

Clinical Commentary Review

Surgery-Related Contact Dermatitis: A Review of Potential Irritants and Allergens

Kevin A. Cook, MD, and John M. Kelso, MD *San Diego, Calif*

Surgical procedures utilize an increasing number of medical products including antiseptics, anesthetics, gloves, suture materials, tissue adhesives, topical antibiotics, and bandages. Many of these products have irritant potential. Allergic contact dermatitis has also been reported. This review covers preoperative, operative, and postoperative exposures that may result in contact dermatitis. Testing with standard patch panels such as T.R.U.E. Test and the North American Contact Dermatitis Group 65 allergen series does not evaluate for all relevant contactants. A thorough understanding of potential exposures is vital to effectively evaluate a patient with surgery-related contact dermatitis. A systematic approach is needed to ensure that standard patch panels and supplementary patches adequately address each encountered contactant. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

Key words: Contact dermatitis; Surgery-related contact dermatitis; Antiseptic; Anesthetic; Adhesive allergy; Cyanoacrylate

The early years of surgery were defined by frequent complications in the absence of anesthesia and antisepsis. Surgery was often considered a last resort with anticipated pain and frequent surgical site infections.¹ Over the last century significant improvements have been made in antiseptics, anesthetics, surgical instruments, and methods of surgical wound closure. A variety of new products continue to improve and refine these areas. Although surgical outcomes and infection rates have improved,¹ a number of these products have been implicated in surgery-related contact dermatitis.^{2,3} Many of these products, such as natural rubber latex (NRL), have been implicated in type I immediate hypersensitivity reactions as well. This review will focus on type IV delayed hypersensitivity related to surgical exposures.

Contact dermatitis related to surgical exposures is typified by delayed onset pruritus and a papulovesicular rash manifesting 48 to 96 hours after surgery.⁵ Inflammatory mechanisms may include a direct irritant effect or a delayed hypersensitivity

reaction resulting in allergic contact dermatitis.⁴ Both may result in poor wound healing and, in some cases, wound dehiscence.⁵ In the case of allergic contact dermatitis, inflammation may persist for weeks after discontinuation or removal of the offending contactant.⁴ Inflammation around the surgical site may sometimes be confused with cellulitis, leading to unnecessary antibiotics and delay in definitive management.

Even when contact dermatitis is suspected, it may be difficult to determine the causative agent. However, because surgical procedures are conducted in a highly systematic fashion, it is possible to identify all the products that were used. This includes preoperative application of antiseptics and anesthetics, operative intervention using sterile metallic instruments, and postoperative wound closure and aftercare. Each step involves exposure to potential irritants and allergenic contactants. Evaluation of surgery-related contact dermatitis requires a thorough understanding of potential exposures and a history detailing all encountered contactants. Complete evaluation may then be conducted by patch testing with contactants and their ingredients. With a growing number of surgical indications and approaches, it has become increasingly important to identify the causative agent of contact dermatitis and to identify acceptable alternative products when available, to recommend for future surgeries to avoid recurrence.

PREOPERATIVE CONTACTANTS

Antiseptics

Antiseptics are applied topically to areas within the planned surgical field to reduce the risk of infection. Many of the first antiseptics contained high levels of elemental iodine. Use of these preparations was limited by a short duration of action and high irritant potential.⁶ Newer preparations utilize an iodophor, a preparation containing iodine complexed with a solubilizing agent such as povidone, which aids in product dispersion and reduces exposure to free iodine. Betadine branded products contain 7.5% to 10% povidone-iodine. The concentration of free iodine in povidone-iodine is highest in its liquid form, with lesser irritant potential on drying.⁶ Thus, the greatest risk of irritant contact dermatitis stems from pooling of iodine containing antiseptics beneath a patient, which may be obscured by a surgical drape.⁷ Although irritant reactions are not uncommon, povidone-iodine has also rarely been implicated as a cause of allergic contact dermatitis.⁸⁻¹² Irritant potential must be considered when patch testing. One study patch-tested 500 patients with 1% povidone-iodine aqueous diluted in water. Fourteen patients tested positive, although only 2 of the 14 reacted during repeat open application testing. From this the authors concluded that patch testing with aqueous povidone-iodine may lead to false positives.¹³ Repeat open application testing ensures clinical relevance, an important consideration

Division of Allergy, Asthma and Immunology, Scripps Clinic, San Diego, Calif
No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication November 1, 2016; revised February 6, 2017; accepted for publication March 1, 2017.

Available online ■■

Corresponding author: Kevin A. Cook, MD, Division of Allergy, Asthma and Immunology, Scripps Clinic, 3811 Valley Centre Dr., S99, San Diego, CA 92130.
E-mail: cook.kevin@scrippshealth.org.

2213-2198

© 2017 American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaip.2017.03.001>

Abbreviations used

NACDG 65-North American Contact Dermatitis Group 65
allergen series
NRL-Natural rubber latex
PABA-Para-aminobenzoic acid

when known irritants are being tested under occlusion.⁴ Patch testing with dried 10% povidone-iodine solution has also been advocated to reduce false-positive results.¹⁴

Another commonly used antiseptic is chlorhexidine. Chlorhexidine demonstrates broad antibacterial activity against both gram-negative and gram-positive organisms. It has been utilized since the 1970s in a wide variety of products including consumer handwash and mouthwash, as well as in medical products such as vascular catheters, sponge dressings, and topical surgical preparations.¹⁵ Surgical preparations such as ChlorPrep and Hibiclens contain 2% to 4% chlorhexidine. These preparations have become increasingly favored in the operating room with demonstrated reduction in surgery-related infections when compared with iodophors.¹⁶ Chlorhexidine also carries the potential for irritant reactions,¹⁷ but is also rarely reported as a cause of patch test-proven allergic contact dermatitis.¹⁸⁻²⁰

Many chlorhexidine-based antiseptics contain isopropyl alcohol. For instance, ChlorPrep and Hibiclens contain 70% and 4%, respectively. Isopropyl alcohol can also be found in presoaked alcohol swabs used at IV insertion sites, injection sites, and for minor dermatologic procedures. Historically, isopropyl alcohol has been cited as a mild skin and eye irritant with little known allergenic potential. However, a large case series of patients with various eczematous skin lesions and a history of isopropyl alcohol exposure demonstrated sensitization by patch testing in 3%.²¹ This suggests that allergic contact dermatitis to isopropyl alcohol is more common than previously thought, although case reports remain rare.

