

Cross-reactivity between gutta-percha and natural rubber latex

Assumptions vs. reality

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Introduced to dentistry in the mid-19th century, gutta-percha is a widely used endodontic material that generally is considered nontoxic and inert.¹ This hard crystalline substance is a major constituent of endodontic points used in the obturation of root canals. Gutta-percha contains the rubber molecule trans 1,4-polyisoprene and is harvested from *Palaquium gutta* trees found in southeast Asia. The purity of the raw gutta-percha; the manufacturing process; and the addition of fillers, opacifiers, waxes, resins and plasticizers all influence the character of gutta-percha points. Gutta-percha point formulations vary by manufacturer, but reportedly contain 56 to 80 percent

zinc oxide, 20 to 30 percent gutta-percha, 1 to 17 percent heavy metal sulfates, 1 to 4 percent waxes and resins and 0.1 to 0.3 percent color pigments (including erythrosin).¹⁻³ Additional variables in commercial gutta-percha point formulations include blends with gutta-balatta or synthetic trans-polyisoprene.⁴ Unfortunately, labels on commercial gutta-percha points provide limited information and do not identify source material, degree of purity or the presence of other plant-based fillers. As a result, the composition and allergenic character of gutta-percha points is difficult for clinicians to evaluate.

As awareness of allergy to natural rubber latex, or NRL, has increased, concerns have been raised about possible cross-reactivity of gutta-percha and NRL anti-

Background. Immunological cross-reactivity between gutta-percha and natural rubber latex, or NRL, has not been demonstrated clearly despite recent concerns and several suspected cases reported in the literature.

Methods. The authors analyzed aqueous extracts of commercial gutta-percha points and raw gutta-percha samples for cross-reactivity to NRL by radioallergosorbent test, or RAST, inhibition; immunoblot inhibition; direct enzyme-linked immunosorbent assay, or ELISA; and ELISA inhibition using sera from NRL-allergic people as the source of anti-NRL immunoglobulin E, or IgE, antibodies. To confirm in vitro results, the authors conducted skin prick testing, or SPT, on a patient with type I NRL allergy using aqueous extracts from raw gutta-percha, ammoniated gutta-percha and gutta-percha points.

Results. Aqueous extracts from commercial gutta-percha points did not cross-react to NRL in RAST inhibition or immunoblot inhibition, ELISA or ELISA inhibition assays. However, three of 13 sera from subjects with type I NRL allergy exhibited IgE binding to raw gutta-percha extracts in direct ELISA. Moreover, in ELISA inhibition, the binding of IgE to raw gutta-percha extracts was inhibited in a dose-dependent manner by raw NRL and vice versa. SPT results from a subject with type I NRL allergy were positive for NRL and raw gutta-percha extracts but negative for gutta-percha point extracts.

Conclusions. The authors found no detectable cross-reactivity between NRL and commercial gutta-percha points. However, their ELISA and SPT results demonstrated that some allergenic cross-reactivity exists between raw gutta-percha and raw NRL.

Clinical Implications. Gutta-percha alone is not likely to induce symptoms in patients with type I NRL allergy. However, other materials used in obturating root canals may be irritating and potentially allergenic in patients with pre-existing allergies.

