

Original Article

Reducing the risk of anaphylaxis during anaesthesia: guidelines for clinical practice

P.M. Mertes¹, M.C. Laxenaire¹, A. Lienhart², and the working group for the SFAR* and W. Aberer³, J. Ring⁴, W.J. Pichler⁵, P. Demoly⁶, for ENDA** and the EAACI interest group on drug hypersensitivity

¹Service d'Anesthésie-Réanimation Chirurgicale, Nancy, France; ²Département d'Anesthésie-Réanimation, Hôpital Saint-Antoine, Paris, France; ³Department of Environmental Dermatology, Graz, Austria; ⁴Klinik und Poliklinik für Dermatologie und Allergologie, Muenchen, Germany; ⁵Clinic for Rheumatology and Clinical Immunology/Allergy, Inselspital, Bern, Switzerland; ⁶Exploration des Allergies -Maladies Respiratoires - INSERM U454, Hôpital Arnaud de Villeneuve, Montpellier, France.

* SFAR: Société Française d'Anesthésie et de Réanimation with the following additional members in the working group: G. Decroix, P. Dewachter, J.L. Guéant, L. Guilloux, D. Laroche, F. Leynadier, D. Longrois, J.M. Malinovsky, D.A. Moneret-Vautrin, C. Pecquet, M. Pinaud, P. Tréchet, D. Vervloet, F. Wessel

** ENDA: European Network for Drug Allergy and the EAACI interest group on drug hypersensitivity with the following additional members in the working group: B.K. Ballmer-Weber, A. Barbaud, B. Biló, J. Birnbaum, M. Blanca, B. Blömecke, K. Brockow, C. Christiansen, A. de Weck, C. Dzvinga, M. Drouet, B. Eberlein-König, A.T. Frew, T. Fuchs, J.L. Guéant, R. M. Guéant-Rodríguez, C. Gutgesell, M. Hertl, G. Kanny, A. Kapp, M. Kidon, M. Kowalski, G. Marone, H. Merk, D.A. Moneret-Vautrin, C. Pascual-Marcos, B. Przybilla, E. Rebelo-Gomes, F. Rueff, A. Sabbah, J. Sainte Laudy, M. L. Sanz, E. Tas, A. Romano, M.J. Torres, D. Vervloet, B. Wedi, B. Wüthrich

Summary: These guidelines represent a consensus of experts in the field of immediate hypersensitivity reactions occurring during anaesthesia. They were based on international science, and implemented in France under the auspices of the French Society for Anaesthesia and Intensive Care (SFAR: Société Française d'Anesthésie et de Réanimation). Their aim was to provide the most valid, widely accepted, effective and easily teachable guidelines that current knowledge, research and experience can provide. This paper presents the main extracts of these recommendations with the most relevant clinical implications.

Key Words: anaphylaxis, anaesthesia, histamine, hypersensitivity, IgE, neuromuscular blocking agents, hypnotics, latex, skin tests, tryptase.

These guidelines are an abridged version of the recently published guidelines for clinical practice for reducing the risk of anaphylaxis during anaesthesia [1, 2], recently developed and implemented in France under the auspices of the French Society for Anaesthesia and Intensive Care (SFAR: Société Française d'Anesthésie et de Réanimation), according to the methodological recommendations of the French National Agency of Evaluation in Medicine (ANAES: Agence Nationale d'Accréditation et d'Evaluation en Santé -<http://www.anaes.fr>).

These guidelines represent a consensus of experts from a variety of disciplines (anaesthetists, allergists, biologists, physiologists...) and were based on international science. Their aim was to provide the most valid, widely accepted, effective and easily teachable guidelines that current knowledge, research and experience can provide. To achieve this goal, experts had to answer a list of pre-established questions. Participants used evidence-based criteria to identify, evaluate, and appraise scientific publications indexed in Medline, Pascal and Excerpta Medica. All experts applied the tools and principles of

Table 1. Levels of evidence and classes of recommendations (SFAR)

Level I	A prospective randomised study with a low positive (α) and negative (β) risk
Level II	A prospective randomised study with high α risk or low or unknown power
Level III	Non-randomized prospective study, must have a control group for comparisons
Level IV	Non-randomized studies, historical control group
Level V	Case series. Expert advice
Classes of recommendations	
A	2 (or more) level I studies
B	1 level I study
C	Level II study(ies)
D	Level III study(ies)
E	Level IV or V study(ies)

evidence-based medicine concerning levels of evidence and classes of recommendations recommended by the SFAR on all proposed guidelines (Table 1). Extensive literature analysis supporting the recommendations was provided by experts. To increase the validity of the results obtained, this version was reviewed by a large panel of 80 lecturers (topic experts, conference leaders, specialists from disciplines concerned with allergy, anaesthesiology, critical care, surgery ...) for scientific accuracy, but also for possible future effects on safety, cost, effectiveness, and teachability. This final version, published as a full text [2], was summarized in a short but more practical version. This paper presents the main extracts of these recommendations with the most relevant clinical implications, following minor adaptations or modifications, as suggested by a panel of experts from ENDA (European Network for Drug Allergy) and the EAACI interest group on drug hypersensitivity.

