OBSERVATION

Allergic Contact Dermatitis to Synthetic Rubber Gloves

Changing Trends in Patch Test Reactions to Accelerators

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Background: Rubber gloves are one of the most frequent causes of occupational allergic contact dermatitis, especially in health care workers.

Observations: We describe 23 patients with allergic contact dermatitis due to rubber accelerators in rubber gloves, some with disseminated dermatitis, treated during a 2-year period. Three had IgE-mediated latex allergies. Sixteen were health care workers from a single institution whose dermatitis was temporally related to the switch to latex-safe gloves. Each had positive patch test reactions to 1 or more rubber accelerators, including carbamates, thiurams, 2-mercaptobenzothiazole, and 1,3-diphenylguanidine. Chemical analysis of 6 glove samples identified 2-mercaptobenzothiazole in 4 and zinc diethyldithiocarbamate in 1. There were discordances between patch test results for glove chemicals and glove swatches and between available information on chemicals used during glove production and chemicals detected during glove analysis. Although these factors may complicate the search for culprit and alternative gloves, dermatitis cleared in each of 9 patients with follow-up data and for whom alternative gloves were provided based on published information of glove composition.

Conclusions: Allergic contact dermatitis due to synthetic rubber gloves occurs even with the use of latex-safe products. More knowledge about chemicals present in these gloves, to which the skin is exposed during use, is necessary to prevent and treat allergic contact dermatitis.

Arch Dermatol. 2010;146(9):1001-1007

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More than 4000 environmental chemicals have been identified as contact allergens.[1] Of these, rubber glove chemicals are among the most frequent causes of allergic contact dermatitis (ACD) in health care workers, usually as a result of frequent glove use.[2,3] The number of rubber gloves used in US health care has increased dramatically during the past 30 years. Contact allergy to rubber gloves is primarily caused by accelerators added to speed up rubber vulcanization, including carbamates, thiurams, 2-mercaptobenzothiazole (MBT), and 1,3-diphenylguanidine (DPG). It may also be caused by antioxidants that prevent rubber deterioration, such as black rubber mix chemicals (*p*-phenylenediamines). Contact allergy should be suspected in any patient who wears rubber gloves and presents with a diffuse or patchy dermatitis on the dorsal surface of the hands (skin over the metacarpal phalangeal joints, thenar, and hypothenar), wrists, and distal forearms.[4] However, many patients present with nonspecific patterns of hand dermatitis for which the diagnosis cannot be made without patch testing.[4]

In 1996, our group described 44 patients with natural rubber latex (NRL) allergy, mostly caused by gloves, of whom 36 had dermatitis on the hand and 26 had relevant positive patch test reactions.[5] In US hospitals, there has been a shift from the use of NRL powdered examination and surgical gloves to the use of NRL powder-free and synthetic gloves (**Table 1**). At the same time, the number of cases of NRL type 1 IgE-mediated allergy has declined dramatically.[6] With the recent mandatory policy shift to synthetic gloves at one institution, largely from a single supplier, we saw an apparent increase in the number of employees reporting putative skin reactions to gloves. There appears to be a shifting trend of type 4 contact allergy to rubber glove accelerators consisting of thiurams only to a combination of carbamates, thiurams, and DPG, indicating that carbamate and DPG levels in specific brands and types of commonly used gloves are high. In this retrospective medical record review and glove analysis approved by the Cleveland Clinic institu-

Table 1. Actual US Hospital Market Percentages for Examination and Surgical Gloves From 1994 to 2008[a]

	1994	1998	2006	2007	2008
Examination gloves, % of market					
NRL powdered	67	30	5	3	3
NRL powder free	26	48	77	74	68
Synthetic	7	22	18	23	29
Surgical gloves, % of market					
NRL powdered	NA	NA	42	38	34
NRL powder free	NA	NA	44	45	45
Synthetic	NA	NA	14	17	21

Abbreviations: NA, not available; NRL, natural rubber latex.
[a] Data were obtained from Robert Milton Hinsch, MS, Technical Services Director, Mölnlycke Health Care, Norcross, Georgia (written communication; June 8, 2009).

tional review board, we report 23 cases of ACD to accelerators in synthetic rubber gloves from May 1, 2007, to May 31, 2009. Our results provide information to individuals, especially health care workers, regarding which types of gloves are more likely to cause ACD and may encourage the avoidance of these gloves and the use of less sensitizing alternatives.

