

Correspondence and Replies

Safety of graded challenge in allergic patients

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TO THE EDITOR:

Graded challenge is a topic that is frequently discussed but lacks formal guidelines and safety data. In an attempt to determine the safety of graded challenge in patients with a questionable history of adverse drug reactions (ADRs), Iammatteo et al¹ performed a retrospective chart review at a single academic institution on patients seen over a 5-year period. The authors concluded, "Our findings, therefore, demonstrated that test doses are safe for evaluation of ADRs and that multistep challenges do not confer additional safety." We question the authors' assertion that they demonstrated safety of any of their protocols for graded challenge.

There were only a small number of bona fide drug-allergic patients in their study population. Of 456 patients, only 29 patients had IgE-mediated reactions to challenge. Those patients with current immediate hypersensitivity were the group at risk of serious ADRs including anaphylaxis. Most of the other patients who were challenged had no reaction, making the primary marker of "safety" the lack of persistent hypersensitivity and not the graded challenge protocol.

Jerschow et al,² Lazarou et al,³ and Ma et al⁴ have shown that the prevalence of fatal drug-induced anaphylaxis is low, and thus in the Iammatteo et al study, a sample size of 29 genuinely allergic patients is not large enough to assert the safety of the techniques.

In this study, various practitioners were able to successfully identify those not truly allergic but carrying an "allergic" label. Criteria for low risk included that the hypersensitivity reaction was distant in time, greater than 10 years, and mild. It can be concluded from this study that the providers were able to identify with high likelihood a population of patients who may undergo drug challenge with a low probability of being allergic. In this study, only 63 challenges resulted in an ADR. None of these ADRs was grade 3 or 4 severity. Although 3 patients in the test dose group received epinephrine, upon chart review the authors found "no documented objective findings that necessitated the administration of epinephrine." No anaphylactic reactions were reported.

In summary, given the lack of a truly allergic population and the small sample size, Iammatteo et al are unable to demonstrate the safety of drug challenge in genuinely allergic patients. Although it is reassuring to think that starting with a low dose of medication as a graded challenge enhances safety, experience with venomous insects has demonstrated that lethal anaphylaxis can occur with microgram quantities of potent allergens in allergic patients.^{5,6} The safety of drug challenge needs to be further addressed with a retrospective review of larger databases, a prospective study in a truly allergic population, or a survey study similar to those assessing the safety of immunotherapy.⁷ The authors deserve to be commended for adding to our understanding of how best to predict which patients are unlikely to react to drug challenge. However, caution is required in interpreting their conclusions regarding the "safety" of drug challenge in those who actually are at risk.

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REPLY

TO THE EDITOR:

We appreciate the opportunity to respond to the concerns raised by Ford et al¹ regarding our recently published retrospective review of all graded challenges and test doses performed over a 5-year period at our institution.² Our analysis demonstrated that test doses are safe in appropriately selected patients for the evaluation of adverse drug reactions. We observed a low rate of adverse drug reactions. When reactions occurred, they were mild and often did not require treatment. In this cohort, we compared multistep challenges to test doses and demonstrated that multistep challenges did not confer additional safety.

Ford et al¹ question our assertion of demonstrating the safety of test doses and graded challenges given the "small number of bona fide drug-allergic patients" in our study population. However, test doses and graded challenges should not be performed in patients

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