1. Reality of the allergic risk during anaesthesia – incidence – morbidity – mortality – responsible agents – clinical picture.

1.1. The reality of the allergic risk during anaesthesia is established on the basis of the

more than 12,000 cases of peranaesthetic hypersensitivity reactions published in the literature over the last 15 years (D).

- 1.2. Among the hypersensitivity reactions occurring during anaesthesia, about 60% are mediated by an IgE-dependent immunologic mechanism (allergic reaction).
- 1.3. Authors from many countries have reported cases of hypersensitivity reactions. The majority come from France, Australia and New Zealand, thanks to the organization established in these countries 25 years ago for reporting these reactions, as well as the strategy of written and oral communication existing in medicine.
- 1.4. Depending on the country, hypersensitivity reactions represent 9 to 19% of complications associated with anaesthesia (D). The mortality rate is about 5 to 7% (D). Morbidity is expressed as more or less severe anoxic cerebral sequelae; its incidence has not been quantified.
- 1.5. In 1996, the incidence of anaphylactic reactions in France was estimated to be 1/13,000 general and local or regional anaesthesia, all types of substances included. The incidence of anaphylaxis caused by muscle relaxants was 1/6,500 anaesthesia in which one of these drugs was administered (D).
- 1.6. The agents responsible for the anaphylactic

- reactions occurring during anaesthesia have been identified in 4,000 cases of anaphylaxis published since 1980. Muscle relaxants are involved in 62% of the total, latex in 16.5%, hypnotics (7.4%), antibiotics (4.7%), plasma substitutes (3.6%) and opioids in 1.9% of cases. Allergy to local anaesthetic agents is exceptional (0.7%). No anaphylactic reaction to inhaled anaesthetics has been published. Various other agents can induce anaphylaxis during anaesthesia such as aprotinine, chlorhexidine, protamine, papain and plasma substitutes.
- 1.7. The importance of each of these different substances in causing anaphylactic reactions appears to be identical in different countries.
 - 1.8. The muscle relaxants most often involved in anaphylaxis in France in 1997-1998 are, in decreasing order of the number of cases reported: rocuronium, suxamethonium, atracurium and vecuronium (D). The relation between the number of patients having had a reaction to each of these agents and the number of patients treated with them is the highest for rocuronium and suxamethonium, the lowest for atracurium, with vecuronium situated in-between (E).
 - 1.9. The clinical manifestations are classified in five stages of increasing severity:
 - I - generalized cutaneous signs: erythema, urticaria with or without angioedema
 - II - moderate multi-organ involvement, with cutaneous signs, hypotension and severe tachycardia, bronchial hyperreactivity (cough, ventilatory impairment)
 - III - severe life-threatening multi-organ involvement that requires specific treatment: collapse, tachycardia or bradycardia, cardiac arrhythmias, bronchospasm; the cutaneous signs may be absent or occur only after the arterial blood pressure recovers normal value.
 - IV - circulatory and/or respiratory arrest
 - V - death due to inefficient cardiorespiratory resuscitation.
 - 1.10. The clinical manifestations are more severe and longer lasting in reactions of immunologic origin than in pharmacologic reactions. The clinical signs do not always fully exist and they may be misleading. The absence of cutaneous signs does not exclude the diagnosis of anaphylaxis.
- for the causal agent, IgE-dependent mechanism and cross-reactive sensitization if the agent is a muscle relaxant (D).
- 2.2. The anaesthetist is responsible for:
 - 2.2.1. initiating the investigation, in collaboration with a consulting allergist;
 - 2.2.2. informing the patient about the nature of the reaction and recommendations for subsequent anaesthesias;
 - 2.2.3. reporting the event to the pharmacovigilance centre if a drug is suspected to be the cause; reporting it to the pharmacovigilance centre of the local institution (when available) if latex is suspected to be involved.
 - 2.3. For patients with clinical signs suggestive of an allergic reaction during anaesthesia, various laboratory examinations, initiated immediately, would be useful for the diagnosis:
 - 2.3.1. The likelihood that the clinical symptoms are connected to a hypersensitivity reaction is substantiated by an increased serum tryptase or plasma histamine concentration (C), even though a normal figure does not totally rule out this diagnosis.
 - 2.3.2. An obvious increase in the level of serum tryptase ($> 25 \mu\text{g}\cdot\text{L}^{-1}$) is in favour of an anaphylactic mechanism (C).
 - 2.3.3. An increased concentration of plasma histamine indicates in vivo histamine release. In the case of a less severe reaction, only a blood sample taken very shortly after the onset of the reaction would be informative.
 - 2.3.4. The plasma histamine assay is not useful in pregnant women and in patients receiving high doses of heparin during extra-corporeal circulation, as in these cases plasma histamine is undetectable (D).
 - 2.3.5. Determination of urinary methylhistamine concentration is no longer recommended, as it is less sensitive for diagnosis than blood histamine and tryptase (D).
 - 2.3.6. These assays require taking 7.5 mL of blood in a dry tube and 7.5 mL in an EDTA tube, as soon as possible after the control of the clinical situation, ideally in the hour following the first signs of the reaction. These tubes should be carried to the local laboratory within 2 hours. If impossible, they can be stored in a refrigerator at $+ 4^\circ \text{C}$, but not for longer than 12 hours. After centrifugation, the plasma (recovered