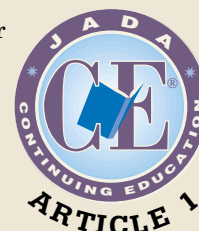


TABLE 1

INGREDIENTS AND RAST* INHIBITION ANALYSIS OF COMMERCIALY AVAILABLE GUTTA-PERCHA POINTS.										
ID NO.†	BRAND NAME	DISTRIBUTOR	MANUFACTURER‡	INGREDIENTS LISTED (% IF GIVEN)					LOT NO.	RAST INHIBITION RESULTS¹
				Gutta-Percha	Barium Sulfate	Zinc Oxide	Coloring Agent	NRL⁵		
01	Chige	R. Chige Inc., Boca Raton, Fla.	Chige	X	X	X	X	N/A#	8347K	ND
02	Super-Dent	Darby-Spencer-Mead Dental Supply Co. Inc., Westbury, N.Y.	Carlisle Laboratories, Westbury, N.Y.	X	N/A	X	X	N/A	8376J	ND ND
03**	Dentsply	Darby	Dentsply International Inc., York, Pa.	X	N/A	X	X	N/A	010598	ND
04	Dia-Dent	Pearson Dental Supplies Co., Sylmar, Calif.	Dia-Dent, Burnaby, B.C., Canada	X	X	X	X	N/A	011198	ND
05**	Hygenic	Darby	Hygenic Corp., Akron, Ohio	X	X	X	X	N/A	1005 315K	ND
06	Hygenic	Patterson Dental Co., St. Paul, Minn.	Hygenic	X	X	X	X	N/A	Not listed	ND
07	Kerr	Darby	Meta Dental Co., Elmhurst, N.Y.	X	X	X	X	N/A	8363G	ND ND
08	Kerr	Patterson	Meta	N/A	N/A	N/A	N/A	N/A	8481E	ND
09	Meta	Pearson	Meta	X	X	X	X	N/A	020596	ND
10	MicroSeal	Sybronendo, Orange, Calif.	Not listed	X	X	X	X	N/A	15698	ND
11	Patterson	Patterson	Patterson	N/A	N/A	N/A	N/A	N/A	P02238	ND
12	Pearson	Pearson	Pearson	N/A	N/A	N/A	N/A	N/A	Not listed	ND
13**	Practice-ware	Practicewares, Sacramento, Calif.	JS Dental Manufacturing Inc., Ridgefield, Conn.	X	X	X	X	N/A	8359R	ND
14	Schein Gutta-Percha Points	Henry Schein Inc., Melville, N.Y.	Schein	N/A	N/A	N/A	N/A	N/A	Not listed	ND
15	Moyco Union Broach	Schein	Produits Dentaires S.A., Vevey, Switzerland	(23.8)	(15.0)	(60.0)	X	N/A	Not listed	ND
16	Moyco Union Broach	Pearson	Not listed	N/A	N/A	N/A	N/A	N/A	621597	ND

Continued on next page

gens. Two case reports in the medical literature attributed adverse reactions to gutta-percha observed in subjects with type I NRL allergy who underwent endodontic treatment.^{5,6} However,

their conclusions most likely were based on assumptions that potential botanical relationships between gutta-percha and NRL implied cross-reactivity; that finished endodontic points

TABLE 1 (CONTINUED)

INGREDIENTS AND RAST* INHIBITION ANALYSIS OF COMMERCIALY AVAILABLE GUTTA-PERCHA POINTS.										
ID NO.†	BRAND NAME	DISTRIBUTOR	MANUFACTURER‡	INGREDIENTS LISTED (% IF GIVEN)					LOT NO.	RAST INHIBITION RESULTS¹
				Gutta-Percha	Barium Sulfate	Zinc Oxide	Coloring Agent	NRL§		
17	Zipperer	Roydent Dental Products, Rochester Hills, Mich.	United Dental Manufacturers Inc., West Palm Beach, Fla.	X	X	X	X	NA	PO2348	ND
18**	Zipperer	Roydent	United Dental Manufacturers	X	X	X	X	NA	P02237	ND
20	Roeko Iso	Roeko GmbH and Co. KG, Langenau, Germany	Roeko	X	X	X	X	NA	159708	ND
22	Premier	PracticeWares	Not listed	X	X	X	X		02265	ND
23	Lone Star	Lone Star Technologies, Westport, Conn.	Lone Star	X	X	X	X	X	030999	ND
24	Towne	Towne International Inc., Baltimore	Towne International	X	X	X	X		061795	ND

* RAST: Radioallergosorbent test.
 † ID: Identification nos. 19 and 21 are not included because it was discovered that these were duplicates of existing lots.
 ‡ Information as supplied with product; for some products, no manufacturer was listed.
 § NRL: Natural rubber latex.
 ¶ ND: Not detectable; the percentage RAST inhibition of the sample was too low for extrapolation. The detection limit of this assay is approximately 1 microgram per gram.
 # N/A: Not applicable.
 ** Indicates brands selected for additional enzyme-linked immunosorbent assay, or ELISA, and ELISA inhibition testing.

contain significant amounts of bioavailable gutta-percha protein; and that other endodontic materials are not allergenic.

