

Diagnosis and Treatment of Perioperative Allergic Complications: A Practical Review

Michael J. Schroeder, MD*

Casey T. Kraft, MD†

Jeffrey E. Janis, MD*

Monica T. Kraft, MD‡

Background: Reported drug allergies are commonly encountered by surgeons and can lead to uncertainty in selecting an appropriate agent due to concerns of associated risks with related and cross-reactive drugs. This uncertainty can ultimately lead to increased infection rates.

Methods: A literature review was conducted in PubMed using a combination of the terms “allergy,” “allergic reaction,” “anaphylaxis,” and “surgery,” “surgical,” or “operating room” for articles published within the last 10 years. Publications identified with these search terms were then filtered for review articles, sorted by “best match,” and a maximum of 100 articles were manually reviewed for each combination of search terms.

Results: Search results yielded 46,484 articles, 676 of which were ultimately included for manual review, based on selection criteria. Specifically, articles selected for inclusion focused on surgical allergic reactions that were either related to mechanism of action, causative agent for the allergic reaction, timing of allergic reaction, or recommendations for appropriate management.

Conclusions: Allergic reactions can be a common occurrence in the operative room. Knowledge of likely causative agents, timing of a reaction to various agents, and appropriate management in the immediate and delayed setting can improve outcomes and safety for plastic surgery patients. (*Plast Reconstr Surg Glob Open* 2024; 12:e5734; doi: 10.1097/GOX.0000000000005734; Published online 15 April 2024.)

INTRODUCTION

Drug allergies are common and can lead to uncertainty when it comes to selection of preferred antibiotic prophylaxis, associated risk with related agents, and recommendations for future care. Anaphylaxis in the operative setting, although rare, can be potentially severe and life threatening. Understanding and awareness of how to navigate these allergic concerns can improve safety and outcomes for plastic surgery patients. The purpose of this article is to provide understanding of the basic physiology of allergic reactions, acute recognition and management of perioperative anaphylaxis, and identification of common causes of allergic reactions within plastic surgery and how to navigate treatment selection.

From the *Department of Plastic and Reconstructive Surgery, Ohio State University, Columbus, Ohio; †Private Practice, Columbus, Ohio; and ‡Department of Otolaryngology, Division of Allergy and Immunology, Ohio State University, Columbus, Ohio.

Received for publication December 6, 2023; accepted February 23, 2024.

Copyright © 2024 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the [Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 \(CCBY-NC-ND\)](#), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/GOX.0000000000005734

METHODS

A scoping literature review was conducted using PubMed to identify all articles published on surgical complications related to allergic reactions to identify common themes with inciting agents or mechanisms. A PubMed database search was performed using a combination of the search terms “allergy,” “allergic reaction,” or “anaphylaxis,” with “surgery,” “surgical,” or “operating room,” with a publication date within the last 10 years. Search term results were filtered for review articles and sorted by “best match.” The goal of the literature review was two-fold: identify articles that (1) discuss recognition and management of perioperative allergic reactions and anaphylaxis and (2) outline causative agents of perioperative allergic reactions. All causative agents were reviewed for relevancy to practicing plastic surgeons by the senior author (M.T.K.) and then agreed upon by the author group. All publications not written in the English language were excluded from review.

RESULTS

These searches yielded a total of 46,484 search results within PubMed. Filtering for review articles yielded 10,469 results. A maximum of the most relevant 100 articles were

Disclosure statements are at the end of this article, following the correspondence information.

reviewed for each combination search result after applying date limits, filtering for review articles, and sorting by “best match,” yielding a total of 676 articles for review (not all combinations yielded 100 results with these criteria). These article titles/abstracts were reviewed by the first and senior author (M.J.S. and M.T.K.) to identify inciting agents of perioperative allergic complications. Agents selected included those commonly used for routine general anesthesia and those specific to plastic surgery operations and agreed upon by the author group (Fig. 1). For each agent, the associated complications, mechanism of allergic reaction, timing of allergic reaction and type of material/medication causing the allergic reaction were reviewed. Agents with special use within plastic surgery were noted when applicable. Seminal articles published within surgical or allergy/immunology journals that were not captured with our search criteria were included in the review based on the authors’ expertise. The identified themes were then categorized based on mechanism, management, or material, and are summarized below.

DISCUSSION

Mechanism of Allergic Reactions

Immediate versus Delayed Hypersensitivity and Pseudoallergic Reactions

Hypersensitivity reactions are characterized by an unrestrained immune response triggered by either foreign or innate antigens and have been classically divided into four groups based on pathophysiologic mechanisms.^{1,2} Type I responses, also known as immediate responses, are IgE-mediated and characterized by anaphylaxis, angioedema, urticaria, asthma, and allergic rhinitis.¹ These reactions occur by an initial sensitization to allergens whereby T cells cause B cells to produce IgE and then, upon re-exposure the allergen, cross-links IgE, leading to release of histamine and other inflammatory cytokines from mast cells and basophils.¹ In contrast, type IV hypersensitivity responses are delayed reactions and are T-cell mediated.¹ Clinical manifestations of type IV hypersensitivities can be mild (eg, contact dermatitis) or severe such as drug reaction with eosinophilia and systemic symptoms, Stevens-Johnson syndrome, or toxic epidermal necrolysis.¹ Type I and IV reactions together comprise the majority of what are commonly called “allergic reactions” and are what would most frequently be encountered by practicing surgeons. Type II and type III reactions involve antibody and immune complex mediated reactions, respectively, and are outside the scope of this overview of allergic reactions in plastic surgery.

In addition to classic allergic reactions, it is important to understand non-IgE-mediated “pseudoallergic” hypersensitivity reactions. These occur through either nonspecific mast cell activation, release of mast cell mediators, or non-IgE-mediated pathways and can result in flushing, hives, or even anaphylaxis.^{1,3} Clinical examples include vancomycin-induced “redman” syndrome, contrast media reactions, pruritis with opiates, vasovagal syncope after local anesthetics, and aspirin/nonsteroidal

Takeaways

Question: How should reported drug allergies affect decision-making when considering the selection of related agents?