Skin pen markers

Skin pen markers are often used preoperatively to mark the planned surgical site and to provide orienting landmarks. A few cases of contact dermatitis have been reported due to these pens, and have identified dye and other components as the offending allergens.^{22,23} The relative paucity of cases may reflect the rather minimal surface area of exposure to the ink and typical removal after surgery.

Anesthetics

Local anesthetics may be applied topically and/or injected into the soft tissues near the surgical site. Both methods may result in an allergic contact dermatitis in sensitized patients.²⁴⁻³⁰ IgE-mediated immediate hypersensitivity reactions have also very rarely been reported.^{31,32} Local anesthetics are typically grouped into structural classes. Para-aminobenzoic acid (PABA)-based anesthetics are commonly referred to as esters, whereas non-PABA anesthetics are referred to as amides.⁴ Amide anesthetics are felt to be uncommon sensitizers,³³ whereas benzocaine, an ester, is the most prevalent anesthetic causing allergic contact dermatitis.³⁴ Anesthetics within each structural group demonstrate some cross-reactivity³⁵ (Table I). Therefore, it is recommended that patients experiencing allergic contact dermatitis to a particular anesthetic should avoid all structurally related anesthetics.⁴

TABLE I. Local anesthetics by the structural group

Esters	Amides
Benzocaine	Bupivacaine
Chloroprocaine	Dibucaine
Cocaine	Lidocaine
Procaine	Mepivacaine
Tetracaine	Ropivacaine

Lidocaine is the most commonly used anesthetic in the surgical setting^{27,31} and is available in an assortment of topical products as well as injectable forms. Lidocaine containing topical products include EMLA (Astra Pharmaceuticals, Wilmington, Del), BLT (Wedgewood Pharmacy, Swedesboro, NJ), LMX-4 (Ferndale laboratories Inc., Ferndale, Mich), and Topicaine (Ebsa Laboratories, Jupiter, Fla) amongst others. Many of these products are now available over the counter. Fortunately, the prevalence of lidocaine sensitization is less than 1%.³⁴

OPERATIVE CONTACTANTS

Gloves

Protective gloves are a common cause of allergic contact dermatitis in the wearer, but rarely in the surgical patient. Gloves are considered a mandatory component of universal precautions and serve to protect the surgeon from blood borne pathogens and to prevent transmission of microorganisms from the surgeon to the surgical site. NRL gloves became popular in the 1980s³⁶ with increasing use spurred by the emergence of HIV. Immediate hypersensitivity reactions became increasingly prevalent with the use of NRL products.³⁷ More recently, regulations for lower protein content in NRL gloves, as well as the use of non-powdered gloves, have reduced rates of NRL sensitization.³⁸ These reactions are due to IgE-mediated sensitization to NRL. Contact dermatitis due to rubber gloves, however, occurs by a different mechanism that does not involve the latex component. Instead, delayed hypersensitivity reactions are due to sensitization to rubber accelerants, including mercapto compounds, thiurams, thioureas, and carbamates, that improve elasticity of rubber products and prevent fracturing.³⁹

Because of increased risk of NRL sensitization in health care workers relative to the general population, there is now a mandate for latex-free alternatives. Nitrile gloves have become an increasingly popular substitute. Notably, production of nitrile gloves also requires the use of many of the same accelerants.⁴⁰ Carbamates are the most common accelerants used in both nitrile and latex gloves, although thiurams are regarded as the most common causes of allergic contact dermatitis due to protective gloves.⁴¹ Accelerant-free gloves may be used in sensitized patients.

Metals

There is much debate regarding the potential role of metal allergy in orthopedic implant failures. Weight bearing orthopedic implants are typically composed of cobalt-chromium alloys (may contain small amounts of nickel) or titanium-aluminum alloys.⁴² Static hardware such as plates and screws may utilize stainless steel made of chromium-iron and nickel.⁴³ Although nickel is the most common metal sensitizer, followed by cobalt and chromium,⁴¹ there is currently an evolving and unclear link with

joint implant failure.^{44,45} However, there are several cases describing dermatitis of the skin overlying the implant site with resolution of dermatitis after explantation, implying a causal relationship.⁴⁶ It is now suggested that patch testing before placement of a metal orthopedic implant be limited to patients with a clear self-reported history of metal allergy.⁴⁷ Although a causative association between metal sensitization and implant failure is often unclear, it seems prudent to avoid implanting metals to which a patient is clearly sensitized preoperatively. Patch testing postoperatively in a patient with evidence of joint failure must be interpreted with caution as sensitization does not confirm a causative role. All factors that may lead to joint failure or overlying dermatitis should be considered before weighing risk-benefit of device explantation.⁴⁷ An extensive review covering the composition of select alloys and proposed diagnostic materials for metal implant hypersensitivity has previously been published.⁴⁸

