

# Frequency and Severity of Acute Allergic-Like Reactions to Gadolinium-Containing IV Contrast Media in Children and Adults

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**OBJECTIVE.** The purpose of our study was to determine the frequency and severity of acute allergic-like reactions to IV-administered gadolinium-containing contrast media in children and adults.

**MATERIALS AND METHODS.** Pediatric (younger than 19 years) and adult department of radiology contrast material reaction forms involving patients who experienced acute allergic-like reactions to gadolinium-containing contrast media from January 1, 2001, through December 31, 2006, were retrospectively evaluated for the specific types of acute allergic-like reactions, reaction management, and patient outcomes. Relevant patient medical information, including documentation of prior gadolinium- or iodine-containing contrast material reaction, premedication before acute allergic-like reaction to IV gadolinium-containing contrast material, previous allergic reactions to substances other than contrast media, and history of asthma, was obtained by reviewing electronic medical records.

**RESULTS.** Seventy-eight thousand three hundred fifty-three (65,009 adult and 13,344 pediatric) IV administrations of gadolinium-containing contrast material were performed during the study period. Acute allergic-like reactions were documented after 54 injections (reaction frequency, 0.07%). Forty-eight reactions involved adult patients (adult reaction frequency, 0.07%), and six reactions occurred in pediatric patients (pediatric reaction frequency, 0.04%). Forty (74%) acute allergic-like reactions were mild, 10 (19%) were moderate, and four (7%) were severe. No gadolinium-containing contrast material-related death occurred during the study period. Twenty-six (50%) of 52 patients had one or more presumed risk factors for contrast material reaction.

**CONCLUSION.** Adult and pediatric acute allergic-like reactions to IV-administered gadolinium-containing contrast media are rare. Most of these reactions are mild; however, moderate and severe reactions that require immediate management do occur.

**T**he use of contrast-enhanced MRI has increased over the past decade as a variety of new applications have been described and put into clinical practice. Consequently, the number of annual pediatric and adult administrations of gadolinium-containing contrast agents has also increased considerably (65% from 2001 to 2006 at our institution). Although the IV administration of gadolinium-containing contrast media has been approved in some form for nearly two decades, it is essential that we continuously reevaluate the safety of these agents.

For many years, gadolinium-containing contrast materials have been considered quite safe, with minimal associated risk. This position may be changing somewhat, however, with the recent recognition of an association between gadolinium-containing contrast agents and nephrogenic systemic fibrosis (NSF) [1–3]. Allergic-like reactions are another risk,

albeit rare, attributed to IV-administered gadolinium-containing contrast materials [4–15]. The risk of allergic-like reaction to gadolinium-containing contrast agents has long been thought to be quite low, particularly when compared with iodinated contrast agents. Review of the literature reveals few recent large prospective or retrospective studies evaluating the frequency and severity of allergic-like contrast reactions to currently used gadolinium-containing contrast agents [13–15]. This is particularly true for the pediatric patient population.

The purpose of this study was to determine the frequency and severity of acute allergic-like reactions to IV-administered gadolinium-containing contrast media in children and adults. In addition, we sought to determine the frequency with which patients who reacted possessed certain presumed risk factors for allergic-like contrast material reaction.

**Keywords:** adults, children, contrast media, contrast reactions, gadolinium

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**TABLE 1: Institutional Classification of Severity and Manifestations of Acute Allergic-Like Reactions to Contrast Media**

Side Effect <sup>a</sup>	Mild <sup>b</sup>	Moderate <sup>c</sup>	Severe <sup>d</sup>
Nausea	Pruritus	Dyspnea	Severe respiratory distress
Vomiting	Rash	Bronchospasm	Unresponsiveness
Altered taste	Urticaria	Mild laryngeal edema	Convulsions
Perspiration	Cough	Symptomatic tachycardia	Arrhythmia
Warmth	Nasal stuffiness	Symptomatic bradycardia	Cardiopulmonary arrest
Flushing	Sneezing	Hypotension	Progressive angioedema
Anxiety	Mild eye swelling, mild facial swelling	Hypertension	

Note—Patients who presented with multiple reaction manifestations are classified according to most severe sign or symptom. Adapted from [16].

<sup>a</sup>Includes physiologic responses to contrast agents that are not considered allergic or allergic-like events.

