

Importance of repeat testing in the diagnosis of penicillin allergy

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SIR, In the May 2005 issue of this Journal Lammintausta and Kortekangas-Savolainen¹ presented an interesting article about the usefulness of skin tests in determining drug hypersensitivity. We have found the results to be very helpful as there are only few reported works about the prevalence of positive skin tests in the context of allergic reactions. However, we have some points of contention.

Although both patch tests (PTs) and intradermal tests (IDTs) are used for the diagnosis of nonimmediate reactions to aminopenicillins, and both tests appear to be valuable, delayed-reading IDTs appear to be somewhat more sensitive² than PTs, but also less specific.³

In the report by Lammintausta and Kortekangas-Savolainen, beta-lactam antibiotics were the drugs more often suspected and tested. However, IDTs with major and minor determinants were carried out only in 31 of 342 patients with suspected penicillin allergy and none of them elicited a positive reaction. The European Network for Drug Allergy (ENDA) recommends testing in most patients in whom penicillin allergy is suspected.⁴ In fact, most diagnoses of penicillin allergy have recently been reported to be obtained by means of the IDT.^{5,6} Between January 2002 and June 2005 we evaluated 604 patients with suspected beta-lactam allergy. In all of them, after written informed consent, skin prick tests and IDTs were performed with benzylpenicilloyl polylysine (PPL), minor determinants mixture (MDM; including benzylpenicillin, benzylpenicilloic acid and sodium benzylpenicilloate), penicillin G and the suspect drug if it was other than penicillin. PPL and MDM were purchased from two different companies (Allergopen®; Allergopharma, Reinbeck, Germany and Diater SA, Madrid, Spain). If the skin tests were negative, controlled drug challenge was performed under strict supervision. After 15 days the skin tests and drug challenge were repeated, as recommended by ENDA.⁴ After completing the study, 66 patients were diagnosed with beta-lactam allergy, 60 by skin testing and 10 of those in the repeat tests. From 1108 challenges with beta-lactams in 554 patients, there were only six positives following a previously negative skin test.

In the report by Lammintausta and Kortekangas-Savolainen, repeat testing was not carried out. ENDA describes that the natural history of allergy to penicillin is such that patients may lose sensitivity or become negative in skin testing.⁴ Because of that, repeat testing has been recommended in patients with a positive history and negative skin and *in vitro* tests, even in those showing a good tolerance after drug provocation testing.⁴ ENDA recommends that repeat testing should follow the same protocol and be performed between 2 weeks and 1 month after the first tests.^{3,7} Our results showed that 16% of subjects (10 of 60) who showed tolerance to beta-lactams in the first challenge were diagnosed as

sensitive after repeat testing. In one patient with an unequivocal history of allergy to penicillin a third evaluation was necessary to produce a positive skin test.

Although penicillin allergy has been vastly overdiagnosed, and too many people are incorrectly labelled as allergic to penicillin,⁸ misdiagnosis is also a risk to consider, as a considerable percentage of patients was able to lose sensitivity or was negative in the first evaluation. Repeat testing, which could be considered as a booster,⁷ and the determination of specific IgE levels,⁹ will help to obtain an accurate diagnosis of beta-lactam allergy, although the majority of the penicillin-allergic donors failed to produce penicillin-specific IgE *in vitro*, when their lymphocytes were cultured in the presence of allergen.¹⁰

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