

Errors of epinephrine administration during severe allergic-like contrast reactions: lessons learned from a bi-institutional study using high-fidelity simulation testing

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Abstract

Purpose: To determine the most common errors of epinephrine administration during severe allergic-like contrast reaction management using high-fidelity simulation surrogates.

Materials and methods: IRB approval and informed consent were obtained for this HIPAA-compliant bi-institutional prospective study of 40 radiology residents, fellows, and faculty who were asked to manage a structured high-fidelity severe allergic-like contrast reaction scenario (i.e., mild hives progressing to mild bronchospasm, then bronchospasm unresponsive to bronchodilators, and finally anaphylactic shock) on an interactive manikin. Intravenous (IV) and intramuscular epinephrine ampules were available to all participants, and the manikin had a functioning intravenous catheter for all scenarios. Video recordings of their performance were reviewed by experts in contrast reaction management, and errors in epinephrine administration were recorded and characterized.

Results: No participant (0/40) failed to give indicated epinephrine, but more than half (58% [23/40]) committed an error while doing so. The most common mistake was to administer epinephrine as the first-line treatment for mild bronchospasm (33% [13/40]). Other common errors were to administer IV epinephrine without a subsequent

IV saline flush or concomitant IV fluids (25% [10/40]), administer an overdose of epinephrine (8% [3/40]), and administer epinephrine 1:1000 intravenously (8% [3/40]). **Conclusion:** Epinephrine administration errors are common. Many radiologists fail to administer albuterol as the first-line treatment for mild bronchospasm and fail to flush the IV catheter when administering IV epinephrine. High-fidelity contrast reaction scenarios can be used to identify areas for training improvement.

Key words: Epinephrine—Epinephrine error—Contrast reaction—High-fidelity simulation

Severe acute allergic-like reactions to contrast media are rare, life-threatening events that demand prompt, directed action by radiologists to ensure a successful outcome [1–3]. Epinephrine is often a critical component of this management and can be life-saving when administered appropriately. Two large studies [2, 4] of contrast medium reactions found an epinephrine use-rate of 0.004% (24/541858) for all IV contrast medium injections. Eight of 24 patients (33%) in those studies were deemed by the authors to have received epinephrine inappropriately (e.g., overdose and/or wrong concentration). The emergency medicine literature estimates that 2.4% of all epinephrine administrations for the treatment of anaphylaxis are associated with inappropriate technique that can result in life-threatening complications [5], including

transient severe systolic dysfunction, cardiac ischemia or infarction, tachydysrhythmia, and labile hypertension [4, 5].

Epinephrine use is uncommon in Radiology Departments [2, 4] and, therefore, data on what represents the most common errors of administration are limited. If common sources of error can be identified, then educational tools could be specifically directed toward correcting those deficits. High-fidelity simulations using interactive manikins can be used to artificially increase the frequency of severe contrast medium reactions, and provide a vehicle for focused assessment [6–10]. The purpose of this study was to determine the most common errors of epinephrine administration during severe allergic-like contrast reaction management using high-fidelity simulation surrogates.

Materials and methods

This was a HIPAA-compliant, institutional review board-approved prospective bi-institutional study (site 1: University of Washington, site 2: University of Michigan) involving volunteer radiology residents, fellows, and faculty who provided written informed consent to participate. The study population consisted of 40 subjects ($n = 23$ from site 1, $n = 17$ from site 2) who were recruited over a one-year period, including 28 radiology residents (out of 44 total possible residents), 9 radiology fellows (out of 9 possible fellows), and 3 radiology faculty (out of 67 possible faculty). No study subject was excluded.

Subject training

All subjects at both institutions were given an identical one-hour-long lecture on contrast reaction management that emphasized the different types of contrast reactions (anaphylaxis, bronchospasm, laryngeal edema, vasovagal, hives), management of the reactions, medication dosing and administration, and how to manage contrast reactions in pediatric patients and sedated patients. This information was derived from the American College of Radiology's Manual on Contrast Media v.8 [11, created prior to release of v.9], as well as other published references [12, 13]. The standardized lecture was administered in addition to the typical contrast reaction instruction given at each respective institution.

