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Cholinergic Urticaria - Clinical Significance in Athletes and Physically Active Individuals: A Narrative Review

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Abstract

Introduction. Cholinergic urticaria (CholU) is a subtype of chronic inducible urticaria triggered by increases in core body temperature and sweating. Its trigger profile, encompassing exercise, passive warming, emotional stress, and hot environments, renders it particularly relevant to athletes and physically active individuals, in whom these stimuli are frequent and often unavoidable.

Purpose. This narrative review aimed to summarize current evidence on the clinical significance, diagnostic challenges, differential diagnosis, and practical management of cholinergic urticaria in athletes and physically active populations.

Current knowledge. CholU predominantly affects young adults and involves heterogeneous pathophysiological mechanisms, including mast cell activation, sweat hypersensitivity, and acetylcholine-mediated pathways. In athletes, recurrent symptoms such as wheals, pruritus, and burning sensations may interrupt training, reduce exercise tolerance, and impair psychological well-being. Diagnosis relies on provocation testing, while differential diagnosis must exclude exercise-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, and other inducible urticarias. Management centers on second-generation antihistamines, trigger modification, and, in refractory cases, omalizumab, which has enabled some patients to resume full athletic participation.

Conclusions. CholU poses a distinct and underrecognized burden in physically active individuals. Individualized management combining pharmacotherapy with exercise modification can allow most patients to maintain safe participation in physical activity, though further research is needed to optimize treatment strategies.

Key words: Urticaria, Exercise, Mast Cells, Anaphylaxis, Histamine Antagonists, Quality of Life

1. Introduction

Regular physical activity is an essential component of health promotion, disease prevention, and athletic performance. During exercise, the human body undergoes predictable physiological changes, including increased heat production, elevation of core body temperature, autonomic activation, peripheral vasodilation, and sweating. In most individuals, these responses enable thermoregulation and support physical performance. In patients with cholinergic urticaria, however, the same physiological processes may become direct triggers of cutaneous symptoms [1,2].

Cholinergic urticaria is classified as a subtype of chronic inducible urticaria, a group of urticarias in which wheals, angioedema, or both occur reproducibly after exposure to specific stimuli [1–3]. It is characterized by recurrent, usually small, pruritic or stinging wheals that appear after an increase in body temperature and activation of sweating mechanisms [1]. Typical provoking factors include physical exercise, passive warming, hot baths, emotional stress, and ingestion of hot or spicy foods [1]. This trigger profile makes cholinergic urticaria particularly relevant for athletes and physically active individuals, because exercise is not an incidental exposure in this population but a repeated and often unavoidable element of daily training, competition, or recreation [1,4].

In physically active individuals, cholinergic urticaria may have consequences that extend beyond transient skin lesions. Symptoms may develop during warm-up, endurance exercise, high-intensity training, sauna exposure, or physical activity performed in warm environments. Pruritus, burning or stinging sensations, visible wheals, and discomfort may interrupt training sessions, reduce exercise tolerance, and discourage further participation in sport. In competitive athletes, even short-lasting symptoms may interfere with preparation, concentration, or performance during an event. In recreationally active individuals, recurrent exercise-related symptoms may reduce adherence to physical activity despite its established role in maintaining health and preventing chronic disease. The development

of a disease-specific quality-of-life questionnaire for cholinergic urticaria supports the view that this condition can impose a distinct burden on daily functioning and patient well-being [5].

The terminology used to describe urticarial symptoms related to exercise or heat exposure requires careful clarification. In patients reporting symptoms during exercise, the term exercise-induced urticaria may be used descriptively to indicate wheals occurring in temporal association with physical exertion. This term indicates the temporal association between physical effort and urticarial lesions, but it does not identify one specific disease mechanism. Exercise-associated urticaria may occur in cholinergic urticaria, exercise-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, or other forms of chronic inducible urticaria [3,4]. Similarly, the informal phrase "heat hives" has been used as an explanatory expression for cholinergic urticaria in the scientific literature, but it is not a standardized medical term and should not be regarded as a formal diagnostic category [6]. Heat-related wheals should be differentiated clinically from localized heat urticaria, in which lesions are provoked by direct contact with a heat stimulus, and from cholinergic urticaria, in which symptoms are typically related to increased core body temperature and sweating [1–3].