Metal implants also include cardiac stents, septal patches, implantable pacemakers and wires, defibrillators, and intrauterine devices. With extended exposure to these devices, metal allergy may potentially be problematic. Currently, reports suggesting allergic reactions to these devices are rare.^{49,50}

The role of metal allergy in other surgical procedures is not well described. Metal instruments serve a variety of utilities and include sharp tools for incision and cutting, retractors, clamps, and ports for laparoscopic surgeries. Although these instruments are also typically made of stainless steel and presumably could result in allergic contact dermatitis in a metal-sensitized patient, a review of the medical literature failed to reveal any cases attributed to transient exposures to metal instruments. Perhaps this is a reflection of the brevity of exposure, with negligible release of free metal ions. One study found that low-sulfur stainless steel, even when containing small amounts of nickel, was a very slow releaser of nickel.⁵¹ Patch testing to low-sulfur stainless steel in nickel-sensitized patients proved negative. Thus, with most surgical procedures metal allergy is an unlikely cause of surgery-related contact dermatitis.

POSTOPERATIVE CONTACTANTS

Sutures

Postoperative exposures primarily include products used for surgical wound closure and subsequent wound care. For major surgical procedures, sutures are routinely used to aid in wound closure. A variety of materials have been used as suture thread. Relevant suture characteristics include natural versus synthetic, braided versus monofilament, absorbable versus nonabsorbable, and coated versus uncoated.⁵² Sutures are more frequently implicated as irritants rather than allergens. The irritant effect is similar to that observed with other foreign bodies within the skin. Product characteristics that increase suture irritant potential include larger caliber, braided rather than monofilament, longer time since placement, and use of natural materials such as silk or catgut. Placement in the upper dermis may also lead to suture "spitting" that may cause further irritation and wound dehiscence.⁵³

Chromic-coated catgut sutures have been implicated as a cause of allergic contact dermatitis.⁵⁴ Contrary to what the name may imply, catgut sutures are derived from purified collagen from the small intestines of ruminant animals such as cattle, sheep, or goats. Chromic salt coating is often applied to enhance tensile

strength and increase time to absorption. Thus, chromic catgut sutures contain 2 materials with allergenic potential: collagen and chromic salts. Chromic salts are commonly used in reflective paints, dyes, and leather tanning providing potential sources for previous sensitization.⁴ Chromic-coated suture products list a history of allergic contact dermatitis to chromium/chromates as a contraindication for use. A review on chromic catgut sutures found increased frequency of postoperative adhesions, wound dehiscence, and infection in patients sensitized to chromate.⁵⁴ There have also been reports of IgE-mediated reactions to catgut collagen with variable cross-reactivity with dietary collagen such as gelatin.⁵⁵ Silk sutures have been reported as a common cause of foreign body reactions and rarely as a cause of allergic contact dermatitis.^{56,57}

Sutures may also be coated with antibiotics. One of every 3 suture products sold in the United States contains an antibiotic coating.⁵⁸ Triclosan, a compound with antibacterial and antifungal properties, is often used.⁵⁹ Triclosan is found in many hygiene products including hand soaps, hand sanitizers, and toothpastes.⁶⁰⁻⁶² Although allergic contact dermatitis has been reported due to triclosan in hygiene products,⁶³ it has also rarely been reported as a cause of dermatitis due to antibiotic-coated sutures.⁵⁸ Nonetheless, product manufacturers recommend avoidance of triclosan-coated sutures in patients reporting a history of triclosan allergy.

Synthetic sutures such as Vicryl and Monocryl are also a rare cause of allergic contact dermatitis.^{64,65} These products are composed of large polymers that slowly degrade to glycolic acid over weeks. Reactions to synthetic sutures are more likely to be irritant, especially if large caliber or braided.

Tissue adhesives

Tissue adhesives containing cyanoacrylates are often used in conjunction with sutures or independently for smaller wound closures. Popular products include Dermabond (2-octyl cyanoacrylate), Indermil (butyl cyanoacrylate), and Histoacryl (butyl cyanoacrylate) amongst others. These products improve approximation of wound edges and enhance the integrity of the healing wound. Medical tissue adhesives are closely related to commercial "super glues" that contain methyl cyanoacrylate.⁶⁶ The R-chain alkane substituent in medical tissue adhesives has been lengthened that slows polymer degradation and produces less toxic degradation products.^{67,68} However, the increasing frequency of the use of tissue adhesives has coincided with a growing number of cases of allergic contact dermatitis due to cyanoacrylate-containing products.^{5,69-76}

Tissue adhesives such as Dermabond contain a number of ingredients in addition to the cyanoacrylate adhesive. Although the precise composition of these proprietary products is not publically available, they are known to contain dyes, plasticizers, polymerization inhibitors, and small amounts of formaldehyde.⁵ Accordingly, although patch testing with tissue adhesive products "as is" may confirm sensitization, it fails to identify the causative ingredient. More than 30 cases of allergic contact dermatitis to Dermabond have been published to date, although none have definitively identified the allergenic ingredient.^{5,69-76} However, an abstract presented in 2012 confirmed cyanoacrylate as the allergenic ingredient in 2 cases of allergic contact dermatitis due to tissue adhesives, by patch testing to high-purity cyanoacrylates.⁷⁷ Patch testing to Dermabond on intact skin has been reported to yield some false negatives, with sensitization

confirmed when repeat patch testing was performed on abraded skin.^{74,78} If the index of suspicion remains high despite negative patch testing on intact skin, it would be reasonable to repeat testing on abraded skin to more accurately replicate clinical use.

