

# Occupational Dermatitis in Health Care Workers Evaluated for Suspected Allergic Contact Dermatitis

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Background: Contact dermatitides occur commonly among health care workers (HCWs).

<u>Objective</u>: To contrast the atopic status and incidence, location, and final diagnosis of skin diseases afflicting HCWs versus non-HCWs (NHCWs) evaluated for suspicion of allergic contact dermatitis (ACD); and among the population diagnosed with ACD, to compare the incidence and occupational relatedness of allergens found in HCWs with the rates observed in NHCWs.

<u>Methods</u>: Between July 1, 1994, and May 30, 2014, 2611 patients underwent patch testing by the senior author. Of these, 165 were classified as HCWs based on their primary occupation. Statistical analysis was done using a  $\chi^2$  test.

<u>Results:</u> Health care workers were more likely than NHCWs to be women and to have hand dermatitis. Women, but not men, HCWs suffered more irritant contact dermatitis. Health care workers had significantly more work-related ACD, especially to formaldehyde, quaternium-15, 2-bromo-2-nitropropane-1,3-diol, cocamide diethanolamine (DEA), thiuram mix, carba mix, thimerosal, benzalkonium chloride, glutaraldehyde, and bacitracin.

<u>Limitations</u>: Only patients suspected of having ACD were tested. Our population was geographically limited to metropolitan Kansas City, MO and metropolitan New York, NY.

<u>Conclusions</u>: Health care workers suffer more from occupational ACD, especially of the hands, than do NHCWs, including to allergens not present on available standard allergen series.

ccupational skin disease among health care workers (HCWs) has a prevalence estimated to be approximately 30%.<sup>1</sup> Health care workers are exposed to a variety of agents that are capable of leading to a disease spectrum that includes allergic contact dermatitis (ACD), irritant contact dermatitis (ICD), and allergic contact urticarial (ACU), as well as exacerbations of a variety of endogenous diseases including atopic dermatitis (AD), dyshidrotic eczema, and psoriasis. For some patients, dermatitis can be multifactorial, as endogenous disease may coexist and be exacerbated by exogenous disease. Positive patch test reactions among HCWs have been reported to have prevalence rates from 17% to 63%.<sup>2-5</sup> Despite such high rates of positive reactions, few published studies are available that correlate the patch test response with a clinical diagnosis of relevant ACD, especially relevant occupational disease. In this retrospective study, we looked at the demographics of, and dermatitides afflicting, HCWs evaluated for suspicion of ACD.

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Among HCWs found to have ACD, we identified the most common allergens and their relevance.

#### **METHODS**

Between July 1, 1994, and May 30, 2014, a total of 2611 patients, who presented with a clinical suspicion of ACD, underwent patch testing to the North American Contact Dermatitis Group standard allergen series and supplemental allergens, as clinically indicated, by the senior author in metropolitan Kansas City, MO (July 1, 1994 to March 31, 2011) and New York, NY (April 1, 2011 to May 30, 2014). Before being patch tested, all patients completed a standardized questionnaire that included demographic, occupational, and medical data. Patients were assessed for AD, asthma, and hay fever; the diagnosis of AD was determined using the criteria set forth by Hanifin and Rajka.<sup>6</sup>

Patients were patch tested in a standardized manner using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Bard Medical, Covington, GA).<sup>7</sup> Patches were applied to the back of patients in areas that were free of dermatitis. Test allergens were purchased from Chemotechnique Diagnostics AB, Malmö, Sweden (1994–2007), or from SmartPractice, Calgary, Alberta, Canada (2008–2014). Allergens were applied to patients on Mondays, and patients were examined at both 2 and 4 days after placement. Reactions were graded on reaction morphology as previously

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# TABLE 1. Professions Included as HCWs

#### Professions Considered to be HCWs

Registered Nurses	
Physicians	
Dentists	
Podiatrists	
Health diagnosing practitioners	
Physician assistants	
Dental hygienists	
Licensed practical nurses	
Dental assistants	
Health aides (except nursing)	
Nursing aids, orderlies, and attendants	

described.<sup>7</sup> Reactions of 1+, 2+, or 3+ were considered positive allergic responses.