METHODS

PATIENTS

From May 1, 2007, to May 31, 2009, a total of 626 patients with suspected ACD underwent patch testing in the Department of Dermatology at the Cleveland Clinic, of whom 37 were identified by our patch test database to have positive patch test reactions to 1 or more rubber chemicals. Twenty-three of the 37 were found to present with primary hand/wrist dermatitis due to currently relevant contact allergy to 1 or more chemicals in the rubber gloves they were wearing. Data recorded on these 23 individuals included patient demographics; a personal medical history of atopy; NRL type 1 allergy; the locations, timing, and duration of the presenting dermatitis; whether the patient suspected gloves as the cause of dermatitis; whether dermatitis was occupationally or domestically related, or both; positive patch test results at the final reading to standard tray allergens and other rubber allergens when indicated; patch test results to glove and other materials; and final diagnoses, treatments, and follow-up results if available.

PATCH TESTS

All patients underwent patch testing with the standard screening tray of the North American Contact Dermatitis Group,[7] which was purchased from Chemotechnique Laboratories, Malmö, Sweden, and SmartPractice Canada, Calgary, Alberta Canada (AllergEAZE). Patch tests were applied to a disease-free site on the upper back with the use of aluminum disks (Finn Chambers; Epitest Ltd, Hyryla, Finland) on acrylic-based, pressure-sensitive adhesive medical tape (Scanpor; Norgesplaster AIS, Aksjeselskap, Norway). Patch tests were removed after 48 hours of occlusion, and results were read twice in most cases, usually on day 2 or 3 and again on day 6 or 7. Other suspected allergens, such as DPG (5 patients), zinc diethyldithiocarbamate (ZDEC) (1 patient), zinc dibutyldithiocarbamate (ZDBC) (1 patient), and postage stamp–sized glove pieces (15 patients) were tested in some patients. Glove pieces were moistened and occluded for 48 hours and, in some cases, moistened and occluded for an additional 48 hours if results were negative. In most cases, only the insides of the gloves were tested. Reading and interpretation of the patch test results were performed according to previously published methods of the North American Contact Dermatitis Group.[8]

TYPE 1 NRL ALLERGY TESTS

Patients suspected of having a type 1 NRL allergy underwent testing with a latex radioallergosorbent test or a prick test. A commercial in vitro NRL radioallergosorbent test with allergen disks (Pharmacia CAP system; Pharmacia Diagnostics AB, Uppsala, Sweden) was used on 10 patients. Results in classes 0 and 1-0 were negative, whereas results in classes 1 through 6 were positive. Prick testing was performed on 2 patients with extracts of *Hevea brasiliensis* in the Department of Allergy at the Cleveland Clinic.

GLOVE ANALYSIS

The 6 gloves we analyzed to detect rubber chemical levels were collected from 2 patients, consisted of 4 brands (2 of which were obtained from 2 different lots each), and were representative of gloves worn by most of our patients. A 55-mm rectangular area of each glove was cut using a standard form and weighed to obtain the mass for calculation of density. The chemical accelerator/allergen content of each glove was determined by a modification of the method of Depree et al.[9] In short, material from each glove was cut into small pieces and extracted for 2 hours at room temperature in acetonitrile (ACN) (1 g/10 mL). Extracts were centrifuged at 1000*g* for 10 minutes at room temperature to remove residual material or powder. Extracts were screened in the presence of cobalt for carbamates, thiurams, and MBT at UV λ 320 and 370 nm.[10]

