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Allergic contact reactions in health personnel

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Increasing numbers of physicians, nurses, and dentists are becoming allergic to rubber (latex) gloves because of the increase in the use of such gloves with the advent of acquired immunodeficiency syndrome (AIDS). Seven percent of such personnel now acquire a delayed allergic, eczematous contact dermatitis, whereas 3% show an immediate allergic urticarial reaction to the aqueous protein fraction of latex obtained from the rubber tree *Hevea brasiliensis*. This urticarial reaction may be accompanied by anaphylaxis. Sensitized individuals give positive scratch and prick skin tests and in vitro positive RAST and IgE reactions. Iatrogenic and intraoperative contact urticaria and anaphylaxis as a result of patients reacting to rubber gloves worn by physicians and surgeons are being reported with more frequency. In March of 1991 the Food and Drug Administration (FDA) alerted health care professionals about the potential of severe allergic reactions to medical devices made of latex. These include surgical and examination gloves, catheters, intubation tubes, anesthesia masks, and dental dams. Individuals sensitive to rubber are also allergic to rubber condoms. Hospital personnel and patients sensi-

tive to rubber can be safely exposed only to synthetic nonrubber elastomer gloves, which are more reliable than vinyl gloves. Corn starch powder in gloves will rarely produce urticarial reactions. Health personnel are also subject to allergic dermatitis from antiseptics, antibiotics, and anticancer drugs.

RUBBER GLOVE ALLERGY

Because the epidemic of AIDS has led to a marked increase in the use of rubber (latex) gloves, allergic contact dermatitis to rubber gloves has become the most common cause of allergic contact dermatitis in physicians. Nurses, hospital personnel in general, and dentists are included among those in whom contact dermatitis to rubber gloves is being reported with increasing frequency.

The allergic dermatoses that occur in the medical profession may be either a delayed eczematous type IV dermatitis or an immediate type I urticarial reaction, or a combination of both.¹

Delayed eczematous rubber glove dermatitis

Any patient who wears rubber gloves and has a diffuse or patchy eczema on the dorsum of hand and fingers may be sensitive to rubber. Although this typical pattern may have an abrupt cutoff above the wrist, the classic distribution of rubber glove dermatitis may extend onto the forearms. Many have a nonspecific pattern of hand eczema, and in most patients a diagnosis could not have been made with certainty with-

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out routine patch testing. The eruption may mimic a photodermatitis.

Rubber chemicals such as the accelerators and antioxidants in rubber gloves are the usual sensitizers. Mercaptobenzothiazole and tetramethylthiuram are the most common causes of eczematous contact dermatitis from gloves. Patch testing with a 1-inch square of rubber glove may also produce positive results. The "use" test, in which the patient wears the suspected rubber gloves, often reproduces the dermatitis.

Contact urticaria caused by the protein component in latex rubber gloves

The onset of symptoms occurs from 5 minutes to 1 hour after the subject puts on the gloves. The urticaria may last from 30 minutes to 2 hours. Associated systemic symptoms, such as rhinitis, dizziness, and eyelid edema, have occurred in some patients.

The diagnosis of contact urticaria caused by rubber gloves is made on the basis of the history and results of a physical examination, and is confirmed by positive results of a provocative test that involves putting the rubber gloves on the subject's damp hands for 15 to 30 minutes. The gloved hands may be held in hot water to stimulate perspiration. Positive results of intracutaneous tests (prick or scratch) with a piece of rubber glove consist of a urticarial wheal.

Incidence of immediate rubber (latex) sensitivity

Turjanmaa² studied the frequency of immediate latex sensitivity at the Tampere Hospital, Finland. Five hundred thirty persons using rubber (latex) gloves in their work were examined. The scratch skin test gave positive results in 24 (4.5%) persons; the highest frequency (17%) was among operating room nurses. Control tests were performed on 139 dermatologic patients suspected of being atopic; only two (1.4%) showed positive test results. Most with positive reactions had a history of glove allergy. They had experienced pruritus and skin irritation when using latex gloves. More detailed skin tests were performed with the sap and leaf of the rubber tree; 15 of 24 persons had clearly positive prick test results. Radioallergo-sorbent tests with use of the latex glove gave positive results in nine of 15 of these subjects; results of the use test with a latex glove confirmed the allergy in 14 of 15 persons.

