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Suspected perioperative allergic reactions: nomenclature and terminology

Vito Sabato[1,*], Peter Platt[2], Tomaz Garcez[3] and Peter Cooke[4]

[1]Department of Immunology, Allergology and Rheumatology, University Antwerp, Antwerp University Hospital, Antwerp, Belgium, [2]Anaesthesiology, Sir Charles Gairdner Hospital, Anaesthetic Allergy Referral Centre of Western Australia, Perth, Western Australia, Australia, [3]Manchester University NHS Foundation Trust, Manchester, UK and [4]Department of Anaesthesia and Perioperative Medicine, Auckland City Hospital, Auckland, New Zealand

*Corresponding author. E-mail: vito.sabato@uantwerpen.be

Standardising nomenclature facilitates diagnostic and therapeutic algorithms, improves comparisons of data in scientific research and reduces misunderstanding. Here, we propose a nomenclature for suspected perioperative allergic reactions.

Importance of harmonised nomenclature

Nomenclature in medicine changes over time and is based on understandings of scientific reality. The acceptance of harmonised consensus nomenclature facilitates the usefulness of diagnostic and therapeutic algorithms, promotes the ability to compare data in scientific research, and reduces misunderstanding. Although uniformity has been recommended by allergy-related scientific societies,[1,2] variation in the usage of key terminology remains. For example, the words hypersensitivity, allergy, and anaphylaxis are frequently used interchangeably without uniformity in their meaning, as are allergy-like, pseudoallergy, and anaphylactoid.

Adverse drug reactions after administration of a compound for diagnostic, prophylactic, or therapeutic purposes can be classified as type A (dose-dependent, predictable, non-immune mediated) and type B (dose-independent, unpredictable, possibly immune-mediated), but some drug reactions may have features that overlap these categories.

The term hypersensitivity encompasses reproducible symptoms or signs resulting from effects beyond the predicted pharmacological targets (intended therapeutic or side-effects) of a compound and implies involvement of immune system/cells or inflammatory mechanisms. Non-allergic hypersensitivity implies involvement of immune cells and release of mediators by direct mechanisms but does not include the adaptive (specific) immune system response. Allergic hypersensitivity implies specific involvement of the adaptive immune system and is further categorised according to the Gell and Coombs[3] classification. Pichler[4] has subsequently substratified type IV (T-cell mediated) reactions. From a clinical point of view hypersensitivity reactions are also categorised as immediate or non-immediate. Immediate reactions occur within 2 h (usually within minutes), and the clinical presentation varies from single organ system features (e.g. urticaria, bronchospasm) to anaphylaxis.

Anaphylaxis is a potentially life-threatening clinical condition resulting from either specific (allergic) or non-specific (non-allergic) activation of mast cells/basophils, inflammatory pathways, or both. It is characterised by the rapid onset of a number of signs and symptoms after exposure to a trigger (Table 1). The National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network[5] consensus meeting defined three clinical scenarios that make the classic presentation of anaphylaxis likely, but these are not necessarily useful in the perioperative context.[6,7]

Non-immediate reactions occur more than 2 h after the exposure (often 48–72 h later) and include maculopapular exanthema, serious cutaneous adverse reactions, drug rash (or reaction) with eosinophilia and systemic symptoms (DRESS), and severe exanthems such as Stevens–Johnson syndrome and toxic epidermal necrolysis. Although some overlap exists, the effector cells involved in immediate reactions are mast cells and basophils, whereas the effector cells involved in non-immediate reactions are T cells.

A sequence of events does not infer causality

When reporting and evaluating adverse events after exposure to a medication, one has to consider that causality cannot necessarily be inferred from a sequence of events. For example, urticaria occurring during a course of penicillin does not mean that penicillin is the cause. This concept is particularly true in the perioperative context where symptoms and signs could be explained by pharmacological or pathophysiological responses. For example, severe hypotension could be either the consequence of an immediate hypersensitivity reaction or surgical complication (i.e. bleeding); and bronchospasm could be either the consequence of an immediate hypersensitivity reaction or a consequence of tracheal intubation in a patient with hyper-reactive airways. Therefore, detailed documentation of signs and symptoms together with time between exposure to the medication and onset of the symptoms is of utmost importance. As clinical presentations of different underlying mechanisms of immediate drug hypersensitivity reactions are indistinguishable, it is not appropriate to assume a mechanism until an allergological work-up has been completed.

