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Management of Severe Allergic-Like Contrast Media Reactions: Pitfalls and Strategies, From the *AJR* Special Series on Contrast Media

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Abstract

Adverse reactions to contrast media are often high-acuity events that are uncommon potentially life-threatening. Nonetheless, these events are treatable, and radiologists may be called upon to manage a contrast media reaction. However, because these events are infrequent, they are prone to management errors. This article highlights common pitfalls and practical tips for the management of acute contrast media reactions in children and adults. Recognition of frequent management errors and implementation of the mitigation strategies presented can ameliorate risk and improve patient outcomes. These measures include proper training on reaction management and medication administration, the prompt use of IM epinephrine autoinjectors whenever a severe allergic-like reaction is suspected, the use of visual aids for quick reference in the setting of a reaction, and the recognition of adverse events that are not allergic-like reactions, which commonly require only supportive care.

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Highlights:

- IM epinephrine is the first-line therapy for any patient demonstrating potential signs of a severe allergic-like contrast media reaction, and administration should not be delayed.
- Knowledge of the correct dose and route of administration of epinephrine is crucial to avoid medication errors, which can result in high patient morbidity.
- Epinephrine autoinjectors, reaction treatment algorithm visual aids, and reaction management training programs are effective tools to help mitigate the risk of errors.

Introduction

Adverse reactions to contrast media are uncommon. When combining physiologic and allergic-like reactions, overall reaction rates for intravascular administration of iodinated contrast material (ICM) are approximately 0.2-0.7% and 0.07-2.4% with gadolinium-based contrast agents (GBCA) [1-4]. Severe reactions are even more infrequent, with an incidence of approximately 0.04% for ICM and 0.001-0.01% for GBCA [1, 4]. Although fatal reactions occur, these events are fortunately very rare, estimated at 0.0002-0.0009% for ICM and 0.00027% for GBCA [1, 4]. Ionic ICM have higher rates of allergic-like reaction than non-ionic ICM [1]. Macrocyclic GBCAs have higher reaction rates compared to linear GBCAs [4]. Moreover, allergic-like reactions to contrast media are more commonly seen in adults compared to children, and rates in children increase with greater patient age [5-8]. Nonvascular contrast media administration is associated with a lower incidence of adverse reactions than intravascular administration [9], but the management strategies are similar.

When discussing contrast media reactions, it is important to note the distinction between true allergies or anaphylaxis (IgE-mediated events) and “allergic-like” or “anaphylactoid” reactions. Nonallergic hypersensitivity reactions (which comprise the bulk of non-physiologic events classified as contrast media allergies) are due to histamine release from mast cells and basophils, which may have direct (contrast media osmolality or membrane receptor binding) or indirect (complement-kinin activation) causes [10, 11]. As true IgE-mediated allergies are rare after contrast media administration, and treatment of allergic-like reactions is the same as for true allergic reactions [1], this article will refer to all such reactions as allergic-like for simplicity. An anaphylactoid reaction is considered a severe allergic-like reaction, akin to true anaphylaxis. Some guidelines advocate testing for evidence of true allergies, including serum tryptase and histamine levels at the time of the event, as well as skin testing, which may also help identify appropriate alternative contrast media for future use [12].

As outlined in the American College of Radiology (ACR) Manual on Contrast Media, allergic-like contrast media reactions may be classified by severity as mild, moderate, or severe (Table 1). Mild reactions are self-limited manifestations without progression. Moderate reactions typically require medical management and may progress to become severe. Allergic-like contrast reactions may have other manifestations beyond those listed, and symptoms could progress to cardiopulmonary arrest. If the etiology is unclear, it is generally considered prudent

to assume an allergic-like cause [1]. Severe reactions require treatment with epinephrine (also known as adrenaline). Epinephrine may also be used to treat moderate reactions that do not respond to other treatments, or as first-line therapy in some patients [1]. Supportive care measures include delivering oxygen by face mask (rate of at least 6-8 liters per minute) for patients with respiratory symptoms. Patients with hypotension may benefit from leg elevation and IV administration of isotonic fluid (0.9% normal saline, Lactated Ringer's solution) [13].

All patients who experience an adverse reaction to contrast media should be assessed by a qualified healthcare professional who is familiar with both the signs and symptoms of allergic-like and non-allergic adverse reactions to contrast media and proper management for such events.

Inadequate knowledge relating to contrast media reaction management and errors during attempted treatment of reactions have been well described [14, 15]. Although most radiologists correctly identify epinephrine as an initial drug of choice for a severe allergic-like contrast media reaction, one survey showed that only 41% provided the correct dose and route of administration. Seventeen percent would have given potentially fatal overdoses of epinephrine [16]. In another study that assessed radiology practitioners' knowledge regarding anaphylaxis treatment, only half knew the proper dose of intramuscular (IM) epinephrine and only 29% identified the correct dose and administration rate of IV epinephrine [17]. Studies of other medical specialties have shown a similar lack of knowledge in managing severe allergic reactions [18, 19]. These gaps have important relevance to radiologists in hospital settings, who may rely upon the knowledge of urgent or emergent response ("code") teams to provide care, as they may be similarly ill-prepared to manage a severe allergic-like contrast media reaction. Emergency medical service (EMS) personnel, who may be called to assist in managing a reaction at an outpatient radiology center, have shown similar errors in management. In one retrospective study, EMS dispatchers proposed use of an epinephrine autoinjector to only 38% of patients deemed to have a clinical presentation consistent with anaphylaxis [20].

To better prepare radiologists to manage acute allergic-like contrast media reactions and understand where mistakes typically occur, we have classified errors and knowledge gaps into common pitfalls (Table 2).

Pitfall 1: Unprepared to Manage a Reaction

Inadequate Training or Knowledge Refreshment

Confident and safe management of contrast media reactions requires both robust initial training and ongoing knowledge refreshment. Many studies have demonstrated the benefits of contrast media reaction training for improving radiologist performance and adherence to recommended management guidelines, with high fidelity simulation training having a greater impact [21-25]. Although computer-based training improves performance (and may be more widely accessible), hands-on training is better rated as a tool for teaching contrast media

reaction management and team communication skills [21]. Barriers to universal adoption of high-fidelity simulation training include cost, access to simulation labs, and availability of trained instructors [26]. However, when available, simulation-based training allows participants to engage in more realistic scenarios and provides hands-on opportunities to practice medication administration. Hands-on practice with medication administration is particularly important because most radiologists rarely handle medications used to treat anaphylaxis. This type of training allows individuals to learn from their mistakes during a simulation and to become more comfortable managing a contrast media reaction [22]. The time and financial costs of training are small considerations in comparison to the potential morbidity of a severe contrast media reaction, as well as in comparison to the malpractice costs if there is a litigation suit related to negligence in management [27]. Contrast media reactions are an infrequent (less than 1%) but possible driver of medical litigation [28]. Knowledge and confidence in treating allergic-like contrast media reactions has been shown to decline 6 months after training, supporting the need for biannual refresher training [22, 29].