The additional symptoms in these 15 persons include rhinitis in two (14%), Quincke's edema in one (7%), and conjunctival edema in five (33%) persons.

The overall frequency of immediate surgical latex glove allergy found in this study was 3%. As expected, the highest prevalence (6.2%) occurred in op-

erating units where latex gloves are in daily use. Allergic persons were from the units of main surgery, gynecology and obstetrics, and otorhinolaryngology. The total allergy frequency was 7.4% in doctors and 5.6% in nurses working in operating units.

TESTING FOR IMMEDIATE RUBBER ALLERGY

The use test

The use test consists of wearing a rubber glove on a wet hand. A positive reaction consists of itching and possibly urticaria within one half hour. Correlation between the use test and prick test is usually good.³⁻⁷

Caution in applying the use test. In two patients that I observed, severe urticaria occurred from the use test. At present, I apply only one finger of the glove on the patient's hand. If there is no reaction after ½ hour, then the entire glove may be applied to the wet skin of one hand.

Scratch and prick skin tests for contact urticaria

Turjanmaa et al.⁸ reported the classic techniques for these skin tests for contact urticaria.

IN VITRO TESTING FOR THE LATEX PROTEIN ALLERGEN

Recent studies have suggested that the allergen is a water-soluble protein derived from natural rubber and that the sensitized persons have specific IgE antibodies that can be detected by skin prick test or RAST.⁹ Frosh et al.⁴ reported that serologic studies were performed in three patients with typical contact urticaria to a latex surgical glove. Specific IgE antibodies to natural latex as well as to vulcanized glove material have been detected by radioimmunoassay.

Cuevas et al.¹⁰ concluded that latex used in the manufacture of surgical gloves should be included in a list of allergens found in the tree *Hevea brasiliensis*. They reported that in one case, for approximately the last year, minutes after using surgical gloves a female doctor had severe pruritus followed by a rash and angioedema of the contact areas. During the last 4 months, on opening the glove bag she had severe rhinitis and respiratory distress. The symptoms ceased in 1 hour. Standard patch tests with substances used in the manufacture of rubber were negative.

Prick tests with glove and natural latex were strongly positive. The presence of specific IgE against natural latex was demonstrated by means of a histamine release assay as well as by immunoenzymatic methods. The antigen seems to have a molecular weight higher than 30,000 d and is sensitive to trypsin.

TABLE I. Synthetic nonrubber elastomer gloves

Brand name	Manufacturer	Composition
Tactylon	Smart Practice, 3400 E. McDowell, Phoenix, AZ 85008, 1 (800) 822-8956	Synthetic block copolymer—a thermoplastic elastomer
Elastyren	Allerdam Labs, P.O. Box 931, Mill Valley, CA 94942, 1 (800) 365-6868 (sold NW USA) Hermal Labs, Route 145, Oak Hill, NY 12460, 1 (800) HERMAL-1	Styrene butadiene block polymer; also available as a nonsterile examination glove Styrene butadiene block polymer; also available as a nonsterile examination glove

These facts suggest that the allergen could be a protein present in the crude natural latex.

FDA MEDICAL ALERT ON LATEX ALLERGY

On March 29, 1991, the FDA issued the following medical alert:

ALLERGIC REACTIONS TO LATEX-CONTAINING MEDICAL DEVICES

Because of reports of severe allergic reactions to medical devices containing latex (natural rubber), FDA is advising health-care professionals to identify their latex-sensitive patients and be prepared to treat allergic reactions promptly. Patient reactions to latex have ranged from contact urticaria to systemic anaphylaxis. Latex is a component of many medical devices, including surgical and examination gloves, catheters, intubation tubes, anesthesia masks, and dental dams.

Reports to FDA of allergic reactions to latex-containing medical devices have increased lately. One brand of latex-cuffed enema tips was recently recalled after several patients died as a result of anaphylactoid reactions during barium enema procedures. More reports of latex sensitivity have also been found in the medical literature. Repeated exposure to latex both in medical devices and in other consumer products may be part of the reason that the prevalence of latex sensitivity appears to be increasing. For example, it has been reported that 6% to 7% of surgical personnel and 18% to 40% of spina bifida patients are latex sensitive.

Proteins in the latex itself appear to be the primary source of the allergic reactions. Although it is not now known how much protein is likely to cause severe reactions, FDA is working with manufacturers of latex-containing medical devices to make protein levels in their products as low as possible.