At site 1, off-study contrast reaction training consists of 2 annual mandatory didactic lectures for all radiology residents and fellows (1-contrast reaction management and pediatric-specific contrast material-related information, 2-contrast-induced nephrotoxicity, nephrogenic systemic fibrosis, and corticosteroid prophylaxis). Only residents who had not been previously exposed to high-fidelity simulation contrast reaction scenarios were recruited for this study. All subjects in site 1 had partici-

pated in the annual training course a minimum of one time.

At site 2, off-study contrast reaction training consists of an annual mandatory course two weeks long for all radiology residents and fellows that consist of six lectures (1-general contrast material-related information, 2-contrast-induced nephrotoxicity, 3-nephrogenic systemic fibrosis, 4-pediatric-specific contrast material-related information, 5-corticosteroid prophylaxis, and 6-contrast reaction management) and a series of hands-on scenarios providing training in basic life support and contrast reaction management. All subjects at site 2 had participated in the annual training course a minimum of one time.

High-fidelity severe contrast reaction scenario. Four months after receiving the standardized study lecture on contrast reaction management, all study subjects were tested on the same standardized high-fidelity severe contrast reaction scenario using a mechanical simulation manikin (Sim Man, Laerdal Medical, Wappinger Falls, NY) in a controlled environment. The contrast reaction scenario was designed by the study team prior to study initiation, and followed a detailed stepwise algorithm progressing from minor hives, to mild bronchospasm, to bronchospasm unresponsive to albuterol, to anaphylactic shock. It included real-time vital sign fluctuations (blood pressure, pulse, pulse oximetry), artificial lung (e.g., wheezing) and heart (e.g., sinus tachycardia) sounds, and manikin vocalization. In all cases, the manikin began the scenario with a functioning intravenous catheter in the antecubital fossa. Equipment available to the study subjects included oxygenation paraphernalia (e.g., nasal cannula, oxygen tubing, Venturi mask, non-rebreather mask), intravenous catheterization tubing and fluids, and institutional "contrast reaction kits" composed of medications typically administered in a Radiology Department by a radiologist or radiology nurse during a contrast reaction.

The contents of the contrast reaction kits at each site were slightly different, but both were modeled after the recommendations in the Manual on Contrast Media v.9 [14], and included among other things: 1:1000 epinephrine ampules, 1:10,000 epinephrine injector kits (1 mg, Hospira Lake Forest, IL), intravenous fluids and tubing, vials of 10 mL normal saline, 10 and 20 mL syringes, a tuberculin syringe, 18–22 gage needles, albuterol inhalers, 25–50 mg diphenhydramine tablets and vials, and atropine injector kits (1 mg, Hospira Lake Forest, IL). EpiPen® (Pfizer, NY, NY) auto-injectors were not included in the kits.

Each simulation was proctored by a contrast reaction expert (a member of the ACR Committee on Drugs and Contrast media and published in the field) or critical care expert (completed a critical care fellowship) at site 1, or a contrast reaction expert at site 2 (a member of the ACR

Committee on Drugs and Contrast media and published in the field) (site 1: University of Washington, site 2: University of Michigan). Geographic separation precluded the same proctor from administering testing at both sites. The proctor at each site was responsible for manipulating or overseeing the manipulation of the Sim Man controls (e.g., vital signs, heart/lung sounds) to conform the scenario algorithm. Specific vital sign and auscultatory findings for each stage of the scenario were prescribed by the study team prior to testing, and adhered to by each proctor in real-time. The subjects were required to obtain vital signs, and draw-up and administer all medication(s) given during their management. Due to minor differences in technologist availability and equipment at each institution, there were slight differences in the testing protocol, but overall the format, scenario, and algorithm were the same for all study subjects.

