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Perspective

Contemporary approaches to the diagnosis and management of physical urticaria

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Clinical Problem

Physical urticaria is considered a subgroup of chronic urticaria (CU) and is characterized by lesions reproducibly triggered by physical stimuli, including cold, heat, physical pressure, vibration, sunlight, water, and exercise. This physical stimulation of the skin incites the characteristic pruritic wheal and flare (ie, hive) response characteristic of urticaria; physical triggers also can provoke angioedema. Physical urticaria can occur alone or concomitantly with other types of chronic or spontaneous urticarial syndromes. The exact pathogenesis of the various physical urticarial syndromes is unknown. The diagnosis of physical urticaria is established by history and physical examination, and in many physical urticaria subtypes, the diagnosis can be confirmed by specific skin provocation testing. As with CU in general, the goals of treatment of physical urticaria are focused on symptom control from identifying and avoiding provocative physical stimulation and from managing symptoms with medical therapy to maximize symptom relief with the least possible toxicity.

Strategies and Evidence

The prevalence of physical urticaria is likely underestimated in the general population. Less severe cases may not come to medical attention or may be treated by primary care providers and thus under-reported. Studies on physical urticaria in the literature are derived largely from specialist experience at tertiary care centers,

predisposing to centripetal bias in reports of the severity and duration of the various physical urticarial syndromes. With this in mind, up to 0.5% of the general population has been estimated to have a physical urticaria/angioedema condition and in up to 20% of patients with CU a physical urticaria component is present.^{1,2}

The prevalence of the various physical urticaria syndromes also varies. Simple dermatographism, a subgroup of dermatographic urticaria, is likely the most common form of physical urticaria, occurring in up to 5% of the general population.³ Cholinergic urticaria is also common, accounting for approximately 5% of all cases of CU and up to 30% of all cases of physical urticaria.⁴ It affects the 2 sexes equally.⁵ Delayed pressure urticaria and angioedema (DPUA) has been described in up to one third of all patients with CU.⁶

The other physical urticaria and angioedema syndromes are less common. The frequency of acquired cold urticaria may be affected by climate and geographic location, with various studies estimating a frequency of cold urticaria from 5% to 30% among the physical urticarias.⁷ Cold urticaria affects the 2 sexes equally, with studies suggesting that cold urticaria often begins in younger adults (<30 years of age).^{8,9} Aquagenic urticaria is rare, with fewer than 100 cases in the literature; it may be more common in women, with age of onset after puberty; and familial cases have been reported.^{10,11} Solar urticaria is a rare form of urticaria and rare among the photodermatoses, with studies suggesting that it can be found in only 0.08% of patients with CU.¹² Most patients develop the disorder in young adulthood, with a higher prevalence in women.¹³ Local heat or heat contact urticaria is also rare, with fewer than 100 cases in the literature, with familial cases also reported.¹⁴ Urticaria may occur as a manifestation of exercise-induced anaphylaxis, and exercise-induced anaphylaxis may occur in up to 5% of all anaphylaxis cases.¹⁵ Vibratory urticaria and angioedema is also rare, with fewer than 50 cases in the literature, and may be acquired or hereditary.^{1,16}

Evaluation

In many cases, a diagnosis of a physical urticaria and angioedema syndrome can be established by history. Different challenge

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procedures may be used to confirm a diagnosis of a specific syndrome and/or to monitor response to treatment. The sensitivity and specificity of these procedures have not been established. Moreover, the recommended protocol for most physical urticaria and angioedema challenges is based on convention (eg, pressure challenge with a stimulus of 15 lb for an exposure time of 15 minutes) rather than a documented need to perform the procedure in a rigid or specific fashion.

The diagnostic procedures that can be carried out to confirm a diagnosis of a physical urticaria and angioedema syndrome are described below and presented in Table 1.

Aquagenic Urticaria

A diagnosis of aquagenic urticaria can be confirmed by applying a water compress at 35°C to the skin of the upper body for 30 minutes.¹⁷ The appearance of “pinpoint” (1–3 mm) hives at the site of challenge is a positive response. Water immersion of a hand or distal upper extremity also may be performed to confirm the diagnosis. Aquagenic urticaria should be distinguished from several other conditions, including (1) aquagenic pruritus, in which provocation of itching occurs in the absence of wheal formation¹⁸; (2) cold urticaria, in which an exaggerated reaction to ice cube challenge can be elicited (see below); and (3) cholinergic urticaria, in which pinpoint lesions manifest but in response to heat (see below). However, it should be noted that cases of aquagenic and coexisting cold urticaria and cholinergic urticaria have been reported.^{19,20}

Cholinergic Urticaria

Intradermal injection of methacholine 0.01 mg in saline 0.1 mL can provoke the formation of at least 1 “satellite wheal”; although this is commonly used as a provocation test, it is associated with suboptimal sensitivity. As few as 1 in 3 patients with cholinergic urticaria may exhibit a “positive” response to a methacholine intradermal challenge, and those who do may not do so consistently.²¹ Because of a poor negative predictive value, a methacholine intradermal challenge may confirm but cannot rule out the diagnosis of cholinergic urticaria.

