylthiuram disulfide (TMTD)	1.0 pet	1+	1+
2	Tetramethylthiuram monosulfide (TMTM)	1.0 pet	1+	1+
3	Tetraethylthiuram disulfide (TETD)	1.0 pet	1+	1+
4	Dipentamethylenethiuram disulfide	1.0 pet	—	—
5	N-Cyclohexyl-N-phenyl-4-phenylenediamine	1.0 pet	—	—
6	N,N-Diphenylpphenylenediamine (DPPD)	1.0 pet	—	—
7	N-Isopropyl-N-phenyl-4-phenylenediamine (IPPD)	0.1 pet	—	—
8	2-Mercaptobenzothiazole (MBT)	2.0 pet	—	—
9	N-Cyclohexyl-2-benzothiazolesulfenamide	1.0 pet	—	—
10	Dibenzothiazyl disulfide (MBTS)	1.0 pet	—	—
11	2-(4-Morpholinylmercapto)benzothiazol (MOR)	1.0 pet	—	—
12	1,3-Diphenylguanidine	1.0 pet	—	—
13	Zinc diethyldithiocarbamate (ZDC)	1.0 pet	—	—
14	Zinc Dibutyldithiocarbamate (ZBC)	1.0 pet	—	—
15	N,N-Di-2-naphtyl-4-phenylenediamine (DBNPD)	1.0 pet	—	—
16	N- Phenyl-2-naphtylamine (PBN)	1.0 pet	—	—
17	Methenamine (Hexamethylenetetramine)	2.0 pet	2+	2+
18	4,4-Diaminodiphenylmethane (MDA)	0.5 pet	—	
19	N,N-Diphenylthiourea (DPTU)	1.0 pet	—	—
20	Zinc dimethyldithiocarbamate (Ziram)	1.0 pet	—	—
21	2,2,4-Trimethyl-1,2-dihydroquinoline	1.0pet	—	—
22	N,N-Diethylthiourea	1.0 pet	—	—
23	N,N-Dibutylthiourea	1.0 pet	—	—
24	Dodecyl mercaptan	0.1 pet	—	—
25	N-(Cyclohexylthio) phthalimide	1.0 pet	—	—
26	Thiourea	0.1 pet	—	—
27	4,4 Dithiodimorpholine	1.0 pet	—	—
28	Petrolatum	100	—	—

Read by: ISM ISM.

Figure 4. Patient responses to the rubber additives series skin patch tests 2022

All these compounds are accelerators used in the manufacture of rubber gloves and have been reported to cause dermatitis in sensitised people.[2]

Clinical course and management

During investigation, the patient continued doing laboratory work, had flare-ups of dermatitis, and required ongoing treatment. The negative tests of sensitisation to PGM salts (both skin prick and skin patch tests), together with the temporal association of dermatitis with glove use and positive patch tests to constituents of rubber gloves, led to a diagnosis of nitrile glove dermatitis.

Soon after diagnosis the patient stopped working for about two months, during which time her rash improved substantially (Figure 5). She returned to work but to tasks that did not require glove use. As of mid-2023, she was clear of dermatitis.

DISCUSSION

We diagnosed a case of nitrile glove-related ACD in a laboratory analyst based on a history of glove-related hand rash, clinical features of dermatitis, positive allergic skin patch tests to rubber accelerators with negative tests to alternative occupational exposures, including PGM, and improvement of rash on cessation of glove use.

The patient had a family history of atopy and skin prick tests were positive for aeroallergens. Atopy is known to be a strong predisposing factor for the development of ACD.[8]

Glove-related ACD is well documented,[2,3,9,10] and South Africa is no exception to its occurrence.[11] The most common cause in synthetic rubber glove users – including those who use nitrile gloves[2] – is exposure to accelerators; thiurams have been the most common culprits, followed by dithiocarbamates.[9] This pattern has changed in some regions, however, as thiuram use has been reduced or substituted by certain glove manufacturers. The most common sensitiser in healthcare workers using synthetic rubber gloves in Brussels in 2010–2017 was 1,3-diphenylguanidine.[10]

