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Topical steroid withdrawal syndrome: developing diagnostic criteria through a modified Delphi method

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Abstract

Background Topical steroid withdrawal syndrome (TSW) is an adverse event following discontinuation of topical corticosteroids (TCS) and is of growing interest among patients and dermatologists. The absence of well-defined diagnostic criteria and limited insights into the pathomechanisms make diagnosis and future research challenging.

Objectives To propose preliminary diagnostic criteria for TSW with the erythemato-oedematous subtype applicable for adult and paediatric populations using a Delphi consensus approach informed by a thorough literature review that summarizes the signs, symptoms and histology of TSW.

Methods Eleven clinicians experienced in diagnosing and treating suspected TSW in both children and adults participated in a three-round modified Delphi process. Two rounds of surveys were conducted, with items ranked using a 5-point Likert scale. A predefined consensus threshold of ≥75% was established for any one feature to be deemed important. The third round involved a live video conference where the panel reached a consensus on essential diagnostic criteria.

Results The panel identified 18 critical diagnostic items, encompassing elements from the patient's clinical history, signs and symptoms. This includes history of escalating TCS requirement, morphology and distribution differing from primary condition, regional or generalized spontaneous neuropathic pain and severe burning sensation of the skin.

Conclusions Differentiating TSW from conditions such as severe atopic dermatitis remains challenging. By emphasizing the common signs and symptoms of TSW, we aim to encourage discussions among healthcare professionals and progress towards the development of a reliable diagnostic tool.

An author video to accompany this article is available online.

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Lay summary

Topical steroid withdrawal (TSW) syndrome can occur in people with eczema. TSW happens when the skin becomes inflamed, itchy and flaky following use of creams or ointments known as topical steroids. It often looks similar to eczema flare-ups. This makes it hard for doctors to tell the difference between the two.

In this study, a group consisting of several healthcare professionals came together to try to better understand TSW. Our goal was to figure out which symptoms are most important for diagnosing TSW. We first completed two rounds of surveys to rate the importance of the different symptoms. Then we discussed the results in a meeting to agree on the key signs and symptoms of TSW. We reviewed relevant research and discussed key symptoms.

We found that TSW has some unique features that help to distinguish it from other skin conditions (such as eczema). One such feature was the rash no longer responding to the standard use of topical steroids. Additional features included different patterns and locations of skin changes, thick wrinkled skin folds and exfoliation or shedding of skin and a strong burning sensation. Other symptoms are also seen in TSW, but are not specific to this syndrome. These include improvement of the skin after cessation of topical steroid use, oozing, fatigue or swollen lymph nodes.

In conclusion, our findings shed light on some of the common signs and symptoms of TSW. This study also highlights the need for the development of a reliable diagnostic tool.

What is already known about this topic?

- Topical steroid withdrawal (TSW) syndrome is a burdensome condition characterized by erythematous, pruritic, burning and/or excessively flaking skin.
- It can develop either during topical corticosteroid use or after discontinuation.

What does this study add?

- Owing to its similarity to other dermatitides, identifying TSW remains challenging, as no diagnostic criteria have been established to guide research.
- This study aims to characterize TSW and identify key features for potential inclusion in diagnostic criteria through consensus reached by a panel of healthcare providers.

Topical steroid withdrawal (TSW) syndrome, also referred to as 'red skin syndrome' and 'topical steroid addiction', is a poorly understood entity with a significant impact on patient wellbeing and quality of life.[1,2] TSW presents a challenging situation for patients and clinicians, as the signs and symptoms of TSW mimic the chronic dermatoses that are commonly treated with topical corticosteroids (TCS). Although TSW has been formally recognized by the US National Eczema Association, the British Association of Dermatologists and the UK's National Eczema Society,[3] no formal diagnostic criteria have been established to date, despite a clear need.[4,5] The lack of formal guidelines for diagnosis impedes efforts to educate providers about the disease and hampers research into prevalence, risk factors and treatment. Furthermore, lack of awareness of the condition among physicians may foster distrust between the patient and healthcare professional, resulting in lack of treatment, self-diagnosis and use of home remedies or untested alternative medical approaches, which may negatively impact the skin and the patient's overall health. While some healthcare professionals dismiss the diagnosis of TSW, there is a pressing need to understand what it is that so many patients are reporting. In recent years, a growing number of publications have recognized TSW as a potential clinical entity and emphasized the need for further research into its pathophysiology, diagnostic criteria and management.[6–10] These studies advocate for open communication between healthcare providers and patients, along with continued investigation into steroid-sparing treatment options.[11,12]

Given the limited literature on diagnostic guidelines for TSW and conflicting viewpoints on the condition, a modified Delphi survey was conducted to identify key findings that can be used to develop future diagnostic criteria. At the time of this Delphi process, no other consensus exercise had been conducted for TSW diagnostic criteria. The Delphi method was chosen to ensure anonymity among participants, reducing biases such as dominance and group conformity, which can occur in in-person meetings. The goal of this process was to achieve a dependable consensus among experienced clinicians through a repeated cycle of questionnaires with structured feedback.[13]

Two main subtypes of TSW have been described in the literature – papulopustular and erythemato-oedematous.[14] In this study, we chose to focus on the erythemato-oedematous subtype. This form is the most clinically dominant, associated with significant morbidity, and is often challenging to distinguish from conditions such as severe atopic dermatitis, rebound flares or a recurrence of a prior diagnosis. Additionally, we propose the inclusion of several nonstandard terms into the dermatology lexicon, discuss the challenges in achieving formal recognition of TSW and highlight key symptoms that differentiate this disease from similar conditions.