Methacrylates, such as methyl methacrylate, are commonly found in bone and dental cements and share structural similarities to cyanoacrylates. However, there is no consensus regarding cross-reactivity.^{79,80}

Staples

Surgical wounds may also be closed by metallic staples. Staples may be preferred for longer incisions and lacerations to facilitate rapid closure. Staples are typically composed of stainless steel, although titanium alloys may also be used particularly in patients with known allergy to nickel or chromium.⁴⁸ Reaction to surgical staples may be the first indication of a metal allergy. A detailed history should identify all components of wound closure, including sutures, staples, and tissue adhesives, that may be used alone or in combination.

Topical antibiotics

Topical antibiotics are notorious skin sensitizers leading to allergic contact dermatitis.⁸¹ In fact, many preparations that have historically been used have been removed from the market for this reason. Topical penicillins were frequently prescribed in the first half of the 20th century, but are no longer used because of high rates of sensitization. There are reports of systemic eczematous reactions in patients sensitized to topical penicillins on re-exposure with parenteral preparations.⁸² More recently, over-the-counter topical antibiotics have become popular with preparations including neomycin, bacitracin, and polymyxin B. Bacitracin may also be added to sterile saline and used for wound irrigation.⁸³ Aminoglycosides, such as gentamicin and tobramycin, may be impregnated into bone cement.

Neomycin has emerged as one of the most common causes of allergic contact dermatitis in the United States.⁴¹ It is the most sensitizing of all topical antibacterials since topical penicillin was banned. The prevalence of sensitization is estimated as 1% of the general population,⁸⁴ with much higher rates in patients with frequent use and/or poor skin integrity. For example, neomycin sensitization is reported in 30% of patients with stasis ulcers, 15% with chronic otitis externa, and 5% with eczema.^{85,86} Although bacitracin does not exhibit cross-reactivity with neomycin, high rates of cosensitization have been reported.⁸⁷ This is likely a reflection of frequent concurrent use in products such as Neosporin and other triple antibiotics. Polymyxin B is a less common cause of contact dermatitis despite being the third component of triple antibiotic preparations.⁸⁸

High rates of sensitization to topical antibiotics and concerns related to increasing antibiotic resistance have led to more selective use. Petroleum-based antibiotic preparations may also result in dissolution of cyanoacrylate tissue adhesives. For these reasons, topical antibiotics are no longer routinely used in the postsurgical setting.^{89,90} However, their broad availability as home first aid products may lead to patient use, even in the absence of a physician recommendation. Consequently, topical antibiotics remain a frequent cause of surgery-related contact dermatitis.⁸¹

Wound dressings

Wound dressing products include tapes, self-adhesive bandages, and liquid adhesives such as Mastisol. Bandages are

TABLE II. Standard patch series and included surgery-related contactants

Contactant	T.R.U.E. Test	NACDG 65 series
Antiseptics	None	None
Anesthetics	PABA derivatives	PABA and non-PABA derivatives
Rubber accelerants	Carba-, mercapto-, thiuram mixes	Carba-, mercapto-, thiuram, thiourea mixes
Metals	Nickel, chromium, cobalt, gold	Nickel, chromium, cobalt
Sutures	Chromic salt	Chromic salt
Cyanoacrylate tissue adhesives	None	None
Bandages	Colophony	Colophony, methacrylate
Topical antibiotics	Neomycin, bacitracin	Neomycin, bacitracin

NACDG 65, North American Contact Dermatitis Group 65 allergen series; PABA, para-aminobenzoic acid.

composed of padding, backings (which may contain rubber products), and adhesives (methacrylate, epoxy diacrylate, etc.) and may also be impregnated with medications including antibiotics.⁹¹ Wound dressings have been identified as an emerging source of methacrylate sensitization.⁹² Although there is certainly allergenic potential with the use of many of these products, it appears that allergic contact dermatitis due to wound dressings is less common than reported. In a series of 24 patients with self-reported allergic contact dermatitis to medical adhesive bandages, patch tests were performed with 158 potential contactants and 10 tapes and bandages in their whole form.⁹³ A clinically relevant allergen was identified in only 4 patients: Mastisol (contains gum mastic, styra, methyl salicylate, and alcohol), neomycin/bacitracin (2 different patients), and cortisone-10 cream. There were no positive allergic reactions to tapes or bandages. However, 8 of 11 patients who left bandages and tape in place for 7 days experienced an irritant reaction. This suggests that many of the reported reactions to wound dressing products may be irritant rather than allergic contact dermatitis.

DIAGNOSTIC EVALUATION

The diagnostic evaluation for surgery-related allergic contact dermatitis begins with a thorough history regarding potential exposures as outlined above. It is important to understand which contactants may then be assessed by a standard patch panel and which products must be tested separately (Table II). T.R.U.E. Test is currently the only FDA-approved test for contact dermatitis. Additional patch test reagents may be purchased from abroad, including the North American Contact Dermatitis Group 65 allergen series (NACDG 65) that is available in Canada (Dormer Laboratories Inc., Toronto, and SmartPractice Canada, Calgary). Targeted patch test panels, such as a dental series, may also be purchased for more focused testing.

