educating patients about the management of possible systemic reactions, are followed when treating patients. Moreover, further investigations concerning the in-season administration of the five-grass pollen tablet will be needed.

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No need for skin and *in vitro* tests in most children with suspected allergy to beta-lactam antibiotics

To the Editor,
Zambonino et al. have reported the results of their large experience evaluating children for suspected hypersensitivity to beta-lactam antibiotics. In line with others and our own experience, most of them (about or more than 90%) were confirmed as tolerant. At last, they reinforce the well-known conclusion that drug provocation tests are an essential tool for diagnosis (1). We fully agree with this but, even more, we challenge the need for *in vitro* and skin tests for most of these children. In the work of Zambonino, specific IgE determinations were performed in 66 children (suspected of immediate reactions) and skin tests in 781 children (all but two with positive *in vitro* tests). As a result, hypersensitivity to beta-lactam antibiotics was diagnosed by these means in only six patients, and drug provocation tests were performed in the remaining 777 children. In view of these figures, we wonder:

- Are those six children really allergic to beta-lactam antibiotics? There is no answer because we do not know sensitivity, specificity, and predictive values of *in vitro* and skin tests. It has been stated that approximately 50% of patients with a positive penicillin skin test result will have an immediate-type hypersensitivity reaction when rechallenged with penicillin (2). Oral provocation test with beta-lactam antibiotics in 11 children with positive skin tests gave only four mild, mainly delayed, skin reactions (positive predictive value of 36%) (3). The reliability of specific IgE test is probably very low (4). A recent study showed a positive predictive value of 0% for intradermal tests with cephalosporins (5).
- What are the use and the costs (direct and indirect, for sanitary system and for families, money, and time) of performing such amount of negative *in vitro* and skin tests?
- Why not perform drug provocation test on every child? Only six more drug provocation tests would have meant 66 *in vitro* tests and 781 skin tests avoided. And a more conclusive diagnosis.
- Would a drug provocation test have been dangerous in those six children with *in vitro* or skin positive tests? Maybe this is the great question, but nobody really knows. First, it depends on the positive predictive value. If this is low, most of those children probably could tolerate beta-lactam antibiotics. Second, for really allergic children, how safe or dangerous a drug provocation test is? Again, nobody knows. But if we look at reports as this presented by Zamborino et al. (1), and by others (3, 6), positive drug provocation tests have never resulted in severe reactions or death. The probability of a severe reaction, according to published studies, seems very low.

From our point of view, the paper of Zambonino et al. greatly contributes to question the usefulness of *in vitro* or skin tests in most children with suspected hypersensitivity to beta-lactam antibiotics. Drug provocation test should be the standard of care for the evaluation of these children, providing a conclusive diagnosis with less time, suffering (for children) and resources consumed. Under controlled conditions, it is a safe procedure, probably even more than that commonly performed with foods. We suggest that skin tests may have a role in the setting of an acutely ill child declaring a history of any reaction related to beta-lactam exposure. Given the high negative predictive value for immediate reactions (2, 7) and fast results, it would be greatly useful to urgently decide the right treatment for a child with a severe infection. Maybe there is a role for *in vitro* and skin tests for those very rare children with a clear history of severe anaphylaxis with beta-lactam antibiotics, to confirm the diagnosis avoiding an uncertain provocation

test. On the contrary, most children evaluated for suspected beta-lactam antibiotic hypersensitivity (excluding those with a history of severe IgE or not IgE-mediated reaction) should have a drug provocation test performed to verify, easily and undoubtedly, whether they should or should not be treated with such antibiotic if needed.

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Possible recurrence of symptoms after discontinuation of omalizumab in anti-IgE-assisted desensitization to egg

To the Editor,

Procedures of desensitization to food in children who do not spontaneously outgrow their food allergy are increasingly being used. Some patients, especially those with severe allergy, have reactions during this process and must quit the procedure (1, 2). An alternative for these cases is to use omalizumab, as an off-label indication, and there are reports of successful and safe results in this type of patients (3–6). We report three cases of children with successful anti-IgE-assisted desensitization to egg who experienced reactions after discontinuation of omalizumab.

Case 1: A 9-yr-old girl was referred to our hospital for desensitization. She had been diagnosed with egg allergy when she was 11 months of age, because she had had vomiting and abdominal pain when first fed egg and had shown positive skin test and specific IgE. When first seen at our clinics, she had had symptoms of abdominal pain, vomiting, and oral pruritus with inadvertent ingestion of egg. Her skin tests were positive to ovoalbumin (OVA) and ovomucoid (OVM), and specific IgE was 155 kUA/l for OVA and 135 kUA/l for OVM. After informed consent, we tried a desensitization procedure, on prophylactic H1 antihistamines, with doubling doses of raw pasteurized egg white, starting from 0.5 ml diluted 1/100 (0.5 mg of protein). With 8 ml diluted 1/100 (8.5 mg of protein), she had repeated vomiting and the procedure was interrupted. A course of omalizumab, using doses recommended by the manufacturer, was started, and 2 months later, we performed the procedure again, which was successful, and the girl could tolerate a final dose of 50 ml of raw egg white (5400 mg of protein). She was challenged with an omelet, which was also well tolerated. She was instructed to eat at least an egg three times a week, and additional amounts were allowed at her own will. Omalizumab was administered 2 months after reaching the final dose, and it was then discontinued. The girl went on having the recommended amount of egg with good tolerance. Four months after stopping omalizumab, she started having symptoms of abdominal pain and vomiting when having egg. The symptoms persisted, so we decided to perform an open challenge with egg. The patient experienced the same symptoms with 5 ml of raw egg white. She was put on omalizumab again, and 2 months later, she underwent an open challenge with 1, 2, 4, 8, and 16 ml or raw egg white at one-h intervals, with good tolerance. The next day she tolerated one whole egg omelet. She is currently on the maintenance dose of at least one egg three times a week while receiving omalizumab.

Case 2: A 10-yr-old girl with egg allergy was referred to our hospital for desensitization. Her specific IgE was 23 kUA/l for OVA and 18 kUA/l for OVM. She was unable to tolerate the procedure, despite prophylactic H1 antihistamines, because of repeated vomiting with 8 ml diluted 1/100 of raw egg white. She was administered omalizumab for 3 months and could