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Reply to: Medication contaminants as a potential cause of anaphylaxis to vincristine. What about drug specific antigens?

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To the Editor

We appreciate the informative letter by Dr. Nicholas Kounis and colleagues in response to our manuscript entitled "Medication contaminants as a potential cause of anaphylaxis to vincristine" [1]. Dr. Kounis *et al.* propose some questions about our report, and discuss it broadly in the context of drug allergy [2]. They first note that vincristine has been associated with allergic reactions of the Kounis type, which are characterized by acute myocardial infarction [3–5]. This is an important consideration given that one of the patients in our report experienced cardiac arrest following vincristine administration. However, multiple physicians documented circumstances and options that suggest the patient in question experienced a hypoxemic arrest. In addition, an EKG performed just after the event was normal, without signs of cardiac ischemia. Together, these additional considerations make a Kounis-type reaction less likely.

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The authors also raise the question as to whether premedicating with antihistamines or steroids could contribute to the anaphylaxis events observed in our study. There are rare examples of allergy to these medications [6]. However, the four patients in our study who were premedicated after their initial reaction to vincristine tolerated subsequent infusions. As such, allergy to antihistamines or steroids was not a contributing factor in our cases.

Lastly, Dr. Kounis and colleagues discuss the value of various testing modalities in evaluation of drug allergy. We agree that drug provocation testing is the gold standard for establishing the presence of an allergy. In the case of our study, seven of the eight patients tolerated vincristine subsequently, leading us to suspect a contaminant as the etiology of the reactions. Other major testing strategies in the field of allergy include cutaneous testing, and evaluation of serum levels of specific IgE molecules. However, commercially available and validated reagents for such testing are only available for penicillin [7]. Basophil activation testing has had mixed results, and additional studies with commercially available tests are needed prior to its acceptance as a diagnostic tool [7]. In the context of chemotherapeutics, taxanes (paclitaxel, docetaxel), platinum compounds (cisplatin, carboplatin, oxaliplatin), and asparaginase are known to cause allergic reactions. Validated testing approaches for these medications are limited at this time [7].

Though not commonly used in the context of chemotherapeutics, primary prevention is another testing modality relevant to drug-related adverse reactions. Perhaps the best examples of such screening come in the form of HLA typing, which is available for abacavir and carbamazepine hypersensitivity [8, 9]. Screening is advantageous if, among other things, a valid, rapid, inexpensive, and easily interpretable laboratory test exists, and the population frequency of the allele in question is relatively high [10]. In the context of HLA typing, this latter criterion is most often achieved by focusing on individuals of similar genetic background [9, 11].

In sum, the field drug-related adverse reactions is important and growing. Future research efforts should focus on understanding the immunologic mechanisms that underlie specific reactions. This will facilitate the development of new testing modalities for use in primary prevention, diagnosis, and management.

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