All deidentified Health Insurance Portability and Accountability Act-compliant data were entered, retrieved, and evaluated using a computer database (Access 2010; Microsoft Corp, Seattle, WA), and, as a result, this study was exempt from institutional review board approval at Columbia University Medical Center, New York, NY. Health care workers were defined as belonging to the occupational groups listed in Table 1. These individuals were chosen because of their likely exposure to water, detergents, antimicrobial agents and gloves. A  $\chi^2$  test was performed to determine significant differences between HCWs and non-HCWs (NHCWs) using statistical software (R, Version 2.15.1; R Foundation for Statistical Computing, Vienna, Austria). A *P* value of 0.05 or less was considered significant.

## RESULTS

Of the 2611 patients who underwent patch testing, 165 (6.3%) were classified as HCWs based on their primary occupation. As shown in Table 2, when compared to the NHCWs, HCWs were more likely to be women. Male, but not female, HCWs had a higher rate of a history of AD when compared to their respective sex in the general population. Female HCWs, but not male HCWs, were

statistically more likely to have hand dermatitis than females NHCWs. With these exceptions, there were no significant demographic differences between HCWs and NHCWs who underwent patch testing.

As shown in Table 3, among the population with a final diagnosis that included ACD, female HCWs were more likely than their NHCW counterparts to have hand dermatitis, whereas the incidence of hand dermatitis in male HCWs barely missed significance. Although more male HCWs than male NHCWs undergoing patch testing had a history of AD (Table 2), there was no difference between these 2 groups with respect to a final diagnosis of ACD (Table 3). Except for hand dermatitis in female HCWs, among those patients with a final diagnosis of ACD, there were no statistically significant differences in the other demographic parameters that were measured.

Among our study population, there was a statistically greater rate of female HCWs with ICD compared to females in the general population, as can be seen in Table 4. Although there was a striking tendency for female HCWs to have ICD of hands as compared to NHCWs, this was not statistically significant. There were no other demographic differences between HCWs and NHCWs with a final diagnosis of ICD.

As shown in Table 5, female HCWs were more likely to suffer from both ACD and ICD than their NHCW counterparts. This difference was not observed in male HCWs. Overall, there was no difference between the HCWs and NHCWs with both ACD and ICD in atopic markers.

We looked at 2 additional subgroups of concomitant diseases: HCWs with both ACD and active AD and HCWs with both ICD and active AD. Compared to the NHCW population, there was no statistical difference in these diagnostic combinations (data not shown).

The most common allergens among HCWs and NHCWs, as well as their relevance (including occupational relevance), are shown in Table 6. Health care workers were statistically more likely to demonstrate relevant allergic reactions to quaternium-15, thiuram mix, carba mix, thimerosal, benzalkonium chloride, 2-bromo-2nitropropane-1,3-diol, cocamide DEA, and glutaraldehyde. When

TABLE 2.	Demographic Data	(MOAHLFA Index)	) for HCWs and NHCWs
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	HCW Male (N*)	HCW Male %	NHCW Male (N*)	NHCW Male (%)	Р	HCW-Female (N*)	HCW Female (%)	NHCW Female (N*)	NHCW Female (%)	Р
Total	28	17.0	876	35.8	≤0.001	137	83.0	1570	64.2	0.004
Asthma†	5	17.9	100	11.4	0.537	15	11.0	231	14.7	0.353
Eczema†	5	17.9	50	5.7	0.047	25	18.2	269	17.1	0.872
Hay fever†	7	25.0	177	20.2	0.790	44	32.1	402	25.6	0.250
Hand‡	13	46.4	252	28.7	0.220	65	47.4	289	18.4	≤0.001
Leg‡	2	7.1	48	5.5	1.000	2	1.5	64	4.1	0.200
Face‡	5	17.9	60	6.9	0.110	18	13.1	294	18.7	0.210
Age, > 40 y	15	53.6	569	65.0	0.663	69	50.4	1012	64.5	0.123

\*N, number of unique patients.

†History of past or active disease.

‡Location of primary dermatitis.

