Special Article

Management and Prevention of Hypersensitivity Reactions to Radiocontrast Media: A Consensus Statement From the American College of Radiology and the AAAAI

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KEY TAKEAWAYS

1. Documentation of iodinated contrast media (ICM) hypersensitivity reactions, including symptoms and the specific inciting agent in the electronic medical record, is recommended to optimize future ICM reaction management.
2. High-quality evidence and methodologically rigorous studies are lacking owing to: (1) the rarity of moderate and severe reactions to low-osmolality iodinated contrast agents; (2) the paucity of methodologically sound studies; and (3) the heterogeneity of published studies, including the multiplicity of premedication and skin testing regimens, variations in patient selection for premedication, and differing contrast agents used in switching methodology.
3. For patients with a history of mild immediate ICM hypersensitivity reactions, premedication is not recommended; this is a change from prior American College of Radiology recommendations. Switching the contrast agent is recommended when the inciting agent(s) is known and when feasible.
4. For patients with a history of severe immediate ICM hypersensitivity reactions, it is recommended first to consider alternative imaging studies. If there is no acceptable alternative study that does not entail exposure to the same class of contrast, premedication is recommended and switching the contrast agent is recommended when feasible; this is a change from the most recent Joint Task Force Practice Parameters on Anaphylaxis. The study should be performed in a hospital setting with a rapid response team available, including personnel, equipment, and supplies to treat anaphylaxis.
5. No premedication is necessary for patients with prior chemotoxic or physiologic reactions or an isolated history of shellfish allergy or iodine allergy including topical povidone-iodine.

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SUMMARY

Key outcomes from a multidisciplinary task force on hypersensitivity reactions to iodinated contrast media include recommendations to document reactions thoroughly in the electronic health record, including symptoms and the specific inciting agent, and a discussion of varying strategies for avoidance of repeat acute hypersensitivity reactions to iodinated contrast media according to the severity of the index reaction; importantly, no corticosteroid premedication is generally recommended for patients with a prior mild acute hypersensitivity reaction.

Intravenous iodinated contrast media (ICM) is widely used in the United States, and it is imperative to provide guidance on the management of adverse reactions to ICM as well as the preparation, planning, and potential premedication for patients with previous reactions. Currently there is a discordance between the American College of Radiology Contrast Manual, which recommends premedication to prevent repeat hypersensitivity reactions to ICM, and the Anaphylaxis 2020 Practice Parameters Update, which recommends against routine administration of glucocorticoids and/or antihistamines to prevent anaphylaxis with prior ICM hypersensitivity reactions. A task force of experts from radiology who are also members of the American College of Radiology Committee on Drugs and Contrast Media and expert allergists/immunologists including members of the Adverse Reactions to Drugs, Biologics and Latex Committee of American Academy of Allergy, Asthma & Immunology evaluated the scientific evidence to develop consensus recommendations that are endorsed by both organizations. The task force took into account the strength of evidence and balanced the potential risks of recurrent reactions with those of premedication and product avoidance when making these recommendations to improve and standardize the care of patients who experience or have a history of reaction to ICM. **(J Allergy Clin Immunol Pract 2025;■:■-■)**

Key words: *Contrast allergy; Contrast hypersensitivity; Iodinated contrast allergy; Iodinated contrast hypersensitivity; Anaphylaxis; Contrast skin testing; Contrast switching; Contrast reaction; Delayed contrast reaction; Immediate contrast reaction*

INTRODUCTION

Intravenous iodinated contrast media (ICM) is widely used across the United States. Eighty million computed tomography (CT) scans were performed in the United States in 2019, an estimated 37.5% of which used ICM.[1,2] Adverse reactions to ICM can occur immediately after exposure or may be delayed. Reactions have decreased in incidence as high-osmolality contrast media (HOCM) have been replaced by low-osmolality contrast media (LOCM), with current rates of acute reactions reported at 0.2% to 0.7%.[3-6] However, it remains imperative to provide guidance on the management of immediate and delayed reactions to ICM as well as the preparation, planning, and potential premedication for patients who have experienced adverse reactions. Patients labeled as having an ICM allergy in the medical record pose a multidisciplinary clinical problem requiring health care professionals to obtain a comprehensive history and to balance the potential risks of recurrent reactions with those of premedication and product avoidance, as appropriate. A consequence is the increased use of glucocorticoid prophylaxis. Currently there is a discordance between the American College of Radiology (ACR) Contrast Manual, which recommends premedication to prevent repeat hypersensitivity reactions (HSRs) in patients with a prior reaction to ICM, and the Anaphylaxis 2020 Practice Parameters Update, which recommends against routine administration of glucocorticosteroids and/or antihistamines to prevent anaphylaxis in patients with prior ICM HSRs. Notably, this was a conditional recommendation with a low certainty rating of evidence.[7,8] Although there are standardized regimens, discrepancies exist between allergy/immunology and radiology practices, as well as between European and North American recommendations.[7-9] In addition, whereas the ACR Manual mentions that switching contrast media within the same class may help reduce the likelihood of a subsequent contrast reaction, the Anaphylaxis Practice Parameters do not discuss this strategy.

As evidence continues to evolve, there are persistent gaps between clinical care based on best evidence and normative care observed in clinical practice.[10] In addition, many myths persist related to ICM, such as an association with iodine and shellfish. To address these gaps, we convened a multidisciplinary task force of allergy/immunology physician representatives with ICM expertise from the American Academy of Allergy, Asthma & Immunology (AAAAI) and radiology physician representatives from the ACR Committee on Drugs and Contrast to evaluate the latest scientific evidence and develop consensus recommendations to guide ordering providers, allergy/immunology physicians, and radiologists in the use of contrast media and the prevention and management of contrast-associated reactions. This document contains joint statements endorsed by the ACR and AAAAI to improve and standardize the care of patients who experience or have a history of an adverse reaction to ICM. High-quality evidence and methodologically rigorous studies are lacking. Therefore, these recommendations should not be taken as definitive standards of practice because they may be subject to change as additional evidence becomes available. Although risk reduction strategies detailed here have been shown to be efficacious for reducing the frequency and severity of HSRs in prior reactors, serious reactions may still occur. Also, individuals who are not prior reactors are also at risk for iodinated contrast reactions. For these reasons, all imaging centers should be prepared to manage an adverse contrast reaction related to the administration of intravenous contrast material in any patient regardless of the history of a prior adverse reaction and should include personnel, equipment, and supplies to treat anaphylaxis. This includes adequate training of all personnel who may be involved in the care of the patient as it relates to contrast reaction management, such as the technologist, radiologist, and any nursing staff according to their scope of practice.

METHODOLOGY

Task force composition

The task force consisted of five representatives from the ACR and five from the AAAAI, who have specialized expertise in adverse reactions to ICM. All radiology members of the task force are practicing radiologists and members of the ACR Committee on Drugs and Contrast Media and have collectively authored 39 peer-reviewed journal articles related to intravenous ICM, adverse reactions to contrast media, or contrast reaction management. The AAAAI representatives include practicing allergists/immunologists who are known experts in the field, and who are also members of the AAAAI Adverse Reaction to Drugs, Biologics, and Latex Committee (A.R., M.K., A.C., and R.S.), who collectively have authored 35 relevant publications. None of the authors have relevant financial conflicts of interest.

Literature review

An initial literature review was performed of PubMed with the search terms (Iodinated Contrast Media) AND ((contrast reaction) OR (allergic[keyword] AND iodinated contrast media) OR (contrast AND (premedication AND reaction))), (Skin testing OR Patch testing OR skin prick testing OR Contrast challenge) AND (Severe cutaneous adverse reaction OR Anaphylaxis OR Immediate reaction OR IgE-mediated reaction OR Stevens Johnson Syndrome OR Toxic Epidermal Necrolysis OR Acute Generalized Exanthematous pustulosis OR Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)). The results of the literature search was divided among the members of the task force, who reviewed the titles and abstracts, identified relevant articles, and added references that were also applicable. If there was a question about relevance, this was brought to the larger group for reconciliation. The articles relevant to each subsection were reviewed in full by the authors who initially drafted those subsections (each subsection was assigned to a two-person team of a radiologist and an allergist). All articles that were relevant to the recommendations listed in the supplemental material were initially reviewed for study quality per trained ACR staff and then the full articles were reviewed for completeness and validity independently by all authors.

Strength of evidence evaluation of literature

The study quality and strength of evidence were determined following the ACR Appropriateness Criteria Evidence Document.[11] A concise adaptation of the Evidence document for grading an example study is provided in Supplemental Appendices A and B of that document; however, we recommend that reader refer to the full document for further details of this structured approach, which was developed using the principles of Grading of Recommendations, Assessment, Development, and Evaluations and the National Academy of Medicine Institute of Medicine Trustworthy Guideline standards.

Recommendation development

Common clinical scenarios related to ICM HSRs were considered by the task force and recommendations were proposed based on the literature review of the topic and the relative strength of the evidence. The task force limited the recommendations to intravenous ICM administration, which was the focus of the literature review, excluding intraarterial, intrathecal, enteric, and intra-articular injections, and excluded consideration of contrast material classes other than ICM (eg, gadolinium-based contrast agents or ultrasound contrast agents). The task force also considered the balance between the potential for benefit compared with the potential for harm or burden relevant for the decision to recommend premedication versus no premedication or contrast avoidance (more specifically, balancing the risk of recurrent iodinated contrast reactions and direct and indirect adverse effects of premedication, in the context of considering the low-quality nature of studies designed to assess reaction prevention). The practicality and feasibility of the recommendation in real-world radiology practice were also debated. After structured discussions in which all stakeholders shared perspectives and explored options, we achieved recommendations via unanimous consensus of task force members.

DEFINITIONS, CLASSIFICATION, AND DOCUMENTATION

For this document, we rely on terminology outlined in a recent AAAAI (EHR) documentation workgroup report, Anaphylaxis and Drug Allergy Practice Parameters. Broadly, the term "adverse reaction" to ICM encompasses various subcategories including immediate reactions (occurring within 1 hour of administration) regardless of whether these are IgE-mediated or non−IgE mediated, delayed (occurring more than 1 hour after administration), nephrotoxic, hemodynamic fluid shift, and others such as extravasation.[9,12,13]

An adverse drug reaction includes unintended effects of a drug that occur owing to its inherent pharmacologic properties.[12,13] Drug HSRs are immune-mediated adverse reactions that can be immediate in onset (within 1 hour) or delayed (more than 1 hour).[14,15] Symptoms of immediate-onset HSR, including hypotension, tachycardia, bradycardia, and bronchoconstriction, can all occur after the administration of ICM through other mechanisms. It may be difficult to determine whether a reaction is an immune-mediated response to ICM or has another underlying cause. Thus, it is important for the treating health care professional to document all symptoms and the time of onset of the reactions[16] in the EHR allergy field or module. This information, including the reaction treatment and monitoring time, may also be included in the radiology report if workflow permits. If there is uncertainty, symptoms should be treated as a drug HSR in the acute response and further evaluation by an allergist may be helpful once the patient is stable.

Throughout this report, we will refer to immediate ICM HSRs and delayed ICM HSRs as immediate reactions and delayed reactions, respectively. When we discuss premedication throughout the document, we are referring to glucocorticosteroids with or without antihistamine, which is reflective of the variable use of antihistamines within premedication regimens in the literature.

IMMEDIATE REACTIONS

Epidemiology of immediate reactions

Immediate reactions to LOCM and iso-osmolar contrast media have been reported to occur in 0.3% to 1.4% of injections and are most commonly mild (0.2% to 0.5%) or moderate (0.04% to 0.1%) in severity.[5,17-20] Reports of severe reactions (0.005% to 0.06%) are uncommon, as are fatalities (0.0006%).[17,18,21]

TABLE I. Categories of acute reactions to iodinated contrast media adapted from American College of Radiology Contrast Manual[7]

Type of adverse reaction	Severity	Physical findings	Vital signs
Hypersensitivity	Mild	Localized urticaria or pruritic, or few scattered hives	Normal
Hypersensitivity	Mild	Sensation of itchy or scratchy throat	Normal
Hypersensitivity	Mild	Nasal congestion, sneezing, conjunctivitis, rhinorrhea	Normal
Hypersensitivity	Moderate	Diffuse, rapid spreading urticaria (ie, ≥50% body surface area)	Normal
Hypersensitivity	Moderate	Facial angioedema	Normal
Hypersensitivity	Moderate	Throat tightness or hoarseness	Normal
Hypersensitivity	Moderate	Wheezing/bronchospasm	Normal
Hypersensitivity	Severe	Facial angioedema with dyspnea	Hypoxia
Hypersensitivity	Severe	Throat tightness or hoarseness (laryngeal edema) with or without stridor	Hypoxia
Hypersensitivity	Severe	Wheezing or bronchospasm	Hypoxia
Hypersensitivity	Severe	Hypotension	Tachycardia
Hypersensitivity	Severe	Systemic reaction involving two or more of moderate symptoms listed earlier*	May be normal or altered
Nonallergic	Mild	Limited nausea or vomiting	Normal
Nonallergic	Mild	Isolated flushing, warmth, or chills	Normal
		Headache, anxiety, or altered taste	Normal
		Subjective dizziness	Normal
Nonallergic	Mild or Moderate (if not self-limiting)	Vasovagal reaction (hypotension)	Bradycardia
Nonallergic	Moderate	Chest pain	Normal
Nonallergic	Severe	Arrhythmia	normal
Nonallergic	Severe	Convulsions or seizure	Normal
Nonallergic	Severe	Hypertensive emergency	Hypertensive with end-organ ischemia symptoms

*Systemic symptoms refer to involvement of any other body systems in addition to the system mentioned.