Materials and methods

Proposing potential diagnostic criteria via modified Delphi

A three-round modified Delphi process was conducted to identify features of TSW that could eventually shape a validated diagnostic criteria applicable to both paediatric and adult global populations. Our modified Delphi study protocol was not proactively registered because it did not involve enrolment of human participants or the collection of identifiable private information. A steering committee, composed of a board-certified dermatologist (P.L.), an advocate for patients with TSW (S.H.), Traditional Chinese Medicine doctor (O.H.F.) and two medical students (C.H. and L.G.) worked together to develop the study timeline and determine panel selection. The steering committee was formed based on interest, experience and knowledge of TSW. Two of five individuals in the steering committee (P.L. and O.H.F.) were involved in the voting process. There were no further subgroups. Panellists were able to recommend other members at any point. Prior to the first survey, 35 statements were generated by the steering committee, informed by the literature review conducted on 5 August 2022 (Table 1). PubMed, Ovid MEDLINE, and the Cochrane Library were searched using the key terms 'TSW', 'topical steroid withdrawal', 'red skin syndrome', 'topical steroid addiction', 'topical steroid rebound', 'topical steroid abuse' and 'topical steroid dependence'. No time limits were set, and the search included all types of studies ranging from case reports and observational studies to reviews. The reference lists of key articles were hand-searched to find additional articles. These methods were adapted from two large systematic reviews conducted for TSW.[14,15] A total of 45 articles were identified. The articles were then screened by L.G. and C.H. to identify those that specifically highlight clinical features of TSW. Additionally, The International Topical Steroid Awareness Network website was referenced to identify patient-reported signs and symptoms.[1]

A group of 15 individuals identified via professional connections, network recommendations, scholarly authorship and their clinical experience were invited to participate in the panel via personalized emails describing the study purpose, Delphi process and the number of planned rounds.

Table 1 Topical steroid withdrawal (TSW) literature search

Author	Type	Title	TSW features reported
Rapaport (2003)	Case series	Corticosteroid addiction and withdrawal in the atopic: the red burning skin syndrome	Long-term TCS, usually with escalating dosage and frequency of application; pruritus evolving into severe burning sensation; atrophy and telangiectasia; marked localized and systemic oedema; headlight sign; history of atopy
Fukaya (2014)	Review	Topical steroid addiction in atopic dermatitis	Itching more uncomfortable than before; TCS not working as effectively as before; intractable nodules with severe itching; rebound eruption extending to skin where TCS have never been applied; flushing or erythema; papules, pustules, or erosions; High fever (102 °F); thickened, desquamative skin; excessive sweating; itchy weals; rebound eruption stopping at the margin of the dorsal and palmar (or solar) sides
Hajar (2015)	Systematic review	A systematic review of topical corticosteroid withdrawal ('steroid addiction') in patients with atopic dermatitis and other dermatoses	Burning/stinging; exacerbation with heat or sun; pruritus; pain; facial hot flashes; diminished tolerance for lubrication; tightness; hyperaesthesia; erythema; papules with or without nodules; pustules; swelling/oedema; dryness/friable/cracked skin; telangiectasia; desquamation/peeling; scaling; vesicles/oozing/crusting; hyperpigmentation; atrophy; striae; increased hair growth; blackheads
Sheary (2016)	Review	Topical corticosteroid addiction and withdrawal: an overview for general practitioners	Headlight sign; red sleeve; elephant wrinkles; red skin; burning pain or stinging; itch; skin peeling or exfoliation; oozing areas; oedema; papulopustules; hives; excessive sweating; depression; insomnia
Dhossche (2017)	Case report	Topical corticosteroid withdrawal in a paediatric patient	Confluent erythematous oedematous plaques; coalescing pustules; lack of signs of steroid-induced atrophy (e.g. skin thinning, increased vascular prominence)
Sheary (2018)	Cross-sectional study	Steroid withdrawal effects following long-term topical corticosteroid use	History of long-term regular TCS use (months to years) where TCSs were initially effective, but over time, either increased amounts or potencies (or both) were required to reduce severity of skin symptoms; itch; erythema; history of atopy, especially atopic dermatitis; history of TCS use on the face, especially potent TCSs; history of oral prednisone use for skin symptoms; burning pain on the skin; skin sensitivity to previously tolerated skin products; excessive skin exfoliation (shedding); oozing skin; oedema, especially of the eyelids or ankles; elephant wrinkles of the extensor elbows and anterior knees; red sleeve sign; sleep disturbance; mood disturbance; skin pain, other than burning pain; papules and pustules; headlight sign
Lio (2019)	Review	TSW in atopic dermatitis	Burning; confluent erythema spreading to areas where TCS have not been applied; history of frequent and prolonged TCS use, especially on the face; oedema; skin exfoliation; papules or pustules; skin sensitivity; elephant wrinkles; red sleeve; sleep and mood disturbances; headlight sign[a]
Hwang (2022)	Systematic review	TCS withdrawal ('steroid addiction'): an update of a systematic review	Pruritus; sleep disturbance; dysaesthesia; erythema/red skin; acneiform papules; scaling; elephant wrinkle; red sleeve; headlight sign; burning pain; pain other than burning; mood disturbance; skin sensitivity; photosensitivity; oedema/swelling; weeping; telangiectasias; pus; hypertrichosis

TCS, topical corticosteroids. [a]Headlight sign: erythema of the full face, with sparing of the nasal and perioral regions; sleeve sign; erythematous eruptions of the upper or lower limb with sharp, well-defined cutoffs at the palms and soles; elephant wrinkles, thickened, loose skin with reduced elasticity classically on extensor surfaces.