	+ ACD* HCW	+ ACD* HCW	+ ACD* NHCW	+ ACD* NHCW		+ ACD* HCW	+ ACD* HCW	+ ACD* NHCW	+ ACD* NHCW	
	Male (N†)	Male (%)	Male (N†)	Male (%)	ط	Female (N†)	Female (%)	Female (N†)	Female (%)	٩
Total	19	67.9	418	47.7	0.313	72	52.6	811	51.7	0.970
Asthma‡	ო	15.8	44	10.5	0.789	8	11.1	132	16.3	0.407
Eczema‡	4	21.1	45	10.8	0.402	16	22.2	164	20.2	0.859
Hay fever‡	9	31.6	85	20.3	0.518	24	33.3	216	26.6	0.437
Hand§	11	57.9	105	25.1	0.052	39	54.2	167	20.6	≤0.001
Leg§	2	10.5	22	5.3	0.683	<del>.    </del>	1.4	27	3.3	0.599
Face§	4	21.1	34	8.1	0.191	12	16.7	158	19.5	0.743
*+ ACD, Final D †N, number of un *Uiston of soot	liagnosis Allergic Cc nique patients.	ontact Dermatitis.								
ELOCATION OF PRIN	or active disease. nary dermatitis.									

TABLE 4.	Demographi	ics (MOAHLF/	A Index) of HCV	Ws and NHCWs	s With a	Final Diagnos	is of Irritant (	Contact Derma	titis	
	Irritant HCW Male (N*)	Irritant HCW Male (%)	Irritant NHCW Male (N*)	Irritant NHCW Male (%)	ط	Irritant HCW Female (N*)	Irritant HCW Female (%)	Irritant NHCW Female (N*)	Irritant NHCW Female (%)	ط
Total	0	7.1	97	11.1	0.774	28	20.4	101	6.4	≤0.001
Asthma†	-	50.0	വ	5.2	0.407	ო	10.7	21	20.8	0.451
Eczema†	-	50.0	ო	3.1	0.245	ო	10.7	12	11.9	1.000
Hay fever†	-	50.0	15	15.5	0.889	7	25.0	25	24.8	1.000
Hand‡	-	50.0	57	58.8	1.000	24	85.7	53	52.5	0.178
Leg‡	0	0.0	ო	3.1	1.000	0	0.0	0	0.0	0.504
Face‡	0	0.0	5	5.2	1.000	-	3.57	13	12.9	0.349
*N, number of u †History of past ‡Location of prir	nique patients. or active disease. nary dermatitis.									

	Male HCW (N)*	Male HCW (%)	Male NHCW (N)	Male NHCW (%)	Р	Female HCW (N)	Female HCW (%)	Female NHCW (N)	Female NHCW (%)	Р
Total	1	3.6	25	2.9	1.000	7	5.1	31	2.0	0.045
Asthma	1	100.0	1	4.0	0.309	0	0.0	2	6.5	1.000
Eczema	1	100.0	1	4.0	0.309	2	28.6	4	12.9	0.767
Hay fever	1	100.0	5	20.0	0.819	1	14.3	6	19.4	1.000

# TABLE 5. Atopic Demographics for HCWs and NHCWs With a Final Diagnosis of Both Allergic Contact Dermatitis and Irritant Contact Dermatitis

\*N, number of unique patients.

assessed for occupational relevance to the current dermatitis, all of these allergens were statistically more relevant in HCWs, as were formaldehyde and bacitracin.

Regarding the rubber accelerators, HCWs almost reached statistical significance for an increased rate of allergic reactions to carba mix between 2005 and 2014 as compared to between 1994 and 2004 (Table 7). During this same period, for HCWs, there was no difference in the rate of allergic reactions to thiurams. Rates of allergic reaction to thiurams statistically decreased in NHCWs during the period from 2005 to 2014 as compared to 1994 to 2004. During this same time for NHCWs, there were no significant changes in the rate of allergic reactions to carba mix. The rate of positive patch test reactions to the other allergens delineated in Tables 6 did not significantly change in either HCWs or NHCWs between these 2 periods (data not shown).

There were a total of 19 patients in our database with an initial diagnosis of ACU to latex (data not shown); all of these were diagnosed in the 1994 to 2004 period. Sixty-eight percent of patients in our database with latex ACU were HCWs, 70% were female, and 21% of the patients had a history of AD. The hand (74%) was the most common site for dermatitis among patients with ACU. The average age for this subset of patients was 41.9 years.

