

REVIEW

Allergy during anaesthesia

J. BIRNBAUM, F. PORRI, M. PRADAL, D. CHARPIN and D. VERVLOET

Department of Chest Diseases and Allergy, Hôpital Sainte-Marguerite, Marseille, France

The use of anaesthetic agents, drugs and chemicals during anaesthesia induce a certain number of anaphylactoid reactions. The incidence of anaphylaxis to intravenous agents used during general anaesthesia is about 1 : 6000. Despite appropriate treatment mortality is about 6%. Different mechanisms are involved. There are multiple risk factors. The main agents used for induction of anaesthesia are neuromuscular blocking agents (muscle relaxants: MR), hypnotics, morphinomimetics, neuroleptics and benzodiazepines. However, other drugs may be used including plasma substitutes such as fluid gelatins or dextrans, latex, ethylene oxide, protamine.

Main substances involved in anaphylactoid shock

Reactions to intravenous agents most often occur within minutes after the induction of anaesthesia. Studies from Australia, France and the UK have reported a great number of cases. All mechanisms included, the incidence of adverse reactions was evaluated to be 1/1250, 1/3500, 1/3500, respectively. A French epidemiological study has collected 1585 cases of anaphylactoid shock over a period of 2 years (1990–1991) [1]. An anaphylactoid mechanism has been demonstrated in 52% of cases. The agents involved were: muscle relaxants (70.3%), latex (12.6%) and at a lower rate the other drugs and substances used during anaesthesia.

Muscle relaxants

They represent a family of agents such as suxamethonium, vecuronium, pancuronium and atracurium widely used in general anaesthesia to achieve muscle relaxation. In France, suxamethonium is the cause of 43% of those anaphylactic shocks involving MR, followed by vecuronium (37%), pancuronium (13%), alcuronium (7.6%), atracurium (6.8%), gallamine (5.6%) [1]. Suxamethonium remains the one most often implicated. The incidence of shocks involving vecuronium is on the increase. These figures should be corrected for the relative amounts of

each MR used in each country: vecuronium is being increasingly used in France, whereas alcuronium and gallamine are no longer administered.

Hypnotics

Since cremophor EL, used as a solvent of some non-barbiturate hypnotics, was replaced by other lipidic solutions, many previous reported anaphylactoid reactions disappeared. The incidence of general adverse reactions with thiopentone is estimated between 1/23 000 and 1/29 000 administrations. Propofol like thiopentone can induce a true anaphylactic shock [2,3].

Morphinomimetics

Although opioid analgesics are among the most commonly prescribed drugs in hospitals, anaphylactoid reactions to these drugs are rare. The incidence of intraoperative shocks to these drugs was similar in 1989 and 1993 [1]. The use of poor histamine releaser morphinomimetics as for instance fentanyl decreases the incidence of anaphylactoid reactions [4]. However, some IgE dependant anaphylactic reactions have been reported.

Neuroleptics and benzodiazepines

Sedative neuroleptics of the family of butyrophenons as for instance droperidol are often used in anaesthesia. The incidence of adverse reactions is exceedingly rare. Adverse reactions reported with some benzodiazepines were usually observed when cremophor EL was used as a solvent.

Plasma substitutes

The most commonly used colloid volume substitutes are dextran and gelatins. Dextrans are glucose polymers with molecular weights ranging from 40 000 to 70 000 kDa used for blood volume expansion. They are produced by bacterium *leuconostoc mesenteroides*. The incidence of anaphylactoid reactions due to dextran was evaluated between 0.008% and 0.069% [5]. Skin tests are rarely positive with immediate reaction. Fluid gelatins are used as fillers in emergency situations. They are produced by

Correspondence: D. Vervloet, Département des Maladies Respiratoires, Hôpital Sainte-Marguerite, BP 29, F-13277 Marseille Cedex 9 France.

hydrolysis of collagen and chemical modification. The frequency of anaphylactoid reactions has been evaluated to be between 0.03% and 0.14% [5].

