Drug Allergy Management on the Move

Pascal Demoly, MD, PhD, and Allison Ramsey, MD

Consensus to manage drug allergies are in place in most countries. This has allowed (1) major improvements in the understanding and management of drug allergy and hypersensitivity reactions and (2) productive collaboration among multiple specialties. Thus, although most data concerning drug allergy acquired over the past decade are being validated, some are being challenged, and some are evolving. The 2021 Drug Allergy Theme Issue aims to consider the past, current, and evolving drug allergy knowledge. This knowledge has strengthened the allergy/immunology specialty, given it more visibility, and promoted collaboration with other specialties.

Indeed, the relevance of the diagnosis and management of drug allergy to clinical medicine is supported by the rising number of articles published in drug allergy and hypersensitivity (Figure 1). As an example, the diagnosis of allergy to beta-lactams has been optimized over the past 20 years and simple flow diagrams developed to label and delabel as many patients with a suspicion of allergy as possible. Anaphylaxis to coronavirus disease 2019 mRNA vaccines in the context of the pandemic and vaccine safety surveillance programs is additional proof of the importance of drug allergy expertise, although with a completely different time frame. It has immediately led to numerous recommendations in different countries, led by allergists. The fear this new type of vaccine has aroused following the first cases of anaphylaxis has led to overprotective agency messages worldwide. The allergy community has reacted with careful messages to support the vaccination program and with research of reported reactions. Calls to allergy centers have exploded! This has actually strengthened surveillance programs and referrals to our clinics to detect, measure, understand, and prevent vaccine adverse events. The allergy/immunology impact on vaccine policy will be considerable, keeping in mind that more than a quarter of the world population is allergic to something.

In their timely article, Caballero et al reviewed the role of excipients in the field of drug allergies and vaccines. They provide an evidence-based review of the literature, covering epidemiology, mechanisms of these so-called hidden allergens, and for clinicians, clear strategies to recognize and test. They make the important distinction that excipients are rarely causes of reactions to most drugs, whereas they are usually the cause of hypersensitivity reactions to vaccines. Their thorough review details the excipients that should be considered in hypersensitivity reactions to drugs, including carboxymethylcellulose, gelatin, polyethylene glycol, and polyethylene glycol derivatives, with the addition of gelatin, polysorbate-80, and galactose-alpha-1,3-galactose for vaccines. The tables in this article are a valuable resource summarizing the current literature regarding immediate and delayed reactions to excipients in drugs and vaccines.

Caballero et al’s article and the other articles in the 2021 Drug Allergy Theme Issue center on the new and evolving knowledge that is challenging traditional drug hypersensitivity understanding and management. Many of these theme articles address difficult clinical scenarios, offering strategies regarding how to best proceed. Trubiano et al use a case-based approach to summarize the evidence and offer expert opinion regarding “treating through” reactions in the age of increasing antimicrobial resistance, complicated infections, and novel therapies where the historically recommended “avoid future use” may not be possible. Although the bulk of evidence exists for treating through mild maculopapular eruptions with trimethoprim/sulfamethoxazole, the authors also bring up the more challenging scenarios of a fixed drug eruption, symmetrical drug-related intertriginous and flexural exanthema, acute generalized exanthematous pustulosis, drug rash with eosinophilia and systemic symptoms, and Stevens-Johnson syndrome/toxic epidermal necrolysis, that is, potential severe T-cell-mediated drug reactions. Trubiano et al end their article with a helpful approach for the clinician considering a treating through strategy.