Both male and female HCWs were statistically more likely than their respective sex in the NHCW population to have occupational ACD, as can be seen in Table 8. Female, but not male, HCWs were statistically more likely than NHCWs to have occupational ICD. Female HCWs were also statistically more likely than female NHCWs to have both occupational ACD and ICD, while male HCWs were not more likely than male NHCWs to have occupational ACD and ICD. Of interest, the incidence of occupational ICD among male HCWs and NHCWs was identical.

#### DISCUSSION

In this study, we tested only patients suspected of having ACD. Furthermore, our population was geographically limited to metropolitan Kansas City, MO and metropolitan New York, NY. The results are therefore not necessarily pertinent to all HCWs or to HCWs in other geographic areas.

We found that HCWs that were referred for patch testing were statistically more likely to be women. The trend of having more female HCWs has been seen in other investigations.<sup>5,8–10</sup> In our population, the hands were the most common site for dermatitis in

both HCWs and NHCWs, but, overall, HCWs were more likely to have hand dermatitis. Although male HCWs were more likely to have hand dermatitis than male NHCWs, this difference was not statistically significant, most likely due to the low number of male HCWs resulting in loss of statistical power. Other authors have also noted that HCWs have higher rates of hand dermatitis than NHCWs.<sup>10,11</sup>

Male HCWs were more likely to have a history of AD than were male NHCWs. When compared to female NHCWs, female HCWs had similar rates of AD. The reason for this difference in atopic status among our male population is unclear. Although this study has an inherent selection bias (suspicion of ACD), there was no difference in the incidence of a final diagnosis of ACD or ICD among our male HCWs and NHCWs, suggesting that we did not have a lower threshold for testing atopic-prone patients, as is also substantiated by the fact that the incidence of AD among our female patients was similar.

Female HCWs had a greater rate of ICD when compared to female NHCWs. This most likely occurred as frequent hand washing, gloves, aggressive disinfectants, and detergents are known to be irritants.<sup>11</sup> Irritant contact dermatitis is also more common in women, as many occupations involving wet work are femaledominated.<sup>12–14</sup> We were not able to see a statistically significant difference in ICD among male HCWs when compared to male NHCWs, most likely due to the fact that our population of male HCWs with ICD was too small, as well as the fact that many of the men evaluated for ACD were manual laborers, where ICD is also common (eg, machinists).

In our study, HCWs were no more likely to have ACD than their NHCW counterparts. This most likely occurred as a result of selection bias: only patients with suspected ACD were patch tested. However, HCWs were more likely to have occupationally relevant reactions to formaldehyde, quaternium-15, 2-bromo-2-nitropane-1,3,-diol, thiuram mix, carba mix, thimerosal, benzalkonium chloride, glutaraldehyde, cocamide DEA, and bacitracin.

In European studies, contact sensitivity in the general population to formaldehyde varies from 2% to 3.1%, whereas areas of North America report up to 9%.<sup>15,16</sup> In our study, we found the rate among NHCWs to be 4.3% and a statistically increased incidence of 8.5% among HCWs. Formaldehyde, which is present in many medical laboratories and in biocides that may be present in hospitals, likely resulted in this finding. Furthermore, certain health care occupations (eg, pathologists) have constant exposure

D (Belevant/O	NHCW Occupationally	NHCW Total	NHCW Total	HCW Occupationally	HCW Total	HCW Total	
		of NHCWs	ared to That	ong HCWs as Comp	lergens Amo	Relevance of the Top 15 All	TABLE 6.