2. Diagnostic investigation

- 2.1. Every patient presenting with a hypersensitivity reaction during anaesthesia must undergo an immediate as well as a secondary investigation

- from above the leukocyte pellet) and the serum should be frozen and stored at - 20° C in several aliquots.
- 2.3.7. In case of a reaction after injection of a muscle relaxant, an aliquot of serum should be obtained and stored for assay for quaternary ammonium ion-specific IgE (D).
- 2.3.8. If the patient is at risk to die, the blood samples should be obtained before resuscitation is detained rather than post-mortem.
- 2.3.9. Because of the potential seriousness of the situation and the short half-life of certain mediators, it is recommended that a package containing tubes for the blood samples, the blood sampling protocol and a form for clinical data recording are continuously available in the operating room.
- 2.3.10. Quality control at a national level of assays for histamine, tryptase and specific IgE is worth being established.
- 2.4. Skin tests are best done after a delay of at least six weeks (D). If necessary, they can be carried out earlier, but with an increased risk of false negative results. Therefore only positive results can be taken into account. If the skin tests are done before six weeks, then they should be repeated after the sixth postoperative week.
- 2.4.1. Anaesthetists should identify local allergists capable of performing the investigations necessary to diagnose the cause of a hypersensitivity reaction occurring during anaesthesia. This list should be readily available when such a consultation is needed.
- 2.4.2 The investigations for allergy diagnosis include:
- 2.4.2.1. Appropriate training, experience and continuing education providing updated knowledge of allergy problems specific to anaesthesia of the allergist performing the skin testing and interpreting the results;
- 2.4.2.2. A supply of the products required for the skin tests, stored under conditions that comply with good pharmaceutical practice (accepting that these are not licensed products) and with the rules of hygiene and asepsis;
- 2.4.2.3. An environment permitting rapid resuscitation in the place where challenge tests are done.
- 2.4.3. Given the present state of knowledge, skin tests (prick and intradermal reaction) remain the golden standard for the detection of IgE-dependent allergies. However, they can be used neither for the detection of allergy to dextrans nor for the detection of delayed hypersensitivity reactions, which are investigated by a different method (D).
- 2.4.3.1. Skin tests are done after obtaining a detailed clinical history and information on the chronology of the event furnished by the anaesthetist, accompanied by a copy of the anaesthesia record and the results of the laboratory tests on blood samples obtained at the time of the reaction.
- 2.4.3.2. Before carrying out these tests, the following preliminary conditions must be met: the patient's informed consent must be obtained, and drugs that are known to inhibit skin test reactivity, such as antihistamines and psychotropic drugs, must be stopped several days before the test (E). Pregnancy, young age and treatment with beta-adrenergic blocking agents, oral corticosteroids and inhibitors of enzyme conversion are not contraindications to doing skin tests.
- 2.4.3.3. Skin tests must include all drugs listed in the anaesthesia record (with the exception of inhalational agents), as well as with latex and other agents administered during this procedure.
- 2.4.3.4. Investigation of latex as a cause of anaphylaxis is performed by prick test, using two different commercial extracts (E).
- 2.4.3.5. Investigation of anaesthetic agents as a cause of anaphylaxis is performed by prick test and/or intradermal reaction using commercial solutions either undiluted or diluted in aqueous phenol. Intradermal reactions are first done with a 1/1000 dilution of the agent, except with muscle relaxants and morphine, for which a 10,000 dilution is used. If the first intradermal reaction is negative, then successive ten-fold lower dilutions are used, with a 20-minute interval between each test. The maximal concentrations not to be exceeded, to avoid false positive results, are given in *Table 2* (E).
- 2.4.3.6. Interpretation of the skin tests requires preliminary verification of the normal reactivity of the patient's skin (E) by a negative control test (prick or intradermal, using an equal

Table 2. Concentrations of anaesthetic agents normally non-reactive in practice of skin tests.