THE USE OF SYNTHETIC NONRUBBER GLOVES IN THE MANAGEMENT OF RUBBER (LATEX) GLOVE ALLERGY¹¹⁻¹⁸

Although vinyl gloves are safe for individuals sensitive to rubber, such gloves may fatigue easily, developing cracks or holes that may admit the AIDS virus. Also, the tactile feel of vinyl is not satisfactory to many surgeons. The nonrubber synthetic (Aller-derm Labs., Mill Valley, Calif.) gloves mentioned in Table I are as strong as natural latex gloves and have

a satisfactory tactile feel for the surgeon. These gloves protect the surgeon and patient from both the immediate urticarial and the delayed eczematous reaction. Thus both the surgeon and patient are protected against iatrogenic and intraoperative allergic latex rubber reactions.¹⁹⁻²¹

ALLERGIC REACTIONS TO RUBBER (LATEX) CONDOMS

The incidence of condom dermatitis is likely to escalate as a result of the increase in the use of condoms because of the rise in publicity concerning the use of condoms to prevent infection from sexually transmitted diseases. Condoms, popularly called "sheaths," "French letters," "prophylactics," "rubbers," "skins," or "safes," are made of rubber.

On acquiring a rubber dermatitis most individuals not realizing that they may be allergic to rubber mistakenly fear that they have acquired a venereal disease.

As in allergic reactions to rubber gloves, sensitized individuals may acquire an immediate urticarial reaction or a delayed eczematous reaction.

Immediate-contact urticaria caused by rubber condoms

Turjanmaa and Renula²² investigated the occurrence of latex allergen in condoms, the symptoms caused by contact with condoms, and 46 patients with latex-glove contact urticaria. Seven (24%) of the 29 patients with a history of condom use had had local swelling and/or pruritus during intercourse, confirming that condoms can cause local symptoms in subjects allergic to latex. Prick tests performed on 16 different condom brands showed that four brands caused positive reactions in 52 (67%) of patients. The remaining 12 brands were not as allergenic, and one brand was totally negative on prick testing. One highly allergenic condom brand was examined by high pressure liquid chromatography, which showed similar protein profiles to those detectable in latex gloves and natural rubber. These results show that, in addition to rubber gloves and balloons, condoms should also be considered as possible sources of latex.

Cornstarch as a cause of contact urticaria in rubber gloves and condoms

Most surgical gloves contain corn starch powder, whereas most condoms contain talc, with the exception of the transparent variety.²³

Recently the first cases of allergic contact urticaria caused by cornstarch in surgical rubber gloves in this country were reported.²⁴ One surgeon who acquired an allergic contact urticaria from surgical gloves containing cornstarch also had marked itching, edema, and urticaria within 15 minutes after using a translucent condom containing cornstarch. Fortunately, most condoms are opaque and contain talc, which is not a sensitizer.

Most gloves contain powder, a cornstarch derivative composed of the polysaccharides amylose and amylopectin. One percent magnesium oxide and 1% calcium phosphate are added to the powder by the manufacturer for "flow control" and absorption. A small amount of this powder rubbed into intact skin on the forearm of the patient sensitive to cornstarch produced a large wheal in 20 minutes. Twelve control powders gave negative reactions. The patients did not react to full-strength magnesium oxide or tricalcium phosphate powders.

It should be noted that the powder is used not only to assure smooth donning of the gloves but also to release the mold used in the production process. Most surgical gloves on the market are dusted with starch, but some are still dusted with talc.

Pristine powder-free surgical gloves are manufactured by a molding method that does not use powder as a mold-release agent but rather chemically processes the outer and inner surfaces of the gloves to different degrees of slipperiness for smooth donning and secure holding of instruments. This new method produces surgical gloves that are completely free from talc, starch, and other foreign materials. Pristine gloves, made in Japan, are available in the United States (World Medical Supply, Inc., San Jose, Calif.).

Van der Meeren and Van Erp²⁵ reported life-threatening contact urticaria from glove powder in the Netherlands. Their patient was a 29-year-old male nurse who occasionally had a mild dermatitis. He worked in the intensive care department of a hospital. One hour after starting work, he noted erythema and swelling of both hands that extended to his thorax, head, and neck. The reaction was violent, resulting in a speech disturbance leading to aphonia, glottal edema, and dyspnea with an inspiratory and expiratory stridor.