The initial email contained a summary of existing scientific evidence on TSW in a slideshow format. All communications were conducted in English. Panel selection criteria included board-certified healthcare providers who had experience treating adult and paediatric patients with probable TSW. We aimed to recruit a diverse, multidisciplinary group of individuals to achieve a broader perspective and generalization of consensus. Those invited were given 2 weeks to respond. Follow-up emails were sent out 1 week prior to the first round of surveys to encourage participation. A final panel of 12 individuals including 10 board-certified dermatologists (D.A., D.D., L.E., R. Serrao, V.S., R. Sidbury, E.S., J.Y., P.L., L.M.), a general practitioner (B.S.), and a Traditional Chinese Medicine doctor (O.H.F.) with extensive experience in acute and chronic inflammatory dermatological conditions, were selected and surveyed using personalized anonymous links via Qualtrics online survey software. Three members of the steering committee (C.H., L.G. and S.H.), who were not involved in the voting process, collected and analysed responses. All survey responses were kept anonymous, and each participant reported having some experience with TSW. On average, participants had 13 years of dermatology experience (ranging from 6 to 25 years) and had treated between two and more than 100 probable cases where TSW diagnostic criteria would have been useful. Half of the participants reported working in an academic setting, while the remaining half were employed in private group or solo practice.

The first round of surveys was emailed on 25 October 2022 (File S1; see Supporting Information). No pilot was conducted prior to the initiation of the first round and there were no deviations from the study protocol. A reminder email was sent on 3 November 2022. All 12 individuals completed the survey. The second survey was distributed on 14 November 2022, with 11 individual responses collected directly on Qualtrics (File S2; see Supporting Information). One panellist withdrew from the study because of time constraints. A participant retention rate of over 90% was achieved between the first and second rounds. The questionnaire asked panellists to rank the statements on a 5-point Likert scale. Examples of questions included 'Rank degree of importance of diagnostic items related to patient history when making a diagnosis of TSW: history of topical corticosteroid use'. Responses included 'not important', 'less important', 'not sure', 'important' and 'very important'. The 'not sure' option was only chosen if the participant did not feel qualified to rank a statement. A criterion was included if it met the a priori threshold of consensus, which was set to ≥75% of participants rating a diagnostic item as 'very important' or 'important' and a median > 4. A criterion was excluded if ≥50% of participants rated the item as 'not important' or 'less important' and a median < 2.5. Participants were also able submit anonymous comments during each round (e.g. rephrase certain items). If a participant's response fell outside the interquartile range, a brief explanation of their rating was requested. All data were compiled and quantitatively analysed using Microsoft Excel. Free-text responses were qualitatively analysed for content, anonymized and presented in the subsequent Delphi round as part of the survey. Additionally, a structured data summary from round one was made available in the form of interquartile scores during the second round. In the second round of surveys, all statements that had not achieved consensus in the first round were reintroduced, along with the addition of a binary choice of 'Yes' (include) or 'No' (exclude). Items that reached clear consensus or items with clear disagreement were not revoted during round two in order to minimize survey fatigue. The anonymous feedback was compiled and discussed during the last round, which was held on 16 January 2023, on a live online video platform to increase accessibility. While rounds one and two were anonymized through personal links and emails, the last round was not anonymous, and panellists were able to interact with one another. The meeting was moderated by our patient advocate and steering committee member (S.H.) who had not participated in the survey. All items presented in both previous rounds were reassessed during this meeting, including those with clear agreement and disagreement. Items that had not previously reached consensus were discussed until a decision was reached. Additionally, participants were able to propose new items during this round, which were then considered for inclusion. A final list of the important diagnostic features of TSW was proposed (Figure 1).

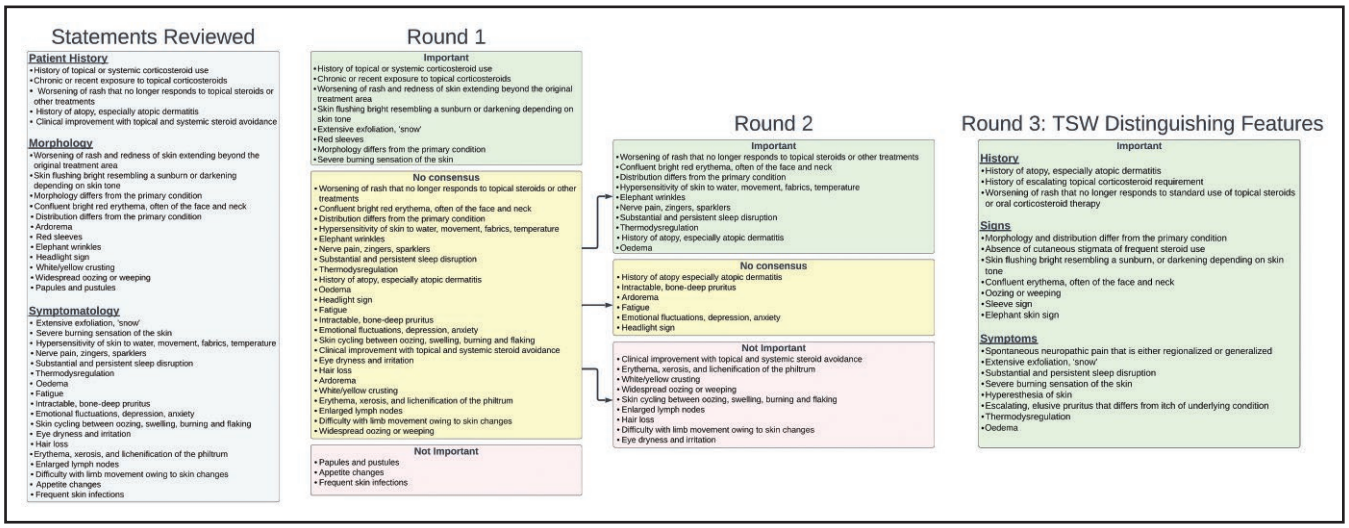

Figure 1 Modified Delphi process. Categorization of items by their significance in topical steroid withdrawal diagnosis.