<sup>b</sup>Requires no medical intervention with exception of possible antihistamine administration for cutaneous reaction.

<sup>c</sup>Requires immediate medical treatment or transfer to emergency department if an outpatient.

<sup>d</sup>Life-threatening, potentially fatal event typically requiring hospitalization if an outpatient.

## Materials and Methods

Institutional review board approval was obtained before the initiation of this HIPAA-compliant investigation. The requirement for participant informed consent was waived because of the retrospective nature of the study.

Our department policy is that all pediatric and adult patients having allergic-like reactions to contrast media, whether gadolinium- or iodine-containing, must be evaluated in person by a radiologist. After patient assessment and management of the contrast reaction, the treating physician is required to document the details of the event by completing a standardized departmental contrast material reaction form. This method of handling allergic-like reactions was established well before January 1, 2001, and has not significantly changed.

All contrast material reaction forms completed on adult and pediatric (younger than 19 years) patients who experienced acute allergic-like reactions to gadolinium-containing contrast agents between January 1, 2001, and December 31, 2006, were examined retrospectively. Forms were evaluated for the specific acute allergic-like reaction manifestation, the contrast agent administered, any medical treatment initiated, and whether the patient (if an outpatient) was discharged, transferred to the emergency department, or admitted to the hospital. An allergic-like reaction was considered acute if its symptoms began before the patient left the department of radiology. Delayed allergic-like reactions, chemotoxic reactions (e.g., NSF), and contrast material extravasations were excluded from this investigation.

Each patient's acute allergic-like reaction was then categorized as mild, moderate, or severe on the basis of a departmental reaction classification system adapted from the American College of Radiol-

ogy (ACR) "Categories of Reactions" [16] (Table 1). According to this classification, mild reactions were self-limited events, exhibited no significant progression, and required no medical treatment (except administration of an antihistamine for cutaneous manifestations). Moderate reactions necessitated medical management (other than or in addition to antihistamine administration) or eventual outpatient transfer to the emergency department. Severe reactions were life-threatening events (typically requiring hospital admission of an outpatient or emergency department patient). If a patient experienced more than a single contrast reaction manifestation, the reaction was categorized on the basis of the most medically significant sign or symptom. Adverse events to contrast material administration, such as nausea, vomiting, altered taste, perspiration, warmth, flushing, and anxiety, are considered physiologic side-effects according to departmental policy. Such adverse events are not thought to be allergic-like in cause, do not typically require medical management, and do not necessitate mandatory documentation.

For each documented reaction during the study period, our institutional comprehensive electronic medical record system was accessed for additional pertinent patient medical history. Specifically, the electronic medical records were searched for evidence of previous contrast material (iodine- or gadolinium-containing) allergic-like reaction, documentation of premedication (corticosteroid and/or antihistamine) administered before the patient received gadolinium-containing contrast material, prior allergic reaction to substances other than contrast media, and history of asthma. In addition, information was gathered pertaining to any further reaction management occurring after the patient left the department of radiology (e.g., in the emergency department or as a hospital inpatient) and to estab-

lish each patient's final disposition (e.g., Was the patient discharged from our institution in their baseline state of health? Did the patient suffer acute allergic-like reaction-related permanent disability? Did the patient die?).

The total number of pediatric and adult IV injections of gadolinium-containing contrast materials and the sex distribution of recipients were determined for the study period by querying the Radiology Information System (RIS). The frequencies of pediatric and adult acute allergic-like reactions at our institution were then compared. The relative risk between the pediatric and adult rates was calculated. Confidence intervals were determined using the normal approximation to the binomial distribution.