Pathophysiology

Controversy persists regarding the pathogenesis for immediate reactions to ICM. In most patients, these reactions are non−IgE mediated, although IgE-mediated reactions also occur.[22] The symptoms of non−IgE mediated reactions are suspected to result from mediator release from mast cells and basophils owing to the nonspecific binding of contrast to membrane receptors, the osmolality effect of the contrast media, or indirectly by complement-kinin activation.[23-25] Reports of positive skin tests with nonirritating concentrations of ICM support an IgE-mediated pathogenesis for some reactions, particularly severe ones.[26,27] Skin testing (ST) is more likely to be positive in severe reactions, particularly life-threatening ones with cardiovascular symptoms.[26,28,29]

Identifying and grading immediate reactions

Immediate reactions are referred to in the ACR Manual on Contrast Media[7] as allergic-like, based on heterogeneous mechanisms, and categorized as mild, moderate, or severe. Mild reactions are characterized by self-limited, nonprogressive symptoms (Table I). Moderate reactions exhibit signs and symptoms that are more pronounced than mild reactions but do not result in altered vital signs (eg, generalized urticaria). These reactions commonly require medical management with the potential to become severe if not treated.[7]

Severe reactions have signs and symptoms that are often life-threatening and can result in permanent morbidity or death if not managed appropriately. Severe reactions include symptoms fulfilling the criteria for anaphylaxis, as discussed subsequently.

Other non−immune mediated adverse reactions or intolerances (synonymous with physiologic reactions) are reactions that generally do not require treatment (eg, isolated nausea or vomiting with no other systemic symptoms, chills or a sensation of warmth, headaches, altered sense of taste, dizziness or lightheadedness without hypotension) as well as reactions that may require attention by appropriately trained medical personnel (eg, vasovagal reactions, panic reactions, hypertension, chest pain, arrhythmias, and seizures).[7] These physiologic reactions do not require premedication for future ICM administrations because they are non−immune mediated adverse reactions.

Treatment of mild or moderate immediate reactions and non−immune mediated reactions varies depending on the patient's symptoms and clinical circumstances. Specific recommendations are beyond the scope of this document, and potential treatment algorithms can be found in the ACR Contrast Manual.[7]

Anaphylaxis

Anaphylaxis is a specific terminology with accepted criteria well known in the allergy/immunology literature that is not as well defined in radiology literature. A summary is given next.

TABLE II. Anaphylaxis vs vasovagal

Presentation	Vasovagal	Anaphylaxis
Onset	Prompt	Within 15-30 min, more serious reactions have more rapid onset
Level of alertness	Lightheaded, transient syncope	May lose consciousness Ranges from alert to persistent loss of consciousness
Respiratory	Slowed, not labored	Dyspnea, cough, rhinorrhea, chest constriction, wheezing, stridor
Skin	Pallor, diaphoresis, clammy	Pruritus, urticaria, or flushing (>90%), angioedema
Gastrointestinal	Nausea, emesis	Nausea, emesis, cramps, diarrhea
Cardiovascular	Hypotension and alertness improve when supine	Hypotension and persistent loss of consciousness
Management	Supine with legs elevated, cold washcloth on face, reassurance, in severe cases intravenous fluids and oxygen may also be needed	Intramuscular epinephrine, supine with legs elevated, intravenous fluid, oxygen, and other measures as warranted

Clinical symptoms. Anaphylaxis is an acute life-threatening systemic allergic reaction. The National Institute of Allergy and Infectious Disease and Food Allergy and Anaphylaxis Network published anaphylaxis diagnosis criteria in 2006, and this definition remains the most widely accepted current framework. The ACR Contrast Manual does not specifically address the criteria for anaphylaxis and refers to hypotension with tachycardia as an "anaphylactoid reaction." The formal definition applies to all allergens including ingested medications or food exposure, which is why the onset could occur up to hours later. However, for our purposes we will adapt the formal definition as it applies to intravenously administered ICM.

Anaphylaxis to ICM should be considered when the acute onset of illness occurs within minutes after intravenous ICM administration and in the absence of other known allergens or triggers. In such situations, anaphylaxis is considered likely if any two or more of these criteria are met:

- Involvement of skin or mucosal tissue, or both.
- Respiratory compromise.

Reduced blood pressure or associated symptoms of end-organ dysfunction. (Note that severe hypotension may preclude the manifestation of any other anaphylaxis symptoms, and anaphylaxis should be considered when there is no other source for the acute onset of severe hypotension within minutes of intravenous ICM administration [eg, shock, sepsis, or vasovagal reaction] [Table II]).

Significant or persistent vomiting and/or severe diarrhea. (Note that these gastrointestinal symptoms in isolation do not meet the criteria for anaphylaxis and should be significantly more severe than the typical quickly resolving vomiting that can be a side effect of ICM.)

These criteria should be considered when evaluating and treating an acute ICM reaction in real time and retrospectively when determining the optimal approach to preventing an acute reaction before future contrast-enhanced radiologic studies.

Because most anaphylaxis cases to ICM have been shown to occur within 15 to 30 minutes after administration of contrast, and the mean delay between injection and reaction has been shown to be shorter with higher-grade reactions, the monitoring of routine patients who have received intravenous ICM regardless of a reaction history should fall within this time frame and comply with all federal or state laws or regulations and local, institutional, site, and facility policies, guidelines, or rules.[26,30]

A serum tryptase value elevated above baseline collected between 30 minutes and several hours (ideally 2 hours but potentially up to 4 to 6 hours) after symptom onset supports a diagnosis of anaphylaxis,[31] although this laboratory value has no role in acute diagnosis and management. A serum tryptase that is not elevated lacks optimal sensitivity to rule out a diagnosis of anaphylaxis.[8,32]

Anaphylaxis versus vasovagal reaction. The vasovagal reaction is an important condition to differentiate from acute anaphylaxis, as detailed in Table II.[33] Features of a vasovagal event may include pallor, weakness, nausea, vomiting, diaphoresis, bradycardia, and hypotension. These reactions can usually be distinguished from anaphylaxis by the absence of skin manifestations: urticaria, angioedema, flush, and pruritus, which are seen in most cases of anaphylaxis cases.[34] Patients with vasovagal reactions typically exhibit bradycardia rather than tachycardia generally observed with anaphylaxis,[33] although bradycardia rarely occurs during anaphylaxis owing to a cardioinhibitory reflex. A distinguishing feature is that bradycardia is observed immediately with a vasovagal event whereas in anaphylaxis, tachycardia precedes the onset of bradycardia. Proper recognition of patients with anaphylaxis is important because a delay in administering epinephrine is a risk factor for adverse outcomes.[35] It is also important to recognize a vasovagal reaction and treat it appropriately. Patients who are prone to vasovagal reactions are not candidates for premedication before re-exposure to contrast. In addition to vasovagal reactions, there is a differential diagnosis for anaphylaxis that must be considered, as reviewed in Table III.

Management of anaphylaxis. The presentation of anaphylaxis is heterogeneous and dynamic, and the treating clinician should continuously reassess the clinical scenario. Although other therapies such as oxygen and antihistamines may be given as the clinical situation unfolds, the two most important steps in ICM anaphylaxis management are stopping the ICM infusion (if ongoing) and administering epinephrine. There is widespread consensus that epinephrine is the first line of treatment for anaphylaxis.[8] No absolute contraindications exist for using epinephrine to treat anaphylaxis[36,37] including patient comorbidities (eg, cardiac disease, age, frailty). Epinephrine counteracts the effects of the myriad of mediators of anaphylaxis and arrests further mediator release. All other therapies, including antihistamines, glucocorticoids, and bronchodilators should be secondarily considered after stabilization. An intramuscular injection of 0.01 mg/kg of a 1:1,000 concentration (1 mg/mL) of

TABLE III. Differential diagnosis of anaphylaxis

Differential diagnosis	Distinguishing features
Exacerbation of asthma	History of asthma
Exacerbation of chronic urticaria	History of chronic urticaria
Inducible laryngeal obstruction or vocal cord dysfunction	No associated cutaneous symptoms
Panic attack	No significant vital sign changes
Munchausen stridor	Factitious anaphylaxis, no significant vital sign changes
Cardiovascular	Chest pain with precordial radiation, diaphoresis, shortness of breath and absence of cutaneous symptoms
Cerebrovascular	Focal neurologic deficit
Flushing syndromes	Preexisting conditions (eg, carcinoid, mastocytosis, pheochromocytoma)
Reaction to other recent medication or food ingestion	Temporal relationship to other medications or foods
Postural tachycardia syndrome	Postural tachycardia without orthostatic hypotension; no associated cutaneous symptoms; history of postural tachycardia syndrome

epinephrine should be administered, with a maximum single dose of 0.5 mg (for >50 kg) which may need to be repeated in severe cases.[8,38] These doses may be drawn from an ampule via a syringe. Alternatively, epinephrine autoinjectors are available from several manufacturers with prespecified epinephrine doses of 0.3 mg for patients greater than 30 kg and 0.15 mg for children less than 25 to 30 kg.[39-41] If staff experience in drawing and administering epinephrine is limited, an autoinjector may minimize errors and expedite epinephrine delivery.[42,43] It is nonetheless important that staff be adequately trained on autoinjectors (through training devices or simulation) because there is a risk for accidental finger injection,[44] although even accidental autoinjection has an overall low risk of permanent morbidity. Epinephrine should be administered into the vastus lateralis in the anterolateral thigh, to allow optimal absorption.[8,45,46] Intramuscular epinephrine is the first-line therapy for anaphylaxis, but in rare cases of protracted anaphylaxis, intravenous epinephrine infusion (1:10,000 concentration (1 mg/10mL)) may be necessary.[8] Delay in administering epinephrine has been associated with anaphylaxis fatalities and increased risk of biphasic reactions,[8,35,47] but this is not specific to ICM anaphylaxis.

Other treatments should be employed as necessary for anaphylaxis. Fluid resuscitation should commence immediately in patients presenting with hypotension, and patient positioning should be changed to supine or Trendelenburg. Supplemental oxygen may be necessary for patients with respiratory symptoms. H1 and H2 antihistamines are commonly administered in cases of anaphylaxis, but there is only indirect evidence supporting this practice and H1 antihistamines will address only cutaneous manifestations of anaphylaxis, none of which are life-threatening. An attempt at a systematic review of the efficacy of H2 antihistamines in anaphylaxis identify no high-quality evidence supporting this practice.[8,48] Glucocorticoids have no role in treating acute anaphylaxis given the slow onset of action.[8] The recent practice parameter update on anaphylaxis also recommended against the administration of glucocorticoids to prevent biphasic anaphylaxis, because multiple studies, including systematic reviews, have not demonstrated clear evidence that glucocorticoids prevent biphasic anaphylaxis.[49-52] After suspected anaphylaxis, patients should be kept under observation until signs and symptoms have fully resolved. Because most imaging centers are not staffed or designed for extended observation of patients, any patient suspected of having had anaphylaxis to ICM should be sent to the nearest emergency department.

