

Placebo effects were not observed in patients with asthma compared with no treatment in a recent study by Hróbjartsson and Gøtzsche.³ It is unlikely that a placebo effect had any significant effect in our analysis. Some symptomatic improvement at the end of the extension phase can be a result of the reversible nature of the disease.

Our study was carefully designed and conducted. For the reasons described, it is unlikely that the cost-effectiveness of omalizumab is significantly greater than we suggested. It is very unlikely that this agent will prove to be cost-effective if given to a broad population either in a study setting or in a real world setting.

A prospective study evaluating the direct as well as indirect costs of severe asthmatic employees treated with omalizumab would be valuable to address some of the concerns raised by Asche et al.¹

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REFERENCES

1. Asche CV, Brixner DI, Oderda GM. Has the cost-effectiveness of Xolair (omalizumab) been underestimated? *J Allergy Clin Immunol* 2005;115:1095.
2. Birnbaum HG, Berger WE, Greenberg PE, Holland M, Auerbach R, Atkins KM, et al. Direct and indirect costs of asthma to an employer. *J Allergy Clin Immunol* 2002;109:264-70.
3. Hróbjartsson A, Gøtzsche PC. Is the placebo powerless? An analysis of clinical trials comparing placebo treatment with no treatment. *N Engl J Med* 2001;344:1594-602.

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Cold temperature challenges for acquired cold urticaria

To the Editor:

I agree with Siebenhaar et al¹ that the use of an objective electronic device for cold stimulation has appeal when testing patients with acquired cold urticaria. The Peltier device as described by the authors¹ apparently can apply a specific calibrated cold temperature stimulus directly to a subject's skin. This methodology has the advantage of providing reproducible standardized cold stimulation, which is especially important when retesting a subject to determine medication suppression and/or evidence of spontaneous remission. Use of ice or other cold stimuli does not provide a standardized temperature stimulus, and immersion of a hand in an ice slurry can induce systemic reactions.

The Peltier device apparently has the capacity to stimulate skin over a wide range of temperatures (0°C to 45°C). This capacity is of particular interest when evaluating patients with negative cold stimulation test results

(0°C to 4°C) despite convincing histories of urticaria after cold exposure. However, testing at a higher threshold temperature can induce wheals in some of these patients. This observation is important, because some patients with acquired cold urticaria may be missed with 0°C to 4°C ice testing but may be diagnosed by use of a cold stimulus with temperatures above freezing.

I believe there is still value in performing a graduated time threshold test, referred to as the *cold stimulation time test*.² Patients with acquired cold urticaria exhibit a time threshold for induction of wheals after application of a cold stimulus. Briefly, an ice cube in a beaker or plastic bag is applied to the forearm for 5 minutes. After rewarming of the skin to normal skin temperature, the reaction is read. If a confluent wheal is induced, the test is repeated at 1 minute decrements at different skin locations on the arm (to avoid cold-induced desensitization) to determine the minimum time required to induce a confluent wheal. Conversely, if the 5-minute cold test result is negative, the test is repeated at 1 minute increments at different skin locations on the arm to a 10-minute time test. If the test result is negative after 10 minutes, these patients may need testing with cold temperatures that are higher than 0°C to 4°C. Once the minimum time threshold is established, the patient can be placed on an antihistamine and be retested 2 or 3 weeks later. The repeat cold stimulation time test is often prolonged compared with baseline, which establishes the suppressive effect of the therapy. In addition, one can determine whether the patient is improving spontaneously by discontinuing suppressive medications and repeating the cold stimulation time test to determine whether the time required to induce a confluent wheal is longer than baseline. Prolongation of the cold stimulation time test as compared with baseline correlates with remission of acquired cold urticaria.

In summary, I concur that the Peltier method can provide a standardized cold test for patients with acquired cold urticaria and for patients with convincing histories of cold urticaria who have a negative test result at 0°C to 4°C. However, I believe there is also value in performing the cold stimulation time test, either with the Peltier device or with ice in a plastic bag, to test for therapeutic efficacy and to predict spontaneous remission.

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REFERENCES

1. Siebenhaar F, Staubach P, Metz M, et al. *J Allergy Clin Immunol* 2004; 114:1224-6.
2. Wanderer AA, Hoffman HM. The spectrum of acquired and familial cold-induced urticaria/urticaria-like syndromes. *Immunol Allergy Clin North Am* 2004;23:259-86.

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