This distinction is clinically important because exercise-related urticaria and systemic reactions during physical activity differ in risk profile, diagnostic approach, and recommendations regarding further activity. Cholinergic urticaria is often limited to cutaneous manifestations, whereas exercise-induced anaphylaxis and food-dependent exercise-induced anaphylaxis may involve systemic symptoms and require different preventive strategies [4]. For athletes and physically active individuals, misclassification may lead either to unnecessary restriction of physical activity or to underestimation of potentially serious exercise-associated reactions. Therefore, recurrent wheals, pruritus, or systemic complaints occurring during or after exertion should prompt careful clinical assessment rather than being dismissed as a benign or purely cosmetic problem [3,4].

The pathophysiology of cholinergic urticaria remains heterogeneous and incompletely understood. Proposed mechanisms include sweat hypersensitivity, mast cell activation related to sweat components, altered cholinergic signaling, impaired sweating, and variants associated with hypohidrosis or anhidrosis [1]. Clinical expression may also vary between patients, with differences in symptom severity, reproducibility, associated features, and impact on quality of life [1,5,7]. Atopic predisposition has been reported as one factor associated with more severe disease characteristics and greater impairment in patients with cholinergic urticaria, suggesting that individual patient factors may influence the clinical burden of the condition [7].

From the perspective of sports medicine, cholinergic urticaria should be considered relevant not only to dermatology and allergology, but also to the assessment and management of symptoms occurring during physical activity. Its triggers overlap with normal physiological responses to exercise, and its symptoms may influence training continuity, performance, psychological comfort, and safety during exertion. Although cholinergic urticaria is included in broader classifications of chronic inducible urticarias, available literature appears to address cholinergic urticaria mainly within dermatological and allergological frameworks, with less emphasis on its practical implications for athletes and physically active individuals. [1–4] Therefore, this narrative review aims to summarize current evidence on the clinical significance, diagnostic challenges, differential diagnosis, and practical implications of cholinergic urticaria in athletes and physically active individuals.

2. Methods

This paper presents a narrative review of the available literature focusing on contemporary scientific evidence concerning Cholinergic urticaria. The literature review covered studies published between 2016 and 2026. Scientific databases searched included PubMed, Scopus, Web of Science, and the Cochrane Library. Additional sources such as ClinicalTrials.gov, Google Scholar, and ResearchGate were also examined to identify potentially relevant publications. Furthermore, a manual review of reference lists from selected papers was performed to detect additional eligible studies through citation tracking.

The search strategy incorporated core keywords as "cholinergic urticaria", "heat hives" and "exercise-induced urticaria". These were integrated with queries related to epidemiology, pathophysiology, clinical presentation, diagnosis, treatment and prevention, as well as the impact of cholinergic urticaria on sport and physical performance. Boolean operators were applied to optimize the search strategy, with synonymous terms combined using OR and thematic categories connected using AND to ensure comprehensive identification of relevant literature.

The database search was carried out during April and May 2026. Eligible publications included randomized controlled trials, observational and quasi-experimental studies, as well as review papers, systematic reviews, and meta-analyses. Only studies involving human participants were included in the review. Articles published in languages other than English or Polish were excluded from the analysis.

The objective of this review was to summarize and critically evaluate current evidence regarding cholinergic urticaria in order to support clinical practice and improve understanding of available management options, especially in patients with persistent symptoms or reduced quality of life.

3. Overview

3.1. Epidemiology

Cholinergic Urticaria usually affects young adults [8–11]. Seo and Kwon's study showed that urticaria is most common in the 20-29 age group, with a significant predominance of men. Women, on the other hand, had an average age of onset of 40 [10]. In another study by Kumaran and colleagues, the average age for men was 19 and for women was 36.25, indicating that the onset of the disease occurs in the second decade of life. The authors also referred to previously available reports, which also showed that 80% of the study participants had onset during adolescence [8]. A study by Rujitharanwond and colleagues also reported a mean age of onset of 28 years, consistent with reports from temperature zones [9]. This shows that all study results are similar. The researchers agree on the duration of urticaria, citing a figure of 46 months, which is consistent with earlier studies by Kim Zand colleagues and Silpa-arch and colleagues, which reported remission in half of patients within 5 years of disease onset [8]. Studies in tropical regions report a median duration of 4.3 years [9].