<i>Available agents</i>		<i>Prick-tests</i>		<i>Intradermal tests</i>	
INN	C (mg mL ⁻¹)	Dilution	MC (mg mL ⁻¹)	Dilution	MC (µg mL ⁻¹)
atracurium	10	1/10	1	1/1000	10
cis-atracurium	2	undiluted	2	1/100	20
mivacurium	2	1/10	0,2	1/1000	2
pancuronium	2	undiluted	2	1/10	200
rocuronium	10	undiluted	10	1/100	100
suxamethonium	50	1/5	10	1/500	100
vecuronium	4	undiluted	4	1/10	400
etomidate	2	undiluted	2	1/10	200
midazolam	5	undiluted	5	1/10	500
propofol	10	undiluted	10	1/10	1000
thiopental	25	undiluted	25	1/10	2500
alfentanil	0.5	undiluted	0.5	1/10	50
fentanyl	0.05	undiluted	0.05	1/10	5
morphine	10	1/10	1	1/1000	10
remifentanil	0.05	undiluted	0.05	1/10	5
sufentanil	0.005	undiluted	0.005	1/10	0.5
bupivacaine	2.5	undiluted	2.5	1/10	250
lidocaine	10	undiluted	10	1/10	1000
mepivacaine	10	undiluted	10	1/10	1000
ropivacaine	2	undiluted	2	1/10	200

INN = International Non proprietary Name; C= concentration; MC = maximal concentration

volume of the solvent) and a positive control test (prick or intradermal, with 9% codeine phosphate solution and/or a 10 mg·mL⁻¹ solution of histamine, that produces a wheal with a diameter of at least 3 mm after 20 minutes).

2.4.3.7. The place on the skin where the tests are to be done is of no special importance, provided that interpretation of the results takes into account the size of the bleb induced by the intradermal injection of the product being tested and the normal reactivity of the skin at the test sites.

2.4.3.8. The criteria of a positive prick test are the appearance after 20 minutes of an oedematous wheal with a diameter at least 3 mm greater than that induced by the negative control solution and with a diameter equal to or larger than half the diameter of the wheal induced by the positive control solution.

2.4.3.9. Intradermal tests are done by injecting into the dermis 0.03 to 0.05 mL of a diluted commercial preparation of the test substance, this being enough to produce an injection papule no larger than 4 mm in diameter. The criteria for positivity of an intradermal test are the appearance after 20 minutes of a wheal with a diameter of at least 8 mm and which is also at least double the diameter of the bleb produced by the injection. The anaesthetic drugs used in these tests are diluted, when necessary, in physiologic salt solution containing 5% phenol. They can nevertheless be stored at + 4°C for no more than 3 months, except for atracurium, rocuronium, mivacurium and cis-atracurium, for whom the stability has not been established (E).

