In conclusion, although there was slightly low hair regrowth in the poliosis group, no significant association was revealed between poliosis and alopecia areata prognosis. We believe that our data are valuable as they suggest an association between poliosis and prognosis of alopecia areata, for which limited information is available. Further well-controlled studies are required to confirm our findings.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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Provocation testing for chronic inducible urticaria: 5-year experience of a Singapore tertiary dermatological centre

Dear Editor,

Chronic inducible urticaria (CIndU) is a sub-group of chronic urticaria in which wheals and/or angioedema develop in response to specific stimuli.[1] We describe our 5-year experience of performing provocation tests for patients with suspected CIndU at our tertiary dermatological centre in Singapore.

This is a retrospective analysis of patients who were referred to the urticaria clinic of our centre between January 2012 and December 2017. Cases that fulfilled the definition of chronic urticaria were enrolled and a provocation test was performed if they were suspected of having one or more CIndU. Their electronic medical records were reviewed and the following data were collected: age, gender, occupation, type(s) of CIndU, disease onset, results of their physical challenge tests and response to treatment given. Cases were excluded if they had been diagnosed with another urticaria-related condition such as urticarial vasculitis, hereditary periodic fever syndrome or acquired autoinflammatory syndrome. The study was approved by the local ethics committee.

Table 1 summarises the methodology used for provocation tests.[1] Prior to testing, informed consent was obtained from all patients. Consumption of medications used to treat urticaria was deferred for at least three days in the case of antihistamines, or at least seven days in the case of other medications (including glucocorticoids). Tests were performed at sites unaffected by urticaria in the last 24 hours.

A total of 168 patients underwent provocation testing during the study period. There was a predominance of males ($n = 140$,

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Table 1: Provocation tests in chronic inducible urticarias[1]

Subtype	Test	Reading time
Symptomatic dermographism	Moderate stroking of either volar forearm skin with a closed ballpoint pen tip	10 min
Cold urticaria	Melting ice cube in a thin plastic bag, applied onto either volar forearm for 5 min	10 min
Heat urticaria	Beaker of water at 45°C, applied to either volar forearm for 5 min	10 min
Delayed pressure urticaria	Suspension of 7 kg of weights over either shoulder with a 3 cm strap for 15 min	6 hours
Solar urticaria	UVA 6 J/cm^2 and UVB 60 mJ/cm^2 to separate buttocks, and visible light to either upper arm	10 min
Vibratory urticaria/ angioedema	Placement of either volar forearm on a laboratory vibrator plate, vibrate at 1000 rpm for 10 min	10 min
Aquagenic urticaria	Immersion of either volar forearm in water for 5 min	10 min
Cholinergic urticaria	1. Exercise on a bicycle trainer for 30 min 2. Immersion in a 42°C bath for 15 min after recording a rise in body temperature of 1°C above baseline.	Immediately and 10 min

83.3%) compared to females (n = 28, 16.7%). The average age was 26 (range 7–69). The mean duration from symptom onset to the formal diagnosis of their CIndU was 41.4 months (range 2–240 months). The most common suspected CIndU referred for provocation testing was cholinergic urticaria (n = 92, 54.8%), followed by cold urticaria (n = 57, 33.9%), heat urticaria (n = 15, 8.9%), solar urticaria (n = 8, 4.8%) and aquagenic urticaria (n = 4, 2.4%) [Table 2].

Ninety-nine out of 168 (58.9%) of the patients referred for provocation tests had at least one positive result [63/92 (68.5%) for cholinergic urticaria; 32/57 (56.1%) for cold urticaria; 5/8 (62.5%) for solar urticaria; 2/4 (50%) for aquagenic urticarial]. Four were eventually diagnosed with more than one CIndU (one each with cholinergic and cold urticaria, cold urticaria and symptomatic dermographism, cholinergic and heat urticaria, and heat and delayed pressure urticaria). One patient had a history of angioedema with exercise although his exercise provocation test was negative. His final diagnosis was idiopathic angioedema. Another patient had a clinical history suggestive of food-dependent exercise-induced anaphylaxis, although his exercise test was negative. He was nonetheless prescribed standby epinephrine on clinical grounds and was referred to an allergist.

Eighty-six out of the 99 (86.9%) of our patients with at least one positive provocation test achieved quiescent disease subsequently with avoidance of the identified trigger along with regular use of H1 antihistamines up to a four-fold increase in the dose. In cases where physical triggers were unavoidable, patients were advised to take antihistamines at least one hour prior to exposure to prevent the recurrence of symptoms. Patient education was also done in our subspecialty clinic to provide strategies to avoid potential physical triggers. One patient with cold urticaria responded well to a combination of H1 and H2 antihistamines (desloratadine and cimetidine), while another with cold urticaria required the addition of a leukotriene receptor antagonist (montelukast). One patient with cholinergic urticaria did not respond to H1 antihistamines (fexofenadine) despite a four-fold increase in the dose. He subsequently received omalizumab for five months with a good response and was subsequently lost to follow-up. There were 10 patients (10.1%) who were lost to follow-up after their provocation tests.