A geographic relationship has also been noted [8–10]. In tropical regions, the incidence of cholinergic urticaria ranges from 0.023% to 11.2%. In this particular study, the prevalence of this condition is 0.7%. Previous studies by these researchers from 2007 and 2011 reported prevalence rates of 0.9% and 0.5%, respectively [9]. Indian studies differ significantly: in the study by Kumaran and colleagues, the prevalence was 1.7%, while the study by Godse and colleagues found a prevalence of 4.16%. Kumerman and colleagues study also found that cholinergic urticaria accounts for 30% of induced urticaria cases, accounting for 5-7% of all urticaria cases. These studies have shown that the prevalence of CholU in India is lower than in Western countries [8]. Scientists from tropical zone suspect that the reason for the lower incidence in this zone may be that patients are accustomed to hot environments, which causes the severity of cholinergic urticaria to be mild. Unfortunately, some people misinterpret the symptoms and do not seek medical attention. Therefore, the incidence may be higher in this zone. As early as 1926, Duke suggested that temperature changes, rather than the constant temperature of the tropical climate, may be a factor in inducing the onset of urticaria [9]. Additionally, in 2022, Sirufo and colleagues also believe that CHolU is a subtype of chronic induced urticaria, triggered by increased temperature. It can occur with physical exertion, emotional stress, and hot baths—situations where the sweating reflex is activated [12].

A risk factor for cholinergic urticaria is atopy [9,11,13,14]. According to Takahagi and colleagues, approximately half of the patients with CholU have atopic diathesis [11]. In a study of differences in bronchial reactivity between CholU subtypes, researchers showed that palpebral angioedema (CholU-PA) is closely associated with atopic diseases such as atopic dermatitis, asthma, and allergic rhinitis. Additionally, the researchers noted that almost all Cholinergic Urticaria patients in the study were women [13]. The Indian study found atopy in 20% of patients, citing previous studies that the correlation could be misleading due to misperceptions of hot bath sensations and interpretations of Cholinergic Urticaria [8]. Research by Rujitharanawong and colleagues shows that the rate of atopy in tropical countries is lower than in temperate climates. This is demonstrated by the results of a study by Zuberbier and colleagues, who found a high prevalence of atopy in German patients with cholinergic urticaria, reaching 45.5%.[9].

An important risk factor in the development of CholU is sweat allergy [8,9,11,13,14]. It is defined as an immediate, IgE-dependent reaction to sweat contents [9,11,14]. The exact mechanism underlying the wheal response in CholU has not yet been fully elucidated; however, hypersensitivity to sweat has been suggested as a potential factor involved in its pathogenesis [11].

Hiragun and colleagues reported that the fungal protein MGL-1304 secreted by Malassezia globosa, which is found in human sweat, induces histamine release from basophils in patients with atopic dermatitis [11,15].

CholU is sometimes associated with cold-induced urticaria [1]. A study by Ramam and colleagues indicated an increased frequency and severity of symptoms during the winter months - from October to January [8]. The

pathophysiology of CholU includes acetylcholine (Ach), histamine, serum factors, obstruction or damage to the sweat duct opening, sweat allergy, and dyshidrosis, with each subtype of CholU having different causes [1,13,14]. Unfortunately, the etiology of each is not yet well understood [1,13].

3.2. Pathophysiology

Pathogenesis of cholinergic urticaria remains incompletely understood and appears to be multifactorial [14,16,17].