Chemical speciation and quantifications were performed using high-performance liquid chromatography (HPLC) coupled to a photodiode array detector (Shimadzu Instruments Inc, Columbia, Maryland). Chemical separation was performed using a 250×4.6-mm column (Discovery C18 column; Superlco, Bellefonte, Pennsylvania). Three different gradient elution methods were used. Solvent flow at a rate of 1 mL/min was used for all HPLC elutions. Zinc dithiocarbamates were eluted from the HPLC column using a linear gradient starting with 85% ACN/15% water that changed to 100% ACN during a span of 3 minutes and maintained at 100% ACN for 12 minutes. Before injection of samples or standards and intermittently thereafter, injections of zinc dimethyldithiocarbamate were made to bind nickel from the HPLC stainless steel components. We assayed MBT and MBT disulfide using a step gradient starting with 100% water that changed to 50% ACN/50% water during a span of 5 minutes, to 80% ACN/20% water during the next 5 minutes, and to 100% ACN during the next 9 minutes and held at 100% ACN for 2 minutes. All other species were determined using a linear gradient from 100% wa-

ter to 100% ACN for 60 minutes. The gloves were analyzed for the following chemicals using this method: MBT, MBT disulfide, tetramethylthiuram disulfide, tetraethylthiuram disulfide, zinc dimethyldithiocarbamate, ZDEC, ZDBC, zinc pentamethylenedithiocarbamate, 1,3-diethylguanidine, DPG, 1,3-diethyl-2-thiourea, 1,3-dibutyl-2-thiourea, *N*-isopropyl-*N*-phenyl-*p*-phenylenediamine, phenylenediamine, diethylamine, and 4,4′-dithiodimorpholine. In addition, direct probe and gas chromatographic mass spectrometry were used on ACN and dichloromethane extracts to confirm the chemical species present and to screen for other potential chemical species for which standards were not available.

RESULTS

Demographic data, the presence of atopy and type 1 NRL allergy, dermatitis characteristics, and occupational relevance data for the 23 patients presenting with primary hand/wrist dermatitis due to currently relevant contact allergy to 1 or more rubber glove chemicals are presented in **Table 2**. Three patients had IgE-mediated latex allergies. Summaries of major results are listed in **Table 3** (patch test reactions to rubber glove chemicals and chemical mixes) and **Table 4** (chemical analysis results of 6 representative gloves).

Table 2. Demographic and Dermatitis Information for 23 Patients With ACD Due to Glove Chemicals

Characteristic	Data[a]
Age, mean (SD) [range], y	47.5 (12.7) [24-72]
Sex	
Male	9 (39)
Female	14 (61)
Race	
White	20 (87)
African American	1 (4)
Other	2 (9)
Occupation	
Health care worker	16 (70)
Nurse	6 (26)
Physician	4 (17)
Surgical scrub technician	3 (13)
Dentist	1 (4)
Phlebotomist	1 (4)
Histology laboratory technician	1 (4)
Machinist	2 (9)
Bus driver	1 (4)
Cement worker	1 (4)
Chemical mixer	1 (4)
Homemaker	1 (4)
Teacher	1 (4)
Personal history of atopy[b]	14 (61)
Eczema	8 (35)
Asthma	4 (17)
Allergic rhinitis	10 (43)
NRL type 1 allergy	5 (22)
Symptoms (eg, contact urticaria, rash, wheezing)	5 (22)
Testing	
RAST	10 (43)
RAST positive result	2 (9)
Skin prick	2 (9)
Skin prick positive result	1 (4)
Duration of dermatitis, mean (range), mo	10.9 (0.75-36)
Sites of presenting dermatitis	
Hands/wrists	23 (100)
Arms	17 (74)
Face/neck	9 (39)
Feet	4 (17)
Trunk and legs	11 (48)
Occupational relevance of glove-induced dermatitis	
Occupational glove-induced dermatitis only	17 (74)
Domestic glove-induced dermatitis only	1 (4)
Occupational and domestic glove-induced dermatitis	5 (22)

Abbreviations: ACD, allergic contact dermatitis; NRL, natural rubber latex; RAST, radioallergosorbent test.
[a] Unless otherwise indicated, data are expressed as number (percentage) of 23 patients. Percentages have been rounded and may not total 100.
[b] Some patients had more than 1 type of atopy.