T.R.U.E. Test includes a panel of 36 allergens. This panel includes PABA-derived anesthetics, rubber accelerants, metals, chromic salt, colophony adhesive, neomycin, and bacitracin. However, sensitization to antiseptics, non-PABA-derived anesthetics, cyanoacrylate and methacrylate adhesives, and suture materials are not assessed. With regard to the NACDG 65 series, this panel includes both PABA- and non-PABA-derived anesthetics, rubber accelerants, metals, chromic salts, methacrylates,

TABLE III. Recommended concentration and vehicle for patch testing of selected surgery-related contactants not included in a standard patch series

	Contactant (product)—recommended patch test concentration and vehicle
Antiseptics	- Povidone-iodine (Betadine)—10% aq dried before application¹⁴ - Chlorhexidine gluconate (Chloraprep, Hibiclens)—1% aq¹⁷ - Chlorhexidine acetate (Nolvasan)—0.5% aq¹⁷ - Isopropyl alcohol (Chloraprep, Hibiclens)—10%⁴
Anesthetics	Depends on -caine, examples: - Lidocaine (Xylocaine)—5%-15% pet^{27,29,94} - Benzocaine—5% pet^{95,96} Consider a standard patch series
Rubber accelerants	Consider a standard patch series (see Table II for included contactants)
Metals	Consider a standard patch series (see Table II for included contactants)
Sutures	- Potassium dichromate for chromic coated - Otherwise single interrupted stitch with suspected product
Cyanoacrylate tissue adhesives	- Tissue adhesive product (Dermabond, Indermil, Histoacryl)—“as is”^{5,70-72,74,76,78} - Ethyl cyanoacrylate—10% pet⁷⁷ - Other cyanoacrylate (if available)—10% pet⁷⁷ Consider testing on abraded or tape-stripped skin if negative
Bandages	Dressings/bandages—square piece “as is” Consider leaving tapes and adhesive bandages in place for 7 d for irritant evaluation ⁹³
Topical antibiotics	Consider a standard patch series (see Table II for included contactants)

aq, Aqueous; pet, petrolatum.

colophony, neomycin, and bacitracin. It is estimated that 25% to 33% of reactions detected by the NACDG series would be missed by the T.R.U.E. test series because of omitted allergens.⁴¹ However, the NACDG series still fails to assess for sensitization to antiseptics, suture materials, and cyanoacrylates. Thus, neither the T.R.U.E. Test nor the NACDG 65 series alone adequately evaluate all surgery-related exposures.

It is therefore critical to expand testing by placing additional patches. Placement of additional patches should be guided by the history of exposures and “gaps” in the standard panel used (T.R.U.E. Test or NACDG 65 series). Surgical materials may sometimes be acquired from the referring surgeon. It is worth noting that many of these products are composed of a mix of active and inactive ingredients. Definitive evaluation of reactions to such materials also requires testing to individual ingredients. However, manufacturers may be unwilling to provide a complete list of inactive ingredients in their proprietary products.

Patch testing with contactants that are not available through allergen suppliers often requires selection of an appropriate diluent and subsequent dilution to a nonirritating concentration. Fortunately, many contactants have been previously tested at varying concentrations, and recommended test concentrations have reported in the literature.⁴ A compilation of these recommendations is provided in Table III. When suture materials are suspected as a cause of allergic contact dermatitis, a single

interrupted suture may be placed in lieu of a patch to more accurately replicate common use.⁶⁴

Lastly, a high index of suspicion despite negative patch testing may necessitate additional specialized testing to simulate surgery-related exposure. Surgery-related allergic contact dermatitis is unique in that it involves contactant exposure on an open surgical wound. This almost certainly increases allergenic and irritant potential. Patch or repeat open application testing on skin prepped with adhesive tape-stripping or abrasion may be considered to evaluate for false negatives that can occur on intact skin.^{74,78} Tape-stripping allows for slight disruption of the epidermal barrier enhancing allergen penetration. Alternatively, the skin may be lightly abraded with a sharp instrument such as a prick test applicator. A negative result on abraded or tape-stripped skin satisfactorily rules out clinically relevant sensitization.⁷⁴

CONCLUSIONS

Modern surgical procedures utilize an assortment of products to reduce the risk of infection, anesthetize incision sites, and close surgical wounds. Although these products have improved surgical outcomes, they sometime result in contact dermatitis. Irritant potential must first be considered as many of these contactants have harsh chemical properties, particularly at higher concentrations and with extended exposure. Cases of allergic contact dermatitis have also been reported. A thorough understanding of all potential contactants is vital to effectively evaluate a patient with surgery-related contact dermatitis. A systematic approach is needed to ensure that standard patch panels and supplementary patches adequately address each potential contactant. Supplementary patches utilizing products and their ingredients aid in precise identification of the offending contactant. Identification of the allergenic ingredient may allow a recommendation of alternative products to avoid recurrence.

REFERENCES

- Gawande A. Two hundred years of surgery. *N Engl J Med* 2012;366:1716-23.
- Butler L, Mowad C. Allergic contact dermatitis in dermatologic surgery: review of common allergens. *Dermatitis* 2013;24:215-21.
- Rouhani P, Kirsner RS, Amado A, Fleming LE, Nouri K, Jacob SE. Knowledge of surgery-related allergic contact dermatitis among Florida dermatological surgeons: a pilot Study. *J Clin Aesthet Dermatol* 2009;2:33-6.
- Rietschel RL, Fowler JF, Fisher AA. *Fisher's Contact Dermatitis*. 6th ed; Hamilton, Canada: Decker Inc.; 2008.
- Bowen C, Bidinger J, Hivnor C, Hoover A, Henning JS. Allergic contact dermatitis to 2-octyl cyanoacrylate. *Cutis* 2014;94:183-6.
- Fleischer W, Reimer K. Povidone-iodine in antiseptics—state of the art. *Dermatology* 1997;195(Suppl 2):3-9.
- Corazza M, Bulciolu G, Spisani L, Virgili A. Chemical burns following irritant contact with povidone-iodine. *Contact Derm* 1997;36:115-6.
- Ancona A, Suarez de la Torre R, Macotella E. Allergic contact dermatitis from povidone-iodine. *Contact Derm* 1985;13:66-8.
- Erdmann S, Hertl M, Merk HF. Allergic contact dermatitis from povidone-iodine. *Contact Derm* 1999;40:331-2.
- Marks JG Jr. Allergic contact dermatitis to povidone-iodine. *J Am Acad Dermatol* 1982;6(Pt 1):473-5.
- Tosti A, Vincenzi C, Bardazzi F, Mariani R. Allergic contact dermatitis due to povidone-iodine. *Contact Derm* 1990;23:197-8.
- Velazquez D, Zamberk P, Suarez R, Lazaro P. Allergic contact dermatitis to povidone-iodine. *Contact Derm* 2009;60:348-9.
- Lachapelle JM. Allergic contact dermatitis from povidone-iodine: a re-evaluation study. *Contact Derm* 2005;52:9-10.
- Kozuka T. Patch testing to exclude allergic contact dermatitis caused by povidone-iodine. *Dermatology* 2002;204(Suppl 1):96-8.
- Silvestri DL, McEnery-Stonelake M. Chlorhexidine: uses and adverse reactions. *Dermatitis* 2013;24:112-8.

16. Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, Carrick MM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med* 2010;362:18-26.
17. Knudsen BB, Avnstorp C. Chlorhexidine gluconate and acetate in patch testing. *Contact Derm* 1991;24:45-9.
18. Ebo DG, Stevens WJ, Bridts CH, Matthieu L. Contact allergic dermatitis and life-threatening anaphylaxis to chlorhexidine. *J Allergy Clin Immunol* 1998;101(Pt 1):128-9.
19. Goon AT, White IR, Rycroft RJ, McFadden JP. Allergic contact dermatitis from chlorhexidine. *Dermatitis* 2004;15:45-7.
20. Toholka R, Nixon R. Allergic contact dermatitis to chlorhexidine. *Australas J Dermatol* 2013;54:303-6.
21. Garcia-Gavin J, Lissens R, Timmermans A, Goossens A. Allergic contact dermatitis caused by isopropyl alcohol: a missed allergen? *Contact Derm* 2011;65:101-6.
22. Komericki P, Kern T, Aberer W, Kranke B. Contact dermatitis from Solvent Yellow 146 in a permanent marker. *Contact Derm* 2001;44:256.
23. Martin-Garcia C, Conde Salazar L, Gonzalez-Mendiola R, Hinojosa M, Sanchez-Cano H. Contact dermatitis due to Edding 3000. *Allergy* 2004;59:235-6.
24. Amado A, Sood A, Taylor JS. Contact allergy to lidocaine: a report of sixteen cases. *Dermatitis* 2007;18:215-20.
25. Bircher AJ, Messmer SL, Surber C, Ruffi T. Delayed-type hypersensitivity to subcutaneous lidocaine with tolerance to articaine: confirmation by in vivo and in vitro tests. *Contact Derm* 1996;34:387-9.
26. Garcia F, Iparraguirre A, Blanco J, Alloza P, Vincent J, Bascones O, et al. Contact dermatitis from prilocaine with cross-sensitivity to pramocaine and bupivacaine. *Contact Derm* 2007;56:120-1.
27. Mackley CL, Marks JG Jr, Anderson BE. Delayed-type hypersensitivity to lidocaine. *Arch Dermatol* 2003;139:343-6.
28. Perez-Perez LC, Fernandez-Redondo V, Ginarte-Val M, Paredes-Suarez C, Toribio J. Allergic contact dermatitis from EMLA cream in a hemodialyzed patient. *Dermatitis* 2006;17:85-7.
29. Sanchez-Morillas L, Martinez JJ, Martos MR, Gomez-Tembleque P, Andres ER. Delayed-type hypersensitivity to mepivacaine with cross-reaction to lidocaine. *Contact Derm* 2005;53:352-3.
30. Weightman W, Turner T. Allergic contact dermatitis from lignocaine: report of 29 cases and review of the literature. *Contact Derm* 1998;39:265-6.
31. Haugen RN, Brown CW. Case reports: type I hypersensitivity to lidocaine. *J Drugs Dermatol* 2007;6:1222-3.
32. Warrington RJ, McPhillips S. Allergic reaction to local anesthetic agents of the amide group. *J Allergy Clin Immunol* 1997;100(Pt 1):855.
33. Sobanko JF, Miller CJ, Alster TS. Topical anesthetics for dermatologic procedures: a review. *Dermatol Surg* 2012;38:709-21.
34. Fransway AF, Zug KA, Belsito DV, Deleo VA, Fowler JF Jr, Maibach HI, et al. North American Contact Dermatitis Group patch test results for 2007-2008. *Dermatitis* 2013;24:10-21.
35. Melamed J, Beaucher WN. Delayed-type hypersensitivity (type IV) reactions in dental anesthesia. *Allergy Asthma Proc* 2007;28:477-9.
36. Rolland JM, O'Hehir RE. Latex allergy: a model for therapy. *Clin Exp Allergy* 2008;38:898-912.
37. Liss GM, Sussman GL, Deal K, Brown S, Cividino M, Siu S, et al. Latex allergy: epidemiological study of 1351 hospital workers. *Occup Environ Med* 1997;54:335-42.
38. LaMontagne AD, Radi S, Elder DS, Abramson MJ, Sim M. Primary prevention of latex related sensitisation and occupational asthma: a systematic review. *Occup Environ Med* 2006;63:359-64.
39. Heese A, van Hintzenstern J, Peters KP, Koch HU, Hornstein OP. Allergic and irritant reactions to rubber gloves in medical health services. Spectrum, diagnostic approach, and therapy. *J Am Acad Dermatol* 1991;25(Pt 1):831-9.
40. Ponten A, Hamnerius N, Bruze M, Hansson C, Persson C, Svedman C, et al. Occupational allergic contact dermatitis caused by sterile non-latex protective gloves: clinical investigation and chemical analyses. *Contact Derm* 2013;68:103-10.
41. Warshaw EM, Maibach HI, Taylor JS, Sasseville D, DeKoven JG, Zirwas MJ, et al. North American contact dermatitis group patch test results: 2011-2012. *Dermatitis* 2015;26:49-59.
42. Krecisz B, Kiec-Swierczynska M, Chomiczewska-Skora D. Allergy to orthopedic metal implants—a prospective study. *Int J Occup Med Environ Health* 2012;25:463-9.
43. Corcos A. Metallic Alloys. *Drugs & Diseases—Orthopedic Surgery* 2015. Available from: <http://emedicine.medscape.com/article/1230554-overview#a1>. Accessed December 1, 2016.
44. Bravo D, Wagner ER, Larson DR, Davis MP, Pagnano MW, Sierra RJ. No increased risk of knee arthroplasty failure in patients with positive skin patch testing for metal hypersensitivity: a matched cohort Study. *J Arthroplasty* 2016;31:1717-21.