2.4.3.10. When the prick or intradermal test with a muscle relaxant

- is positive, investigation for cross-reactivity with other commercialised muscle relaxants must be done by the intradermal route, taking into account the maximal concentration of the drug that must not be exceeded (*Table 2*).
- 2.4.3.11. In the case of a patient who has had an anaphylactic reaction to a muscle relaxant, proven by skin test, before giving a newly commercialised muscle relaxant to the patient it is essential to do an intradermal test with it to look for possible cross-sensitization to other muscle relaxants. The maximal concentration of this new drug that is not to be exceeded must first be determined in non-sensitized healthy controls.
- 2.4.3.12. Before any new anaesthetic drug is introduced on the market, their cutaneous reactivity in healthy volunteers should be studied in order to standardize the skin test method and its interpretation.
- 2.5. Laboratory tests
- 2.5.1. Assays for IgE antibodies in the patient's serum of the patient for muscle relaxants (with quaternary ammonium ions), thiopentone and latex. The results of assays for these specific IgEs can be helpful in the interpretation of negative or doubtful skin test results, especially when the clinical signs were highly suggestive of anaphylaxis (E). It is preferable to use only assays with the highest sensitivity for IgE specific for muscle relaxants: QAS-RIA (quaternary ammonium sepharose - radio-immuno-assay) and PAPP-RIA (P-aminophenylphosphoryl-choline - radio-immuno-assay). For anti-latex IgE, the commercial assays are quite satisfactory.
- 2.5.2. The leukocyte histamine release assay, using the patient's basophils, is not the first choice diagnostic test. In rare cases, it might be useful as a complement to skin tests to confirm the diagnosis. It might also help with the choice of a muscle relaxant for a subsequent anaesthesia in case cross-sensitization is found.
- 2.5.3. Other cellular assays based either on flow cytometry or on the release of sulphidoleukotrienes are not sufficiently validated to be recommended for routine use.
- 2.6. Provocation tests
- 2.6.1. A document designed for the patient and containing information on the test methods and on the risks is essential for obtaining the patient's informed consent. The document containing this information should be available to be handed to the patient before the tests are carried out.
- 2.6.2. Indications for progressive challenge tests are limited to local anaesthetics and latex, and they should be done only after being certain that skin tests are negative.
- *Test with a local anaesthetic: inject 0.5 to 1.0mL of test solution undiluted and containing no epinephrine subcutaneously (E)*. The test is negative if no anaphylactic reaction occurs during the 30 minutes following the injection. In pregnant patients, the test is to be done in the delivery room 30 minutes before the induction of epidural anaesthesia (E).
 - *Test with latex: wearing a natural rubber latex glove for 15 minutes*. The test is negative if there is no sign of a local allergic reaction (urticaria) occurring within the following 30 minutes. If the patient experienced bronchospasm during the course of the initial reaction, and both skin test and provocation test are negative, consider bronchial provocation test.
- 2.7. Results of the allergy investigation
- 2.7.1. A positive diagnosis of anaphylaxis depends on positive skin tests, laboratory results and coherence of these results with the clinical history and the anaesthesia protocol.
- 2.7.2. Close collaboration between the allergist and the anaesthetist is essential within the frame of an allergy consultation (E).
- 2.7.3. A full report of the results written by the allergist is to be addressed to the anaesthetist. This report must be included in the patient's medical records. Copies must also be sent by the anaesthetist to the regional pharmacovigilance centre (if available) accompanied by a clinical description of the reaction, and also to the patient's attending physician.
- 2.7.4. The conclusions must be transmitted to the patient by the anaesthetist, giving the patient a written copy of the document. The patient should be encouraged to carry this written document with his identity papers. He

- should also be encouraged to wear a bracelet (example: Medic-Alert) or a tag signalling this allergy (E).
- 2.7.5. Advice concerning matters of anaesthetic technique and indications can only come from the anaesthetist (E).
- 2.7.6. When there is difficulty in interpretation of the results of the allergy workup and of the consequences on a subsequent anaesthesia, appeal to a local or regional group of reference anaesthetist who has had training and is updated in the knowledge of allergic reactions associated with anaesthesia should be made. A list of such specialists should be readily available to physicians who might need it.
- 2.8. It would be desirable to ascertain regularly the incidence of the number of allergic reactions occurring during anaesthesia:
- 2.8.1. by collecting data from referral centres and regional pharmacovigilance centres;
- 2.8.2. by considering them in relation to anaesthesia-associated mortality and morbidity data.

3. Predisposing factors for anaphylaxis during anaesthesia and the value of the preanaesthetic allergy investigation.

- 3.1. Patients at risk for anaphylaxis during anaesthesia.
- 3.1.1. Patients who are allergic to one of the drugs or products likely to be administered or used during anaesthesia and for which the diagnosis had been established by a previous allergy investigation.
- 3.1.2. Patients who have shown clinical signs suggesting an allergic reaction during a previous anaesthetic.
- 3.1.3. Patients who have experienced clinical manifestations of allergy when exposed to latex (D), whatever the circumstances in which this occurred.
- 3.1.4. Children who have had multiple operations, especially those with spina bifida, because of the high rate of sensitization to latex (D) and of the high incidence of anaphylactic shock caused by latex in such patients.
- 3.1.5. Patients who have experienced clinical manifestations of allergy to avocado, kiwi, banana, chestnut, buckwheat, etc., because of the high rate of cross-reactivity with latex (D).
- 3.2. Patients who are atopic (for example, those with allergic asthma or hay fever) or those who are allergic to a drug or other product that is not likely to be used during the course of the anaesthesia are not to be considered at risk for anaphylaxis during preanaesthesia.
- 3.3. Preanaesthesia allergy investigation
- 3.3.1. Risk factors for allergy must be investigated in a systematic manner before every anaesthesia.
- 3.3.2. Concerning anaesthesia for members of the general population, it is not necessary to do a systematic screening for sensitivity to drug(s), and/or other products used in anaesthesia. This policy is justified by the absence of sufficient information on the positive and negative predictive values of allergy skin tests and laboratory tests for these substances in the general population. Indeed, false negative results and/or false positive results can have disastrous consequences for anaesthesia by leading to change to an inadequate anaesthesia technique. Because of this, the risk/benefit ratio of such an approach is unknown.
- 3.3.3. In those patients who are atopic or allergic to a drug or product that will *not* be used during the course of the anaesthesia, it is not necessary to look for sensitivity to anaesthetic drugs or other products that are to be used during the course of anaesthesia.
- 3.3.4. For those patients who are at risk as defined above (3.1.), an allergy investigation looking for specific sensitization should be proposed before any anaesthetic procedure. Nevertheless, no matter which tests are used, they do not guarantee an absolutely correct diagnosis. Indeed, skin tests done some time after a reaction can be negative. A work-up done six weeks after an incident is always preferable.
- 3.3.4.1. Investigations for patients in category 3.1.1.
- Follow the conclusions of the previous allergy investigation.
 - In case of allergy to muscle relaxants, test recently commercialized muscle relaxants.

