

Letter to the Editor

A survey of allergists regarding the association of thyroid autoimmunity with chronic urticaria

To the Editor:

The Urticaria and Angioedema Committee of American Academy of Allergy, Asthma & Immunology (AAAAI) developed a questionnaire to survey the opinions of the members of the AAAAI regarding the possible association of chronic urticaria (CU) and thyroid autoimmunity. The objectives of this preliminary survey were to determine whether there was consensus or variability in the opinions of interested AAAAI members about the link between thyroid autoimmunity and CU and whether there was consensus or variability regarding treatment of such patients with thyroxine. The questionnaire was created *de novo* and has not been previously validated. Although it is currently known that thyroid autoantibodies are present at a relatively high frequency in patients with CU, there has been considerable controversy about whether there is a causative link and whether treatment with thyroxine might benefit the patient. We hypothesized that a survey of the opinions of AAAAI members with interest in the treatment of CU would be of benefit to readers.

Two e-mail messages were sent to AAAAI physician members with registered e-mail addresses in February and March 2007, encouraging them to click the link to the 8-question Zoomerang survey and submit their opinions. The survey was sent to the 3388 physician members of the AAAAI, with 828 responses (24.5% response rate, assuming no individual completed the survey more than once). We recognize that the responders might well represent a self-selected subpopulation of the AAAAI membership who are particularly interested in the clinical management of urticaria. The results of our study cannot be generalized to the entire AAAAI membership without a relatively high likelihood of introducing bias.¹ A similar survey initiated by the Immunotherapy and Allergy Diagnostics Committee of the AAAAI has been previously published.² The design of these surveys does not allow for statistically powered comparisons but permits a general assessment of interested members' opinions on key clinical topics.

Eight hundred sixteen of the 828 responders indicated that they are clinically active in seeing patients with CU. Seven hundred seventy-eight (95%) responders were United States-based members, and the majority of the non-United States responders were Canadian. Regarding academic affiliation, 401 reported no affiliation, 274 reported part-time affiliation, and 153 reported full-time academic appointments. The number of years in practice was queried, which spanned the range from the first year in practice to 40 or more years.

There were 5 multiple-choice questions regarding clinical opinions, each with 4 possible answer choices, as follows:

- 1) Do you think that the presence of antithyroid antibodies in euthyroid patients with CU is evidence of thyroid-related pathogenesis leading to urticaria, or is it an epiphenomenon (ie, there is no causal link between the two)?
 - A. Generally is an epiphenomenon (ie, no causal link)
 - B. Could be both
 - C. Generally is thyroid-related pathogenesis leading to urticaria
 - D. Do not know
- 2) Do you personally see and treat patients with CU?
 - A. Yes (If you select yes, please answer all remaining questions.)
 - B. No (If you select no, please exit. Thank you for completing this part of the questionnaire.)
- 3) Do you test for antithyroid antibodies as part of the CU laboratory work-up?
 - A. Never
 - B. 1% to 50% of the time
 - C. 51% to 99% of the time
 - D. Always
- 4) What percentage of your euthyroid patients who have antithyroid antibodies and CU do you treat with thyroid hormone?
 - A. None
 - B. 1% to 50%
 - C. 51% to 99%
 - D. All
- 5) If you treat with thyroid hormone, what is your target level for thyroid-stimulating hormone (TSH)?
 - A. I do not treat
 - B. Less than the normal range
 - C. Low end of the normal range
 - D. Mid-normal range
 - E. I treat but do not monitor TSH

The number of answers to each question is shown in Table I. The scatter of responses to question 1 shows that there is variability as to opinion regarding whether there is a pathogenic link between thyroid autoimmunity and CU. However, only a minority (11%) believed strongly that there is a pathogenic link. After answering question 2, only those responders who personally treat patients with CU were to answer the remaining 3 questions. The scatter of responses to question 3 shows variability in diagnostic work-up among responders. Combining answers C and D, 531 (65%) of 823 responders test for antithyroid antibodies at least 50% of the time. We find this relatively high proportion to be interesting, given the low proportion of responders to question 1 who believed that there was a pathogenic link between thyroid autoimmunity and CU. This might be explained by the 52% of respondents to question 1 who stated that there could be a link.

The answers to question 4 show an overall low rate of treating antithyroid antibody-positive euthyroid patients with thyroid hormone, but there was variability. These results suggest to us that there might be some physicians who believe that thyroid pathogenesis leads to urticaria who might be more likely to treat with thyroid hormone, whereas physicians who believe that the 2 are an epiphenomenon might order the laboratories to look for possible subclinical thyroid autoimmunity but might not think that treatment with thyroxine will make any difference to the disease course of urticaria. In this sense some physicians might order thyroid autoantibodies because they consider it a marker of autoimmunity. The presence of thyroid autoantibodies has been shown to correlate with the presence of other autoantibodies, such

TABLE I. Enumeration of the responses to the 5 multiple-choice questions

Question no.	Total responses	Answers				
		A	B	C	D	E
1	828	261	429	89	49	—
2	823	816	7	—	—	—
3	823	42	250	256	275	—
4	819	420	310	60	29	—
5	802	432	42	189	101	38

as anti-FcεR1 and anti-IgE, although the strength of the association has been variable depending on the study, and the exact role of the latter autoantibodies in patients with CU has still not been fully elucidated.^{3,4}

The range of answers to question 5 shows that of the 370 responders who do treat with thyroid hormone, there is variability in their target TSH level. Some clinicians have no clear target level and do not monitor TSH.

The detection of an increased prevalence of thyroid autoantibodies in patients with CU versus control subjects was first reported more than 20 years ago and has now been sufficiently replicated in case-control studies.⁵⁻⁷ Therefore it is now generally accepted that there is an association between CU and thyroid autoantibodies, but the nature of the association is still unknown: Is there a direct pathogenic link, or is the association indirect? Does autoimmune inflammatory activity at the site of the thyroid gland directly cause urticaria in some patients, or are thyroid autoimmunity and CU independent but coexisting phenomena indicative of an overall autoimmune diathesis? These questions have not been studied directly, and as shown by our survey, the opinions of interested AAAAI members vary.

Despite the lack of consensus on pathogenesis, 65% of responders order thyroid autoantibodies in the work-up of the majority of their patients with CU, but relatively few treat euthyroid patients with thyroid hormone. The evidence regarding whether treatment with thyroxine is effective in improving urticaria is still conflicting,⁶ and no large-sized controlled trials have been published. When clinicians do treat with thyroid hormone, there appears to be variability in their target TSH levels. Evidenced-based guidelines are clearly needed.

As indicated, the response rate to this survey was low (24.5%), which raises the possibility of biases and precludes generalization of the results to all AAAAI members. With that caveat, the survey data demonstrate variability among AAAAI members with interest in urticaria. The data presented show that clinicians are indeed prescribing thyroid hormone in some cases when increases of antithyroid antibody levels are found during diagnostic work-up, despite the lack of consensus regarding possible mechanism and conflicting data to date on the clinical effectiveness of thyroid hormone in this situation. Furthermore, there are minimal data on what dose of thyroid hormone to use in these patients (who are

often clinically euthyroid) and no consensus as to what should be the target TSH level. Our findings underscore a significant need for further large-scale research in this area.

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