Review

Water-Induced Itching Without Cutaneous Signs

Aquagenic Pruritus

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• **Aquagenic pruritus is now a well-recognized symptom complex, usually of unknown origin. A few prove to have polycythemia rubra vera. We describe an important and distinct subset, termed *aquagenic pruritus of the elderly,* in which old age, dry skin, and seasonal weather conditions are major factors. Unlike other varieties, aquagenic pruritus of the elderly responds to appropriate local measures.**

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No event seems more innocuous than contact of the skin with water. For some people, however, contact with water may be accompanied by distressing signs (wheals) and symptoms (itching). In some cases, it is not the wetting of the skin that is responsible but an associated factor. For example, in cold urticaria, it is not the water but the lowered temperature that elicits the reaction. Likewise, in urticarias triggered by hot water, namely cholinergic and heat urticaria, the water is merely coincidental. Symptomatic dermatographism from powerful jets during showering illustrates another situation in which water is merely the vehicle for delivering the triggering mechanical force. On the other hand, in aquagenic urticaria, it is the water itself that is the provocative agent by some unknown mechanism. In all these, the wheal is the stereotyped response.

Contact with water may have adverse effects in the absence of visible signs. We refer here to aquagenic pruritus (AP), which has only recently been described.[1] It is the rare physician who perceives a connection between water exposure and bouts of intense itching. Aquagenic pruritus is a newcomer to the dermatologic vocabulary. Knowledge about water-induced pruritus is most advanced in association with polycythemia rubra vera (PRV).[2-5]

A hitherto undescribed, to our knowledge, variety of AP occurs frequently in the elderly and is the source of much distress. It is our intention in this article to summarize knowledge about AP, with emphasis on its expression in the aged.

AP

A detailed analysis of 36 patients with AP has recently been reported.[6] Patients experience intense skin discomfort after contact with water regardless of temperature. This is usually described as itching, but other symptoms may be mixed in, such as burning and pricking. There are no visible skin changes; the symptoms are limited to sites of water contact. Urticaria is absent. The patients have none of the cutaneous or internal disorders associated with pruritus. Drugs are not causative. However, PRV, a specific type of AP, has to be excluded.

The following is a synopsis of the main features of pure AP reported recently. The mean age (±SE) at onset was 29.4 ± 13.4 years for women and 34.5 ± 20.0 years for men. Most patients had complained of AP for approximately ten years. One third had a family history of AP. There was no relationship to atopy. The patients experienced itching, burning, tingling, or prickling quality after contact with

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Comparison of Clinical Features of Aquagenic Pruritus and Aquagenic Pruritus of the Elderly

Clinical Feature	Aquagenic Pruritus	Aquagenic Pruritus of the Elderly
Age at onset	Young/middle-aged	Elderly
Sex incidence	50% male	75% female
Family history	33%	None
Seasonal incidence	None	Winter
Relationship to water contact	During contact (50%)	Invariably during drying
Appearance of skin	Normal	Dry, scaly
Psychiatric symptoms	Common	None
Emollients	Ineffective	Effective

water, fresh or seawater, at any temperature. The condition was generally unremitting, though in some, freedom from pruritus periodically lasted a few months. In about half, the pruritus began about five minutes after exposure to water. In the remainder, symptoms occurred two to 15 minutes after water contact had ceased. The itching lasted about 40 minutes on the average, but could persist up to two hours. It is important to note that water was not the sole incitant in many cases. Sudden changes in temperature, as when getting in or out of bed, might start a bout of itching. Heat produced pruritus in about 30% and cold in 35%. The occurrence of AP after exertion in a few patients is probably attributable to sweating. Emotional upsets were triggering factors in a small minority.

Aquagenic pruritus often began in the legs and thighs before spreading elsewhere. The trunk, shoulders, and arms were affected in most patients. Careful inspection of the body surface revealed nothing of significance. Dry skin was noted in only one person.

One of the most striking features of AP was unpleasant psychological changes during attacks. Fifty-five percent of patients noted feelings of aggression, irritability, anger, and depression. Examination during episodes of itching revealed no skin abnormalities.

Neither H_1 nor H_2 antihistamines alone or in combination were of value. Neither emollients nor other topical treatments seemed to provide protection against attacks. Preliminary results suggest that ultraviolet radiation may be useful, as in some other types of intractable pruritus.

The pathogenesis of AP is unknown. Pharmacological analysis of blood before and during attacks of AP in four patients revealed elevated levels of histamine. Skin biopsy specimens showed an increased population density of degranulated mast cells before and during attacks, although total numbers of mast cells were within normal limits. Nonetheless, it is unlikely that histamine is the sole mediator of AP. First, the quality of itching is unlike that induced by histamine. Second, antihistamines are ineffective. One possibility is the release of proteases by plasminogen activation, as described by Lotti et al.[7]

Although we do not yet know how to prevent the itching, it is very important to make a firm diagnosis. Patients with AP are usually considered by their medical attendants and relatives alike as being psychoneurotic. Since there are no objective skin changes, it is easy to believe that the symptoms arise entirely in the mind. The psychological concomitants of AP also tend to reinforce a diagnosis of psychoneurosis. Emotional persons are doubly disturbed by AP. Patients are invariably relieved to be told that their symptoms have a physical causation.