Provocative challenges that increase core body temperature, including exercise or hot water immersion, may be associated with more optimal sensitivity. Partial immersion of a patient in a hot bath (42°C) to increase the body temperature by at least 0.7°C can be used if a challenge procedure with greater sensitivity is desired.²

Patients with a “follicular” subtype of cholinergic urticaria may exhibit a wheal or flare reaction to autologous diluted sweat, implying that in these patients sweat contains factors that can elicit

histamine release.²² In such patients who have refractory cholinergic urticaria, rapid desensitization to autologous sweat may be as efficacious as a therapeutic intervention.²³

Cold Urticaria

Provocative cold testing (ie, cold stimulation or ice-cube challenge) can be used to confirm a diagnosis of primary or secondary acquired cold urticaria. The most common protocol entails a 0°C to 4°C stimulus (eg, an ice cube in a plastic bag) placed on the forearm for 5 minutes and then observing the challenge site as the skin rewarms to ambient temperature. The development of a wheal or flare response during rewarming is a positive test result.²⁴ If an exaggerated reaction is not observed with a 5-minute challenge, the test can be repeated incrementally up to 10 minutes. The optimal or maximal duration of challenge testing to exclude the presence of cold urticaria has not been determined.²⁵ A caveat concerning this challenge is that a cold stimulus should not be reapplied at a previously challenged site, to avoid a “false negative” result owing to local desensitization of the skin.

Acquired cold urticaria variants have been described in which provocative cold testing is negative, including systemic atypical acquired cold urticaria, cold-dependent dermatographism, cold-induced cholinergic urticaria, acquired delayed cold urticaria, and localized cold reflex urticaria.

A cold stimulation time test may have utility in the management of patients with cold urticaria. If an ice cube challenge result is positive at 5 minutes, it can be repeated serially at 1-minute intervals to identify the minimum exposure time for a positive challenge. Alternatively, if a result is negative at 5 minutes, it can be performed serially at 1-minute intervals to determine the minimum exposure time for response, up to a maximum of 10 minutes.^{8,24} The cold stimulation time test can be used to assess response to therapeutic interventions (eg, antihistamine medications). Prolongation of cold stimulation time to longer than 3 minutes may be used as a goal of pharmacologic therapy, although patients who achieve this goal of therapy should still be considered at risk for systemic reactions from aquatic activities.⁸ Hand immersion in a 10°C water bath for 5 minutes also may be used to confirm a diagnosis; angioedema during rewarming is regarded as a positive test result. Because systemic reactions may occur, this challenge is not preferred.^{26,27}

Delayed Pressure Urticaria and Angioedema

Patients with DPUA develop swelling with exposure of the skin to a pressure stimulus, but do so at a delay of 0.5 to 12 hours, with a peak at 4 to 6.5 hours.^{28–32} Biopsy of angioedema lesions provoked

Table 1
Characteristics of physical urticarias

Type	Clinical features	Familial	Angioedema	Diagnostic test	Transfer factor ^a
Aquagenic	more common in women than in men	yes	no	application of room-temperature wet compress to upper body for 30 min at 35°C	no
Cholinergic	itchy, small 3- to 5-mm monomorphic pale center with surrounding erythema	yes	yes	methacholine intradermal injection, exercise, or hot water immersion	yes
Cold (primary vs secondary)	itchy, pale lesions (5% with cyroglobulins)	yes	yes	5- to 10-min ice-cube test	yes
Delayed pressure	large painful or itchy lesions	no	yes	dermographometer; application of weight or force to a skin area, eg, 15-lb weight for 15 min	no
Dermatographism	linear lesions	yes	no	light stroking of skin	yes
Exercise-induced urticaria and anaphylaxis	hives distinguishable from cholinergic lesions	yes	yes	treadmill exercise challenge; can be performed without or after ingestion of inciting food or other agent	no
Solar	itchy pale or red swelling	yes	yes	irradiation by solar simulator	yes
Vibratory	erythema and edema sharply demarcated from normal skin	yes	yes	vortex mixer for 1–5 min	no