A key mechanism in CholU is mast cell activation with subsequent release of histamine and other inflammatory mediators. Increased serum histamine levels during symptom development and after exercise have been demonstrated in patients with CholU, supporting the important role of histamine in disease pathophysiology [16]. However, incomplete response to antihistamine therapy suggests that mediators other than histamine are also involved. IgE-mediated mast cell activation is considered an important pathogenic mechanism, as supported by passive transfer experiments and the clinical efficacy of omalizumab [17].

Acetylcholine (ACh) plays a central role in CholU. Physiologically, ACh released from sympathetic cholinergic nerves stimulates eccrine sweat glands through muscarinic acetylcholine receptor M3 (CHRM3). In some patients, especially those with hypohidrosis or anhidrosis, reduced expression of CHRM3 and acetylcholinesterase has been demonstrated in eccrine glands [14,16]. This leads to insufficient binding of acetylcholine within sweat glands and possible “overflow” of ACh to adjacent mast cells, resulting in mast cell degranulation and wheal formation [14,16]. This mechanism is characteristic of the acetylcholine-direct, depressed sweating type of CholU.

Another important mechanism is hypersensitivity to sweat. Studies demonstrated positive autologous sweat skin tests and basophil histamine release in response to autologous sweat in many patients with CholU, indicating a type I hypersensitivity reaction to sweat antigens [14,16,17]. Sweat allergy appears particularly relevant in patients with atopic predisposition [14,16]. Leakage of sweat into the dermis due to obstruction or damage of sweat ducts may further enhance mast cell activation and local inflammation.

Sweating dysfunction, including acquired idiopathic generalized anhidrosis (AIGA) and hypohidrosis, is strongly associated with some CholU phenotypes [14,16,17]. Histopathological studies revealed lymphocytic and mast cell infiltration around eccrine sweat glands together with decreased CHRM3 expression [14]. These findings suggest immune-mediated dysfunction of the sweat apparatus. In affected patients, wheals tend to occur mainly in hypohidrotic rather than completely anhidrotic skin areas [14,16,17].

Based on pathogenesis and clinical presentation, several subtypes of CholU have been proposed [1]:

conventional sweat allergy-type CholU,

follicular-type CholU,

CholU with palpebral angioedema,

CholU with acquired anhidrosis and/or hypohidrosis (CholU-Anhd).

3.3. Clinical Presentation

Clinical presentation of cholinergic urticaria is characterized by the rapid appearance of numerous small wheals, usually 1–3 mm in diameter, surrounded by erythematous halos. In some patients, lesions may enlarge and coalesce into larger plaques. The eruptions most commonly affect the trunk and proximal extremities, while the palms, soles, and axillae are usually spared [16]. Symptoms are triggered by situations associated with sweating, including exercise, emotional stress, hot baths, sauna exposure, spicy foods, and elevated ambient temperature [17].

Lesions typically develop within minutes and resolve within approximately one hour [17]. Unlike other forms of urticaria, many patients describe stinging, tingling, or burning sensations rather than intense pruritus. CholU frequently coexists with atopic diseases such as atopic dermatitis, allergic rhinitis, and bronchial asthma, especially in moderate-to-severe cases [16].

Morphological presentation of CholU is heterogeneous. Shurmelova et al. identified six different skin reaction patterns after provocation testing, including classic pinpoint wheals with erythema, confluent erythematous plaques, and small aggregated red papules. Most patients exhibited more than one lesion type simultaneously. Lesions were most commonly localized on the trunk, neck, and upper extremities [18]. Nagai et al. on the other hand described two major clinical phenotypes: a classic red wheal/erythema type associated with pruritus, atopy, and positive autologous sweat skin tests, and a goosebump-like rash type associated with male sex, hypohidrosis, and painful sensations rather than itching [19].

Although CholU is usually limited to the skin, severe systemic reactions may occur. Patients can develop angioedema, dyspnea, dizziness, hypotension, gastrointestinal symptoms, and anaphylaxis, particularly after intense or prolonged trigger exposure. A distinct phenotype, CholU with palpebral angioedema, is associated with female sex, atopy, and a particularly high risk of anaphylaxis [17].