Grant et al.²⁶ indicated that starch can cause hypersensitivity reactions in patients and also in surgeons who use gloves with cornstarch powder. The implan-

tation of starch powder can produce granulomas in various organs of the patient.²⁷⁻³⁰

It should be emphasized, however, that talc is much less immunogenic than cornstarch powder.²³

Cornstarch urticaria may be tested by applying cornstarch powder "as is" to a scratch on the skin and observing for 45 minutes for urticaria.

Consort condom contact dermatitis

Condom contact dermatitis in patients' sexual partners includes any dermatitis shared by partners of either or both sexes. The sites of condom dermatitis in either sex may include the thighs, lower abdomen, and perianal or anal areas, and such reactions as cheilitis or stomatitis. The dermatitis that can occur at these sites can be either a delayed, eczematous variety caused by rubber sensitizers, or an immediate urticarial variety. The urticarial type of condom dermatitis occurring in the oral mucosa may be accompanied by anaphylactic shock.²³

Delayed eczematous contact dermatitis caused by condoms

In men, contact dermatitis from condoms is usually easy to diagnose, because there is a clear relationship with intercourse, and it is often accompanied by marked penile edema. Allergic reactions to condoms may produce itching and edema of the prepuce or distal part of the shaft of the penis and may also initiate an eczematous dermatitis that may spread to the scrotum, inguinal area, and inner aspects of the thighs. In one patient, the eruption spread to the face, sides of the neck, axillae, and antecubital fossae.²³

Differential diagnosis of condom dermatitis in women

The differential diagnosis of condom allergy includes pubic and groin dermatitis and vulvitis from other contraceptive agents such as spermicidal jellies, creams, and foams, diaphragms and lubricants.

Although the vulvar and vaginal mucosae appear to be somewhat less susceptible to allergic contact sensitivity than the skin, allergic mucosal reactions do occur from rubber condoms. Often, in mild cases, the patient complains of pruritus vulvae or a burning vaginal sensation; little is noted on examination. In more severe degrees of allergic reactions, redness and edema of the vulva occur, and the adjacent skin shows an eczematous reaction.

Women sensitive to rubber can also acquire an acute diffuse dermatitis of the vulva and inner thighs from contact with a rubber condom worn by her partner. In one instance, a vulvitis attributed to an allergic reaction to a condom was actually due to perfume in

a feminine hygiene spray that had been used before and after intercourse.

Patch testing for eczematous condom dermatitis

Table II lists patch test series for condom dermatitis. Two 1-inch squares of the condom should be tested, covered, and left in place for 48 hours. One of the squares used should be from the outside portion of the condom and the other should be from the inside portion. If both squares produce sensitivity, the cause is probably a rubber chemical.

With regard to the inside portion of the condom, the patient should be observed for 45 minutes to determine whether an immediate reaction has taken place. If the patient complains of itching, the patch should be removed and the site inspected for an urticarial reaction that would implicate cornstarch powder. If there is some itching but no urticarial reaction, the patch may be replaced.

If at the end of 48 hours the outside portion of the condom produces a positive reaction but the inside produces a negative reaction, a chemical in the lubricant of the condom is the most likely cause.

Nonrubber condoms

Nonrubber condoms popularly known as "fish skins" include the following:

1. Fourex Natural Lamb Skins (Schmidt, Sarasota, Fla.)
2. Trojan Natural Lamb Skins (Young Drug Products, New York, N.Y.)

These condoms, made of processed sheep intestine (caecum), are not sensitizers. However, they may contain a lubricant that includes perfume, Bronopol (a preservative), and propylene glycol, which may be sensitizers.³¹

These nonrubber condoms can prevent transmission of sperm, but the FDA has ruled that the use of nonrubber condoms may not prevent transmission of the virus that causes AIDS.

Men sensitive to rubber have to use a nonrubber condom with a rubber condom worn over it to protect themselves from AIDS.³²

Sexual partners who are allergic to rubber condoms should require their partner to wear a rubber condom, with a nonrubber variety worn over it.

Future prospects for condoms

With the increased incidence of AIDS there has been an increase in the use of rubber gloves and condoms accompanied by an increase of condom and rubber glove dermatitis.

