Correspondence and Replies

Direct challenge in children with β-lactam allergies: Consensus is reached, but now it is time for accurate results

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To the Editor:

The remarkable work of Lucas et al[1] reinforces the uselessness of skin and serum testing for the evaluation of children with suspected non-anaphylactic β-lactam (BL) allergy and confirms the recommendation to perform a direct oral provocation test in most of them, including patients with a history of immediate reactions. I have some minor questions about the article. The authors stated that, to the best of their knowledge, it was the largest study examining children with immediate IgE-mediated reactions (n = 143). But immediate reactions were not defined in their work and are not inferred from data in Table II, where 84 reactions occurred in the first hour and 163 occurred in the 6 hours after the dose. Another confusing issue is the statement that 24 children had had a severe immediate reaction. Ignoring the fact that these data are presented in the discussion but not in the results, it is not clear how a severe immediate reaction is defined when severe reactors had been excluded for the evaluation, according to Table I. We recently reported[2] the largest cohort of children studied for suspected BL allergy, (n = 2,133), including 238 unquestionable immediate reactions (first hour after the dose), with a direct oral provocation test safely performed in 172 of them. The safety of this procedure is also confirmed by recent systematic reviews.[3,4] Direct oral provocation test is now the recommended procedure for children with non-severe immediate and non-immediate reactions to β-lactams in most recent guidelines.[5]

Lucas et al[1] observed that 8.3% of children had BL allergy confirmed by an oral provocation challenge: 2.1% in the single-day challenge and another 6.3% in a 5-day extended challenge. All reactions in the challenges were mild, mainly skin reactions. There is a possibility that some of the mild unspecific manifestations observed during BL challenges may not be caused by the BL, and may be a false-positive result of the challenge.[6] The possibility of a false-positive result increases as the challenge is extended a number of days, if any manifestation occurring on the days of the challenge (or even on the days after the challenge, as in the work of Lucas et al) is attributed to the drug. Extending the drug challenge may improve the sensitivity but at the expenses of declining specificity. It is hard to know whether the global accuracy of the drug challenge increases or decreases by extending the challenge by a number of days. A recent review[7] reported no conclusive benefit of extended compared with single-day challenges. Irrespective of the length of the challenge, as a way to obtain accurate results, we proposed that mild positive challenges should be repeated promptly (in a few weeks or months) to confirm the test, to avoid a wrong label for the patient and know the real rate of true allergy in children evaluated for suspected BL allergy.[2,6] It is time for more accurate BL allergy results in children.

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Reply to "Direct challenge in children with β-lactam allergies: Consensus is reached, but now it is time for accurate results"

To the Editor:

We read the comments on our report[1] by Moral et al[2] with interest. Regarding the first query concerning the 143 children with immediate IgE-mediated reactions, this number was derived from the sum of children with a clinical history indicative of a type 1 IgE-mediated reaction. Specifically, this total was calculated using data from Table II: initial reactions categorized by urticarial rash (grade 1: 79 + grade 2: 40 = 119), combined with initial reactions classified as grade 2 and grade 3 (19 + 5 = 24), resulting in a total of 143. We did not classify immediate IgE-mediated reactions based on the timing between dose and reaction owing to the significant number of children with missing data regarding an accurately reported time frame between dose and reaction. Additionally, in some cases in which reactions were reported within 6 hours, maculopapular rashes were described, which are not consistent with typical IgE-mediated reactions.

The 24 children with severe immediate reactions are listed in Table II[1] under Index Reaction as grade 2 and grade 3 reactions. This classification was based on parent-reported history.