Protamine

Recent advances in medicine, such as cardiac catheterization, phoresis, dialysis and cardiopulmonary bypass technology, have increased the need for heparin anticoagulation. To antagonize heparin's effect and prevent haemorrhagic complications after the procedure, protamine has likewise been used more frequently. With its increased use have come increasing reports of adverse reactions to protamine consisting of rash, urticaria, elevation of pulmonary artery pressure, systemic hypotension and, at times, death [6].

Latex and ethylene oxide

Immediate hypersensitivity to latex was first described in 1979 by Nutter [7]. Clinical manifestations are various and result from direct contact between skin or mucosa and latex, or from inhalation of airborne latex allergens attached to the cornstarch powder used to lubricate surgical gloves [8]. Reactions can be local or general such as urticaria and angioedema, rhinitis, asthma or even anaphylactic shock. These manifestations, especially anaphylactic shock, have been described during surgical procedures [9], gynaecological and obstetric procedures [10], vaginal examination [11], barium enema [12], rectal manometry, dental procedures and also after exposure to balloons, adhesive bandages, condoms, baby pacifiers [11]. Shocks involving latex now account for 12.6% of intraoperative anaphylactic reactions, whereas it was rare in 1989 (0.5%) [1]. They occur between 30 min and 2 h after induction of anaesthesia [13,14]. The rationale for the increase of latex allergy during these last years could be the better knowledge of clinical manifestations, the increasing use of latex gloves and condoms because of acquired immune deficiency syndrome (AIDS), and modification in rubber and gloves industry or in growing of *Hevea brasiliensis*.

Ethylene oxide, a gas used for sterilization of medical material, is involved in severe but non-fatal reactions in 4.2% out of 1 000 000 dialysers sold [4]. Association of latex and ethylene oxide was described especially in some children with myelodysplasia.

Mechanisms

IgE-dependent reactions

Muscle relaxants Presence of IgE antibodies was

suggested by passive transfer tests and leucocyte histamine release [15,16]. However, direct proof of the presence of IgE antibodies was brought about by an Australian group [17]. Data to check the specificities of IgE antibodies were obtained from inhibition studies, in which patient's sera were preincubated with each of the muscle relaxants. Quantitative inhibition studies showed that IgE antibodies from most patients crossreacted with all muscle relaxants tested and with unrelated agents containing ammonium ions [18]: many drugs (neostigmine, pentolinium, trimetaphan and morphine) or substances as well as cell membrane constituents contain ammonium ions. In this case, inhibition studies revealed that the binding of IgE to the drug on the drug support could be diminished or prevented by this wide variety of compounds containing quaternary or tertiary ammonium ions. Since these compounds are commonly found in drugs, foods, cosmetics, industrial materials, contact or inhalation of these compounds could provide an opportunity to become sensitized. The rigidity of the chain linking quaternary ammoniums plays a triggering role in allergic reactions. Flexible molecules with simple carbon chains like suxamethonium can stimulate sensitized cells more strongly than rigid molecules as pancuronium [19].

Thiopentone Two antigenic determinants on the thiopentone molecule were demonstrated. The determinants were the secondary pentyl and ethyl groups attached in position 5 of the pyrimidine ring nucleus and the region of the ring encompassing and including the attached hetero atom. Thus, the thiopentone-allergic determinants so far recognized are on opposite sides of the molecule. At high pH thiopentone binding of the immunoabsorbent material can generate substituted ammonium ions that are normally internalized within the molecule. Specific IgE against quaternary ammonium ions in subjects sensitive to muscle relaxants can bind these substituted ammonium ions thus simulating allergy to thiopentone [2].

Morphine and related opioids IgE antibodies to morphine and meperidine have been detected [20]. Allergic determinant identified on morphine encompass the *N*-methyl group and the cyclohexenyl ring with a hydroxyl at C-6. Crossreactivity between morphine, codeine and other narcotics has been alleged.

