Received: 15 March 2024 | Revised: 16 May 2024 | Accepted: 30 May 2024

DOI: 10.1111/all.16191

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

NEWS & VIEWS

Algorithms in Allergy and Clinical Immunology

An algorithm for the management of radiocontrast media hypersensitivity, 2024 update

Radiocontrast media (iodinated contrast media, RCM) are rapidly given as highly concentrated solutions in large volumes to highlight radiographic contrast. Adverse reactions after administration are classified into immediate hypersensitivity reactions (IHR) occurring within 1 h after RCM administration, non-immediate hypersensitivity reactions (NIHR) presenting >1 h after exposure, toxic reactions (e.g., generalized pruritus, flushing, nausea), or events unrelated to RCM exposure (e.g., spontaneous urticaria).[1] IHR presents with symptoms seen in anaphylaxis, most commonly mild skin reactions. NIHR present with exanthema variants, predominantly with maculopapular exanthem (MPE).[2,3] IHR and NIHR occur each in about 0.5%–2% of patients receiving RCM.[1,2,4] In patients with severe anaphylaxis, skin tests indicating an IgE-mediated mechanism are often positive, whereas they mostly remain negative in those with mild reactions. NIHR are often caused by T cell-mediated allergy. Patients with previous hypersensitivity reaction (HR) have a high risk of a repeat reaction in the next RCM examination. These patients, but not those with prior mild toxic symptoms only (e.g., generalized pruritus, heat sensation, flushing, nausea), should be investigated and counselled (Table 1 and Figure 1) to reduce the risk of repeat reactions.[2]

There is insufficient evidence on the degree of effectiveness of premedication in patients with NIHR to RCM; numerous breakthrough reactions have been described.[2] Thus, premedication should be no principal strategy to avoid further reactions after NIHR. After IHR, premedication had been advocated to prevent repeat reactions.[2] Some efficacy has meanwhile been reported also for low-osmolar RCM after IHR if using at least two doses of corticosteroids (32–50 mg prednisolone or methylprednisolone given 1–2 h and 4–12 h before) in a meta-analysis and for antihistamine premedication after mild reactions.[5] However, the effect has not been consistently found in all studies indicating a probable weak effect. In direct comparison, changing to a RCM with a different side chain (DSC) structure in the subsequent examination has demonstrated a clearly superior efficacy, which is robust in different studies.[4,5] This is also effective in patients with NIHR. Interestingly, the side chain structures are of importance. Pairs of RCM with higher or lower cross-reactivity have been reported. Whereas the results are influenced by the RCM chosen in different publications, the carbamoyl side chain appears to be relevant for IHR and NIHR: a change from a RCM carrying this side chain to one without or vice versa reduced subsequent reactions, whereas a change to an agent with similar side chain may be insufficient (Figure S1).[5]

Skin testing with non-irritant concentrations (Table S1) and using a skin test-negative RCM for the next imaging has been shown to greatly reduce, but not eliminate, the risk of repeat reactions in patients with previous IHR or NIHR and to reduce its severity in IHR.[6,7] Whereas it is recommended for NIHR as well as for moderate and severe IHR, its additional value after mild IHR and after changing to a RCM with different side chain structure still has to be confirmed. The negative predictive value (NPV) is better for IHR than for NIHR.[2] Thus, applying a DSC RCM, ideally skin test-negative, is now the first choice for prevention of repeat reactions. In contrast, premedication prior to RCM reexposure for patients with previous IHRs to low-osmolar RCM may possibly add a lower level of protection. It can be given in urgent need for RCM without test possibility and may additionally be considered after allergy testing.

Drug provocation tests (DPTs) with a skin test-negative RCM in experienced allergy departments have been established as an alternative to reexposition in the radiology department for identifying a safe alternative and provide more safety for the patient. They should be performed in patients after severe anaphylaxis and in those with RCM with positive skin test and may be done in patients with mild to moderate non-allergic reactions depending on availability. Its NPV depends on the maximum dose used.[8] Lowering the computertomogram (CT) voltage to 100 kVp, the dose to 1.5 mL/kg (max, 130 mL), and speed to 2.5 or 3 mL/s may be an additional approach to reduce repeat reactions in IHR. The effect was more pronounced in moderate to severe IHRs (relative risk 0.62), where it can be recommended, if applicable.[9]