In 1992, a nonlatex condom, which will resist the

TABLE II. Condom dermatitis patch test series

Rubber chemicals	
Mercaptobenzothiazole	1% in petrolatum
Tetramethylthiuram	1% in petrolatum
Zinc dithiocarbamate	1% in petrolatum
Lubricant sensitizers	
Perfume "mix"	As is
Parabens "mix"	15% in petrolatum
Guar gum	50% in aqueous solution
Nonoxynol 9 (spermicide)	0.9% in aqueous solution

AIDS virus will become available from the manufacturers of Tactylon nonlatex gloves (Smart Practice, Phoenix, Ariz.).

Preliminary testing has shown that these nonrubber condoms made of the same elastomer as Tactylon gloves are well tolerated by individuals sensitive to rubber.

In addition, a new vaginal pouch (female condom) made of polyurethane is being tested and may also become available in the near future (Reality Pouch, Wisconsin Pharmacal, Jackson, Wis.).

MISCELLANEOUS ALLERGIC DERMATITIS IN HEALTH PERSONNEL

Contact dermatitis, particularly of the hands, is an occupational hazard of physicians and surgeons. Frequent washing of the hands with various soaps, detergents, or disinfectant solutions can produce either an irritant or an allergic contact dermatitis. Physicians and surgeons often assume that their hand dermatitis is solely due to occupational exposure. In fact, other etiologic factors may be the actual cause of the dermatitis. Patch testing is required to prove the etiology of such dermatoses.

Antiseptics producing allergic dermatitis in medical personnel

Table III lists those antiseptics that have produced allergic dermatitis in medical personnel.

Glutaraldehyde (patch test 1% aqueous). Health workers are exposed to this antiseptic, particularly in Sporocidin and Cidex used to disinfect endoscopes.³³ Cross reactions may occur with formaldehyde.^{34,35}

Chlorhexidine (patch test 0.5%, prick test 0.005%). Chlorhexidine is unusual in that its salts may produce the following reactions: (1) delayed, eczematous, contact dermatitis; (2) contact urticaria; (3) combined delayed eczematous and immediate urticarial reaction, and anaphylaxis.^{36,37}

TABLE III. Antiseptics that cause allergic dermatitis

Glutaraldehyde
Chlorhexidine
Povidone-iodine (Betadine)
Alcohol
Benzalkonium chloride
Hexachlorophene

Chlorhexidine is at present most commonly used as the diglicomate (Hibiclens, Corrody, Hibidil, Hibistat, Hibiscrub, Plac out, Plurex, Rotersept). Chlorhexidine may produce both an eczematous dermatitis and urticaria.³⁶

Ohtoshi et al.³⁷ encountered a 24-year-old woman who had generalized urticaria and anaphylactic shock shortly after 0.5% chlorhexidine was applied to an elbow wound. These investigators state that the Prausnitz-Kustner test and the radioallergosorbent test gave positive results. In addition, IgE antibodies against chlorhexidine were demonstrated. These authors claim that in Japan 30 cases of anaphylactic shock after exposure to chlorhexidine used in various procedures have been reported.

Cheung and O'Leary³⁸ reported a man who was anesthetized to undergo plastic surgery and went into anaphylactic shock shortly after chlorhexidine acetate was used on the wound and the donor graft site. An intracutaneous test with 0.005% solution of chlorhexidine gave strongly positive results.

Betadine (povidone iodine) (patch "as is" open). Betadine, iodine in polyvinyl pyrrolidone, is an irritant under a closed patch test. Betadine is a rare sensitizer but can irritate the skin, particularly in surgeons who use this antiseptic and put on surgical gloves.³⁹

Alcohol (patch test "as is"). Although it is widely recognized that alcohol can dry and irritate the skin, the possibility of alcohol being a cutaneous sensitizer is usually overlooked. Externally applied alcohol is usually ethyl alcohol, which for this purpose is denatured and is unfit for drinking because of the addition of chemicals. For industrial use, 5% methyl alcohol or acetone is often added to denature ethyl alcohol; for ordinary medicinal use approximately 40 chemicals are available for denaturing it. Most of these substances have a bitter taste or cause emesis. Rubbing alcohol is 70% ethyl alcohol with a denaturing agent. In alcohol used in cosmetics, the added chemicals are odorless and nontoxic. Denatured alcohols used for perfumes and other cosmetics often contain diethyl phthalate.⁴⁰

