POSITION PAPER

General considerations on rapid desensitization for drug hypersensitivity – a consensus statement

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To cite this article: Cernadas JR, Brockow K, Romano A, Aberer W, Torres MJ, Bircher A, Campi P, Sanz ML, Castells M, Demoly P, Pichler WJ, for the European Network of Drug Allergy and the EAACI interest group on drug hypersensitivity. General considerations on rapid desensitization for drug hypersensitivity – a consensus statement. *Allergy* 2010; DOI: 10.1111/j.1398-9995.2010.02441.x

Keywords
desensitization; drug hypersensitivity; graded challenge; tolerance induction

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‡The paper was first drafted by Josefina Rodrigues Cernadas, Portugal, and revised by Knut Brockow, Germany and Antonino Romano, Italy. Important input was added by Werner Aberer, Austria, Maria José Torres, Spain, Andreas Bircher, Switzerland, Paolo Campi, Italy, Maria Luisa Sanz, Spain, Mariana Castells, USA, Pascal Demoly, France, and Werner Pichler, Switzerland.

Accepted for publication 4 June 2010

DOI:10.1111/j.1398-9995.2010.02441.x

Edited by: Hans-Uwe Simon

Abstract

Drug hypersensitivity reactions can occur with most drugs, are unpredictable, may affect any organ or system, and range widely in clinical severity from mild pruritus to anaphylaxis. In most cases, the suspected drug is avoided in the future. However, for certain patients, the particular drug may be essential for optimal therapy. Under these circumstances, desensitization may be performed. Drug desensitization is defined as the induction of a temporary state of tolerance of a compound responsible for a hypersensitivity reaction. It is performed by administering increasing doses of the medication concerned over a short period of time (from several hours to a few days) until the total cumulative therapeutic dose is achieved and tolerated. It is a high-risk procedure used only in patients in whom alternatives are less effective or not available after a positive risk/benefit analysis. Desensitization protocols have been developed and are used in patients with allergic reactions to antibiotics (mainly penicillin), insulins, sulfonamides, chemotherapeutic and biologic agents, and many other drugs. Desensitization is mainly performed in IgE-mediated reactions, but also in reactions where drug-specific IgE have not been demonstrated. Desensitization induces a temporary tolerant state, which can only be maintained by continuous administration of the medication. Thus, for treatments like chemotherapy, which have an average interval of 4 weeks between cycles, the procedure must be repeated for every new course. In this paper, some background information on rapid desensitization procedures is provided. We define the drugs and drug reactions indicated for such procedures, describe the possible mechanism of action, and discuss the indications and contraindications. The data should serve as background information for a database (accessible via the EAACI-homepage) with standardized protocols for rapid desensitization for antibiotics, chemotherapeutic agents, monoclonal antibodies/fusion proteins, and other drugs.

Drug hypersensitivity accounts for more than 15% of all adverse drug reactions, affecting more than 7% of the general population and 10 to 20% of all hospitalized patients (1–3).

According to the nomenclature of the task force of the EAACI (European Academy of Allergy and Clinical Immunology) and the AAAAI (American Academy of Allergy Asthma and Immunology), drug hypersensitivity reactions are classified as allergic and nonallergic (4, 5). The latter are those in which an immunologic pathogenic mechanism is not demonstrated. Allergic hypersensitivity reactions can be classified as either IgE- or nonIgE mediated.

For practical reasons, drug hypersensitivity reactions are also classified as immediate and nonimmediate. The former are those occurring within 1 h after the last drug administration. Many immediate reactions are IgE mediated. The main clinical presentations of IgE-mediated reactions include cutaneous, respiratory, gastrointestinal and systemic (anaphylaxis) manifestations (6–8). NonIgE–mediated reactions can present the same symptoms as IgE-mediated ones (formerly called ''anaphylactoid''). Nonimmediate reactions (9) are those occurring more than 1 h after the last drug intake; they include skin reactions, such as delayed-appearing urticaria, maculopapular exanthemas, fixed drug eruption, bullous exanthemas, acute generalized exanthematous pustulosis (AGEP), drug reaction (or rash) with eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DIHS), symmetrical drug-related intertriginous flexural exanthema (SDRIFE), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) (10, 11). However, they are also manifested as interstitial nephritis, pancreatitis, pneumonitis, hepatitis, vasculitis, different forms of blood cell dyscrasias, and autoimmune reactions (12–14). In some of these manifestations, such as maculopapular exanthemas and AGEP, a T-cell-mediated pathogenic mechanism has been demonstrated (15–17).