Epinephrine administration errors. All scenarios were video recorded and later reviewed by two of the study authors at site 1 (CW, SC) to determine what, if any, errors in epinephrine administration occurred. Possible errors of epinephrine administration were determined prior to study initiation based on consensus opinion from 4 contrast reaction experts and are listed in Table 1. Errors were predominantly recorded as binary (present or absent) with the exception of dosing errors in which the actual doses were recorded. The proper treatment actions for this scenario expected by the study team are listed in Table 2. Deviations in the treatment algorithm (as indicated in Tables 1, 2) were tabulated.

Table 1. Common errors of epinephrine administration relevant to the high-fidelity scenario as identified by pre-study expert consensus

1	Failure to give indicated epinephrine
2	Attempting to give epinephrine before albuterol for the initial management of mild bronchospasm
3	Administering the wrong dose of epinephrine
4	Administering epinephrine 1:1000 intravenously
5	Administering subcutaneous epinephrine to a hypotensive patient
6	Failure to flush the intravenous catheter with either concurrently running intravenous fluids or a separate saline flush during the administration of intravenous epinephrine
7	Administration of a second dose of epinephrine before waiting at least five minutes after the first dose

Table 2. Expected treatment approach for the severe contrast reaction scenario administered to the study subjects as defined by pre-study expert consensus

1	Observation for hives
2	When bronchospasm develops, administer oxygen by facemask, 6–10 L/min
3	Administer albuterol inhaler (2 puffs) (can repeat up to 3 times)
4	When hypotension develops, administer intravenous fluids
5	Administer epinephrine (0.3 mg 1:1000 IM vs. 0.1–0.3 mg 1:10,000 IV followed by a flush or with fluids concurrently running)
6	Raise legs

Data analysis. Categorical data (e.g., error rates) are expressed as counts and percentages. All calculations were conducted using statistical software (SPSS v.20, IBM Corporation).

Results

All study subjects ($n = 40$) administered epinephrine at some point during the scenario, but more than half of the subjects (58% [23/40; Site 1 13/23 (57%) and Site 2 (10/17 (59%))] committed an error while doing so. Table 3 lists the frequency and type of errors observed. The most common errors of epinephrine administration were as follows: trying to give epinephrine as the first-line treatment for bronchospasm (33% [13/40]), and giving a 2nd dose of epinephrine before five minutes had elapsed since the first dose (30% [12/40]); more than half (7/12, 60%) repeated the dose prematurely after failing to flush the IV catheter. Because the scenario mandated that unflushed IV catheters following small volume epinephrine administrations (e.g., 1 mL of 1:10,000) would be considered equivalent to no drug delivery (i.e., retention of epinephrine in the dead space of the cannula [15]), the simulated patient did not improve in this setting, likely prompting these subjects to attempt a second dose before doing so was indicated. Four of the participants improperly administered epinephrine to the manikin when the only presenting signs were mild hives without significant vital sign alterations (10% [4/40]).

Two subjects initially administered 0.1 mg of 1:1000 SC epinephrine when the manikin was hypotensive, and later administered 0.1 mg of 1:10,000 epinephrine IV to the same manikin, resulting in 42 total epinephrine administrations. However, these 2 subjects are recorded as having given IV epinephrine in the analysis since the first dose was ineffective. Figure 1 demonstrates the

Table 3. Types and frequency of errors seen in the administration of epinephrine out of 40 subjects

Error	Subjects $n = 40$
Gave epinephrine when not indicated	17 (43%)
Mild hives only	4
First line for bronchospasm	13
Gave an improper dose of epinephrine	3 (8%)
Dose: 1 mg of 1:10,000 IV	2
1 mg of 1:1000 IV	1
Gave an improper concentration of epinephrine for the route of administration	4 (10%)
1:1000 IV	3
1:10,000 SC	1
Gave subcutaneous epinephrine to a hypotensive patient	3 (8%)
Dose: 0.3 mg of 1:10,000	1
0.1 mg of 1:1000 ^a	2
Did not flush or have IV fluids running following administration of IV epinephrine	10 (25%)
Gave 2nd dose of epinephrine without waiting at least five minutes	12 (30%)
Any error	23 (58%)