45. Middleton S, Toms A. Allergy in total knee arthroplasty: a review of the facts. *Bone Joint J* 2016;98-B:437-41.
46. Atanaskova Mesinkovska N, Tellez A, Molina L, Honari G, Sood A, Barsoum W, et al. The effect of patch testing on surgical practices and outcomes in orthopedic patients with metal implants. *Arch Dermatol* 2012;148:687-93.
47. Schalock PC, Crawford G, Nedorost S, Scheinman PL, Atwater AR, Mowad C, et al. Patch testing for evaluation of hypersensitivity to implanted metal devices: a perspective from the American Contact Dermatitis Society. *Dermatitis* 2016;27:241-7.
48. Schalock PC, Menne T, Johansen JD, Taylor JS, Maibach HI, Linden C, et al. Hypersensitivity reactions to metallic implants—diagnostic algorithm and suggested patch test series for clinical use. *Contact Derm* 2012;66:4-19.
49. Honari G, Ellis SG, Wilkoff BL, Aronica MA, Svensson LG, Taylor JS. Hypersensitivity reactions associated with endovascular devices. *Contact Derm* 2008;59:7-22.
50. Kaaber K. Allergic manifestations caused by nickel hypersensitivity in women with a copper intrauterine device [in Danish]. *Ugeskr Laeger* 1990;152:688.
51. Haudrechy P, Mantout B, Frappaz A, Rousseau D, Chabeau G, Faure M, et al. Nickel release from stainless steels. *Contact Derm* 1997;37:113-7.
52. Kudur MH, Pai SB, Sripathi H, Prabhu S. Sutures and suturing techniques in skin closure. *Indian J Dermatol Venereol Leprol* 2009;75:425-34.
53. Semchyslyn NL. Dermatologic Surgical Complications. Medscape. Available from: <http://emedicine.medscape.com/article/1128404-overview>. Accessed December 1, 2016.
54. Engler RJ, Weber CB, Turnicky R. Hypersensitivity to chromated catgut sutures: a case report and review of the literature. *Ann Allergy* 1986;56:317-20.
55. Mullins RJ, Richards C, Walker T. Allergic reactions to oral, surgical and topical bovine collagen. Anaphylactic risk for surgeons. *Aust NZ J Ophthalmol* 1996;24:257-60.
56. Katsunuma T, Iikura Y. Delayed allergic reaction to silk sutures; a case report [in Japanese]. *Arerugi* 1995;44:630-2.
57. Tubbs RS, Verma K, Riech S, Mortazavi M, Oakes WJ, Cohen-Gadol AA. Reaction to silk suture in children undergoing neurosurgery: case reports and review of the literature. *Childs Nerv Syst* 2011;27:497-9.
58. Bhutani T, Jacob SE. Triclosan: a potential allergen in suture-line allergic contact dermatitis. *Dermatol Surg* 2009;35:888-9.
59. Sprowson AP, Jensen CD, Parsons N, Partington P, Emmerson K, Carluke I, et al. The effect of triclosan coated sutures on rate of surgical site infection after hip and knee replacement: a protocol for a double-blind randomised controlled trial. *BMC Musculoskelet Disord* 2014;15:237.
60. Steinkjer B, Braathen LR. Contact dermatitis from triclosan (Irgasan DP 300). *Contact Derm* 1988;18:243-4.
61. Veronesi S, de Padova MP, Vanni D, Melino M. Contact dermatitis to triclosan. *Contact Derm* 1986;15:257-8.
62. Wong CS, Beck MH. Allergic contact dermatitis from triclosan in antibacterial handwashes. *Contact Derm* 2001;45:307.
63. Buhl T, Fuchs T, Geier J. Contact hypersensitivity to triclosan. *Ann Allergy Asthma Immunol* 2014;113:119-20.
64. Ogbechie OA, Paul S, Schalock PC. A technique for identifying vicryl suture hypersensitivity. *Dermatitis* 2014;25:370-1.
65. Sanchez-Morillas L, Reano Martos M, Rodriguez Mosquera M, Iglesias Cadarso A, Perez Pimiento A, Dominguez Lazaro AR. Delayed sensitivity to Prolene. *Contact Derm* 2003;48:338-9.
66. Hivnor CM, Hudkins ML. Allergic contact dermatitis after postsurgical repair with 2-octylcyanoacrylate. *Arch Dermatol* 2008;144:814-5.
67. Leggat PA, Kedjarune U, Smith DR. Toxicity of cyanoacrylate adhesives and their occupational impacts for dental staff. *Ind Health* 2004;42:207-11.
68. Mehdizadeh M, Yang J. Design strategies and applications of tissue bio-adhesives. *Macromol Biosci* 2013;13:271-88.
69. Caton AM, Dauphine C. Allergic contact dermatitis after repeated exposure to Dermabond. *Am Surg* 2014;80:520-2.
70. Davis MD, Stuart MJ. Severe allergic contact dermatitis to Dermabond Prineo, a topical skin adhesive of 2-octyl cyanoacrylate increasingly used in surgeries to close wounds. *Dermatitis* 2016;27:75-6.
71. Durando D, Porubsky C, Winter S, Kalymon J, O'Keefe T, LaFond AA. Allergic contact dermatitis to Dermabond (2-octyl cyanoacrylate) after total knee arthroplasty. *Dermatitis* 2014;25:99-100.
72. El-Dars LD, Chaudhury W, Hughes TM, Stone NM. Allergic contact dermatitis to Dermabond after orthopaedic joint replacement. *Contact Derm* 2010;62:315-7.