^aTransfer factor refers to the ability to passively transfer a physical urticaria by intracutaneous injection of serum from a patient with a specific physical urticaria to a naive patient.

by pressure display a more intense inflammatory infiltrate than that seen in biopsies of typical CU lesions and do not show findings seen in lesions from patients with leukocytoclastic vasculitis. Histopathology shows an eosinophil- and neutrophil-rich infiltrate in the dermis and subcutaneous tissues.^{33,34}

DPUA can be confirmed by a challenge procedure that involves the application of a pressure stimulus, typically a weight or force to a specific area of skin. Development of angioedema at the challenge site can confirm this diagnosis. However, published protocols vary in the pressure stimulus used, the duration of the challenge, and the area of the body to which the stimulus is applied. Positive and negative likelihood ratios for the challenge procedure have not been determined.

A commonly recommended challenge procedure entails the suspension of a 15-lb weight across the shoulder for 10 or 15 minutes.^{29,32} A deep painful reaction at the challenge site, occurring 2 to 12 hours later, with peak swelling at 4 to 6.5 hours, is considered a positive response. Some protocols recommend ambulation with weights suspended over the shoulder, but whether ambulation enhances the sensitivity of the challenge procedure is unknown. The challenge procedure should be performed when chronic idiopathic urticaria and angioedema, which also may be present in patients with DPUA, is stable. Other challenge procedures include the use of a calibrated dermatographometer or an apparatus with weighted metal rods.^{35–37}

Dermatographia

The diagnosis of dermatographia may be confirmed by stroking the skin with a firm object, such as a tongue blade or another instrument with a firm edge. A white line develops on the skin as a consequence of reflex vasoconstriction; this is followed promptly by the development of a wheal and flare reaction at the challenge site. The wheal-and-flare response should develop within 1 to 3 minutes.²

Exercise-Induced Urticaria and Anaphylaxis

The diagnosis of exercise-induced urticaria and angioedema can be confirmed by an exercise challenge in a controlled environment.^{38,39} Because an exercise challenge entails the risk for anaphylaxis, this challenge should be performed only in an environment in which appropriate personnel, equipment, and supplies are in the immediate vicinity.

In patients with food-specific exercise-induced urticaria and angioedema, the clinical relevance of a specific food suspected by history can be evaluated with immediate hypersensitivity skin testing or detection of in vitro serum-specific IgE antibody. If food-associated exercise-induced urticaria and angioedema is suspected, a challenge procedure can be performed with and without food consumption. The development of urticaria during a treadmill exercise challenge also may be provoked in patients with cholinergic urticaria, because exercise increases body temperature; however, the morphology of the lesions that appear can be used to distinguish these 2 conditions.^{39–41} A diagnosis of cholinergic urticaria also can be confirmed by passive heating and/or intradermal injection of methacholine.

Solar Urticaria

The diagnosis of solar urticaria can be confirmed with phototesting, to simulate provocation of urticarial lesions with sunlight. Reactions are more frequently observed with ultraviolet (UV) A or visible wavelengths, less commonly with UVB or infrared radiation.⁴² A commonly used provocative method uses a xenon arc lamp with a monochromator to ascertain the minimal urticarial dose at different wavelengths of light. Phototesting is performed on an area of non-sun-exposed skin, such as the mid and lower

back.⁴³ If a xenon lamp with monochromator is not available, other light sources, such as a slide projector light bulb (for visible light), fluorescent black light (UVB and UVA wavelengths), fluorescent sunlamp (UVB and UVA wavelengths), or infrared lamp (infrared wavelengths), can be used.^{43–45} For each wavelength or light source used, the minimal urticarial dose can be determined by exposing a 1-cm² area of skin at a distance of 10 cm from the light source. Provocative light exposure also can be used to confirm the diagnosis without determining the minimal urticarial dose. Response is assessed immediately after light exposure. A pruritic erythematous wheal developing during or shortly after irradiation, that fades within a few minutes after the light stimulus is removed, is accepted as a positive challenge result.⁴³ If this provocative test result is negative (no response after 1–3 minutes), it should be repeated on the originally affected skin area; if still negative, the test should be repeated with direct sun exposure before a diagnosis of solar urticaria can be ruled out.^{46,47} It is important to distinguish solar urticaria from polymorphous light eruption.^{48,49} Lesions of polymorphous light eruption typically last longer than 24 hours. In patients with erythropoietic protoporphyria, lesions may be painful rather than pruritic, symptom onset is early in life and in association with a positive family history, and the diagnosis can be confirmed by elevated protoporphyrin levels.