^a These 2 subjects later also gave 0.1 mg of the 1:10,000 epinephrine IV, intravenous; SC, subcutaneous; IM, intramuscular

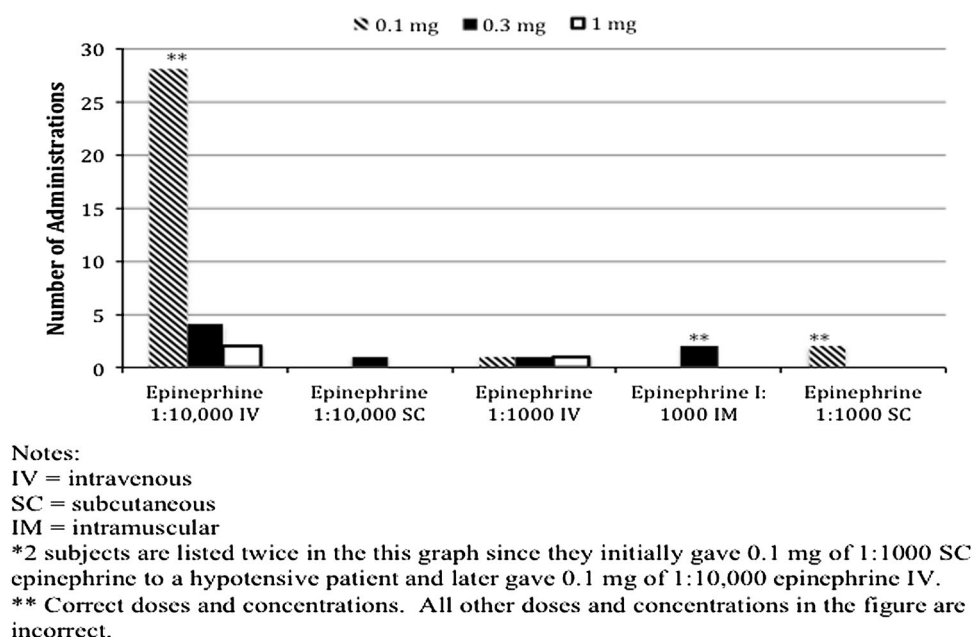


Fig. 1. Concentration, doses, and routes of epinephrine administration used by the subjects during the simulation. Epinephrine was available in both 1:1000 and 1:10,000 concentrations. There were 42 administrations of epinephrine by 40 subjects. All subjects administered some form of epinephrine during the simulation.

various doses, concentrations, and routes of epinephrine administration used by the study subjects. The majority chose to administer epinephrine intravenously (IV: 93% [37/40], IM: 5% [2/40], SC: 2% [1/40]). One of the subjects attempted to administer an initial dose of 0.3 mg of 1:10,000 IM, but after realizing he was unable to without an exposed needle for IM injection, he correctly administered 0.1 mg of 1:10,000 IV. The most commonly administered dose was 0.1 mg ($n = 31/42$ administrations), followed by 0.3 mg ($n = 8$ administrations). Four doses were given with the incorrect concentration (1:10,000 $n = 1$ [subcutaneous], 1:1000 $n = 3$ [intravenous]). Three subjects overdosed the manikin with 1 mg IV (1:10,000 IV $n = 2$, 1:1000 IV $n = 1$). Two additional subjects announced that they intended to give 1 mg of 1:10,000 IV, but only gave 0.1 mg IV after the simulated patient showed initial improvement.