Latex and ethylene oxide Radioallergosorbent test (RAST) to latex and ethylene oxide are commercially available. Immediate allergic reactions to these substances are IgE dependent [14]. However, *in vitro* determination of IgE antibodies to latex is less sensitive

than skin tests. One candidate for the major latex allergen has been identified as the rubber elongation factor of the rubber tree *Hevea brasiliensis*. Allergens adhere to the powder of latex gloves and can be transported into the respiratory tract [21].

Non-specific histamine release

With hypnotics and morphinomimetics an histamine release mechanism is possible in some cases. Of the MR, atracrium induces more non-specific histamine release than vecuronium. An *in vitro* study showed that atracurium released within 1 min five times more histamine from the skin, lung and heart mast cells than vecuronium [22]. Other substances injected before or during anaesthesia may give non-specific release: prophylactic antibiotics (metronidazole, cefuroxime), plasma substitutes (gelatins) and blood products. Simultaneous injection of different drugs is likely to increase the level of histamine up to the threshold of clinical manifestations.

Complement activation

Complement activation is no longer thought to be involved in anaphylactoid reactions involving anaesthetic agents. This mechanism is involved in reactions to protamine, dextrans and vascular prostheses.

Diagnostic tests

Screening is mainly based on clinical findings but in some cases skin tests and/or laboratory tests are available.

Skin tests

Following intradermic injection of the suspected allergen, an immediate reaction characterized by the appearance of weal-and-flare is highly predictive of sensitivity. In experimental studies such reactions were frequent in allergic subjects whereas they were extremely uncommon in controls at the same concentrations.

A number of studies have demonstrated the usefulness of skin tests to retrospectively confirm allergy to muscle relaxants, barbiturics and latex [2,8,23]. The concentrations necessary to conclusively prove allergy to muscle relaxants have been rigorously defined [23]. Recently, a good correlation was found to exist between intradermal tests and prick tests [24]. However, it should be stated that, in a few cases, positive intradermal tests have been observed for vecuronium and pancuronium only at 400 and 200 $\mu\text{g/ml}$, respectively. In these cases prick tests using commercially available solutions at 4

and 2 mg/ml may be negative. Thus, if only prick tests were performed, it may be wrongly concluded that the subject is not allergic to muscle relaxants. Similarly intradermal tests with tracrrium must be performed at a maximal concentration of 10 $\mu\text{g/ml}$. Prick tests performed using commercially available solution at 10 mg/ml lead to false positive reactions.

Debate about the value of systemic preoperative skin testing for predicting muscle relaxants allergy has been opened a few years ago. Before accepting to do it the following questions should be answered: is the test valid? what is its predictive value, which population should be tested, is screening feasible? In order to be valid, a screening test must be cheap, reproducible, sensitive and specific. Prick tests have been advocated, because they are easy to perform, safe, sensitive and specific. However, sensitivity and specificity of prick tests are not the same whether prick tests are performed by anaesthetists or by allergologists, because performing and reading skin tests is not always easy (personal data). In order to be efficient, a test has to have both a high positive and negative predictive value. Given a valid test, a high predictive value will be obtained if the prevalence of the disease in the population under study is high enough. In order to identify such a population at higher risk, we need to know what are the risk factors. A good negative predictive value to MR has been demonstrated when the skin tests were performed by an allergologist [25].

Concerning latex allergy, latex extracts for skin tests are now commercially available in Europe (Laboratories Stallergènes, France) but they need to be standardized. To identify latex allergic subjects, skin test to latex has to be performed because symptoms have a low positive predictive value for predicting true latex sensitization [26]. It should be borne in mind that the predicting value of latex sensitization for the occurrence of peroperative anaphylactic reactions is unclear.