The aim of involving a patient advocate in this modified Delphi study was to ensure that the criteria prioritized for inclusion reflected the perspectives and lived experiences of individuals affected by TSW, an emerging and poorly understood condition. Our patient advocate was involved in the initial generation of diagnostic items and the final consensus meeting. Their input led to the inclusion of items that may otherwise have been overlooked, such as 'intractable, bone-deep pruritus' and 'hypersensitivity of skin to water, movement, fabrics and temperature'. These two patient-suggested items reached consensus for inclusion in the final proposed diagnostic criteria with editing from our panel. As the moderator, our patient advocate did not participate in the voting process directly. Including a patient advocate helped validate patient-reported symptoms that are not yet widely recognized in clinical guidelines.

Results

Some of the patient-reported features that reached consensus include diffuse skin peeling and flaking, commonly referred to by patients as 'snow'.[16] This extensive exfoliation often affects the entire face, including the eyebrows and lips, and spares the nasal tip. What are commonly referred to by patients as 'zingers' or 'sparklers' were summarized as hyperesthesia of the skin, referring to localized or generalized nerve pain. 'Red sleeves' is colloquially used by patients to refer to erythematous eruptions of the upper or lower limb with sharp, well-defined cutoffs at the palms and soles, seen in up to 75% of adults with TSW.[2] 'Sleeve sign' provides a more accurate description of this symptom unique to TSW, as erythema varies based on skin tone.

Up to 80% of adults with TSW report thickened, loose skin with reduced elasticity classically on extensor surfaces, a symptom patients describe as 'elephant skin' or 'elephant wrinkles.'[2] When present on the thighs and shoulders this can mimic the redundant, inelastic skin seen in cutis laxa or in Ehlers–Danlos syndrome. 'Elephant skin sign' was proposed to describe this finding (Figure 2).

Features considered nondiagnostic or nonspecific to TSW include the presence of the 'headlight sign', which refers to erythema on the face that spares the nasal and perioral areas. Although commonly observed in patients with TSW, this sign is part of Hanifin and Rajka's diagnostic criteria for atopic dermatitis and was considered too nonspecific to be useful for diagnosing TSW. Raw data, along with a summary of the changes made to the criteria during round three, are provided in Tables S1–3 (see Supporting Information).

Discussion

TSW syndrome is often confused with other dermatological conditions, most commonly atopic dermatitis and steroid rebound flares. Up to 96% of dermatologists surveyed believe that TSW is ordinary eczema that has relapsed in some or most cases.[17] The goal of the diagnostic criteria is to distinguish TSW from similar conditions. In contrast to TSW, steroid rebound flares are a well-described adverse effect of cessation of TCS. Pharmacological rebound flares can be attributed to one or more of the following aetiologies:

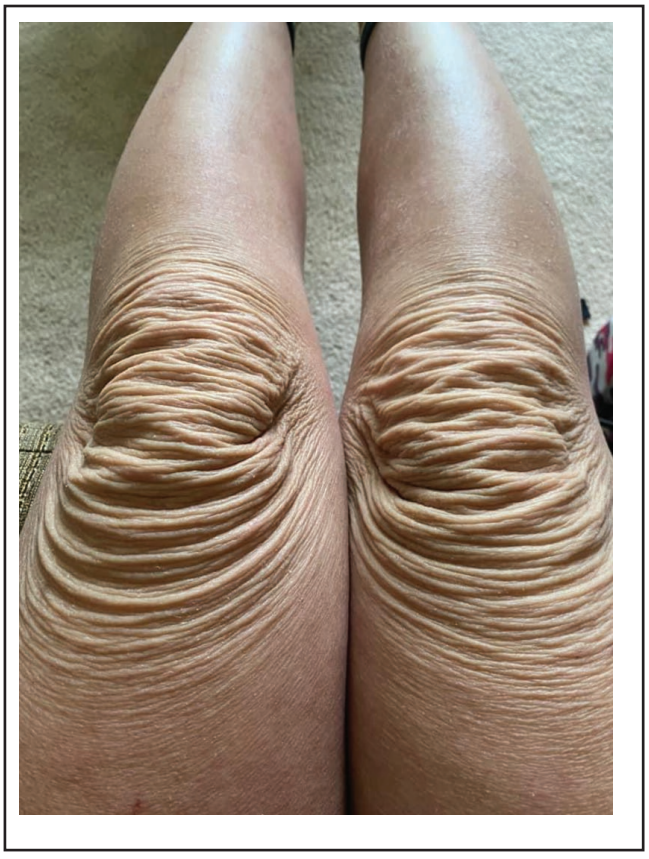

Figure 2 Elephant skin sign: erythematous, oedematous skin with prominent skin thickening and wrinkling.

eczema worsening owing to cessation of treatment; a papulopustular eruption commonly seen around the mouth and genital region after stopping TCS and lasting several weeks; rebound vasodilation and rebound cytokine cascade following TCS cessation;[9,10] and/or systemic adrenal insufficiency.[18,19]

In contrast to pharmacological rebound, patients with TSW often have symptoms that last far longer, sometimes lasting up to years postcessation. When TCS are reintroduced, the patient's condition often fails to improve. The loss of clinical effects of TCS in inflammatory skin disease, termed 'tachyphylaxis', has been an accepted principle in dermatology; however, there is no evidence from clinical trials to support the idea that topical glucocorticoids lose effectiveness over time.[20] Of the large population of patients who have used steroids, those who develop TSW appear to represent only a small fraction. Additionally, TSW presents with a unique constellation of symptoms not typically seen in the preceding condition, which is most commonly atopic dermatitis. There are reports of TSW across different diseases (e.g. psoriasis, vitiligo) but this is exceedingly rare. Symptoms unique to TSW include oedematous folds, referred to as the elephant skin sign; well-demarcated erythema sparing the palms and soles, or sleeve sign; and skin flaking or 'snow', all in the absence of the typical signs of frequent steroid use. We aim to formalize and standardize these patient-originated descriptions as part of the dermatological lexicon in order to provide the clinical language needed to identify and describe this novel condition. In addition to

these distinguishing symptoms, the morphology and distribution of skin affected by TSW often differs from the initial presentation and can spread to areas where TCS were never applied.[21–25] Furthermore, those with severe TSW often report weakness and fatigue in addition to cutaneous symptoms, which may also be attributed to systemic steroid absorption resulting in hypothalamic–pituitary–adrenal axis suppression and secondary hypoadrenalism.[21–25]