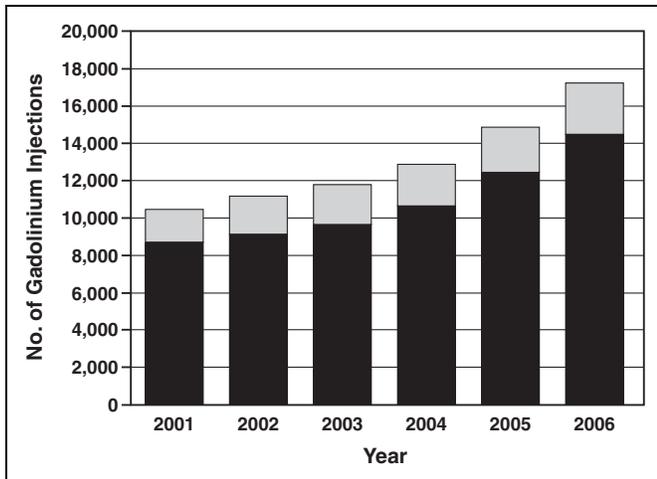
Three gadolinium-containing contrast materials were used in both pediatric and adult patients at our institution during the time of the investigation. Gadopentetate dimeglumine (Magnevist, Bayer HealthCare), a linear ionic gadolinium chelate, constituted more than 90% of gadolinium-containing contrast media administrations during the study period (as determined by department of radiology purchasing records). Gadobenate dimeglumine (MultiHance, Bracco Diagnostics), also a linear ionic gadolinium chelate, constituted fewer than 10% of gadolinium-containing contrast material administrations and was used only for specific examinations, including MRI of the liver, enhanced MR angiography of the body (chest, abdomen, pelvis, and extremities), enhanced MR angiography of the neck, enhanced MR venography of the brain, and perfusion MRI of the brain. Gadodiamide (Omniscan, GE Healthcare), a linear nonionic gadolinium chelate, was used in fewer than 0.1% of injections during the study period. The exact number of administrations of each agent is unknown. Gadolinium-containing contrast agents were typically given at a dose of 0.1 mmol/kg at our institution. Rarely, higher double doses (0.2 mmol/kg) were used for applications such as MR angiography and cardiac MR infarct and viability studies.

## Results

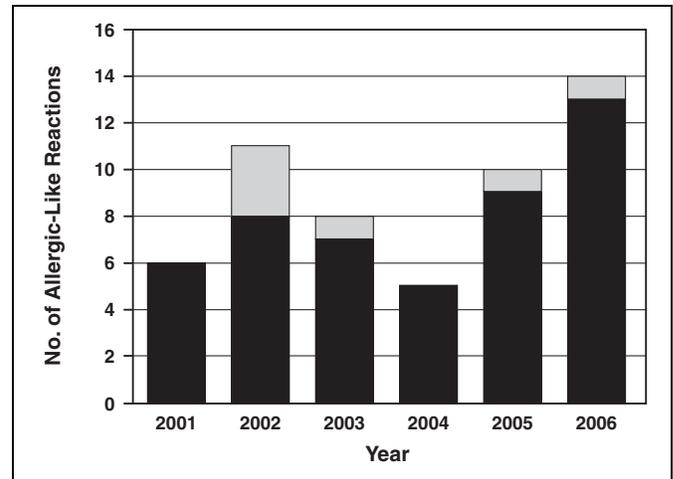
There were 78,353 IV administrations of gadolinium-containing contrast material performed between January 1, 2001, and December 31, 2006, in the department of radiology at our institution, 65,009 in adult patients and 13,344 in children (Fig. 1). Fifty-four percent of injections were given to female patients and 46% to male patients.

Fifty-four acute allergic-like reactions were recorded during the study period, for a frequency of 0.07%. The pediatric frequency of acute allergic-like reactions was 0.04% (six reactions for 13,344 contrast material

## Reactions to Gadolinium-Containing Contrast Media



**Fig. 1**—IV gadolinium-containing contrast media administrations in pediatric (gray bars) and adult (black bars) patients per year from January 1, 2001, through December 31, 2006.



**Fig. 2**—Acute allergic-like reactions to IV gadolinium-containing contrast media in pediatric (gray bars) and adult (black bars) patients per year from January 1, 2001, through December 31, 2006.

administrations), and the adult frequency was 0.07% (48 reactions for 65,009 contrast material administrations) (Fig. 2). A single adult patient experienced three acute allergic-like reactions during the study period. Consequently, 52 separate patients experienced acute allergic-like reactions.

Thirty-five reactions involved female patients and 19 involved male patients. The mean age of patients who experienced acute allergic-like reactions was 43 years (range, 7 months–74 years). The mean age of adult patients who experienced acute allergic-like reactions was 47 years (range, 22–74 years), and the mean age of pediatric patients was 9 years (range, 7 months–15 years). Most reactions occurred in the outpatient setting (49/54 reactions, 91%). A single reaction (2%) involved an emergency department patient, whereas four reactions involved hospital inpatients (7%). Outpatients account for approximately 84% of MRI examinations performed at our institution annually.