To date, no study has conclusively demonstrated that gutta-percha is a causative agent of adverse allergic reactions. Moreover, in other case reports, no adverse effects were observed when gutta-percha was used in people with type I NRL allergy.^{7,8} Consistent with these observations, a recent investigation by Costa and colleagues⁴ reported no evidence of immunological cross-reactivity in vitro between NRL and gutta-percha points using radioallergosorbent test, or RAST, inhibition analysis.⁴

Several patient groups are considered at risk of experiencing a type I NRL allergy, including health care workers; patients with myelodysplasia (for instance, spina bifida and myelomeningocele), urogenital congenital abnormalities or a history of multiple surgeries during early childhood; and people with a history of skin

or whole-body allergic reactions to rubber, fruits, plants and pollens.⁹ The prevalence of type I NRL allergy is highest in patients with myelodysplasia or urogenital congenital abnormalities, in whom it ranges from 25 to 55 percent.¹⁰⁻¹² The prevalence of type I NRL allergy in health care workers varies with each specialty, ranging from 4 percent to 17 percent in hospital personnel and laboratory workers and from 6 percent to 12 percent in dental professionals.¹³⁻¹⁷ Assuming an average prevalence of 10 percent, more than 800,000 health care workers in the United States may have a type I NRL allergy. However, a type IV allergy (that is, allergic contact dermatitis) to one or more of the chemicals found in dental and health care products—such as gloves and disinfectants—may be twice as common.^{18,19} Many symptoms of a type IV chemical allergy are similar to those of a type I NRL allergy, confounding appropriate diagnosis and treatment.

Of the 15 million endodontic therapy pro-

TABLE 2

IMMUNOLOGICAL ANALYSES APPLIED TO DIFFERENT TYPES OF GUTTA-PERCHA SAMPLES.

EXTRACT DESCRIPTION	ANALYSIS APPLIED					
	Protein Analysis	RAST* Inhibition Analysis	Immunoblot Inhibition Analysis	ELISA† Analysis	ELISA Inhibition Analysis	Skin Prick Tests
Dried Raw Gutta-Percha	X	X	N/A‡	X	X	X
Ammoniated Raw Gutta-Percha	N/A	N/A	X	N/A	N/A	X
Commercial Gutta-Percha Points	X	X	N/A	X	X	X

* RAST: Radioallergosorbent test.
† ELISA: Enzyme-linked immunosorbent assay.
‡ N/A: Not applicable.

cedures performed annually in the United States, a portion involves these groups at high risk.²⁰ As a result, it is important that dental professionals better understand the allergenic potential of endodontic materials. Therefore, we undertook an investigation of the immunological cross-reactivity between NRL and gutta-percha using both in vitro and in vivo methods. In this article, we report our results; we also review dental treatment strategies for patients with this allergy, including recognition of symptoms and potential allergens used during endodontic procedures.

MATERIALS AND METHODS

Materials. Through collaboration with the Forest Research Institute of Malaysia in Kepong, we obtained raw gutta-percha samples by collecting either liquid or coagulated gutta-percha gel from tapped mature *Palaquium gutta* trees. We obtained ammoniated gutta-percha samples by rinsing off the partially coagulated gel. In addition, we purchased 22 lots of commercial gutta-percha points from different distributors to obtain a reasonable representation of the material available for sale in dentistry (Table 1, page 1358). Because information on foreign production sources is not readily available and manufacturers may obtain gutta-percha from multiple sources, we tried to sample multiple lots from each manufacturer. According to manufacturer labels or technical information, the principal ingredients were zinc oxide, gutta-percha, barium sulfate and a coloring agent. One package label noted that the gutta-percha points contained “dry

natural rubber.” We coded commercial gutta-percha point packages with identification numbers and removed the brand labels.

Gutta-percha extraction methods. We first pulverized (using a KSM2 grinder, Braun, Boston) or homogenized (using the Ultra-Turrax T8 homogenizer, IKA-Werke GMBH & Co., Staufen, Denmark) commercial gutta-percha points and raw gutta-percha samples in extraction buffer, which was either 20-millimolar ammonium bicarbonate (pH 8.5) or phosphate-buffered saline, or PBS (10 mmol phosphate, pH 7.4). We extracted 1-gram samples in at least 5 milliliters of extraction buffer for 24 hours at 23 C with constant shaking.