PRV

Pruritus without visible skin changes is a well-recognized symptom of patients with PRV.[2-5] Forty-three of 325 untreated patients with PRV, observed by the Polycythemia Vera Study Group, suffered itching, typically triggered by baths or showers. The itch, which is also of a prickling or burning quality, is sufficiently severe to prohibit some patients from wetting the skin. It develops within minutes of contact with water and lasts for 15 to 60 minutes. The temperature of the water is immaterial. Many patients find that avoidance of rapid cooling after emerging from a bath reduces the itching. Some note that pruritus starts when undressing to go to bed. Perspiring after exercise is another precipitating factor. The pruritic episodes often precede diagnosis of PRV by many years. As in AP, patients with PRV and water-induced itching have elevated concentrations of histamine in the venous blood. Pruritus in PRV may be associated with iron deficiency. In such instances, administration of iron supplements relieves the itch. Iron, however, has the disadvantage of increasing red blood cell mass in PRV. Antihistamines (eg, cyproheptadine hydrochloride) may be effective in relieving the itch. A double-blind crossover study suggested that aspirin might be an effective treatment. Every patient with water-induced itching should be examined for underlying PRV.

AP OF THE ELDERLY

One of us (A.M.K.), involved over a 20-year period in dermatological care of institutionalized elderly persons, has had occasion to observe many patients who complain of itching after water exposure. The Table shows the differences from and similarities to ordinary AP. Three quarters of the patients are female, and their symptoms are more severe. Those with fair skins were most susceptible. Aquagenic pruritus of the elderly (APE) was unusual in dark-complexioned people of Mediterranean origin. It was never seen in blacks.

The age at onset was usually after 60 years, and the severity of symptoms increased with age. A distinguishing feature of all these patients was persistently dry skin, sometimes called senile xerosis. The surface is roughened and scaly, with a cracked, whitish, dry appearance. Symptoms are directly related to the severity of xerosis, much worse in the

winter, probably because of the high ambient temperature (23.9 to 26.7 °C) and particularly the low relative humidity (<30%) in the institutional environment. Elderly persons with xerosis often experience intermittent itching, frequently resulting in uncontrolled scratching excoriations. Itching in xerotic patients may be triggered by temperature changes (undressing), light stroking, rough clothing, and insomnia. However, the dominant provocative event in all these xerotic patients was a hot bath or shower that invariably unleashed an episode of pruritus. The intensity of itching was proportional to the duration of exposure. However, when the bath was brief, less than five minutes, itching failed to occur or was mild. Notably, pruritus is absent as long as the patient stays in the bath. On emergence, soon after toweling or air drying, especially if the bathroom is cool enough to incite shivering, the pruritus starts up and mounts rapidly. Showering sometimes causes pruritus, but its effect is unpredictable. Heat, exercise, and emotions did not provoke symptoms in these patients. The itching almost always began on the lower extremities, extending to the thighs, then to the trunk and upper extremities. The head was rarely affected. Itching usually lasted for ten to 20 minutes, but could persist for an hour or more. Aquagenic pruritus of the elderly runs a consistent course, with regular exacerbations, getting more severe each winter with increasing age. The condition is persistent and presumably accompanies the elderly xerotic patient to the grave.

Systemic treatment with antihistamines (H_1 with or without H_2), hypnotics, or tranquilizers was unhelpful and may have been aggravating in some cases. Apart from avoidance of bathing, modification of bathing habits, including brief sponge baths and avoidance of total immersion and soaping, were valuable. Topical corticosteroids were ineffective. The most helpful regimen is directed to improvement of the xerosis, namely, the use of nonmedicated emollients. These did not completely prevent the pruritus, but made the bouts shorter and milder. Hydrophobic ointments, especially petrolatum and, to a lesser extent, lanolin, were the most effective. Mineral oil was unimpressive despite being hydrophobic. Water-in-oil emulsions (eg, Eucerin, hydrophilic ointment) were nearly as good and more pleasant to use. Relief of itching corresponded to remission of the xerosis by the emollients. The lighter oil-in-water creams, though more aesthetic, were also less effective. Although actinic damage was a prominent feature in some patients, its severity was unrelated to the presence and severity of the pruritus. Some of the severest cases had little or no actinic damage.