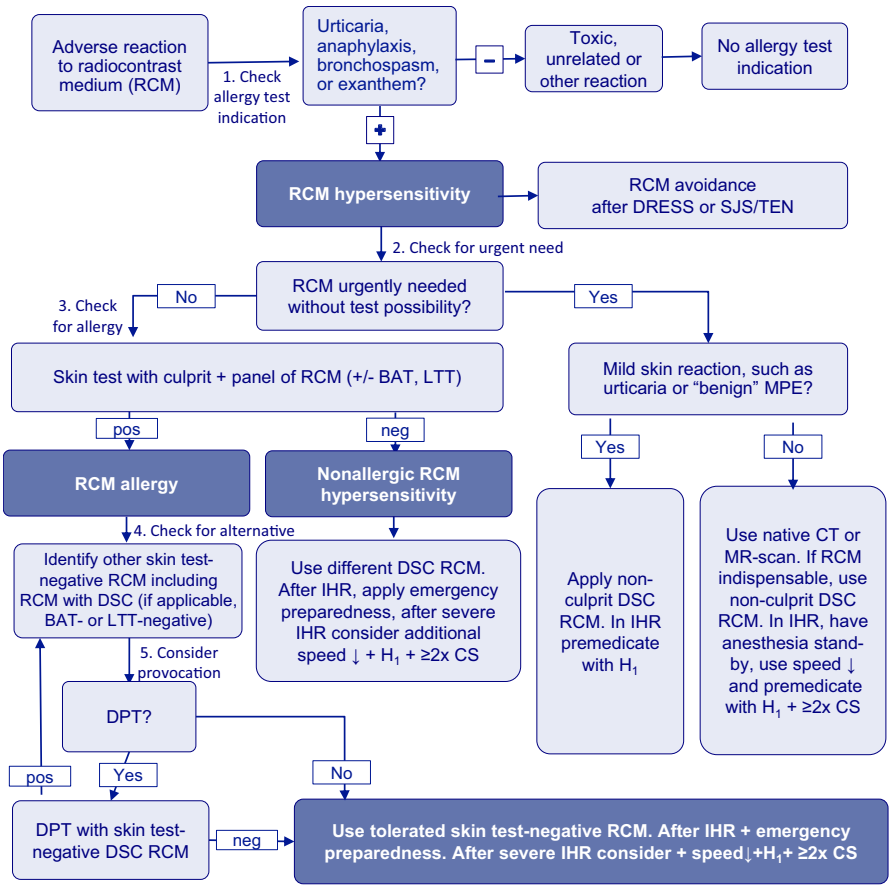
(1) Patients with history of anaphylaxis, bronchospasm, urticaria/angioedema, and exanthems to RCM should undergo allergological work-up. Those with severe NIHRs, as bullous exanthems (SJS/TEN) or with systemic symptoms (DRESS), should avoid future RCM application, whereas skin tests can be done. (2) In patients with mild IHR (urticaria +/− angioedema) or NIHR (maculopapular exanthema, MPE) and urgent need for RCM-based imaging, a non-culprit RCM with different side chain (DSC) has to be given, in IHR after applying H_1-premedication (H_1). In patients with anaphylaxis, RCM should be avoided and native CT- or magnet resonance (MR)-scan considered. If RCM is indispensable, administer a non-culprit DSC RCM; in IHR,

TABLE 1 Indications for allergy testing in suspected radiocontrast media hypersensitivity.

Previous reaction after radiocontrast media application	Indication (yes/no)
Food, respiratory, cutaneous, drug allergies, but no previous reaction to radiocontrast media, alleged "iodine" allergy	No
Unspecific symptoms (e.g., generalized pruritus, heat sensation, transient erythema, flushing, dizziness, nausea, sneezing, rhinorrhea, chest tightness)	No
Localized cutaneous injection site reaction (e.g., isolated wheal, erythema)	No
Generalized cutaneous reaction (urticaria, angioedema, erythema)	Yes[a]
Isolated bronchospasm	Yes[a]
Anaphylaxis	Yes
Delayed-appearing urticaria and angioedema	Yes[a]
Maculopapular exanthem	Yes
Morphological variants of exanthems (FDE, SDRIFE, AGEP)	Yes
Severe bullous skin reactions, DRESS (normally no reexposition, no provocation)	Yes

[a]More data desired to confirm the additional value of allergy testing in this indication.