Any remaining particulate was removed by filtration and the clear supernatant used for subsequent analysis. We subjected gutta-percha samples to different analyses, as summarized in Table 2.

Protein analysis. We conducted an initial analysis of the raw gutta-percha samples and all 22 lots of gutta-percha points (Table 1) for total protein content. We then selected four brands of gutta-percha points (identification nos. 3, 5, 13 and 18) from the same original lots for secondary protein analysis. We assayed protein level using a modified Lowry analysis based on acid precipitation (equal volumes 72 percent trichloroacetic acid and 72 percent phosphotungstic acid) of a 0.15 percent deoxycholate-solubilized sample.²¹ The limit of detection of this assay is 4 micrograms per mL. Excessive precipitation after the addition of acid to ammoniated gutta-percha samples pre-

cluded subsequent protein analysis.

RAST inhibition analysis. We analyzed aqueous extracts from raw gutta-percha and commercial gutta-percha points by RAST inhibition assay for their ability to competitively inhibit the binding of immunoglobulin E, or IgE, anti-NRL antibody to a solid-phase NRL allergen.^{22,23} We diluted NRL reference allergen (nonammoniated NRL, ProGene Corp., Lenexa, Kan.) or gutta-percha extracts in PBS containing 1 milligram/mL human serum albumin and incubated for one hour with a 50-microliter aliquot of pooled high-positive human sera. These sera were determined by technicians at IBT Reference Laboratory (Lenexa, Kan.) to contain a high titer of anti-NRL IgE levels by one of three routine latex-specific IgE immunoassays: radioimmunoassay, or RIA; Pharmacia CAP System (Pharmacia Diagnostics, Kalamazoo, Mich.); or AlaSTAT (Diagnostic Products Corp., Los Angeles). We transferred incubated extracts to nonammoniated NRL-coated microwells, incubated them for four hours and washed them with tris-buffered saline containing 0.5 percent polyethylene glycol sorbitan monolaurate (Tween-20, ICI Americas Inc., Bridgewater, N.J.). Microwells were incubated overnight with 50 μ L of I¹²⁵-labeled equine anti-human IgE (Kallestad-Sanofi, Chaska, Minn.), washed repetitively and counted for five minutes. We quantified cross-reacting NRL allergen levels by comparing them with the quantity of the NRL reference allergen required for 50 percent inhibition. If inhibition by undiluted samples was below 30 percent, we considered antigen content not detectable. The detection limit of the assay is approximately 1 μ g/g.

Immunoblot inhibition analysis. We evaluated extracts from ammoniated gutta-percha by the immunoblot inhibition using reagents from the AlaBlot immunoblotting kit (Diagnostic Products Corp.). We incubated nonammoniated NRL nitrocellulose strips (AlaBlot) sequentially with 50 μ L of either NRL reference allergen (1.96 mg/mL) or gutta-percha extract; a 50- μ L aliquot of pooled high positive human sera; and 400 μ L of diluent buffer. After a two-hour incubation at 20 C, we processed the strips and visualized the bands with the enzyme-labeled anti-IgE reagent system provided by the manufacturer.

Direct ELISA. We analyzed raw gutta-percha and four randomly selected commercial gutta-percha points (nos. 3, 5, 13 and 18) for their ability to directly bind IgE in sera from 13 sub-