Eight patients (five of them female) were investigated in greater detail. Dermographism was absent. The local reaction and itching response to intradermal injection of 0.1 mL of 1:10,000 histamine phosphate (1 and 10) did not differ from the reaction in four controls. Local itching could not be produced by applying cold, warm, or hot compresses to the calves or arms. However, immersing a leg in warm water (30 °C) for ten minutes regularly induced a bout of itching, beginning a few minutes after the leg was towel dried, and lasting ten to 30 minutes. Pruritus was invariably confined to the area exposed to water. By increasing water exposure to 20 minutes, both the intensity and duration of itching could be increased. Three subjects immersed a leg in cold water at 15 °C for ten minutes. This induced itching, but of a lesser intensity than at 30 °C. However, when in the same three patients the other leg was immersed at 45 °C for ten minutes, the itching came on sooner, was more intense, and lasted longer than at lower temperatures. These observations suggest that the pruritus may be related to rehydration, and especially to the amount of water imbibed by the stratum corneum. Itch intensity was clearly related to rapid drying of the skin and was especially acute when a forced warm air draft from a conventional hair dryer was used after water exposure. Vigorous towel drying was not as pruritogenic as a current of warm dry air.

Attempts to induce tolerance (20 minutes' immersion of both legs in warm water five days weekly for two weeks) were largely unsuccessful. However, when the immersions were followed by emollients after drying, the xerosis was much improved with a corresponding decrease in pruritus. Administration of 1 minimum erythema dose from a lamp (FS20 Westinghouse, 280 to 340 nm) to one leg on Mondays, Wednesdays, and Fridays for three weeks in five subjects did not relieve pruritus induced by a 20-minute immersion of both legs in warm water. Occlusion of one leg under an impermeable plastic film (Saran Wrap) for one to three days triggered exceptionally severe pruritus on removal and proved the most potent stimulus of any that have been tried.

Punch biopsy specimens (3 mm) were taken from three patients with APE and three with skin of equal dryness but without itching. Stains for mast cells, elastic fibers, small vessels (alkaline phosphatase), and glycosaminoglycans (Mowry's) revealed no difference between the symptomatic and asymptomatic subjects. A spotty mild lymphocytic perivenular infiltrate was observed in two of the controls and three of the symptomatic patients, but was probably of no significance in this age group.

Four subjects immersed both legs in warm water for 20 minutes thrice weekly for two weeks. After each immersion, one was washed for two minutes with a harsh soap (Eubos, which is high in anionic surfactants), using a nonwoven cloth, followed by water rinsing and towel drying. There was no difference between the sides for the first two washings. After the third, one subject had worsened pruritus on the soaped site. Two had intensified itching after the fourth washing, and three of the four had severe, persistent itching by the last washing, accompanied by increased scaling and dryness. Washing with fast-lathering, highly detergent soap bars is certainly contraindicated in subjects with AP. Aggravation

of pruritus is directly related to aggravation of the xerosis by harsh soaps.

Aquagenic pruritus of the elderly can be disabling since it usually leads to an ever-accelerating itch-scratch cycle. Irritability, fatigue, and depression are common, leading to prescription of hypnotics that eventually aggravate the problem by reducing inhibition of scratching.

The program for moderating APE is as follows: (1) Baths are never to exceed five minutes, with avoidance of highly detergent soaps. (2) Sponge baths or quick warm showers are advisable for intractable cases. (3) Twice-daily application of hydrophobic moisturizers is effective for reducing the intensity and duration of the itching. (4) Topical corticosteroids, while helpful at first, will invariably worsen the xerosis and, in turn, the itching. (5) Moisturizers containing potential irritants, including more than 20% propylene glycol, more than 5% salicylic acid, more than 2.5% crude coal tar, or more than 20% urea are contraindicated; they may be helpful for a few weeks, but eventually become aggravating for most patients.

COMMENT

Itching induced by water contact is a distressing problem clinically. We have highlighted three clinical categories. Aquagenic pruritus and its senile variant have common features, but the differences are sufficiently great to warrant taxonomic separation. These include the different age incidences, different relationships to wetting of the skin, and differences in clinical appearance. The APE is invariably associated with dryness and scaling, while the skin in AP is clinically normal. This argues against lumping them together.

It is of practical importance to make the correct diagnosis. Although there is no satisfactory treatment of AP, patients suffer the additional affliction of being labeled as psychoneurotic by friends, family, and doctors alike. Correct diagnostic labeling relieves these patients of a social stigma, for which they are usually very grateful. Patients with APE can be helped by regular liberal applications of emollients during the winter months.

We wish to stress the importance of excluding PRV in all patients who present with water-induced itching. To date, none of our patients originally diagnosed by us as having AP has subsequently developed PRV, but this sequence of events remains a possibility.

Finally, we speculate that water contact mobilizes some pruritogenic mediator from the stratum corneum. We shall be searching for this hypothetical substance.

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