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Commentary

Modern Approaches to Drug Hypersensitivity Diagnosis

Serena Takahashi*

Department of Clinical Pharmacology, Sakura University School of Medicine, Kyoto, Japan

DESCRIPTION

Drug Hypersensitivity Reactions (DHRs) represent a challenging and often perplexing area within clinical medicine due to their varied presentation, unpredictable occurrence and complex pathophysiology. In recent years, there has been growing awareness of the importance of accurate diagnosis to avoid unnecessary drug avoidance, which can limit treatment options and adversely affect patient outcomes. Effective diagnosis is a precise and thorough clinical history. The article reiterates that while history-taking may seem elementary, it remains the cornerstone for identifying DHRs. Main components such as the onset of symptoms, temporal relationship to drug exposure, prior tolerance to the suspected agent and the nature of the symptoms whether immediate-type or non-immediate-type help guide the clinician toward the appropriate diagnostic pathway. However, history alone is often insufficient to confirm the diagnosis or to distinguish between immune-mediated and non-immune-mediated reactions, necessitating the use of validated testing methods.

Skin testing, including Skin Prick Tests (SPTs) and Intradermal Tests (IDTs), continues to serve as an essential diagnostic tool, especially in IgE-mediated reactions such as beta-lactam allergy. The review appropriately underscores the variable sensitivity and specificity of these tests depending on the drug class involved. For example, penicillin skin testing is well standardized and demonstrates high negative predictive value, yet the same cannot be said for many non-beta-lactam antibiotics or chemotherapeutic agents, for which standardized reagents are lacking. The article also notes the limited utility of skin testing in non-immediate reactions, where delayed immune responses play a larger role.

Patch testing is another modality emphasized in the review, particularly relevant for diagnosing T cell-mediated reactions like maculopapular exanthema, fixed drug eruptions and Stevens-Johnson syndrome. While patch testing can offer supportive evidence, its sensitivity remains modest and interpretation often requires experience. Furthermore, the lack of standardized drug concentrations for various agents contributes to variability in outcomes, as the review rightly points out.

In vitro testing holds potential in improving the safety and specificity of diagnostics. The specific IgE assay, though useful for a select group of drugs like penicillin and a few muscle relaxants, is generally limited by the availability of validated tests and a high rate of false negatives. The article outlines advances in cellular assays such as the Basophil Activation Test (BAT) and the Lymphocyte Transformation Test (LTT), which aim to detect cellular immune responses to drugs. BAT is particularly relevant for immediate reactions, while LTT has potential utility in non-immediate hypersensitivities. Despite encouraging results from research settings, these assays are hampered by the need for specialized laboratories, technical variability and limited accessibility in routine clinical practice.

One of the most critical aspects explored in the review is Drug Provocation Testing (DPT), which remains the high standard in many cases where other tests fail to provide conclusive answers. The article cautiously advocates for its use, given the inherent risks of inducing a hypersensitivity reaction. It highlights the necessity of performing DPT in controlled environments with experienced personnel and emphasizes that its application must be judicious and individualized. Despite its risks, DPT plays an essential role in de-labeling patients with suspected drug allergies, particularly antibiotics, which often carry lifelong and unfounded labels.

Another emerging theme in the article is the role of pharmacogenetic testing in preventing severe idiosyncratic reactions. The association of HLA-B alleles with severe cutaneous adverse reactions, such as HLA-B57:01 with abacavir hypersensitivity and HLA-B15:02 with carbamazepine-induced Stevens-Johnson syndrome, has created the path for pre-treatment genetic screening in certain populations. These developments exemplify the transition toward personalized medicine, although the review wisely cautions that pharmacogenomic testing is not yet universally applicable and must be guided by ethnicity, drug-specific risk and population prevalence.

Correspondence to: Serena Takahash, Department of Clinical Pharmacology, Sakura University School of Medicine, Kyoto, Japan, E-mail: s.takahashi@sakurauniv.jp

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In summary, this updated review highlights that while significant advances have been made in the diagnosis of DHRs, no single test suffices in isolation. A comprehensive approach that integrates clinical acumen with a combination of skin, in vitro and, when necessary, provocation testing remains the current standard. Emerging techniques like cellular assays and pharmacogenomics hold potential but require further standardization and accessibility. Ultimately, accurate diagnosis of drug hypersensitivity is pivotal not only for patient safety but also for ensuring optimal therapeutic choices and stewardship of drug resources. The authors of the review successfully highlight the need for continued research, collaboration and guideline development to navigate the evolving area of drug allergy diagnostics.