Measurement of specific serum IgE

Recently, in the field of anaphylactic reactions to MR, laboratory tests have proven their usefulness both with regard to the study of the offending epitopes and molecular structures.

As for all allergens, a good correlation is usually observed between skin tests and specific IgE levels, but no generalization should be made in this regard. Since measurement of specific IgE is less sensitive than skin testing in most cases, discordant results with positive skin tests and negative RAST are possible. To solve this problem, a new test using a structural analogue of insolubilized choline on sepharose as a solid support

has been developed in Nancy (France). This support which is called sepharose-quaternary ammonium (SQA) is used to detect the presence of specific quaternary ammonium ions in the serum based on the radio-immunological method of RAST. Inhibition of specific IgE binding is systematically controlled by placing the tested serum in the presence of offending molecule in soluble form. The concordance rate with skin tests is reported to be about 83% [27]. Recently, another solid phase for detecting antiquaternary ammonium IgE, using *p*-aminophenylphosphoryl-choline immobilized on agarose beads has been proposed [28].

Some patients with IgE against quaternary ammonium ions may have positive RAST and negative skin tests especially for MR with rigid structures such as pancuronium or vecuronium [23]. These drugs may not bridge two specific IgE molecules, thus preventing the release of mediators.

A radioimmunoassay for the detection of thiopentone-reactive IgE antibodies is available. In the sera of some patients allergic to MR, but not allergic to thiopentone, specific IgE to thiopentone were found [20]. These results suggest that the IgE antibodies in the sera of MR allergic subjects recognize determinants on both thiopentone and MR. Substituted ammonium group in cyclic form are present in the barbiturate ring of thiopentone.

A latex radioallergosorbent test is commercially available but, as expected, it is less sensitive than a skin test, detecting these antibodies in only about 50–70% of cases [14]. Latex specific IgE is more frequently found in ragweed, blue grass and ficus-allergic patients [29].

Measurement of serum tryptase and urinary methylhistamine

Tryptase is a neutral protein which, like histamine occurs in mast cells. Unlike histamine which is contained within other cells, notably basophils tryptase is more than 99% confined to the mast cells. The long half-life of tryptase permits the investigation of anaphylactic or anaphylactoid reactions and its measurement may be used to distinguish mast cell dependant adverse reactions from others. However, this assay does not permit to identify the agent responsible for the adverse reaction [30].

Risk factors

Despite appropriate treatment, about 6% of the patients who suffered such anaphylactoid reactions die. Thus, it is of the utmost importance to develop a rational approach to try to minimize the risk by identifying possible risk factors before surgery: sex, age, genetic background,

previously administered general anaesthesia, history of drug reaction at large and atopy. Drug reactions in general, and perioperative drug reactions in particular, are more frequent in women. The most frequent age for perioperative drug reactions in large series are the third, fourth and fifth decades. No data are available concerning the role of genetic factors in immunological responses to anaesthetic drugs. Data concerning the incidence of atopic disease associated with anaesthetic agent hypersensitivity is contradictory. This disagreement may stem mainly from the definition of atopy [31,32].

Muscle relaxants

Sex A female predominance has been demonstrated in perioperative reactions. Anaphylactic reactions to muscle relaxants occur in females three times out of four [33,34]. The presence of specific IgE towards natural constituents containing quaternary ammoniums ions has been suggested: acetylcholine, membrane phospholipids, food lecithins from soy or egg. A possible sensitization to cosmetics and other substances containing ammonium ions has been put forward.

Age Reactions to muscle relaxants used during general anaesthesia have rarely been reported in young children. This could be because of injection of lower doses, a lower number of general anaesthetics, or a natural loss of sensitization as it has been described in the field of hymenoptera allergy.