Findings: Selection of alternative agents due to a reported drug allergy may be unnecessary and can lead to worse clinical outcomes. Unnecessary avoidance of certain drugs can be attributed to uncertainty regarding cross reactivity and the propagation of outdated data and misinformation. In certain situations, referral to an allergy and immunology specialist can help clarify a reported allergy and direct future care.

Meaning: Staying up to date with current recommendations, maintaining accurate knowledge of medication cross reactivities, and recognizing situations for specialist referral can lead to improved outcomes for patients.

antiinflammatory-associated exacerbations of respiratory disease or urticaria/angioedema, among others.

Perioperative Anaphylaxis: Recognition and Management

Recognition

One of the most severe forms of allergic reaction encountered by surgeons is perioperative anaphylaxis (POA). POA is rare (1:10,000 to 1:20,000);⁴ however, consequences can be severe, with a mortality rate as high as 9%.⁵ Clinical presentations include cutaneous rashes and swelling, bronchospasm, airway swelling, hypotension, and cardiovascular collapse.⁶ Early recognition may be limited, as patients are unable to report symptoms and visibility of cutaneous symptoms may be either nonexistent or limited by surgical drapes. Up to 46% of POA may present with isolated hypotension or cardiovascular collapse without skin symptoms.⁴ Furthermore, many drugs are administered in close succession, confounding identification of the offending agent. Most likely etiologies vary depending on timing within a case and may be related to intraoperative surgical events⁷⁻⁹ (Table 1).

Management

The first step in treating POA is identification and removal of the offending agent and early administration of epinephrine. Epinephrine 5–10 µg (0.2 µg/kg) should be administered intravenously and titrated to effect in cases of mild/moderate hypotension. With cardiovascular collapse, 0.1–0.5 mg should be administered intravenously.⁶ Airway should be secured and supported with 100% oxygen and intravenous crystalloids (2–4L), bronchodilators (if bronchospasm present), and glucocorticoids (hydrocortisone; Table 2).⁶

After the acute management of anaphylaxis, confirmatory testing is critical for accurate diagnosis and future avoidance of the offending agent. Serum mast cell tryptase levels should be obtained within 4 hours from first signs and symptoms.¹⁰ Elevated tryptase is suggestive of an anaphylactic event and should be compared with baseline levels drawn 24 hours after the event; persistently elevated levels may suggest a mast cell disorder.¹⁰ A list and timing

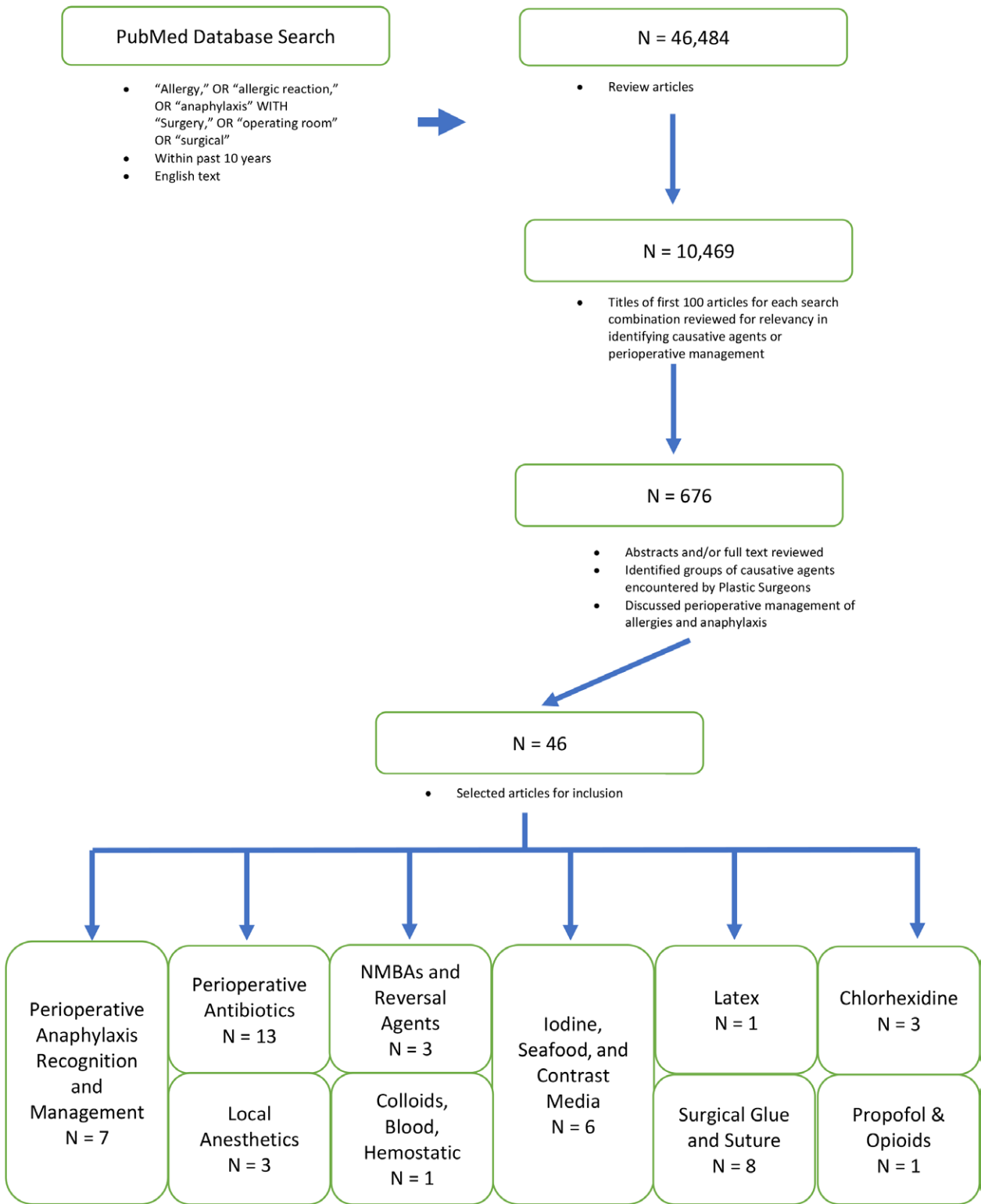


Fig. 1. Literature review selection process.

