

Correspondence

Is the autologous plasma skin test in patients with chronic urticaria really useless?

To the Editor:

We read with interest the letter by Metz et al¹ about autologous serum and plasma skin testing in patients with chronic urticaria (CU), which was prompted by one of our previous articles also published in the *Journal*.² We appreciate that our recent work has elicited interest in other groups of researchers; however, because Metz et al¹ have obtained results that are not completely in line with our findings and have argued about the interpretations we gave of our recent findings in patients with CU, we think that a response is warranted. To this end, we wish to point out the following.

First, regarding the differences in the prevalence of positive autologous plasma skin test (APST) results in our versus the authors' hands, the authors themselves state that the prevalence of a positive autologous serum skin test (ASST) result ranges from 7% to 76% in the literature, "possibly reflecting patient selection and differences in methodology and response interpretation." For example, as a difference from previous reports, in a recent article³ ASST results were positive in 55.5% of healthy subjects versus 52.5% of patients with CU. Clearly, methodology and interpretation are especially important because, in our hands, the APST often produces a clear-cut flare (up to 30 × 30 mm in diameter) with little wheal; needless to say, saline scores totally negative and histamine skin prick testing causes a normal wheal-and-flare reaction in these patients. We classify these patients as having positive APST results; if Metz et al¹ consider skin reactions positive only if a large wheal is present, this might explain the differences between our findings and theirs.

As a matter of fact, in the Metz et al¹ study, the ASST and the APST score differently in 47 of 200 (about one fourth) patients, which suggests that irrespective of their higher or lower prevalence, the 2 tests do not overlap. Unfortunately, Metz et al¹ refrain from commenting on this point.

We have never claimed, either in the first study² or in the subsequent study,⁴ that results on the APST are more frequently positive than those on the ASST because of the presence of thrombin. On the contrary, in the Discussion section of the first article, we pointed out that "because of its extremely short half-life, it is unlikely that the wheal-and-flare reaction ... is caused by thrombin itself."² The observation of a different prevalence of positive skin test results with autologous plasma and serum in patients with CU simply prompted us to investigate the coagulation cascade, which in effect turned out to be activated and to parallel the disease severity.^{2,4} We cannot exclude that a positive APST result has nothing to do with thrombin and that we had only a lucky strike, but the fact remains that the coagulation cascade is activated and that eosinophils seem the main actors in this sense.⁵ These findings were recently confirmed by

independent researchers.^{6,7} Interestingly, we found a more marked thrombin generation, as indicated by higher F1+2 levels, in patients with positive ASST and positive APST results than in patients with negative ASST and positive APST results, indicating that the coagulation cascade is more activated in the former than in the latter and suggesting that probably thrombin is not responsible for skin reactivity to autologous plasma. As previously pointed out, the mediator of skin reactivity is probably another molecule, and the activation of coagulation might represent an intermediate stage in CU pathophysiology.

The fact that in the Metz et al¹ study patients with positive ASST results show a more impaired quality of life is not surprising because the ASST (but not the APST) is associated with the presence of autoantibodies the presence of which is associated with more severe disease. This point as well was stressed in our study.²

In conclusion, we think that the observations by Metz et al¹ do not tarnish the relevance of our recent findings about the possible role of coagulation and eosinophils in the pathogenesis of CU in patients with or without detectable autoantibodies.

Riccardo Asero, MD^a

Alberto Tedeschi, MD^b

Massimo Cugno, MD^{b,c}

From ^aAmbulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano (MI), Italy;

^bUnità Operativa di Allergologia e Immunologia Clinica, Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Fondazione IRCCS, Milano, Italy; and ^cDipartimento di Medicina Interna, Università di Milano, Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Fondazione IRCCS, Milano, Italy. E-mail: r.asero@libero.it.

Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

REFERENCES

- Metz M, Gimenez-Arnau A, Borzova E, Grattan CEH, Magerl M, Maurer M. Frequency and clinical implications of skin autoreactivity to serum versus plasma in patients with chronic urticaria. *J Allergy Clin Immunol* 2009;123:705-6.
- Asero R, Tedeschi A, Riboldi P, Cugno M. Plasma of patients with chronic urticaria shows signs of thrombin generation and its intradermal injection causes wheal and flare reactions much more frequently than autologous serum. *J Allergy Clin Immunol* 2006;117:1113-7.
- Taskapan O, Kutlu A, Karabudak O. Evaluation of autologous serum skin test results in patients with chronic idiopathic urticaria, allergic/non-allergic asthma or rhinitis and healthy people. *Clin Exp Dermatol* 2008;33:754-8.
- Asero R, Tedeschi A, Coppola R, Griffini S, Paparella P, Riboldi P, et al. Activation of the tissue pathway of blood coagulation in patients with chronic urticaria. *J Allergy Clin Immunol* 2007;119:705-10.
- Cugno M, Marzano AV, Tedeschi A, Fanoni D, Venegoni L, Asero R. Expression of tissue factor by eosinophils in patients with chronic urticaria. *Int Arch Allergy Immunol* 2009;148:170-4.
- Wang F, Tang H, Xu J, Kang K. Activation of the blood coagulation cascade is involved in patients with chronic urticaria [letter]. *J Allergy Clin Immunol* 2009; [Epub ahead of print].
- Fujii K, Usuki A, Kan-No Y, Ohgou N. Elevation of circulating thrombin-antithrombin III complex and fibrin degradation products in urticaria. A laboratory finding unrelated to intravascular coagulopathy. *J Dermatol* 2008;35:308-10.

doi:10.1016/j.jaci.2009.02.039