History of previous general anesthesia using the drug that has elicited the reaction Previous exposure does not seem to be a risk factor for reaction to muscle relaxants since many of patients presenting anaphylactic shock had never been given the drug before [35]. In Fisher's study [36] among 46 patients who reacted to muscle relaxants, only six were previously exposed to this group of drugs. In our own study [34], 25% of 32 patients who developed an anaphylactic reaction to muscle relaxants had no history of surgery. In addition, the mean number of previous general anaesthetics was comparable in the case and control groups.

Atopy Atopy has been recognized by some authors as a risk factor, whereas it has been denied as such by others. If atopy is only defined on clinical grounds, i.e. history of perennial or seasonal rhinitis or bronchial asthma, then in some reports it appears to be a risk factor for anaphylactic reactions. In contrast, if atopy is defined on a biological criteria, i.e. positive skin tests to common aeroallergens or positive Phadiatop® (Kabi Pharmacia, Uppsala, Sweden) test, then it does not seem to be so [34].

Thiopental

Sex Anaphylactic reactions have been reported three times more frequently in females than in males.

Previous general anaesthesia Thiopental anaphylaxis is frequently associated with previous general anaesthesia or drug exposure. Baldo found that 29 of 31 patients (97%) who reacted to thiopentone had received the drug before. In Dundee's study 13 out of 19 cases (68%) had been previously exposed [2].

Latex

Sex Most of the patients sensitized to latex are female, 80% of the cases reported by Wrangsjö [37] were female, 70% of those reported by Jaeger *et al.* [38] and 100% of cases in the study of Beaudouin [39]. However, most of the published reports concern hospital personnel where women are over-represented.

Age Latex allergy appears to cluster in young people who are also over-represented in health care personnel especially paediatric nurses and children and babies [8]. Anaphylactic shock during surgical procedures in children are most often related to latex allergy [1].

Atopy Many reports of latex allergy concern atopic subjects. Lagier *et al.* [27] showed that 47% of atopic nurses (history of allergic rhinitis and/or asthma) exposed to latex had a positive skin-prick test to latex. This percentage was equal to 10.7% overall. In a recent study [40], it was shown that atopy multiplies the risk of latex sensitization by 25 in a group of non-exposed subjects: 9.44% in the atopic group vs 0.37% in the non-atopic group. Beaudouin *et al.* [39] studied 907 subjects working in an hospital. The incidence of atopy was significantly greater in the group with a positive test to latex (58.3%) than in the whole group (29%).

Occupation Health care workers are at risk for latex allergy. Even if the prevalence of latex sensitization in the general population is unknown, several studies conducted in hospital personnel have showed a high rate of sensitization, between 2.5 and 10.7% [27,39,41].

Workers in glove manufacturing plants are also at risk to develop a latex allergy. Eleven per cent of the workers skin tested by Tarlo *et al.* [42] were sensitized to latex and three had an occupational asthma related to this allergen. Other occupations at risk include dentists, cleaners gardeners ..., all people who were frequently exposed to latex at work.

The prevalence of latex allergy among workers on rubber tree farms in latex processing facilities is unknown. Atopy seems to act synergistically with frequent exposure to latex [40].

Spina bifida (SB) Many anaphylactic shocks to latex in SB children have been described during the last 10 years [40,43–47]. The prevalence of latex sensitization in SB children was found extremely high between 28 and 35%. Risk factors could be more repeated surgical procedures than a genetic predisposition (personal data). In these children, latex allergy is also frequently associated with allergy to ethylene oxide [47].

Food allergy Food allergy could be associated with latex allergy. A cross-allergenicity has been demonstrated for banana [48], chestnut [49], kiwi and avocado. Wrangsjö *et al.* [37] found a food allergy in 75% of cases among 30 patients with contact urticaria to natural rubber.

Fluid gelatins and dextrans

Food allergy Cross-allergy between dietary gelatin and fluid gelatins used for plasma has been observed [50].

Personal pathological conditions Chronic inflammatory signs such as osteomyelitis, gallstones, arthritis, urinary infections, gastrointestinal signs and cardiopulmonary diseases may be risk factors for dextran allergy [4].