An easily accessible visual aid can facilitate knowledge refreshment and minimize mistakes that are more likely to occur in a stressful scenario [30]. One high-fidelity simulation study proved the value of visual aids, showing improved radiologist confidence, faster administration time of epinephrine and fewer management errors [30]. Visual aids can be posted in clinical areas and/or stored in contrast media reaction kits and may include treatment algorithms, medication dosing, instructions for medication administration, and phone numbers to call for assistance (Fig. 1). Pocket-sized cards management guides are available from several institutions and the ACR [31]. Smartphone apps providing guidance for management of contrast media reactions have also been developed [32].

Equipment

In addition to quality contrast media reaction training, facilities need to ensure that the necessary equipment and medications are available to properly diagnosis and manage allergic-like contrast media reactions. Many hospitals or advanced imaging centers have contrast media reaction kits readily available in imaging suites. Others maintain “code carts.” Some facilities require certain medications to be stored within automated medication dispensing systems (i.e., Pyxis). Radiologists should be familiar with the locations where contrast media reaction medications are maintained in their facility. Specialized contrast media reaction kits allow for a portable solution with easy access to the critical drugs necessary for appropriate reaction management.

The kit contents may vary based on the patient population imaged at the site (adult vs pediatric) and availability of emergency response (“code”) team support. The ACR provides guidance on what medications and equipment should be stocked in areas where contrast media are being injected [1]. These items include epinephrine (1 mg/mL) for IM injection, inhaled short-acting beta-agonists, and antihistamines. Staff should also have access to oxygen, a stethoscope, blood pressure and pulse monitor, pulse oximeter, and a defibrillator or

automated external defibrillator (AED). Other equipment and medications may be included within kits at the discretion of each practice [1].

It is also important for radiologists to know how to call for help. In the hospital setting, this process may entail activating a medical emergency (or code) team or a rapid response team. Radiologists and staff must be familiar with the number to call to initiate the process. At ambulatory or outpatient facilities, the only available assistance may be via EMS staff and ambulance arrival. Proper acute management by onsite radiology staff is critical, as arrival of the EMS team can be variable based on geography and availability of EMS staff.

Pitfall 2: Errors in Medication Administration

Delay in Epinephrine Administration

Nearly every radiology and allergy or immunology society guideline emphasizes prompt administration of IM epinephrine as the most critical step for any patient with potential signs of anaphylaxis [1, 12, 33-35]. Importantly, IM epinephrine is suggested even when the diagnosis of anaphylaxis is in doubt, as there are no absolute contraindications to IM epinephrine [36]. Failure to recognize and promptly treat a severe contrast media reaction is a critical pitfall. Omission of, or delay in, epinephrine use has been shown to increase patient morbidity and mortality [37]. For example, a U.K. registry study on anaphylaxis found that nearly 40% of fatal reactions were not treated with epinephrine, and only 14% were treated with epinephrine prior to arrest [38]. Epinephrine administration should not be delayed due to diagnostic uncertainty or in favor of other treatments such as albuterol, antihistamines, or corticosteroids. Corticosteroids are not useful in the acute treatment of contrast media reactions and, in fact, may potentially be harmful in anaphylaxis management. For this reason, many authors have recommended complete removal of corticosteroids in anaphylaxis management guidelines [1, 12, 33-35, 39-41]. While radiologists and other clinicians may perceive antihistamines or steroids as a safer first choice of medication, it cannot be overemphasized that this view is incorrect, and that IM epinephrine should be the first-line treatment for any potential severe allergic-like contrast media reaction [1, 12, 33-35, 39-41]. Antihistamines can be used as an adjunct after IM epinephrine administration, to help manage cutaneous or nasopharyngeal symptoms [42].

Misadministration of Epinephrine

Even when epinephrine is administered early, misadministration errors can still occur. Two concentrations of epinephrine are available for use: 1 mg/mL and 1 mg/10 mL (0.1 mg/mL). These concentrations were previously often expressed as ratios (1:1,000 and 1:10,000, respectively), but the labeling was recently changed by the U.S. FDA in an effort to avoid confusion and medication errors [43].

Wrong concentration or route—A major pitfall in epinephrine administration is the selection of the incorrect concentration for the chosen route of administration. The 1 mg/mL (formerly labeled 1:1,000) concentration of epinephrine is designed for IM or subcutaneous injection. This concentration of epinephrine should never be injected directly IV. Accidental IV administration of this form of epinephrine has been reported to occur in 25% of epinephrine-related events and in 63% of events resulting in patient harm, more than any other error type [44]. Multiple case reports have also described patient harm secondary to misadministration of this form of epinephrine IV [42]. Injecting a full 1 mg dose of the 1 mg/mL concentration of epinephrine IV results in a rapid catecholamine surge that may lead to vasoconstrictive complications such as myocardial infarction, arrhythmia, and hypertension [42, 45]. The most effective way to avoid this error is to exclude 1 mg/mL epinephrine vials from contrast media reaction kits altogether, and to only use commercially available autoinjectors for IM administration. In simulation studies, use of an autoinjector reduced the time to administration of epinephrine by 70 seconds, reducing the error rate by 33-46%, and improving practitioner comfort [46, 47]. The main disadvantage to autoinjector use is cost. In the United States, many of these devices are nearly 100-times more expensive than traditional 1 mg/ml epinephrine vials [48]; this difference is amplified by the need to routinely replace these devices annually secondary to medication expiration dates. Hospitals may also continue to stock 1 mg/ml epinephrine vials because this concentration is commonly used in emergency department and ICU settings to create epinephrine drips when mixed with 250 ml of dextrose 5% in water [42]. For radiology departments that are unable to replace vials with autoinjectors due to cost or other factors, the authors suggest that the hospital pharmacy supply a premixed, IM formulation or that the drug be explicitly labeled to remind the treating radiologist of the correct dose and route of administration when treating an acute contrast media reaction.