'Suspected perioperative allergic reactions' as a pragmatic clinical descriptor

We concur with Cook and colleagues[8] that in the current context it is appropriate to define the perioperative period as the time when the patient is under the care of an anaesthetist, rather than from the moment of contemplation of surgery until full recovery.[9] During the perioperative period, when clinical features compatible with immediate hypersensitivity occur, for example hypotension, the best descriptor may be 'suspected perioperative allergic reaction' (Fig. 1).[10] The clinical features could be related to (1) the pharmacological effect of the medication or to surgical factors; (2) specific activation

Table 1 Definitions of key terms.

Anaphylaxis	Severe, life-threatening generalised or systemic hypersensitivity reaction which is characterised by being rapid in onset with life-threatening airway, breathing or circulatory problems, usually associated with skin and mucosal changes.
Hypersensitivity reaction	Reproducible clinical features resulting from effects beyond the pharmacological activity of a medication. It implies activation of immune cells, inflammatory pathways, or both.
Allergic hypersensitivity	Clinical features resulting from specific activation of immune cells.
Non-allergic hypersensitivity	Clinical features resulting from non-specific activation of immune cells, inflammatory pathways, or both.

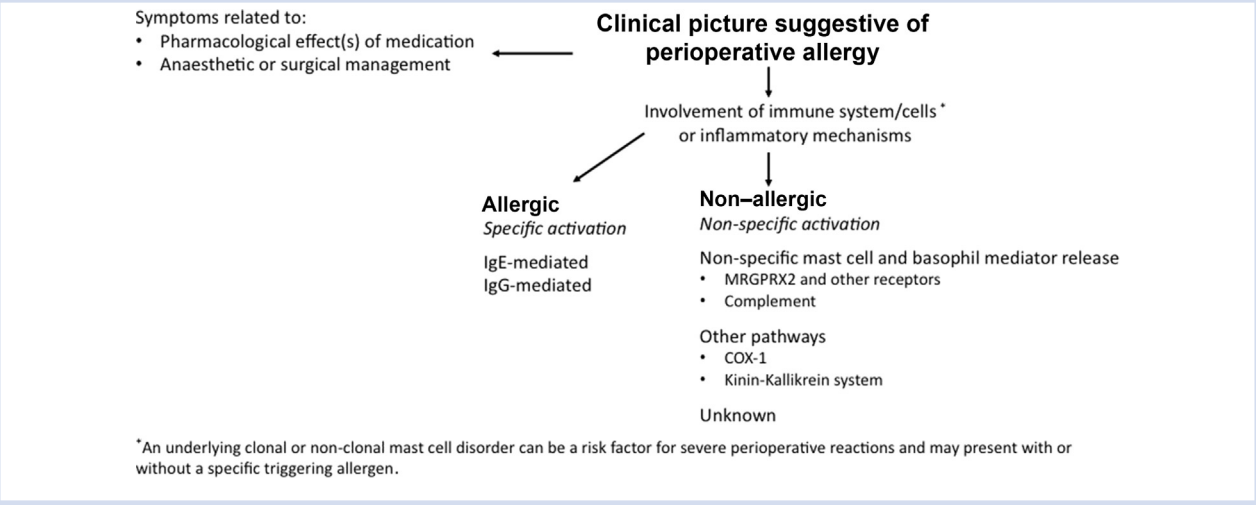

Fig 1. Possible pathomechanisms for clinical picture suggestive of perioperative allergy.

(immunoglobuin [Ig] E/IgG) mediated by mast cells/basophils, namely allergy; or (3) non-specific activation of immune cells (mast cells and basophils) or inflammatory mechanisms (see earlier discussion of mechanisms). Although clinical manifestations of allergic and non-allergic mechanisms are indistinguishable, they follow different rules in terms of risk of reoccurrence, risk of cross-reactivity with related compounds, the role of facilitating factors, and the response to desensitisation. Therefore a clinically oriented, comprehensive allergological evaluation of those patients is mandatory.

The subsequent categorisation of suspected perioperative allergic reactions relies on evaluation of the clinical picture and the allergological investigation. The investigation includes analysis of markers of mast cell release (serum tryptase is the most used and accessible) and deduction of the underlying immunological mechanisms by undertaking skin tests, specific IgE measurement, basophil activation testing, and when indicated drug provocation testing.

Authors' contributions

Conception, design, and drafting of paper: all authors.
Approval of the final version of the paper: all authors.

Declaration of interest

The authors declare that they have no conflict of interests.

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