Patients should be educated regarding the possibility of biphasic anaphylaxis. Biphasic anaphylaxis occurs when the initial symptoms of anaphylaxis resolve completely but then recur up to 72 hours later, with a mean of 11 hours.[53,54] Protracted anaphylaxis (when anaphylaxis symptoms remain continuous and intravenous epinephrine may be required) occurs even more rarely.[55] An analysis of 145 patients with ICM anaphylaxis demonstrated that 10.3% developed biphasic anaphylaxis and 4.1% developed refractory anaphylaxis.[56] Biphasic anaphylaxis is associated with greater severity of the initial reaction and requirement of more than one dose of epinephrine to treat initial symptoms (odds ratio = 4.82; 95% CI, 2.70-8.58). Evidence suggests that epinephrine administration early in the course of acute anaphylaxis may improve clinical outcomes by reducing the risk of biphasic reaction.[57-59]

Based on available evidence, it would be prudent to extend observation to up to 6 hours or longer (including hospital admission) for a patient with severe anaphylaxis and/or requiring more aggressive treatment (eg, one or more doses of epinephrine) for potential biphasic event after complete resolution of signs and symptoms.[8,60] Regardless of severity, all patients should be observed until signs and symptoms of anaphylaxis have fully resolved.

Prevention of immediate reactions to ICM

Historical context for corticosteroid prophylaxis. The initial studies evaluating corticosteroid prophylaxis were done to prevent recurrent immediate reactions with HOCM.[61-63] The protocols involved premedication with oral glucocorticoids and H1 antihistamines, with or without H2 antihistamines and ephedrine, to prevent the nonspecific release of histamine and other mediators from circulating basophils, which is the presumed mechanism in most contrast reactions.[61-64] Studies evaluating the efficacy and safety of premedication entailed substantial variation in medications used and the timing of their corticosteroid administration (eg, prednisone 50 mg 13 hours, 7 hours, and 1 hour before ICM; methylprednisolone 32 mg 12 and 2 hours before ICM).[61,64-66] Moreover, glucocorticoids take several hours to work.[67] Glucocorticoid administration is associated with acute basopenia, providing a basis for the efficacy of these premedication regimens.[68]

The risk of adverse immediate ICM reactions has been dramatically reduced with the universal use of LOCM. There is no high-quality evidence supporting the benefit of corticosteroid

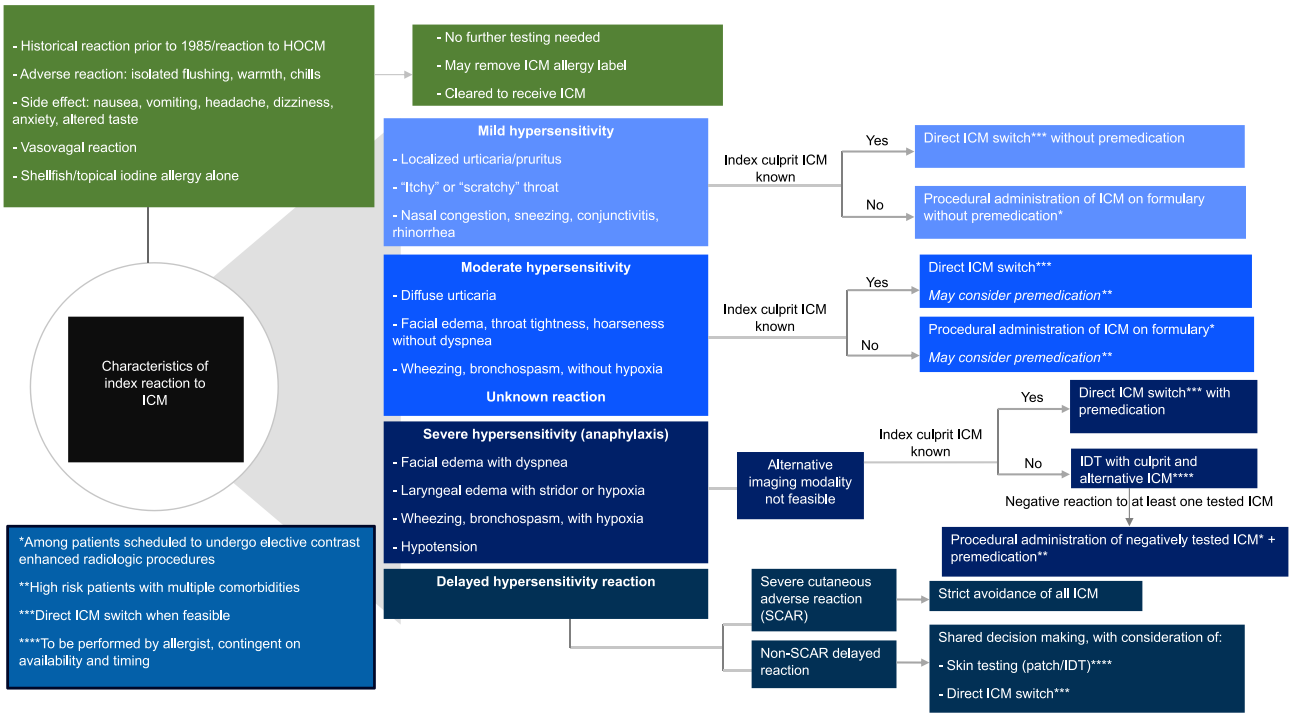

FIGURE 1. Flowchart for management of reactions to iodinated contrast media (ICM). *HOCM*, high-osmolality contrast media; *IDT*, intradermal testing.

premedication in preventing recurrent reactions in patients receiving LOCM, owing to variations in premedication protocols and the low rate of severe reactions to LOCM.[10,17,64,65,69] Despite these unproven and modest benefits, a survey of radiologists in 2009 showed increasing support for using premedication regimens compared with 1995.[10]

Is premedication recommended for prior reactors in association with the administration of LOCM?

In making management recommendations, our task force has prioritized the potential for benefit of premedication for severe prior reactors (reduced likelihood of severe immediate reaction) based on very low-quality evidence from HOCM studies being extrapolated to LOCM and very low-quality evidence from LOCM studies, compared with the potential for harm (risk for untoward effects from corticosteroid and antihistamine premedication and burden (diagnostic delay, needing a driver, etc).

Direct risks of corticosteroid premedication are generally considered to be minor. One of the most studied effects is transient asymptomatic hyperglycemia, generally lasting 48 hours or less.[70,71] Transient leukocytosis, sleeplessness, mood changes, and potential for increased infection risk have been studied as possible effects of short-term oral corticosteroids, although many reports define short-term as up to 30 days rather than the 12- or 13-hour treatment regimen recommended by the ACR and, until recently, the Joint Task Force on Practice Parameters.[7,8,65,72-75] Additionally, although considered optional by the ACR, some premedication regimens include diphenhydramine (or other antihistamines, including second-generation ones). Direct risks of diphenhydramine include anticholinergic and sedative effects, which may impair a patient's ability to drive and necessitate coordination with a driver. Indirect risks of premedication include diagnostic delay because of the time required to complete the premedication regimen.[76] For this reason, the role of premedication has become controversial, with questions raised as to whether the potential benefit (reduction in risk for immediate reaction) outweighs the potential for harm (untoward effects from corticosteroid and antihistamine administration and prolonged length of hospital stay for inpatients).[77,78] Given the substantially lower rate of immediate reactions with routine use of LOCM, premedication may pose a greater risk for indirect harm than the direct harm this regimen is intended to prevent. Overall, there is limited evidence that premedication for immediate reactions is helpful.[79]

Is premedication recommended for prior reactors with moderate and severe reactions?

A comprehensive analysis carried out by the Joint Task Force on Practice Parameters[8] did not demonstrate benefit from premedication to prevent immediate reactions in prior reactors (relative risk = 1.07; 95% CI, 0.67-1.71) and suggested against routine administration of glucocorticoids and/or antihistamine premedication to prevent immediate reaction before re-exposure to ICM for prior reactors, with a very low certainty of evidence. Considering this, and weighing the potential benefits with the potential for harm or burden with premedication, premedication may still be an option for moderate reactions, but this evidence is of low quality and certainty. We also acknowledge that previous reaction severity may not predict future reaction severity.[80] We recommend premedication for patients with a history of severe reactions to ICM for whom an alternative imaging study is not an option and when the untoward consequences of premedication and delayed diagnosis are small (Figure 1),[78] while acknowledging that the evidence supporting this recommendation is of very low

quality. One early landmark trial in LOCM in 1994 was underpowered to evaluate the efficacy of corticosteroids to prevent reactions and included chemotoxic, vasovagal, or other reactions as well as immediate reactions, with decreases seen in physiologic reactions as well as mild to moderate symptoms, but no significant reduction in severe immediate reactions.[65] A pooled analysis of 736 patients in five retrospective studies included some moderate and severe reactions. Patients who did not receive premedication had initial pooled HSR rates of 0.16 (95% CI, 0.07-0.35), compared with 0.02 in association with premedication (95% CI, 0.01-0.06); patients who had prior HSRs and received premedication were significantly less likely to experience HSRs (odds ratio = 0.09; 95% CI, 0.03-0.25; $P < .00001$). However, methodologic shortcomings were present in all five studies: (1) There was substantial heterogeneity in corticosteroid and antihistamine premedication regimens across and within these studies; and (2) indications for premedication were not limited solely to moderate or severe reactions. In addition to prior ICM reactions, pretreated patients included those with previous "allergic-like or unknown-type reactions" to ICM, "history of bronchial asthma," or "a history of allergies requiring medical treatment." Although a statistically significant reduction in the rate of moderate or severe reactions was observed compared with no treatment in this recent systematic review and meta-analysis,[78] these regimens reduce but do not eliminate the risk for an immediate reaction, with breakthrough reactions occurring in approximately 2.1% of this patient group.[7,69,79,81] Nearly half (48%) of breakthrough reactions may be moderate or severe despite premedication and can be acutely life-threatening or require prompt medical attention.[81] Repeat immediate reactions have been shown to occur in up to 12% of patients with moderate or severe breakthrough reactions and occur more often in patients with moderate or severe index reactions.[79,81]

When circumstances imply a high risk for serious anaphylaxis based on a history of severe reaction and one or more comorbid conditions (eg, mastocytosis) that imply the greater risk for more serious immediate reaction is present, the balance between the potential for benefit and the potential for harm or burden favors administering premedication with systemic corticosteroids with or without antihistamines. For patients with a history of moderate reaction, a shared decision-making approach, weighing risks versus benefits from an individualized standpoint, allowing the patient to participate in the medical decision-making process by expressing values and preferences, is most appropriate.

Is premedication recommended for prior reactors with mild reactions?

Based on the evidence for benefit compared with the potential for harm or burden, premedication is not recommended for patients with a history of mild reaction (Figure 1). As is the case with the previous recommendation for moderate to severe prior reactors, additional studies that are methodologically sound are required to determine whether the benefit from premedication before administration of LOCM for prior reactors exceeds the harm or burden associated with this treatment. Given the low confidence in the certainty of evidence, future studies may lead to a change in this recommendation. Although premedication is not generally recommended in this patient group, we acknowledge that such patients may be premedicated in rare instances after shared medical decision-making between the patient and the health care provider or because of strong patient preferences or clinical circumstances.

Should direct switching from incriminated ICM to an alternative agent be performed?

A direct switch away from the incriminated ICM agent may protect against a repeat breakthrough reaction and may also be more effective than premedication. Abe et al[82] reported that a direct switch to an alternative agent was associated with greater protection against recurrent HSR compared with corticosteroids premedication. However, most patients had a mild reaction without a standardized switching protocol. The overall breakthrough reaction rate was 28% when the same ICM was administered without corticosteroids premedication compared with 17% when the same ICM was given with steroid premedication and an 8% recurrence rate with a direct switch between LOCM and no premedication. Concordantly, a multicenter study reviewed the incidence of breakthrough reactions among patients with re-exposure to ICM and a history of moderate to severe HSR.[83] This study similarly noted that directly changing from the culprit agent to an alternative ICM led to a significantly decreased breakthrough rate of 13.4% compared with 27.6% when the same ICM was used.

The most substantive evidence thus far comes from a study by McDonald et al.[80] The authors performed a retrospective evaluation of 1,973 patients with immediate ICM-induced HSR who underwent 4,360 contrast-enhanced CT scans and compared outcomes with corticosteroids prophylaxis versus direct ICM switch. Premedication alone was not effective at preventing breakthrough reactions in patients who received the same ICM agent as the index reaction: 26% (44 of 172) versus 25% without prophylaxis (73 of 298). However, the direct ICM switch was highly effective at preventing breakthrough reactions and resulted in breakthrough reactions in 3% of patients with premedication and 6% without premedication.