COMMENT

UNDERREPORTING OF CASES

Despite the recent shift from use of NRL to synthetic gloves, there are still associated skin problems, especially ACD due to rubber glove accelerators. Our impression is that the actual number of cases of ACD due to glove chemicals is underreported because patients (1) are switching to alternative gloves on a trial-and-error basis, (2) are reluctant to declare occupational relationships, and (3) may be unable to keep patch test appointments because of time or financial constraints.

OCCUPATIONAL PREDOMINANCE

Studies have shown that ACD due to rubber glove chemicals is primarily occupational, with health care workers being particularly affected.[3,5,12-20] This is consistent with our current results as presented in Table 2, in which 17 cases of rubber glove chemical-induced dermatitis (74%) were solely occupationally related and 5 (22%) were due to work and household gloves. Of these, 16 cases (70%) were in health care workers. In contrast, only 1 case (4%) was considered to be caused solely by household gloves. Proksch et al[21] also reported that ACD due to household gloves was rare compared with occupational (especially health care) gloves. They attributed this finding to (1) the inner cotton linings present in most household gloves; (2) new production techniques such as leaching to reduce allergen content, especially from the inner household glove surface; (3) intermittent use of the same pair of household gloves for short durations; (4) the loose fit of household gloves; and (5) conditions associated with household glove use that induce less skin irritation.[21]

PATCH TESTING WITH GLOVE CHEMICALS

Worldwide, thiurams followed by carbamates have been deemed the most common rubber contact allergens.* Most positive patch test reactions to carbamates have been found in patients with positive reactions to thiurams as well,[3,22,27,28] which may be due to coreaction (ie, concomitant sensitization to both accelerators in gloves)[3,27] or to cross-

*References 3, 7, 12, 13, 15-17, 19, 22-26.

Table 3. Positive Patch Test Reactions[a] to Rubber Chemicals and Chemical Mixes

Rubber Chemicals or Chemical Mixes by Reaction	No. (%) of Patients With Specified Positive Patch Test Reaction[b]
CM	**20** (87)
1+	9
2+	6
3+	5
ZDEC (of 1 patient tested)	0/1
ZDBC (of 1 patient tested)	0/1
TM	**14** (61)
1+	5
2+	8
3+	1
2-MM	0
MBT	**2** (9)
1+	2
MDTU	**1** (4)[c]
1+	1
Black rubber mix (PPD mix)	0
DPG (of 5 patients tested)	**5**/5 (100)
1+	1
2+	4
Combination of rubber chemicals or chemical mixes	
CM+ and TM–	9 (39)
CM– and TM+	3 (13)
CM+ and TM+	11 (48)
CM+ and DPG– (of 5 patients tested with DPG)	0/5
CM– and DPG+ (of 5 patients tested with DPG)	0/5
CM+ and DPG+ (of 5 patients tested with DPG)	5/5 (100)[d]

Abbreviations: CM, carba mix; DPG, 1,3-diphenylguanidine; MBT, 2-mercaptobenzothiazole; MDTU, mixed dialkyl thioureas; MM, 2-mercapto mix; PPD mix, *p*-phenylenediamine mix; TM, thiuram mix; ZDBC, zinc dibutyldithiocarbamate; ZDEC, zinc diethyldithiocarbamate; –, negative; +, positive.

[a] Indicates final reading.

[b] Percentages are based on 23 patients with allergic contact dermatitis due to glove chemicals, unless otherwise stated.

[c] This 1+ reaction to MDTU may be a spillover from the neighboring 3+ reaction to bacitracin.

