

PERIOPERATIVE ANAPHYLAXIS UPDATE

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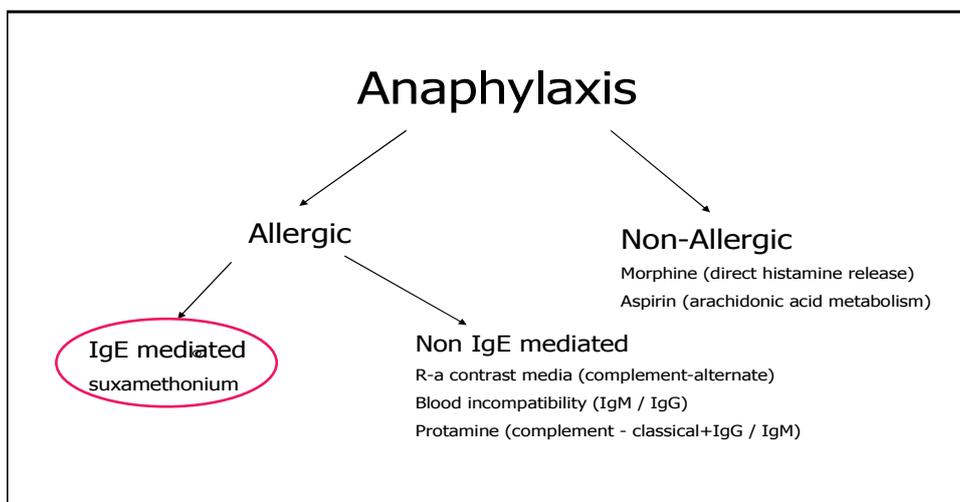
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ANZCA has approved the formation of a SIG which will be called the Australian and New Zealand Anaesthetic Allergy Group – ANZAAG. The challenging aims, in the first instance, will be to standardise testing, reporting and produce a data-base. The New Zealand Group, which now consists of 10 centres, has been in existence for five years, and has already produced a referral form. The draft was produced by Lucas Sikiotis from Waikato.

Definitions

These have been altered. However, the fundamental definition of anaphylaxis still remains: a severe life-threatening generalised or systemic hypersensitivity reaction.

The European group of allergists and immunologists (2003) defined this condition according to the pathological cause: allergic or non-allergic.



Two years later the Americans (SNAID / FAAN 2005) preferred a more clinical definition, based on the signs, which include skin changes, respiratory and / or cardiovascular responses. It was considered that, if these signs were apparent, therapy would be more rapidly instituted. The word "anaphylactoid" has now been eliminated.

