



Progress in the understanding of hypersensitivity drug reactions

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The present issue on drug allergy deals with four major topics of major relevance to the understanding and evaluation of hypersensitivity drug reactions.

The first article dealing with the multiple drug hypersensitivity (MDH) syndrome is quite opportune as it is the first time that this entity is being reviewed in the Current Opinion of Allergy and Clinical Immunology's Drug Allergy series. Chiriac and Demoly [1] attempt to provide a definition of the syndrome in order to differentiate it appropriately from other adverse reactions induced by drugs, mainly cross reactivity and multiple drug intolerance. Although the definition of this syndrome can be a matter of debate [2], and is relatively uncommon in clinical practice, well defined cases with appropriate immunological work-up have been published in the literature.

It is difficult to define a syndrome in which multiple unrelated drugs are involved, and different apparently unrelated clinical manifestations occur. From the conceptual point of view, it is easier to understand this syndrome when similar pathophysiological mechanisms are involved, for instance those reactions in which only T cells are responsible; in contrast to T-cell mediated responses with IgE-mediated reactions or other types of responses. The review provides a list of the most relevant publications on this topic. When there is an underlying disease such as a viral infection, the pathogenesis of MDH appears clearer compared with when no background diseases coexist [3]. Although progress has been made in the understanding of the genes that predispose to hypersensitivity drug reactions [4,5], no studies are yet available for MDH.

The second review is dedicated to toxic epidermal necrolysis (TEN) [6]. Although previous articles in the Current Opinion of Allergy and Clinical Immunology series have analyzed TEN in detail [7–9], the authors provide new insights into the understanding of the pathophysiology of TEN [6]. It is clear that the number of causative drugs remains limited, although in general many drugs can be implicated. In this sense, they constitute well defined prototypes in which the genetics provide

valuable information. In these reactions there is not only very high mortality but also significant sequelae for survivors [7]. The information that the authors provide clearly indicate that we are making progress in understanding the pathomechanisms, particularly the genetic aspects [6], and monitoring of the acute response as has been pointed out in previous reviews in this journal [10]. The authors provide information about granulosa, a molecule clearly involved in the pathogenesis of the disease. The importance of monitoring the response is because we can identify putative markers that may in future be targets for therapeutic interventions. Other studies [11,12] have shown through monitoring the response in the acute stage and resolution period the involvement of a number of genes that are either up or downregulated during the process.

The third review is dedicated to nonimmediate reactions to contrast media [13]. This topic has also been reviewed in a previous issue [14] but the relevance of the subject deserves an update. Again the role of T cells is emphasized as in previous publications. Although contrast media are diagnostic rather than therapeutic agents, they are a very important group of organic chemical compounds involved in hypersensitivity drug reactions. As occurs with NSAIDs, in addition to IgE and T-cell mediated reactions, other mechanisms exist. In the case of these drugs is the activation of the complement and the kinin system in addition to other possible mechanisms. Contrast media produce accelerated reactions as do β -lactams with few series reported so far [15]. There are reasons to believe that nonimmediate reactions to contrast media are on the increase [13]. As alternative contrast media are often not available and cross-reactivity does not

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always occur, the search for an alternative is important. The value of skin testing may be limited and a controlled administration is often required to assess tolerance or cross-reactivity. Again as the authors mention in the article, monitoring of the acute phase provides important clues on the underlying pathophysiological mechanisms as has been shown in other hypersensitivity reactions to drugs [11,12,15].

The last article deals with angioedema induced by angiotensin-converting enzyme (ACE) inhibitors [16]. There is increasing interest in this entity and in fact it was a topic discussed at the EEC program last year. Drug-induced angioedema is common, and a significant proportion of patients with NSAID hypersensitivity develop angioedema in the absence of urticaria or any other accompanying symptoms [17]. As the authors state, there has been progressive increase in cases of angioedema due to ACE inhibitors [16]. Whether this is due to the increase in consumption of these drugs or other additional factors, the reasons remain unknown. Pharmacogenetic studies may provide some clues to the underlying mechanisms.

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Conflicts of interest

None declared.

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