# Anaphylaxis to Neuromuscular-blocking Drugs

## *All Neuromuscular-blocking Drugs Are Not the Same*

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IN the current issue of ANESTHESIOLOGY, Reddy *et al.*[1] report a two-hospital, retrospective, observational, cohort study confirming that anaphylaxis is more common with rocuronium and succinylcholine than with atracurium, a topic that is difficult to assess and was first highlighted in this journal in 2003.[2] Although any medication can potentially cause perioperative anaphylaxis, neuromuscular-blocking drugs (NMBDs), antibiotics, latex, and chlorhexidine are the most likely to do so. Regional differences regarding the relative risk of allergic reactions to NMBDs do exist. NMBDs represent the dominant causes of anaphylaxis in several countries and regions such as France,[2–4] Norway,[5] Spain,[6] and Australasia,[7] whereas other agents may be primarily involved in other countries.[8] Nevertheless, allergic reactions to NMBDs remain a serious concern for anesthesiologists because death may occur even when reactions are rapidly and adequately treated.[9] The reported incidence of perioperative anaphylaxis is quite varying, ranging between 1:3,500 and 1:20,000. Part of the variability is likely due to difficulty in determining the exact exposures to the numerous drugs, blood products, and agents used in the operative setting. The number of documented cases of intraoperative anaphylaxis is typically reported in aggregate for a large population, leaving the specifics of the total amount and type of medications the population was exposed to in question.

***"There are many factors that will influence the choice of a specific NMBD, depending on the clinical situation, [including] the likely increased allergic risk associated with succinylcholine and rocuronium...."***

In the study by Reddy *et al.*, the authors take the advantage of their ability to retrieve detailed information concerning new patient exposure to each NMBD from electronic anesthetic records available in the two participating centers over 7 yr. This allowed a more precise estimate of the number of patients exposed as the denominator when calculating the relative risk of allergic reactions associated with the use of each NMBD. This method helps eliminate the primary concern with data based on drug sales, which have the potential to overestimate the exposure resulting in a potential underestimation of anaphylaxis rate. Interestingly, the authors' findings are similar to the estimates of allergic reactions to NMBDs based on drug sales. This study confirms the increased relative risk of allergic reaction to succinylcholine and rocuronium in countries where a high rate of reaction to NMBDs is reported.

The surveillance of intraoperative adverse drug reactions still represents a clinical and statistical challenge[10] because these reactions are rare, random, and mostly independent from the repeated exposure of patients to anesthesia. In addition, possible biases and underreporting make comparison between drugs relatively difficult. Another weakness of any reporting system is that responsible physicians seem to have little understanding of which drug is actually causing the anaphylactic reaction when several drugs are simultaneously administered during anesthesia induction due to a lack of a single confirmatory test.[11] With thorough review in this study, it was noted that 9 of the 21 cases of identified NMBD anaphylaxis did not meet the standard skin test criteria for positivity but correctly warranted inclusion based on clinical picture and adjunct testing.

Because identification of the anaphylactic mechanism, of the responsible drug, and of the alternative safe agents is not always straightforward, a standard use of tryptase measurements in case of suspected allergic reactions and investigation of these reactions in compliance with established guidelines[12] by allergists trained in the field of drug allergy working in close collaboration with anesthesiologists should be promoted.[13,14] Reddy *et al.* confirm that

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allergic reactions are associated with greater tryptase and greater severity than nonallergic cases. Because no predictive test can help us to identify patients at risk before any reaction, reduction of the risk of perioperative anaphylaxis can only be based on secondary prevention.[12] This report provides a strong motivation for a thorough and systematic investigation of any hypersensitivity reactions occurring during the perioperative period[15] to avoid any undesirable subsequent exposure to an offending agent toward which one is already sensitized. This necessity is further supported by the small number of minor reactions diagnosed in this study, probably related to under-referral of mild reactions to all agents, a reality clearly demonstrated in the literature.[4,15] The authors were not able to determine the number of reactors who were receiving anesthesia for the first time, had a history of multiple anesthetic exposure or even history of previous reaction. This information would be helpful in future studies in determining sensitization patterns. Going forward, studies of intraoperative anaphylaxis should include a standard definition of anaphylaxis, uniform skin testing, specific immunoglobulin E drug testing, tryptase measurements, and review by an allergist in conjunction with an anesthesiologist.