of medications administered should be collected and the patient referred to allergy/immunology for confirmatory skin testing (Table 3).¹⁰ Traditionally, testing has been deferred for 4–6 weeks after the event due to concern for

a postanaphylaxis refractory period, which would render the skin test temporarily nonreactive, though this has been called into question with recent studies, and earlier testing is more accepted.¹¹

Table 1. Most Likely Cause of Intraoperative Anaphylaxis Based on Timing within a Case

Time	Causes
0–30 min	Antibiotics, induction agents, hypnotics
>30 min	Latex, chlorhexidine, dyes, intravascular volume expanders, blood products
After surgical events	Reperfusion after tourniquet removal, dye injection, chlorhexidine irrigation, antibiotic irrigation, TXA irrigation, injection, or infusion
End of the case	Sugammadex

Table 2. Allergic Reaction Symptom Management

Allergic Symptom	Treatment
Anaphylaxis*	Removal of offending agent, IV/IM epinephrine, supportive care
Hypotension	IV epinephrine, IV crystalloid fluids, vasopressors
Airway edema	Secure airway, 100% FiO ₂ , IV epinephrine, IV glucocorticoids
Bronchospasm	Bronchodilators, glucocorticoids
Urticaria	H1/H2 antihistamines, glucocorticoids
Contact dermatitis	Removal of offending agent, PO antihistamines, topical steroids, PO steroids (severe)

*First-line treatment of anaphylaxis is epinephrine. Supportive treatment focused on other symptoms (ie, use of bronchodilators for bronchospasm) should not replace first-line therapy if anaphylaxis is suspected.

Specific Causes of Allergic Reactions in Plastic Surgery

Prophylactic Antibiotics

Administration of prophylactic antibiotics has become standard practice in select plastic surgery operations as timely administration has been shown to reduce surgical site infections.^{12–14} In the United States, prophylactic antibiotics are the most frequently cited cause of perioperative anaphylaxis, accounting for up to 50% of reactions.¹⁵ Although overall incidence is exceedingly rare (0.0006%), cefazolin is the most commonly reported offending antibiotic, likely due to its frequent use.^{15,16} In the United States, cefazolin is the prophylactic antibiotic of choice due to its spectrum of common skin flora coverage and favorable pharmacokinetics, resulting in rapid rise to an effective concentration in tissues.¹⁷

It is worth making specific note of a common scenario encountered by surgeons: Can cefazolin, a cephalosporin in the beta lactam family, be safely administered in patients

with reported allergy to penicillin? Up to 10% of the US population reports a penicillin allergy, but only 1%–10% of those reported are true confirmed allergies, making the true incidence closer to 0.1%–1%.^{18,19} Penicillin allergy on a patient’s chart often results in providers choosing alternative and inferior agents, leading to increased risks of surgical site infections and adverse events, including *clostridium difficile* colitis and vancomycin-resistant enterococcus.^{12,17,20} Compliance with optimal timing of antibiotic administration is thought to play a role in the difference in surgical site infections, as optimal timing for cefazolin administration is 30–59 minutes of incision compared with between 60 and 120 minutes for vancomycin.^{17,21–23}

The avoidance of cefazolin in penicillin-allergic patients is founded on outdated research quoting penicillin and cephalosporin cross reactivity as high as 8%–10%; however, this was likely related to manufacturing contaminants (cross-reactive molds) that are no longer used.²⁴ New data suggest that cross reactivity is closer to 1%–3%,^{24,25} and based on the R-side chain, and not the shared beta-lactam ring.²⁴ Despite this, cephalosporin manufacturing still lists a 10% cross reactivity on its packaging. Cefazolin has a unique side chain, which is not shared with any penicillin and shared with only one cephalosporin.²⁴ Therefore, cefazolin does not cross-react with penicillin and has been repeatedly demonstrated to be safe to administer to patients with penicillin allergies across institutions in both adult and pediatric populations (Fig. 2).^{26–30}

Referral to an allergist preoperatively, when able, can help clarify a prior penicillin allergy through skin testing and/or an oral challenge. In many cases, the allergy label may be removed, which will prevent confusion regarding cross reactivity and risk. In cases of prior anaphylaxis to a cephalosporin or severe cutaneous adverse reactions such as drug reaction with eosinophilia and systemic symptoms, Stevens-Johnson syndrome, or toxic epidermal necrolysis to any beta lactam, cefazolin use may be contraindicated and consultation with an allergy specialist is advisable (Table 1 and Fig. 2)

Neuromuscular Blocking and Reversal Agents

Neuromuscular blocking agents (NMBAs) are the most common cause of perioperative anaphylaxis in several international populations, accounting for 50%–70%

Table 3. Reasons to Obtain Allergy and Immunology Referral

When and Why to Consider an Allergy and Immunology Referral		
	When?	Why?
Drug allergy requires selection of an inferior alternative	Patient undergoing elective surgery with a reported cephalosporin allergy	Selection of a cefazolin alternative leads to increased risk of surgical site infection and increased rates of clostridium difficile colitis and vancomycin-resistant enterococcus
	Patient undergoing elective surgery with a reported chlorhexidine allergy	Preoperative prep with a chlorhexidine alternative leads to increased risk of surgical site infection
Drug allergy leads to a potentially unnecessary exposure	Patient with reported contrast allergy undergoing nonurgent contrast imaging	Before contrast administration, patients require exposure to high doses of steroids over 13 h
	Patient with local anesthetic allergy who requires a procedure that could be performed in-office under local	Patient would require potentially unnecessary exposure to general anesthesia for a procedure that could otherwise be done in-office
Drug allergy resulted in acute anaphylaxis	Patient who developed an acute perioperative anaphylaxis reaction	Patient should undergo confirmatory skin-testing to accurately diagnose offending agent to guide future treatment. Traditionally performed 4–6 weeks after reaction