Discussion

Our findings demonstrate that errors of epinephrine administration are extremely frequent (58% [23/40]) during the management of a severe contrast reaction. One of the more common errors that occurred in our study was a failure to administer IV epinephrine with either concurrently running IV fluids or a concomitant IV flush. Failure to do this may result in improper underdosing because the drug solution can remain in the dead space within the IV cannula and tubing, and does not reach the vein. Typical peripheral IV catheters can have a dead-space volume of 0.15–0.30 mL [15]. This, added to

the dead space of any additional IV tubing connected to the cannula, can act as a reservoir for a significant fraction of the intended drug volume. Given that many of the study participants were not aware of this (or were not incorporating this knowledge into their actions), it may be worthwhile to include facts regarding peripheral IV catheter dead space as a part of contrast reaction management training that emphasizes the uses of IV epinephrine. Establishing a general rule about the co-administration of isotonic IV fluids with IV epinephrine also may help obviate this problem.

Improper dosing by the study subjects often resulted in an overdose to the simulated patient, which is consistent with previously published clinical experience. For example, in two large ($n = 541,858$ combined patients) retrospective studies examining contrast reaction management outcomes [2, 4], seven of 24 patients (30%) who were given epinephrine as part of the management of a contrast reaction received a higher than recommended initial starting dose. One of the three subjects in our study who gave the wrong IV concentration (1:1000 instead of indicated 1:10,000) also administered a 1 mg overdose. Although the overdoses in our study occurred within the safety of a simulation laboratory, the patients in the comparator clinical studies [2, 4] suffered related acute complications, including transient cardiac ischemia ($n = 2$), ST-elevation myocardial infarction ($n = 1$), and non-ST-elevation myocardial infarction ($n = 1$). In other disciplines, there are numerous reports of inadvertent epinephrine overdose causing cardiomyopathy, transient left ventricular dysfunction, coronary

infarction and dissection, and ventricular arrhythmias [5, 16–19].

However, some epinephrine administration errors can result in under-dosing (e.g., failure to account for IV catheter dead space). Three subjects gave subcutaneous epinephrine when the simulated patient was hypotensive. Two of these subjects subsequently administered IV epinephrine when the simulated patient failed to improve, but there was a delay in treatment. The third subject attempted to administer 1:10,000 epinephrine subcutaneously twice before the simulated patient developed cardiopulmonary arrest. Since hypotensive patients are usually peripherally vasoconstricted, systemic absorption from subcutaneous epinephrine may not occur or may occur very slowly [20, 21], resulting in less than the intended dose reaching the systemic circulation. Subcutaneous dosing is not appropriate for patients with hypotension [14].

In addition to epinephrine dosing and administration errors, some subjects gave epinephrine when it was not indicated (43% [17/40]) [14]. Specifically, 13 (33%) chose to give epinephrine as the first-line treatment for mild bronchospasm. According to accepted treatment algorithms [14, 22, 23], epinephrine should be reserved for patients who do not respond to supplemental oxygen and inhaled bronchodilators, which was emphasized in the baseline lecture. Four subjects administered epinephrine for the treatment of mild hives, which should be managed instead with observation or antihistamines [14]. Administering epinephrine in lieu of more appropriate, conservative therapies may increase the risk of cardiovascular complications [5, 16–19].

Part of the confusion regarding epinephrine dosing relates to its multiple concentrations (1:1000 and 1:10,000) and the presence of multi-dose vials. Literature demonstrates that physicians are not adept at correctly converting drug doses from a percentage concentration or dilution [24–26]. One possible solution is to have pre-filled syringes with a proper unalterable dose (e.g., EpiPen® (Pfizer, NY, NY) [0.3 mg of 1:1000 epinephrine for IM administration]). IM administration of epinephrine is the only recommended route by the Contrast Committee of the European Society of Urogenital Radiology (ESUR), (0.1–0.5 mg of 1:1000) depending on the severity of the reaction [27].