Twenty-six (48%) acute allergic-like reactions followed the administration of gadopentetate dimeglumine, and four (7%) followed the administration of gadobenate dimeglumine. The injected gadolinium-containing contrast agent was not documented in 24 (44%) instances; however, it is likely, on the basis of purchasing records from the study period, that most of these reactions involved gadopentetate dimeglumine.

Forty (74%) of the documented acute allergic-like reactions were classified as mild, 10 (19%) as moderate, and four (7%) as severe

(Tables 2–4). No gadolinium-containing contrast material–related death occurred during the study period.

A single patient experienced more than one acute allergic-like reaction to gadolinium-containing contrast media during the study period. This adult male patient experienced urticaria on three occasions after the injection of gadolinium-containing contrast material during an 8-month period. As a result of the initial allergic-like reaction, the patient was premedicated with both corticosteroid and antihistamine before the two subsequent examinations. This patient had what has been termed a “breakthrough reaction” on the last two occasions because he experienced acute allergic-like reactions to contrast media despite appropriate premedication [17]. Seven additional patients in this study also experienced breakthrough reactions.

Twenty-six (50%) of 52 individual patients who experienced acute allergic-like reactions to gadolinium-containing contrast media had one or more identifiable presumed risk factors for contrast reaction. Six patients (12%) had a history of previous allergic-like reaction to gadolinium-containing contrast material, three (6%) had experienced prior allergic-like reactions to iodinated contrast media, and two (4%) had a history of asthma. Twenty patients (38%) had documented prior allergic reactions to substances other than gadolinium- or iodine-containing contrast media. Ten patients (19%) had more than one risk factor, and 26 patients (50%) had no identifiable risk factor.

### Discussion

The 0.07% frequency of acute allergic-like reactions to gadolinium-containing contrast media obtained in this study is similar to that described in the few other large studies in the literature on the subject. Murphy et al. [13] described a 0.1% frequency of allergic-like reaction to gadolinium-containing contrast media involving 21,000 patients over an almost 5-year period. Gadopentetate dimeglumine accounted for 98% of contrast material injections in that study. A retrospective survey involving 53 institutions determined that 241 allergic-like reactions occurred after 825,535 injections of gadolinium-containing contrast media (687,255 gadopentetate dimeglumine doses, 64,005 gadoteridol doses, and 74,275 gadodiamide doses), for a reaction frequency of 0.03% [14]. It is likely that the rate of allergic-like reaction established in that study is an underestimate of the actual rate based on the inherent design of the investigation. A more recent study showed 19 allergic-like events involving 9,528 patients, for a slightly higher reaction frequency of 0.2% [15]. Patients in that study experienced allergic-like reactions after the administration of gadoterate meglumine, gadodiamide, or gadopentetate dimeglumine.

The frequency of acute allergic-like reaction to gadolinium-containing contrast media observed in our study is less than that typically observed for iodinated contrast media in adults. In an investigation of IV-administered nonionic iopromide (Ultravist, Bayer Health-Care) in adult patients, Mortelé et al. [18] de-

**TABLE 2: Manifestations of Mild Acute Allergic-Like Reaction to Gadolinium-Containing Contrast Media (n = 40)**

Manifestation	No. of Reactions
Urticaria (hives)	23 <sup>a</sup>
Mild throat symptoms (e.g., itching, tightening) requiring no treatment	4 <sup>a</sup>
Rash (away from injection site)	3 <sup>b</sup>
Mild difficulty breathing requiring no treatment	3
Sneezing and nasal congestion (mucosal edema)	3
Mild perioral or periorbital edema	2 <sup>a</sup>
Mild facial edema and urticaria	2

<sup>a</sup>Including a single pediatric patient.<sup>b</sup>Including two pediatric patients.**TABLE 3: Manifestations of Moderate Acute Allergic-Like Reaction to Gadolinium-Containing Contrast Media (n = 10)**