Most recently, a systematic review and meta-analysis of six studies, including 7,155 adult patients with prior ICM-induced HSR, compared outcomes in 2,826 patients who received the same ICM and 4,329 who received a different ICM agent.[84] The studies were widely heterogeneous with no standardization in either the switching methods or the premedication regimen used, which limits the interpretation of these data. Substitution with an alternative ICM agent decreased the risk of breakthrough reactions by 61% compared with using the same agent in patients with prior immediate HSRs. These data must be interpreted with caution given the observational nature of the studies and limited quality, but they provide support for changing the culprit ICM agent if possible. Severe reactions occurred in about 0.2% of patients (n = 11 of 7,155 patients in the six studies reporting reaction severity), limiting the ability to interpret the effect on severe reactions. A subanalysis in this meta-analysis suggested that premedication did not decrease the risk of recurrent reactions in the aggregate cohort.[84] The strategy of a direct switch is supported by the finding that patients with a positive skin test to the index ICM often test negative to alternative agents.[28,85-87] Overall, the data favor switching ICM agents to decrease recurrent reactions in situations where this is possible and the index agent is known (Figure 1). There is no known direct harm to the patient from switching agents.

The ACR Manual on Contrast Media advises a direct switch to an alternative LOCM in patients with a history of immediate

reaction to ICM when the inciting agent is known, whereas the 2020 Practice Parameter on Anaphylaxis did not discuss this potential strategy. The task force found the data on switching agents compelling enough at this time to recommend it for all levels of severity of index reactions when feasible. This caveat, "when feasible," is in place for several reasons including the absence of a documented culprit ICM in the EHR and the lack of patient knowledge regarding which agent to replace. One study showed that only 1.6% of patients were able to name the contrast agent to which they reacted.[88] Additionally, the task force recognizes from practical experience that switching agents may be logistically challenging or even impossible depending on institutional limitations, as highlighted by the recent ICM severe contrast shortage. In the United States, ICM is supplied by only four companies, two of whom supply 90% of the ICM infusions. This, coupled with the limited distribution channels for ICM and consolidation of buyers into group purchasing organizations, results in many institutions having preferred vendor contracts, which limits the number of alternative contrast agents allowed on formulary and may be cost-prohibitive because certain agents may be significantly more expensive.[89] In addition, it may be workflow-prohibitive to switch agents using multiple-dose injectors, some of which are approved by the Food and Drug Administration for single-vendor contrast agents and could result in large amounts of wasted contrast from needing to switch agents before using up a multiple-dose vial.

DELAYED REACTIONS

Epidemiology of delayed reactions

The incidence of delayed HSRs is difficult to quantify accurately owing to the delayed onset of presentation (anywhere from hours up to 1 week after ICM administration), the difficulty of establishing causality, and missed reporting. Reactions may also not be characterized according to commonly used grading schema, creating a barrier to optimal characterization.[18,83] The available literature does not always distinguish between immediate and delayed reactions. Each of these complicating factors could result in either underestimation or overestimation of the true incidence of this condition.[90]

Noting these limitations, delayed HSRs are thought to be less common than acute HSRs, comprising an estimated 0.5% to 23% of all ICM HSRs.[91] Several retrospective studies and at least one prospective study suggest a prevalence of 0.5% to 46%, although the inclusion of physiologic-type reactions (eg, altered taste sensation or restlessness) and inclusion of both intra-arterial and intravenous administration of ICM may have contributed to the wide range.[92-96]

Pathophysiology of delayed reactions

Delayed HSRs could be related to a T cell−mediated mechanism, with skin biopsies demonstrating a perivascular infiltration of CD4 and CD8 T cells.[15,97] Evidence after allergy investigations, such as ST and drug challenge, implicates an immunologic mechanism in more than 50% of reported HSRs.[22,98-100]

It is suspected that the immunologic mechanism of these delayed reactions is attributed to the structure of the ICM, because nonionic dimeric ICM (eg, iodixanol) is associated with more cutaneous reactions compared with nonionic monomeric ICM, although the exact mechanism for nonallergic urticaria and or angioedema more than 6 hours after ICM administration is unknown.[7]

Identifying delayed reactions to ICM

A retrospective review of more than 74,000 adverse reactions to intravenous LOCM injections throughout Korea suggested that DHRs comprised 11.4% of all contrast reactions; greater than 99% manifested with solely cutaneous symptoms, and 88% in the form of a maculopapular exanthem.[93]

Whereas the vast majority of DHRs would be classified as mild according to the schema described by the ACR,[7] there are case reports of severe cutaneous adverse reactions (SCARs) such as acute generalized exanthematous pustulosis,[101-104] drug reaction with eosinophilia and systemic symptoms,[97] and Stevens-Johnson syndrome/toxic epidermal necrolysis.[105-109] There is no role for extending monitoring patients with a history of a delayed reaction at the time of a subsequent contrast study beyond routine monitoring.

Prevention of delayed reactions

Should premedication and or direct switch be used in patients with a history of delayed reaction to ICM?

Currently, the literature is limited regarding the rate of subsequent reactions after an initial delayed reaction to ICM, the risk factors for or the underlying mechanisms of these subsequent reactions, and the accuracy of allergy testing. The available evidence does not support premedication as a strategy to prevent recurrent reactions. Only a small retrospective study showed a possible benefit for corticosteroid use before and after intervention in nonsevere delayed reactions.[110] Cross-reactivity among the different ICM agents has been described for both immediate and delayed reactions.[85] A higher rate of cross-reactivity has been described in patients with delayed reactions compared with patients with immediate reactions.[111] To date, no formal evidence-based recommendations can be formulated concerning direct switching for patients reporting non-SCAR delayed reactions. The final decision about direct switching in this patient population should be made by the patient and treating physician and depends on the indication for the study.

Summary for delayed reactions

For patients with a history of delayed reactions to ICM, there is no evidence to support premedication as a strategy to prevent recurrent reactions. Patients with a SCAR to ICM should strictly avoid ICM in the future.[112,113] For patients with a non-SCAR reaction, the decision to use contrast and whether to direct switch should be made by the patient and treating physician depending on the need of the study and the reaction history.

IODINATED CONTRAST MEDIA MYTHS

Is allergy a risk factor for immediate or delayed ICM reactions?

In 1975, a prospective study of factors associated with adverse reaction to HOCM in 112,003 patients described an association of allergy with a greater rate of adverse reaction from contrast infusion.[114] An elevated rate of adverse reactions to HOCM was associated with self-reported allergy to medications and foods, such that the authors concluded "the overall incidence of adverse reactions in patients with allergy is about twice that in the general population."[114]

This study had several methodologic weaknesses: (1) the data were obtained via a questionnaire with no corroborative testing performed to confirm the self-reported history of allergy to drugs or foods; (2) there was no evaluation to verify the self-described history of asthma, allergic rhinitis, or general allergy; and (3) patients who experienced a reaction from HOCM consistent with anaphylaxis or symptoms related to the effects of mast cell mediator release were not distinguished from those who experienced vasovagal, hemodynamic, or other adverse reactions.

Is seafood allergy associated with an elevated risk for anaphylaxis for ICM and an indication for premedication before contrast exposure?

Survey data from 2008 demonstrated that most radiology and cardiology participants screen for seafood allergy before the administration of ICM, and a significant subset would either withhold ICM or administer premedication for patients responding affirmatively.[115] The task force believes that the surveillance study by Shehadi[114] is likely the original source for the mistaken belief that seafood allergy is associated with greater risk from contrast infusion.

Self-reported allergy to other foods was also more common in individuals who had contrast media reactions; however, the highest reaction rate (14.98%) was found among those with allergy to seafood or shellfish. A clear association between seafood allergy and greater risk for immediate ICM reactions has not been established. Patients with self-reported seafood allergy and those with confirmed IgE-mediated (allergic or anaphylactic) potential to crustaceans are not at elevated risk for immediate or delayed ICM reaction compared with the general population, and thus should not be regarded as candidates for risk reduction measures.[116]

Is iodine allergy associated with an elevated risk for anaphylaxis from ICM and an indication for premedication before contrast exposure?

It is unclear how seafood allergy and iodine allergy became linked.[117] As older contrast agents disassociated into ions containing an iodinated benzene ring, they were regarded as iodine-based. When the myth developed that seafood allergy was related to contrast reactions,[114] it is possible that a causal link between the iodine content of crustaceans and contrast material was assumed. However, the mechanism for immediate ICM reaction is most likely related to the physiochemical properties of these media and is unrelated to its iodine content.[33] IgE-mediated reaction to crustaceans is unrelated to iodine, but rather to tropomyosin.[118]

Iodine is not an allergen. As a public health intervention, iodine was added to table salt to prevent iodine deficiency, such that the population is universally exposed to iodine. There is no evidence to support the assertion that patients who have been labeled as having iodine allergy are at elevated risk for a contrast media reaction.[119] Patients who have had (1) iodide-induced sialadenitis or (2) an adverse reaction to potassium iodide are also not candidates for premedication before ICM administration.[120,121]

Is a prior gadolinium-based contrast media immediate reaction an indication for premedication before contrast exposure?

A few studies demonstrated an increased risk for immediate reaction to ICM in patients with a history of immediate reaction to gadolinium-based contrast media (GBCM); however, these were self-reported adverse reactions, and some (eg, headache, dizziness, or injection site reaction) were not immune-mediated.[122,123] In addition, it is unclear whether patients who have had non−IgE mediated anaphylaxis from GBCM are at elevated risk from receiving ICM based on an indirect hazard associated with shared risk factors. From a pharmacologic standpoint, there is no similarity between the chemical structures of ICM and GBCM to suggest cross-reactivity. Adverse reactions to GBCM occur at a lower rate than to ICM. The reported rate of anaphylaxis ranges from 0.004% to 0.7%; severe reactions occur in the range of 0.001% to 0.01%.[7,124]

There is currently no clear evidence to support premedication for ICM owing to a history of immediate reaction to GBCM.

SKIN TESTING AND RAPID DRUG DESENSITIZATION

Should ST to ICM be performed for a history of immediate reactions?

The current European guidelines recommend ST with the culprit agent and a panel of alternative contrast media for patients with a history of ICM-induced anaphylaxis, to identify a tolerated agent.[15] Skin testing may be helpful in the evaluation of higher-risk patients with a history of severe HSRs, especially in those with a history of reaction in the past 6 months who need repeat contrast administration.[125-127] However, ST to ICM is not routinely performed in the United States, and access to ST in a timely manner may limit routine implementation.[128]

It is recommended to perform skin prick testing and intradermal testing (IDT) with undiluted ICMs and 1:10 diluted ICM solution (300-320 mg/mL), respectively.[15,26,129-131] Intradermal testing results may lack optimal specificity owing to an irritant effect; conversely, a negative skin test does not preclude a recurrent reaction.[126] The lack of standardized ST methodology and protocols in the literature to date also complicates the comparison of results across the literature and conclusions regarding its diagnostic accuracy. Overall, ST to ICM has a negative predictive value of 80% to 97.3% for immediate reactions; however, the positive and negative likelihood ratios of ICM ST have not been determined.[15,132] Reaction severity appears to correlate with ST positivity,[125] and in one study, 81.8% of patients with ICM-induced anaphylactic shock had positive ST results with ICM, with largely negative results in mild reactors.[26] This was reproduced in a meta-analysis of patients with ICM-induced immediate HSR, in which pooled per-patient ST positivity rates increased from 17% (95% CI, 10% to 26%) in an unselected population to 52% (95% CI, 31% to 72%) among patients with severe index reactions.[127] The timing of the investigation is also important; ST within 6 months of the reaction is recommended owing to higher sensitivity.[15]

Allergist referral for ST in the setting of severe HSRs may be helpful, particularly if the culprit agent is unknown, for the selection of a potentially tolerated agent and for a direct switch to an alternative agent if the ICM used during the index reaction is known. However, a risk-benefit discussion with the patient is important because 7% of patients with negative testing react to contrast on repeat administration, and the benefit of ST needs to be clarified through prospective studies.[133,134] Studies investigating the role of ST in the evaluation of immediate HSRs are listed in Table IV. Figure 1 outlines a suggested workflow.