TSW typically occurs with prolonged use of moderate- to high-potency topical steroids[15] and can emerge during or after the cessation of treatment. An escalating need for steroids (i.e. increased amount, frequency or potency) often precedes the condition. An online survey reported the use of moderate-potency TCS for an average duration of 15 years.[2] Our consensus group recognizes a distinct and limited set of cases where patients experienced prolonged symptoms despite minimal exposure to TCS; these cases warrant further investigation. Owing to insufficient data supporting a dose-dependent effect and acknowledging cases arising from minimal exposure, the consensus decision was made not to specify the frequency and duration of topical steroid use in the diagnostic criteria, but to acknowledge that TSW often results from escalating steroid use. The recommendations for criteria proposed by this panel draw upon, and are consistent with, the clinical findings reported in previous studies.[14,15,26–28]

To investigate the histopathology of TSW, biopsies were taken from the thigh, exhibiting the elephant skin sign, and the arm, showing the sleeve sign. The biopsies revealed minimal parakeratosis and spongiosis, lymphocytic inflammation and a relative scarcity of eosinophils. These histopathological features of TSW are largely nonspecific and do not help to distinguish this condition from disorders with similar features (Figures 3, 4).

We acknowledge that currently TSW remains a diagnosis of exclusion. Therefore, it is important for healthcare providers to carefully consider and rule out other conditions before diagnosing TSW, as several signs and symptoms overlap with those of other eczematous skin conditions (Table 2 and Figure 5).

The limitations of this research include its US-centric nature. Certain tests are not routinely performed depending on the country of practice (e.g. skin scraping for scabies). While we were able to collaborate with a Traditional Chinese

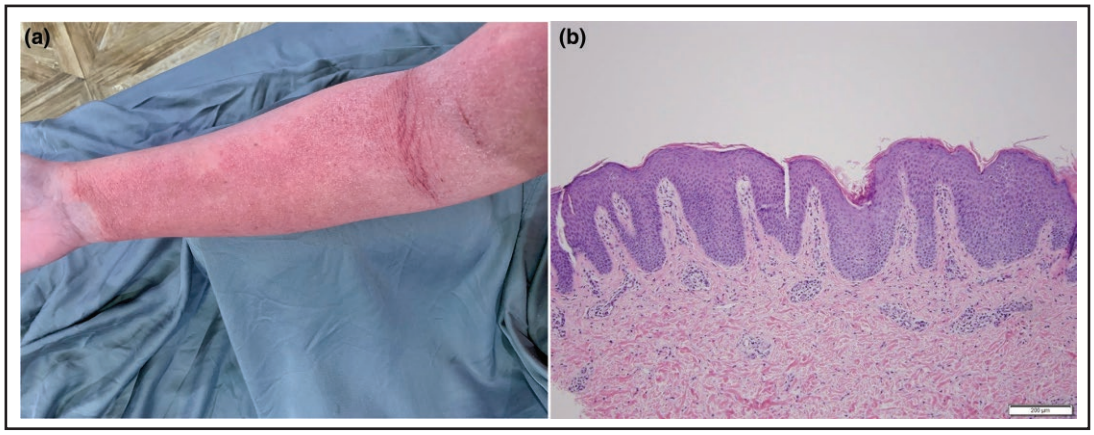

Figure 3 (a) Biopsy of sleeve sign. A 30-year-old female patient with widespread, plaque-like eczematous eruption with sharp demarcation at the wrist. Of note, this may also occur on the lower extremities. (b) Biopsy of the left upper arm shows mild focal parakeratosis overlying an acanthotic and mildly spongiotic epidermis. Mild perivascular and interstitial lymphocytic inflammation with sparse eosinophils present (haematoxylin and eosin staining, original magnification × 100).

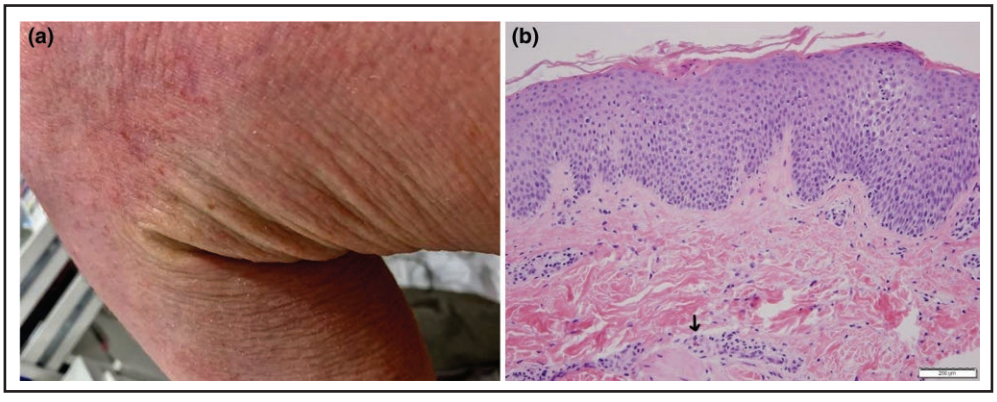

Figure 4 (a) Biopsy of elephant skin sign. An 18-year-old male patient with widespread erythematous eczematous patches with crusting, lichenification and hyperpigmentation. (b) Biopsy of the anterior thigh reveals mild parakeratosis overlying a mildly acanthotic and spongiotic epidermis with a few, small, exocytotic lymphocytes. Sparse, perivascular, lymphocytic infiltrate with rare eosinophils (haematoxylin and eosin staining, original magnification × 100).