3.4. Diagnosis

Diagnosis of cholinergic urticaria (CholU) is primarily based on its characteristic clinical presentation and the reproducible occurrence of symptoms after sweating or an increase in core body temperature [16]. Because symptoms are triggered by exercise, passive warming, emotional stress, or hot environments, provocation testing is recommended both to confirm the diagnosis and to exclude other inducible urticarias.

According to EAACI recommendations, diagnosis should be based on provocation and threshold testing [2]. Standard methods include pulse-controlled ergometry (treadmill or bicycle exercise) or passive warming with a hot bath at 42°C for about 15 minutes, aiming to increase core body temperature by at least 1°C above baseline [3].

Azizi and colleagues proposed a simpler and more accessible provocation test suitable for outpatient settings and developing countries. The protocol consists of repeated stair climbing with progressive heart rate elevation monitored every 5 minutes. The study demonstrated that a body temperature above 37.05°C or an increase of at least 0.35°C from baseline reproduced symptoms with high specificity and good sensitivity, particularly when measured in the forehead region [20].

Additional diagnostic tools include intradermal testing with cholinergic agents such as acetylcholine or methacholine, which may induce satellite wheals in some patients and help assess local sweat gland function [16].

Differential diagnosis includes other inducible urticarias and exercise-related disorders. Food-dependent exercise-induced anaphylaxis (FDEIA) must be excluded using food-specific IgE testing, skin prick tests, and combined provocation challenges. Heat urticaria is limited to areas of direct heat contact and is confirmed by local heat provocation. Aquagenic urticaria is triggered by water exposure regardless of temperature. Adrenergic urticaria presents with pruritic papules and a characteristic white vasoconstrictive halo and can be confirmed by adrenergic intradermal testing. Cold-induced cholinergic urticaria (generalized reflex cold urticaria) should also be considered when symptoms occur after systemic cold exposure rather than heat or sweating [16].

3.5. Impact on Daily Life and Physical Activity

In contrast to other inducible urticarias, in which periods of remission or reduced symptom severity may occur, many patients with cholinergic urticaria experience the disease for many years or throughout life. Consequently, patients may avoid activities that induce urticaria and modify their daily habits without seeking medical treatment [21].

CholU may negatively affect quality of life and can be a source of considerable discomfort [4,9,21,22]. In severe cases, patients may become unable to study, work, or perform household activities [5]. Fear of symptom occurrence may additionally contribute to avoidance behaviours, as patients may avoid potentially stressful situations or activities associated with sweating [22]. Interestingly, despite the moderate-to-severe intensity of symptoms, patients with CholU did not take sick leave days or attend emergency departments, suggesting adaptation to the limitations associated with the disease [21].

In physically active individuals, CholU is particularly relevant because exercise may act as one of the provoking stimuli. Fonseca, Rodrigues and Lemos (2022) reported that the disease may affect participation in physical exercise, while fear of symptom occurrence may additionally contribute to avoidance of activities associated with sweating [22]. Similarly, Minowa et al. (2020) noted that avoidance of provoking stimuli, including exercise, may negatively influence quality of life in affected individuals [23].

Avoidance of causative factors is considered a standard approach in CholU management; therefore, patients often limit or avoid exercise when it triggers symptoms [4,23]. Current recommendations indicate that nonsedating H1-antihistamines together with trigger avoidance should be used as first-line treatment [9].

However, appropriate management may help patients cope with CholU without complete restriction of physical activity. In the case described by Fonseca, Rodrigues and Lemos (2022), the patient continued daily antihistamine therapy and used prophylactic antihistamines before physical activity [22]. Although lesion occurrence remained dependent on exercise intensity, counselling, reassurance, and patient education improved confidence regarding exercise participation and enabled continuation of physical activity [22].

The importance of effective treatment was also illustrated by Koumaki and Seaton, who described a 39-year-old woman with severe CholU whose symptoms were exacerbated by mild heat exposure and physical activity. After unsuccessful treatment with several medications, omalizumab therapy was introduced. Following treatment, the patient became asymptomatic and was able to resume all activities, including exercise, long-distance triathlon participation, and hot baths [24]. These reports suggest that appropriate management may reduce the impact of CholU on daily functioning and help maintain participation in physical activity.