TABLE IV. Summary of evidence for skin testing in evaluation of iodinated contrast media allergy

Study	Study design	Clinical end point	Study groups	Skin test protocol	DPT protocol	Skin test results	DPT results	Conclusion
Ahn et al (2022)[135]	Retrospective cohort study	Compared two DPT doses for challenge with ST-negative ICM. Examined rate of breakthrough reactions (BTR) in ST and challenge-negative patients during CT scans after corticosteroid premedication	Korean cohort (n = 85) with history of ICM-induced anaphylaxis	IDT (1:10) with task force of ICM	IV challenge using two DPT doses (10 vs 30 mL)	ST sensitivity 74%	9.6% ST-negative patients had positive DPTs (3.6%)/BTRs (7.6%)	80% of BTRs were severe with 10-mL DPT dose No severe reactions with 30-mL DPT dose, which may suffice to rule out BTRs
Gamboa et al (2021)[125]	Prospective cohort study	Examined cross-reactivity between iomeprol and iopamidol among patients with iomeprol-induced immediate HSR and tolerance to alternative agents	Spanish cohort (n = 216) with history of ICM-induced immediate HSR	IDT (1:10) with task force of ICM	IV challenge with 100-mL dose (no premedication)	ST sensitivity 20.4% 32 of 36 selective ST-positive iomeprol Low ST cross-reactivity rate (11%) between iomeprol and other ICM	84.7% ST-negative patients with iomeprol-induced reactions tolerated IV challenge	Iomeprol-allergic patients had uneventful CT scans with alternative ICM (no premedication)
Kwon et al (2019)[134]	Retrospective cohort study	Evaluated IDT to ICM in patients with index reaction to a known causative agent Examined the rate of BTRs in patients during CT scans after premedication, grouped by IDT results to the index culprit ICM	Korean cohort (n = 69) with history of immediate HSR to known culprit ICM	IDT (1:10) with task force of ICM	N/A	38 patients with positive IDT to culprit ICM (CULPRIT+) 31 patients with negative IDT to culprit ICM (CULPRIT−) ST sensitivity 87%	N/A	16 CULPRIT+ and 22 CULPRIT− patients had ICM re-exposure CULPRIT+ group: four of five patients had BTRs with IDT-positive alternative ICM, no BTRs with IDT-negative ICM CULPRIT− group: no BTRs with IDT-positive alternative ICM, two BTRs with IDT-negative alternative ICM ST useful in selecting safe alternative only with positive IDT to culprit ICM

(continued)

TABLE IV. *(Continued)*

Study	Study design	Clinical end point	Study groups	Skin test protocol	DPT protocol	Skin test results	DPT results	Conclusion
Trautmann et al (2019)[126]	Retrospective cohort study	Assessed the NPV of ST for ICM	German cohort (n = 45), 32 with history of immediate HSR	IDT (1:10) to battery of ICM	IV challenge with 49-mL total dosed at 30-min increments	ST-positive patients (11) categorized as allergic; ST-negative patients (21) categorized as nonallergic All ST-positive patients had moderate to severe anaphylaxis; ST-negative patients had only urticaria	Of 10 allergic patients, all tolerated IV challenge with ST-negative alternative RCM	IDT highly sensitive in identifying allergic patients DPT with ST negative ICM is safe and helps to identify a tolerated alternative ICM
Clement et al (2018)[26]	Prospective multicenter cohort study	Investigated frequency of immediate ICM-induced HSR Correlation of positive ST with likelihood of true ICM-induced allergic reactions	French cohort (n = 209) with history of immediate HSR	IDT (1:10 and full-strength) to battery of ICM	N/A	41 (19.6%) positive ST results to ICM	N/A	Positive ST correlated with clinical severity, cardiovascular signs, and histamine and tryptase concentrations
Schrijvers et al (2018)[85]	Retrospective cohort study	Assessed the NPV of ST for ICM in predicting reactions during future ICM re-exposure with variable premedication use	French cohort (n = 597), 423 (70.9%) with history of immediate HSR	IDT (1:10) to battery of ICM	N/A	Positive ST: 56 of 423 patients NPV of ST: 94.2%	N/A	172 (40.6%) re-exposed to ICM with BTRs in 10 of cases (5.8%) 16 of 17 ST-positive patients (94.1%) tolerated re-exposure without a reaction 201 of 216 ST=negative patients (93.1%) tolerated re-exposure
Lerondeau et al (2016)[111]	Retrospective cohort study	To analyze ICM cross-reactivity in immediate and delayed HSR based on ST and DPT	n = 38 with history of immediate HSR	IDT (1:10) to battery of ICM	IV challenge with 1/100 to >1/10 final dose	24 (63.1%) ST-positive	Two (5.2%) positive challenges	High rate of cross-reactivity (67%) for immediate and delayed reactions based on ST

Yoon et al (2015)[127]	Meta-analysis	Evaluated the diagnostic potential of ST in patients with ICM-induced immediate HSR in predicting tolerance to ST-negative agents	Meta-analysis of 21 studies investigating ST to ICM	SPT (full strength) and IDT (1:10) with task force of ICM	N/A	ST-positive rate 17% in immediate HSR and 52% with severe immediate HSR	N/A	7% BTR rate to ST-negative ICM
Prieto-Garcia (2013)[136]	Retrospective cohort study	Evaluated the predictive value of IDT in patients with index reaction to a known causative agent Evaluated outcomes with controlled challenge testing using alternative ST-negative ICM in ST-positive ICM reactors	Spanish cohort (n = 106) with history of ICM-induced immediate HSR	IDT (1:10) to battery of ICM	IV challenge with 120-mL dose (no premedication)	IDT-positive to culprit ICM in 11 of 106 patients (10.4%)	Five of 11 patients tolerated DPT with ST-alternative ICM Two additional patients tolerated ST-alternative ICM during subsequent CT	Patients with + IDT to culprit ICM tolerated subsequent exposure to ST- alternative ICM without premedication
Caimmi et al (2010)[87]	Retrospective cohort study	To evaluate the NPV of ICM skin tests	French cohort (n = 24) with history of ST for ICM-induced immediate HSR and subsequent re-exposure to ICM (no premedication)	SPT (full strength) and IDT (1:10) with task force of ICM	N/A	ST positive in 17 of 24 patients	N/A	High NPV of ST ~96% in preventing BTRs following re-exposure to ICM
Brockow (2009)[22]	Prospective cohort study	To evaluate the sensitivity and specificity of ICM ST in previous reactors	European cohort (n = 122) with history of ICM-induced immediate HSR	SPT (full strength) and IDT (1:10) with task force of ICM	N/A	ICM ST had 96% to 100% specificity	N/A	~50% immediate reactors were ST+ on tests performed 2 to 6 months of the index reaction

BTR, breakthrough reaction; *CT*, computed tomography; *DPT*, drug provocation test; *HSR*, hypersensitivity reaction; *ICM*, iodinated contrast media; *IDT*, intradermal testing; *IV*, intravenous; *N/A*, not available; *NPV*, negative predictive value; *RCM*, radiocontrast media; *ST*, skin testing.

Should ST to ICM be performed for patients with a history of delayed reaction?

Although ST has been evaluated in delayed ICM reactions, its accuracy is poorly understood.[87,137-139] Skin test modalities include patch testing and delayed IDT with the culprit and alternative ICM.[15,22,90,98,126,137,140,141] The described nonirritant concentration for IDT and patch testing is 1:10 and undiluted, with reading performed at 24 to 72 hours.[15,90,137,142,143] The specificity of delayed IDT had been calculated at 100%,[86,127,138] but the sensitivity is unknown at this time.[127] A recent meta-analysis demonstrated that *in vivo* investigations were positive in 16.9% to 53.5% of patients, with positive provocation after ST in 0% to 34.6% of them.[98,131] The negative predictive value of a negative skin test and challenge has been calculated at 90% to 96% in some clinical studies.[85,87,98,144] In another meta-analysis looking at patients with positive skin tests, alternative ICMs were tolerated in 71% (75 of 105).[98]

To date, no formal evidence-based recommendations can be formulated concerning the validity of performing ST for patients reporting non-SCAR delayed reactions. The final decision about ST in this patient population should be made by the patient and treating physician and depends on the need of the study.

Should ST be used as a prescreening tool in patients without a reaction history?

Empirical IDT of unselected patients has been shown to have extremely low sensitivity and minimal positive predictive value (both ~0%) and is not predictive of future HSRs.[131] Prescreening is therefore not recommended.

Is there a role for rapid drug desensitization?

Rapid drug desensitization is a procedure used to induce temporary drug tolerance in patients with prior immediate HSR when there are no ideal treatment alternatives. Rapid drug desensitization temporarily modifies the hypersensitivity response to a medication through the administration of gradually incremental drug doses.

Rapid drug desensitization protocols for ICM allergy have been successfully undertaken in patients with a history of breakthrough anaphylaxis despite premedication to enable coronary angiography.[145-149] Corticosteroid or antihistamine premedication was used in all published rapid drug desensitization protocols, which can be found in the cited literature and is beyond the scope of this report.

UNMET NEEDS REQUIRING FUTURE RESEARCH

First and foremost, there is a need to document in the EHR (1) the inciting agent for the contrast reaction, and (2) a description of the type of contrast reaction and treatments received. To standardize for future large-scale studies, the radiology community should use a standard lexicon for symptom descriptors and phenotypes such as adopting those used in the allergy and immunology literature.[150] There continues to be a need to identify those at increased risk for ICM reactions and to establish the utility of risk reduction measures including whether premedication with antihistamines and corticosteroids confers benefits that outweigh the potential for harm or burden, and the value of switching agents. In making this recommendation, we recognize this will require large, methodologically sound multicenter research studies and/or the establishment of a national registry. Because of the rarity of moderate and severe reactions, it may be challenging to perform a large multi-institutional prospective randomized study to achieve the overall number of injections required for statistical significance. Therefore, a national registry may be a more practical solution to acquire similar data retrospectively. Further efforts are needed to incorporate tryptase measurements after a severe ICM reaction in risk stratification for future ICM-enhanced studies. There is also a need to investigate further the value and potential role that ST can have in identifying alternative tolerable ICM agents and the feasibility and impact on the health care system.

SUMMARY STATEMENTS

This document contains joint consensus statements endorsed by the ACR and the AAAAI, which are intended to improve and standardize the care of patients who experience or have a history of an adverse reaction to ICM. These consensus recommendations are based on the best evidence and apply only to intravenous administration of ICM. High-quality evidence and methodologically rigorous studies are lacking owing to (1) the rarity of moderate and severe reactions to low-osmolality iodinated contrast agents; (2) the paucity of methodologically sound studies; and (3) the heterogeneity of published studies, including the multiplicity of premedication and ST regimens, variations in patient selection for premedication, and differing contrast agents used in switching methodology. These recommendations should not be taken as definitive standards of practice; they may be subject to change once additional and more definitive evidence becomes available. Given these limitations, the strength of recommendation is limited for any of the recommendations with limited strength of evidence unless otherwise specified subsequently. The study quality and strength of evidence were determined according to the ACR Appropriateness Criteria Evidence Document. (A concise summary and adaption of the process and the recommendations with associated strength of evidence references can be found in Appendices A, B, and C of the document).[11]

All imaging centers should be prepared to manage an adverse contrast reaction related to the administration of intravenous contrast material in any patient regardless of a history of adverse reaction and should include personnel, equipment, and supplies to treat anaphylaxis. Although specific details are outside the scope of this document, suggested supplies, equipment, and on-site personnel can be found in the ACR Contrast Manual and Statement from the Drugs and Contrast Media Committee on Supervision of Contrast Material Administration.[151]

RECOMMENDATIONS

Documentation

1. The occurrence of an ICM HSR and manifesting symptoms should be documented in the allergy field or module of the EHR by the treating health care professional. This should include the specific inciting agent and avoid the general term “iodinated contrast agent” and the term “iodine” to optimize future ICM reaction management. Furthermore, inaccurate or incomplete historical ICM reactions should be updated in this section of the EHR when additional information

becomes available. Documenting the reaction in the radiology report could also be considered, but only in addition to the allergy field or module in the EHR.

Strength of evidence: Limited
Strength of recommendation: Strong

This is a strong recommendation despite limited strength of evidence, because it is expert consensus that it is necessary to document the index HSR and inciting agent accurately to be able to optimize future management for the patient who returns for a contrast-enhanced CT and to be able to provide optimal management as additional evidence becomes available. This will also aid in research into best practices.

PREMEDICATION (GLUCORTICOSTEROIDS WITH OR WITHOUT ANTIHISTAMINES)

2. For patients with a history of **mild** immediate ICM HSRs, **premedication** is **not recommended.**

   Strength of evidence: Limited
   Strength of recommendation: Limited

3. For patients with a history of **mild** immediate ICM HSRs, **switching the contrast agent is recommended** when feasible (eg, dependent on knowing the inciting agent(s), availability of an alternative agent, and institutional constraints).

   Strength of evidence: Limited
   Strength of recommendation: Limited

4. For patients with a history of **moderate** immediate ICM HSRs, **switching the contrast agent is recommended** when feasible (eg, dependent on knowing the inciting agent(s), availability of an alternative agent, and institutional constraints).