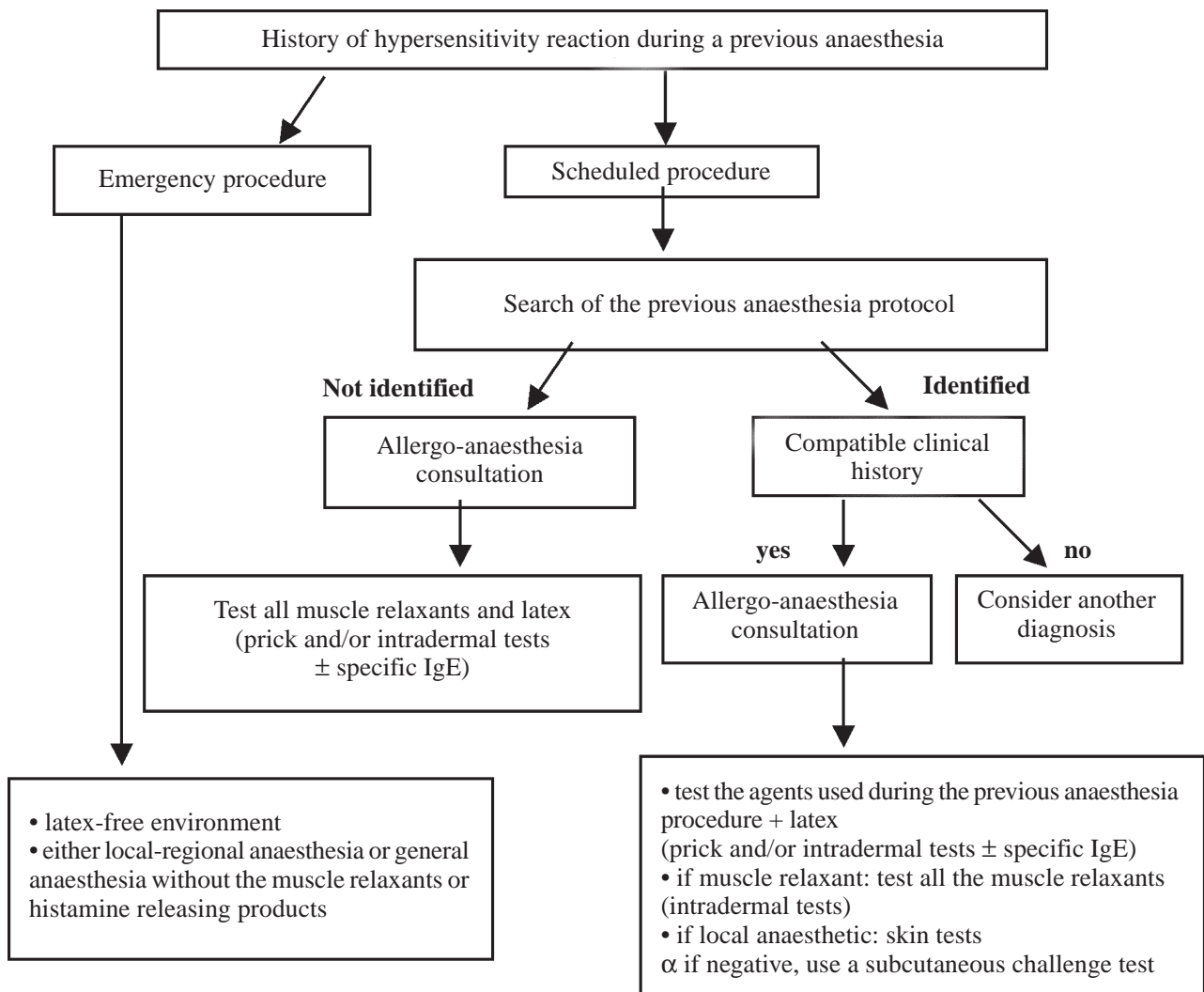


Figure 1. Decisional algorithm for a patient reporting a hypersensitivity reaction during a previous anaesthesia and who has had no allergy investigation.