Autoinjector errors–While replacing 1 mg/mL epinephrine vials with autoinjectors will eliminate the potential for erroneously injecting this concentration IV, autoinjectors can also introduce potential misadministration errors. Radiologists must recognize that autoinjectors are made with variable doses. Each epinephrine autoinjector manufacturers provides autoinjectors with at least two different doses: one adult dose of 0.3 mg, and one pediatric dose of 0.15 mg. The 0.3 mg dose autoinjector is intended for patients weighing 30 kg (66 lbs) or greater, and the 0.15 mg dose is intended for pediatric patients weighing between 15 and 29 kg (33-66 lbs). One manufacturer has an additional autoinjector with a 0.1 mg dose for patients weighing 7.5-15 kg (16.5-33 lbs). Outside of the United States, a 0.5 mg dose is also available, as the recommended dose for adult patients in various guidelines ranges from 0.3-0.5 mg [1, 12, 33, 34]. A common question in infants and young children is what to do if the child weighs less than the designated weight range of the lowest dose autoinjector available (less than 7.5 kg if 0.1 mg dose or less than 15 kg if 0.15 mg dose). The American Academy of Pediatrics supports use of a 0.15 mg dose for children weighing 10 kg (22 lbs) or above [49]. At the lead authors' institution, the decision was made to use this autoinjector dose for any child under 30 kg, as the risks of trying to manually draw and administer IM epinephrine from a vial were felt to be greater than the risks of using the 0.15 mg autoinjector off-label in infants under 15 kg.

The autoinjector size and shape are identical for the various doses, aside from different labeling and subtle color variation. Thus, when stocked together in a contrast media kit or code cart, a practitioner may accidentally choose the autoinjector corresponding with the wrong dose for the patient, especially during a high stress event like a severe contrast media reaction. The best way to prevent this error is to avoid stocking the autoinjectors together. However, this measure may not be possible in departments that care for pediatric and adult patients in the same facility. Users should be alerted to the difference by additional measures such as placement of a sticker inside the contrast media kit (Fig. 2) or creation of a visual aid flowsheet (Fig. 1).

If the wrong autoinjector is chosen, then a pediatric patient will receive a higher dose of epinephrine than intended. This larger dose may result in symptoms such as tremor, anxiety, palpitations or other cardiovascular effects, as well as headache or nausea. Most of these symptoms can be managed expectantly and resolve with time [50]. If a larger patient is underdosed with epinephrine, then repeat dosing is appropriate. Given that the traditionally proposed dosing of IM epinephrine is 0.01 mg/kg body weight, some advocate for routine use of higher doses for large patients than 0.3 mg IM [51]. In addition, for patients who do not improve after a single dose, it is appropriate to administer up to three repeat doses of IM epinephrine, spaced by 5-15 minutes [1].

After choosing the correct autoinjector, it is important understand the device's proper deployment. A pitfall and potential error in autoinjector use is possible accidental self-administration. Self-administration (defined as the drug being administered to the person dispensing the autoinjector) is the most commonly reported autoinjector error. For many devices, self-administration occurs because the person trying to use the autoinjector mistakenly places a digit over the end of the device where the needle fires (Fig. 3). The most commonly injected fingers are the thumb and index finger. Injection of epinephrine into a digit can result in painful ischemia or necrosis and may require medical treatment [52]. Self-administered by an individual other than the patient who is having the allergic-like reaction results in the patient not receiving epinephrine in any form. Self-administered by the patient who is experiencing the reaction describes when the patient administers the drug in a small digit instead of in the lateral thigh musculature, resulting in suboptimal drug delivery and uptake into the blood stream. From 2013 to 2014, over 6800 cases of unintentional autoinjector exposures were reported to U.S. Poison Centers, most commonly involving EpiPen administration in the digits by non-healthcare practitioners [53].

Healthcare practitioners (within and outside of radiology) experience similar self-administration errors as reported for patients. A simulation lab study reported a self-injection rate of 24% by radiologists using an EpiPen trainer [30]. Another study involving pediatric practitioners showed a self-injection rate of 16% [54]. Instructions on how to use the device are printed on the autoinjector itself. Nonetheless, the authors emphasize that practitioners should not first learn to use the device when trying to administer epinephrine in the setting of an actual potential severe allergic-like reaction. For this reason, the authors suggest that all sites stocking an autoinjector device in their contrast media reaction kits ensure that all practitioners undergo

training on the device's proper use. Visual aids and easily available instructions may also reduce the rate of this error [30]. One autoinjector product (Auvi-Q, Kaleo, Inc.) is unique in that the device uses real-time voice instructions to guide administration.

IV epinephrine errors–In rare cases, IV epinephrine may be needed to manage a severe contrast media reaction, particularly in patients who are hypotensive [1, 42]. Errors in IV administration of epinephrine encompass two broad categories: incorrect dose, and incorrect rate (i.e., speed of injection). Differences in dosing of IV epinephrine for severe allergic-like reactions versus for cardiac arrest can be confusing, particularly in the acute setting. The concentration of IV epinephrine (1:10,000 at 1 mg/10 ml) is ten times lower than the concentration of IM epinephrine (1:1000 at 1 mg/1 mL), but the actual dose administered for a cardiac arrest is ten times higher than the dose required for a severe reaction. The proper epinephrine dose for appropriate treatment of severe allergic-like reactions in adults entails separate 1 mL aliquots of 1 mg/10 mL concentration (0.1 mg); this dose can be repeated, if needed. Administration of the entire 10 mL epinephrine vial at once (1 mg) would provide the dose of IV epinephrine used to treat a cardiac arrest. Although a rapid IV push of epinephrine is appropriate for managing cardiac arrest, the recommended method for managing a severe reaction is to administer a slow IV push of epinephrine over several minutes or to administer epinephrine concurrently with IV fluids [1]. When administered via IV push, a slow saline flush should be performed after the epinephrine is administered, to clear any remaining epinephrine in the IV catheter tubing [55].

Errors with IV epinephrine administration in treating moderate-to-severe contrast media reactions are common in radiology departments. In one study, 25% of participants failed to use a saline flush or to provide fluids during IV epinephrine administration [14]; such errors result in underdosing, as a portion of the epinephrine dose will remain in the IV tubing and not reach the patient. Rapid administration can result in a catecholamine surge and associated complications. If the hospital code team or personnel outside of radiology are called to treat a patient, it is imperative that the clinical scenario is clearly conveyed as an allergic-like reaction and not as a cardiac arrest, so that the responders avoid overdosing a patient with epinephrine. As code teams are accustomed to administering code doses (10 mL IV push) of epinephrine, clear communication is critical for patient safety and mitigation of errors.

IV administration of epinephrine for treatment of a severe allergic-like reaction is associated with a significantly higher risk of overdose and adverse cardiovascular events. Therefore, IM epinephrine is recommended for initial use. IV epinephrine is recommended only for extreme circumstances such as profound hypotension, cardiac arrest, or failure to respond to multiple doses of IM epinephrine [42, 56].

