

Clinical Communications

Incidence of suspected perioperative anaphylaxis—a multicenter snapshot study

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Clinical Implication

- Quoted incidence of perioperative anaphylaxis is 1:1300-1:13,000. In this study of 4595 general anesthetic cases, 1:353 cases met referral criteria for the investigation of suspected perioperative anaphylaxis, which suggested that this clinical problem may be underrecognized and underreported.

TO THE EDITOR:

Anaphylaxis associated with general anesthesia (AAGA) is a serious perioperative event with significant morbidity and mortality. Appropriate follow-up and investigation of such events is critical to improve the safety of subsequent anesthetics for the individual.

The Association of Anesthetists of Great Britain and Ireland (AAGBI) has guidelines that state that all suspected cases should be referred to a specialist clinic for investigation.¹ Criteria for referral include unexpected, unexplained hypotension, unexpected bronchospasm resistant to treatment, angioedema, urticaria, severe itch, or widespread erythema (Table E1, found in this article's Online Repository at www.jaci-inpractice.org). Referrals should include serial serum mast cell tryptase (MCT) measurements and a thorough history of the event.

Whilst the incidence of proven AAGA is given as between 1:1380 and 1:13,000,^{2,3} the incidence of adverse perioperative events that meet the criteria for AAGA is not known. It is thought that such events are more common than reported,⁴ and several barriers to referral have been described that may account for this.⁵

We sought to determine the incidence of these events in a multicenter study that involved 12 hospitals. Having gained research and development approval, data were collected about general anesthetics given for elective and emergency surgery between 08:00 and 18:00 hours Monday to Friday, simultaneously in all 12 hospitals, during a 2-week period. Cases where a regional technique was used in addition to general anesthesia were included, but cases where regional anesthesia was the sole technique were not.

Data collection was performed by the Anesthetic Audit and Research Matrix of Yorkshire (AARMY). This is a network of anesthetic trainees and consultants who work collaboratively across a large region within the United Kingdom.⁶

Possible cases were identified using a questionnaire that asked the responsible anesthetist whether any of the criteria, as defined above, had been met for any of the patients on their operating list. The data were collected retrospectively at the end of each list, whilst still fresh in the anesthetist's mind. This was at the end of the morning, or afternoon operating session. Where cases were identified, the anesthetist was then asked whether an MCT sample had been taken and whether the patient had been referred for further investigation.

Data were collected from 4595 general anesthetics. For 7 of the 12 participating hospitals, the total number of general anesthesia cases that met criteria for inclusion were also recorded in the same 2-week period. In those hospitals, the study capture rate was between 80% and 100%.

There were 13 cases that met the criteria for suspected anaphylaxis. The majority of these presented with isolated urticaria or erythema (Figure 1).

Three of the cases identified by the data collectors had serum MCT measurements taken and were referred for further investigation. Of note, these were cases where there was major cardiovascular or respiratory involvement, or both. One case had an MCT rise, but with negative skin testing. A presumptive diagnosis of teicoplanin allergy was made based on the temporal relationship between administration of teicoplanin and the onset of the reaction. The second case had a significant MCT rise and the patient was found to be allergic to penicillin following skin testing. The third case demonstrated no rise in MCT, and skin testing for the agents administered during anesthesia (including neuromuscular blocking agents) was negative; however, this patient had a positive skin prick test to suxamethonium. Interestingly, the patient had experienced a previous episode of suspected anaphylaxis to this agent that had not been investigated. Based on our confirmed cases of anaphylaxis, the incidence of AAGA in our study is therefore 1:2297, higher than most previous work in this area.

The 10 cases not referred for investigation were predominantly those with isolated urticaria or erythema. Two cases not referred had cardiovascular and/or respiratory involvement. In one of these, the data collector was uncertain whether the clinical picture met the criteria for "unexpected" bronchospasm and hypotension, as the patient had a background of hypertension and chronic obstructive pulmonary disease.

The local coordinators for each hospital where cases were not referred were requested to contact the patients and invite them for further investigation; to date no patients have come forward for this.

This study defines an incidence of 1 in 353 adverse perioperative events that meet published criteria for suspected AAGA. To the best of the authors' knowledge, this is the first time such an incidence has been determined. It appears to confirm the suspicion that such events may be underreported, with only 3 of 13 referred on for further investigation with appropriate MCT measurements.

It is not possible to determine from these data why the cases with isolated skin signs were not referred. One explanation may be that anaphylaxis is generally considered by anesthetists to always be a severe clinical syndrome that involves cardiovascular and/or respiratory compromise. It is perhaps not widely known that isolated skin signs might also be due to anaphylaxis, whether IgE mediated