Vibratory Angioedema

Vibratory angioedema can be confirmed by an exaggerated reaction to stimulation of the skin with a vortex mixer. Similar to other physical urticaria and angioedema syndromes, there is a lack of evidence permitting recommendations as to the optimal vibratory stimulus to use, the duration of exposure to vibration, and grading of a positive reaction. A challenge procedure that is generally accepted and has been described in several reports entails supporting a patient's forearm under the wrist and elbow so that the skin of the forearm, hand, or finger rests in the rubber cup of a vortex mixer. Then, the mixer is vibrated at constant speed for at least 1 minute and up to 5 minutes.^{16,50} A positive response to vibration is the development of erythema and edema sharply demarcated from normal skin within 4 minutes of stimulation and persisting for at least 1 hour. The response can be quantified by measuring the change in forearm circumference or finger volume.¹⁶

Normally, patients who undergo this challenge may develop pruritus and erythema, with no angioedema, that resolves in less than 30 minutes. Patients with vibratory angioedema who undergo a challenge with a vortex mixer develop erythema, pruritus, and angioedema in 30 seconds to 5 minutes. In 1 report, forearm erythema and pruritus developed with vibratory provocation that faded within 30 minutes of stimulation, recurred at 1 to 2 hours, and peaked at 4 to 6 hours, suggesting that the delayed onset of vibratory angioedema after provocation should still be interpreted as consistent with the diagnosis.⁵¹

Symptomatic vs Specific Treatment

Treatment of physical urticarias requires avoidance of the inciting agent, in some cases progressive exposure to the stimulus to induce tolerance and/or administration of medications commonly used to treat CU. It has been proposed that pseudoallergens, defined as substances to which individuals are exposed through dietary intake, including food additives, vasoactive substances, fruits, vegetables, and spices, can induce intolerance reactions that provoke and perpetuate CU. Although pseudoallergen-free diets have been recommended because of reports that some patients with CU with a physical component exhibited improvement, when responders underwent pseudoallergen challenge, fewer than 20% reacted. Based on the burden of adhering to such diets, this intervention cannot be

recommended for the management of patients with physical urticaria until the therapeutic utility of this intervention is established in more methodologically sound studies.^{52,53}

Aquagenic Urticaria

The pathogenesis of aquagenic urticaria is unknown but several mechanisms have been proposed. For example, it has been postulated that interaction with water and a component in the stratum corneum or sebum creates a toxic compound, which, after it is absorbed in the skin, can cause mast cell activation. Other studies have shown that enhancement of water's ability to penetrate the stratum corneum increases the severity of the urticarial response. However, none of these proposed mechanisms have been confirmed to explain the cause of aquagenic urticaria. For these reasons, treatment is empiric and includes avoidance measures as feasible. Oral antihistamines are not uniformly effective for all patients.¹¹ Pretreatment with anticholinergic agents, such as scopolamine, has been shown to suppress hives after water exposure. Treatments with petrolatum barrier cream, selective serotonin reuptake inhibitors, and UVA or UVB phototherapy have been reported to be effective in refractory cases.^{17,20,54} A case of aquagenic urticaria refractory to antihistamines, in a patient infected with the human immunodeficiency virus, responded to stanozolol.⁵⁵

Cholinergic Urticaria

Several mechanisms have been postulated for cholinergic urticaria, including increased secretion of acetylcholine, hypersensitivity to acetylcholine, impaired cholinesterase activity, hypohidrosis, and antigen-antibody immune complex reactions.^{21,27,28,56} Effective treatment includes avoidance of triggers. However, this recommendation is not always feasible and does not always prevent outbreaks. Most patients with cholinergic urticaria will benefit from regular use of oral antihistamines. For those patients who exhibit a poor response to antihistamines, more complex antihistaminic regimens, including mast cell-stabilizing agents such as ketotifen, may be effective. Cases showing the effectiveness of the androgen, danazol, and the anti-IgE biologic, omalizumab, have been reported.^{57–59} Contrary to expectations based on the name of this physical condition, anticholinergic agents have not been shown to be effective for cholinergic urticaria.⁶⁰ Patients with severe cholinergic urticaria may manifest systemic symptoms consistent with anaphylaxis and should be provided with a self-administered epinephrine injector.