	HCW, Total	HCW, Total	HCW, Occupationally	NHCW Total	NHCW Total	NHCW, Occupationally	P (Relevant/Occupationally
Allergen	Relevant (N*)	Relevant (%)	Relevant (%)	Relevant (N*)	Relevant (%)	Relevant (%)	Relevant
Quarternium-15	24	14.5	10.3	125	5.1	1.7	≤0.001/≤0.001
Nickel sulfate	15	9.1	0.6	217	8.9	1.0	1.000/0.622
Thiuram mix	20	12.1	10.9	61	2.5	1.0	≤0.001/≤0.001
Carba mix	18	10.9	9.7	63	2.6	1.0	≤0.001/≤0.001
Thimerosal	17	10.3	5.5	15	0.6	0	≤0.001/≤0.001
Fragrance mix	80	4.8	0.6	185	7.6	0.7	0.291/0.881
Cobalt chloride	10	6.1	0.6	124	5.1	0.9	0.729/0.686
Formaldehyde	11	6.7	6.7	102	4.2	1.3	0.211/≤0.001
Balsam of Peru	10	6.1	0.6	138	5.6	0.8	0.969/0.770
Benzalkonium chloride	თ	5.5	3.6	38	1.6	0.1	0.001/≤0.001
Bacitracin	9	3.6	0.6	153	6.3	0	0.666/≤0.001
Sodium gold thiosulfate	-	0.6	0	10	0.4	0.1	1.000/0.713
2-Bromo-2-nitropropane-1,3-diol	£	3.0	1.2	31	1.3	0.2	0.037/0.031
Cocamide DEA	9	3.6	3.6	22	0.9	0	≤0.001/≤0.001
Glutaraldehyde	9	3.6	3.6	0	0.0	0	≤0.001/≤0.001
*N, number of unique patients.							

number of unique patients.

l to 2005 and 2014	CW Total 2005	Current (%) P
2004 as Compared	NHCW Total 2005 NH	to Current (N*) to
een 1994 and	NHCW Total	1994-2004 (%)
a Mixes Betw	NHCW Total	1994-2004 (N*)
l Carb		٩
o Thiuram and	HCW Total 2005	to Current (%)
<b>Ns Responding t</b>	_	
Ws Responding to	HCW Total 2005 to 1	Current (N*)
<b>CWs and NHCWs Responding t</b>	HCW Total HCW Total 2005 to H	1994–2004 (%) Current (N*)
Percent of HCWs and NHCWs Responding to	HCW Total HCW Total HCW Total 2005 to H	1994–2004 (N*) 1994–2004 (%) Current (N*)

≤ .001
0.918

1.5 2.5

20 32

3.8 2.8

43 32

0.614 0.051

17.0 19.7

5 <u>5</u>

12.2 6.7

÷ 9

Thiuram Mix

9	patient
Carba Mix	*N, number of unique

		-			0					
	HCW Male (N*)	HCW Male (%)	NHCW Male (N*)	NHCW Male (%)	P	HCW F (N*)	HCW F (%)	NHCW F (N*)	NHCW F (%)	P
Occupational ACD	10	35.7	122	13.9	0.021	34	24.8	95	6.1	≤0.001
Occupational ICD	2	7.1	65	7.4	1.000	24	17.5	41	2.6	≤0.001
Occupational ACD and ICD	1	3.6	16	1.8	1.000	7	5.1	13	0.83	≤0.001

	TABLE 8. Perce	entage of Occupat	ional ACD and ICD Among	g HCWs as Com	pared to NHCWs
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\*N, number of unique patients.

F indicates Female.

to formaldehyde. Formaldehyde contact sensitivity may play a role in the increased reactivity to formaldehyde-releasers, such as quaternium-15.<sup>17,18</sup>

Quaternium-15 and 2-bromo-2-nitropane-1,3,-diol are formaldehyde-releasing preservatives used in many cosmetics and industrial substances such as liquid soaps, moisturizers, and cleaning supplies. Health care workers may come into contact with these preservatives more than NHCWs because of their constant washing and moisturizing of their hands. Health care workers may also be exposed at higher rates due to products used on patients, such as electrode attachment gels.<sup>19</sup> To reduce rates of ACD, and especially ICD, in HCWs, it has been recommended that HCWs only wash their hands when they are visibly soiled or contaminated with proteinacious material, and to otherwise use alcohol-based hand rubs to reduce the transmission of infectious agents.<sup>11</sup>

Health care workers also had a statistically higher rate of relevant ACD to glutaraldehyde. Glutaraldehyde is used as a cold sterilizing solution for medical and dental equipment. Individuals working in the dental profession are particularly likely to have reactions to glutaraldehyde as compared to both the general population and other HCWs.<sup>20,21</sup> In a recent study, although occupational asthma due to glutaraldehyde was decreasing as more precautions are taken to minimize airborne exposure, the rates of respiratory asthma linked to glutaraldehyde are still the highest among operating theatre, endoscopy, and radiology staff nurses.<sup>22</sup>

