Guidelines for cold urticaria management established by the Centre of Evidence of Dermatology and the Urticaria Group of the French Society of Dermatology

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Dear Editor, Cold urticaria (CU) is a type of chronic inducible urticaria. Lesions can be superficial (weals) and/or deep (angioedema). It is a rare condition and its prevalence is around 0.05% in central Europe. It can occur at any age, with a clear female predominance in most studies. CU can last for several years (approximately 6.3 years), but patients may recover spontaneously.[1] Cold anaphylaxis can be potentially life-threatening, although it is not known whether the severe vasoplegia induced by a systemic reaction to cold exposure is IgE-mediated.[1] About 10–38% of patients with CU have experienced a severe systemic reaction (hypotension, hypotensive symptoms) at least once, and water immersion causes up to 77% of these reactions.[2]

The latest international urticaria management guidelines recommend limited paraclinical examinations in CU [differential blood count (BC), C-reactive protein (CRP), and in specialized care total IgE and IgG antithyroid peroxidase antibody] and ruling out other diseases, especially infections.[3]

However, few publications have addressed CU severity classification or the risks of severe forms, defined as any history of anaphylactic reaction to cold and/or pharyngeal and/or laryngeal manifestations after cold exposure. To date, there is no consensus on the prescription of autoinjectable adrenaline (epinephrine) kits in CU.

Therefore, the Centre of Evidence of Dermatology (CDP) and the Urticaria Group (GUS) of the French Society of Dermatology initiated a standardized recommendation process for CU. A multidisciplinary working group (WG) composed of 13 physicians (dermatologists, allergists, paediatricians, occupational physicians and general practitioners) was formed. The WG members had no conflicts of interest and followed a strict methodology.[4] Firstly, the WG systematically reviewed the literature to identify references in French or English from 1980 to 2022 in the MEDLINE database. Retrospective studies, clinical cases, case series, conference abstracts and oral communications were included, given the limited number of prospective studies available. Genetically determined CU and CU associated with cryopathies were excluded (agglutinin syndrome, cryoglobulinaemias and cryofibrinogenaemia).

After analysing the methods, objectives, results and biases of included studies, the WG established recommendations by grading the evidence levels using the French Haute Autorité de Santé grid[4] [from D (no direct research evidence) to A (several multicentric double-blinded studies with concordant positive results and acceptable risks)]. In cases where it was not possible to decide the level of evidence, the WG consulted nine national urticaria experts; their responses were subsequently integrated into the recommendations. The WG submitted its recommendations to a multidisciplinary panel of 25 reviewers (dermatologists, allergists, emergency physicians, internists and paediatricians) who scored each recommendation from 1 to 10, to assess the internal consistency of the recommendations and their practical applicability.

The main points of the guidelines are as follows:

1 The WG recommends performing an ice cube test, because it is easy to use, cheap and informative. Place an ice cube in a plastic bag and apply to the volar forearm for 5 min. Read the test 10 min after removing the ice cube. If negative, repeat application for up to 10 min or even 20 min (Grade B).[5] Typical CU is defined as a positive cold test, as opposed to atypical CU (Grade A). If available, the more reproductible TempTest® (Medelink, Brossard, QC, Canada) can further provide the temperature threshold as additional but not crucial information (expert agreement).

2 The WG proposes the following CU severity classification (expert agreement):
- Type I: weals and/or angioedema limited to the area of cold contact (without localized life-threatening laryngeal oedema)
- Type II: urticaria and/or generalized angioedema without episodes suggestive of hypotension or respiratory symptoms
- Type III: severe systemic reaction (symptoms included respiratory symptoms of noisy or difficulty breathing and/or cardiovascular compromise following exposure to cold) or localized life-threatening laryngeal oedema.

3 The WG recommends differential BC and CRP tests;[3] cryoglobulin and cold agglutinin should only be tested where a clinical indication exists (Grade C). For a generalized type III CU (according to Wanderer's 1986 classification) reaction, the WG recommends determining tryptase levels in acute and baseline phases (expert agreement).

4 The WG recommends prescribing an autoinjectable adrenaline (epinephrine) kit for patients who have experienced a severe form of CU before, defined as any history of anaphylactic reaction to cold and/or pharyngeal and/or laryngeal manifestations after cold exposure (including ingesting cold foods or beverages) (Grade C).[2]

If a background treatment is indicated (depending on impact on quality of life), a second-generation antihistamine (anti-H1) at conventional dosage, is recommended as first-line treatment for CU (Grade A).[6]

If background treatment response is unsatisfactory, the WG recommends increasing the dosage of anti-H1 medication up to four times the standard dose as second-line treatment;[7] however, issues regarding the various biases in the literature (small study populations, poor clinical relevance of endpoints, etc.) must be taken into account. The anti-H1 bilastine, rupatadine and desloratadine have been studied at quadruple dose in CU (Grade B).