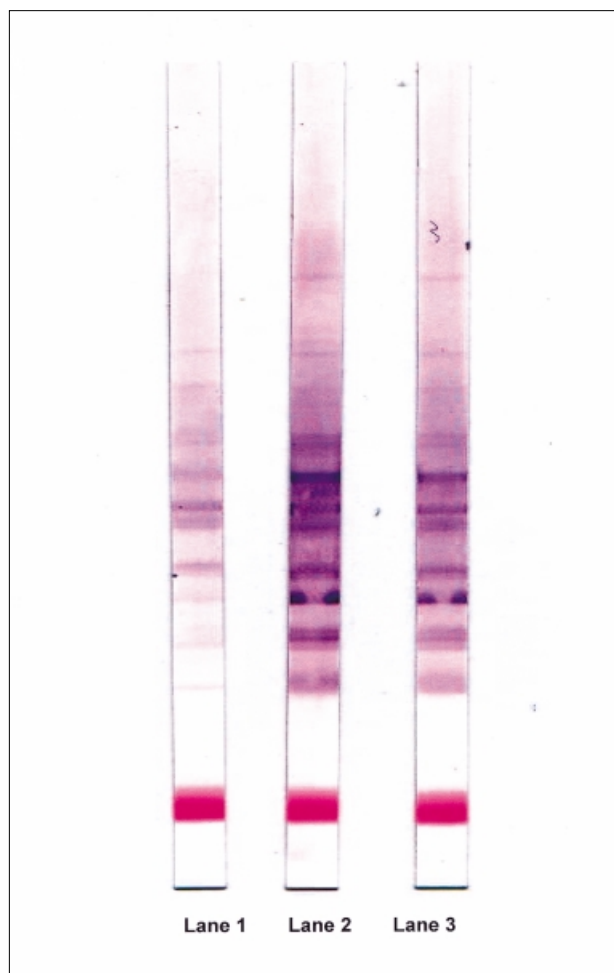


Figure 1. Human immunoglobulin E binding to solid-phase nonammoniated natural rubber latex, or NRL, inhibited by NRL reference allergen (Lane 1, positive control), unaffected by diluent buffer (Lane 2, negative control) and unaffected by ammoniated gutta-percha extract (Lane 3).

jects with type I NRL allergy known to have IgE antibodies to hevein (Hev b 6.02), a major NRL allergen.²⁴ We prepared polystyrene microtiter plates as previously described but coated them with 100 μ L of extracts (10 μ g/mL protein) from either raw gutta-percha or gutta-percha points.²² We prepared reference plates with purified hevein (1 μ g/mL protein) for comparison. After washing, we incubated plate wells with 100 μ L of sera from NRL-allergic patients or non-NRL-allergic control subjects (1:10 dilution). After subsequent washes, we determined binding with biotinylated antihuman IgE and detected it with streptavidin-conjugated alkaline phosphatase (absorbance monitored at 405 nanometers).

ELISA inhibition. We examined cross-reactivity between dried raw gutta-percha and raw NRL by means of competitive inhibition of

RESULTS

Protein extraction and analysis. On the basis of preliminary studies, a 24-hour extraction period was needed to solubilize sufficient protein for detection owing to gutta-percha's low solubility in aqueous solutions. Total protein content extracted from raw gutta-percha varied from 500 $\mu\text{g/g}$ to 2,400 $\mu\text{g/g}$. By comparison to raw gutta-percha, the protein content of commercial gutta-percha point extracts was much lower: 39 $\mu\text{g/g}$ total protein from a single gutta-percha point and 76 $\mu\text{g/g}$ from a subsequent analysis of four commercial gutta-percha points.

RAST inhibition. Neither the raw gutta-percha extracts nor the 22 lots of commercial gutta-percha point extracts competitively inhibited binding of IgE anti-NRL antibody to solid-phase NRL allergen. If these gutta-percha extracts contained any epitopes that cross-reacted with allergens from NRL, their concentrations were below the detection limit of the assay (1 $\mu\text{g/g}$).

Immunoblot inhibition. Ammoniated raw gutta-percha did not inhibit recognition and binding of nonammoniated NRL by pooled high-positive human sera (Figure 1, page 1361).

Direct ELISA. Three of 13 (23 percent) sera from subjects with type I NRL allergy had IgE antibodies that bound solid-phase gutta-percha prepared from raw gutta-percha extracts (Figure 2A). In contrast, none of the sera had IgE antibodies that recognized solid-phase antigen prepared from commercial gutta-percha point extracts (Figure 2B). Simultaneous analysis of IgE binding to solid-phase hevein is shown for comparison (Figure 2, page 1362). Control serum from subjects without a type I NRL allergy did not bind either gutta-percha

