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The autologous serum skin test may be used as a marker for histamine releasing autoantibodies in urticaria and is not relevant to other subject groups

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Taskapan *et al.* recently reported a high frequency of autoreactivity in healthy control subjects, patients with nonallergic asthma and rhinitis (NAAR), allergic rhinitis or bronchial asthma (AR/BA) and chronic idiopathic urticaria (CIU).¹ They concluded that a positive reaction using the autologous serum skin test (ASST) might be a nonspecific phenomenon, and suggest that the significance of the ASST in CIU should be re-evaluated. There are some important misconceptions in their article, which question the conclusions and invite re-inspection of the authors' data.

Firstly, the authors used the definition of a positive ASST response as a serum weal diameter of 1.5 mm larger than a negative normal saline control at 30 min, as reported by Sabroe *et al.* for patients with CIU.² However, in the Sabroe study, this threshold was adopted in order to define the statistical performance characteristics (sensitivity, specificity, positive and negative predictive values) of this test with respect to *in vitro* serum basophil histamine release activity in a prespecified group of patients, namely those with CIU. Any other usage of this test in any other group of individuals, apart from patients with CIU, needs *de novo* examination, clear definition of its role as a predictor of a specific outcome, and subsequent analysis to define the optimum threshold for this outcome of interest. As Taskapan *et al.* did not give data from a basophil histamine-release assay, there is no rational justification for adopting the same criterion as Sabroe *et al.* because the primary purpose of the test in chronic urticaria (CU) is to screen for functional autoantibodies and thereby define a subgroup of patients with autoimmune urticaria. We are not aware of any studies that have demonstrated histamine-releasing autoantibodies in patients with NAAR or AR/AB, or in healthy subjects.

Secondly, the development of an inflammatory response, characterized by redness and swelling, is fundamental to a positive ASST, whereas non-inflammatory oedema due to extravascular injection of serum or saline is not. It is usual to detect some residue

of this at 30 min, whereas a strong ASST response in urticaria will still be present at 2 h.³ There are therefore two components of a biologically important skin test response that should be recorded: redness and duration, but the authors did neither. Sabroe *et al.* defined the criterion for a positive ASST as a red weal response, but neither Taskapan *et al.* nor Guttman-Yassky *et al.*⁴ (who also reported a high frequency of ASST positivity in healthy controls) included redness in their definition. Grattan *et al.* were the first to describe the ASST in patients with CIU in 1986.³ They used a much stricter criterion for defining a positive response (a difference in weal diameters between serum and saline skin tests of ≥ 5.0 mm and the surrounding erythema being ≥ 10 mm at 2 h) to separate biologically important positive reactions from nonspecific responses. They found positive responses in 7 of 12 patients with CIU but in none of 19 healthy controls. It would be interesting to know if any of the ASST-positive subjects reported by Taskapan *et al.* would have met this more stringent criterion. In the Grattan study, venesection and skin testing at different times of urticarial activity were also examined without differences being found.

Although generation of bradykinin and C5a during blood clotting has been proposed as a cause of false-positive ASST results, this has not been studied *in vitro* to our knowledge and therefore remains speculative. It is our experience that short-lived erythematous responses can occur in a minority of subjects without CU but it should not be a surprise that nonspecific mast-cell degranulation might occur after needling the skin and injecting fluids intradermally. The first description of the ASST was in 1946 by Malmros, who tested 956 patients.⁵ In 53 patients, he found a weal response similar to that provoked by histamine, which appeared within 15 min, and typically disappeared within 30–45 min. Late reactions persisted to the next day in a few patients. Of these 53 patients, 16 had asthma and 6 had urticaria, with the rest having a variety of conditions. A group of 35 post-partum women was also tested, and 5 had a positive reaction by his criterion, so there is a precedent for finding an early weal response to ASST in conditions other than urticaria. The real question is not 'how often does it occur?', but rather 'what does it mean?'.

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