As a third-line treatment, the WG recommends adding omalizumab (150 mg subcutaneously every 4 weeks)[8] to anti-H1 therapy (Grade B) for the background treatment. If the response at 12 weeks is inadequate, consider increasing the dosage to 300 mg every 4 weeks (expert agreement).

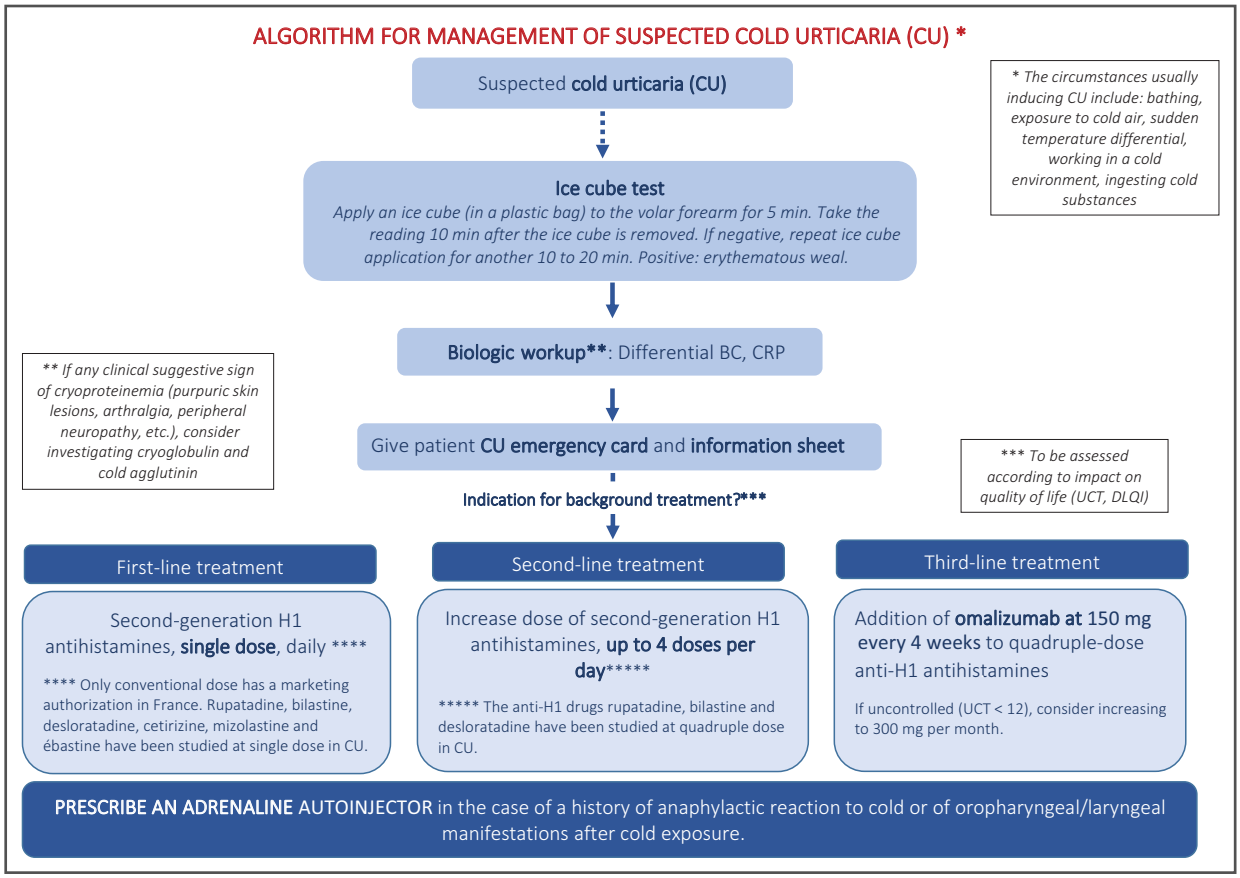

Figure 1 French Society of Dermatology recommendations for the management of cold urticaria (CU) confirmed by examination. Anti-H1, antihistamine; BC, blood count; CRP, C-reactive protein; DLQI, Dermatology Life Quality Index; UCT, Urticaria Control Test.

These data were used to develop a practical decision-making algorithm (Figure 1) and are available on a dedicated website (https://reco.sfdermato.org/). The WG also created an emergency card and information sheet for patients with CU, taking into account the significance of therapeutic education.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

File S1 Full list of affiliations.

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