When a physician has a patient who has had a hypersensitivity reaction to a medication and needs it again, there are two options to consider (18): (i) to administer an unrelated alternative medication; (ii) to administer the same drug by performing drug desensitization.

Although it is increasingly applied, drug desensitization is a controversial issue because of different definitions, various protocols, and lack of clearly defined indications and contraindications, as well as heterogeneous literature data.

This consensus paper aims to clarify uncertain and controversial issues and focuses mainly on drug desensitization in patients with immediate reactions.

However, some protocols of desensitization also include patients with anaphylactic symptoms occurring within 24 h after the last drug administration.

Because controlled studies are lacking, a formal evidence-based review is not possible. Thus, this document represents the collective opinion of the convened expert panel as a consensus statement (19). The expert panel considered their own European and American experience (in a combined European–American effort to standardize procedures), as well as literature data collected by searching the Medline database with the following key words: drug hypersensitivity, desensitization, tolerance induction, and graded challenge. They also took into account chapters in relevant books. The quality of these sources may vary.

Definitions

The term desensitization has traditionally been used for type I allergic reactions only; other terms, such as tolerance induction, have been applied for nonallergic hypersensitivity reactions.

For practical reasons, in this paper, drug desensitization is defined as the induction of a state of unresponsiveness to a compound responsible for a hypersensitivity reaction.

Literature data indicate that most patients who had experienced hypersensitivity reactions within 24 h after the last drug administration achieve tolerance with rapid desensitization. This procedure allows full therapeutic doses to be reached in a relatively short time, typically between 4 and 12 h (20).

Unlike specific immunotherapy with common peptide allergens, such as inhalant allergens and insect venoms, drug desensitization leads only to a temporary state of tolerance. In effect, if the drug concerned is discontinued, the tolerance state is lost within a period of time that can vary from a few hours to a few days.

Drug desensitization must be clearly differentiated from a graded drug challenge, also called incremental test dosing or provocation test, which is a diagnostic tool (21, 22). Graded challenges are performed only for diagnosis, aiming to prove or disprove a suspected hypersensitivity. Moreover, in this procedure, the physician usually starts with low doses to avoid severe reactions, but dose increments are rapid and not aimed at inducing tolerance (Table 1). On the other hand, desensitization protocols are used only for therapeutic purposes in patients with proven or highly suspected hypersensitivity reactions (e.g., in subjects with aspirin hypersensitivity reactions and an acute coronary syndrome, in whom a diagnostic challenge is not feasible).

Mechanisms

As far as immediate reactions are concerned, in the majority of patients who reacted to beta-lactams and platinum salts, an IgE-mediated pathogenic mechanism has been demonstrated on the basis of positive responses to skin tests and/or serum-specific IgE assays (23–25). On the other hand, such pathogenic mechanism has not been demonstrated in most patients with immediate reactions to nonsteroidal anti-inflammatory drugs (NSAIDs), many antibiotics other than beta-lactams, and some antineoplastic drugs, such as taxenes. In fact, most of these patients display negative results in allergologic tests (26–29).

Despite its clinical success, little is known about the mechanisms and molecular targets of drug desensitization.

Mast cells and basophils seem to be targets in the process since mediators from these cells are released during hypersensitivity reactions to drugs, as well as during desensitization procedures.

Table 1 Drug provocation test *vs* desensitization

	Drug provocation test	Desensitization
Hypersensitivity	Unproven	Proven
Purpose	Confirm or disprove hypersensitivity	Produce temporary tolerance
Effect on immune system	None	Tolerance
Risk of allergic reactions	Present	Present
Initial dose	1/100–1/10 of therapeutic dose	1/1000 000–1/10 000 of therapeutic dose
Number of steps	Normally 3–5	Normally > 10
Time interval between doses	According to reaction	15 min to 2 h
Action after an objective reaction	Discontinue test, treat patient	Stop administration, treat when needed, continue procedure after symptoms resolve, consider modification of protocol

Some authors have shown that tissue mast cells become nonreactive to the implicated drug after desensitization has been achieved (30–32). The consecutive administration of suboptimal doses of antigen prior to the optimal dose seems to render these cells unresponsive to the drug compound but not to other stimuli.

