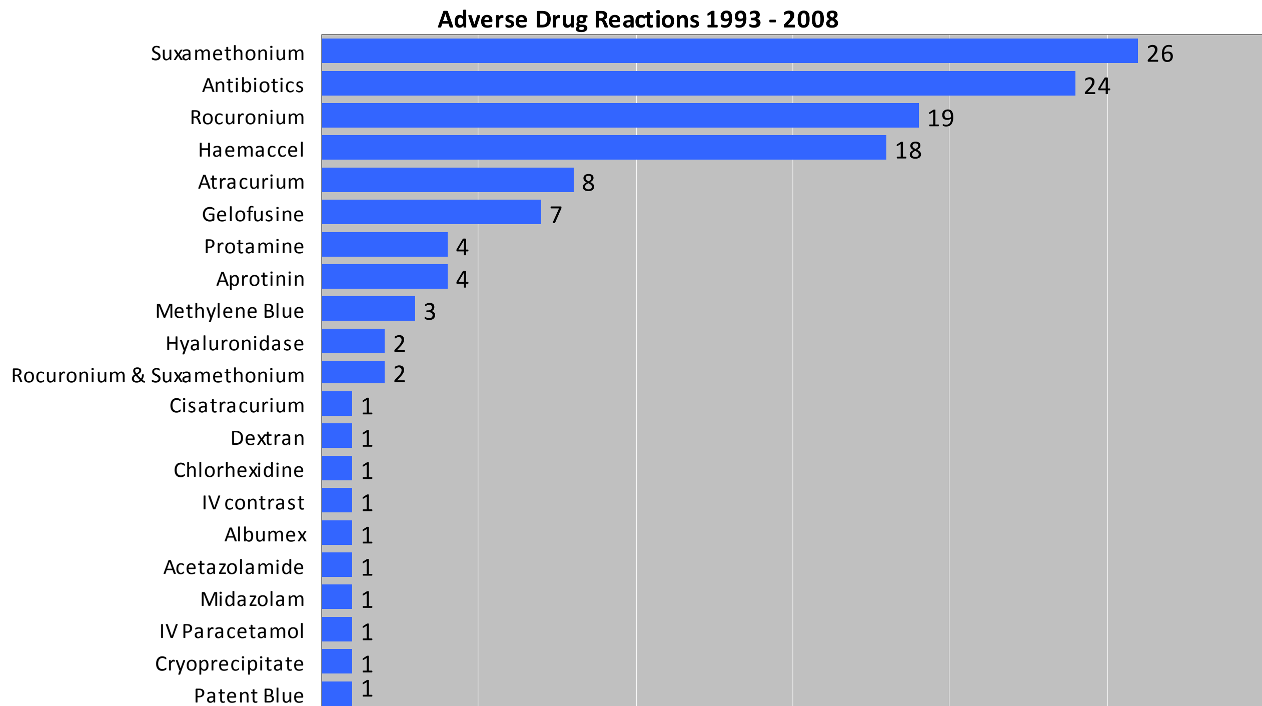
Adverse Drug Reactions

Since 1993 to the end of December 2008, the Victorian Consultative Council on Anaesthetic Mortality and Morbidity (VCCAMM) has received a **total of 127** cases of drug sensitivity.



1. Life threatening anaphylactic reactions to muscle relaxants comprises the highest risk. It is suggested that whenever unexpected hypotension is encountered during induction, it is wise to consider anaphylaxis and institute treatment with adrenaline, even if the diagnosis is in doubt. A number of instances of post-induction hypotension have resulted in myocardial infarction and serum tryptase estimations have revealed the underlying cause.

2. Reactions to intravenous antibiotics are also significant and frequently difficult to manage. In the case of cephalothin, careful inquiry should be made with regards to previous hypersensitivity reactions to cephalosporins and penicillin and previous experience of major allergy to penicillin should be a contraindication to the use of cephalosporins as there is some evidence of cross allergenicity. In addition, any patient who has exhibited any form of allergy, especially to drugs, should receive intravenous antibiotics very cautiously.

   RECOMMENDATIONS: Although there is no recommendation for a prior test dose in the pharmaceutical literature, the Council believes that it is safe and conservative practice to administer a prior test dose with a *diluted* solution. It is also recommended that the drug be administered to the patient *prior* to the induction of anaesthesia but while under the surveillance, so that when there is a reaction, a temporal relationship can be established between the two events. For vancomycin, it is mandatory to always administer the drug as an infusion over 60 mins, to prevent hypotension and florid cutaneous vasodilatation (red man syndrome).

3. Adverse reactions to Haemaccel were only classified as such where there was no other obvious cause for the acute hypotension or where there was evidence of a skin rash. Council is aware that the formulation of the drug was changed several years

ago and many, but not all, of these cases antedate these changes. Haemaccel is no longer manufactured. Although there are less reports of reactions to Gelofusine when compared to Haemaccel, they continue to be reported.

4. Hypotension occurring after the injection of methylene blue has been reported. In one case there was a rise in serum tryptase but in others, rapid infusion was judged to be the cause. Methylene blue should be infused over at least 20 minutes.

5. Aprotinin (Trasylol) is a serine protease inhibitor isolated from bovine lung tissue. It has been used to reduce blood loss and consequent transfusion requirements in patients at risk of significant blood loss, particularly in cardiac surgery and liver transplantation.
   Hypersensitivity reactions due to histamine release ranging from mild skin rashes and urticaria to anaphylaxis and death – occur in < 0.1 - 0.6% of patients on initial exposure. However, re-exposure is associated with an increased incidence of 3 – 9% allergic reactions.
   Aprotinin specific immunoglobulin IgG antibodies have been reported in almost 50% of patients after initial exposure. However its relevance to an allergic reaction is not clear, although one study showed persistence of these antibodies for up to 4 years. It is suggested that an interval between exposures of less than 6 months resulted in a significantly higher incidence of hypersensitivity reactions.
   Skin testing is not a reliable indicator of pre-existing antibodies to Aprotinin and IgG assays are not able to be reliably interpreted.

   RECOMMENDATION: That **NO** patient should receive a second dose of Aprotinin within six months of a prior dose and that all patients should be given a test dose of 1ml (1.4mg) Aprotinin at least 10 minutes prior to the loading dose

   It is noteworthy that aprotinin has now been withdrawn from the market for reasons unrelated to allergic reactions.

VCCAMM
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