The most popular denaturing agents in rubbing alcohol include tartar emetic, salicylic acid, quinine

sulfate, colchicum extract, brucine (an alkaloid resembling strychnine), quassia (the bitter principle of a Jamaica wood), and sucrose octaacetate (an anhydrous adhesive used in lacquers). Isopropyl alcohol, which has a slight odor resembling that of acetone, may also be used as a denaturing agent. Pure ethyl alcohol is used in some hospitals, but coloring matter, such as methylene blue or amaranth pink (an azo dye used to color elixir phenobarbital), is added to discourage drinking. Some individuals who have allergic contact sensitivity to alcohol may react to the ingestion of alcohol with a generalized erythema. Reports indicate that allergic reactions to the alcohols are not as rare as formerly believed.

Richardson⁴¹ reported an allergic eczematous contact dermatitis to a commercially available prepackaged alcohol sponge (Preptic Swab, New Brunswick, Conn.). The dermatitis appeared on the hands of nurses and at the sites of electrocardiogram electrode placement (where the sponges were used as conductors) on cardiac patients. Patch tests indicated that the allergen is probably a volatile substance added to sterilize the swab. The actual sensitizer was not discovered.

Contact dermatitis caused by alcohol. Allergic contact dermatitis is caused occasionally by pure ethyl alcohol, and the allergic sensitivity extends usually to amyl, butyl, methyl, and isopropyl alcohols. The dermatitis may take the form of an eczematous eruption or, rarely, an erythematous flush or contact urticaria at the exposed sites.^{42,43} Alcohols, however, are usually irritant.

Systemic contact dermatitis. The ingestion of alcohol or even beer or wine by individuals sensitized by external contact to alcohol may be accompanied by extensive stomatitis, aphthous stomatitis, urticaria, angioedema, morbilliform eruptions, or a flare of eczematous dermatitis at sites affected previously by the external exposure to alcohol.

Van Ketel and Tan-Lim⁴⁴ reported on a patient with an allergic eczematous contact dermatitis from alcohol. This patient also has positive reactions to beer, red wine, sherry, and acetone. Van Ketel and Tan-Lim state that an external reaction to alcohol does not necessarily mean that systemic contact dermatitis will develop after drinking alcoholic beverages.

Testing for allergic alcohol hypersensitivity. Alcohol may be tested undiluted. Two types of reactions may occur: (1) An immediate urticarial contact reaction. This type of reaction to topical applications of alcohol occurs usually within 15 minutes in the form of a bright red erythema with or without urticarial elements, which may persist for 2 hours or more. It is advisable to test for contact sensitivity to alcohol first by the open patch test method and to keep the

patient under observation for an hour or so; and (2) The second type of reaction to patch testing with alcohol may take place after a delay of 24 or 48 hours with the formation of an erythematous, eczematous patch at the patch test site. Occasionally, there is a combination of the immediate and delayed reaction.⁴⁴

Benzalkonium chloride (patch test 0.1% aqueous). Benzalkonium chloride is a quaternary ammonium cationic detergent that has been used as a preoperative skin disinfectant and as a surgical instrument disinfectant. Solutions of benzalkonium chloride support microbial growth. The Association for Practitioners in Infection Control (APIC) did not approve the use of benzalkonium chloride as a surgical scrub. Benzalkonium chloride has produced allergic contact dermatitis in surgical personnel who handled instruments soaked in this antiseptic.⁴⁵ Benzalkonium chloride is present in many over-the-counter products. Health care workers sensitized to benzalkonium chloride need to avoid both occupational and nonoccupational exposures to this detergent.

Benzalkonium chloride has become a frequent sensitizer in ophthalmic solutions.⁴⁶

Hexachlorophene (G11) (patch test 1% in petrolatum). Surgical "scrubs" of the hands often precipitate atopic dermatitis with superimposed contact dermatitis of the hands in surgical personnel who have been free of atopic dermatitis since childhood.⁴⁷

Hexachlorophene is still a popular preoperating scrubbing agent. Many surgeons complain of dryness of the skin from this agent, an effect that is a primary irritant reaction. Allergic reactions to hexachlorophene are rare. Cross-contact sensitivity and photo-contact sensitivity to hexachlorophene have been observed in guinea pigs with primary photosensitivity to tetrachlorosalicylanilide and tribromosalicylanilide. It is not yet generally accepted that hexachlorophene is a primary photosensitizer, although such photosensitivity has been reported.⁴⁸

DERMATITIS AND PARESTHESIA FROM ACRYLIC BONE CEMENT IN ORTHOPEDIC SURGEONS

Patch test methyl methacrylate monomer 5% in petrolatum

In 1971 the FDA approved the use of acrylic bone cement in artificial hip arthroplasty, and it is still used commonly.⁴⁹

The acrylic bone cement denture material is made by mixing methyl methacrylate monomer with the polymer. The monomer usually contains an inhibitor, such as benzoyl peroxide or dimethyl-p-toluidine.