Table 2 Differential diagnoses: ruling out other conditions

Condition	Features mimicking TSW	Features differing from TSW
Atopic dermatitis[27,29–32]	Oedema, oozing, crusting, scaling, erythroderma, lichenification, headlight sign, chronic or chronically relapsing dermatitis	Relapsing and remitting erythematous and pruritic patches with a propensity for flexural surfaces, often improves with reintroduction of TCS, lack of spontaneous neuropathic pain and hyperaesthesia, lack of elusive pruritus, lack of sleeve and elephant skin sign, lack of thermodysregulation, lack of severe burning sensation of skin
Pharmacological rebound flare after stopping TCS[33,34]	Relapse/worsening of original condition after stopping TCS, papulopustular eruption, facial erythema, telangiectasia	Onset of constellation of symptoms outlined in Figure 1, not present with original condition; TSW symptoms last months to years after cessation of TCS
Papulopustular TSW[14,15,35–43]	Erythroderma; pruritus; burning; papulopustular eruption upon cessation of TCS	Compared with erythemato-oedematous TSW, papulopustular is more common in patients who were using TCS for pigmentary disorders or acneiform conditions; prominent features of pustules, papules and/or nodules; less frequent oedema and burning/stinging
Allergic contact dermatitis to topical steroids[14,15,35–43]	Erythroderma; pruritus; cracks and fissures; lichenification; acute weeping dermatitis with severe oedema	Scaling and visible borders after contact with TCS or its excipients; distribution corresponds to the areas where the offending agent was applied; vesicles and bullae in acute cases, id-like eruptions
Tachyphylaxis[20]	Underlying condition fails to improve with reintroduction of TCS	Lack of the systemic constellation of symptoms highlighted in Figure 1
Erythrodermic eczema (generalized exfoliative dermatitis)[44,45]	Erythroderma, scaling and exfoliation, coalescing erythematous patches, pruritus, fatigue/malaise	Classically involves >90% of the body surface with concurrent metabolic burden, hepatosplenomegaly, lymphadenopathy, fever
Erythrodermic psoriasis[46–50]	Erythroderma, scaling and exfoliation, pruritus	Well-demarcated, erythematous plaques with overlying scales most often distributed on the scalp, elbows and knees; generalized, confluent erythema involving >75% of the body surface area; fever, chills, malaise, tachycardia, arthralgias and lymphadenopathy; histological findings include marked dilation and coiling of vessels within the papillary dermis, epidermal hyperplasia, loss of granular layer and parakeratosis with neutrophilic collections
Seborrhoeic dermatitis[30,51]	Erythroderma, flaking, burning, crusting, pruritus	Distribution on areas rich in sebaceous glands (scalp, face, upper trunk, intertriginous areas); inflamed, erythematous plaques covered with yellowish, greasy scales
Scabies[30,52]	Intense pruritus; secondary infections	Multiple small, erythematous papules, excoriations, burrows, vesicles, pustules and blisters on multiple locations, manifests 2–6 weeks after contact with mites
Pellagra[53]	Extensive erythematous eruption, pruritus, burning, symmetrical, well demarcated	Dementia, diarrhoea, alopecia, bullae, scale, painful fissures of the palms and soles, cheilitis, glossitis, peripheral neuropathy, oesophagitis, anorexia, disorientation, anxiety, irritability
Acrodermatitis enteropathica[54]	Eczematous pink scaly plaques, secondary infections, erosions and crusting, symmetrical eruption	Predilection for intertriginous, periorificial, and acral regions, diarrhoea, nail dystrophy and paronychia, nonscarring alopecia, glossitis, stomatitis, failure to thrive
Hyper-IgE syndrome[30,55]	Pruritus; eczematous lesions, xerosis, lichenification, secondary infections and crusting	Commonly seen in adolescents, episodes of bronchitis and pneumonia, mucocutaneous candidiasis, dental abnormalities, unusual facial appearance, elevated eosinophils and IgE, recurrent staphylococcal skin abscesses
Netherton syndrome[30,56–58]	Chronic eczematous eruptions, erythroderma, pruritus	Seen in newborns and infants, ichthyosis linearis circumflexa characterized by cyclic episodes of reddened, circular skin lesions, trichorrhexis invaginate, predisposition to atopy
Omenn syndrome[30,59,60]	Erythroderma, desquamation, hair abnormalities, secondary infections	Seen in newborns and infants, presence of rash shortly after birth, hepatosplenomegaly, lymphadenopathy
Langerhans cell histiocytosis[56,61,62]	Erythematous rash	Commonly seen in infants and adolescents, isolated skin or bone lesions, can have multisystem involvement, petechiae, bloody crusting, firmly indurated nodules, mucosal ulcers or gingivitis, pulmonary lesions, lymph node involvement, hepatosplenomegaly
Cutaneous T-cell lymphoma[56,63,64]	Erythroderma	Often presents asymmetrically in a 'bathing suit' distribution, progression from patch to plaque to tumour, poikiloderma vasculare atrophicans atrophic patches with increased telangiectasias, weight loss and malaise
Carcinoid syndrome[56,65,66]	Cutaneous flushing, erythema, xerosis	Paroxysmal flushing that can be precipitated by eating, drinking alcohol, stress, liver palpation and anaesthesia; tachycardia, periorbital swelling, increased lacrimation, gastrointestinal symptoms including diarrhoea and malabsorption, cardiac involvement particularly right-sided valvular disease and mostly tricuspid regurgitation; wheezing and dyspnoea associated with flushing episodes
Multiple myeloma[56,67]	Pruritus, plasmacytomas or amyloidosis may resemble eczematous lesions, secondary infections	Hypercalcaemia, renal dysfunction, anaemia, bone pain with lytic lesions
Erythrodermic sarcoidosis[68–70]	Erythroderma, scaling and exfoliation, pruritus, lichenification	Infiltration with noncaseating granulomas, erythema nodosum, weight loss, hepatitis, fever, chills and night sweats, peripheral lymphadenopathy
Superficial fungal infection/tinea corporis[71–73]	Pruritus, erythema, scaling	Pruritic circular or oval, erythematous or hyperpigmented patch or plaque that spreads centrifugally, active raised border with central clearing

TCS, topical corticosteroids; TSW, topical steroid withdrawal.