   Strength of evidence: Limited
   Strength of recommendation: Limited

5. For patients with a history of **moderate** immediate ICM HSRs, **premedication may be considered.**

   Strength of evidence: Limited
   Strength of recommendation: Limited

6. For patients with a history of **severe** immediate ICM HSRs, it is **recommended** first to consider **alternative studies** (eg, contrast-enhanced magnetic resonance imaging, ultrasound, contrast-enhanced ultrasound, non-contrast CT).

   Strength of evidence: Expert consensus

7. For patients with a history of **severe** immediate ICM HSRs, when there is no acceptable alternative study, **switching** the contrast agent is **recommended** when feasible (eg, dependent on knowing the inciting agent(s), availability of an alternative agent, and institutional constraints).

   Strength of evidence: Limited
   Strength of recommendation: Limited

8. For patients with a history of **severe** immediate ICM HSRs, when there is no acceptable alternative study, **premedication is recommended.**

   Strength of evidence: Limited
   Strength of recommendation: Limited

9. For patients with a history of **severe** immediate ICM HSRs, the study should be performed in a hospital setting with a rapid response team available including personnel, equipment, and supplies to treat anaphylaxis regardless of whether the patient underwent agent switching or premedication.

   Severity Table 1
   Strength of evidence: Expert consensus

10. Premedication is **not recommended** for only an isolated history of HSR to HOCM or allergy to an unknown iodinated contrast agent before Food and Drug Administration approval of the first low-osmolality agent in 1985.

    Strength of evidence: Limited
    Strength of recommendation: Limited

11. Premedication is **not recommended** for only an isolated history of delayed ICM HSR.

    Strength of evidence: Expert consensus

12. Premedication is **not recommended** for only an isolated history of HSR to gadolinium-based contrast agents when the patient is to receive ICM.

    Strength of evidence: Limited
    Strength of recommendation: Limited

13. Premedication is **not recommended** for only an isolated history of shellfish or iodine allergy, including topical povidone-iodine allergy.

    Strength of evidence: Limited
    Strength of recommendation: Strong

    No clear association between shellfish allergy and an increased risk of ICM hypersensitivity has been found in clinical studies or via pathogenesis. Iodine is an essential element in thyroid function and is not an allergen. See section on ICM Myths for detailed rationale.

14. Premedication is **not recommended** for only an isolated history of asthma.

    Strength of evidence: Expert consensus

15. Premedication is **not recommended** for any of the following in isolation: drug allergy, food allergy, stinging insect allergy, family history of ICM HSR, female sex, asthma, use of β-blockers or ACE inhibitors, or a history of cardiovascular disease.

    Strength of evidence: Expert consensus

16. Premedication is not recommended for non−immune mediated adverse reaction or intolerances characterized as "physiologic reactions" in the ACR Manual.

Strength of evidence: Expert consensus

ANAPHYLAXIS AND ITS TREATMENT

Anaphylaxis and its treatment

17. Anaphylaxis to ICM should be considered when the acute onset of illness occurs within minutes after intravenous ICM administration and in the absence of other known allergens or triggers. In such situations, anaphylaxis is considered likely if any two or more of the following criteria are met:
    a. Involvement of skin/mucosal tissue or both
    b. Respiratory compromise
    c. Reduced blood pressure or associated symptoms of end-organ dysfunction (Severe hypotension may preclude the manifestation of any other anaphylaxis symptoms and anaphylaxis should be considered when there is no other source for the acute onset of severe hypotension within minutes of intravenous ICM administration such as shock, sepsis, or vasovagal reaction.)
    d. Significant or persistent vomiting and or severe diarrhea (These gastrointestinal symptoms in isolation do not meet criteria for anaphylaxis and should be significantly more severe than the typical quickly resolving vomiting that can be a side effect of ICM.)

Strength of evidence: Limited
Strength of recommendation: Strong
This is the accepted definition of anaphylaxis.

18. Epinephrine is recommended as the first-line treatment for anaphylaxis.

Strength of evidence: Limited
Strength of recommendation: Strong
This is a strong recommendation from the Practice Parameters on Anaphylaxis from the AAAAI and the American College of Allergy, Asthma and Immunology. Epinephrine is the treatment of choice based on the mechanism of action and data demonstrating adverse outcomes when epinephrine is not given or there is a delay in administration.

19. H1 antihistamines should not be administered as the primary and only treatment for anaphylaxis.

Strength of evidence: Limited
Strength of recommendation: Strong
This is a strong recommendation from the Practice Parameters on Anaphylaxis from the AAAAI and the American College of Allergy, Asthma and Immunology. H1 antihistamines should be used primarily for reactions limited to the skin.

FOLLOW-UP IN SEVERE IMMEDIATE ICM HSR

20. After a severe immediate ICM HSR, when feasible, it is recommended that a serum tryptase level is drawn ideally within 2 hours but potentially up to 4 to 6 hours and compared with baseline or recovery level drawn more than 24 hours after all signs and symptoms have resolved to support the diagnosis of anaphylaxis.

Strength of evidence: Limited
Strength of recommendation: Limited

21. After a severe immediate ICM HSR, it is recommended that the radiologist consider referral to a board-certified allergist for further evaluation and consideration of ST to identify alternative ICM agents that can be tolerated for future nonurgent examinations. For higher sensitivity, the testing should be performed within 6 months of the reaction.

Strength of evidence: Limited
Strength of recommendation: Limited

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REFERENCES

1. Goldfarb JW. National trends in contrast media enhanced and unenhanced computed tomography use. Clin Imaging 2023;93:103-5.
2. Harvard Medical School. Radiation risk from medical imaging. Accessed May 1, 2023. https://www.health.harvard.edu/cancer/radiation-risk-from-medical-imaging
3. Li X, Liu H, Zhao L, Liu J, Cai L, Liu L, et al. Clinical observation of adverse drug reactions to non-ionic iodinated contrast media in population with underlying diseases and risk factors. Br J Radiol 2017;90:20160729.
4. Dean KE, Starikov A, Giambrone A, Hentel K, Min R, Loftus M. Adverse reactions to intravenous contrast media: an unexpected discrepancy between inpatient and outpatient cohorts. Clin Imaging 2015;39:863-5.
5. Wang CL, Cohan RH, Ellis JH, Caoili EM, Wang G, Francis IR. Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reactions. AJR Am J Roentgenol 2008;191:409-15.
6. Brockow K. Immediate and delayed cutaneous reactions to radiocontrast media. Chem Immunol Allergy 2012;97:180-90.
7. American College of Radiology. ACR Manual on Contrast Media. Accessed January 7, 2025. Available from: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf
8. Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, et al. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol 2020;145:1082-123.
9. European Society of Urogenital Radiology. ESUR guidelines on contrast agents. Accessed January 26, 2023. https://www.esur.org/wp-content/uploads/2022/03/ESUR-Guidelines-10_0-Final-Version.pdf
10. O'Malley RB, Cohan RH, Ellis JH, Caoili EM, Davenport MS, Dillman JR, et al. A survey on the use of premedication prior to iodinated and gadolinium-based contrast material administration. J Am Coll Radiol 2011;8:345-54.
11. Kurth DA, Karmazyn BK, Waldrip CA, Chatfield M, Lockhart ME. ACR Appropriateness Criteria Methodology. J Am Coll Radiol 2021;18:S240-50.
12. Guyer AC, Macy E, White AA, Kuruvilla ME, Robison RG, Kumar S, et al. Allergy electronic health record documentation: A 2022 Work Group Report of the AAAAI Adverse Reactions to Drugs, Biologicals, and Latex Committee. J Allergy Clin Immunol Pract 2022;10:2854-67.
13. Khan DA, Banerji A, Blumenthal KG, Phillips EJ, Solensky R, White AA, et al. Drug allergy: a 2022 practice parameter update. J Allergy Clin Immunol 2022;150:1333-93.
14. Egbert RE, De Cecco CN, Schoepf UJ, McQuiston AD, Meinel FG, Katzberg RW. Delayed adverse reactions to the parenteral administration of iodinated contrast media. AJR Am J Roentgenol 2014;203:1163-70.
15. Torres MJ, Trautmann A, Böhm I, Scherer K, Barbaud A, Bavbek S, et al. Practice parameters for diagnosing and managing iodinated contrast media hypersensitivity. Allergy 2021;76:1325-39.
16. Staicu ML, Vyles D, Shenoy ES, Stone CA, Banks T, Alvarez KS, et al. Penicillin allergy delabeling: a multidisciplinary opportunity. J Allergy Clin Immunol Pract 2020;8:2858-2868.e16.
17. Katayama H, Yamaguchi K, Kozuka T, Takashima T, Seez P, Matsuura K. Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. Radiology 1990;175:621-8.
18. Cha MJ, Kang DY, Lee W, Yoon SH, Choi YH, Byun JS, et al. Hypersensitivity reactions to iodinated contrast media: a multicenter study of 196 081 patients. Radiology 2019;293:117-24.

