

EDITORIAL

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Towards rationalizing the nomenclature and classification of urticaria: some guidance on guidelines

C. E. H. Grattan^{*†}^{*}St John's Institute of Dermatology, London, UK and [†]Dermatology Centre, Norfolk and Norwich University Hospital, Norwich, UK

This issue of Clinical and Experimental Allergy sees the publication of a third set of national or international guidelines on urticaria in the English language within Europe since 2001 [1–3]. A consensus agreement on the diagnosis and management of acute and chronic urticaria has also been published on behalf of the American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy Asthma and Immunology (ACAAI) in 2000 [4]. While the intention of these guidelines is to help structure and clarify the diagnosis and management of urticaria, a number of anomalies relating to the nomenclature and classification have emerged. These differences are due in some part to historical influences, in some part to exposure of specialties to different populations of patients with urticaria and most importantly to the complexity, breadth and diversity of a condition that may affect up to one in five individuals over their lifetime with multiple causes, associations and aggravating factors. A common platform is needed to amalgamate the experience of allergists, dermatologists, emergency medicine specialists, general physicians, immunologists, paediatricians and primary care doctors so that advances in the understanding of aetiopathogenesis and management can be translated into best clinical practice across specialties and national boundaries.

Divergence of opinion begins with the definition of urticaria itself. The term is used internationally to describe an eruption of superficial weals, with deeper swellings being known as angio-oedema. This leads to the rather untidy use of urticaria and angio-oedema or urticaria/angio-oedema to describe the illness itself. As around 60% of patients presenting with urticaria will have angio-oedema at some stage of their illness, usually when it is most severe, the unifying term urticaria is now used to define an illness that is characterized by superficial swellings of the dermis (weals), deeper swellings of the dermis,

subcutis and submucosa (angio-oedema) or both together in two of the three European guidelines [2, 3]. This nomenclature has the advantage of recognizing that weals and angio-oedema are often expressions of a disease with the same pathogenesis for which the clinical expression depends on the depth of swelling and no more. Recognition that the depth of swelling defines a disease continuum rather than more than one pathogenesis in an individual patient has the added advantage of dispelling the uncertainty of how to classify deeper skin swellings that may be seen in delayed pressure urticaria, for instance, and emphasizing that one treatment approach is appropriate for the different morphological expressions of the same disease. By extension of logical thought on the definition of urticaria, weals and angio-oedema are often features of anaphylaxis. This may be considered as a systemic disorder of capillary leakage that may or may not involve the skin, whereas urticaria defines a capillary leakage problem confined to the skin and mucous membranes. As in so many areas of medicine, complete separation is not possible because severe, widespread urticaria may progress to anaphylaxis, as in cold contact urticaria, allergic contact urticaria and acute allergic urticaria and, furthermore, the rare anaphylactic disorders exercise-induced anaphylaxis and food- and exercise-induced anaphylaxis are included within most classifications of urticaria!

One might think that classifying urticaria by disease duration into acute and chronic is simple, unequivocal and satisfying because it appears to imply an understanding of the disease pathogenesis and its prognosis. In some respects, this is true because patients with acute urticaria are more likely to have an allergic or viral aetiology than chronic urticaria, which is more likely to be autoimmune or remain unexplained (idiopathic). The problem with classifying urticaria in this way is finding agreement on what is meant by chronic. Strictly speaking, chronic urticaria is any pattern of continuous daily or almost daily disease that goes on for 6 weeks or more. This should embrace any aetiology or clinical pattern including the physical urticarias and urticarial vasculitis (where this is included in classifications of urticaria), but this concept

Correspondence:

C. E. H. Grattan, Dermatology Centre, Norfolk and Norwich University Hospital, Colney, Norwich NR4 7UY, UK.
E-mail: clive.grattan@nnuh.nhs.uk

does not account for the intermittent or episodic pattern of short bursts of continuous activity that are not uncommon in clinical practice. The authors of the British Society of Allergy and Clinical Immunology (BSACI) guidelines [1] have accommodated this acute intermittent pattern into their definition of chronic urticaria, whereas it is separated from chronic urticaria in those published by the British Association of Dermatologists (BAD) [2]. The European Academy of Allergology and Clinical Immunology (EAACI) guidelines [3] go further by implying that the term chronic urticaria as a subheading of spontaneous urticaria is a surrogate for those patients who would previously have been labelled as having chronic idiopathic urticaria. With increasing international acceptance that about 30–50% of patients with what was previously called chronic idiopathic urticaria have chronic autoimmune urticaria (and a suspicion that the proportion may be considerably higher but without routine laboratory tests to show this), there is a need for a term that embraces all those patients presenting with continuous urticaria that is not physical, vasculitic or the presentation of an autoinflammatory syndrome, which is independent of aetiology. The use of the term ordinary urticaria to define a group of patients with the usual presentation of continuous disease irrespective of aetiology (be it acute, episodic or chronic), which excludes those with other clinically recognizable subgroups, has been proposed [2] but has not yet been widely accepted. One advantage of separating temporal, clinical and aetiological definitions is that they can be merged or expanded to summarize subgroups of patients appropriately for different purposes. For instance, it may be sufficient to refer to the collective term urticaria for the purpose of separating patients with itchy skin who develop short-lived swellings and respond to antihistamines from those with eczema whose disease does not fluctuate daily and does not respond to antihistamines. In another context, it may be helpful to distinguish those patients with urticaria who have the ordinary presentation of urticaria from those who have a predominantly physical urticaria or those with angio-oedema without weals, from the perspective of management. For the purpose of clinical studies without access to tests to distinguish patients with autoimmune from idiopathic urticaria, the clinical term chronic ordinary urticaria helps to define a clinically homogeneous but aetiotologically heterogeneous subgroup for comparing therapies. Where full facilities are available in specialist centres to separate patients with chronic urticaria presenting similarly but with different definable aetiologies, including autoimmunity, dietary intolerance and infections, a string of terms can be applied for a tighter definition of patient subgroups, such as autoimmune chronic ordinary urticaria, idiopathic episodic ordinary urticaria or cold-induced chronic physical urticaria.

Nor do differences in the guidelines stop at the conceptual level. For the aficionados of urticaria, the sub-

classification of physical urticarias varies in content and emphasis. Even publications on the testing of physical urticarias disagree on some details [3, 5, 6]. Cholinergic urticaria is extracted from the other physical urticarias in the EAACI classification because it may be induced by stimuli that cause sweating, such as stress and spicy foods, as well as the much more common stimulus of overheating resulting in an increase of core body temperature. The exceptionally rare localized heat urticaria remains. Hereditary angio-oedema and urticarial vasculitis are separated from other patterns of urticaria in the EAACI classification as 'diseases related to urticaria for historical reasons' but appear within the BAD and BSACI guidelines as subcategories of 'angio-oedema without weals' and urticaria or vasculitis, respectively. Both are annotated in the algorithm for chronic urticaria/angio-oedema in the joint AAAAI/ACAAI consensus document.

There is a need for agreement and rationalization of the nomenclature and diagnostic classification of urticaria at a cross-specialty and international level for students of the future. It is implausible that urticaria is a different disease across the world, although it is very possible that the predominance of clinical patterns and aetiologies are influenced by environmental and genetic influences. It is only through harmonizing patient groups for selection and analysis in clinical trials that it will be possible to be confident that results from one investigational centre are comparable to those of another with respect to appropriate prescribing, regulatory authorization and pharmaceutical company promotion. A rigorous definition of patient subgroups will also facilitate investigation of genetic markers of disease susceptibility, such as aspirin-induced urticaria, and a better understanding of disease aetiopathogenesis.

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