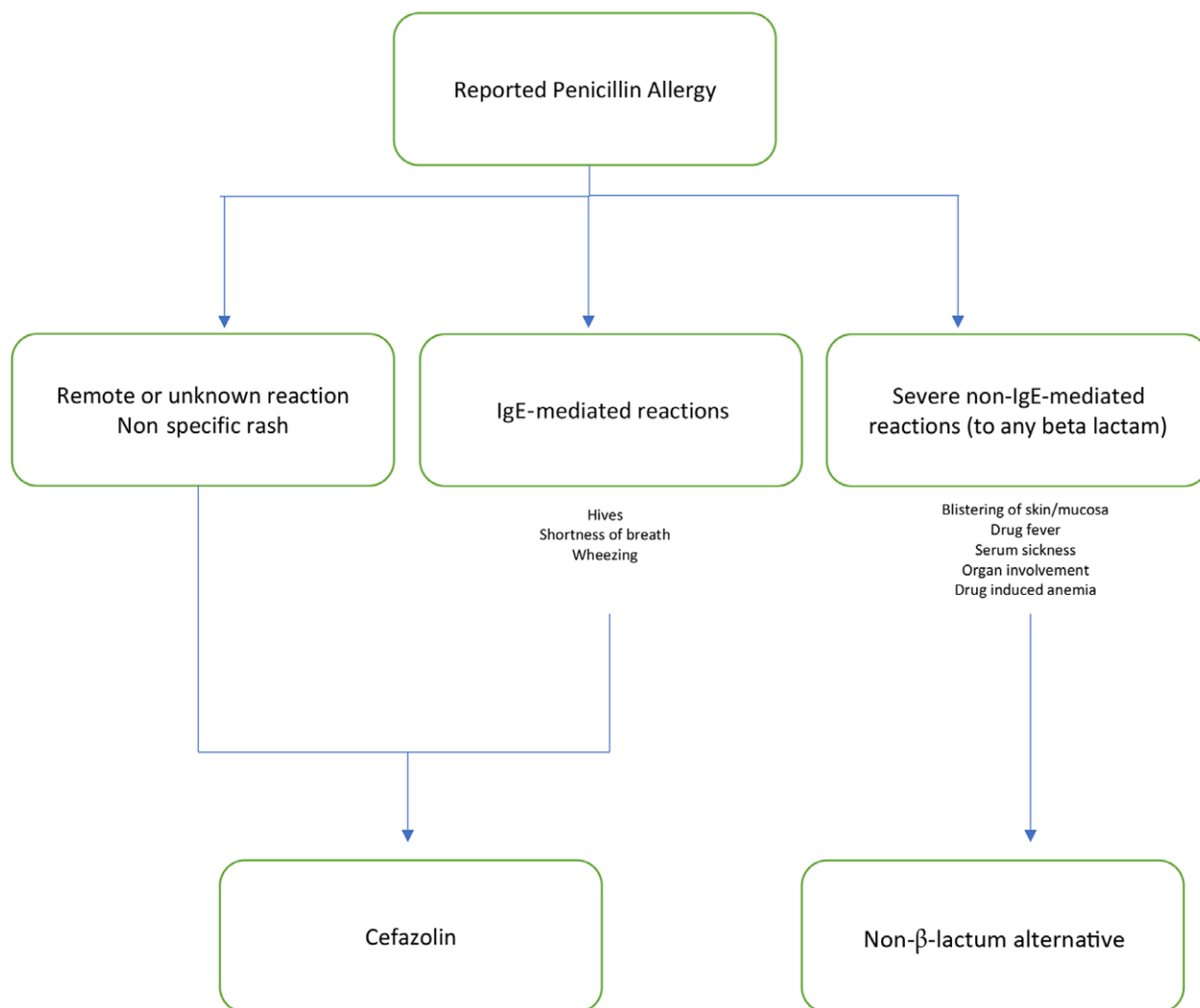


Fig. 2. Selection of preoperative antibiotic prophylaxis with reported penicillin allergy.

of perioperative anaphylaxis cases and the second most common cause in the United States, with around 30% of cases.³¹ Allergic response typically occurs within 5 minutes after induction, making diagnosis of the offending agent challenging, given the concomitant administration of multiple medications.³¹ In some regional studies, rocuronium has shown higher rates of anaphylaxis,³² but this has not been replicated in the United States.³³ NMBA cross reactivities range from 36% to 70%.³¹

Sugammadex is used to rapidly reverse nondepolarizing NMBAs and is a rare (29 per 1,000,000 cases) but increasingly recognized cause of POA.³⁴ Anaphylaxis occurs at the end of a surgical case at which time sugammadex is used for NMBA reversal and may occur without prior exposure due to sensitization through oral ingestion of other cyclodextrin-containing medicinal products or foods.³⁴

Chlorhexidine Products

Chlorhexidine is a highly effective antiseptic used in a wide range of products (Table 4).³⁵ Hypersensitivity reactions can be either immediate reactions (ranging

Table 4. Chlorhexidine-containing Products

Product	Name
Surgical prep	Chloraprep (Beckton Dickson, Franklin Lakes, N.J.)
Medical grade mouthwash	Peridex (3M, St. Paul, Minn.)
Dressings	Biopatch (Ethicon, Raritan, N.J.) Tegaderm CHG dressings (3M, St. Paul, Minn.)
Preoperative body wash	Hibiclens (Molnlycke Health Care, Gothenburg, Sweden)
Irrigation solutions	Irrisept (Irrimax Corporation, Gainesville, Fla.)
Urethral gel	—
Central venous catheters	—

from urticarial angioedema to anaphylaxis) or delayed contact dermatitis.³⁶ Chlorhexidine is one of the most common causes of perioperative anaphylaxis,⁴ with symptoms starting 15–45 minutes after induction of anesthesia and related to its use as a preoperative skin preparation. However, anaphylaxis can occur at any

time during surgery or in the immediate postoperative setting.³⁶

A reported allergy to chlorhexidine may lead to higher postoperative infection rates due to substitution with an inferior preoperative scrub. Demonstrated in a randomized controlled trial, chlorhexidine-alcohol scrub is superior to povidone-iodine scrub and paint in preventing surgical site infections (likely due to the antimicrobial effects of alcohol).³⁷ Therefore, a careful history should be obtained from patients reporting allergies to chlorhexidine or chlorhexidine-containing products, and referral to allergy and immunology should be considered, particularly in surgical cases involving placement of implants.