Manifestation	Management
Difficulty breathing, urticaria <sup>a</sup>	Diphenhydramine, transfer to emergency department
Difficulty breathing, throat symptoms, rash <sup>a</sup>	Diphenhydramine, epinephrine, transfer to emergency department
Difficulty breathing, chest pain <sup>b</sup>	Transfer to emergency department
Difficulty breathing, facial angioedema, urticaria <sup>a</sup>	Transfer to emergency department
Difficulty breathing, facial angioedema, hypotension <sup>b</sup>	Diphenhydramine, epinephrine, transfer to emergency department
Difficulty swallowing, bronchospasm <sup>b</sup>	Epinephrine, inhaled albuterol
Facial angioedema, rash <sup>b</sup>	Diphenhydramine, transfer to emergency department
Throat symptoms, facial angioedema, urticaria <sup>c</sup>	Epinephrine, transfer to emergency department
Throat symptoms, rash, urticaria <sup>a</sup>	Diphenhydramine, methylprednisolone, transfer to emergency department
Throat symptoms, nasal congestion <sup>a</sup>	Transfer to emergency department

Note—All patients in table are adults. Those transferred to emergency department were all subsequently discharged without being admitted to hospital.

<sup>a</sup>Reaction for which exact gadolinium-containing contrast agent is unknown.<sup>b</sup>Reaction to gadopentetate dimeglumine.<sup>c</sup>Reaction to gadobenate dimeglumine.**TABLE 4: Manifestations of Severe Acute Allergic-Like Reaction to Gadolinium-Containing Contrast Media (n = 4)**

Manifestation	Management
Laryngeal edema, urticaria, sneezing, nasal congestion <sup>a</sup>	Diphenhydramine, epinephrine, hospital admission via emergency department
Difficulty breathing, hypoxia <sup>a</sup>	Diphenhydramine, epinephrine, methylprednisolone (hospital inpatient at time of examination)
Difficulty breathing, hypoxia <sup>a</sup>	Hospital admission via emergency department
Difficulty breathing, facial angioedema, urticaria <sup>a,b</sup>	Diphenhydramine, epinephrine, methylprednisolone, hospital admission via emergency department

<sup>a</sup>Reaction for which exact gadolinium-containing contrast agent is unknown.<sup>b</sup>Pediatric patient.

scribed an adverse event rate of 0.7% (of which approximately 90% were allergic-like) in 29,508 patients. A lower frequency of reac-

tion for nonionic iodinated contrast media was shown by Cochran et al. [19] during a 9-year period in which this group observed an

adverse event rate of 0.23% (of which approximately 90% were allergic-like). Although the frequency of acute allergic-like reactions to iodinated contrast media is lower in the study by Cochran et al. than that described by Mortelé et al., both rates are substantially higher than those observed in our study of gadolinium-containing contrast agents.

In the pediatric population, the risk of allergic-like reaction to IV gadolinium-containing contrast media also appears to be less than that previously observed for iodinated contrast agents. In 1975, a large study by Gooding et al. [20] involving 12,419 IV administrations of ionic contrast material described a 0.4% frequency of allergic-like reactions in children undergoing excretory urography. In a recent series, Dillman et al. [21] observed a pediatric incidence of acute allergic-like reaction to low-osmolality nonionic iodinated contrast media of 0.18%. Both rates are higher than the 0.04% frequency of reaction noted for pediatric patients in our study.

The pediatric frequency of acute allergic-like reaction to gadolinium-containing contrast media was 0.04% during our study period, and the adult rate was 0.07% (similar to the combined pediatric and adult rates). Thus, the adult frequency of contrast reactions is nearly two times that of the pediatric population, with a relative risk of reaction in adults compared with children of 1.53 (95% CI, 0.66–3.56). Although this difference in frequencies of reaction is not statistically significant, these results mirror an age-related trend observed in previous studies that evaluated the risk of allergic-like reaction to iodine-containing contrast media. The studies by Dillman et al. [21] and Katayama et al. [22], when stratified by age, both showed that pediatric patients have a decreased risk of contrast reaction when compared with adult patients after the IV administration of iodine-containing contrast media. The factors responsible for this difference in rates of reaction between pediatric and adult patients are uncertain.