One possible explanation implies that increasing sub-therapeutic doses can provide a sufficient amount of antigenic determinants to bind to IgE anchored to the surface FcεRI receptors, but not to cross-link such IgE. Alternatively, the antigen may be able to induce rapid internalization of cross-linked antigen receptors, which depletes the cell surface of these receptors, making the cell unresponsive to the antigen (32).

Interestingly, *in vitro* rapid desensitization of human mast cells decreases the levels of signal transducing molecules, such as Syk and Lyn. This may be because of the degradation of such molecules or other, yet unknown mechanisms (33, 34).

Literature data showed the importance of different signal-transduction pathways for desensitization. Naturally occurring Syk-deficient basophils do not degranulate, and STAT-6-deficient mast cells, although responsive to antigens and releasing beta-hexosaminidase, cannot be desensitized (35–39).

In nonallergic hypersensitivity reactions, the mechanism of rapid desensitization to aspirin and other NSAIDs is thought to be based on a decreased production of leukotrienes and tryptase (40).

Rapid desensitization is also possible for other nonIgE-mediated reactions caused by chemotherapeutic and biologic agents, sulfonamides, as well as non-beta-lactam antibiotics. However, mechanisms are still unknown (41–43).

Indications and contraindications

Indications

Drug desensitization is indicated when:
(1) the drug concerned is irreplaceable (e.g., penicillin in pregnant women with syphilis and platinum salts in patients with platin-sensitive recurrent ovarian cancer);
(2) the drug concerned is more effective than the alternatives (e.g., a specific antibiotic in cystic fibrosis or tuberculosis, cotrimoxazole in HIV-positive patients for Pneumocystis jirovecii prevention, aspirin in patients with cardiovascular complications), or it has a unique mechanism of action (e.g., aspirin in aspirin-exacerbated respiratory disease – AERD or nasal polyps).

Contraindications

Desensitization to culprit drugs should generally not be performed in patients at increased risk because of a co-morbidity, such as those with uncontrolled asthma (FEV1 < 70% of their normal value), hemodynamically unstable ones, or those with uncontrolled cardiac diseases. In patients treated with beta-blockers and subjects who have experienced severe anaphylaxis, as well as in patients with hepatic, renal, or other diseases, in whom exposure might provoke a potentially harmful complication, desensitization should also only be considered after a careful individual risk/benefit evaluation. Desensitization is absolutely contraindicated in patients who have experienced severe, life-threatening immunocytotoxic reactions, vasculitis, or bullous skin diseases like SJS/TEN, and DIHS/DRESS (5, 18, 20, 22, 44, 45).

General rules

Before performing any desensitization procedure, an individual risk-benefit evaluation has to be performed, and the benefits must outweigh the risks. Caution and surveillance are mandatory in all cases. Desensitization is associated with the risk of acute hypersensitivity reactions and should be performed in an adequately controlled setting under the supervision of a well-trained physician who is familiar with the procedures and with the treatment of anaphylaxis.

An intravenous line and continuous monitoring are obligatory. There is still debate whether desensitization must be performed in an intensive care unit (18, 20, 46–48). Many experienced centers do it on an outpatient basis. In any case, for patients who have completed the first procedure with minimal or no symptoms, subsequent procedures can be performed in the outpatient clinic. In both inpatient and outpatient clinics, all nurses should be trained to recognize symptoms of hypersensitivity reactions. At the same time,

patients are taught to recognize early signs and to notify the nurse or doctor.

To provide maximal safety to patients, physicians should be available for immediate consultation, if needed. Equipment to treat allergic reactions and for cardio-pulmonary resuscitation must be easily accessible and include all drugs necessary to treat anaphylaxis.

Desensitization procedures should take into account available protocols (Table 2).

As a general rule, it is preferable to use protocols applied in samples larger than 10 patients (e.g., subjects sensitive to penicillins and antineoplastic agents) (29, 48–55).

Both oral and parenteral routes can be used in the procedure and it seems that both can be equally effective (18, 50, 56). For drugs that can be administered both orally and parenterally, the oral route seems to be safer (50, 57), easier, and less expensive; however, it is not always advisable or feasible (18, 50, 56–59). There are protocols that combine oral and parental routes of administration (50) (Table 3).