Iodine, Seafood, and Contrast Media: Historical Concerns and Current Recommendations

Historically, allergy to an iodine-containing drug or food (most commonly shellfish) has raised concerns for cross reactivity to other iodine-containing drugs. This concept has come under scrutiny because iodine is an atom and physiologically cannot be an allergen, and the concept of iodine cross-sensitivity between iodinated substances is not supported by evidence.³⁸ Shellfish food allergies are related to structural proteins (such as tropomyosin), not iodine, and thus allergy to one iodine-containing product should not be a contraindication for a patient to receive a different iodine-containing drug.

Iodinated Contrast Media

Allergies to iodinated contrast mediums do exist and are indicated by prior reactions, but are not due to iodine.³⁸ Distinct from classic IgE-mediated allergic reactions, these hypersensitivity reactions are often due to direct effect on mast cells and basophils, releasing histamine and other chemicals, and frequently can be prevented with adequate pretreatment with antihistamines and glucocorticoids (Table 5).³⁹ In rare cases of severe or recurrent reactions

despite adequate pretreatment, allergy referral should be considered for the less common possibility of IgE-mediated allergy. Both the American College of Radiology⁴⁰ and the American Academy of Allergy, Asthma, and Immunology⁴¹ have established guidelines that iodinated contrast media is safe to administer to patients with shellfish or povidone-iodine allergies.

Betadine

Povidone iodine is frequently used in plastic surgery as a surgical preparation; pocket, implant, or mesh irrigation; or postoperative ointment.^{42–44} Iodine at a concentration above 1% is considered an irritant and may cause an irritant contact dermatitis, which can mimic a local allergic response and be exacerbated by use of alcohol immediately prior as it removes a protective layer of sebum.³⁸ Allergies to povidone are typically in the form of an allergic contact dermatitis as opposed to an IgE-mediated response and can be managed symptomatically.³⁸

Indocyanine Green

Rare reports of anaphylactoid and urticarial reactions to indocyanine green, which can be used to evaluate tissue perfusion and map lymphatics, have been published, but again, there is no evidence to support iodine as the cause.^{38,45,46} Management is based on symptoms and severity (Tables 2 and 6).

Local Anesthetics

Local anesthetic adverse drug reactions are estimated to occur in 2.5%–10% of patients, but true allergy is rare and occurs in less than 1% of patients.⁴⁷ Nonallergic adverse drug reactions include vasovagal syncope, systemic toxicity, injury to nearby anatomic structures, and side effects of epinephrine. Allergic reactions include contact dermatitis presenting as localized eczematous, pruritic, blistering beginning hours after injection and peaking within 72 hours.⁴⁷ Allergic type I IgE-mediated reactions are rare, typically characterized by generalized urticaria and anaphylaxis occurring within 1 hour of injection.⁴⁷

Local anesthetics are classified as either esters or amides. Esters can be remembered as having only one “i” in their name and are more commonly associated with allergic reactions compared with amides. Although cross reactivity within a group is possible, cross reactivity between amides and esters is very unlikely.⁴⁸ Patients with

Table 5. Pretreatment before Contrast Administration for Patients with Contrast Allergy

Time before Procedure	Medication
13 h	Prednisone 50mg PO
7 h	Prednisone 50mg PO
1 h	Prednisone 50mg PO Diphenhydramine 25–50mg PO/IV

Table 6. Offending Agents in Perioperative Allergic Reactions and Associated Time of Reaction, Symptoms, and Treatment

Agent	Time of Reaction	Symptoms
Prophylactic antibiotics	Immediate, beginning of surgery	Rash, urticaria, hypotension, anaphylaxis
Neuromuscular blockers	Immediate, after induction	Rash, urticaria, hypotension, anaphylaxis
Latex	Immediate, during surgery (anaphylaxis) Delayed 24–48h after exposure (dermatitis)	Anaphylaxis, contact dermatitis, contact urticaria
Chlorhexidine	During or immediately after surgery; delayed hours to days after surgery	Rash, urticaria, hypotension, anaphylaxis, contact dermatitis
Local anesthetics	Immediate within 1 h of injection; delayed hours to 72h after injection (dermatitis)	Vasovagal response, rash, urticaria, hypotension, anaphylaxis (rare), contact dermatitis
Sugammadex	Immediate, end of surgery	Rash, urticaria, hypotension, anaphylaxis
Indocyanine green	Immediate	Hypotension, urticaria, anaphylaxis
Surgical glue	Delayed, 5–14 d after exposure	Contact dermatitis, systemic id reaction or auto-eczematization

a history of reactions to both amides and esters may in fact have an allergy to para-aminobenzoic acid (PABA), as esters are derivatives of PABA, and PABA was previously used in amide anesthetics. PABA is a common additive in sunscreens, lotions, and cosmetics, increasing risk of prior sensitization.