However, proper training is also important to ensure appropriate administration of these pre-filled syringes. Use of these devices has been associated with a substantial number (i.e., 15,190 events over a 14-year period [28]) of unintended epinephrine injections [28, 29]). In addition, many physicians do not know how to properly use an epinephrine auto-injector (EpiPen® (Pfizer, NY, NY) [30]. In a study by Mehr et al. [30], 16% (16/100) of physicians tested would have auto-injected their own thumb, and 37% (37/100) would not have successfully administered epinephrine to the patient.

In addition to pre-filled syringes, proper labeling of the boxes may help to reduce error. For example, Kanwar labeled their pre-filled syringes of 0.3 mg of 1:1000 intramuscular (IM) epinephrine boxes “Use for anaphylaxis” and their 1 mg of 1:10,000 intravenous (IV) epinephrine boxes “Use only for cardiac arrest.” This new labeling system along with numerous teaching sessions stressing the use of IM epinephrine for anaphylaxis and memoranda about the potential for inappropriate administration of epinephrine and the policy changes results in no further adverse events for the next 2 years at their institutions compared to 4 events in the preceding 5 years [5].

The practice of assembling the briojet particularly in the more stressful setting of managing a contrast reaction during a high-fidelity simulation may serve as a teaching aid on the proper assembly and administration of the medication to help prevent error. Therefore, we advocate incorporating some form of hands-on training into the contrast reaction management curriculum in order to give the residents an opportunity to develop muscle memory on the proper assembly and administration of medications. Incorporating high-fidelity simulation into the training will also bring the added benefit of psychomotor learning and activate auditory, visual, and tactile learning pathways to help reinforce the cognitive knowledge. High-fidelity simulation would also be a good method to test for knowledge, identify deficiencies in knowledge and skills, and teach and demonstrate proficiency of skills. Prior studies have shown that high-fidelity simulation training improved residents’ recognition and knowledge in treating patients having severe contrast reactions [7, 9]. The benefits of high-fidelity simulation training include tailoring the teaching to the individual trainee and allowing them to make, detect, and correct errors in a safe-controlled environment where the attending can focus on the trainee and not compromise the safety of the patient [31].

Unfortunately, annual training in contrast reaction management may not be sufficient. Trout et al. [32] demonstrated that following a contrast reaction educational course, there was a measurable decline in knowledge and confidence in managing contrast reactions over time, with a return to baseline after 9 months. The authors advocated biannual refresher training [32]. Segal and Bush [33] suggest posting an outline of medication doses and/or a flowchart of contrast reaction treatment plans in every radiology suite, while Favinger’s et al. [34] use pocket treatment algorithm cards. Although no strategy is clearly superior to another, it is plain that our current methods of preparing radiologists to manage severe contrast reactions are insufficient. It is likely that radiologists will require regular, at least biannual, simulated exposure to these rare events if they wish to be adequately prepared for a real-life occurrence. Due to the potential high cost of hands-on high-fidelity simulation

training [35], incorporating some component of online interactive simulation training may be helpful in offsetting some of the resource, time, and financial costs such as <http://www.contrastrxn.com> [8].

There are several limitations of our study. Since scenario management was graded subsequent to subject performance by watching a video recording, it is possible that there may have been some discrepancies between actual medication administration and what was believed based on video evidence. There were also some minor differences in the simulations at the two study sites (e.g., minor differences in contrast reaction kits, examination proctors, instructors, etc.), but this was unavoidable due to geographic differences. It is unlikely that these differences contributed strongly to our results. Another possible limitation was our relatively small sample size due to the voluntary nature of the study as well as the exclusion of residents and faculty who had previous exposure to high-fidelity simulation. This may have also resulted in a selection bias as those uncomfortable managing contrast reactions may not have volunteered for the study. The numbers of errors may have been more without this bias. Finally, our study did not assess the effect of intramuscular epinephrine auto-injectors. Therefore, we cannot comment on whether use of these auto-injectors would improve or worsen contrast reaction management performance. However, we could conjecture that if intramuscular epinephrine auto-injectors were available in the simulation testing and everyone used the auto-injectors that the dosing errors, lack of flushing, or attempt to give subcutaneous epinephrine with the IV briojet would not have occurred. However, it would be impossible for us to predict how many participants would have chosen to give intramuscular epinephrine rather than intravenous or subcutaneous epinephrine.