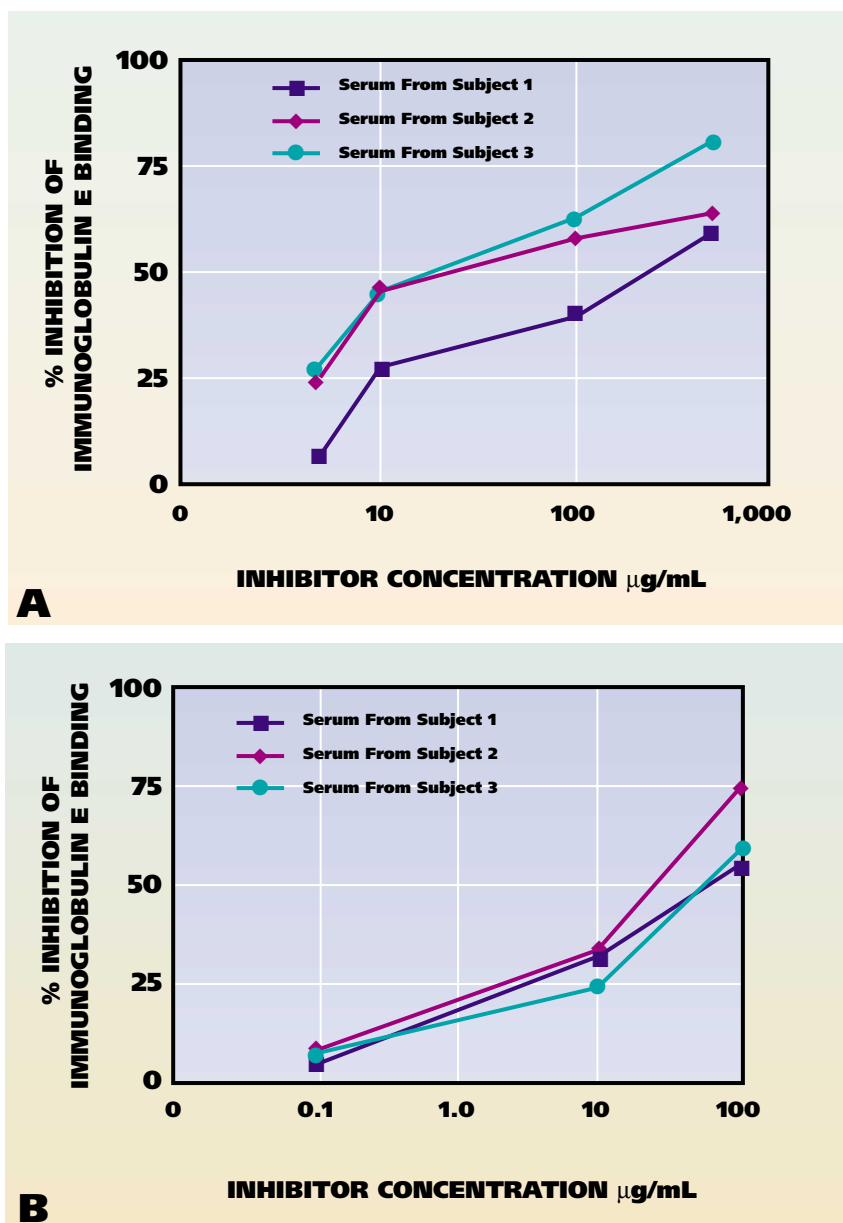


Figure 3. A. Natural rubber latex, or NRL, inhibition of the binding of serum immunoglobulin E, or IgE, to solid-phase raw gutta-percha. Serum samples were obtained from select NRL-allergic patients and incubated with 50 microliters of raw NRL extract solutions of 5, 10, 100 and 500 micrograms per milliliter of protein. **B.** Gutta-percha inhibition of the binding of serum IgE to solid-phase raw NRL. Serum samples were obtained from select NRL-allergic patients and incubated with 50 μL of raw gutta-percha extract solutions of 0.1, 1.0, 10 and 100 $\mu\text{g/mL}$ protein.

extracts or hevein (data not shown).

ELISA inhibition. Using sera from the three subjects with type I NRL allergy that bound solid-phase gutta-percha by direct ELISA, we observed cross-reactivity between raw gutta-percha and NRL. Raw NRL inhibited the binding of IgE to solid-phase gutta-percha antigen (prepared from raw gutta-percha extracts) in a dose-dependent



Figure 4. Skin prick test results in a patient with type I allergy to natural rubber latex, or NRL: histamine (labeled “hist”) positive control, 7-millimeter wheal; NRL (labeled “latex”) standard, 5-mm wheal; extract from commercial gutta-percha point no. 3 (labeled “GP 1”), no wheal observed; extract from dried raw gutta-percha (labeled “GP 2”), 5-mm wheal. No wheal was observed with saline (150 millimolars) negative control (not shown).

manner (Figure 3A, page 1363). In addition, extracts from raw gutta-percha inhibited the binding of IgE to solid-phase raw NRL antigen in a dose-dependent manner (Figure 3B, page 1363).