Specific protocols for parenteral routes have been developed and have been widely used for many drugs, including beta-lactams, insulins, chemotherapeutic agents, and monoclonal antibodies (52–55, 60–63).

Starting dose and dose increments

In published protocols, the starting dose ranges from 1/10 000 to 1/100 of the full therapeutic one (23, 49, 50, 55, 56, 64, 65). The starting dose should be determined by taking into account the severity of reaction: in patients with histories of severe anaphylaxis (such as hypotension with loss of consciousness or severe bronchospasm), the initial dose should be between 1/1 000 000 and 1/10 000 of the full therapeutic one. In patients with a positive skin test to a nonirritating concentration of a drug, the starting dose can be determined on the basis of the endpoint titration. For example, the starting dose of a desensitization protocol to gentamycin, in a patient with a positive skin test, can be determined on the basis of the lowest nonirritative concentration (mg/ml), which elicits the positive intradermal test, and the injected volume for such test (e.g., gentamycin 4 mg/ml × 0.03 ml = 0.12 mg) (66).

The endpoint titration is only applicable in patients with positive skin tests performed according to the available guidelines (67, 68) and using the recommended concentrations (68). In patients with a very low endpoint titration value and/or severe reactions, it is advisable to modify the protocol (e.g., by reducing the initial dose, decreasing the rate of infusion, increasing the time interval between doses in oral-route administration, and/or increasing the number of steps).

Classical protocols for oral and intravenous desensitization to penicillin (Tables 3–5) start at 1/10 000 to 1/100 of the target dose; doubled doses are administered every 15–20 min over the course of several hours until the therapeutic dose is reached (49, 53, 54, 64, 65, 69). The oral route seems to be safer because it is less prone to expose patients to multivalent penicillin conjugates, which are thought to have an important role in IgE-mediated reactions (22).

Most protocols increase doses by doubling. Exceptions are sometimes made in the initial (slower increase) or final steps. In protocols developed by Castells et al. for chemotherapeutic agents and monoclonal antibodies (20, 29, 41, 46, 48, 55, 70) (Table 6), the final step entails both a much larger dose and a much longer time of administration.

Table 2 Successful protocols for drug desensitizations described in the literature

Type of drug	Drugs	References
Antibiotics	Penicillins	(18, 23, 49, 50, 56, 57, 59, 64, 74)
	Aminoglycosides	(53)
	Cephalosporins	(49, 52)
	Vancomycin	(54, 62)
	Anti-tuberculous agents	(80, 81)
	Sulfonamides	(42, 51, 82–87)
	Pentamidine	(87)
Other agents	Aspirin, Lysine-acetylsalicylate (LAS), NSAIDS	(26–28, 75, 95–97)
	Chemotherapeutics	(29, 41, 48, 55, 70, 71, 73, 77, 78, 88, 89, 98)
	Deferoxamine	(90)
	Tetanus toxoid	(91, 92)
	D-penicillamine	(93)
	Heparin	(94)
	Insulin	(60, 61)
	Monoclonal antibodies	(41, 55, 63, 99)

Table 3 Combined oral-subcutaneous-intramuscular penicillin desensitization protocol

Dose*	Units	Route
1	100	P.O.
2	200	P.O.
3	400	P.O.
4	800	P.O.
5	1600	P.O.
6	3200	P.O.
7	6400	P.O.
8	12 800	P.O.
9	25 000	P.O.
10	50 000	P.O.
11	100 000	P.O.
12	200 000	P.O.
13	400 000	P.O.
14	200 000	S.C.
15	400 000	S.C.
16	800 000	S.C.
17	1000 000	I.M.

P.O., oral; S.C., subcutaneous; I.M., intramuscular.
*The interval between doses is 15 min (ref. 50).