In conclusion, despite annual efforts to provide contrast reaction training at our respective institutions, errors of epinephrine administration still occurred frequently in a simulated environment. Training should emphasize the need to administer IV epinephrine with concurrent fluids or a saline chaser, reinforce the proper dose and route of epinephrine administration, advocate an avoidance of subcutaneous epinephrine in hypotensive patients, and explain the proper assembly and use of all contrast reaction-related medications. High-fidelity simulations can be used to address these concerns, while providing radiologists with a platform for regular exposure to what are otherwise rare but serious events.

References

- Hunt C, Hartman R, Hesley G (2009) Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses. *AJR Am J Roentgenol* 193(4):1124–1127
- Wang C, Cohan R, Ellis J, et al. (2008) Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reactions. *AJR Am J Roentgenol* 191(2):409–415
- Jung JW, Kang HR, Kim MH, et al. (2012) Immediate hypersensitivity reaction to gadolinium-based MR contrast media. *Radiology* 264(2):414–422
- Collins MS, Hunt CH, Hartman RP (2009) Use of IV epinephrine for treatment of patients with contrast reactions: lessons learned from a 5-year experience. *AJR Am J Roentgenol* 192(2):455–461
- Kanwar M, Irvin CB, Frank JJ, Weber K, Rosman H (2010) Confusion about epinephrine dosing leading to iatrogenic overdose: a life-threatening problem with a potential solution. *Ann Emerg Med* 55(4):341–344
- Tubbs R, Murphy B, Mainiero M, et al. (2009) High-fidelity medical simulation as an assessment tool for radiology residents' acute contrast reaction management skills. *J Am Coll Radiol* 6(8):582–587
- Wang CL, Schopp JG, Petsavage JM, et al. (2011) Prospective randomized comparison of standard didactic lecture versus high-fidelity simulation for radiology resident contrast reaction management training. *AJR Am J Roentgenol* 196(6):1288–1295
- Wang CL, Schopp JG, Kani K, et al. (2013) Prospective randomized study of contrast reaction management curricula: computer-based interactive simulation versus high-fidelity hands-on simulation. *Eur J Radiol* 82(12):2247–2252
- Tofil N, White M, Grant M, et al. (2010) Severe contrast reaction emergencies high-fidelity simulation training for radiology residents and technologists in a children's hospital. *Acad Radiol* 17(7):934–940
- Sarwani N, Tappouni R, Flemming D (2012) Use of a simulation laboratory to train radiology residents in the management of acute radiologic emergencies. *AJR Am J Roentgenol* 199(2):244–251
- American College of Radiology Committee on Drugs and Contrast Media and Committee on General and Pediatric Radiology (2012) *Manual on contrast media, 8th and 9th ed.* Reston, VA: ACR. <http://www.nxtbook.com/nxtbooks/acr/contrastmediamanual2012/#/0>. Accessed Oct 1 2013
- Bush WH, Swanson DP (1991) Acute reactions to intravascular contrast media: types, risk factors, recognition, and specific treatment. *AJR Am J Roentgenol* 157(6):1153–1161
- Bush WH, Segal AJ (2009) Recognition and treatment of acute contrast reactions. *Appl Radiol* 38:16–21
- American College of Radiology Committee on Drugs and Contrast Media and Committee on General and Pediatric Radiology (2013) *Manual on contrast media 9th ed.* Reston, VA: ACR. http://www.acr.org/~media/ACR/Documents/PDF/QualitySafety/Resources/Contrast%20Manual/2013_Contrast_Media.pdf. Accessed October 1, 2013
- Geggie D, Moore D (2007) Peripheral line dead space: an unrecognized phenomenon? *Emerg Med J* 24(8):448–449
- Arfi AM, Kouatli A, Al-Ata J, Arif H, Syed S (2005) Acute myocardial ischemia following accidental intravenous administration of epinephrine in high concentration. *Indian Heart J* 57(3):261–264
- Budhwani N, Bonaparte KL, Cuyjet AB, Saric M (2004) Severe reversible left ventricular systolic and diastolic dysfunction due to accidental iatrogenic epinephrine overdose. *Rev Cardiovasc Med* 5(2):130–133
- Fyfe AI, Daly PA, Dorian P, Tough J (1991) Reversible, "cardiomyopathy" after accidental adrenaline overdose. *Am J Cardiol* 67(4):318–319
- Nelson LS, Garlich FM (2010) Case studies in toxicology inadvertent IV administration of IM epinephrine. *Emerg Med* 42(11):24–27
- Heilborn H, Hjemdahl P, Daleskog M, Adamsson U (1986) Comparison of subcutaneous injection and high-dose inhalation of epinephrine—implications for self-treatment to prevent anaphylaxis. *J Allergy Clin Immunol* 78(6):1174–1179
- Simons FE, Gu X, Simons KJ (2001) Epinephrine absorption in adults: intramuscular versus subcutaneous injection. *J Allergy Clin Immunol* 108(5):871–873
- Blake K (2006) Review of guidelines and the literature in the treatment of acute bronchospasm in asthma. *Pharmacotherapy* 26(9 Pt 2):148S–155S