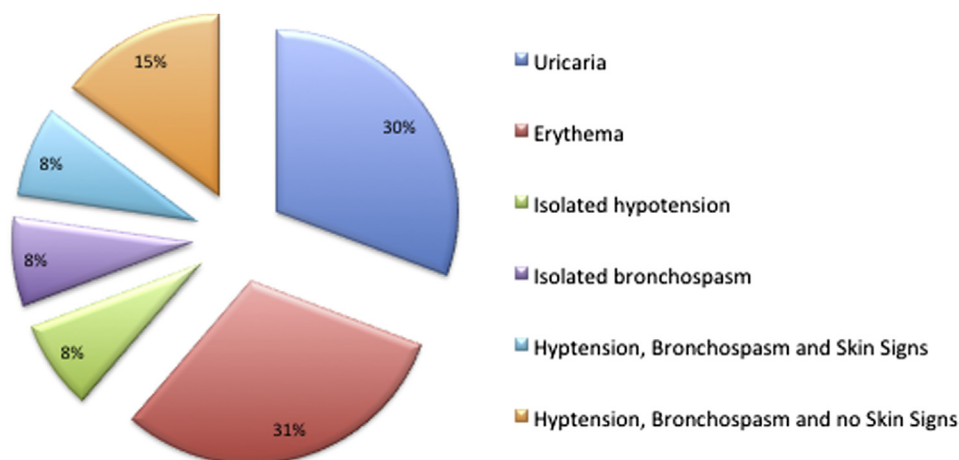


FIGURE 1. Of 4595 general anesthetics given over a 2-week period, 13 met the criteria for suspected anaphylaxis. The clinical presentation of these cases is detailed in the text.

or non-IgE mediated. In addition, it is relatively common to have localized histamine release following injection of many anesthetic drugs, in particular the neuromuscular blocking drugs. It is possible that anesthetists have developed an inappropriately high threshold for referral when skin signs develop in isolation.

These findings highlight the need to improve awareness that such adverse perioperative events may be anaphylactic in nature, and to improve the referral of such cases. This may be facilitated by the use of “anaphylaxis follow-up packs” available in the operating room, containing the necessary paperwork and blood bottles, as well as template letters for the patients and their family doctor with information about the reaction they have had. As well as ensuring appropriate and timely referral to a specialist clinic, the packs can improve the cascade of information to patients and their health care providers.⁷ For many patients, this may prove to be life saving.

Acknowledgments

We thank all those who have contributed to this study as part of the AARMY network: Louise Savic; Philip Hopkins; Andrew Lumb; Liam Allender; Kate Robinson; David Moir; Martyn Robertson; Olga Plotnikova; Alison Lansbury; Manik Chandra; Will Emery; Manojit Sinha; Mike Munro; John Stones; Annelise Wilkins; Andrew Gratrix; Simon Howell; Stephen Fletcher; Nick Freeman; Joanna Gordon; Anne-Mair Hammond-Jones; Louise Jobling; Laura Walton; Mamoon Yusaf; Vikas Kaura; Kate Henderson; Madhu Balasubramaniam; Umakanth Kempanna; Andrew McDonald; John Titterton; Dave Wright; Caden Namwera; Amjad Sami; Sarah Dawson; Jessamine Read; Nagesh Pissay; Lana Vestarkis; Alistair Rose; Robert Jackson; Adam Beaini; Robert Charles; Alice Gilbert; Waisun Kok; Rebecca Lathey; Stephen Murphy; Rachel Rowe; Nabreesa Shafeeu; Simon Timperley; Andrew Brennan; Amit Surah; Ben Brown; Natalie Baldry; Faisal Eshan; Ali White; Michelle Gardener; Nomann Wilson-Baig; Priya Shankar; David Yates; Andy Horne; Gregorz Grzelinski; Gary Reah; Caroline Thomas; Michal Luniewski; Gulia Suleymanova; Mark Southworth; Ibrahim

Mohammed; Abi Kant; Pragna Prakash; Matthew Milsom; Carl Marincowitz; Sarah Peacock; Matt Powell; Ian McNeil; Omer Farooq; James Isherwood; James Lloyd; Harry Mason; Jerry Thomas; Abigail Clarke; Simon May; Andy Quin; Ben Chandler; Daniel Harper; Gary Woods; Naomi Flemming.

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No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts.

Received for publication December 2, 2014; accepted for publication December 30, 2014.

Available online ■ ■ ■

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2213-2198

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<http://dx.doi.org/10.1016/j.jaip.2014.12.016>

REFERENCES

1. Association of Anaesthetists of Great Britain and Ireland. AAGBI safety guideline; 2009. Available from: www.aagbi.org/sites/default/files/anaphylaxis_2009.pdf. Accessed June 19, 2014.
2. Mertes PM, Alla F, Trechot P, Auroy Y, Jougla E. Anaphylaxis during anaesthesia in France: an 8-year national survey. *J Allergy Clin Immunol* 2011;128:366-73.
3. Moneret-Vautrin CA, Mertes PM. Anaphylaxis to general anaesthetics. *Chem Immunol Allergy* 2010;95:180-9.
4. Gurrieri C, Weingarten TN, Martin DP, Babovic N, Narr BJ, Sprung J, et al. Allergic reactions during anesthesia at a large United States referral center. *Anesth Analg* 2011;113:1202-12.
5. Savic L, Wood PM, Savic S. Anaphylaxis associated with general anaesthesia: Challenges and recent advances. *Trends Anaesth Crit Care* 2012;2:258-63.
6. The Anaesthetic Audit and Research Matrix of Yorkshire, www.aarmy.co.uk. February 8, 2015.
7. Savic L, Garside M, Savic S, Hopkins PM. Anaphylaxis follow-up: making it simple—making it better. *R Coll Anaesth Bull* 2014;87:33-7.

TABLE E1. Referral criteria for investigation of suspected perioperative anaphylaxis

System	Cardiovascular	Respiratory	Cutaneous
	Unexplained cardiac arrest during anesthesia	Unexplained, unexpected bronchospasm, particularly if severe, causes decreased saturations and is relatively resistant to treatment	Widespread rash, flushing or urticaria
	Unexplained, unexpected hypotension requiring active treatment		Angioedema

Adapted from Harper et al. Anaesthesia 2009;64:199-211.