Patients who experience a severe allergic-like reaction should be monitored until all symptoms resolve [34]. This monitoring may require that outpatients be transported to the emergency department.

Bronchodilator administration–When lower airway bronchospasm is a manifestation of a contrast media reaction, albuterol (or other short-acting beta-2 agonist) may be indicated. Failing to administer albuterol as first-line treatment for bronchospasm without significant hypoxia was the most common error seen in a study using high-fidelity simulation testing for radiologists [14]. Most radiologists are unlikely to have been responsible for actually administering an albuterol treatment, as this medication is more commonly administered by nurses or respiratory therapists. However, such practitioners may not be available during a contrast media reaction, particularly in an outpatient imaging center. Therefore, it is important for the radiologist to understand how to properly administer albuterol. The two common methods include a metered dose inhaler (MDI) and a nebulizer. The MDI is the more common treatment method for outpatients. Caution should be exercised in the use of MDIs in the acute setting, however, as inhalation necessitates patient cooperation, and lack of cooperation is a common source of errors [57]. Furthermore, children and dyspneic patients may not be able to follow instructions. Therefore, albuterol is more commonly administered in acute settings as a nebulizer treatment. Such treatments involve pouring the albuterol solution into the chamber of the nebulizer, placing the mask on the patient's face, and hooking the mask to oxygen to aerosolize (Fig. 4). In simulation training, radiologists are often observed to be unaware of where or how to put the albuterol in the chamber; this issue is easily mitigated by simply teaching the process. Another common pitfall in administration of albuterol is to attach the mask to flowing oxygen while albuterol is poured into the chamber; this action will result in aerosolizing the albuterol in the room (or in the face of the radiologist). This error can be avoided by either waiting to turn on the oxygen or waiting to connect the tubing until the mask is positioned on the patient.

For moderate-to-severe bronchospasm, administration of IM epinephrine (as adjunct or first-line treatment) is appropriate management, as epinephrine can reverse bronchoconstriction and treat lower airway symptoms [1, 34]. For patients with upper airway obstruction, treatment with nebulized epinephrine may be considered [33]. Nonetheless, if symptoms of laryngeal edema are severe and/or progressing rapidly, then treatment by IM epinephrine remains warranted.

Pitfall 3: Documentation

A commonly overlooked or underemphasized but essential component of contrast media reaction management is appropriate documentation of the event. Documentation should specify the reaction type (physiologic or allergic-like), severity (mild, moderate, or severe) [1], and the specific contrast medium that precipitated the adverse reaction, as well as the treatment that was administered. This documentation is critical for management of future reactions, but such documentation has been shown to be poor. In one study, only 11.5% of contrast media allergies documented in the EHR listed a specific contrast medium, and 69.1% were ambiguous contrast media concepts [58]. Additionally, a significant number of non-allergic-like reactions were listed [58]. Although European radiology and allergy society

guidelines do not recommend routine use of premedication for prior allergic-like contrast media reactions, current ACR guidelines continue to do so if the reaction is categorized as moderate or severe [1, 12, 35]. Additional literature has shown that changing the contrast media may be similar or more effective than premedication in preventing a repeat reaction [59-62]. However, if the specific medium that caused the reaction is not documented, then accurately selecting an alternate medium may be difficult. The ACR Manual on Contrast Media provides additional information on breakthrough reactions [1].

Prior work has shown that improved documentation can be achieved by using standard terminologies and leveraging solutions in the her [58]. Use of a semistructured electronic application for reporting adverse contrast media reactions was shown to significantly increase documentation rate (from 50% to 89%) and completeness [63]. Radiology personnel should be educated on allergy documentation practices and should be empowered to optimize the EHR as appropriate [58].

Pitfall 4: Adverse Event That Is Not an Allergic-Like Contrast Media Reaction

While all allergic-like contrast media reactions are adverse events, not all adverse events are allergic-like reactions. Patients may experience physiologic reactions to contrast media or may have other medical symptoms or conditions that manifest while in the radiology department, but that are unrelated to contrast media injection; these include panic attacks, vasovagal reactions, hypoglycemia, acute coronary syndrome, seizures, air embolism, and other conditions that can mimic allergic-like contrast media reactions. Allergic-like reactions should be a leading consideration in patients who are symptomatic after receiving contrast media. Depending on the clinical scenario, responders should obtain a brief but thorough history when the patient condition allows, perform a focused physical examination, and consider other diagnoses or contributing factors. Review of the images from the imaging examination that was just performed may also aid in diagnosis. For example, a contrast-enhanced chest CT may reveal a large pulmonary embolism in a patient presenting with dyspnea after completion of the CT. However, despite the wide variety of adverse events that can occur from contrast media administration, it should be reemphasized that epinephrine administration, preferably via IM autoinjector, should not be delayed for suspected severe allergic-like reactions. Laboratory testing such as serum tryptase or histamine levels may provide useful information after an atypical presentation of a possible severe reaction [12].

Conclusion

Errors in management of contrast media reactions are common. Recognition of management pitfalls and implementation of the mitigation strategies discussed in this article can ameliorate risk and improve patient outcomes. These measures include proper training on reaction management and medication administration, the prompt use of IM epinephrine autoinjectors whenever a severe allergic-like reaction is suspected, the use of visual aids for quick reference

in the setting of a reaction, and the recognition of adverse events that are not allergic-like reactions, many of which require only supportive care.

References:

1. ACR Committee on Drugs and Contrast Media. ACR Manual on Contrast Media. In, 2023
2. Idée JM PE, Prigent P, Corot C. Allergy-like reactions to iodinated contrast agents. A critical analysis. *Fundam Clin Pharmacol* 2005; Jun;19(3):263-81
3. Wang CL CR, 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; Aug;191(2):409-15
4. Behzadi AH, Zhao Y, Farooq Z, Prince MR. Immediate allergic reactions to gadolinium-based contrast agents: a systematic review and meta-analysis. *Radiology* 2018; 286:471-482
5. Dillman JR, Strouse PJ, Ellis JH, Cohan RH, Jan SC. Incidence and severity of acute allergic-like reactions to iv nonionic iodinated contrast material in children. *American journal of roentgenology* 2007; 188:1643-1647
6. Dillman JR, Ellis JH, Cohan RH, Strouse PJ, Jan SC. Frequency and severity of acute allergic-like reactions to gadolinium-containing iv contrast media in children and adults. *AMERICAN JOURNAL OF ROENTGENOLOGY-NEW SERIES*- 2007; 189:1533
7. McDonald JS, Larson NB, Kolbe AB, et al. Acute reactions to gadolinium-based contrast agents in a pediatric cohort: A retrospective study of 16,237 injections. *American Journal of Roentgenology* 2021; 216:1363-1369
8. Callahan MJ, Poznauskis L, Zurakowski D, Taylor GA. Nonionic iodinated intravenous contrast material–related reactions: incidence in large urban children's hospital—retrospective analysis of data in 12 494 patients. *Radiology* 2009; 250:674-681
9. Kim YS, Choi YH, Cho YJ, et al. Incidence of breakthrough reaction in patients with prior acute allergic-like reactions to iodinated contrast media according to the administration route. *Korean journal of radiology* 2018; 19:352-357
10. Trcka J, Schmidt C, Seitz CS, Bröcker E-B, Gross GE, Trautmann A. Anaphylaxis to iodinated contrast material: nonallergic hypersensitivity or IgE-mediated allergy? *American Journal of Roentgenology* 2008; 190:666-670
11. VI - Definitions of anaphylaxis and anaphylactoid events. *Journal of Allergy and Clinical Immunology* 1998; 101:S481
12. Radiology ESoU. ESUR Guidelines on Contrast Agents, 10.0. March, 2018. In:
13. Dillman JR, Trout AT, Davenport MS. Allergic-like contrast media reaction management in children. *Pediatric radiology* 2018; 48:1688-1694
14. Wang CL DM, Chinnugounder S, Schopp JG, Kani K, Zaidi S, Hippe DS, Paladin AM, Lalwani N, Bhargava P, Bush WH. Errors of epinephrine administration during severe allergic-like contrast reactions: lessons learned from a bi-institutional study using high-fidelity simulation testing. *Abdom Imaging* 2014; Oct;39(5):1127-33
15. Segal AJ BWJ. Avoidable errors in dealing with anaphylactoid reactions to iodinated contrast media. *Invest Radiol* 2011; Mar;46(3):147-51

16. Lightfoot CB AR, Mammen T, Abdolell M, Kapur S, Abraham RJ. Survey of radiologists' knowledge regarding the management of severe contrast material-induced allergic reactions. *Radiology* 2009; Jun;251(3):691-6
17. Nandwana SB WD, Torres WE. Radiology Department Preparedness for the Management of Severe Acute Iodinated Contrast Reactions: Do We Need to Change Our Approach? *AJR Am J Roentgenol* 2015; Jul;205(1):90-4
18. Benkelfat R, Gouin S, Larose G, Bailey B. Medication errors in the management of anaphylaxis in a pediatric emergency department. *The Journal of emergency medicine* 2013; 45:419-425
19. Kanwar M, Irvin CB, Frank JJ, Weber K, Rosman H. Confusion about epinephrine dosing leading to iatrogenic overdose: a life-threatening problem with a potential solution. *Annals of emergency medicine* 2010; 55:341-344
20. Dami F, Enggist R, Comte D, Pasquier M. Underuse of Epinephrine for the Treatment of Anaphylaxis in the Prehospital Setting. *Emergency Medicine International* 2022; 2022
21. Wang CL, Chinnugounder S, Hippe DS, et al. Comparative effectiveness of hands-on versus computer simulation–based training for contrast media reactions and teamwork skills. *Journal of the American College of Radiology* 2017; 14:103-110. e103
22. Pfeifer K, Staib L, Arango J, et al. High-fidelity contrast reaction simulation training: performance comparison of faculty, fellows, and residents. *Journal of the American College of Radiology* 2016; 13:81-87
23. Kruse DE, Scriver G, Walsh R. High-fidelity simulation training improves resident knowledge of contrast reaction management, especially for junior residents. *European Journal of Radiology Open* 2022; 9:100444
24. Wang CL, Schopp JG, Petscavage JM, Paladin AM, Richardson ML, Bush WH. Prospective randomized comparison of standard didactic lecture versus high-fidelity simulation for radiology resident contrast reaction management training. *American Journal of Roentgenology* 2011; 196:1288-1295
25. Tofil NM WM, Grant M, Zinkan JL, Patel B, Jenkins L, Youngblood AQ, Royal SA. Severe contrast reaction emergencies: high-fidelity simulation training for radiology residents and technologists in a children's hospital. *Acad Radiol* 2010; Jul;17(7):934-40
26. Chinnugounder S, Hippe DS, Maximin S, O'Malley RB, Wang CL. Perceived barriers to the use of high-fidelity hands-on simulation training for contrast reaction management: why programs are not using it. *Current Problems in Diagnostic Radiology* 2015; 44:474-478
27. Petscavage JM, Wang CL, Schopp JG, Paladin AM, Richardson ML, Bush Jr WH. Cost analysis and feasibility of high-fidelity simulation based radiology contrast reaction curriculum. *Academic radiology* 2011; 18:107-112
28. Whang JS, Baker SR, Patel R, Luk L, Castro III A. The causes of medical malpractice suits against radiologists in the United States. *Radiology* 2013; 266:548-554
29. Trout AT CR, Ellis JH, Khalatbari S. Teaching management of contrast reactions: does it work and how often do we need to refresh? *Acad Radiol* 2012; Apr;19(4):498-504
30. Gardner JB, Rashid S, Staib L, et al. Benefit of a visual aid in the management of moderate-severity contrast media reactions. *American Journal of Roentgenology* 2018; 211:717-723
31. American College of Radiology. Contrast Reaction Cards. In:

32. American College of Radiology. ACR Contrast Reaction Mobile App. In:
33. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. *World allergy organization journal* 2020; 13:100472
34. Shaker MS, Wallace DV, Golden DB, et al. Anaphylaxis—a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. *Journal of Allergy and Clinical Immunology* 2020; 145:1082-1123
35. Muraro A, Worm M, Alviani C, et al. EAACI guidelines: Anaphylaxis (2021 update). *Allergy* 2022; 77:357-377
36. Dalal R, Grujic D. Epinephrine. In: *StatPearls [Internet]*: StatPearls Publishing, 2023
37. Chooniedass R, Temple B, Becker A. Epinephrine use for anaphylaxis: too seldom, too late: current practices and guidelines in health care. *Annals of Allergy, Asthma & Immunology* 2017; 119:108-110
38. Pumphrey R. Lessons for management of anaphylaxis from a study of fatal reactions. *Clinical and experimental allergy* 2000; 30:1144-1150
39. Auth RD, Zheng T, Berk J. Things We Do for No Reason™: Routine use of corticosteroids for the treatment of anaphylaxis. *Journal of Hospital Medicine* 2022; 17:211-214
40. Mo Y-Y, Byrd AM, Stephens K, Shahid W, Mahdavinia M, Tobin MC. Steroid Management of Allergic Reactions and Anaphylaxis in the Emergency Room. *Journal of Allergy and Clinical Immunology* 2018; 141:AB41
41. Gabrielli S, Clarke A, Morris J, et al. Evaluation of prehospital management in a Canadian emergency department anaphylaxis cohort. *The Journal of Allergy and Clinical Immunology: In Practice* 2019; 7:2232-2238. e2233
42. Wood JP, Traub SJ, Lipinski C. Safety of epinephrine for anaphylaxis in the emergency setting. *World journal of emergency medicine* 2013; 4:245
43. U.S. Food & Drug Administration. Single Entity Injectable Drug Products. In:
44. An Update on the "Epi"demic: Events Involving Epinephrine. *PA Patient Saf Advis*; 6:102-103
45. Collins MS HC, Hartman RP. Use of IV epinephrine for treatment of patients with contrast reactions: lessons learned from a 5-year experience. *AJR Am J Roentgenol* 2009; Feb;192(2):455-61
46. Asch D, Pfeifer KE, Arango J, et al. JOURNAL CLUB: benefit of epinephrine autoinjector for treatment of contrast reactions: comparison of errors, administration times, and provider preferences. *American Journal of Roentgenology* 2017; 209:W363-W369
47. Restauri N LE, Glueck D, Lind KE, Sachs P, Vargas D, Suby-Long T. Best Practice for Safe and Effective Administration of Epinephrine for the Treatment of Anaphylaxis in the Radiology Department. *J Am Coll Radiol* 2016; Mar;13(3):303-6
48. Institute for Safe Medication Practices. What Price Must We Pay for Safety? Excessive Cost of EPINEPHrine Auto-Injectors Leads to Error-Prone Use of Ampuls or Vials and Unprepared Consumers. In, 2016
49. Sicherer SH, Simons F, Mahr TA, et al. Epinephrine for first-aid management of anaphylaxis. *Pediatrics* 2017; 139

50. Simons FER, Gu X, Silver NA, Simons KJ. EpiPen Jr versus EpiPen in young children weighing 15 to 30 kg at risk for anaphylaxis. *Journal of allergy and clinical immunology* 2002; 109:171-175
51. Dreborg S, Walter G, Kim H. International recommendations on epinephrine auto-injector doses often differ from standard weight-based guidance: a review and clinical proposals. *Allergy, Asthma & Clinical Immunology* 2022; 18:102
52. Walsh K, Baker BG, Iyer S. Adrenaline Auto-injector injuries to digits; a systematic review and recommendations for emergency management. *The Surgeon* 2020; 18:305-310
53. Anshien M, Rose SR, Wills BK. Unintentional epinephrine auto-injector injuries: a national poison center observational study. *American journal of therapeutics* 2019; 26:e110-e114
54. Mehr S, Robinson M, Tang M. Doctor–how do I use my EpiPen? *Pediatric Allergy and Immunology* 2007; 18:448-452
55. Institute for Safe Medication Practices. Safe Practice Guidelines for Adult IV Push Medications. In, 2015
56. Campbell RL, Bellolio MF, Knutson BD, et al. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. *The Journal of Allergy and Clinical Immunology: In Practice* 2015; 3:76-80
57. Sanchis J, Gich I, Pedersen S, Team ADMI. Systematic review of errors in inhaler use: has patient technique improved over time? *Chest* 2016; 150:394-406
58. Deng F LM, Wong A, Kowalski LT, Lai KH, Digumarthy SR, Zhou L. Quality of Documentation of Contrast Agent Allergies in Electronic Health Records. *J Am Coll Radiol* 2019; Aug;16(8):1027-1035
59. Umakoshi H, Nihashi T, Takada A, et al. Iodinated contrast media substitution to prevent recurrent hypersensitivity reactions: a systematic review and meta-analysis. *Radiology* 2022; 305:341-349
60. McDonald JS, Larson NB, Kolbe AB, et al. Prevention of allergic-like reactions at repeat CT: steroid pretreatment versus contrast material substitution. *Radiology* 2021; 301:133-140
61. Abe S FH, Tobe K, Ibukuro K. Protective effect against repeat adverse reactions to iodinated contrast medium: Premedication vs. changing the contrast medium. *Eur Radiol* 2016; Jul;26(7):2148-54
62. Park SJ KD, Sohn KH, Yoon SH, Lee W, Choi YH, Cho SH, Kang HR. Immediate Mild Reactions to CT with Iodinated Contrast Media: Strategy of Contrast Media Readministration without Corticosteroids. *Radiology* 2018; Sep;288(3):710-716
63. Lang M, Deng F, Singh R, DeFuria CL, Saini S, Alkasab TK. Implementation of a Semistructured Clinical Event Documentation Tool for Acute Adverse Contrast Reactions. *Journal of the American College of Radiology* 2022; 19:655-662

Tables:

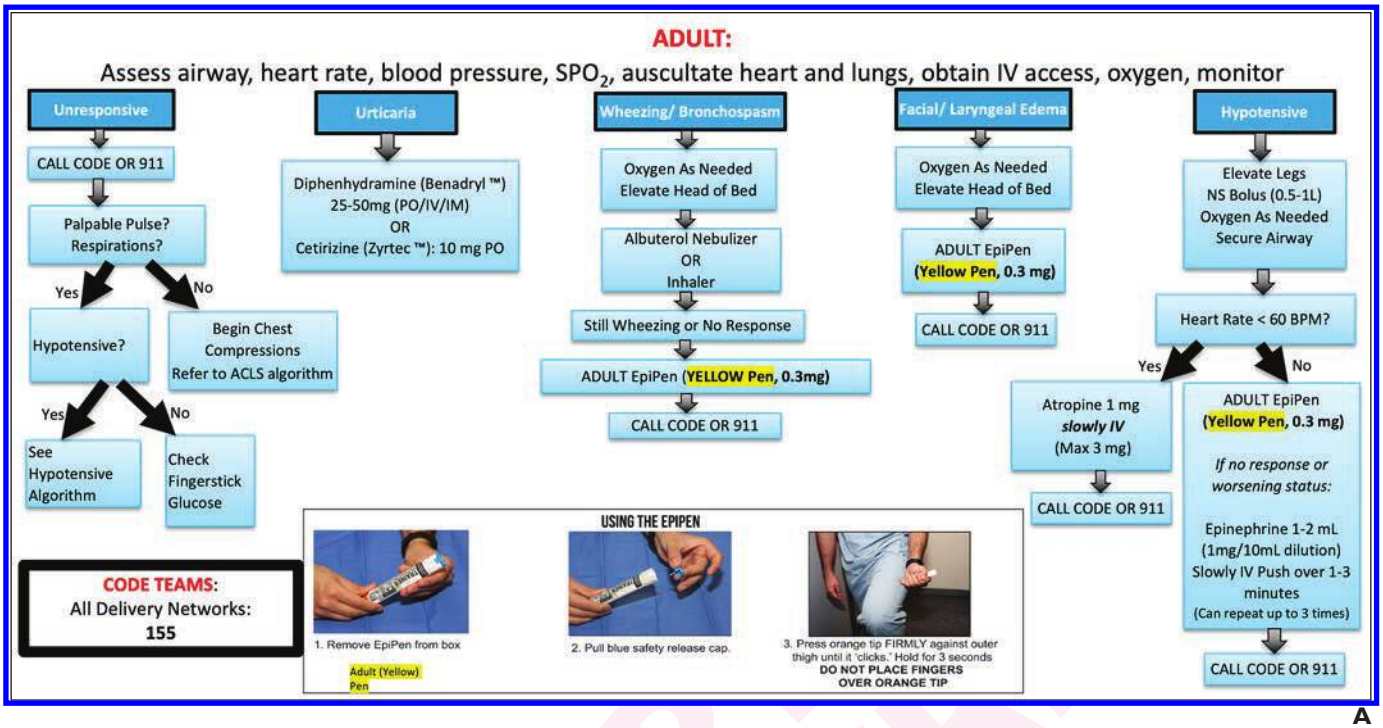
Table 1. Classification of allergic-like contrast media reactions by severity [1].