Cold Urticaria

Treatment of cold urticaria depends on the specific type manifested by the patient. Avoidance of cold temperatures is the main treatment for acquired cold urticaria, with or without positive cold provocation testing. These patients are at risk for developing hypotension and shock while engaging in aquatic sports and other cold-weather work or leisure activities.^{8,24} Patients who manifested a positive result after a cold stimulation time test shorter than 3 minutes were reported to be at greater risk for developing vascular collapse when exposed to cold temperatures.⁸ Laryngeal attacks can be precipitated by exposure to cold foods or drinks.⁶¹ Treatment with antihistamines is usually effective in preventing episodes. Specifically, cyproheptadine, hydroxyzine, doxepin, or combinations of these antihistamines with H₂ antagonists have been reported to be effective in preventing symptoms and achieving a delay in cold stimulation time tests.^{62–65} Other agents, including ketotifen and montelukast and combination treatment with cetirizine and zafirlukast, have been reported to be effective.^{66–68} Corticosteroids have not been found to be effective in preventing primary or secondary acquired cold urticaria

outbreaks.⁶⁹ Successful treatment with omalizumab has been described.⁷⁰ Gradual immersion in cold water at regular intervals has been shown to induce tolerance in some individuals.^{71,72} Continuous exposure is essential to maintain tolerance and prevent recurrence of cold-induced urticaria.^{69,72} Therefore, cold tolerance protocols should be recommended only for very compliant patients, given the risk of cold-induced systemic reactions. For patients undergoing surgery, the operating room temperature should be increased and all fluids and blood products should be prewarmed to prevent cold-induced symptoms. Pretreatment with H₁ and H₂ antagonists and corticosteroids has been reported to prevent reactions during surgery.^{73,74} Case reports of leukotriene receptor antagonists alone or in combination with antihistamines have suggested benefit in cold urticaria.⁶⁷

Delayed Pressure Urticaria and Angioedema

Delayed pressure urticaria and angioedema is one of the more challenging forms of physical hives to manage. This condition can have a significant impact on daily work and leisure activities, resulting in an impaired quality of life.^{4,75} Patients should be advised to avoid prolonged pressure to different body sites or trauma, which can elicit swelling episodes. H₁ and H₂ antagonists alone are typically not effective.^{29,30,32} One double-blinded controlled study comparing cetirizine with placebo in patients with DPUA found that cetirizine 30 mg was associated with greater efficacy.⁷⁶

Two randomized controlled trials showed that leukotriene receptor antagonists in combination with antihistamines were more effective than antihistamine monotherapy in patients with DPUA.^{77,78}

Some studies have reported clinical improvement in patients with localized delayed pressure urticaria treated with different preparations of potent topical corticosteroids.^{79–81} Short courses of oral corticosteroids may be required, but long-term use of oral corticosteroids is not recommended. Some cases of DPUA may benefit from nonsteroidal anti-inflammatory drugs, but no statistically significant benefit was found in a double-blinded trial with indomethacin 25 mg 3 times a day compared with placebo.^{30,32} Because many patients with physical urticaria also have spontaneous CU outbreaks, which may be exacerbated by the administration of cyclooxygenase-1-inhibiting drugs, prescribing aspirin or aspirin-like drugs to patients with DPUA should be approached cautiously.⁸² A randomized, double-blinded trial showed benefit in patients with DPUA using nimesulide, a cyclooxygenase-2 inhibitor, and ketotifen, which was equivalent to outcomes observed with high-dose prednisone.⁸³ Other therapeutic agents that have been anecdotally reported to be effective include montelukast, sulfasalazine, chloroquine, dapsone, intravenous gamma globulin, tranexamic acid, anti-tumor necrosis factor- α and omalizumab.^{84–89}

Dermatographism

Treatment of dermatographism includes moisturizing the skin in combination with daily H₁ antagonists to increase the itch threshold response and prevent scratching, which triggers lesions. Although this approach is clinically very effective, there are few controlled studies documenting the efficacy of these interventions. First- and second-generation H₁ antagonists, including hydroxyzine and cetirizine, respectively, have been shown to improve symptom control.^{90–93} The addition of H₂ antagonists to H₁ antagonists has been found to be of benefit, but not consistently, in all studies.^{94–96} Use of UVB phototherapy also has been reported to be effective in some cases.⁹⁷

Potent topical corticosteroids have been shown to decrease mast cell numbers and welting of the skin after stroking in 6 patients with dermatographism.⁹⁸