Notably, the patient had positive skin patch test reactions to three of four thiuram allergens in the rubber additives series, but was negative to the thiuram mix in the ESS, which combined into one patch test: tetramethylthiuram disulfide, tetramethylthiuram monosulfide, tetraethylthiuram disulfide, and dipentamethylenethiuram disulfide. Sensitisation to thiurams would have been missed had only the ESS been used. Under-detection of thiuram sensitisation (false negatives) by the thiuram mix, compared to individual thiurams, has been reported; 17% false-negative reactions were reported in one case series.[12] In a French multi-centre study, almost 45% of the sensitisations to glove allergens were detected only by a rubber series.[13] Testing with a dedicated rubber series, using individual thiurams – preferably at 1% in petroleum jelly – is recommended in patients with suspected contact allergies to rubber, to avoid false-negative results.[12,13,14,15]

A possible explanation for the contradictory patch test results is the low concentration of thiurams in the mix – 0.25% for each of the four (Figure 3) versus 1% for each of the individual thiuram allergens in the rubber additives series (Figure 4).

Considerations

Distinguishing between allergic and irritant skin patch test reactions can be difficult. In the case reported here, an experienced scientist interpreted the patch test reactions and identified typical allergic reactions (Figure 6).

The patient had positive allergic skin patch test reactions to formaldehyde in the ESS and quaternium 15, and to the metal salts, cobalt chloride, and nickel sulphate. Formaldehyde and the formaldehyde releasing quaternium 15 are commonly used preservatives in many household products and cosmetics. They are regarded as problematic patch test substances with poor reproducibility, and a cause of irritant reactions.[16] The patient was not exposed to these substances at work and recovered when away from work and not wearing gloves. The PGM ore dust might have contained nickel as the metal has been found in platinum refinery dust,[17] and South African PGM ores may also contain cobalt.[18] Nickel and cobalt are commonly found in electroplated items such as jewelry, zips, coins, and metal buttons and their contribution to her ACD cannot be excluded. However, her sensitisation to thiurams, hand dermatitis, and frequent use of nitrile gloves strongly support the diagnosis of glove dermatitis.

Potential interventions

Besides job relocation or re-allocation of tasks that require gloves, substitution of nitrile gloves with those that do not contain rubber components and are accelerator-free or have low allergenic accelerators may be successful. There are several options.[2,19] The choice is partly informed by work requirements (e.g. tactility), and the need for protection against chemicals or microbes.[2] Numerous guides exist to inform protective glove selection, including that of the US Occupational Safety and Health Administration.[20] Kersch et al. (2018) provide some recommendations for glove selection.[3] Increased cost and limited availability may, however, be hindrances to the use of gloves that are accelerator-free or contain low allergenic accelerators. Non-nitrile synthetic rubber gloves, e.g. polyisoprene and polychloroprene (neoprene), may contain high concentrations of accelerators, and cause hand dermatitis.[10] Replacing nitrile gloves with other synthetic rubber gloves may, therefore, be unhelpful if those gloves contain allergenic accelerators. Gloves without accelerators have been shown to reduce or eliminate allergic reactions.[10] A possible solution, if suitable accelerator-free protective gloves are not obtainable, is to use polyethylene gloves as liners underneath the accelerator-containing protective gloves.[2]

CONCLUSION

Testing with a dedicated rubber series with individual additives at a suitable concentration (typically 1% petroleum jelly), is recommended for patients with suspected contact allergies to rubber to avoid false-negative results.[12,14]

Figure 5. Improved hand dermatitis while away from work
Photograph: courtesy of patient

Figure 6. Positive skin patch test reactions to ESS 2022
Photograph: Anna Fourie

KEY MESSAGES

1. ACD occurs due to exposure to chemicals in nitrile gloves.
2. Skin patch testing is necessary for the identification of the causative allergen.
3. Targeted allergens are needed in addition to the ESS in patients with features consistent with ACD but with unhelpful ESS test results.
4. There are interventions that can potentially manage nitrile glove-related ACD.

DECLARATION

The authors declare that this is their own work; all the sources used in this paper have been duly acknowledged and there are no conflicts of interest. The investigation of the patient was conducted at the National Institute for Occupational Health without commercial gain.

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AUTHOR CONTRIBUTIONS

Data acquisition: AF, HAC, NN
Interpretation of the data: DR, AF, HAC, NN
Drafting of the paper: DR
Critical revision of the paper: DR, AF, HAC, NN

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