Health care workers were statistically more likely than NHCWs to have relevant allergic reactions to benzalkonium chloride. Benzalkonium chloride is widely used in hand sanitizers, as a preservative in pharmaceuticals, hygienic towelettes, cosmetics, deodorants, and mouthwashes, and as a disinfectant for floors and surgical equipment. As a result, individuals in the health care industry are more likely exposed to benzalkonium chloride than others. Of note, some alcohol-free hand sanitizers use benzalkonium chloride as an alternative.<sup>23</sup>

Thimerosal is an antiseptic and antifungal agent that is used as a preservative in vaccines, cosmetics, skin test antigens, tattoo inks and ophthalmic medications.<sup>24</sup> Because of allergic reactions, poisoning, and mercurial content, its use has declined during the past 2 decades.<sup>25</sup> Health care workers are overrepresented among thimerosal-allergic patients. Because HCWs are at higher risk for diseases, such as influenza and hepatitis B, the main strategy to prevent high-risk groups from disease is vaccination.<sup>26–28</sup> As a result, the increased rate of thimerosal allergy among HCWs could be explained by higher rates of vaccination. These findings match what has been previously noted with HCWs.<sup>4,28</sup>

Cocamide DEA is a surfactant used in industrial, household, and cosmetic products. Although there are few reports of ACD to cocamide DEA, in a recent publication, it was found to be a relatively common allergen in patients with occupational hand dermatitis in which the primary source of sensitization was hand cleansers.<sup>29</sup> This was also the case for HCWs in the current study, where cocamide DEA in hand soaps was the culprit in all occupationally relevant cases.

In our study, HCWs had statistically higher rates of ACD to both carba mix and thiuram mixes relative to the general population. The higher rates are most likely due to the greater use of gloves among HCWs, as carbamates and thiurams are rubber accelerators. Since the 1990s, thiuram use in gloves (especially nitrile) has decreased with carbamates and diphenylguanidine replacing thiurams. This could explain why rates of positive patch tests have increased for carba mix in HCWs between 1994 to 2004 and 2005 to 2014. However, this does not explain why positive patch test reactions to thiurams in HCWs have remained constant over these 2 periods. From 1994 to 2004 and 2005 to 2014, allergic reaction to thiuram, but not carba, mix has significantly decreased in the NHCW population. It is possible that we did not detect a decrease in thiuram reactivity among HCWs because many of these individuals had previously been sensitized and "solved" their problem by switching to thiuram-free gloves, which are likely to have carbamates or diphenylguanidine as accelerators, only to subsequently become sensitized to these allergens.

Among our patients, no HCWs were diagnosed with ACU to latex after 2004. This is in contrast to research done before 2004, which found that ACU to latex had not declined over time.<sup>4</sup> A decrease in the use of nonsterile latex gloves in the health care sector, together with manufacturing processes that reduce the protein content (viz., hevein) in latex gloves, are likely responsible for curbing this epidemic in the United States.

Overall, HCWs undergoing patch testing for suspected ACD do not have a higher incidence of allergy than do NHCWs. However, HCWs are more likely than NHCWs to be allergic to many of the allergens listed in Table 6. When it comes to gloves, we recommend use only when needed. Vinyl gloves do not have rubber accelerators, such as thiurams, carbamates, or diphenylguanidine, and should be preferentially used when appropriate. When working with formaldehyde or glutaraldehyde, HCWs should be cautioned to minimize contact because these allergens readily permeate most gloves. To reduce sensitization to formaldehyde-releasing preservatives, as well as to reduce water/surfactant induced ICD, alcohol-based (benzalkonium-free) hand sanitizers should be used instead of antimicrobial soaps and water as much as possible. Health care workers would also be well advised to carefully choose moisturizers without formaldehyde-releasers, such as quaternium-15. Finally, despite the higher rate of thimerosal sensitization among HCWs, we encourage HCWs to be vaccinated as appropriate. As has been previously reported, allergic patch test reactions to thimerosal are rarely relevant,<sup>5,30,31</sup> and most individuals with a positive patch test reaction to thimerosal do not react when vaccinated to thimerosal.<sup>32</sup>

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