Specific IgG The presence of specific IgG antibodies to dextran is a major risk factor [5].

Prevention

In this area, no recommendation except drug avoidance can be formulated. No treatment reliably prevents anaphylactic reactions.

Pretreatment with H1 antihistamines before injecting anesthetic agents does not prevent anaphylactic shock. Their only action is to decrease the effect of a non-specific histamine release [51]. The association with H2 antihistamine has been proposed [52], however, the efficacy of this association compared with H1 antihistamine given alone was not proven. Infusion of monovalent hapten dextran (Promit®) was demonstrated as effective in the prevention of adverse reaction to dextrans [53].

The possibility to prevent anaphylaxis to MR by monovalent haptens [54] needs confirmation.

As there is no preventive treatment, particular caution is necessary to identify the high risk groups for a given

allergen and eviction of drugs or substances (latex for instance) to which the patient is allergic remains the best way of prevention.

Conclusion

Anaphylaxis is frequent during general anaesthesia, occurring in about 1/6000 procedures. Muscle relaxants are by far the worst offenders, followed by latex and thiopentone. Diagnosis procedure are now efficient at least for some substances (muscle relaxants, ethylene oxide, thiopentone, latex). Evaluation of possible risk factors needs further work. A systemic preoperative screening is not justified at this time except screening for latex allergy in high risk groups.