Severity	Symptoms
Mild	•Limited urticarial or pruritus •Nasal congestion •Cutaneous edema •Sneezing, conjunctivitis, or rhinorrhea •Limited itchy or scratchy throat
Moderate	•Diffuse urticarial or pruritus •Diffuse erythema, stable vital signs •Facial edema without dyspnea •Throat tightness or hoarseness without dyspnea •Wheezing or bronchospasm, with mild or no hypoxia
Severe	•Diffuse edema, or facial edema with dyspnea •Diffuse erythema with hypotension •Laryngeal edema with stridor and/or hypoxia •Wheezing or bronchospasm, with significant hypoxia •Anaphylactic shock (hypotension and tachycardia)

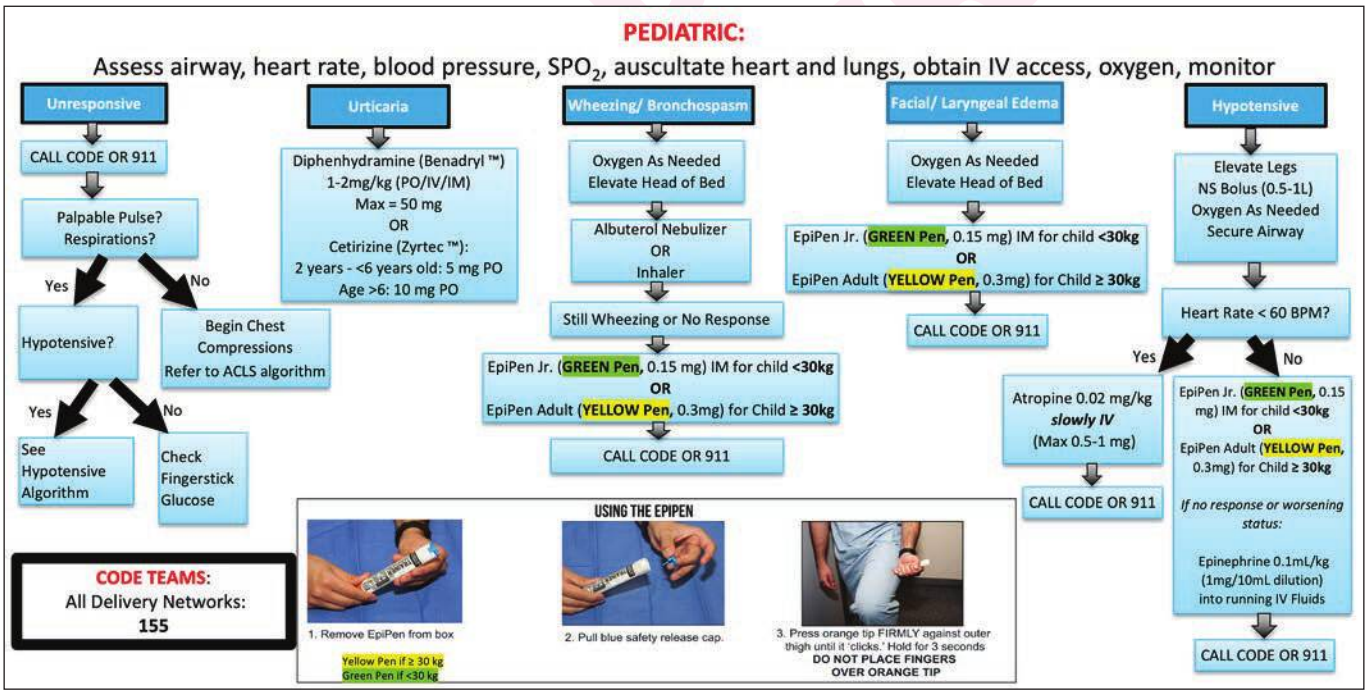
Table 2. Pitfalls in management of allergic-like contrast media reactions and respective mitigation strategies.

Pitfall	Mitigation Strategies
Unprepared to manage reaction	• Annual or biannual training that is preferably simulation-based • Visual aids • Contrast media kits with essential equipment and medications
Delayed administration of IM epinephrine	• Prompt recognition of a severe allergic-like reaction • Administration of IM epinephrine as first-line agent for any suspected severe allergic-like reaction, even if the diagnosis is in doubt
Wrong dose or route of IM epinephrine	• Use of autoinjectors • Premixed IM vials with labeling
Misadministration of IV epinephrine (wrong injection rate or wrong dose)	• Avoid IV epinephrine administration unless patient does not respond to IM epinephrine or has severe hypotension • When given, administer 1 ml (0.1 mg) concurrently with IV fluids or as slow IV push followed by saline flush
Autoinjector errors	• Color-coded labeling to better differentiate adult and pediatric injectors • Autoinjector training and visual aids • Always hold autoinjector in the center of cylinder to prevent self-administration
Misadministration of albuterol	• Use nebulizer (not inhalers) in acute setting
Inadequate documentation	• Train staff on proper information to document (reaction type, severity, and causal contrast media agent) • EHR solutions to improve documentation
Allergic-Like reactions mimics	• Avoid tunnel vision and recognize mimics that can be confused with reactions • Treat any suspected severe allergic-like reaction with IM epinephrine, even if the diagnosis is in doubt

IM = intramuscular



A



B

Figure 1. Examples of one institution's adult (A) and pediatric (B) visual aids posted on and in contrast media reaction kits. Practices vary in code team and emergency medical service phone numbers and procedures as well as in available equipment and medications such as autoinjectors. Although visual aids are useful for reference, they are not intended to replace sufficient training on prompt and appropriate management.