Clinically, a local anesthetic allergy is relevant for surgeons who have patients requiring a minor procedure. Patients reporting a history of local anesthetic allergy should be prompted to recall the specific agent to determine its classification, as well as the timing and symptoms of the reaction. For example, a patient reporting tachycardia or syncope immediately after injection of lidocaine during a dental procedure without other systemic symptoms is more consistent with a vasovagal reaction or side effect of local epinephrine absorption. If there is uncertainty, a referral to allergy and immunology for further evaluation with skin testing would help elucidate their candidacy for a procedure under local. For a patient with a true allergy to local anesthetics, 1% diphenhydramine with 1:100,000 epinephrine solution has been reported as a safe and effective alternative.⁴⁹

Latex

Latex sensitivities affect approximately 4% of the general population and, notable for pediatric plastic surgeons, 40%–65% among the spina bifida pediatric population.⁵⁰ In the 1980s and 1990s, rampant use of powdered latex gloves lead to high sensitization rates through direct skin contact and airborne exposure (made worse by aerosolization effects of added cornstarch powder).⁵⁰ Hypersensitivity reactions can be type I IgE-mediated, leading to life-threatening anaphylaxis; or delayed type IV developing 24–48 hours after exposure and limited to localized dermatitis. Reactions in the healthcare setting have substantially decreased through the introduction of primary preventative measures by replacing latex gloves with powder-free nonlatex alternatives.⁵⁰

Surgical Glue

Cyanoacrylate glues are used as dressings or adjuncts to closure and can expedite closing times, lead to improved scars, and provide an antibacterial barrier to skin pathogens.^{51–53} There are multiple reports of contact dermatitis as a result of cyanoacrylate glue products,^{53–57} with rates ranging from 0.5% to 14%, and have been hypothesized to

vary based on anatomic location due to skin thickness.^{53,58} A prospective study of cosmetic and reconstructive breast surgery found 14% developed contact dermatitis, with allergy to cyanoacrylate confirmed by allergy scratch testing.⁵³ Presentation is characterized by eczematous to urticarial dermatitis 5–14 days after surgery and can progress to a systemic response known as id reaction or auto-eczematization characterized by widespread macular/papular eruption and generalized pruritis.⁵⁷ Treatment includes removal of the glue product by applying petroleum or acetone to loosen the adhesive. Additional treatment should consist of either topical and/or oral formulations of antihistamines and steroids, with oral steroids reserved for severe, widespread, systemic, and/or recalcitrant reactions.⁵⁷

Suture

Sutures are frequently skin irritants, whereas cases of true allergies are limited to case reports.⁵⁹ Potential allergenic components include triclosan (antibiotic coating), animal-derived collagen (eg, natural gut sutures), and chromic salts (eg, chromic gut suture). Use of natural gut sutures should be cautioned in patients with gelatin allergies because collagen may cross react with gelatin.⁵⁹

Colloids, Hemostatic Agents, and Blood Products

Colloids, such as gelatin, dextran, and albumin, are uncommon causes of perioperative anaphylaxis. Gelatin is the highest risk and found in topical hemostatic agents, including Surgiflo (Ethicon, Raritan, N.J.) and Gelfoam (Pfizer, New York, N.Y.), which have been implicated as rare causes of intraoperative anaphylaxis.³¹ Anaphylaxis to blood products is estimated to occur in 0.6 per 1000 transfusions and may be more frequent in patients with IgA deficiency or with previous exposure through pregnancy or prior transfusions.³¹

Propofol and Opioids

Propofol is an inductive agent for general anesthesia and contains soybean oil and egg lecithin, raising concerns for patients with soy and/or egg allergies. However, patients with food allergies react to proteins in the foods, not the oils (eg, soybean oil) or fats (eg, egg lecithin). The American Academy of Allergy, Asthma, and Immunology have stated that patients with soy/egg allergies can receive propofol without special precautions (Table 7).

Table 7. Common Allergy Misconceptions

Myth	Truth
For penicillin-allergic patients, there is a 10% cross reactivity rate with cephalosporins	True cross reactivity rate is 1%–3% and related to the R-side chain (not beta lactam ring)
Penicillin-allergic patient should not receive cefazolin for preoperative prophylaxis	Except in rare situations, most penicillin-allergic patients can safely receive cefazolin. Cefazolin is not cross reactive with penicillin as it does not share an R-side chain with any known penicillin
Patients with allergies to certain foods (eg, shellfish) or drugs (eg, betadine-povidone ointment, iodinated contrast media) should avoid iodine-containing drugs due to concerns for iodine cross reactivity	Iodine is an atom and not an allergic antigen. The concept of iodine cross-sensitivity between iodinated substances is not supported by evidence
Patients with egg or soy allergies should not receive propofol	According to the American Academy of Allergy, Asthma, and Immunology, patients with soy or egg allergies can receive propofol without any special precautions

Opioids are rare causes of intraoperative anaphylaxis (one in every 100,000 to 200,000 cases of anesthesia).³¹ Endogenous production of opioid-like substances make true IgE-mediated reactions exceedingly rare to nonexistent, but may mimic allergic reactions via opioid-receptor-mediated vasodilation, causing generalized flushing.⁶⁰ One study reviewed 499 patients with previously noted opioid allergies and found 92.5% of patients tolerated re-administration, and allergy to one clinical class of opioid (natural, semisynthetic, or synthetic) did not predict cross reactivity with another (Table 6).⁶⁰

CONCLUSIONS

Allergic complications and anaphylactic events can be extremely stressful for patients and surgeons. By staying up to date with current recommendations and accurate knowledge of medication cross reactivities, mechanisms of allergy, and management options, surgeons can be well prepared to optimize outcomes for their patients and manage these rare incidents expeditiously.

Monica T. Kraft, MD

915 Olentangy River Road, Suite 400

Columbus, OH 43212

E-mail: monica.kraft@osumc.edu

Twitter: @drmonicakraft

DISCLOSURES

Dr. Janis receives royalties from Thieme and Springer Publishing. All the authors have no financial interest to declare in relation to the content of this article.