References

- 1 Laxenaire MC. Drugs and other agents involved in anaphylactic shock occurring during anaesthesia. A French multicenter epidemiological inquiry. *Ann Fr Anesth Reanim* 1993; 12:91-6.
- 2 Baldo BA, Fisher MM, Harle DG. Allergy to thiopentone. *Clin Rev Allergy* 1991; 9:295-308.
- 3 Laxenaire MC, Guéant JL, Bermejo E, Mouton C, Navez MT. Anaphylactic shock due to propofol. *Lancet* 1988; ii:739-40.
- 4 Pradal M, Vervloet D. Drug allergy. Kabi Pharmacia Diagnostics. 1992.
- 5 Ring J. Anaphylactoid reactions to intravenous solutions used for volume substitution. *Clin Rev Allergy* 1991; 9:397-414.
- 6 Weiss ME, Adkinson NF. Allergy to protamine. *Clin Rev Allergy* 1991; 9:339-55.
- 7 Nutter AF. Contact urticaria to rubber. *Br J Dermatology* 1979; 101:597-8.
- 8 Levy DA, Charpin D, Pecquet C, Leynadier F, Vervloet D. Allergy to latex. *Allergy* 1992; 47:579-87.
- 9 Gold M, Swartz JS, Braude BM, Dolovich J, Schandling B, Gilmour RF. Intraoperative anaphylaxis: an association with latex sensitivity. *J Allergy Clin Immunol* 1991; 87:662-6.
- 10 Turjanmaa K, Reunala T, Tuimala R, Karkkainen T. Allergy to latex gloves: unusual complication during delivery. *Br Med J* 1988; 297:1029.
- 11 Axelsson JGK, Johansson SGO, Wrangsjö K. IgE-mediated anaphylactoid reactions to rubber. *Allergy* 1987; 42:46-50.
- 12 Ownby DR, Tomlanovich M, Sammons N, McCullough J. Anaphylaxis associated with latex allergy during barium enema examinations. *AJR*, 1991; 156:903-8.
- 13 Slater JE, Mostello LA, Shaer C, Honsinger RW. *Ann Allergy* 1990; 65:411-4.
- 14 Moneret-Vautrin DA, Finet JF, Maria Y. L'allergie au latex. *Rev Fr Allergol* 1988; 283:235-6.
- 15 Vervloet D, Arnaud A, Vellieux P, Kaplanski D, Charpin J. Anaphylactic reactions to muscle relaxants under general anaesthesia. *J Allergy Clin Immunol* 1979; 63:348-53.
- 16 Vervloet D, Nisankowska E, Arnaud A, Senft M, Charpin J. Adverse reactions to suxamethonium and other muscle relaxants under general anaesthesia. *J Allergy Clin Immunol* 1983; 71:552-9.
- 17 Harle DG, Baldo BA, Fisher MC. Detection of IgE antibodies to suxamethonium after anaphylactoid reactions during anaesthesia. *Lancet* 1984; i:930.
- 18 Baldo BA, Fisher MC. Anaphylaxis to muscle relaxants drugs: cross reactivity and molecular basis of binding of IgE antibodies detected by radioimmunoassay. *Mol Immunol* 1983; 20:1393-400.
- 19 Didier A, Cador D, Bongrand P, Philip-Joet F, Charpin J, Vervloet D. Role of the quaternary ammonium ion determinants in allergy to muscle relaxants. *J Allergy Clin Immunol* 1987; 79:578-84.
- 20 Fisher MM, Harle DG, Baldo BA. Anaphylactoid reactions to narcotic analgesics. *Clin Rev Allergy* 1990; 9:309-18.
- 21 Baur X, Ammon J, Chen Z, Bekmann U, Czuppon AB. Health risk in hospitals through airborne allergens for patients presensitized to latex. *The Lancet* 1993; 342:1148-9.
- 22 Marone G, Stellato C, Mastronardi P, Mazzarella B. Non-specific histamine-releasing properties of general anesthetic drugs. *Clin Rev Allergy* 1991; 9:269-80.
- 23 Birnbaum J, Vervloet D. Allergy to muscle relaxants. *Clin Rev Allergy* 1991; 9:281-93.
- 24 Leynadier F, Sansarricq M, Didier JM, Dry J. Prick tests in the diagnosis of anaphylaxis to general anaesthetics. *Br J Anaesth* 1987; 59:683-9.
- 25 Leynadier F, Calinaux C, Dry J. Valeur prédictive des tests intradermiques aux curarisants. *Ann Fr Anesth Reanim* 1989; 8:98-101.
- 26 Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol*. 1992; 90:319-22.
- 27 Guéant JL, Mata E, Monin B et al. Evaluation clinique et biologique d'un test radio-immunologique de détection des IgE sériques spécifiques des curarisants. In: Biologic prospective. M. Galteau, G. Siest J. Henny, eds. Libbey Eurotext, Paris, 1989; 737-40.
- 28 Guilloux L, Ricard-Blum S, Ville G, Mottin J. A new radioimmunoassay using commercially available solid supports for detection of IgE antibodies against muscle relaxants. *J Allergy Clin Immunol* 1992; 90:153-9.
- 29 Appleyard JK, McCullough JA, Ownby DR. Cross-reactivity between latex, ragweed and blue grass allergens. *J Allergy Clin Immunol* 1994; 93:A119.
- 30 Watkins J, Wild G. Improved diagnosis of anaphylactoid reactions by measurement of serum tryptase and urinary methylhistamine. *Ann Fr Anesth Reanim* 1993; 12:169-72.
- 31 Charpin D, Pradal M, Vervloet D. Risk factors for allergic or pseudoallergic reactions in the perioperative period. *Clin Rev Allergy* 1991; 9:259-68.
- 32 Haddi E, Charpin D, Tafforeau M et al. Atopy and systemic reactions to drugs. *Allergy* 1990; 45:236-9.
- 33 Laforest M, More DG, Fisher MM. Predisposing factors in anaphylactoid reactions to anaesthetic drugs in an Australian population: the role of allergy, atopy and previous anaesthesia. *Anaesth Intensive Care* 1980; 8:454-59.