In our study, cholinergic urticaria was the most common CIndU both referred for testing and diagnosed on positive provocation. The proportion of cholinergic urticaria in our cohort (63.6%) is much higher compared to other published studies. In Singapore, all male citizens are required to serve a period of compulsory service in the uniformed services when they reach the age of 18 years. The pre-enlistment medical check-up includes screening for exercise-induced conditions. They would be referred to relevant specialists for diagnosis and evaluation if needed. Rigorous physical training in the uniformed services, especially in our tropical climate, may also unmask occult cases of cholinergic urticaria. This heightened surveillance of the local young, male population explains why there is an over-representation of men in our cohort of patients who have undergone provocation tests. In this group, we would recommend taking vocations that do not require exposure to excessive heat or physical activities.

Table 2: Characteristics of patients with CIndU who had provocation tests (n = 168)

Types of CIndU	Number of patients who underwent provocation tests, N (%)*	Number of patients with positive provocation tests, N (%)	Mean age, years (range)	Male:Female ratio
Cholinergic urticaria	92 (54.8)	63 (68.5)	25.1 (7–60)	8.0
Cold urticaria	57 (33.9)	32 (56.1)	26.7 (9–69)	2.9
Heat urticaria	15 (8.9)	5 (33.3)	22 (15–36)	14.0
Solar urticaria	8 (4.8)	5 (62.5)	35.2 (20–57)	7.0
Aquagenic urticaria	4 (2.4)	2 (50)	17 (12–20)	3.0

*Numbers exceed 100% due to >1 types of suspected CIndU per patient

Table 3: Prevalence of CIndUs in other studies compared to our study

Study	Miles LM, 2021[3] *n* = 64	Bal F, 2021[4] *n* = 117	Pereira ARF, 2020[5] *n* = 118	Napolitano M, 2018[6] *n* = 32	Current study, *n* = 168
Dermographism	–	76	83	16	–
Cold	40	10	9	8	57
Cholinergic	27	14	21	3	92
Solar	10	–	2	–	5
Pressure	2	1	6	–	–
Aquagenic	–	2	–	3	4
Heat	–	–	1	1	15
Vibratory	–	–	–	1	–

Cold urticaria was the second most frequent CIndU amongst all test-positive cases in our cohort (32.3%). This is slightly higher in frequency when compared to the existing literature. The reason for this is unknown, although we speculate that our predominantly warm, tropical climate may reduce tolerance to cold temperatures in people susceptible to urticaria, who are then triggered by movement into ubiquitous air-conditioned indoor spaces. In an in vitro study, skin biopsy samples were challenged to various temperatures prior to the measurement of mast cell degranulation of histamine. The most significant mast cell release was seen in skin biopsy samples rewarmed to 37°C after chilling at 4°C for 10 minutes.[2] Our sunny weather may also provoke more cases of solar urticaria, which is also slightly higher in frequency in our study cohort (5.0%) compared to the published literature. On the other hand, we did not detect any cases of delayed pressure urticaria, vibratory urticaria and contact urticaria in our study. Heat urticaria and aquagenic urticaria were rare (≤2.0%), consistent with the published literature. Finally, symptomatic dermographism was omitted from our study due to methodical reasons; it is in fact very commonly encountered in our chronic urticaria patients, consistent with the published literature, and can easily be diagnosed via point-of-care testing with a ballpoint pen. Such cases were thus not specifically referred for provocation testing. Table 3 lists the frequency of CIndU subtypes in selected published studies compared to our study.

In our study, the mean time from symptom onset to diagnosis of CIndU was 41.4 months. This reflects the protracted course of most types of CIndU, which can last from 3–9 years.[1] The clinical outcome in our patients was generally good with a combination of avoidance of stimuli along with regular H1 antihistamine use, reflecting the importance of recognising and identifying potential triggers, including performing provocation tests where indicated.

In conclusion, cholinergic urticaria, cold urticaria and solar urticaria were the most common forms of CIndUs diagnosed in our centre, possibly due to social and environmental factors in Singapore. Provocation testing has a valuable role to play in the accurate identification of specific triggers in CIndU and can greatly help in the management of these patients.

Declaration of patient consent

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Conflict of interest

There are no conflicts of interest.

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