Table 4 Oral penicillin desensitization protocol

Step	Penicillin (mg/ml)	Amount (ml)	Dose (mg)	Cumulative dose (mg)
1	0.5	0.1	0.05	0.05
2	0.5	0.2	0.1	0.15
3	0.5	0.4	0.2	0.35
4	0.5	0.8	0.4	0.75
5	0.5	1.6	0.8	1.55
6	0.5	3.2	1.6	3.15
7	0.5	6.4	3.2	6.35
8	5.0	1.2	6.0	12.35
9	5.0	2.4	12.0	24.35
10	5.0	5.0	25.0	49.35
11	50.0	1.0	50.0	100.0
12	50.0	2.0	100.0	200.0
13	50.0	4.0	200.0	400.0
14	50.0	8.0	400.0	800.0

Observe patient for 30 min, then give full therapeutic dose by the desired route.
*The interval between doses is 15 min (ref. 59).

Table 5 Intravenous penicillin desensitization protocol using a continuous infusion pump

Step	Penicillin (mg/ml)	Flow rate (ml/h)	Dose (mg)	Cumulative dose (mg)
1	0.01	6	0.015	0.015
2	0.01	12	0.03	0.045
3	0.01	24	0.06	0.105
4	0.1	50	0.125	0.23
5	0.1	10	0.25	0.48
6	0.1	20	0.5	1.0
7	0.1	40	1.0	2.0
8	0.1	80	2.0	4.0
9	0.1	160	4.0	8.0
10	10.0	3	7.5	15.0
11	10.0	6	15.0	30.0
12	10.0	12	30.0	60.0
13	10.0	25	62.5	123.0
14	10.0	50	125.0	250.0
15	10.0	100	250.0	500.0
16	10.0	200	500.0	1000.0

Observe patient for 30 min, then give full therapeutic dose by the desired route.
*The interval between doses is 15 min (ref. 22).

Other protocols with tenfold increments do exist, but appear to be associated with more side-effects. In theory, the pharmacokinetic and pharmacodynamics of the drug have to be considered to establish the time interval between doses (e.g., of aspirin), as well as to prevent overdosing (e.g., of insulins).

Recent studies support the importance of defining the starting dose and time interval between doses. Using a murine model, Morales et al. (38) showed that the process was both dose and time dependent since statistically significant differences were seen in mediator release when dose delivering times were different. When doses are too high and delivered too fast, the state of unresponsiveness may be delayed; this can explain breakthrough reactions during desensitization. In effect, a certain time interval between doses of the drug antigen is needed to achieve maximum tolerance of the therapeutic dose (38).

Table 6 Desensitization protocol for rituximab I.V. (851 mg): Solution preparation

Total dose	851 mg	Solution concentration	Total dose in each solution (mg)
Solution 1	250 ml	0.034 mg/ml	8.150 mg
Solution 2	250 ml	0.340 mg/ml	85.100 mg
Solution 3	250 ml	3.377 mg/ml	844.303 mg

Step	Solution	Rate (ml/h)	Time (min)	Administered dose (mg)	Cumulative dose (mg)
1	1	2	15	0.0170	0.0170
2	1	5	15	0.0426	0.0596
3	1	10	15	0.0851	0.1447
4	1	20	15	0.1702	0.3149
5	2	5	15	0.4255	0.7404
6	2	10	15	0.8510	1.5914
7	2	20	15	1.7020	3.2934
8	2	40	15	3.4040	6.6974
9	3	10	15	8.4430	15.1404
10	3	20	15	16.8861	32.0264
11	3	40	15	33.7721	65.7986
12	3	75	186	785.2014	851.0000

Total time = 351 min (5.85 h).
From ref. 55, with permission from the author.

Concomitant medications and pretreatments

Before beginning any desensitization procedure, patients should be in a stable clinical condition (e.g., FEV1 $\geq$ 70% of the normal value for asthmatics, controlled cardiac insufficiency). Any concomitant medication used for treating underlying diseases must be continued. However, drugs such as beta-blockers, which can interfere with the treatment of a severe hypersensitivity reaction, should be discontinued whenever possible. Indications should be strictly observed, e.g., sudden withdrawal of beta-blocker therapy in patients with arrhythmia may be life threatening.

For most drugs, pretreatment with systemic steroids and antihistamines is not necessary and may mask early signs of a hypersensitivity reaction (22, 71, 72). It is also unclear whether anti-histamines may actually interfere with rapid desensitization. However, many chemotherapy regimens already include medication with corticosteroids, antihistamines, and proton-pump inhibitors for other reasons (41, 46, 55, 70, 73).