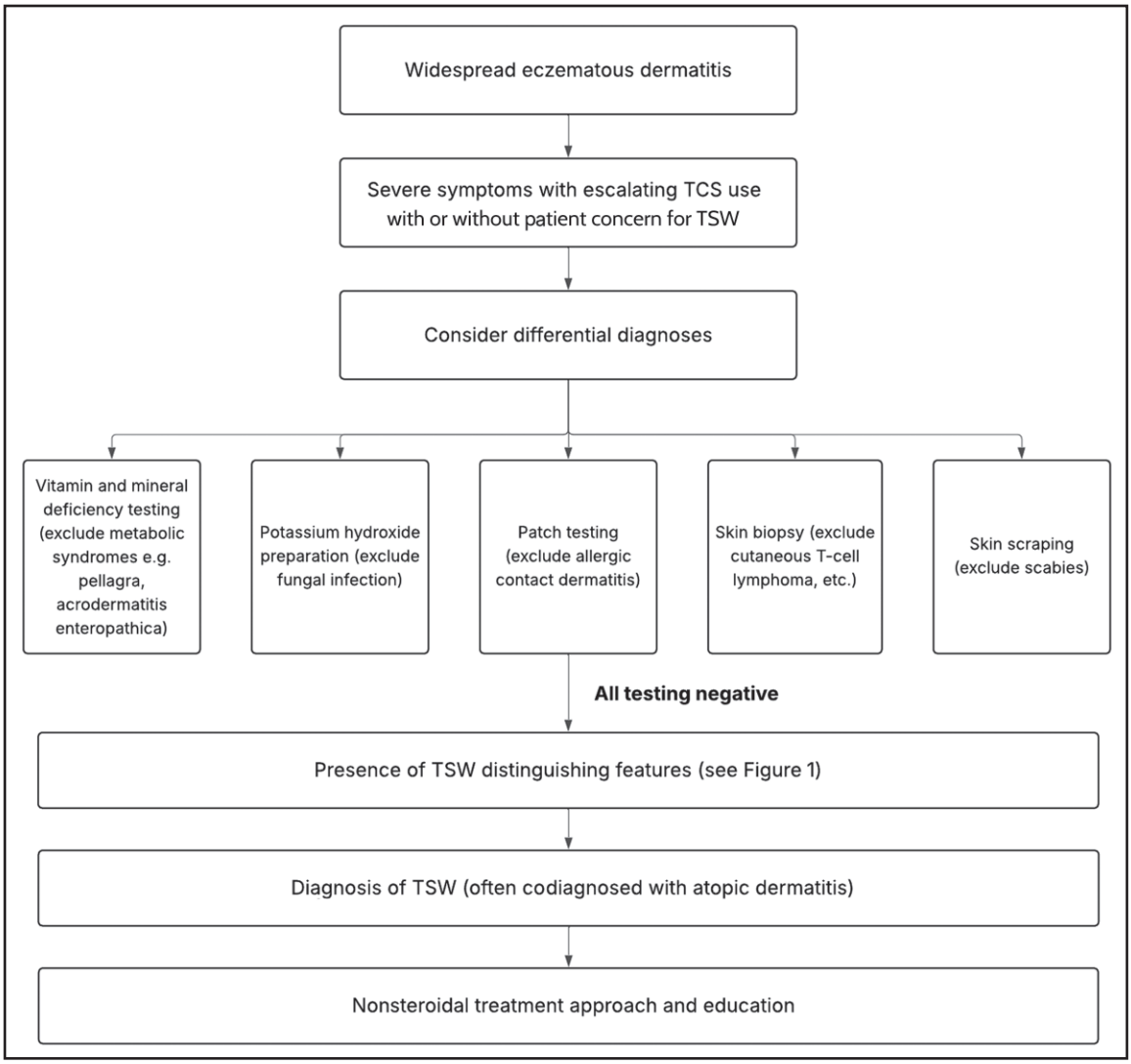

Figure 5 Proposed diagnostic framework for topical steroid withdrawal (TSW). TCS, topical corticosteroids. Patch testing may be limited by presence of diffuse red skin and burning.

Medicine doctor and a patient advocate with significant TSW experience, there is room for greater collaboration with patients with TSW and more clinicians from other disciplines who have treated this patient population. Furthermore, the literature review was limited by a deficiency in existing research and the lack of consensus regarding the existence of this relatively novel condition. There are other limitations inherent in Delphi studies, including results based on group consensus rather than 'best', 'expert' or 'correct' outcomes. The size of the panel was limited by the complexity of the disease and the need for participants with specific knowledge of the condition, but it aligns with recommendations in the literature.[18] Additionally, several panel participants are frequent collaborators, which may have led to nonanonymous interactions and could potentially influence consensus responses.

By highlighting the common signs and symptoms of TSW, we hope to encourage further research and ultimately develop a sensitive and specific diagnostic tool. This will require testing the criteria against a population of individuals clinically diagnosed with TSW, and involving individuals with other proven dermatoses as negative controls. This process may be limited by the lack of a gold standard for comparison.