REFERENCES

- Dispenza MC. Classification of hypersensitivity reactions. *Allergy Asthma Proc.* 2019;40:470–473.
- Coombs RR. Immunopathology. *Br Med J.* 1968;1:597–602.
- McNeil BD, Pundir P, Meeker S, et al. Identification of a mast-cell-specific receptor crucial for pseudo-allergic drug reactions. *Nature.* 2015;519:237–241.
- Harper NJN, Cook TM, Garcez T, et al. Anaesthesia, surgery, and life-threatening allergic reactions: epidemiology and clinical features of perioperative anaphylaxis in the 6th National Audit Project (NAP6). *Br J Anaesth.* 2018;121:159–171.
- Mertes PM, Tajima K, Regnier-Kimmoun MA, et al. Perioperative anaphylaxis. *Med Clin North Am.* 2010;94:761–789, xi.
- Volcheck GW, Hepner DL. Identification and management of perioperative anaphylaxis. *J Allergy Clin Immunol Pract.* 2019;7:2134–2142.
- Bansal RA, Nicholas A, Bansal AS. Tranexamic acid: an exceedingly rare cause of anaphylaxis during anaesthesia. *Case Reports Immunol.* 2016;2016:7828351.
- Imbesi S, Nettis E, Minciullo PL, et al. Hypersensitivity to tranexamic acid: a wide spectrum of adverse reactions. *Pharm World Sci.* 2010;32:416–419.
- Li PH, Trigg C, Rutkowski R, et al. Anaphylaxis to tranexamic acid—a rare reaction to a common drug. *J Allergy Clin Immunol Pract.* 2017;5:839–841.
- Kalagara J, Vanijcharoenkarn K, Lynde GC, et al. Approach to perioperative anaphylaxis in 2020: updates in diagnosis and management. *Curr Allergy Asthma Rep.* 2021;21:4.
- van der Poorten MM, Walschot M, Faber M, et al. Reliability of early and late testing for suspected perioperative hypersensitivity. *J Allergy Clin Immunol Pract.* 2022;10:1057–1062.e2.
- Bratzler DW, Dellinger EP, Olsen KM, et al; American Society of Health-System Pharmacists (ASHP). Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect (Larchmt).* 2013;14:73–156.
- Harrison B, Khansa I, Janis JE. Evidence-based strategies to reduce postoperative complications in plastic surgery. *Plast Reconstr Surg.* 2016;138(3 Suppl):51S–60S.
- ElHawary H, Hintermayer MA, Alam P, et al. Decreasing surgical site infections in plastic surgery: a systematic review and meta-analysis of level 1 evidence. *Aesthet Surg J.* 2021;41:NP948–NP958.
- Kuhlen JL, Jr, Camargo CA, Jr, Balekian DS, et al. Antibiotics are the most commonly identified cause of perioperative hypersensitivity reactions. *J Allergy Clin Immunol Pract.* 2016;4:697–704.
- Gurrieri C, Weingarten TN, Martin DP, et al. Allergic reactions during anesthesia at a large United States referral center. *Anesth Analg.* 2011;113:1202–1212.
- Blumenthal KG, Ryan EE, Li Y, et al. The impact of a reported penicillin allergy on surgical site infection risk. *Clin Infect Dis.* 2018;66:329–336.
- Macy E, Ngor EW. Safely diagnosing clinically significant penicillin allergy using only penicilloyl-poly-lysine, penicillin, and oral amoxicillin. *J Allergy Clin Immunol Pract.* 2013;1:258–263.
- Macy E. Penicillin and beta-lactam allergy: epidemiology and diagnosis. *Curr Allergy Asthma Rep.* 2014;14:476.
- Schlosser KA, Maloney SR, Horton JM, et al. The association of penicillin allergy with outcomes after open ventral hernia repair. *Surg Endosc.* 2020;34:4148–4156.
- Malhotra NR, Piazza M, Demoor R, et al. Impact of reduced pre-incision antibiotic infusion time on surgical site infection rates: a retrospective cohort study. *Ann Surg.* 2020;271:774–780.
- Seidelman JL, Mantyh CR, Anderson DJ. Surgical site infection prevention: a review. *JAMA.* 2023;329:244–252.
- Weber WP, Marti WR, Zwahlen M, et al. The timing of surgical antimicrobial prophylaxis. *Ann Surg.* 2008;247:918–926.
- Sousa-Pinto B, Blumenthal KG, Courtney L, et al. Assessment of the frequency of dual allergy to penicillins and cefazolin: a systematic review and meta-analysis. *JAMA Surg.* 2021;156:e210021.
- Shenoy ES, Macy E, Rowe T, et al. Evaluation and management of penicillin allergy: a review. *JAMA.* 2019;321:188–199.
- Grant JM, Song WHC, Shajari S, et al. Safety of administering cefazolin versus other antibiotics in penicillin-allergic patients for surgical prophylaxis at a major Canadian teaching hospital. *Surgery.* 2021;170:783–789.
- Jones R, Quartuccio KS, Stern JL, et al. Antibiotic stewardship interventions improve choice of antibiotic prophylaxis in total joint arthroplasty in patients with reported penicillin allergies. *Clin Orthop Relat Res.* 2021;479:1484–1494.
- Beltran RJ, Kako H, Chovanec T, et al. Penicillin allergy and surgical prophylaxis: cephalosporin cross-reactivity risk in a pediatric tertiary care center. *J Pediatr Surg.* 2015;50:856–859.
- Pagani NR, Moverman MA, Puzitiello RN, et al. Preoperative allergy testing for patients reporting penicillin and cephalosporin allergies is cost-effective in preventing infection after total knee and hip arthroplasty. *J Arthroplasty.* 2021;36:700–704.
- Anstey KM, Anstey JE, Doernberg SB, et al. Perioperative use and safety of cephalosporin antibiotics in patients with documented penicillin allergy. *J Allergy Clin Immunol Pract.* 2021;9:3203–3207.e1.
- Pitlick MM, Volcheck GW. Perioperative anaphylaxis. *Immunol Allergy Clin North Am.* 2022;42:145–159.
- Reddy JI, Cooke PJ, van Schalkwyk JM, et al. Anaphylaxis is more common with rocuronium and succinylcholine than with atracurium. *Anesthesiology.* 2015;122:39–45.
- Bhananker SM, O'Donnell JT, Salemi JR, et al. The risk of anaphylactic reactions to rocuronium in the United States is

