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Chronic idiopathic urticaria (CIU) is no longer idiopathic: time for an update

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MADAM, During recent years our knowledge of the aetiology and pathogenesis of urticaria has advanced considerably, allowing us to better characterize urticaria subtypes. However, although the classification of urticaria has undergone some revisions during this time,¹ authors still use different names for the same type of urticaria, which has implications for comparing study outcomes and for drug licensing. Consequently, there is an urgent need for a harmonized and universally accepted nomenclature and classification of urticaria and to avoid the routine use of the outdated aetiological term, chronic idiopathic urticaria (CIU).

The current European Academy of Allergy and Clinical Immunology (EAACI), Global Allergy and Asthma European Network (GA²LEN), European Dermatology Forum (EDF) and World Allergy Organization (WAO) guidelines for urticaria¹ recommend that urticaria should be classified initially by its duration, viz. whether the condition is acute (lasting < 6 weeks) or chronic (lasting more than 6 weeks). Chronic urticaria is then divided into its two primary subgroups according to whether symptoms occur spontaneously or are induced by a demonstrable stimulus (Table 1). Individual conditions are then listed in one of these subgroups according to their underlying aetiology or purported mechanism of induction. In its 2011 consensus paper, the GA²LEN taskforce on unmet needs in urticaria² reiterated the classification and the associated changes in urticaria nomenclature recommended by the above guidelines. The nomenclature of each individual type of urticaria should contain two terms in addition to 'urticaria' as its universal last word. The first defines its duration as either *acute* or *chronic* and the second states whether the condition is *spontaneous*, in that it occurs without demonstrable provocation, or if it is *induced* by a demonstrable stimulus. For chronic spontaneous urticaria (CSU) the purported trigger cause, or mechanism of induction should also be included when identified, e.g. chronic spontaneous urticaria *due to infection*. For physical, aquagenic and cholinergic urticarias the aetiology remains unknown. This nomenclature should be accepted globally and used consistently throughout the medical literature.

Table 1 Classification and nomenclature of chronic urticaria

Chronic urticaria (CU)	
Chronic spontaneous urticaria (CSU)	Chronic inducible urticaria (CINDU)
CSU due to known causes ^a	Physical urticarias
	Symptomatic dermographism ^b
	Cold urticaria ^c
	Delayed pressure urticaria ^d
	Solar urticaria
	Heat urticaria ^e
CSU due to unknown cause	Vibratory angio-oedema
	Cholinergic urticaria
	Contact urticaria ^f
	Aquagenic urticaria

Based on the current European Academy of Allergy and Clinical Immunology (EAACI), Global Allergy and Asthma European Network (GA²LEN), European Dermatology Forum (EDF) and World Allergy Organization (WAO) guidelines for urticaria.¹ ^aKnown causes for chronic spontaneous urticaria include, for example, autoimmunity as defined by the presence of mast cell-activating autoantibodies.⁷ For more information on other factors, such as infection, food components, stress or fatigue as underlying causes, aggravating factors or eliciting triggers, alone or in combination, see references 1 and 2. ^bAlso called urticaria factitia. ^cAlso called cold contact urticaria. ^dAlso called pressure urticaria. ^eAlso called heat contact urticaria. ^fIt is recognized that most cases of contact urticaria will present acutely, especially allergic contact urticaria, which is usually recognized very early.

A major reason for recommending these changes is to avoid the problems resulting from the use of the outdated, inaccurate and ambiguous term 'CIU'. Previously, the term 'chronic idiopathic urticaria' was used to describe what is now called chronic urticaria,³ chronic ordinary urticaria,⁴ chronic spontaneous urticaria⁵ or chronic spontaneous urticaria due to unknown cause.⁶ In many publications, information on how patients with CIU were aetiologically investigated and clinically described is missing. These inconsistencies have made it hard, and sometimes impossible, to compare the findings of such studies. Furthermore, the term 'chronic idiopathic urticaria' has been used as a group name for all chronic urticarias containing separate and distinct entities and subgroups of entities (i.e. spontaneous vs. inducible urticarias) that differ in their course and patterns as well as diagnostics and management approaches.