Breakthrough reactions

Breakthrough reactions are drug hypersensitivity reactions that occur despite the desensitization procedure. They most often occur during the first course of desensitization. In subsequent procedures, reactions are usually less severe (46, 48, 55). Breakthrough reactions seem to be dose dependent as they often appear when a substantial increment in the dose is attempted. Breakthrough reactions have to be treated immediately. Stopping the infusion or oral intake is considered mandatory, and over 90% of the reactions resolve without further treatment (46, 48, 55).

Although, there is no common approach concerning further management, some authors choose to treat through reactions without modifying the protocol. Others interrupt the procedure, treat the reactions, and then modify the desensitization protocol by introducing intermediate dosing steps, going back one or two steps, or re-starting at the stopping point with a lower dose (41, 45, 46, 48, 55, 70, 71).

There are some data suggesting that decelerating the dose escalation by duplicating problematic doses reduces the incidence of reactions and improves tolerability (41, 48, 55, 56). In patients with near fatal reactions or clinical syndromes, such as serum sickness and blood cell dyscrasias, the desensitization has to be definitely stopped.

Outcomes of desensitization

Complete successful desensitization is achieved when the patient reaches the full therapeutic dose and tolerates repeated administrations of such dose until the therapeutic course is completed.

It must be remembered that desensitization is dose and drug dependent; it is also an active and quickly reversible process, dependent on the continuous administration and presence of the drug. When the drug is discontinued, tolerance is lost over hours or days. Therefore, for further treatments, repeating desensitization with the drug is mandatory. It is possible to sustain a state of ongoing tolerance by daily administration of the drug, such as penicillin in patients with recurrent infections (57, 74) or aspirin in patients with AERDs (26–28, 75).

In both adults and children, the efficacy of therapy with chemotherapeutic agents administered after desensitization has been shown to be the same as without a prior desensitization (41, 55).

Desensitization procedures are high-risk procedures that can induce anaphylaxis.

Side-effects occurring during desensitization are usually mild-to-moderate and easily treated. Mild reactions were reported in 30–80% in some series of penicillin-allergic patients undergoing desensitization (64, 69, 76). To avoid repeating desensitization, physicians should consider treating through selected mild-to-moderate reactions (e.g., urticaria) (55) and continue the procedure.

In a recent study by Castells et al. (55), the rate of adverse reactions during 413 rapid desensitizations to chemotherapeutic agents was: 26.9% (111 of 413) were mild and only 5.8% (24 of 413) were severe anaphylactic reactions. The vast majority (75%) of reactions occurred in the final steps of desensitization procedures. Most procedures (67%) were tolerated without any symptoms.

A desensitization procedure fails when the target therapeutic dose cannot be achieved and has to be stopped because of systemic allergic reactions (e.g., severe life-threatening reactions to carboplatin). If the recommended precautions are followed, fatal outcomes should be extremely unlikely. Specifically, no deaths have been reported because of desensitization for cancer therapy or chronic inflammatory diseases in the last 10 years (41, 55, 77, 78).

Desensitizations have been successfully performed in large samples of patients with hypersensitivity reactions to beta-lactams and chemotherapeutic agents (20, 23, 29, 41, 46, 48, 55, 64, 69). As far as drugs other than beta-lactams, taxenes, and platinum salts are concerned, there are only reports of single cases or case series with less than 10 patients.

It must be stressed that immediate desensitization is not known to prevent the occurrence of non-IgE-mediated reactions, like MPEs or severe cutaneous bullous reactions (SJS or TEN). Serum-sickness-like reactions and hemolytic anemia have been reported in patients who were otherwise successfully desensitized (18, 55, 56, 79).

Research needs

The need for general recommendations to perform such procedures has increased in recent years, but many questions remain to be answered. Research is needed to uncover the cellular and molecular mechanisms that might explain why drug desensitization is an active, rapid, often successful, but temporary and reversible phenomenon. The duration of tolerance for different drugs is unknown. Moreover, open questions remain regarding the starting dose, additional value of endpoint titration, dose increments, number of subsequent doses, the time interval between doses, and the total duration of the procedure. In addition, the role of any co-medications and/or drugs used in premedication, including anti-IgE, in breakthrough symptoms, as well as the possible influence of such drugs on the efficacy of desensitization should be studied. It is unclear if drug-specific protocols are needed or if general rules can be applied. The efficacy of treatment of underlying diseases should also be studied.