- comparable to that of vecuronium: an analysis of food and drug administration reporting of adverse events. *Anesth Analg*. 2005;101:819–822.
34. Ue KL, Kasternow B, Wagner A, et al. Sugammadex: an emerging trigger of intraoperative anaphylaxis. *Ann Allergy Asthma Immunol*. 2016;117:714–716.
 35. Chiewchalermrsri C, Sompornrattanaphan M, Wongsa C, et al. Chlorhexidine allergy: current challenges and future prospects. *J Asthma Allergy*. 2020;13:127–133.
 36. Opstrup MS, Jemec GBE, Garvey LH. Chlorhexidine allergy: on the rise and often overlooked. *Curr Allergy Asthma Rep*. 2019;19:23.
 37. Darouiche RO, Wall MJ, Jr, Itani KM, et al. Chlorhexidine-alcohol versus povidone-iodine for surgical-site antisepsis. *N Engl J Med*. 2010;362:18–26.
 38. Wulf NR, Schmitz J, Choi A, et al. Iodine allergy: common misperceptions. *Am J Health Syst Pharm*. 2021;78:781–793.
 39. Hsu Blatman KS, Hepner DL. Current knowledge and management of hypersensitivity to perioperative drugs and radiocontrast media. *J Allergy Clin Immunol Pract*. 2017;5:587–592.
 40. ACR Committee on Drugs and Contrast Media. *ACR Manual on Contrast Media*. Reston, VA: American College of Radiology; 2023. Available at: https://www.acr.org/-/media/acr/files/clinical-resources/contrast_media.pdf. Accessed September 4, 2023.
 41. Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma, and Immunology, American College of Allergy, Asthma, and Immunology, Joint Council of Allergy, Asthma, and Immunology. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol*. 2010;105:259–273.
 42. Venkataram A, Lahar N, Adams WP. Enhancing patient outcomes in aesthetic breast implant procedures using proven antimicrobial breast pocket irrigations: a 20-year follow-up. *Aesthet Surg J*. 2023;43:66–73.
 43. Saeg F, Schoenbrunner AR, Janis JE. Evidence-based wound irrigation: separating fact from fiction. *Plast Reconstr Surg*. 2021;148:601e–614e.
 44. Schneeberger SJ, Kraft CT, Janis JE. No-touch technique of mesh placement in ventral hernia repair: minimizing postoperative mesh infections. *Plast Reconstr Surg*. 2020;145:1288–1291.
 45. Bjerregaard J, Pandia MP, Jaffe RA. Occurrence of severe hypotension after indocyanine green injection during the intraoperative period. *A A Case Rep*. 2013;1:26–30.
 46. Garski TR, Staller BJ, Hepner G, et al. Adverse reactions after administration of indocyanine green. *JAMA*. 1978;240:635.
 47. Koca Kalkan I, Koycu Buhari G, Ates H, et al. Identification of risk factors and cross-reactivity of local anesthetics hypersensitivity: analysis of 14-years' experience. *J Asthma Allergy*. 2021;14:47–58.
 48. Thyssen JP, Menné T, Elberling J, et al. Hypersensitivity to local anaesthetics—update and proposal of evaluation algorithm. *Contact Dermatitis*. 2008;59:69–78.
 49. Bina B, Hersh EV, Hilario M, et al. True allergy to amide local anesthetics: a review and case presentation. *Anesth Prog*. 2018;65:119–123.
 50. Nucera E, Aruanno A, Rizzi A, et al. Latex allergy: current status and future perspectives. *J Asthma Allergy*. 2020;13:385–398.
 51. Rushbrook JL, White G, Kidger L, et al. The antibacterial effect of 2-octyl cyanoacrylate (Dermabond) skin adhesive. *J Infect Prev*. 2014;15:236–239.
 52. Perez JL, Rohrich RJ. Optimizing postsurgical scars: a systematic review on best practices in preventative scar management. *Plast Reconstr Surg*. 2017;140:782e–793e.
 53. Nigro LC, Parkerson J, Nunley J, et al. Should we stick with surgical glues? The incidence of dermatitis after 2-octyl cyanoacrylate exposure in 102 consecutive breast cases. *Plast Reconstr Surg*. 2020;145:32–37.
 54. Lake NH, Barlow BT, Toledano JE, et al. contact dermatitis reaction to 2-octyl cyanoacrylate following 3 orthopedic procedures. *Orthopedics*. 2018;41:e289–e291.
 55. Knackstedt RW, Dixon JA, O'Neill PJ, et al. Rash with DERMABOND PRINEO skin closure system use in bilateral reduction mammoplasty: a case series. *Case Rep Med*. 2015;2015:642595.
 56. Liu T, Wan J, McKenna RA, et al. Allergic contact dermatitis caused by Dermabond in a paediatric patient undergoing skin surgery. *Contact Dermatitis*. 2019;80:61–62.
 57. Chalmers BP, Melugin HP, Sculco PK, et al. Characterizing the diagnosis and treatment of allergic contact dermatitis to 2-octyl cyanoacrylate used for skin closure in elective orthopedic surgery. *J Arthroplasty*. 2017;32:3742–3747.
 58. Park YH, Choi JS, Choi JW, et al. Incidence and risk factor of allergic contact dermatitis to 2-octyl cyanoacrylate and n-butyl cyanoacrylate topical skin adhesives. *Sci Rep*. 2021;11:23762.
 59. Cook KA, Kelso JM. Surgery-related contact dermatitis: a review of potential irritants and allergens. *J Allergy Clin Immunol Pract*. 2017;5:1234–1240.
 60. Powell MZ, Mueller SW, Reynolds PM. Assessment of opioid cross-reactivity and provider perceptions in hospitalized patients with reported opioid allergies. *Ann Pharmacother*. 2019;53:1117–1123.