The acrylic bone cement used in orthopedic surgery is self cured and develops considerable heat in the process. Some residual monomer usually remains un-

polymerized. A warning on the package of the bone cement states: "This preparation should not be allowed to come into contact with rubber or rubber gloves." The acrylic bone cement readily penetrates rubber gloves and is capable of actually dissolving several plastic and synthetic rubber compounds.⁵⁰

Pegum and Medhurst⁵¹ and Fisher⁵² reported that these monomers penetrate practically all rubber and polyvinyl gloves. Many orthopedic surgeons have acquired allergic contact dermatitis from the acrylic monomers and have shown strongly positive patch test reactions to methyl methacrylate.

Some sensitized physicians resort to wearing two and even three pairs of gloves. One surgeon reported that by allowing the cement to stiffen before use, there is less penetration of rubber gloves, presumably because a small amount of free liquid monomer is available. Other surgeons with severe hand dermatitis have resorted to having a colleague handle the bone cement during the surgery.

To prevent dermatitis, Maibach and Gellin⁵³ advise mixing the orthopedic cement mechanically and applying it with a spatula. Two pairs of cotton gloves and another pair of rubber gloves over them should be worn. These three pairs of gloves should be removed as soon as possible and discarded. Contaminated instruments should be cleaned immediately, first with dry cotton balls and then with cotton balls wetted with an appropriate solvent (methylethyl ketone or alcohol). Skin contamination should be cleaned locally in the same way and the hands washed with ample soap and water.

Persistent paresthesia occurring in acrylic bone cement dermatitis

Fries et al.⁵⁴ and Fisher⁵⁵ reported that paresthesia of the affected fingers of medical personnel in some cases lasted for months after discontinuation of contact with the cement. After it penetrates the skin, monomethylmethacrylate may have an untoward effect on naked myelinated nerve fibers and on the nodes of Ranvier.⁵⁶ Edwards⁵⁷ has reported neurologic effects from related acrylamide compounds. Several neurologists have suggested in anecdotal reports that since the acrylic monomer is a powerful solvent, it may penetrate deep into the cutis, producing a peripheral neuritis caused by an inflammatory effect on the nerve endings.

Allergic reactions of acrylic bone cement in patients

Some controversy exists as to whether the rejection of an artificial hip joint might be caused by an allergic reaction to the methyl methacrylate monomer. Monteny et al.⁵⁸ have suggested such a possibility.

Rapaport⁵⁹ has reported that numerous patients have been studied in various centers for potential allergic sensitizations to either the metals or the acrylic monomers. There have been several isolated reports of sensitivity to cobalt, an ingredient of the prosthetic devices. There have been no reports of cases of sensitivity to acrylic bone cement in patients.

Fitzgerald and Kelly⁶⁰ state that fixation of prosthetic devices with methyl methacrylate appears safe. Recently Waterman and Schrik⁶² performed a prospective study in 85 patients of the relationship between implantation of metal-to-polyethylene hip prostheses and the incidence of delayed type of allergy to components of the prostheses. This report showed that sensitization to cobalt, nickel, chromate, and methylmethacrylate can develop as a result of such implantation. Loosening did not occur in any of the cases of possible sensitization. Evidence of allergy in prosthetic components was not found in any of the 10 cases of loosening.

Maibach and Gellin⁵³ theorized that perhaps the delayed type of allergy to methyl methacrylate monomer has been found only infrequently in patients undergoing hip surgery because the sensitizers in these glues initially come in contact with the bloodstream and may promote the production of repressor cells. When the number of repressor cells exceeds the number of effector T cells there is no danger of allergy. A second possibility is that other acrylic compounds, their metabolites, or additives present in the commercial cements are responsible for sensitization.

In a personal communication, Dr. Rudolph Baer of New York University Medical Center, suggested that the paucity or absence of Langerhans' cells in the acetabulum may explain the rarity of allergic sensitization of patients to acrylic bone cement.