[d] Of the 5 patients who underwent patch testing with CM and DPG, 3 had 2+ reactions to CM and DPG, of whom 1 underwent testing with and had negative reactions to the CM ingredients ZDEC and ZDBC. In addition, 1 patient had a 1+ reaction to CM and a 2+ reaction to DPG, and 1 patient had a 2+ reaction to CM and a 1+ reaction to DPG.

reaction of structurally similar chemicals.[27,29,30] However, since the mid-1990s, the sensitization frequency of thiurams appears to be generally on the decline,[7,14,31,32] whereas relevant patch test reactions to carba mix, which includes ZDEC, ZDBC, and DPG, appears to be on the rise, especially in health care workers.[13,33] This changing trend may be partly caused by the changes of chemicals used during glove manufacturing. According to Geier et al,[32] surveillance of ingredient lists of medical and chemical protective gloves has revealed that most international rubber glove manufacturers have replaced thiurams with dithiocarbamates, MBT, or both and their derivatives in recent years. A glove analysis study published in 2000 supports this trend, demonstrating that ZDEC, ZDBC, MBT, and zinc pentamethylenedithiocarbamate were the most frequently detected chemicals in gloves, whereas thiurams were detected in only a minor fraction of the analyzed gloves.[34] Chemical analyses of commercially available rubber gloves published in 2005 and 2006 further support this trend. The authors did not detect thiurams in any of the sampled glove brands, but did detect ZDEC, ZDBC, MBT, and/or zinc pentamethylenedithiocarbamate alone or in various combinations.[9,35]

Our study confirms previous findings of a changing trend in patch test results from primarily reactivity to thiurams to reactivity to carbamates, thiurams, and DPG. As shown in Table 3, 20 patients (87%) had positive reactions to carba mix, whereas only 14 (61%) had positive reactions to thiuram mix. In contrast to earlier studies that showed that patients with positive reactions to carba mix usually also reacted to thiuram mix (whereas the converse was not true[3]), 11 of our patients (48%) had positive reactions to both carba mix and thiuram mix, 9 (39%) had positive reactions to carba mix but negative reactions to thiuram mix, and only 3 (13%) had positive reactions to thiuram mix and negative reactions to carba mix.

Because carba mix contains ZDEC, ZDBC, and DPG,[36] positive patch test reactions may be based on DPG alone, as noted by Cronin.[29] In fact, all 5 patients who underwent patch testing with DPG showed positive reactions to DPG and carba mix (Table 3). Of these 5 patients, only 1 underwent testing with ZDEC and ZDBC, with negative reactions to both. Also, the use of carba mix for patch testing may miss approximately 10% of DPG sensitizations (Don Belsito, MD, University of Missouri–Kansas City Department of Medicine [Division of Dermatology]; written communication; July 17, 2008). In addition, DPG is suspected of being a mild skin irritant,[32] which may partly account for the higher rate of irritant reactions to carba mix when compared with other rubber allergens.[36(pp581-604)] Ideally, carbamates and DPG should be tested separately rather than as a mixture. Our findings suggest that carbamate and possibly DPG levels in certain glove types may be high, which leads to sensitization and elicitation of ACD in many individuals who wear them.

Although MBT use during glove manufacturing has reportedly increased in recent years,[32] only 2 of our 23 cases (9%) exhibited positive reactions to MBT on patch testing (Table 3). This is consistent with other reports, which have noted that contact allergy and sensitization to MBT and its derivatives continue to be rare and appear to be declining.[32,37] Also, our cases were limited to those with primary hand/wrist dermatitis induced by rubber glove chemicals, whereas MBT and its derivatives may have elicited more positive reactions in ACD induced by other products such as shoes.[37]

Allergic contact dermatitis to thioureas has occasionally been noted from exposure to rubber, especially neoprene. Gloves have been reported as the most common occupational source and third most common overall source of relevant positive patch test reactions after shoes and medical devices.[38] However, in our study, despite patients' use of neoprene gloves and gloves in which diphenylthiourea was used during manufacturing, only 1 (4%) positive patch test reaction to thioureas was noted (Table 3). One reason for this apparent lack of thiourea reactions may result from the inability of mixed dialkyl thioureas (MDTU), which contain only diethylthiourea and dibu-

Table 4. Chemical Compositions According to Our Analysis of 6 Representative Gloves

