

Letter to the editor

As investigators and members of the European Network for Drug Allergy (ENDA) of the European Academy of Allergy and Clinical Immunology, we wish to express our disagreement and concerns regarding the article recently published by Macy and Burchette in *Allergy* 2002;57:1151.

First, several assertions are poorly supported while other references containing relevant information are omitted. Reference (3), for example, does not report that penicillin allergic subjects have a major incidence of adverse drug reactions to non-betalactam antibiotics, and when discussing the decay in penicillin allergy and skin test sensitivity with time, other valuable information is omitted (1). When they mention that anaphylaxis with oral penicillins is rare, they base this on single case reports or old references, omitting data from large series indicating that amoxicillin, taken orally, is the most common drug inducing penicillin allergy and can give rise to severe systemic reactions (2). The statement that 'penicillin skin testing accurately identifies individuals who make anti-penicillin IgE' is not correct, because there are patients with specific IgE antibodies who are skin test negative (3).

They report the results of penicillin skin testing in 1081 patients between November 1994 and May 2000, finding that 17.8% were skin test positive to amoxicillin. In a previous study, performed by the same authors in 265 of these same patients between 1994 and 1996, only one (1.7%) responded to amoxicillin (4). How do the authors explain this large difference in such a short period of time? Nevertheless, we are pleased to read the authors' confirmation that skin testing

with amoxicillin identifies amoxicillin allergic patients.

The statement that 'the history is a poor predictor of who will be penicillin skin test positive' is too general. If the history is not taken by a trained person or is simply reported by the patient, this may be the case, but if the history is taken by specialists, the situation may well be different, especially in cases of anaphylaxis.

They state that penicillin skin testing is safe to evaluate any potential IgE-mediated adverse drug reaction. We strongly disagree with this, and reports exist of systemic reactions with skin test material (3). In fact, Macy himself found that 4% of the patients with positive skin tests developed systemic reactions, and even in patients with negative skin tests some patients suffered reactions (16 of 980; 1.6%), possibly allergic in origin. Do the authors still believe that skin testing in drug allergy involves 'risks well within those tolerated with any skin testing procedure'? Furthermore, in the group of patients that Macy describes in Table 1 with skin test positive, only 18 had clearly had an immediate reaction, 64 had developed a non-immediate reaction, and in 19 the timing was unknown, thereby confounding the results as skin test sensitivity varies according to the type of reaction.

Many important questions arise concerning the methodology of skin testing. First, the amoxicillin used was obtained from Sigma (4). This is a trihydrate amoxicillin that, as the authors state, cannot be dissolved beyond 4%, unless the pH is raised to 8.5, which converts it into a sodium salt. As far as we are aware, Sigma only provides amoxicillin for laboratory use, and it has not been approved for human purposes. Sec-

ondly, the amoxicillin currently used for skin testing in several European countries is a sodium salt, obtained from that used for parenteral administration. The final concentration of this parenteral drug, for therapeutic purposes, ranges from 100 to 200 mg/ml, so obtaining a solution of 20 mg/ml is perfectly possible. The authors have inexcusably confused two different types of amoxicillin. The concentration of 20 mg/ml used in amoxicillin and ampicillin intradermal testing has been widely validated (2, 3, 5), and is the one recommended by the European Network of Drug Allergy (ENDA) (6).

Many other statements or assumptions are not supported by the data, such as the fact that only 33% of penicillin skin test-positive patients will react after oral penicillin intake. The suggestion that there is a low degree of cross reactivity between penicillins and cephalosporins is oversimplification. Last, but by no means least, the assumption that penicillin can be administered safely in penicillin skin test-negative individuals is not supported, as skin testing sensitivity is not 100% accurate, and the possibility of a person having a negative skin test but being truly allergic is 30% (3). We believe that it is the duty of any researcher to mention all recent data, whether they agree or otherwise with the results reported, in order to provide the reader with adequate information.

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