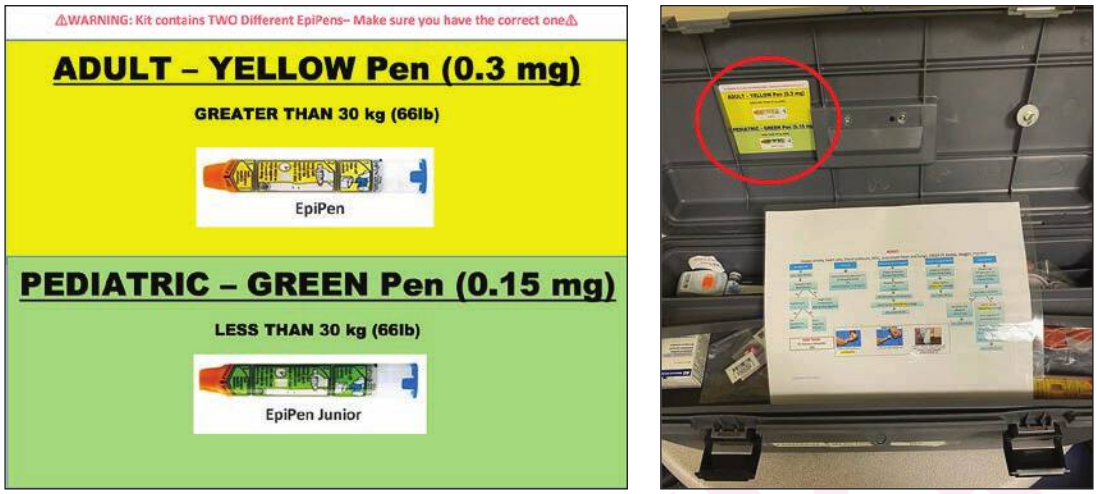


Figure 2. Sticker (A) shown within contrast media kit (B) alerting users to two different autoinjector doses available.

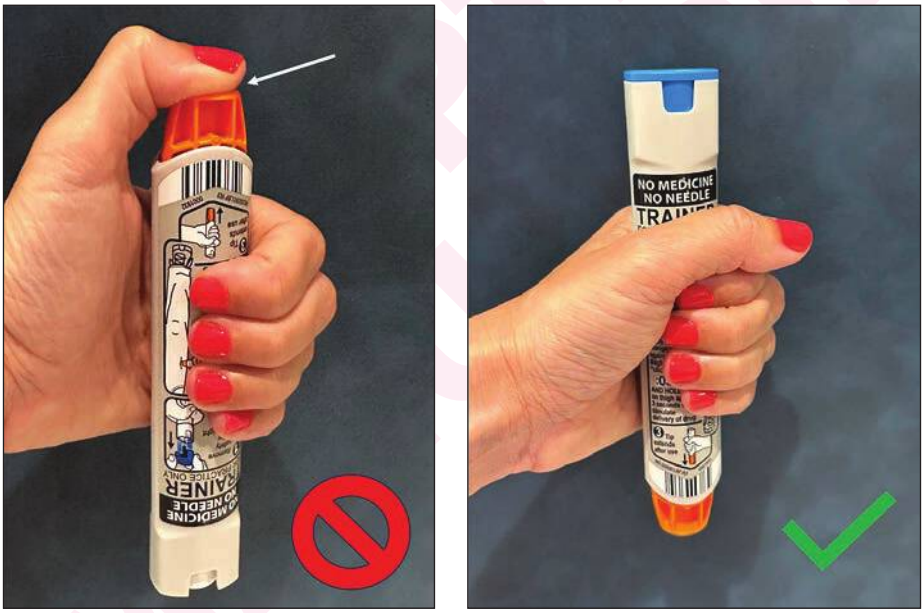


Figure 3. Autoinjector self-administration. Self-administration occurs when the device is erroneously held with operator's finger over end of device with needle (A). When device is pressed against patient, needle fires into operator's thumb (arrow). Operators should hold midportion of devices, avoiding both ends (B), to avoid this error.

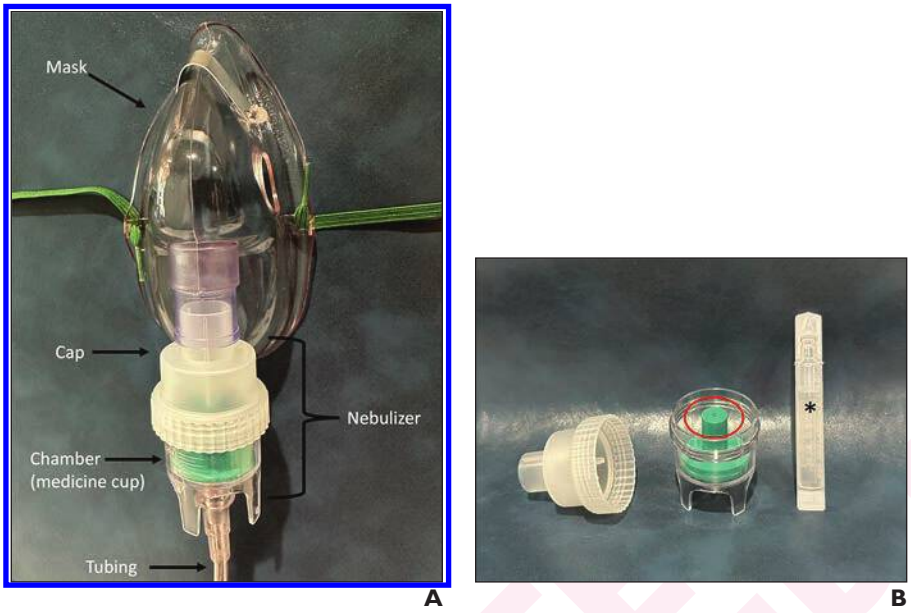


Figure 4. Nebulizer mask components and use. (A) Assembled device with mask attached to nebulizer and tubing (oxygen connection not shown). (B) Separate components of device. To use, nebulizer cap is removed, medicine solution (*) is poured into medicine cup (red oval), and cap is replaced. Once mask is placed over patient's nose and mouth with tubing connected, oxygen is turned on and then delivered to patient.

AJR

Management of Severe Allergic-Like Contrast Media Reactions: Pitfalls and Strategies, From the AJR Special Series on Contrast Media

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