Because of the limited number of patients in each centre, only multicentre studies can answer these questions, improving outcomes and establishing common, effective standardized protocols.

Concluding remarks

Drug desensitization is the induction of a temporary state of tolerance of a compound responsible for a hypersensitivity reaction. This is achieved by the administration of increasing doses of the offending drug over a short period of time until the full therapeutic dose is reached (Fig. 1). A high success rate has been reported in series of patients sensitive to beta-lactams or platinum salts but failures and

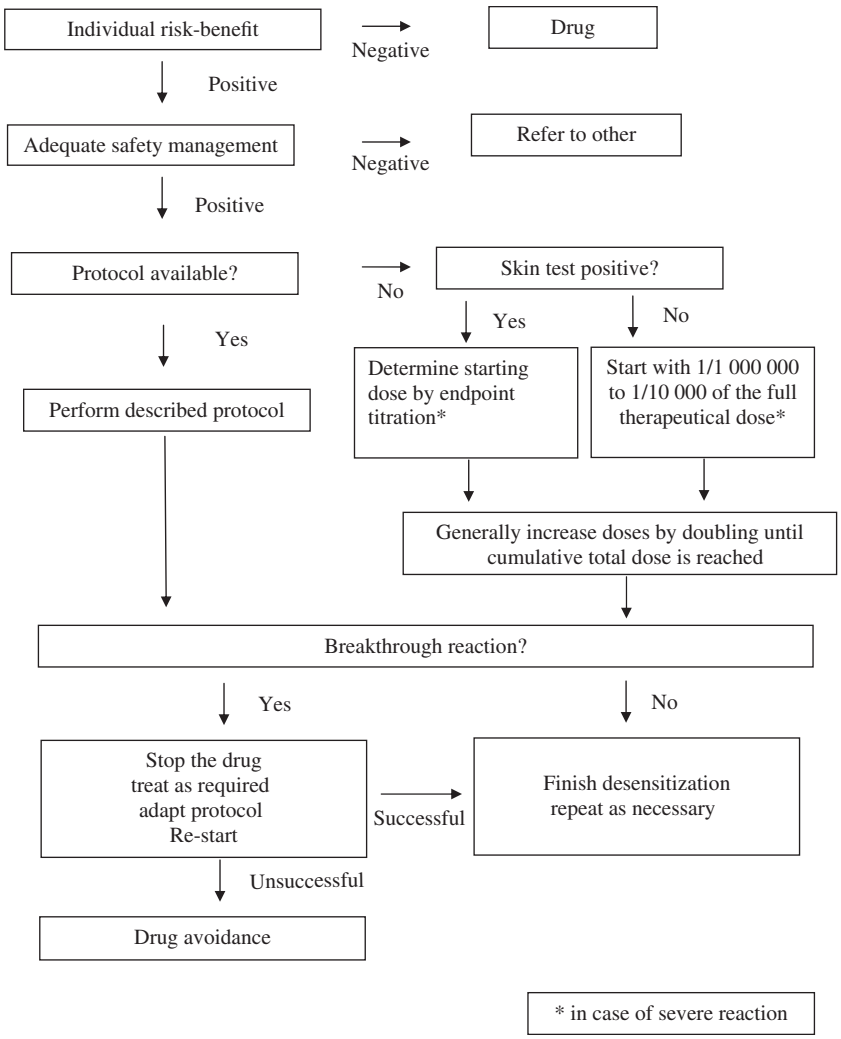

Figure 1 General algorithm for drug desensitization.

life-threatening anaphylaxis have also been described. Thus, it is a high-risk procedure and should be used only by well-trained doctors in selected patients in whom alternatives are less effective or not available and after establishing a risk/benefit analysis.

At present, it is advisable to use successful desensitization protocols applied in large samples (more than ten patients).

The selection of candidates for desensitization by allergy and immunology specialists, the stabilization of concomitant diseases, the training of personnel (doctors and nurses), the treatment of breakthrough reactions, and the availability of validated protocols are crucial for the success of this procedure. To further improve desensitization, the desensitization database of the EAACI http://www.eaaci.net/v2/activities/task-forces/drug allergy should help in collecting more data and in exchanging experiences.

Conflict of interest

There is no conflict of interest for any member of the consensus group. The desensitization task force was financially supported by EAACI.

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