Trubiano et al discuss strategies to address a known hypersensitivity reaction to a drug, whereas Thong et al discuss prevention strategies. The evidence supporting prescreening is currently primarily in the area of HLA’s in drug- and ethnicity-specific patterns, such as HLA-B*57:01 genotyping before the use of abacavir. The authors bring up evolving work in the areas of nonsteroidal anti-inflammatory drug and beta-lactam hypersensitivity, as well as the lack of effective prescreening tools in perioperative anaphylaxis. The common practice of predemecating before radiocontrast exposure in patients with a history of an immediate reaction is challenged in this review, given the scant evidence supporting this practice. A paradigm shift in identifying alternative contrast agents through allergy/immunology input and potential skin testing, rather than using a predemecation strategy, is recommended. Radiocontrast allergy is an important area of evolving knowledge in which allergy/immunology physicians can lead clinical practice change through collaboration with colleagues from radiology and hospital-based medicine.
Thong et al discuss the lack of prescreening strategies for perioperative anaphylaxis in their work, whereas Vitte et al offer a further nuanced analysis of the role of tryptase measurement in this setting. The authors provide a succinct background on the genetics, structure, and role of serum tryptase, along with clinical phenotypes of tryptase gene mutations. A comprehensive discussion of the history and current state of laboratory assays for serum tryptase, along with timing of tryptase measurement, leads to the authors’ discussion of the rationale for use of acute and baseline tryptase measurements to aid in the diagnosis of perioperative hypersensitivity reactions. The authors’ recommendation that acute and baseline tryptase measurements should be obtained challenges the historical approach of the sole use of an acute tryptase, which itself may not even be widely used in centers without expertise in perioperative hypersensitivity. The analysis by Vitte et al brings up another opportunity for collaboration: between allergy/immunology and anesthesiology to better characterize perioperative hypersensitivity reactions through the use of baseline and acute tryptase measurements.

Penicillin allergy has illustrated, in many ways, the reach of allergy/immunology drug hypersensitivity expertise to diverse medical specialties. It has also been an area of evolving approaches and management. Allergy/Immunology practitioners initially challenged the penicillin allergy label through the use of penicillin skin testing, but more recent approaches have illustrated a role for direct penicillin challenges. Iammatteo et al take readers through the existing evidence for direct challenges in pediatric and adult patients with both delayed and immediate historical reactions. The authors synthesize this data into pediatric and adult management algorithms that risk stratify on the basis of reaction history. Penicillin allergy delabeling remains an opportunity for prime collaboration with allergy/immunology and other specialties. Our specialty has an opportunity to educate other medical specialties regarding penicillin allergy, particularly surrounding the identification of low-risk reaction histories, because these patients could potentially undergo delabeling through allergy/immunology-led formal institutional guidelines without a need for case-by-case allergy/immunology input. Such a systematic delabeling approach would represent a shift from the current approach in many institutions.

Ramsey et al discuss another important aspect of drug allergy: appropriate documentation in the electronic health record (EHR). Although the EHR drug allergy field exists to protect patients from recurrent adverse drug reactions, it has become clear that inaccurate and incomplete documentation in this EHR allergy module is a barrier to optimal medical care. The authors in this review examine the evidence regarding the current suboptimal state of EHR documentation, and discuss ways to improve the EHR allergy module with a focus on harnessing technology to do so. The use of technology, such as telemedicine and e-consults, in aiding the delabeling of drug allergies is also presented, along with proposed solutions to this complicated issue.

Most of the drug allergy literature addresses the use of traditional prescription or over-the-counter drugs used to treat medical conditions. Our last theme article challenges that very characteristic with a review of the current data surrounding cannabis and cocaine allergy, along with opioids and alcohol. Decuyper et al detail how, in some cases, the physiological effects of these drugs may be difficult to differentiate from hypersensitivity reaction symptoms, as is the case for cannabis and cocaine. They also discuss the current state of hypersensitivity testing for these drugs. Allergy/Immunology practitioners may increasingly encounter cannabis allergy, due to both its medical use and increasing legalization in several US states. Decuyper et al also detail immunologic and other adverse reactions to alcohol and potential etiologies for these reactions (eg, fining agents and sulfa). The discussion of medical conditions exacerbated by alcohol is particularly clinically relevant for our specialty, because they include chronic urticaria, mastocytosis, and systemic contact dermatitis.

Together, the carefully chosen reviews in the 2021 Drug Allergy Theme Issue summarize hundreds of original articles, bringing us a comprehensive digest accompanied by straightforward recommendations issued from the authors’ readings and clinical expertise in diverse areas of drug allergy. We hope you enjoy and learn from the series!

REFERENCES