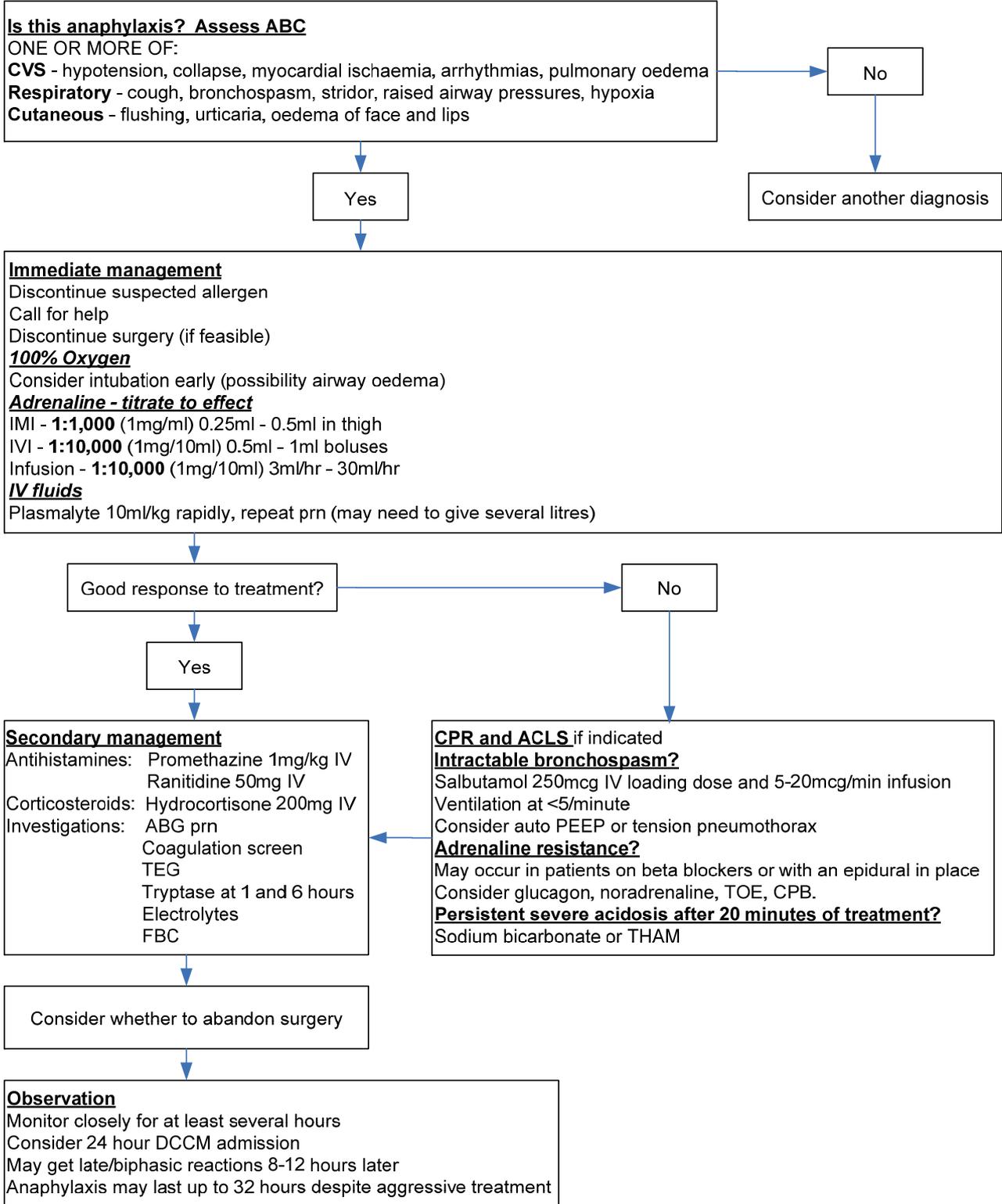
Tryptase

Many mediators are released in an anaphylactic reaction, both pre-formed and newly formed. From a clinical view-point, the most useful is tryptase, as it is a stable protease which reaches its maximum level 1 to 2 hours after the event. Tryptase is present in mast cells, which are found in skin, mucous membranes and connective tissue. It is not present in basophils which also are involved in anaphylactic reactions.

It is therefore important to know when to take blood samples for serum tryptase: 1-2 hours after the event; a second one at 6-8 hours later and a third sometime after 24 hours. This last sample is the base-line level of this mediator for that patient. Our Clinic has picked up at least 4 patients with systemic mastocytosis by noting that the base-line level is abnormally high.



Guidelines for the management of anaphylaxis in adults



- THIS IS A LIFE THREATENING EMERGENCY -**
- 1. Prompt recognition of signs and symptoms of anaphylaxis is crucial.**
 - 2. Adrenaline administered early and in adequate doses is the mainstay of treatment of anaphylaxis.**
 - 3. Appropriate volume replacement is essential.**



Incidence of Peri-operative Anaphylaxis

Reports vary widely; 1:4,000 (France) to 1:20,000 (Boston Collaborative Study 1989). It is estimated that in the Greater Auckland region the incidence is around 1:4,500.

The Auckland Anaesthetic Allergy Testing Clinic (AATC)

The tests performed are prick tests, intradermal tests and, when appropriate, specific IgE tests. These latter tests which are used by the AATC are for latex, penicillin G & V, suxamethonium and chlorhexidine. Auckland is the only centre to have the chlorhexidine specific test.

Around 100 patients are referred to the AATC each year. These referrals are triaged and between 70 – 80 patients are tested annually. Referrals are received, not only from anaesthetists and intensivists, but also from many other medical practitioners. There is a close collaboration with the Department of Clinical Immunology and occasionally referrals overlap. The clinic is held every 4 weeks when usually 6 patients are skin-tested. Auckland is very fortunate in having a strong laboratory Immunology Department. The specialist technicians produce the dilutions required for intra-dermal testing and also perform the testing.

Results

35% of all patients test positive. However, the figure rises to 51% when referrals from anaesthetists and intensivists only are assessed.

Suxamethonium is still the most frequent cause of peri-operative anaphylaxis. Rocuronium is the second most frequent culprit, but its incidence appears to be declining in recent years. Whether this is due to reduced use of this drug or a change in formulation, is unknown. Reasons as to why this muscle relaxant produces anaphylaxis, not only on its first administration, but also at the first general anaesthetic for that patient are outlined. International studies are still on-going. It appears that the ancillary agents used peri-operatively are becoming more of a problem in causing anaphylaxis. These include chlorhexidine, Patent Blue Dye (which is reported to have an incidence of 1:100 for sentinel node localisation), antibiotics, especially penicillins and cephalosporins, and gelatine-containing solutions.

Some unexpected conditions, such as systemic mastocytosis, reactions to local anaesthetics and cold urticaria, have been diagnosed.

A few case reports are presented.

“Anaphylaxis Boxes”

It is worth considering providing an ‘anaphylaxis box’ in a readily accessible area. We provide: blood request forms, appropriate blood sample tubes, guide-lines for intractable cases and a reminder when to take samples for serum tryptase levels. No drugs are kept in these boxes as adrenaline is in the emergency drawer of the anaesthetic locker.



Referral Forms

Other centres may modify this to suit their hospital and situation –

Referrals to the AATC

- New four page referral form: public and private
- www.healthpoint.co.nz Go to
 - Anaesthesia
 - Auckland DHB Anaesthesia
 - *(under quick links)* Referral Expectations
 - *(hyperlink at bottom of section)* Referral Form

Summary

Increasing awareness, improved skin-testing techniques and the avoidance of certain agents will hopefully reduce the incidence of life-threatening peri-operative anaphylaxis.