Most acute allergic-like reactions to gadolinium-containing contrast media in our study were mild. This is not dissimilar to results presented in other studies that evaluated both gadolinium-containing and iodinated contrast material allergic-like reactions [13–15, 18, 19, 21, 22]. In our investigation, 40 (74%) of the 54 documented acute allergic-like reactions were mild. Most of these mild events were self-limited isolated cutaneous reactions (65%, or 26/40 mild allergic-like reactions) such as urticaria or rash. Five of six pediatric

acute allergic-like reactions were mild, but a sixth reaction was severe.

Overall, 10 acute allergic-like reactions were moderate in severity and four were severe. Consequently, 26% of reactions required either medical management, transfer to the emergency department, or hospital admission. It is essential that institutions and individual radiologists who perform contrast-enhanced MRI examinations be prepared to appropriately manage such acute reactions. Acute allergic-like reactions to gadolinium-containing contrast agents are typically treated in a manner identical to that for treating similar reactions after the administration of iodinated contrast material [16]. Although no gadolinium-containing contrast material-related death occurred during the study period, such occurrences have been described [23].

Twenty-four (52%) of 46 adult patients who experienced acute allergic-like reactions had one or more apparent risk factors for allergic-like contrast reaction, such as a history of previous allergic-like reaction to either gadolinium- or iodine-containing contrast media, a prior allergic reaction to a substance other than contrast media, or documented asthma. Twenty-two percent of adults who experienced an acute allergic-like reaction had more than one risk factor. In comparison, two (33%) of six pediatric patients had an identifiable risk factor, including a patient with a history of prior allergic-like reaction to gadolinium-containing contrast media and a patient with a history of prior allergic reaction to a substance other than contrast medium. No pediatric patient had more than a single risk factor. Four (67%) of six pediatric and 22 (48%) of 46 adult patients had none of the described presumed risk factors.

Interestingly, in our study we found that female patients experienced 63% of adult and 83% of pediatric acute allergic-like reactions. When combining both the pediatric and adult rates, 65% of reactions involved female patients, whereas only 35% of reactions involved males. Although this sex difference is not statistically significant (the relative risk of reaction in women compared with men is 1.57 [95% CI, 0.90–2.74]), it may be a real finding. It is likely that this difference would be significant in a slightly larger patient population. The cause of such a difference between sexes is uncertain.

Both gadopentetate dimeglumine and gadobenate dimeglumine are linear (open-chain) ionic gadolinium chelates. No cyclic or nonionic gadolinium-containing contrast agents were included in this study (only a minimal

number of doses of gadodiamide were administered at our institution during the study period). Some evidence suggests that cyclic chelates are generally more stable compounds than linear chelates. This difference in stability has been implicated by some as playing an important role in the pathogenesis of NSF. However, no definitive evidence in the literature suggests that this difference in structure between various gadolinium-containing contrast agents affects the observed rates of allergic-like reactions [24].

Our study has a few limitations. First, it is possible that certain allergic-like reactions included in this study were not directly related to the IV administration of gadolinium-containing contrast material. Although this is thought to be unlikely, if such an event occurred, it would artificially increase the frequency of reaction established in the study. Second, our results depend on the completion of a contrast material reaction form. If an acute allergic-like reaction was not documented (or if a contrast material reaction form was completed but lost), such a reaction would not be included in our investigation. Such occurrences would falsely lower the frequency of reaction calculated in this study. Third, when attempting to assess apparent risk factors for acute allergic-like reaction to gadolinium-containing contrast media, the prevalence of certain conditions, including history of asthma, history of allergic-like reaction to contrast media, and history of allergic reaction to substances other than contrast media, is not known over our entire pediatric or adult patient populations. Finally, the offending gadolinium-containing contrast agent was not documented for 44% of the reactions included in this study.

In conclusion, acute allergic-like reactions related to IV-administered gadolinium-containing contrast media in both children and adults are rare. They occur less frequently than do reactions to IV-administered iodinated contrast media. Most of these acute allergic-like reactions to gadolinium-containing contrast media are mild; however, moderate and severe reactions do occur. Although reactions were more frequent in adult than in pediatric and in female than in male patients, these differences were not statistically significant. Potential factors that may increase an individual's risk of an acute allergic-like reaction include a history of previous allergic-like reaction to IV-administered contrast medium (either gadolinium- or iodine-containing) and prior allergic reaction to a substance other than contrast media.