SPT. The type I NRL-allergic subject exhibited positive SPT reactions to histamine (7 mm), NRL standardized allergen (5 mm) and raw gutta-percha extract (5 mm) as shown in Figure 4. We observed a smaller reaction (approximately 2 mm) at the site associated with diluted ammoniated gutta-percha. We observed no reactions in response to saline (150 mmol) negative control or extracts of commercial gutta-percha points no. 3 or no. 13.

DISCUSSION

Gutta-percha generally is viewed as a nontoxic

obturator material. Although more than 100 years have passed since its introduction, gutta-percha still is considered the material of choice for filling root canals. In 1994, Boxer and colleagues⁵ reported diffuse urticaria, or hives, and swelling in a type I NRL-allergic dental hygienist during endodontic surgery.⁵ Symptoms persisted after surgery but apparently resolved when the gutta-percha was removed one month later. In the 1980s, Gazelius and colleagues⁶ recorded a similar case of a long-term reaction to gutta-percha in a nurse with a type IV allergy to rubber-compounding chemicals. By comparison, other clinicians have described successful root canal placement of gutta-percha in patients with type I NRL allergy.^{7,8} These divergent clinical outcomes could be caused by variations in patients' immunological sensitivity, the allergenicity of gutta-percha, endodontic chemical allergens or procedural differences such as NRL-allergy management procedures.

We examined the potential cross-reactivity between different gutta-percha sources and NRL using the *in vitro* techniques of RAST inhibition, immunoblot inhibition, direct ELISA and ELISA inhibition (Table 2). Our results showed that no detectable cross-reactivity exists between NRL and the 22 lots of commercial gutta-percha points we tested according to RAST inhibition, direct ELISA and ELISA inhibition. These results are similar to the RAST inhibition findings recently reported by Costa and colleagues.⁴ In addition, our *in vivo* SPT results confirm that a patient with type I NRL allergy is unlikely to react to commercial gutta-percha points.

Our direct ELISA and ELISA inhibition results suggest that some allergenic cross-reactivity exists between raw gutta-percha and raw NRL. Our *in vivo* SPT results also confirmed this potential cross-reactivity. This is not unexpected; patients with type I NRL allergies have been shown to have allergic reactions and antibodies to related proteins such as the chitinases from ficus plants, avocados and bananas.²⁵⁻²⁷ However, the cross-reactivity between raw gutta-percha and raw NRL is not likely to have clinical relevance. Raw gutta-percha is processed through a combination of heat and petroleum-based-solvent extractions during the manufacture of endodontic points. As a result, any remaining proteins in the solvent-extracted, fully refined gutta-percha are probably highly denatured with minimal antigenic character.

TABLE 3

CHARACTERISTICS OF TYPE I AND TYPE IV ALLERGIES AND POTENTIAL DENTAL ALLERGENS THAT CAN EVOKE SYMPTOMS IN ALLERGIC PATIENTS.

ALLERGY FACTORS	TYPE I ALLERGY	TYPE IV ALLERGY
Potential Dental Allergens	Natural rubber latex proteins Chlorhexidine Eugenol Formaldehyde derivatives	Rubber-compounding chemicals such as thiurams, carbamates, thioureas and thiazoles Disinfectants such as glutaraldehyde and chlorhexidine Formaldehyde derivatives Eugenol Methacrylates
Symptoms Occur	Within minutes or hours	Within hours or days
Symptoms Subside	Within hours	Within weeks or months
Sources of Exposure	Mouth, eyes, nose and skin Injection Lungs via aerosolization Ingestion	Skin and epithelial surfaces Oral mucosa
Dermatologic Symptoms	Swelling or tightness Hives (raised red itchy bumps) Burning or tingling Itching or redness	Swelling and thickening Cracking, peeling, scabbing, crusting, scaling, fissures and vesicles Itching, soreness and redness
Eye and Respiratory Symptoms	Asthma, wheezing Coughing, throat constriction Itchy red eyes Runny nose, sneezing Rhinitis	None
Gastrointestinal Symptoms	Nausea, vomiting Diarrhea, cramps	None
Cardiovascular Symptoms	Hypotension Tachycardia Shock	None
Means of Diagnosing Allergy	Medical history Symptom assessment Skin prick testing, serologic testing or both	Medical history Symptom assessment Patch testing