- 34 Charpin D, Benzarti M, Hemon Y et al. Atopy and systemic reactions to suxamethonium. *J Allergy Clin Immunol* 1988; 82:356-60.
- 35 Moneret-Vautrin DA, Laxenaire MC. The risk of allergy related to general anaesthesia. *Clin Exp Allergy* 1993; 23:629-33.
- 36 Fischer MM. The epidemiology of anaesthetic anaphylactoid reactions in Australia. *Klin Wochenschr* 1982; 60:1017-20.
- 37 Wrangsjö K, Wahlberg JE, Axelsson JGK. IgE-mediated allergy to natural rubber in 30 patients with contact urticaria. *Contact Dermatitis* 1988; 19:264-71.
- 38 Jaeger J, Kleinhaus D, Czuppon AB, Baur X. Latex specific proteins causing immediate type cutaneous, nasal, bronchial and systemic reactions. *J Allergy Clin Immunol* 1992; 89:759-68.
- 39 Beaudouin E, Pupin P, Jacson F, Laxenaire MC, Moneret-Vautrin DA. Allergie professionnelle au latex - Enquête prospective sur 907 sujets du milieu hospitalier. *Rev Fr Allergol* 1990; 30:157-61.
- 40 Moneret-Vautrin DA, Beaudouin E, Widmer S et al. Prospective study of risk factors in natural rubber latex hypersensitivity. *J Allergy Clin Immunol* 1993; 92:668-77.
- 41 Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; 17:270-5.
- 42 Tarlo SM, Wong L, Roos J, Booth N. Occupational asthma caused by latex in a surgical glove manufacturing plant. *J Allergy Clin Immunol* 1990; 85:626-31.
- 43 Gerber AC, Jorg W, Seger RA, Dangel PH. Severe intra-operative anaphylaxis to surgical gloves: latex allergy and unfamiliar condition. *Anesthesiology* 1989; 71:800-2.
- 44 Slater JE. Rubber anaphylaxis. *N Engl J Med* 1989; 320:1126-9.
- 45 Meeropol E, Kelleher R, Bell S, Leger R. Allergic reactions to rubber in patients with myelodysplasia. *N Engl J Med* 1990; 323:1072.
- 46 Slater J, Mostello L, Sheer C. Rubber specific IgE in children with spina bifida. *J Urol* 1991; 146:578-9.
- 47 Moneret-Vautrin DA, Laxenaire MC, Bavoux F. Allergy shock to latex and ethylene oxide during surgery for spina bifida. *Anesthesiology* 1990; 73:556-8.
- 48 M'Raihi L, Charpin D, Pons A, Bongrand P, Vervloet D. Cross-reactivity between latex and banana. *J Allergy Clin Immunol* 1991; 87:129-30.
- 49 Anibarro B, Garcia-Ara MC, Pascual C. Associated sensitization to latex and chestnut. *Allergy* 1993; 48:130-31.
- 50 Wahl R, Kleinhaus D. IgE-mediated allergic reactions to fruit gums and investigation of cross-reactivity between gelatine and modified gelatine containing products. *Clin Exp Allergy* 1989; 19:77-80.
- 51 Hatano Y, Fukuda K, Arai T, Tamai S, Harioka T. Histamine H1 agonist alone attenuates d-tubocurarine induced hypotension. *Anesthesiology* 1985; 63:731-2.
- 52 Hosking MP, Lennon RL, Gronert GA. Combined H1 and H2 receptor blockade attenuates the cardiovascular effects of high dose atracurium for rapid sequence endotracheal intubation. *Anesth Anal* 1988; 67:1089-92.
- 53 Ljungström KG, Willman B, Hedin H. Hapten inhibition of dextran anaphylaxis. Nine years of post-marketing surveillance of dextran 1. *Ann Fr Anesth Réanim* 1993; 12:219-22.
- 54 Moneret-Vautrin DA, Motin J, Mata E et al. Preventing muscle relaxant anaphylaxis with monovalent haptens. A preliminary study. *Ann Fr Anesth Réanim* 1993; 12:190-202.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.