The term CIU has also commonly been used to describe CSU. However, the word idiopathic in CIU, when used synonymously with CSU, doesn't make it clear that the weals and other symptoms in this group of urticarias occur spontaneously, and are not reproducibly induced by a specific trigger. More importantly, in many patients with CSU the underlying cause can nowadays be identified, thus the designation idiopathic (i.e. of unknown cause) is no longer appropriate⁶ because a patient cannot have an illness that is idiopathic and have a known cause at the same time.

Today, some underlying causes of CSU are known and may be used for subtyping. Only in an increasingly small number of patients with CSU is the underlying cause not identifiable. For this subtype, we recommend the use of the term 'CSU due to unknown cause'. Although this subtype could be called chronic spontaneous idiopathic urticaria, we advise against the use of this term to avoid confusion.

The changes in the nomenclature of urticaria, and specifically to end the use of the term CIU, have several important implications: (i) patients with CSU (formerly sometimes known as CIU) are more frequently checked and treated for underlying causes; (ii) novel urticaria drugs should no longer be licensed for the treatment of patients with CIU. Instead, the indication for use should be chronic spontaneous urticaria, chronic urticaria or simply urticaria, depending on the drug's mechanism of action and/or efficacy profile. Interestingly, many nonsedating H₁-antihistamines, including desloratadine, ebastine, levocetirizine and rupatadine, have recently seen a change of their therapeutic indication from CIU to urticaria, and new antihistamines, such as bilastine, are no longer licensed for CIU but for urticaria; (iii) the use of the recommended classification and nomenclature (and thereby the avoidance of the term CIU) will benefit urticaria research, as it will allow the comparison of findings obtained from the investigation of better-defined patient populations.

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References

- 1 Zuberbier T, Asero R, Bindslev-Jensen C et al. EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. *Allergy* 2009; **64**:1417–26.
- 2 Maurer M, Weller K, Bindslev-Jensen C et al. Unmet clinical needs in chronic spontaneous urticaria. A GA²LEN task force report. *Allergy* 2011; **66**:317–30.
- 3 Spector SL. Management of chronic idiopathic urticaria. *West J Med* 1989; **150**:337.
- 4 Grattan C, Powell S, Humphreys F. Management and diagnostic guidelines for urticaria and angio-oedema. *Br J Dermatol* 2001; **144**:708–14.
- 5 Magen E, Mishal J. The effect of L-thyroxine treatment on chronic idiopathic urticaria and autoimmune thyroiditis. *Int J Dermatol* 2012; **51**:94–7.
- 6 Staubach P, Dechene M, Metz M et al. High prevalence of psychosomatic disorders and emotional distress in patients with chronic spontaneous urticaria. *Acta Derm Venereol* 2011; **91**:557–61.
- 7 Konstantinou GN, Asero R, Maurer M et al. EAACI/GA²LEN task force consensus report: the autologous serum skin test in urticaria. *Allergy* 2009; **64**:1256–68.

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A severe familial phenotype of Ichthyosis Curth–Macklin caused by a novel mutation in the *KRT1* gene

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MADAM, Ichthyosis Curth–Macklin (ICM; Mendelian Inheritance in Man database #146590) is a rare genetic disorder that is clinically characterized by severe palmoplantar keratoderma. The skin of patients with ICM is characterized by extensive dark spiky or verrucous plaques that affect the large joints and the trunk. In some cases these lesions can cover the entire body. Differentiating keratinocytes of ICM tissues display ultrastructural anomalies such as keratin intermediate filaments (KIF), aggregation into peripheral shells, perinuclear vacuolization and binucleated cell formation.¹ ICM, as well as other keratinopathic ichthyoses, is caused by mutations of the keratin 1 gene (*KRT1*) that lead to an impairment of the KIF network assembly in the cytoplasm of keratinocytes.² At the protein level, these mutations are located in the variable (V2) domain of the protein.^{1,3,4}

In this study, we report two related women of Colombian origin, affected by a severe ICM phenotype, who present a novel *KRT1* mutation. These patients attended the Dermatology Unit of the Carlos Ardila Lulle Clinic of Bucaramanga (Colombia). This study has been approved by the Ethical Committee at Universidad del Rosario and was conducted according to