19. Sodagari F, Mozaffary A, Wood CG III, Schmitz B, Miller FH, Yaghmai V. Reactions to both nonionic iodinated and gadolinium-based contrast media: incidence and clinical characteristics. AJR Am J Roentgenol 2018;210:715-9.
20. McDonald JS, Larson NB, Schmitz JJ, Kolbe AB, Hunt CH, Hartman RP, et al. Acute adverse events after iodinated contrast agent administration of 359, 977 injections: a single-center retrospective study. Mayo Clin Proc 2023;98: 1820-30.
21. Fukushima Y, Taketomi-Takahashi A, Suto T, Hirasawa H, Tsushima Y. Clinical features and risk factors of iodinated contrast media (ICM)-induced anaphylaxis. Eur J Radiol 2023;164:110880.
22. Brockow K. Immediate and delayed reactions to radiocontrast media: is there an allergic mechanism? Immunol Allergy Clin North Am 2009;29:453-68.
23. Morcos SK. Review article: acute serious and fatal reactions to contrast media: our current understanding. Br J Radiol 2005;78:686-93.
24. Laroche D, Vergnaud MC, Lefrançois C, Hue S, Bricard H. Anaphylactoid reactions to iodinated contrast media. Acad Radiol 2002;9(Suppl 2):S431-2.
25. Lieberman PL, Seigle RL. Reactions to radiocontrast material. Anaphylactoid events in radiology. Clin Rev Allergy Immunol 1999;17:469-96.
26. Clement O, Dewachter P, Mouton-Faivre C, Nevoret C, Guilloux L, Bloch Morot E, et al. Immediate hypersensitivity to contrast agents: the French 5-year CIRTACI study. EClinicalMedicine 2018;1:51-61.
27. Salas M, Gomez F, Fernandez TD, Doña I, Aranda A, Ariza A, et al. Diagnosis of immediate hypersensitivity reactions to radiocontrast media. Allergy 2013; 68:1203-6.
28. Kim MH, Lee SY, Lee SE, Yang MS, Jung JW, Park CM, et al. Anaphylaxis to iodinated contrast media: clinical characteristics related with development of anaphylactic shock. PLoS One 2014;9:e100154.
29. Morales-Cabeza C, Roa-Medellín D, Torrado I, De Barrio M, Fernández-Álvarez C, Montes-Aceñero JF, et al. Immediate reactions to iodinated contrast media. Ann Allergy Asthma Immunol 2017;119:553-7.
30. Fukushima Y, Suto T, Hirasawa H, Tsushima Y. Contrast-induced anaphylaxis: does it occur in the medical environment and is it being responded to appropriately? Jpn J Radiol 2023;41:1022-8.
31. Vitte J, Sabato V, Tacquard C, Garvey LH, Michel M, Mertes PM, et al. Use and interpretation of acute and baseline tryptase in perioperative hypersensitivity and anaphylaxis. J Allergy Clin Immunol Pract 2021;9:2994-3005.
32. Buka RJ, Knibb RC, Crossman RJ, Melchior CL, Huissoon AP, Hackett S, et al. Anaphylaxis and clinical utility of real-world measurement of acute serum tryptase in UK emergency departments. J Allergy Clin Immunol Pract 2017;5:1280-1287.e2.
33. Lieberman P, Nicklas RA, Randolph C, Oppenheimer J, Bernstein D, Bernstein J, et al. Anaphylaxis–a practice parameter update 2015. Ann Allergy Asthma Immunol 2015;115:341-84.
34. Gonzalez-Estrada A, Silvers SK, Klein A, Zell K, Wang XF, Lang DM. Epidemiology of anaphylaxis at a tertiary care center: a report of 730 cases. Ann Allergy Asthma Immunol 2017;118:80-5.
35. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. Fatal anaphylaxis: mortality rate and risk factors. J Allergy Clin Immunol Pract 2017;5:1169-78.
36. Shaker M, Toy D, Lindholm C, Low J, Reigh E, Greenhawt M. Summary and simulation of reported adverse events from epinephrine autoinjectors and a review of the literature. J Allergy Clin Immunol Pract 2018;6:2143-2145.e4.
37. Simons FE, Ebisawa M, Sanchez-Borges M, Thong BY, Worm M, Tanno LK, et al. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J 2015;8:32.
38. Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report–second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Ann Emerg Med 2006;47:373-80.
39. Brown JC. Epinephrine, auto-injectors, and anaphylaxis: challenges of dose, depth, and device. Ann Allergy Asthma Immunol 2018;121:53-60.
40. Edwards E, Kessler C, Cherne N, Dissinger E, Shames A. Human factors engineering validation study for a novel 0.1-mg epinephrine auto-injector. Allergy Asthma Proc 2018;39:461-5.
41. Dreborg S, Kim H. The pharmacokinetics of epinephrine/adrenaline auto-injectors. Allergy Asthma Clin Immunol 2021;17:25.
42. Masch WR, Ellis JH, Wang CL, Cohan RH, Davenport MS. Effect of available intravenous access on accuracy and timeliness of epinephrine administration. Abdom Radiol (NY) 2016;41:1133-41.
43. Asch D, Pfeifer KE, Arango J, Staib L, Cavallo J, Kirsch JD, et al. JOURNAL CLUB: benefit of epinephrine autoinjector for treatment of contrast reactions: comparison of errors, administration times, and provider preferences. AJR Am J Roentgenol 2017;209:W363-9.
44. Muck AE, Bebarta VS, Borys DJ, Morgan DL. Six years of epinephrine digital injections: absence of significant local or systemic effects. Ann Emerg Med 2010;56:270-4.
45. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. J Allergy Clin Immunol 2001;108:871-3.
46. Simons FE, Roberts JR, Gu X, Simons KJ. Epinephrine absorption in children with a history of anaphylaxis. J Allergy Clin Immunol 1998;101:33-7.
47. Ma L, Danoff TM, Borish L. Case fatality and population mortality associated with anaphylaxis in the United States. J Allergy Clin Immunol 2014;133: 1075-83.
48. Nurmatov UB, Rhatigan E, Simons FE, Sheikh A. H2-antihistamines for the treatment of anaphylaxis with and without shock: a systematic review. Ann Allergy Asthma Immunol 2014;112:126-31.
49. Nagata S, Ohbe H, Jo T, Matsui H, Fushimi K, Yasunaga H. Glucocorticoids and rates of biphasic reactions in patients with adrenaline-treated anaphylaxis: a propensity score matching analysis. Int Arch Allergy Immunol 2022;183: 939-45.
50. Choo KJ, Simons E, Sheikh A. Glucocorticoids for the treatment of anaphylaxis: Cochrane systematic review. Allergy 2010;65:1205-11.
51. Choo KJ, Simons FE, Sheikh A. Glucocorticoids for the treatment of anaphylaxis. Evid Based Child Health 2013;8:1276-94.
52. Sheikh A. Glucocorticosteroids for the treatment and prevention of anaphylaxis. Curr Opin Allergy Clin Immunol 2013;13:263-7.
53. Wood RA, Camargo CA Jr, Lieberman P, Sampson HA, Schwartz LB, Zitt M, et al. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immunol 2014;133:461-7.
54. Lieberman P. Biphasic anaphylactic reactions. Ann Allergy Asthma Immunol 2005;95:217-26. quiz 26, 58.
55. Pouessel G, Deschildre A, Dribin TE, Ansotegui IJ, Cardona V, Chinthrajah RS, et al. Refractory anaphylaxis: a new entity for severe anaphylaxis. J Allergy Clin Immunol Pract 2023;11:2043-8.
56. Kim TH, Yoon SH, Lee SY, Choi YH, Park CM, Kang HR, et al. Biphasic and protracted anaphylaxis to iodinated contrast media. Eur Radiol 2018;28: 1242-52.
57. Fleming JT, Clark S, Camargo CA Jr, Rudders SA. Early treatment of food-induced anaphylaxis with epinephrine is associated with a lower risk of hospitalization. J Allergy Clin Immunol Pract 2015;3:57-62.
58. Hochstadter E, Clarke A, De Schryver S, La Vieille S, Alizadehfar R, Joseph L, et al. Increasing visits for anaphylaxis and the benefits of early epinephrine administration: a 4-year study at a pediatric emergency department in Montreal, Canada. J Allergy Clin Immunol 2016;137:1888-1890.e4.
59. Robinson M, Greenhawt M, Stukus DR. Factors associated with epinephrine administration for anaphylaxis in children before arrival to the emergency department. Ann Allergy Asthma Immunol 2017;119:164-9.
60. Golden DBK, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, et al. Anaphylaxis: a 2023 practice parameter update. Ann Allergy Asthma Immunol 2024;132:124-76.
61. Lieberman P. Anaphylactoid reactions to radiocontrast material. Clin Rev Allergy 1991;9:319-38.
62. Bush WH, Swanson DP. Acute reactions to intravascular contrast media: types, risk factors, recognition, and specific treatment. AJR Am J Roentgenol 1991; 157:1153-61.
63. Greenberger PA, Patterson R, Tapio CM. Prophylaxis against repeated radiocontrast media reactions in 857 cases. Adverse experience with cimetidine and safety of beta-adrenergic antagonists. Arch Intern Med 1985;145: 2197-200.
64. Greenberger PA, Patterson R. The prevention of immediate generalized reactions to radiocontrast media in high-risk patients. J Allergy Clin Immunol 1991;87:867-72.
65. Lasser EC, Berry CC, Mishkin MM, Williamson B, Zheutlin N, Silverman JM. Premedication with corticosteroids to prevent adverse reactions to nonionic contrast media. AJR Am J Roentgenol 1994;162:523-6.
66. Jung JW, Choi YH, Park CM, Park HW, Cho SH, Kang HR. Outcomes of corticosteroid prophylaxis for hypersensitivity reactions to low osmolar contrast media in high-risk patients. Ann Allergy Asthma Immunol 2016;117: 304-309.e1.
67. Williams DM. Clinical pharmacology of corticosteroids. Respir Care 2018;63: 655-70.
68. Dunsky EH, Zweiman B, Fischler E, Levy DA. Early effects of corticosteroids on basophils, leukocyte histamine, and tissue histamine. J Allergy Clin Immunol 1979;63:426-32.
69. Mervak BM, Davenport MS, Ellis JH, Cohan RH. Rates of breakthrough reactions in inpatients at high risk receiving premedication before contrast-enhanced CT. AJR Am J Roentgenol 2015;205:77-84.

70. Davenport MS, Cohan RH, Caoili EM, Ellis JH. Hyperglycemic consequences of corticosteroid premedication in an outpatient population. AJR Am J Roentgenol 2010;194:W483-8.
71. Davenport MS, Cohan RH, Khalatbari S, Myles J, Caoili EM, Ellis JH. Hyperglycemia in hospitalized patients receiving corticosteroid premedication before the administration of radiologic contrast medium. Acad Radiol 2011;18:384-90.
72. Richards RN. Side effects of short-term oral corticosteroids. J Cutan Med Surg 2008;12:77-81.
73. Buchman AL. Side effects of corticosteroid therapy. J Clin Gastroenterol 2001;33:289-94.
74. Waljee AK, Rogers MA, Lin P, Singal AG, Stein JD, Marks RM, et al. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study. BMJ 2017;357:j1415.
75. Schrijvers R, Demoly P, Chiriac AM. Premedication for iodinated contrast media induced immediate hypersensitivity reactions. Curr Treat Options Allergy 2019;6:538-53.
76. Davenport MS, Mervak BM, Ellis JH, Dillman JR, Dunnick NR, Cohan RH. Indirect cost and harm attributable to oral 13-hour inpatient corticosteroid prophylaxis before contrast-enhanced CT. Radiology 2016;279:492-501.
77. Davenport MS, Cohan RH. The evidence for and against corticosteroid prophylaxis in at-risk patients. Radiol Clin North Am 2017;55:413-21.
78. Hsieh C, Wu SC, Kosik RO, Huang YC, Chan WP. Pharmacological prevention of hypersensitivity reactions caused by iodinated contrast media: a systematic review and meta-analysis. Diagnostics (Basel) 2022;12:1673.
79. Freed KS, Leder RA, Alexander C, DeLong DM, Kliewer MA. Breakthrough adverse reactions to low-osmolar contrast media after steroid premedication. AJR Am J Roentgenol 2001;176:1389-92.
80. McDonald JS, Larson NB, Kolbe AB, Hunt CH, Schmitz JJ, Maddox DE, et al. Prevention of allergic-like reactions at repeat CT: steroid premedication versus contrast material substitution. Radiology 2021;301:133-40.
81. Davenport MS, Cohan RH, Caoili EM, Ellis JH. Repeat contrast medium reactions in premedicated patients: frequency and severity. Radiology 2009;253:372-9.
82. Abe S, Fukuda H, Tobe K, Ibukuro K. Protective effect against repeat adverse reactions to iodinated contrast medium: premedication vs. changing the contrast medium. Eur Radiol 2016;26:2148-54.
83. Park HJ, Park JW, Yang MS, Kim MY, Kim SH, Jang GC, et al. Re-exposure to low osmolar iodinated contrast media in patients with prior moderate-to-severe hypersensitivity reactions: a multicentre retrospective cohort study. Eur Radiol 2017;27:2886-93.
84. Umakoshi H, Nihashi T, Takada A, Hirasawa N, Ishihara S, Takehara Y, et al. Iodinated contrast media substitution to prevent recurrent hypersensitivity reactions: a systematic review and meta-analysis. Radiology 2022;305:341-9.
85. Schrijvers R, Breynaert C, Ahmedali Y, Bourrain JL, Demoly P, Chiriac AM. Skin testing for suspected iodinated contrast media hypersensitivity. J Allergy Clin Immunol Pract 2018;6:1246-54.
86. Brockow K, Romano A, Aberer W, Bircher AJ, Barbaud A, Bonadonna P, et al. Skin testing in patients with hypersensitivity reactions to iodinated contrast media - a European multicenter study. Allergy 2009;64:234-41.
87. Caimmi S, Benyahia B, Suau D, Bousquet-Rouanet L, Caimmi D, Bousquet PJ, et al. Clinical value of negative skin tests to iodinated contrast media. Clin Exp Allergy 2010;40:805-10.
88. Ruff C, Banayan E, Overdeck D. Patients have very limited knowledge of their contrast allergies. Clin Imaging 2021;79:319-22.
89. Grist TM, Canon CL, Fishman EK, Kohi MP, Mossa-Basha M. Short-, mid-, and long-term strategies to manage the shortage of iohexol. Radiology 2022;304:289-93.
90. Gómez E, Ariza A, Blanca-López N, Torres MJ. Nonimmediate hypersensitivity reactions to iodinated contrast media. Curr Opin Allergy Clin Immunol 2013;13:345-53.
91. Webb JA, Stacul F, Thomsen HS, Morcos SK. Late adverse reactions to intravascular iodinated contrast media. Eur Radiol 2003;13:181-4.
92. Lapi F, Cecchi E, Pedone C, Attanasio F, Banchelli G, Vannacci A, et al. Safety aspects of iodinated contrast media related to their physicochemical properties: a pharmacoepidemiology study in two Tuscany hospitals. Eur J Clin Pharmacol 2008;64:723-37.
93. Loh S, Bagheri S, Katzberg RW, Fung MA, Li CS. Delayed adverse reaction to contrast-enhanced CT: a prospective single-center study comparison to control group without enhancement. Radiology 2010;255:764-71.
94. Schild HH, Kuhl CK, Hübner-Steiner U, Böhm I, Speck U. Adverse events after unenhanced and monomeric and dimeric contrast-enhanced CT: a prospective randomized controlled trial. Radiology 2006;240:56-64.
95. Sakai N, Sendo T, Itoh Y, Hirakawa Y, Takeshita A, Oishi R. Delayed adverse reactions to iodinated radiographic contrast media after coronary angiography: a search for possible risk factors. J Clin Pharm Ther 2003;28:505-12.
96. Hosoya T, Yamaguchi K, Akutsu T, Mitsuhashi Y, Kondo S, Sugai Y, et al. Delayed adverse reactions to iodinated contrast media and their risk factors. Radiat Med 2000;18:39-45.
97. Soria A, Bernier C, Veyrac G, Barbaud A, Puymirat E, Milpied B. Drug reaction with eosinophilia and systemic symptoms may occur within 2 weeks of drug exposure: a retrospective study. J Am Acad Dermatol 2020;82:606-11.
98. Bansie RD, Karim AF, van Maaren MS, Hermans MA, van Daele P, Gerth van Wijk R, et al. Assessment of immediate and non-immediate hypersensitivity contrast reactions by skin tests and provocation tests: a review. Int J Immunopathol Pharmacol 2021;35:20587384211015061.
99. Lerch M, Keller M, Britschgi M, Kanny G, Tache V, Schmid DA, et al. Cross-reactivity patterns of T cells specific for iodinated contrast media. J Allergy Clin Immunol 2007;119:1529-36.
100. Kanny G, Pichler W, Morisset M, Franck P, Marie B, Kohler C, et al. T cell-mediated reactions to iodinated contrast media: evaluation by skin and lymphocyte activation tests. J Allergy Clin Immunol 2005;115:179-85.
101. Machet P, Marcé D, Ziyani Y, Dumont M, Cornillier H, Jonville-Bera AP, et al. Acute generalized exanthematous pustulosis induced by iomeprol with cross-reactivity to other iodinated contrast agents and mild reactions after rechallenge with iopromide and oral corticosteroid premedication. Contact Dermatitis 2019;81:74-6.
102. Peterson A, Katzberg RW, Fung MA, Wootton-Gorges SL, Dager W. Acute generalized exanthematous pustulosis as a delayed dermatotoxic reaction to IV-administered nonionic contrast media. AJR Am J Roentgenol 2006;187:W198-201.
103. Hammerbeck AA, Daniels NH, Callen JP. Ioversol-induced acute generalized exanthematous pustulosis: a case report. Arch Dermatol 2009;145:683-7.
104. Poliak N, Elias M, Cianferoni A, Treat J. Acute generalized exanthematous pustulosis: the first pediatric case caused by a contrast agent. Ann Allergy Asthma Immunol 2010;105:242-3.
105. Pop M, Hemenway A, Shakeel F. Probable parenteral and oral contrast-induced Steven Johnson syndrome/toxic epidermal necrolysis. Am J Emerg Med 2021;45:684.e5-6.
106. Rosado A, Canto G, Veleiro B, Rodríguez J. Toxic epidermal necrolysis after repeated injections of iohexol. AJR Am J Roentgenol 2001;176:262-3.
107. Laffitte E, Nenadov Beck M, Hofer M, Hohl D, Panizzon RG. Severe Stevens-Johnson syndrome induced by contrast medium iopentol (Imagopaque). Br J Dermatol 2004;150:376-8.
108. Demoly P, Adkinson NF, Brockow K, Castells M, Chiriac AM, Greenberger PA, et al. International Consensus on drug allergy. Allergy 2014;69:420-37.
109. Tasker F, Fleming H, McNeill G, Creamer D, Walsh S. Contrast media and cutaneous reactions. Part 2: delayed hypersensitivity reactions to iodinated contrast media. Clin Exp Dermatol 2019;44:844-60.
110. Kim JH, Choi SI, Lee YJ, Kim BK, Park HW, Cho SH, et al. Pharmacological prevention of delayed hypersensitivity reactions caused by iodinated contrast media. World Allergy Organ J 2021;14:100561.
111. Lerondeau B, Trechot P, Waton J, Poreaux C, Luc A, Schmutz JL, et al. Analysis of cross-reactivity among radiocontrast media in 97 hypersensitivity reactions. J Allergy Clin Immunol 2016;137:633-635.e4.
112. Broyles AD, Banerji A, Barmettler S, Biggs CM, Blumenthal K, Brennan PJ, et al. Practical guidance for the evaluation and management of drug hypersensitivity: specific drugs. J Allergy Clin Immunol Pract 2020;8:S16-116.
113. Banerji A, Solensky R, Phillips EJ, Khan DA. Drug allergy practice parameter updates to incorporate into your clinical practice. J Allergy Clin Immunol Pract 2023;11:356-368.e5.
114. Shehadi WH. Adverse reactions to intravascularly administered contrast media. A comprehensive study based on a prospective survey. Am J Roentgenol Radium Ther Nucl Med 1975;124:145-52.
115. Beaty AD, Lieberman PL, Slavin RG. Seafood allergy and radiocontrast media: are physicians propagating a myth? Am J Med 2008;121:158.e1-4.
116. American Board of Internal Medicine. Choosing wisely. Accessed January 12, 2023. https://www.choosingwisely.org/clinician-lists/american-academy-allergy-asthma-immunology-low-or-iso-osmolar-radiocontrast-media/
117. Schabelman E, Witting M. The relationship of radiocontrast, iodine, and seafood allergies: a medical myth exposed. J Emerg Med 2010;39:701-7.
118. Reese G, Jeoung BJ, Daul CB, Lehrer SB. Characterization of recombinant shrimp allergen Pen a 1 (tropomyosin). Int Arch Allergy Immunol 1997;113:240-2.
119. Wulf NR, Schmitz J, Choi A, Kapusnik-Uner J. Iodine allergy: common misperceptions. Am J Health Syst Pharm 2021;78:781-93.