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## References

1. Marckmann P, Skov L, Rossen K, et al. Nephrogenic systemic fibrosis: suspected causative role of gadodiamide used for contrast-enhanced magnetic resonance imaging. *J Am Soc Nephrol* 2006; 17:2359–2362
2. Kuo PH, Kanal E, Abu-Alfa AK, Cowper SE. Gadolinium-based MR contrast agents and nephrogenic systemic fibrosis. *Radiology* 2007; 242:647–649
3. Broome DR, Girquis MS, Baron PW, Cottrell AC, Kjellin I, Kirk GA. Gadodiamide-associated nephrogenic systemic fibrosis: why radiologists should be concerned. *AJR* 2007; 188:586–592
4. Weiss KL. Severe anaphylactoid reaction after i.v. Gd-DTPA. *Magn Reson Imaging* 1990; 8:817–818
5. Tishler S, Hoffman JC Jr. Anaphylactoid reactions to i.v. gadopentetate dimeglumine. *Am J Neuroradiol* 1990; 11:1167
6. Salonen OL. Case of anaphylaxis and four cases of allergic reaction following Gd-DTPA administration. *J Comput Assist Tomogr* 1990; 14:912–913
7. Tardy B, Guy C, Barral G, Page Y, Ollagnier M, Bertrand JC. Anaphylactic shock induced by intravenous gadopentetate dimeglumine. *Lancet* 1992; 339:494
8. Shellock FG, Hahn HP, Mink JH, Itskovich E. Adverse reaction to intravenous gadoteridol. *Radiology* 1993; 189:151–152
9. Witte RJ, Anzai LL. Life-threatening anaphylactoid reaction after intravenous gadoteridol administration in a patient who had previously received gadopentetate dimeglumine. *Am J Neuroradiol* 1994; 15:523–524
10. Meuli RA, Maeder P. Life-threatening anaphylactoid reaction after IV injection of gadoterate meglumine. (letter) *AJR* 1996; 166:729
11. Runge VM. Allergic reactions to gadolinium chelates. *AJR* 2000; 175:1513–1517
12. Rahman SL, Harbinson MT, Mohiaddin R, Pennell DJ. Acute allergic reaction upon first exposure to gadolinium-DTPA: a case report. *J Cardiovasc Magn Reson* 2005; 7:849–851
13. Murphy KJ, Brunberg JA, Cohan RH. Adverse reactions to gadolinium contrast media: a review of 36 cases. *AJR* 1996; 167:847–849
14. Murphy KP, Szopinski KT, Cohan RH, Mermillod B, Ellis JH. Occurrence of adverse reactions to gadolinium-based contrast material and management of patients at increased risk: a survey of the American Society of Neuroradiology Fellowship Directors. *Acad Radiol* 1999; 6:656–664
15. Li A, Wong CS, Wong MK, Lee CM, Au Yeung MC. Acute adverse reactions to magnetic resonance

- contrast media: gadolinium chelates. *Br J Radiol* 2006; 79:368–371
16. American College of Radiology. *Manual on contrast media*, 5th ed. Reston, VA: American College of Radiology, 2004
  17. Freed KS, Leder RA, Alexander C, DeLong DM, Kliewer MA. Breakthrough adverse reactions to low-osmolar contrast media after steroid premedication. *AJR* 2001; 176:1389–1392
  18. Mortel  KJ, Oliva MR, Ondatequi S, Ros PR, Silverman SG. Universal use of nonionic iodinated contrast medium for CT: evaluation of safety in a large urban teaching hospital. *AJR* 2005; 184:31–34
  19. Cochran ST, Bomyea K, Sayre JW. Trends in adverse events after IV administration of contrast media. *AJR* 2001; 176:1385–1388
  20. Gooding CA, Berdon WE, Brodeur AE, Rowen M. Adverse reactions to intravenous pyelography in children. *AJR* 1975; 123:802–804
  21. 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. *AJR* 2007; 188:1643–1647
  22. 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; 175:621–628
  23. Jordan RM, Mintz RD. Fatal reaction to gadopentetate dimeglumine. *AJR* 1999; 164:743–744
  24. Morcos SK. Nephrogenic systemic fibrosis following the administration of extracellular gadolinium-based contrast agents: is the stability of the contrast agent molecule an important factor in the pathogenesis of this condition? *Br J Radiol* 2007; 80:73–76