COMMENTS

Although orthopedic surgeons frequently become sensitized to the acrylic bone cement used in artificial hip operations and experience severe dermatitis and paresthesia, patients very rarely, if ever, become sensitized. The presence of numerous Langerhans' cells in the skin and their absence in the acetabulum may explain this difference.

FORMALDEHYDE (PATCH TEST) 1% AQUEOUS

One half million American hospital workers are routinely exposed to formaldehyde. Exposure may occur in areas such as autopsy rooms, pathology laboratories, and renal dialysis units. Formaldehyde is a strong cutaneous irritant.⁶² Allergic contact dermatitis

to formaldehyde used to sterilize hemodialysis equipment and thermometers has been reported in nurses.^{63,64} Formaldehyde was the most common cause of allergic contact dermatitis among medical personnel at the Municipal Hospital Schwabing in Munich, Germany, and among nurses in Warsaw, Poland. Formaldehyde has been discontinued as a disinfectant in some hospitals and dental offices, and allergic contact dermatitis to formaldehyde has become less commonly reported.⁶⁵ Most work gloves appear to provide adequate protection against formaldehyde.

ANTINEOPLASTIC DRUGS

Many antineoplastic drugs are cutaneous irritants. Mechlorethamine, chlorambucil, N, N-bis (2-chloroethyl)-N-nitrosourea (BCNU), N-(2-chloroethyl)-N'-cyclohexyl-N-nitrosourea (CCNU), 5-(dimethyl-triazene) imidazole-4-carboxamide (DTIC), methotrexate, vindesine, actinomycin D, daunorubicin, bleomycin, mitomycin C, l-asparaginase, hexamethylmelamine, and hydroxyurea are reported to cause irritant contact dermatitis. 5-Fluorouracil (5-FU) and cyclophosphamide were considered to be less irritating to intact skin. Antineoplastic drugs are potential mutagens and teratogens for health care workers. Protective clothing and disposable gloves should be used during preparation and administration of antineoplastics. Chemotherapy solutions should be prepared in specialized work areas by pharmacists with special training.⁶⁶

Nitrogen mustard dermatitis in dermatologists (patch test "as is" open)

Several dermatologists were studied who, although they wore rubber gloves, acquired an allergic contact dermatitis to nitrogen mustard, which they had applied to their patients for the treatment of mycosis fungoides. It should be emphasized that rubber gloves are readily penetrated by nitrogen mustard. However, heavy-duty vinyl gloves will protect the physician. Contact urticaria and anaphylactoid reactions may develop in individuals sensitized to nitrogen mustard.^{67,68}

Mitomycin-C (patch test 0.1% aqueous)

Mitomycin-C (Mutamycin) is classified as an antibiotic aminoquinone alkylating agent that is instilled intravesically for the treatment of superficial bladder cancer. Mitomycin is isolated from *Streptomyces caespitosus*.⁶⁹

CASE REPORT

A 60-year-old man noted a severe eruption on the penis, thighs, lower abdomen, and buttocks. The unusual feature of the eruption is that it began after the first instillation of

mitomycin-C, whereas in previous case reports the allergic reaction occurred only after several instillations of the agent. This patient had previously handled mitomycin-C in his job as a nurse and gave a history of dermatitis of his hands. This may have been an allergic reaction from occupational exposure to mitomycin-C. Thus his severe allergic reaction after initial treatment with mitomycin-C may have been due to the fact that he was already sensitized to the drug.⁷⁰

The dermatitis is probably of a delayed contact variety from contact of the urine containing mitomycin-C.^{71,72}

Patch testing should be performed with freshly prepared 0.1% aqueous solution, which is the same concentration as that used therapeutically.

The handling of antitumor drugs by health personnel without proper protection is hazardous. The patient was probably sensitized by handling mitomycin-C and subsequently had a severe allergic contact dermatitis after the initial instillation of mitomycin. The patient described here probably was sensitized by previous handling of mitomycin-C in his work as a nurse, so that the initial instillation of mitomycin-C produced a widespread dermatitis.

Most recently, the FDA has approved the instillation of bacillus Calmette-Guerin for treatment of superficial bladder carcinoma. Thus patients who do not tolerate mitomycin-C may now be treated with bacillus Calmette-Guerin.

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