120. Jiao A, Farsad K, McVinnie DW, Jahangiri Y, Morrison JJ. Characterization of iodide-induced sialadenitis: meta-analysis of the published case reports in the medical literature. Acad Radiol 2020;27:428-35.
121. Curd JG, Milgrom H, Stevenson DD, Mathison DA, Vaughan JH. Potassium iodide sensitivity in four patients with hypocomplementemic vasculitis. Ann Intern Med 1979;91:853-7.
122. Nelson KL, Gifford LM, Lauber-Huber C, Gross CA, Lasser TA. Clinical safety of gadopentetate dimeglumine. Radiology 1995;196:439-43.
123. Ahn YH, Kang DY, Park SB, Kim HH, Kim HJ, Park GY, et al. Allergic-like hypersensitivity reactions to gadolinium-based contrast agents: an 8-year cohort study of 154 539 patients. Radiology 2022;303:329-36.
124. Fok JS, Smith WB. Hypersensitivity reactions to gadolinium-based contrast agents. Curr Opin Allergy Clin Immunol 2017;17:241-6.
125. Gamboa P, Sánchez de Vicente J, Galán C, Jáuregui I, Segurola A, García-Lirio E, et al. Tolerance to iopamidol in patients with confirmed allergic immediate hypersensitivity to iomeprol. J Allergy Clin Immunol Pract 2021;9:2101-2103.e1.
126. Trautmann A, Brockow K, Behle V, Stoevesandt J. Radiocontrast media hypersensitivity: skin testing differentiates allergy from nonallergic reactions and identifies a safe alternative as proven by intravenous provocation. J Allergy Clin Immunol Pract 2019;7:2218-24.
127. Yoon SH, Lee SY, Kang HR, Kim JY, Hahn S, Park CM, et al. Skin tests in patients with hypersensitivity reaction to iodinated contrast media: a meta-analysis. Allergy 2015;70:625-37.
128. Evans MA. Decreasing wait times for new referrals to an outpatient specialty clinic. Accessed January 26, 2023. https://repository.usfca.edu/cgi/viewcontent.cgi?article=1375&context=capstone
129. Trcka J, Schmidt C, Seitz CS, Bröcker EB, Gross GE, Trautmann A. Anaphylaxis to iodinated contrast material: nonallergic hypersensitivity or IgE-mediated allergy? AJR Am J Roentgenol 2008;190:666-70.
130. Dewachter P, Laroche D, Mouton-Faivre C, Bloch-Morot E, Cercueil JP, Metge L, et al. Immediate reactions following iodinated contrast media injection: a study of 38 cases. Eur J Radiol 2011;77:495-501.
131. Lee JH, Kwon OY, Park SY, Seo B, Won HK, Kang Y, et al. Validation of the prescreening intradermal skin test for predicting hypersensitivity to iodinated contrast media: a prospective study with ICM challenge. J Allergy Clin Immunol Pract 2020;8:267-72.
132. Srisuwatchari W, Vo T, Gauthier A, Molinari N, Schrijvers R, Demoly P, et al. Hypersensitivity reactions to iodinated radiocontrast media: cluster analysis reveals distinct clinical phenotypes. World Allergy Organ J 2022;15:100680.
133. Han S, Yoon SH, Lee W, Choi YH, Kang DY, Kang HR. Management of adverse reactions to iodinated contrast media for computed tomography in Korean referral hospitals: a survey investigation. Korean J Radiol 2019;20:148-57.
134. Kwon OY, Lee JH, Park SY, Seo B, Won HK, Kang Y, An J, et al. Novel strategy for the prevention of recurrent hypersensitivity reactions to radiocontrast media based on skin testing. J Allergy Clin Immunol Pract 2019;7:2707-13.
135. Ahn KM, Ahn YH, Cho MK, Kang DY, Lee SY, Kang HR. Validation of practical pathway in patients with anaphylaxis to low osmolar contrast media: a retrospective cohort study. J Allergy Clin Immunol Pract 2022;10:2685-2692.e2.
136. Prieto-García A, Tomás M, Pineda R, Tornero P, Herrero T, Fuentes V, et al. Skin test-positive immediate hypersensitivity reaction to iodinated contrast media: the role of controlled challenge testing. Investig Allergol Clin Immunol 2013;23:183-9.
137. Vernassiere C, Trechot P, Commun N, Schmutz JL, Barbaud A. Low negative predictive value of skin tests in investigating delayed reactions to radiocontrast media. Contact Dermatitis 2004;50:359-66.
138. Soyyigit S, Goksel O, Aydin O, Gencturk Z, Bavbek S. What is the clinical value of negative predictive values of skin tests to iodinated contrast media? Allergy Asthma Proc 2016;37:482-8.
139. Meucci E, Radice A, Fassio F, Sibilio M, Iorno MLC, Testi S, et al. Diagnostic approach to hypersensitivity reactions to iodinated contrast media: a single-center experience on 98 patients. Eur Ann Allergy Clin Immunol 2020;52:220-9.
140. Brockow K. Medical algorithm: Diagnosis and treatment of radiocontrast media hypersensitivity. Allergy 2020;75:1278-80.
141. Kvedariene V, Orvydaite M, Petraityte P, Rudyte J, Edvardas Tamosiunas A. Inherent clinical properties of non-immediate hypersensitivity to iodinated contrast media. Int J Clin Pract 2021;75:e14766.
142. Voltolini S, Cofini V, Murzilli F, Bignardi D, Borro M, Calamari M, et al. Hypersensitivity reactions to iodinate contrast media in Italy: a retrospective study. Characteristics of patients and risk factors. Eur Ann Allergy Clin Immunol 2022;54:60-7.
143. Torres MJ, Gomez F, Doña I, Rosado A, Mayorga C, Garcia I, et al. Diagnostic evaluation of patients with nonimmediate cutaneous hypersensitivity reactions to iodinated contrast media. Allergy 2012;67:929-35.
144. Doña I, Bogas G, Salas M, Testera A, Moreno E, Laguna JJ, et al. Hypersensitivity reactions to multiple iodinated contrast media. Front Pharmacol 2020;11:575437.
145. Uppal S, DeCicco AE, Intini A, Josephson RA. Rapid desensitization to overcome contrast allergy prior to urgent coronary angiography. Int Heart J 2018;59:622-5.
146. Saad A, Mahdi AS, Nasr I. Successful desensitization to the radiocontrast material iohexol (Omnipaque). Cureus 2022;14:e32356.
147. Gandhi S, Litt D, Chandy M, Nguyen BM, Jindal NL, Tarlo SM, et al. Successful rapid intravenous desensitization for radioiodine contrast allergy in a patient requiring urgent coronary angiography. J Allergy Clin Immunol Pract 2014;2:101-2.
148. Sanan N, Rowane M, Hostoffer R. Radiologic contrast media desensitization for delayed cardiac catheterization. Allergy Rhinol (Providence) 2019;10:2152656719892844.
149. Al-Ahmad M, Bouza TR. Successful desensitization to radiocontrast media in two high-risk cardiac patients. Ann Saudi Med 2017;37:333-5.
150. Blumenthal KG, Peter JG, Trubiano JA, Phillips EJ. Antibiotic allergy. Lancet 2019;393:183-98.
151. American College of Radiology. Statement from Drugs and Contrast Media Committee on Supervision of Contrast Material Administration. Accessed May 5, 2024. Available from: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/FINAL_Statement-from-Drugs-and-Contrast-Media-Committee-on-Supervision-of-Contrast-Administration.pdf