Changing Assessment of Diet in Chronic Spontaneous Urticaria

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I would like to thank the authors for the recent systematic review of the effect of diet in chronic spontaneous urticaria (CSU) (1). In chronic disease, medicine has always offered classical pharmacological treatment options accompanied by lifestyle measures, in which dietary recommendations have been the most important or approachable. Now, in the era of biologicals, some of which are highly useful, physicians and specialists are beginning to forget the importance of lifestyle recommendations, frequently fostered by not sufficiently proven or too rapidly held statements about the futility of dietary recommendations. This seems to be the case in CSU.

Scientific evidence seeks for causes, aetiology and characterization of disease. CSU is still a clinical entity without a specific ultimate cause, and therefore research on treatment options has focused on the only unifying, but highly reductionist, cause, which is the apparently inappropriate activation of mast cells.

Over the last decades, several dietary recommendations have been proposed in CSU, and these have been reviewed by the authors. However, I would like to highlight the difficulties in assessing the results of many of the included studies. By citing the last European Academy of Allergy and Clinical Immunology (EAACI) consensus the authors claim that some of the previous dietary proposals are "untested in well-designed double-blind placebo-controlled studies" (1, 2). But contrary to pharmacological studies, double-blind studies are not possible when assessing dietary measures. Therefore, the seeming lack of evidence is not due to methodological shortcomings, but to the inherent difficulties in clinical studies assessing dietary changes.

According to the authors "the European guidelines … do not recommend diet for managing CSU". This is a recently repeated statement, which is not adopted as such by the original consensus (2). In the last consensus the mention is about "Those diets are controversial and as yet unproven in well-designed double blinded placebo-controlled studies". However, controversy does not automatically mean uselessness. A lack of evidence can be due to methodological difficulties, geographical and cultural differences, or publication bias. Therefore, caution should be in the mind before fuelling an attitude that discards from the beginning any possible lifestyle recommendations.

The lack of useful and convincing studies and the difficulties of validating diets in CSU should be interpreted in its historical context. The focus has largely been on allergy, but it has long been proven that immunoglobulin E (IgE)-mediated allergy is extremely rare in CSU. Subsequently the focus was still on specific external causes, and therefore dietary amines, pseudo-allergens and other eliciting agents have been proposed and studied with more or less success. Certain foods containing aromatic components or alcohol have been identified as triggering factors (3). Even if the current state of the art is to recognize that a pseudo-allergen-free diet is "only" controversial, the future will probably show that the pseudo-allergen-free diet or other proposals will become increasingly discredited if the published studies and interpretation are still biased on the assumptions of intolerance (pseudo-allergen) or an external specific stimulus being responsible for CSU. However, this does not mean that diet as a potential modifying measure is not implicated in positive results, as has been the case for many published trials in high-impact journals. The problem arises as to how to interpret the potential effects of diets or changing habits. These should be studied in future not as an intolerance or allergy, but as a potential modifying factor. Change in dietary habits has been proven to change metabolic parameters, to affect microbiota composition and diversity or even inflammation-associated characteristics. Any of these endpoints could affect the activity of urticaria, which is a chronic inflammatory condition (4).

It is otherwise of interest, that the authors conclude that personalized diets could be of benefit in individual patients, and extending this idea should not discard that in the future urticaria would not be seen as disease entity, but as a guiding symptom, which could have multiple underlying (otherwise subclinical) aetiologies, including metabolic disease, intolerance reactions, and dysbiosis. No clinical study would reveal statistically relevant differences as no unique specific cause would be the reason. Otherwise personalized treatment options of underlying, often subclinical, disease could justify personalized diets.

Seen in this light, one of the assessed studies did not show improvement in urticaria with a fish-free diet, but, on the contrary, showed a potential beneficial effect of including (mainly oily) fish in the diet of some patients with CSU (5). In fact, this study showed how inflammatory parameters were associated with fish intake as well as with Urticaria Activity Score. Other previously published data could be re-interpreted in the light of different effects of dietary habits on the course of urti-

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caria. In fact, as an example, recent research focuses on ultra-processed food as a risk factor for several chronic diseases (6), and pseudo-allergens could have been an epiphenomenic marker of other dietary habits.

Changes in lifestyle can be very cheap, but need more time and training for physicians and other health professions, and are, on the whole, a neglected field in less-funded medical research, such as in CSU.

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The author of the original article (Hélène Cornillier) was given the opportunity to comment in response to this Correspondence, but chose not to do so.