However, there will always be the unexpected!

References

1. Intradermal testing after severe histamine reactions to IV drugs used in anaesthesia. M Fisher. *Anaes Intens Care* 1976; 4: 97 (historical)
2. The diagnosis of acute anaphylactoid reactions to anaesthetic drugs. M Fisher. *Anaes Intens Care* 1981; 9:235
3. Intradermal testing after anaphylactoid reactions to anaesthetic drugs: Practical aspects of performance. M Fisher. *Anaes Intens Care* 1984; 12: 115
4. Anaphylaxis during anaesthesia: current aspects of diagnosis and prevention. M Fisher & BA Baldo. *Europ J Anaesthesiol.* 1994; 11:263
5. Anaphylactoid reactions during anaesthesia. M Fisher & BA Baldo. *Clinics in Anaesthesiology.* 1984; 2 (3): 677
6. Histaminoid reactions in anaesthesia. McKinnon RP & Wildsmith JAW. *BJA.* 1995; 74: 217
7. Anaphylactic and anaphylactoid reactions occurring in France 1999 – 2000. Mertes PM et al. *Anesthesiology.* 2003; 99(3) 536
8. Anaphylaxis during anaesthesia. Results of a 2 year survey in France. Laxenaire MC Mertes PM et al *BJA* 2001; 87(4) 549
9. Immunoassays in the diagnosis of anaphylaxis to neuromuscular blocking drugs: The value of morphine for the detection of IgE antibodies in allergic subjects. M Fisher & BA Baldo. *Anaes Intens Care;* 2000; 28(2): 167
10. Mast cell tryptase in anaesthetic anaphylactoid reactions. M Fisher & BA Baldo. *BJA;*1998; 80: 26
11. Review article: Mast cell tryptase: a review of its physiology and clinical significance. Payne V, Kam PCA. *Anaesthesia* 2004; 59: 695
12. Anaphylactic reactions to neuromuscular blocking drugs. Are we making the right diagnosis? Levy J. *Anesth Anal.* 2004; 98(4): 881
13. Prevention of anaphylactic reactions to anaesthetic drugs. M Fisher & GS Dorg. *Drug Safety.* 2004; 27(6): 393
14. Anaphylactic reactions during anaesthesia – let us treat the problem rather than debating its existence. PM Mertes. *Acta Anaesthesiol Scand;* 2005; 49(4):43 (Ed)
15. Prevalence of IgE antibodies to morphine. Relation to the high and low incidences of NMBA anaphylaxis in Norway and Sweden, respectively. Florvaag E et al. *Acta Anaesthesiol Scand;* 49(4): 437
16. Skin testing and the anaesthetist. Watkins J. (Editorial 2) *BJA.* 2000; 85(6): 814
17. Weal and flare responses to intradermal rocuronium and cisatracurium in humans. JH Levy et al. *BJA.* 2000; 85(6): 844
18. Rocuronium: high risk for anaphylaxis? M Rose & M Fisher. *BJA.* 2001; 86(5): 678
19. Histaminoid reactions associated with rocuronium. S Neal et al. *BJA.* 2000; 84(1): 108



20. Anaphylaxis to rocuronium. C Baillard et al. BJA 2002; 88(4): 600
21. Danish Anaesthesia Allergy Centre – preliminary results. LH Garvey et al. Acta Anaesthesiol Scand; 2001; 45(10): 1204
22. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization. October 2003. J Allergy Clin Immunol. 2004; 113(5): 832
23. The basophil activation test by flow cytometry: recent developments in clinical studies, standardization and emerging perspectives. R Boumisa et al. Clinical and Molecular Allergy. 2005, 3:9
24. Update on genetics of allergy and asthma: A potential clinical role? J E James. CMC.medscape.com/viewarticle/474406
25. Clinical value and measurement of specific IgE. M Plebani. Clinical Biochemistry, 36(6); Sept 2003: 453
26. The Immune System – first of Two Parts. Delves PJ and Roitt IM. NEJM, 343(1); July6 2000: 37
27. Second symposium on the definition and management of anaphylaxis: Summary report – Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Sampson HA et al. J Allergy Clin Immunol 2006; 117: 391-7
28. Anaphylaxis and Anaesthesia. What Can We Do Better? Rose MA and Fisher MM. Australasian Anaesthesia 2009
29. Anaphylactic reactions during general anaesthesia. Florvaag E. New Horizons – Allergy. 2005; No 2
30. Anaphylaxis: diagnosis and management. Brown SGA et al. MJA 2006; 185 (5): 283-289
31. Anaphylaxis during anaesthesia: diagnostic approach. Ebo DG, Fisher MM et al Allergy May 2007; 62(5): 471-487
32. Use of cephalosporins, carbapenems and monobactams in penicillin allergic patients. Roland Solensky. www.uptodate 2009