Glove Chemicals[b]	Glove[a]					
	SMT (Synthetic PI) Surgical		Blue With Neu-Thera (Synthetic PI) Surgical			
	Lot 1	Lot 2	Lot 1	Lot 2	Microsurgical	Stretchy Nitrile Examination
ZDEC	ND[c]	ND[c]	ND[c]	ND[c]	ND[c]	903 μg/g[c]
ZDBC	ND[c]	ND[c]	ND[c]	ND[c]	ND[c]	ND[c]
MBT	11.2 μg/g[c,d]	314.9 μg/g[c]	198.7 μg/g[c]	ND[c]	381.6 μg/g[c]	ND
MBTS	ND	ND	ND	ND	ND	ND
TETD	ND	ND	ND	ND	ND	ND
TMTD	ND	ND	ND	ND	ND	ND
DPG	ND	ND	ND	ND	ND	ND

Abbreviations: DPG, 1,3-diphenylguanidine; MBT, 2-mercaptobenzothiazole; MBTS, mercaptobenzothiazole disulfide; ND, none detected; PI, polyisoprene; SMT, surface modification technology; TETD, tetraethylthiuram disulfide; TMTD, tetramethylthiuram disulfide; ZDBC, zinc dibutyldithiocarbamate; ZDEC, zinc diethyldithiocarbamate.

[a] All gloves are Esteem brand from Cardinal Health, Dublin, Ohio.

[b] Other glove chemicals analyzed but not detected in any of the 6 gloves and not giving any positive reactions on patch testing included zinc dimethyldithiocarbamate, zinc dipentamethylenedithiocarbamate, 1,3-diethylguanidine, 1,3-diethyl-2-thiourea, 1,3-dibutyl-2-thiourea, 4,4′-dithiomorpholine, phenylenediamine, *N*-isopropyl-*N*-phenyl-*p*-phenylenediamine, and diethylamine.

[c] This rubber glove chemical was added during glove manufacturing according to available published information.[11]

[d] This low detected MBT level in our glove analysis may be due to MBT being added as a preservative into the bucket when the rubber tree is tapped rather than during glove manufacturing.

tylthiourea, to detect sensitizations to other thioureas including diphenylthiourea and ethylenethiourea. As reviewed by McClesky and Swerlick,[39] up to 25% of thiourea-induced ACD cases may be missed by screening with MDTU alone. However, Warshaw et al[38] concluded that the relatively low prevalence (24.9%) of cosensitizations to thioureas and other rubber allergens reflects the need to continue using MDTU—and possibly other thioureas—in detecting thiourea-induced rubber ACD.

Our study confirms that ACD to black rubber mix is uncommon in health care workers (Table 3). However, sensitization is more common with the use of black-colored industrial rubber products, including heavy black rubber gloves, boots, tires, and pipes.[3,11]

PATCH TESTING WITH GLOVE PIECES

The importance of testing glove pieces is illustrated by the case reported by Rich et al,[40] which demonstrated 2 newer sensitizing chemicals—the antioxidants Lowinox 44S36 and butylhydroxyanisole—in a latex glove. Both were identified by obtaining and testing chemical glove constituents after initial positive patch test reactions to pieces of the glove.

Our case series shows inconsistent results between patch test results to glove chemicals and those to pieces of gloves. There were 12 instances in which the patient had a negative reaction to the glove piece tested but a positive reaction to 1 or more accelerators used during glove manufacture according to available information.[11] For example, 1 patient had a negative reaction to a synthetic polyisoprene surgical glove to which carbamates and DPG were added during glove production[11] but had positive reactions to carba mix. Similar discrepancies in patch test reactions to glove chemicals and gloves have been reported by others.[2,28] Our recommendation is that patients should not wear gloves to which they had negative patch test results if they had positive results to a chemical listed as present in the glove.[11]

GLOVE CHEMICAL ANALYSIS

Likewise, there were discordances among chemicals detected in our glove analysis (Table 4), chemicals used during glove production (Table 4),[11] and patch test reactions to chemicals (Table 3) and glove pieces. Chemical analysis of 6 representative gloves detected ZDEC in 1, MBT in 4, and DPG in none. On patch testing, 20 patients (87%) reacted to carba mix whereas only 2 (9%) reacted to MBT; 5 of 5 patients (100%) undergoing testing with DPG had positive reactions.