3.6. Treatment and Prevention

Cholinergic urticaria is a chronic, episodic condition whose symptoms can significantly impact daily functioning. The goal of treatment is to control symptoms and improve quality of life. For athletes and physically active individuals, it is important to maintain the ability to engage in physical activity.

Treatment is based on second-generation antihistamines, which block H1 receptors, alleviating itching and skin symptoms [25]. Preparations containing cetirizine, levocetirizine, loratadine, and desloratadine are used. Second-generation antihistamines are preferred for athletes because, compared to first-generation antihistamines, they have less sedative effects and thus do not significantly impair the ability to perform physical activity [25]. If the standard dose does not provide sufficient symptom control, it is recommended to increase the dose of antihistamines up to four times the standard dose [2]. In cases resistant to treatment with antihistamines, omalizumab - an antibody that reduces mast cell activation - may be used [26]. During intense exercise, exercise-induced anaphylaxis may occur. In such a situation, exercise should be stopped immediately and epinephrine administered [16].

Non-pharmacological management primarily involves avoiding triggers such as excessive physical exertion, overheating, and high ambient temperatures [27]. For athletes and physically active individuals, it is crucial to adjust the type, intensity, and conditions of physical activity to prevent the onset of an urticaria attack. This can be achieved through proper warm-ups, gradually increasing training intensity, training in cooler conditions, adequate hydration, and wearing breathable clothing [28].

Cholinergic urticaria can significantly affect exercise tolerance in athletes and physically active individuals. The occurrence of skin lesions, itching, and a burning sensation during training leads to discomfort and, in some cases, the need to interrupt physical activity. These symptoms may limit the ability to maintain an appropriate training intensity and affect training regularity. Additionally, some patients experience reduced psychological well-being due to fear of symptom onset during exercise. This may lead to avoidance of intense forms of physical activity, which in turn can affect physical fitness levels and quality of life.

Prevention of cholinergic urticaria in athletes and physically active individuals is a key component of treatment, as physical exertion is the primary trigger for the condition's symptoms. In addition to non-pharmacological management, pre-exercise pharmacological prophylaxis is used, which involves administering second-generation antihistamines before engaging in physical activity [2]. This may reduce the risk of symptoms occurring during training.

The treatment of cholinergic urticaria in athletes and physically active individuals requires a comprehensive approach that includes both pharmacotherapy and appropriate modification of physical activity. The condition can limit exercise tolerance, affect training comfort, and impact patients' quality of life. Pharmacotherapy plays a key role in management, primarily using second-generation antihistamines, which enable symptom control and often allow for the continuation of physical activity. Non-pharmacological management is also an important component, including proper preparation for exercise and patient education. Appropriately selected treatment and management strategies allow most patients to safely maintain physical activity and improve their quality of life.

4. Conclusions

Cholinergic urticaria remains a complex and not fully understood disorder, with an incompletely elucidated pathophysiology involving multiple interacting mechanisms. Despite advances in understanding disease mechanisms, significant gaps in knowledge persist, particularly regarding the relative contribution of individual pathogenic pathways and the reasons for clinical heterogeneity.

Clinically, CholU can be highly burdensome. Recurrent symptoms often significantly impair quality of life and may lead to avoidance of physical activity, reduced exercise tolerance, and limitations in daily functioning. In more severe cases, the disease may be associated with systemic symptoms, including angioedema, respiratory compromise, and potentially life-threatening anaphylaxis.

At the same time, therapeutic options are continuously evolving. In addition to standard antihistamine therapy, newer treatment approaches, including biologics such as omalizumab and other targeted strategies, have shown promising results.

Nevertheless, there is a clear need for further well-designed studies to better characterize the pathophysiology, improve phenotypic classification, and optimize individualized treatment strategies for cholinergic urticaria.

Disclosure

Supplementary Materials

Not applicable.

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During the preparation of this work, the authors used OpenAI's ChatGPT for the purpose of editorial assistance, including language editing, improving clarity and conciseness, and minor stylistic revisions. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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