23. Holley AD, Boots RJ (2009) Review article: management of acute severe and near-fatal asthma. *Emerg Med Australas* 21(4):259–268
24. Rolfe S, Harper NJ (1995) Ability of hospital doctors to calculate drug doses. *BMJ* 310(6988):1173–1174
25. Jones SJ, Cohen AM (2001) Confusing drug concentrations. *Anaesthesia* 56(2):195–196
26. Wheeler DW, Carter JJ, Murray LJ, et al. (2008) The effect of drug concentration expression on epinephrine dosing errors: a randomized trial. *Ann Intern Med* 148(1):11–14
27. Thomsen HS (2006) European Society of Urogenital Radiology (ESUR) guidelines on the safe use of iodinated contrast media. *Eur J Radiol* 60(3):307–313
28. Simons FE, Edwards ES, Read EJ, Clark S, Liebelt EL (2010) Voluntarily reported unintentional injections from epinephrine auto-injectors. *J Allergy Clin Immunol* 125(2):419–423
29. Simons FE, Lieberman PL, Read EJ, Edwards ES (2009) Hazards of unintentional injection of epinephrine from autoinjectors: a systematic review. *Ann Allergy Asthma Immunol* 102(4):282–287
30. Mehr S, Robinson M, Tang M (2007) Doctor—how do I use my EpiPen? *Pediatr Allergy Immunol* 18(5):448–452
31. Issenberg S, McGaghie W, Petrusa E, Lee Gordon D, Scalese R (2005) Features and uses of high-fidelity medical simulations that lead to effective learning: a BEME systematic review. *Med Teach* 27(1):10–28
32. Trout AT, Cohan RH, Ellis JH, Khalatbari S (2012) Teaching management of contrast reactions: does it work and how often do we need to refresh? *Acad Radiol* 19(4):498–504
33. Segal AJ, Bush WH (2011) Avoidable errors in dealing with anaphylactoid reactions to iodinated contrast media. *Invest Radiol* 46(3):147–151
34. Favinger J, Bastawrous S, Bhargava P (2013) Management of acute contrast media reactions: assessing preparedness of a tertiary care Veterans Affairs medical center. *J Am Coll Radiol* 10:872–874
35. Petscavage JM, Wang CL, Schopp JG, et al. (2011) Cost analysis and feasibility of high-fidelity simulation based radiology contrast reaction curriculum. *Acad Radiol* 18(1):107–112