3.3.4.2. Investigations for patients of category 3.1.2.

Depending on the circumstances of the surgical procedure, the course to follow is explained in Figure 1.

3.3.4.2.1. In the well-prepared situation, the anaesthetist should check the previous anaesthesia record for evidence of the cause of the reaction and transmit this information to the allergist who is going to do the tests.

- When the previous anaesthesia record is not available: test all the muscle relaxants and latex (skin tests \pm specific IgE).

- When the previous anaesthesia record is available: test latex and the drugs used in the previous protocol (skin tests \pm specific IgE). In case of local anaesthesia, perform a progressive challenge test (E) after ascertainment that the skin tests are negative (paragraph 3.4.)

- A pregnant woman at risk of intolerance of local anaesthetics and scheduled for epidural anaesthesia/analgesia during labour, the local anaesthetic agents should be tested by the

allergist, using the intradermal route. When the tests are negative, a progressive challenge test can be done in the delivery room by the anaesthetist before the insertion of epidural catheter, after having obtained informed consent from the patient.

3.3.4.2.2. In an emergency, the precautionary approach would be to exclude all latex products from the patient's environment, use local/regional anaesthesia or general anaesthesia, excluding muscle relaxants or histamine-releasing agents.

3.3.4.3. Investigations for patients in categories 3.1.3 to 3.1.5.

Prick test with latex \pm latex-specific IgE.

4. Can prevention of allergy risk during anaesthesia be obtained by premedication and/or a particular environment?

- 4.1. Primary prevention of sensitisation.
 - 4.1.1. Total avoidance of contact with latex from the first surgical procedure and in the medical environment of infants with spina bifida prevents the acquisition of latex sensitivity (E).
 - 4.1.2. Latex particles carried by cornstarch glove powder is the factor of sensitization by inhalation. Reduction of the incidence of sensitization in professionals exposed to this powder can be achieved by the use of non-powdered latex gloves.
 - 4.1.3. There is actually no way to prevent primary sensitization to muscle relaxants. Anaphylactic reactions to these agents can occur in the absence of their prior administration.
- 4.2. Secondary prevention for patients already sensitized:
 - 4.2.1. The only effective secondary preventive measure is to identify the responsible allergen and then completely avoid it. When this is possible, subsequent allergic reactions to this allergen can be avoided (E).
 - 4.2.2. For patients sensitized to latex, a latex-free environment is effective for the prevention of an anaphylactic reaction (E). The latex-free environment must include the operating rooms, the postoperative recovery room and some other sectors of the hospital. To facilitate the transmission of the orders for preventive measures in these various sectors, a "check-list" providing information on management of the patient is recommended. Every anaesthesia service, in collaboration with the hospital's pharmacy, should establish a list of latex-free medical and surgical material, and update it regularly.
 - 4.2.3. In order to identify patients sensitized to anaesthetic drugs and/or products planned to be administered during the procedure, the principle of an intravenous test dose is prescribed, as a very low dose of allergen can induce anaphylaxis in sensitized patients (E).
- 4.3. Premedication
 - 4.3.1. For patients allergic to latex and to drugs, premedication with an H1 anti-histamine alone, an H2 anti-histamine alone, a corticosteroid or association of two or more of these drugs does not guarantee that an anaphylactic reaction will not occur (C, D).
 - 4.3.2. The administration of an H1 anti-histamine alone, or combined with an H2 anti-histamine could prevent bronchospasm and haemodynamic variations caused by non-specific histamine release (C).
 - 4.3.3. Premedication with a monovalent substance
 - 4.3.2.1. Dextrans

The rate of severe reactions to dextrans can be decreased by administering dextran I (Promit[®]), which is a monovalent inhibition of dextran binding.
 - 4.3.2.2. Muscle relaxants

The concept of protection with a hapten ("haptenic protection") including only a single quaternary ammonium has been used for the prevention of anaphylaxis in some patients allergic to muscle relaxants (E). However, in the absence of controlled clinical studies, such "haptenic protection" cannot be recommended for routine use at present.

- 4.4. Special cases
- 4.4.1. The intravenous administration of antibiotics for preoperative prophylaxis should be started in the operating room with the patient awake and being monitored, 5 to 10 minutes before anaesthesia induction.
- 4.4.2. Because there is no evidence of cross reactivity between propofol and muscle relaxants, the use of propofol in patients allergic to a muscle relaxant is not contraindicated.