Our analysis of Esteem SMT synthetic polyisoprene surgical gloves (Cardinal Health, Dublin, Ohio) revealed the presence of MBT in both lots (Table 4). Carbamates were not detected in our analysis, although available information indicated that they were added during manufacture along with MBT (Table 4).[11] Besides 1 patient with a positive reaction to MBT who demonstrated a questionable reaction to the glove piece, all other patients had positive reactions to carba mix and negative reactions to MBT while demonstrating positive reactions to the glove piece.

Similarly, although we detected only MBT in 1 lot of Esteem Blue with Neu-Thera synthetic polyisoprene surgical gloves (Cardinal Health), we did not detect any of the chemicals for which we had analyzed in the other lot of this glove (Table 4). Available information indicates that carbamates and MBT were both used during glove production (Table 4).[11] All patients who reacted to the glove piece exhibited negative reactions to MBT but positive reactions to carba mix.

Moreover, we detected MBT in Esteem Micro surgical gloves (Cardinal Health), which is consistent with available information indicating the addition of MBT during glove manufacturing (Table 4).[11] However, we did not detect carbamates, which were also added during glove production (Table 4).[11] Although 5 patients with positive reactions to the glove piece on patch testing also re-

acted to carba mix, 1 had a negative reaction to the glove piece but a positive reaction to carba mix and MBT.

With the Esteem Stretchy Nitrile examination glove (Cardinal Health), our analysis revealed the presence of ZDEC, which is consistent with available information on glove composition (Table 4).[11] However, although all 4 patients who underwent patch testing with the glove piece had positive reactions to carba mix, 3 had negative reactions and 1 exhibited a questionable reaction to the glove piece.

These discrepancies are in accordance with the results of other studies.[34,35,41] Some manufacturers list their gloves as accelerator free, stating that accelerators such as carbamates and thiurams, which are initially used during production, are undetectable in the final product. Discordances between patch test reactions to glove chemicals and glove pieces and between glove composition based on available manufacturing information[11] and chemicals detected by glove analysis may be accounted for by (1) batch-to-batch variation in the exact formulation of the gloves; (2) changes of chemical structures during vulcanization; (3) impurities or contaminants during glove manufacture; (4) preservatives added shortly after tapping rubber trees; (5) lack of regulations requiring that glove chemicals be listed as ingredients in consumer products; (6) protection of glove ingredient information as proprietary; (7) presence of additional rubber glove chemicals that may serve as contact allergens; and (8) differences between glove use patterns and glove piece patch test conditions (eg, a difference in allergic sensitivity between the skin on the back vs the hands and failure to patch test with both sides of the glove piece), which may result in false-positive or negative patch test results for gloves. Consequently, the search for culprit and alternative gloves for patients with ACD due to glove chemicals is complicated, and a high index of clinical suspicion must be used throughout the investigative process. Also, the importance of patch testing with glove pieces used by patients under similar conditions is highlighted.

CLINICAL FINDINGS

When evaluating contact allergies to glove chemicals, it is important to determine the site of the patient's initial dermatitis. Seven of our patients (30%) had autoeczematization with dissemination of their dermatitis, whereas others presented with hand/wrist dermatitis before spread to their arms (3 [13%]) or face and neck (2 [9%]). Not all patients suspected gloves as the cause of their dermatitis. Natural rubber latex allergy, concomitantly or separately, should not be overlooked.

Hand dermatitis often has multiple causes. As demonstrated by our patients, skin diseases that may coexist with or be exacerbated by ACD due to glove chemicals include ACD due to other chemicals (eg, nickel or fragrance mix), irritant contact dermatitis, contact urticaria, skin infections, atopic dermatitis, dyshidrotic eczema, asteatotic eczema, nummular dermatitis, psoriasis, lichenoid eruptions, and Sweet syndrome. Also, in examination of patients with glove allergy, it is important to look for other causes directly related to work, such as topical medications, scrubs and scrub agents, surgical gowns and other attire, and alcohol disinfectants.

