



Guest Editorials

Priority role of epinephrine in anaphylaxis further underscored—the impact on biphasic anaphylaxis



Anaphylaxis, the most severe manifestation of IgE-mediated hypersensitivity, is a condition that allergists have tremendous respect for, and as a result, are the practitioners perhaps most well versed in its appropriate management. Recommendations from national and international allergy organizations have long underscored the priority role of epinephrine in the treatment of this systemic allergic response.^{1–4} The importance of prompt administration of epinephrine in the setting of anaphylaxis is further emphasized from the findings of Alquarashi et al in their study published in this month's issue of the *Annals*.⁵

Alquarashi et al conducted a well-designed retrospective evaluation of 484 patients presenting to the emergency department with a diagnosis of anaphylaxis at 2 pediatric centers in Canada during the course of 2011. Patients needed to meet the 2006 National Institute of Allergy and Infectious Diseases and Food Allergy and Anaphylaxis Network diagnostic criteria for anaphylaxis to be enrolled, and all were children younger than 18 years. Charts were reviewed in detail to determine the presence or absence of biphasic reactivity. Baseline characteristics, comorbid conditions, inciting antigen, and detailed assessment of management strategies used were compared between children who developed a subsequent biphasic anaphylactic reaction with those who did not.

The overall incidence of biphasic anaphylaxis in this cohort was 14.7%, which is generally in keeping with other larger studies of this condition. The median time to onset of the second phase was 4.7 hours if it occurred while the patients were still in the emergency department and 18.5 hours if it occurred after discharge. Other prospective evaluations of biphasic anaphylaxis have similarly noted that these reactions can be quite delayed after the beginning of the asymptomatic window.⁶ Important predictors of biphasic reactivity included a longer time from the onset of symptoms to presentation in the emergency department, severity of the initial reaction (as noted by a wider pulse pressure, an increased rate of epinephrine use, and the need for >1 dose of epinephrine and a higher rate of intravenous fluid in the biphasic reactors compared with the uniphasic reactors), and, importantly, a time delay longer than 90 minutes was significantly associated with the biphasic response.

Delay to the administration of epinephrine in the setting of anaphylaxis has long been known to be a risk factor for fatality from anaphylaxis,^{1–3} and the study by Alquarashi et al adds to the growing body of literature suggesting that it also is a risk factor for biphasic reactions.^{7,8} Indeed, the converse has been shown

previously, in that if patients used a self-administration of epinephrine through an auto-injector and symptoms resolved within 20 minutes, then these individuals were identified as a subset who were universally protected from biphasic reactivity.⁶

There are multiple reasons to give epinephrine in the setting of anaphylaxis—the most important being that it is the only treatment that provides inhibition of further inflammatory mediator release from mast cells and basophils through increased cyclic adenosine monophosphate production owing to its stimulation of β -adrenergic receptors, in addition to the beneficial end-organ effects of α - and β -adrenergic stimulation.⁹ With this publication, clinicians are reminded of yet another reason to give epinephrine and promptly in the setting of anaphylaxis—the potential decreased risk for biphasic responses.

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Disclosures: Dr Ellis is on the speaker's bureau of Pfizer, Canada.