FIGURE 1 Management of patients with previous radiocontrast medium reaction.



emergency preparedness including anesthesia standby and premedicate with H_1 and with two times corticosteroids (2×CS). (3) Skin prick test and, if negative, intradermal tests are performed, in NIHR additionally patch tests; best sensitivity is 2–6 months after the reaction (Table S1). The culprits of previous reactions together with a panel of available RCM including an DSC alternative are tested. Basophil activation test (BAT) and lymphocyte transformation tests (LTT) may optionally be used. If no RCM allergy can be demonstrated (nonallergic RCM hypersensitivity), skin tests are not helpful to select an alternative. Thus, use a non-culprit DSC RCM. In IHR, apply emergency preparedness, and after severe reactions additionally consider premedication with H_1 and 2×CS as well as speed ↓. (4) If skin tests are positive to the culprit, RCM allergy is diagnosed, and alternative skin test-negative (+/− BAT- or LTT-negative) alternative RCMs are looked for. (5) Drug provocation tests (DPT) confirm tolerability to a skin test-negative RCM, preferably with a DSC, e.g.,

after severe reactions, whereas in patients with mild to moderate non-allergic reactions, reexposition in the radiology department is normally sufficient. Otherwise, a skin test-negative alternative DSC RCM is administered under emergency preparedness; after severe IHR, consider additional speed↓, H_1, and 2×CS premedication.

ACKNOWLEDGEMENTS

Open Access funding enabled and organized by Projekt DEAL.

FUNDING INFORMATION

No funding.

CONFLICT OF INTEREST STATEMENT

No conflict of interest.

DATA AVAILABILITY STATEMENT

None.

Knut Brockow

Department of Dermatology and Allergy Biederstein, School of Medicine and Health, Technical University of Munich, Munich, Germany

Correspondence

Knut Brockow, Department of Dermatology and Allergy Biederstein, Technical University of Munich, Biedersteiner Strasse 29, Munich 80802, Germany.

Email: knut.brockow@tum.de

ORCID

Knut Brockow https://orcid.org/0000-0002-2775-3681

REFERENCES

1. Brockow K, Christiansen C, Kanny G, et al. Management of hypersensitivity reactions to iodinated contrast media. *Allergy*. 2005;60:150-158.
2. Torres MJ, Trautmann A, Böhm I, et al. Practice parameters for diagnosing and managing RCM hypersensitivity. *Allergy*. 2021;76:1325-1339.
3. Brockow K, Ardern-Jones MR, Mockenhaupt M, et al. EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity. *Allergy*. 2019;74:14-27.
4. Cha MJ, Kang DY, Lee W, et al. Hypersensitivity reactions to iodinated contrast media: a multicenter study of 196 081 patients. *Radiology*. 2019;293:117-124.
5. Kim S, Jeon KN, Jung JW, et al. Substitution with low-osmolar iodinated contrast agent to minimize recurrent immediate hypersensitivity reaction. *Radiology*. 2023;309:e222467.
6. Lee JH, Yoo Y, Kim SR, et al. Skin test-guided strategy to select alternative iodinated contrast Media in Patients with Immediate Hypersensitivity Reaction: a prospective confirmative study. *J Allergy Clin Immunol Pract*. 2023;11:3454-3462.
7. Trautmann A, Brockow K, Behle V, Stoevesandt J. Radiocontrast media hypersensitivity: skin testing differentiates allergy from non-allergic reactions and identifies a safe alternative as proven by intravenous provocation. *J Allergy Clin Immunol Pract*. 2019;7:2218-2224.
8. Ahn KM, Ahn YH, Cho MK, Kang DY, Lee SY, Kang HR. Validation of practical pathway in patients with anaphylaxis to low osmolar contrast media: a retrospective cohort study. *J Allergy Clin Immunol Pract*. 2022;10:2685-2692.
9. Park HJ, Son JH, Kim TB, et al. Relationship between lower dose and injection speed of iodinated contrast material for CT and acute hypersensitivity reactions: An observational study. *Radiology*. 2019;293:565-572.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.