The risk of allergic reactions is not the only drug characteristic that anesthesiologists must take into account when making their clinical choice. In view of the number of side effects associated with the use of succinylcholine, a controversy exists concerning replacing this old drug by rocuronium for rapid sequence induction.[16] Nevertheless, because of their rapid onset of effect, both drugs will remain essential in the anesthesiologists' armamentarium. Another interesting point that must be considered is that rocuronium can be rapidly reversed by sugammadex, a possibility that can make rocuronium a drug of choice in countries where sugammadex is available.[17] Sugammadex has also recently been proposed to improve recovery in case of anaphylaxis to rocuronium[18]; however, its ability to play a role in reaction reversal remains controversial.[19,20] Moreover, hypersensitivity reactions, either allergic or not, have been reported with sugammadex,[21] and this drug has not been approved in the United States at present.

Due to the amount of vecuronium exposures, Reddy *et al.* were not able to provide specific information concerning the risk associated with its use. This drug has been shown to have a lower risk of anaphylaxis than rocuronium in large epidemiologic studies[22] and its effect can also be effectively reversed by sugammadex.[23] They considered atracurium to be a safe alternative but were not able to comment on the relative risk associated with cisatracurium because this drug is not in use in Australasia. Cisatracurium has been shown to have the lowest risk of hypersensitivity reactions, either allergic or not, in large cohort studies,[3,22] and has also been shown to have the lowest rate of cross-sensitization with other NMBDs in allergic patients.[7,22] There are many factors that will influence the choice of a specific NMBD, depending on the clinical situation, but the likely increased allergic risk associated with succinylcholine and rocuronium, and the relatively low risk associated with atracurium and even more so with cisatracurium must be part of the clinical reasoning when considering the use of a NMBD.

## Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

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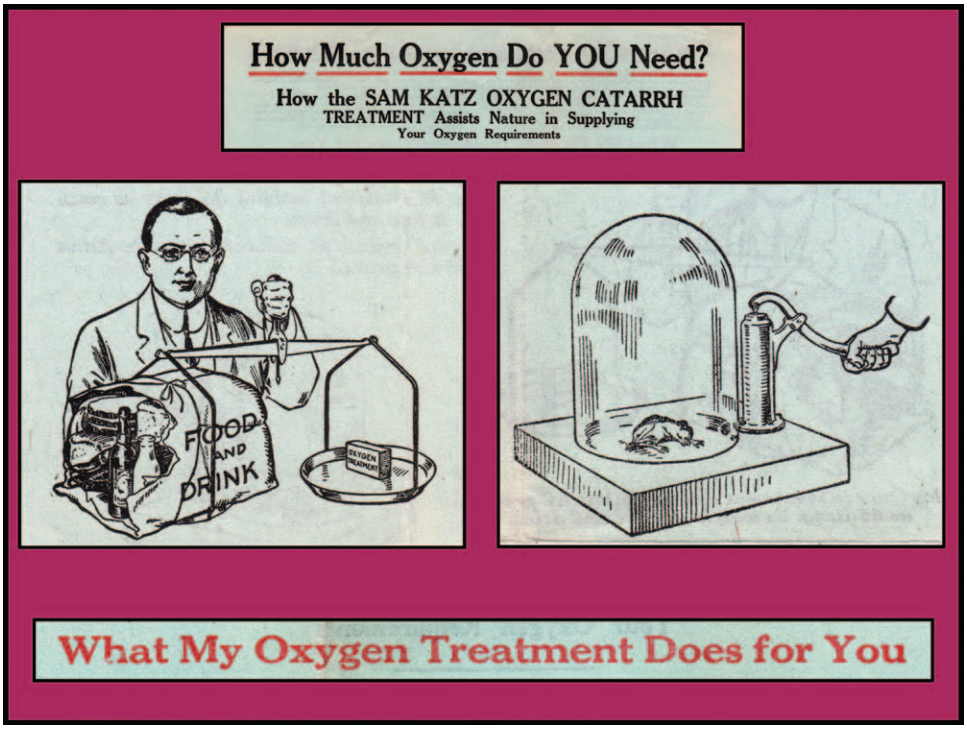
# Katz Oxygen Treatment for Catarrh




Just before World War I, the company of Chicago's Samuel Katz peddled his "Oxygen Treatment for Catarrh" as an oxygenating panacea. He advertised that his cure-all contained "as much Oxygen as 86 times its weight in food and drink" (*left*). Katz reminded his readers that if they placed "any living thing in a vacuum, without oxygen … it will die" (*right*). In 1917 another Chicago-based organization, the American Medical Association (AMA) published analyses of Katz Oxygen Treatment revealing it to consist of four discrete boxes, consisting chiefly of (1) "aloes," (2) "magnesium dioxide, magnesium carbonate and … calcium salts, with acacia," (3) "sodium perborate and tartaric acid," and (4) "cotton soaked in menthol." So ironically, Chicago provided a home to promoters (Katz and Company) and discreditors (the AMA) of the Katz Oxygen Treatment. (Copyright © the American Society of Anesthesiologists, Inc.)

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