Exercise-Induced Urticaria and Anaphylaxis

Patients with this form of physical urticaria should be advised not to exercise in close proximity to the ingestion of known factors that can induce an attack, such as a specific food or drug. Although the period that affected patients should not exercise after eating is controversial, it generally recommended patients wait at least 4 hours after exposure. However, the duration from eating to exercise-induced symptoms can be as long as 24 hours, so this recommendation should be individualized for each patient.⁹⁹

Patients with exercise-induced urticaria and anaphylaxis should exercise with a partner knowledgeable about their condition, has a cell phone, and is capable of treating an episode if it occurs. Self-injectable epinephrine should be carried by the patient, and medical identification jewelry should be worn. Furthermore, patients should avoid exercising on warm, humid days, avoid concomitant use of aspirin and aspirin-like drugs, and stop exercising immediately if early symptoms of anaphylaxis, such as flushing, pruritus, or urticaria, develop. Treatment of a severe exercise-induced episode is similar to the management of anaphylaxis and may require the administration of epinephrine, intravenous fluids, oxygen, antihistamines, corticosteroid, endotracheal intubation, and/or other resuscitative measures. A refractory case successfully managed with omalizumab has been reported.¹⁰⁰

Solar Urticaria

Avoidance of relevant wavelengths of light or using protective sunscreens may be of benefit.³⁹ H₁ antihistamine therapy may have variable effectiveness in preventing or attenuating solar urticaria.^{101–107} Desensitization to induce tolerance using different bands of light, including broadband UVB, narrowband UVB, UVA and visible light therapy, by gradually increasing exposure over time, has been reported to be effective.⁴³ Skin exposed to natural sunlight on a consistent basis may become less reactive than skin normally covered from the sun.¹⁰⁸ Treatment typically begins using 3% to 5% UVA/UVB beginning for short periods (approximately 3–5 minutes) and gradually increasing the intervals (10–15 minutes) 3 times a week for up to 30 treatments. Tolerance dissipates if controlled phototherapy or natural exposure to sunlight is not continued.¹⁰⁹ Photochemotherapy with 8-methoxypsoralen given orally before UVA irradiation may be more effective but frequently requires maintenance treatment that is associated with drug-specific adverse risks of burns or skin cancer.¹¹⁰ In severe cases, benefit with plasmapheresis with or without 8-methoxypsoralen plus UVA irradiation, cyclosporin A, and intravenous immunoglobulin has been reported.^{111–114} Omalizumab has been found to have a variable therapeutic benefit for the treatment of solar urticaria.^{70,115–117}

Vibratory Angioedema

Treatment of vibratory angioedema includes avoidance of provocative stimuli. It has been suggested that vibratory angioedema triggered by running can be attenuated by “warming up” before exercise.¹¹⁸ Progressive exposure to vibratory stimuli has been shown to induce tolerance.¹¹⁹ Some case reports have suggested that H₁ antagonists may be effective, whereas others have found no benefit.^{120–122} A recent case reported no benefit using omalizumab but described a salutary effect when ketotifen was administered.¹²³

Areas of Uncertainty

Although the provocative stimuli and challenge methodologies for diagnosis of physical urticarias are well accepted, the pathogenic mechanisms for the development of urticaria and

angioedema with exposure to relevant physical factors are not well understood. This has hindered the development of specific treatments that could lead to improved control. The need for improved therapies is quite apparent when the long-term prognosis of patients with CU and a physical component is compared with those without a physical component. A longitudinal study found that the prognosis of uncomplicated CU was relatively favorable for improvement or remission.¹²⁴ After 1 year, 35% of patients with CU without a physical component were free and 30% had decreased symptoms. After 3 years, 47% of patients with CU without a physical component had spontaneous remission compared with only a 16% remission rate of patients with a physical urticarial component.¹²⁴ These data imply the prognosis for complete resolution of CU is significantly impaired for those patients with a component of physical urticaria.

Guidelines

Several US, European, and international guidelines for urticaria have been published that include recommendations for the evaluation and treatment of physical forms of urticaria.^{125–127} These documents are relatively in agreement regarding the current scientific literature and recommendations pertaining to the evaluation and management of the physical urticarias.

Conclusions and Recommendations

Physical urticaria is a perplexing form of urticaria that requires additional research to better understand its mechanisms and to develop more efficacious therapies. The current treatment approach is to avoid inciting triggers as feasible and to use therapies shown to be effective for the specific form of physical urticaria, taking into consideration the burden of disease and safety of each treatment. Patients with CU should be advised that the duration of their urticaria may be prolonged if it is associated with a physical component.

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