Our study involved multiple stakeholders, including general dermatologists, paediatric dermatologists, a general practitioner, a Traditional Chinese Medicine practitioner and a patient advocate dedicated to advancing the recognition, diagnosis, treatment and ultimately the prevention of TSW. After reviewing the literature and engaging in discussion, the group recognized that many features of TSW overlap with severe atopic dermatitis and other dermatological conditions. The listed features are merely factors to consider; dermatologists and other healthcare professionals are currently limited by the absence of formal diagnostic criteria. Therefore, TSW remains a diagnosis of exclusion at this time. Given that TCSs are a primary treatment for atopic dermatitis, it is crucial for clinicians to practice diligent steroid stewardship and closely monitor the use of topical steroids in patients with chronic, recurrent eczema. We followed recommended guidelines for consensus development and assembled a diverse panel to ensure a thorough process in identifying diagnostic features of this condition. Ultimately, we hope that the outcomes of

this Delphi process will help clinicians more effectively diagnose and treat TSW in the future.

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Author contributions

Cynhia Hsu (Data curation, Formal analysis, Investigation, Methodology, Writing—original draft [equal]), Lily Guo (Data curation, Formal analysis, Investigation, Methodology, Writing—original draft [equal]), Derrick Adams (Investigation, Validation [equal]), Dawn Davis (Investigation, Validation [equal], Writing—review & editing [lead]), Lawrence F. Eichenfield (Investigation, Validation, Writing—review & editing [equal]), Olivia Hsu Friedman (Conceptualization, Investigation, Methodology, Writing—review & editing [equal]), Sarah Harris (Conceptualization, Investigation, Methodology, Writing—review & editing [equal]), Rocco Serrao (Investigation, Validation [equal]), Belinda Sheary (Investigation, Validation, Writing—review & editing [equal]), Vivian Y. Shi (Investigation, Validation [equal], Writing—review & editing [lead]), R. Sidbury (Investigation, Validation, Writing—review & editing [equal]), Eric Lawrence Simpson (Investigation, Validation [equal], Writing—review & editing [lead]), Jiade Yu (Investigation, Validation [equal], Writing—review & editing [lead]) and Peter Lio (Conceptualization, Investigation, Methodology, Resources, Supervision, Validation, Writing—review & editing [lead]).

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Conflicts of interest

L.E. has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Amgen, Arcutis, Aslan, Bristol Myers Squibb, Castle Biosciences, Dermavant, Eli Lilly, Forte, Galderma, Incyte, Janssen, Johnson & Johnson, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Target RWE and UCB. S.H. is an employee of Gladskin. R. Serrao has served as an investigator, consultant or speaker for Abbot, AbbVie, Aclaris, Asana BioScience, Arcutis, Bristol Myers Squibb, Chemocentryx, Concert, Dermavant, Eli Lilly, Incyte, Janssen, L'Oreal, LEO Pharma, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme. V.S. is on the Board of Directors for the Hidradenitis Suppurativa Foundation, an advisor for the National Eczema Association, is a stock shareholder of Learn Health and has served as an advisory board member, investigator, speaker and/or received research funding from Sanofi Genzyme, Regeneron, AbbVie, Genentech, Eli Lilly, Novartis, SUN Pharma, LEO Pharma, Pfizer, Incyte, Boehringer Ingelheim, Alumis, Aristea Therapeutics, Menlo Therapeutics, Dermira, Burt's Bees, Galderma, Kiniksa, UCB, Target-PharmaSolutions, Altus Lab/cQuell, MYOR, Polyfins Technology, GpSkin and Skin Actives Scientific. R. Sidbury reports being an investigator for Regeneron, Pfizer, Galderma, UCB and Castle; a consultant for Leo, Lilly, Arcutis and Dermavent; and a speaker for Beiersdorf. E.S. reports personal fees from AbbVie, Amgen, Arena Pharmaceuticals, ASLAN, Benevolent AI Bio Limited, BiomX Ltd, Bluefin Biomedicine, Boehringer Ingelheim, Boston Consulting Group, Collective Acumen, LLC, Connect Biopharma, Coronado, Dermira, Eli Lilly, Evidera, ExcerptaMedica, Galderma, GlaxoSmithKline, Forte Bio RX, Incyte Dermatologics, Janssen, Kyowa Kirin Pharmaceutical Development, Leo Pharm, Medscape LLC, Merck, Novaris, Ortho Galderma, Pfizer, Physicians World LLC, Pierre Fabre Dermo Cosmetique, Regeneron, Roivant, Sanofi Genzyme, SPARC India, Trevi therapeutics, WebMD and Valeant; grants from AbbVie, Amgen, Arcutis, ASLAN, Castle Biosciences, Celegene, CorEvitas, Dermavant, Dermira, Eli Lilly, Galderma, Incyte, Kymab, Kyowa Hakko Kirin, Leo Pharmaceuticals, Merck, Novartis, Pfizer, Regeneron, Sanofi and TARGET-DERM outside the submitted work. J.Y. has served on the advisory boards for Arcutis, Sanofi and Incyte; been an investigator for AbbVie, Sol-Gel and Eli Lilly; a consultant for National Eczema Association, O'Glacee, Edvyce; and is on the Board of Directors for the American Contact Dermatitis Society and Pediatric Dermatology Research Alliance. P.L. reports research grants/funding from AbbVie and AOBiome. P.L. is also on the speaker's bureau for AbbVie, Arcutis, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oreal, Pfizer, Pierre Fabre Dermatologie and Regeneron/Sanofi Genzyme. P.L. reports consulting/advisory board roles for Alphyn, AbbVie, Almirall, Amyris, Arcutis, ASLAN, Boston Skin Science, Bristol Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosci, Dermavant, Eli Lilly, Galderma, Janssen, Johnson & Johnson, LEO Pharma, Lipidor, L'Oreal, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Skinfix, Theraplex, UCB, Unilever, Verrica and Yobee Care. P.L. reports holding stock options with Codex, Concerto Biosciences and Yobee Care. In addition, P.L. has a patent pending for a Theraplex product with royalties paid and is a board member and scientific advisory committee member of the National Eczema Association.

Data availability

The data underlying this article are available in the article and in its online supplementary material.

Ethics statement

Not applicable.

Patient consent

Written patient consent for publication was obtained.

Supporting Information

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

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