73. Howard BK, Downey SE. Contact dermatitis from Dermabond. *Plast Reconstr Surg* 2010;125:252e-3e.
74. Lefevre S, Valois A, Truchetet F. Allergic contact dermatitis caused by Dermabond(R). *Contact Derm* 2016;75:240-1.
75. McDonald BS, Buckley DA. Severe dermatitis from Dermabond (R) surgical glue. *Br J Dermatol* 2014;170:739-41.
76. Sachse MM, Junghans T, Rose C, Wagner G. Allergic contact dermatitis caused by topical 2-octyl-cyanoacrylate. *Contact Derm* 2013;68:317-9.
77. Shaw DW. Allergic contact dermatitis from butyl and octyl cyanoacrylate tissue adhesives. *Dermatitis* 2012;23:141.
78. Studer M. Comment tester l'allergie de contact à la colle tissulaire au 2-octylcyanoacrylate (Dermabond)? *Revue Française d'Allergologie* 2010;50:75-6.
79. Kanerva L. Ethyl cyanoacrylate does not cross-react with methacrylates and acrylates. *Am J Contact Derm* 1997;8:54-5.
80. Koppula SV, Fellman JH, Storrs FJ. Screening allergens for acrylate dermatitis associated with artificial nails. *Am J Contact Derm* 1995;6:78-85.
81. Gilissen L, Goossens A. Frequency and trends of contact allergy to and iatrogenic contact dermatitis caused by topical drugs over a 25-year period. *Contact Derm* 2016;75:290-302.
82. Vickers HR, Bagratuni L, Alexander S. Dermatitis caused by penicillin in milk. *Lancet* 1958;1:351-2.
83. Falagas ME, Vergidis PI. Irrigation with antibiotic-containing solutions for the prevention and treatment of infections. *Clin Microbiol Infect* 2005;11:862-7.
84. Menezes de Padua CA, Schnuch A, Lessmann H, Geier J, Pfahlberg A, Uter W. Contact allergy to neomycin sulfate: results of a multifactorial analysis. *Pharmacoepidemiol Drug Saf* 2005;14:725-33.
85. Fisher AA. Prevention of contact dermatitis. *NY State J Med* 1978;78:1739-41.
86. Wereide K. Neomycin sensitivity in atopic dermatitis and other eczematous conditions. *Acta Derm Venereol* 1970;50:114-6.
87. Pirila V, Pirila L. Sensitization to the neomycin group of antibiotics. Patterns of cross-sensitivity as a function of polyvalent sensitization to different portions of the neomycin molecule. *Acta Derm Venereol* 1966;46:489-96.
88. Jiaravuthisan MM, DeKoven JG. Contact dermatitis to polymyxin B. *Contact Derm* 2008;59:314-6.
89. Draelos ZD, Rizer RL, Trookman NS. A comparison of postprocedural wound care treatments: do antibiotic-based ointments improve outcomes? *J Am Acad Dermatol* 2011;64(Suppl):S23-9.
90. Nijhawan RI, Smith LA, Mariwalla K. Mohs surgeons' use of topical emollients in postoperative wound care. *Dermatol Surg* 2013;39:1260-3.
91. Jacob SE, Amado A, Cohen DE. Dermatologic surgical implications of allergic contact dermatitis. *Dermatol Surg* 2005;31(Pt 1):1116-23.
92. Spencer A, Gazzani P, Thompson DA. Acrylate and methacrylate contact allergy and allergic contact disease: a 13-year review. *Contact Derm* 2016;75:157-64.
93. Widman TJ, Oostman H, Storrs FJ. Allergic contact dermatitis from medical adhesive bandages in patients who report having a reaction to medical bandages. *Dermatitis* 2008;19:32-7.
94. Kaufmann JM, Hale EK, Ashinoff RA, Cohen DE. Cutaneous lidocaine allergy confirmed by patch testing. *J Drugs Dermatol* 2002;1:192-4.
95. Gonzalez-Rodriguez AJ, Gutierrez-Paredes EM, Revert Fernandez A, Jorda-Cuevas E. Allergic contact dermatitis to benzocaine: the importance of concomitant positive patch test results. *Actas Dermosifiliogr* 2013;104:156-8.
96. Wilkinson JD, Andersen KE, Lahti A, Rycroft RJ, Shaw S, White IR. Preliminary patch testing with 25% and 15% 'caine'-mixes. The EECDRG. *Contact Derm* 1990;22:244-5.