5. Treatment of allergic reactions occurring during the course of anaesthesia

- 5.1. Recommendations for the treatment of allergic reactions occurring during the course of anaesthesia must not be established on a rigid scheme. Treatment must be adapted to the severity of the clinical situation, to the patient's history, to the associated treatment and to the patient's response to the emergency treatment. It is understood that the patient is monitored as required in any anaesthetic procedure.
- 5.2. General measures used in all cases (E)
- 5.2.1. Discontinue the administration of the drug and/or product that is suspected of being the causative factor.
- 5.2.2. Information from the surgical team (depending on the situation: cancel, simplify, accelerate or stop surgery).
- 5.2.3. Administer 100 vol% oxygen.
- 5.3. In grade I reactions, the measures described in *paragraph 5.2.* are generally sufficient.
- 5.4. In more severe cases (grade II or III) (E):
- 5.4.1. Rapidly control the airways.
- 5.4.2. Administer epinephrine intravenously by bolus in titrated doses. The initial dose, determined as a function of the severity of the hypotension (10 to 20 µg for grade II reactions; 100 to 200 µg for grade III reactions), to be repeated every 1 to 2 minutes until restoration of convenient arterial blood pressure. In case of ineffectiveness of this treatment, the dose should be increased rapidly. Intravenous perfusion at a dose of 0.05 to 0.1 µg·kg⁻¹·min⁻¹ might be used instead of repeated bolus administration of epinephrine. In case an effective intravenous route is not immediately available, the

intramuscular route can be used (0.3 to 0.5 mg), with injections repeated after 5 to 10 min, depending on the patient's haemodynamic status. In the same situation, the intratracheal route can be used if the trachea is intubated, knowing that only one third of the dose will enter the systemic circulation.

- 5.4.3. Ask for help from competent staff.
- 5.4.4. Elevate the patient's legs.
- 5.4.5. Rapidly restore the vascular volume with isotonic crystalloid. Colloids should replace salt solutions when the volume of salt solution exceeds 30 mL·kg⁻¹, avoiding the administration of the substance or substances that are suspected to be the cause of the reaction.
- 5.4.6. In case of bronchospasm without arterial hypotension, a beta2-adrenergic agonist (such as salbutamol) can be administered through an inhalation chamber adapted to the ventilatory circuit. In case of resistance to this treatment, or immediately severe reaction, the intravenous route can be used: administer a 100 to 200 µg bolus of salbutamol, followed by continuous perfusion of this drug (5 to 25 µg·min⁻¹). The most severe forms can be reversed by continuous perfusion of epinephrine.
- 5.4.7. In pregnant women, because of the risk of hypoperfusion of the placenta caused by epinephrine, treatment of the hypotension should be started with intravenous ephedrine (10 mg, repeated every 1 to 2 min, with a maximum cumulative dose of 0.7 mg·kg⁻¹). In addition, the patient should be placed in left lateral decubitus. In case of ineffectiveness, switch to epinephrine.
- 5.4.8. In some patients with beta-adrenergic blocking agents, it may be necessary to increase the dose of epinephrine rapidly: a first bolus of 100 µg, followed when necessary by 1 mg or even 5 mg, at 1 to 2 min intervals. If not efficient, glucagons could be effective (1 to 2 mg intravenously, repeated every 5 min).
- 5.4.9. In case of hypotension, resistant to high doses of epinephrine, various other vasoconstrictor drugs can be tried, as norepinephrine (starting with 0.1 µg·kg⁻¹·min⁻¹).
- 5.5. In case of cardiac arrest (grade IV) (E):

- 5.5.1. External cardiac massage
- 5.5.2. Epinephrine: intravenous bolus of 1 mg every 1 to 2 min, or even 5 mg bolus after the third injection. The cumulative dose can reach 50 even 100 mg.
- 5.5.3. Follow the usual resuscitation measures for cardio-circulatory insufficiency
- 5.6. Additional secondary treatment in severe cases (E) :
 - 5.6.1. Corticosteroids may be given to decrease delayed manifestations: administer hydrocortisone hemisuccinate, 200 mg intravenously every six hours.
 - 5.6.2. Intensive monitoring must be assured for at least 24 hours, due to the risk of unstable blood pressure.

- 2. Prévention du risque allergique peranesthésique. recommandations pour la pratique clinique. *Ann Fr Anesth Reanim* 2002; 21 Suppl 1: 1s-180s.

Paul Michel Mertes

Paul Michel Mertes, Service d'Anesthésie-Réanimation Chirurgicale, Hôpital Central, 54035 Nancy Cedex, France.
 Tel : +33-383851531; Fax : +33-383858559;
 Email: pm.mertes@chu-nancy.fr or
 Pascal Demoly, *ENDA secretary*, Exploration des Allergies - Maladies Respiratoires - INSERM U454, Hôpital Arnaud de Villeneuve, CHU de Montpellier, 34295 Montpellier cedex 5, France.
 Tel : +33-467336127; Fax : +33-467042708;
 E.mail: demoly@montp.inserm.fr

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