RAST inhibition and immunoblot inhibition results differed from ELISA inhibition results, most likely caused by IgE differences in the serum pools used. For our ELISA inhibition testing, we selected sera obtained from three patients with a type I NRL allergy confirmed by both clinical history and positive in vivo skin prick test results. These serum samples also contained antihevein IgE antibodies and recognized and bound to raw gutta-percha. In contrast, our RAST and immunoblot inhibition methods used pooled human sera with high overall anti-NRL IgE levels determined by in vitro immunoassays. However, this sera was not selected for specific antibodies to gutta-percha or major NRL allergens such as hevein. Therefore, this pooled human sera probably did not contain sufficient quantities of specific anti-NRL antibodies that could recognize and bind the cross-reacting struc-

tures in raw gutta-percha.

While our results showed minimal potential for commercial gutta-percha points to elicit a response in people with type I NRL allergy, these patients can have an allergic reaction to other materials used in endodontic treatment. Patients with type I NRL allergies can have concomitant allergies to certain foods, plants, pollens, chemicals and fragrances.⁹ As shown in Table 3, endodontic chemicals that are potential allergens include eugenol (in fragrances and root canal sealers), disinfectants such as glutaraldehyde and chlorhexidine, methacrylates in bonding agents and epoxy resins, formaldehyde derivatives (in root canal sealers and resins) and the rubber-compounding chemicals thiurams, carbamates, thioureas and thiazoles that are used in synthetic and natural rubber products (such as gloves, carpule stoppers and dental dams).^{19,28-30} Routes of

exposure could include direct contact with skin or oral mucosa, apical leakage or injection. In patients with a type IV allergy to one or more of these chemicals, the oral mucosa and facial skin may redden, burn, swell, itch, crack, scale or scab within a few hours of exposure. These symptoms can take weeks or months to subside. And acute allergic reactions such as hives and anaphylaxis, while uncommon, have been reported after exposure to eugenol, formaldehyde and chlorhexidine.³¹⁻³³ If not allergenic, the remaining chemicals used in endodontic treatment—including zinc oxide, disinfecting hypochlorite (bleach) solutions and softening solvents such as chloroform and halothane—often are strong irritants.^{6,34,35}

Dental professionals must evaluate patients' medical histories carefully for documented allergies. They also should be aware of critical signs of undocumented allergies such as unexplained rashes, breathing problems, hives or anaphylactic reactions.⁷ When treating patients with a documented or suspected type I NRL allergy, dentists should pay attention to potential reactions to dental chemicals and materials, including rubber dams, rubber anesthetic cartridge stoppers, epoxy resins, anesthetics and disinfectants.^{30,35} Dentists should address any concerns regarding the content of gutta-percha points or other dental materials with the manufacturers before proceeding to treat patients with the materials. Dental professionals also may need to confer with primary care providers for optimal patient management. In general, dental patient care should follow guidelines outlined by an NRL allergy management protocol established by the dental practitioner. Moreover, patients with type I NRL allergy should be educated with regard to the dental materials used and their allergenic or irritant potential. This strategy is essential in lowering anxiety, reducing symptoms that falsely mimic an allergic reaction and improving endodontic treatment outcomes in patients with an NRL allergy.³⁶

CONCLUSION

Consistent with the results of a recent study by Costa and colleagues,⁴ we found that commercial gutta-percha points did not contain allergens that cross-reacted to NRL in immunological testing. Furthermore, when using sera selected for recognizing antigens in raw gutta-percha and purified NRL allergen, we still were unable to demonstrate cross-reactivity in finished commercial gutta-percha points. Therefore, gutta-percha

points alone are unlikely to cause an allergic response in patients with an existing or suspected type I NRL allergy. However, these patients often have a strong and lengthy history of allergies and, as a result, may react to one or more of the dental chemicals used in root canal obturation. Therefore, these patients may require careful management before, during and after root canal obturation procedures. ■

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