ALTERNATIVE GLOVES

Although topical, systemic, and UV light therapies may be helpful in alleviating diagnosed chemical-induced ACD due to gloves, the only cure is to avoid using gloves or to use alternative gloves free of established allergens for the patient. In our case series, dermatitis in 9 of 9 patients (100%) improved at follow-up with changes to recommended accelerator-free alternative rubber gloves based on available glove composition information,[11] whereas 2 of 2 patients (100%) exhibited clearing of their dermatitis because of job changes that removed the need to wear rubber gloves.

Patch testing is performed to identify specific allergenic rubber accelerators or antioxidants. Our approach is to perform patch testing in patients with the standard screening patch test tray and pieces of their gloves. Alternative gloves that do not contain the patch test–positive allergens may be substituted. Lists of specific chemicals used in the manufacture of specific brands of gloves have been published[11] or the manufacturer may be contacted directly for this information. Our patients who were allergic to the synthetic nitrile examination gloves from Cardinal Health were primarily provided with vinyl gloves from Cardinal Health or from other vendors. Accelerator-free nitrile gloves (eg, N-DEX Free; Showa Best Glove, Menlo, Georgia) are another possible alternative. Polyurethane examination gloves, a previous substitute for accelerator-allergic patients, are no longer available. Individuals allergic to synthetic surgical gloves from Cardinal Health were primarily provided with neoprene gloves (Dermaprene Ultra; Ansell Healthcare Products, Dothan, Alabama), which were mostly successful in clearing patients' dermatitis. Accelerator-free block polymer surgical gloves are no longer available. Positive patch test reactions to gloves are helpful in confirming definite relevance to patients' hand dermatitis. Almost all medical gloves are currently manufactured outside the United States, where vendors frequently consolidate. Hence, alternative glove information is subject to change.

In conclusion, our data suggest a changing trend in ACD and sensitization to rubber glove accelerators consisting of thiurams only to a combination of carbamates, thiurams, and DPG, a change particularly apparent in the health care setting. As health care facilities shift from the use of NRL to synthetic gloves, more knowledge on the spectrum of rubber chemicals present in synthetic gloves, to which the skin is exposed during use, is necessary for preventing and treating rubber glove chemical-induced ACD and sensitization.

Accepted for Publication: December 23, 2009.
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Author Contributions: Ms Cao and Dr Taylor had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Cao and Taylor. *Acquisition of data:* Cao, Taylor, Sood, Murray, and Siegel. *Analysis and interpretation of data:* Cao, Taylor, and Sie-

gel. *Drafting of the manuscript:* Cao, Taylor, Murray, and Siegel. *Critical revision of the manuscript for important intellectual content*: Taylor, Sood, and Siegel. *Administrative, technical, and material support:* Taylor and Siegel. *Study supervision:* Taylor.

Financial Disclosure: Dr Taylor has served on the advisory boards of Novartis, Shire Labs, and United Health Care; served as an author for HMP Communications, Unitech Communications, and Web MD; has served as a consultant to the AMA Press, BASF, Betco, Inc, Consumer Product Safety Commission, ConvaTec, Inc, National Institute for Occupational Safety and Health, Novartis, Procter and Gamble, Regent Medical, and Shire Labs; has served as an investigator for Guidant, Mekos Lab Denmark, and Shire Labs; has served as a speaker for Aula Medica Spain, Hermal Labs Germany, Medicis, and Watson Labs; and owns or has owned stock in Amgen, Bristol Myers Squibb, GlaxoSmithKline, Johnson and Johnson, Keithley Instruments, Medco Health Solutions, Merck, Renovo, and Wyeth. He is also a director of the North American Contact Dermatitis Group, past vice president of the American Academy of Dermatology, and past president of the Academy of Medicine of Cleveland and Northern Ohio. His department has received investigator funds from Amgen, Astellas, Bristol Myers Squibb, Centocor, Genentech, Pfizer, and Procter and Gamble, for which he was not a participant.

Additional Contributions: Robert Milton Hinsch, MS, technical services director of Mölnlycke Health Care, Norcross, Georgia, provided valuable data on glove composition and use.

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