

Correspondence

Reply

To the Editor:

The correspondence by Francuzik et al¹ interrogates sex as a risk factor for anaphylaxis severity using an Anaphylaxis Registry database.² They confirm the increased incidence of anaphylaxis in premenopausal women compared with men found in other epidemiological studies. These findings had prompted us to evaluate the effect of sex in anaphylaxis in a controlled mouse model³ because sex biases in other allergic and nonallergic human diseases have been reproduced in mice and it allows for testing sex in the absence of other confounding factors. We demonstrated more severe reactions in female mice that were dependent on estrogens.³ Even though our mouse data, we would argue, may relate to the increased incidence of anaphylaxis in women because severe reactions are more likely to be recognized, the actual effect of sex on the severity of anaphylaxis in humans is of interest. Francuzik et al¹ report that unlike mice, males aged between 13 and 56 years have a slightly higher risk of severe anaphylaxis. As discussed below, we believe their registry cannot unequivocally address this question.

The registry includes patients who presented at specialized medical centers with anaphylaxis, a situation that may itself skew the assessment of severity because it may be influenced by differences between men and women in the initial recognition of symptoms or willingness to seek medical help. In addition, the reference describing the Anaphylaxis Registry² states that most patients received medical treatment, thus bringing into consideration the possibility that sex-related responses to therapy could affect assessment of severity grading.

Furthermore, this registry does not appear to have included questions relating to the reproductive phase nor gathered data on diet and medications that influence sex hormone levels of individual patients. Rather, to address such issues, they selected ages 1 to 12 years as prepubertal and 57 years and above as postmenopausal, when the reported median age at menopause is 51.3 years.^{4,5} It would have been much preferable to obtain such information from each patient during the course of study because the possibility exists that these selected ages for onset of puberty and menopause do not accurately reflect the study population.

In addition, the cases in the registry include a preponderance of anaphylaxis from insect venom,² a proportion unlikely representative of the most common elicitors in the general population.

Insect venom is reportedly an independent predictor of severity,⁶ and anaphylaxis elicited by insect stings has been recently associated with clonal mast cell disorders (diagnosed by bone marrow biopsy),⁷ thus possibly affecting the conclusion of this analysis.

We do, however, much appreciate this effort to assess anaphylaxis severity related to sex and would encourage that future epidemiological studies on anaphylaxis prevalence and severity consider sex and be designed to consider life events, diet, and medications that influence the levels of estrogens and androgens.

Valerie Hox, MD, PhD

Dean D. Metcalfe, MD

Ana Olivera, PhD

From the Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. E-mail: Ana.Olivera@nih.gov.

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