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Reply

To the Editor: We appreciate the interest shown by Levis et al in our article.¹ The letter will be informative for the medical community regarding leprosy in native-born Americans in the United States.

We agree with Levis et al that for many new leprosy patients in the United States, the source of the infection cannot be established. We concur that armadillos are a most unlikely source of leprosy infection in New York City. In our article we observed, however, that in the southern and southeastern United States, armadillos are an important reservoir for *Mycobacterium leprae*. As we noted, most studies on leprosy in wild armadillos have been conducted on populations from the Texas–Louisiana area; however, as early as 1984, it was reported that this population of armadillos had migrated into western Florida, and could import leprosy-infected armadillos.² Therefore it is reasonable to assume that contiguous areas of Georgia could be similarly invaded.

Based on this knowledge, we applied Occam's razor, in which speculations on the explanation of phenomena of unknown origin should be sought first in terms of known quantities. In this case, our patient had leprosy, she had no known contact with human cases, she had close association with wild armadillos in southern Georgia, and some of the armadillos could be reasonably suspected of carrying *M leprae*.

To our knowledge, only a few armadillos in southern Georgia have been surveyed, and only by methods with low sensitivity for *M leprae*. Those armadillos were negative for *M leprae* infection. More extensive surveys using highly sensitive techniques would seem to be indicated.

Finally, for clarity, we suggest that Levis et al could have indicated that leprosy had not been found in armadillos east of the state of Mississippi. Their

statement as it stands may be misconstrued to mean the Mississippi River. The large river is viewed by some as a natural barrier. The reported *M leprae*–infected armadillo found east of the Mississippi River, thus, is relevant to our hypothesis.

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Chronic urticaria: One step forward and two steps back

To the Editor: In their article Guerra et al¹ suggest that contact sensitization to chemicals, metals, or additives (often without clinical symptoms of eczema) may play a role in the pathogenesis of chronic urticaria (CU) and that routine patch tests and patch test–driven avoidance measures should be considered in patients with CU. However, several perplexities arise from a careful evaluation of the study design and the results obtained. Patch tests proved positive in 50 of 121 patients with CU (41%), a percentage similar to that found in the general population (40%) in another large study.² Avoidance measures were considered effective if remission occurred within 10 to 30 days. However, the duration of the remission was not specified; a control group with CU and showing contact sensitization but not submitted to avoidance measures was not included; only 4% of patients showed autologous serum skin test (ASST) positivity

(this proportion is about 10 times lower than that found in most previous studies); and diseases such as diabetes, *Helicobacter pylori* and other bacterial infections, Hashimoto's thyroiditis, malignancies, as well as other entities were considered as the possible cause of CU in 50 of 121 patients with negative patch tests (notably, the role of such conditions in CU is unproven, debated, or even questioned).

During the past few years there has been a worrying tendency to go backward in our approach to CU. After several decades spent considering CU as a mysterious disease possibly caused by anxiety and intolerance to foods, food dyes, or food additives (and prescribing useless and distressing restriction diets to entire legions of patients), the groups of Greaves³ and Kaplan⁴ finally demonstrated the presence of circulating histamine-releasing factors in a proportion of patients with CU. Such factors were subsequently characterized as functionally active IgG autoantibodies specific for the high-affinity IgE receptor, FcεRI, or for IgE, able to induce degranulation of mast cells and basophils.^{3,4} Since then, ASST has become an established, simple, and rapid means to detect autoreactivity in-vivo in patients with CU. Since functionally active autoantibodies can be detected in only a proportion of ASST-positive patients, and ASST itself is positive in about 50% of CU patients, the following challenge was to try to understand what happens in the remaining 50%. In this sense we recently demonstrated that the proportion of autoreactive patients rises dramatically if autologous plasma rather than autologous serum is used for skin testing. This suggested the existence of some circulating histamine-releasing factors that were more abundant in plasma than in serum. Since this ruled out autoantibodies, we investigated coagulation factors and found that CU patients show signs of thrombin generation as the result of an activation of the extrinsic pathway of coagulation; we also found that tissue factor is overexpressed in skin biopsy specimens from patients with CU.^{5,6}

The observations of Guerra et al¹ are of interest but need to be confirmed by other controlled studies before routine patch testing and avoidance measures are recommended; otherwise, we take the risk of going some 20 years back in our approach to patients with CU.

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