REVIEW

A systematic review of topical corticosteroid withdrawal ("steroid addiction") in patients with atopic dermatitis and other dermatoses

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Background: The National Eczema Association has received increasing numbers of patient inquiries regarding "steroid addiction syndrome," coinciding with the growing presence of social media dedicated to this topic. Although many of the side effects of topical corticosteroids (TCS) are addressed in guidelines, TCS addiction is not.

Objective: We sought to assess the current evidence regarding addiction/withdrawal.

Methods: We performed a systematic review of the current literature.

Results: Our initial search yielded 294 results with 34 studies meeting inclusion criteria. TCS withdrawal was reported mostly on the face and genital area (99.3%) of women (81.0%) primarily in the setting of long-term inappropriate use of potent TCS. Burning and stinging were the most frequently reported symptoms (65.5%) with erythema being the most common sign (92.3%). TCS withdrawal syndrome can be divided into papulopustular and erythematoedematous subtypes, with the latter presenting with more burning and edema.

Limitations: Low quality of evidence, variability in the extent of data, and the lack of studies with rigorous steroid addiction methodology are limitations.

Conclusions: TCS withdrawal is likely a distinct clinical adverse effect of TCS misuse. Patients and providers should be aware of its clinical presentation and risk factors. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2014.11.024.)

Key words: atopic dermatitis; pruritus; red face; side effects; steroid addiction; topical corticosteroid withdrawal; topical corticosteroids.

Topical corticosteroids (TCS) are the first-line therapy for the treatment of atopic dermatitis according to various independently published international guidelines from both dermatology and allergy groups worldwide[1-6] and have been shown to have a positive impact on the quality of life of patients.[7,8] TCS have been shown to be a safe treatment option both in short-term daily use and long-term intermittent application.[9]

There has been a growing presence of social media addressing side effects from chronic TCS use, especially when TCS are withdrawn. This concern for possible "steroid addiction" may contribute to reduced adherence and therapeutic failure.[10,11] Several Internet sites and patient blogs recommend that TCS not be used in the management of atopic dermatitis to avoid steroid addiction. Such recommendations and commentaries are in stark

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contrast to the published evidence-based atopic dermatitis treatment guidelines,[1-4,6,12] which state that proper use of TCS is integral to the treatment of most patients with atopic dermatitis.

A clearer understanding of this adverse effect will allow for fully informed choices by providers, parents, and patients during the management of atopic dermatitis and other dermatoses.

The objective of this systematic review was to better define the steroid addiction/withdrawal syndrome, outline its signs and symptoms, identify potential risk factors, and review existing therapies based on the scientific literature.

CAPSULE SUMMARY

- Little is known about steroid withdrawal syndrome and there is a growing presence of social media around this topic.
- This systematic review suggests it is a distinct adverse effect of steroid misuse.
- Patients and providers should be aware of the clinical features and risk factors to identify and prevent this complication.

METHODS

This systematic review was registered with PROSPERO International prospective register of systematic reviews (CRD42013005370). We searched Ovid MEDLINE, PubMed, the Cochrane Library, and grey literature from January 1946 to April 2014, using search terms relating to TCS withdrawal, addiction, abuse, tolerance, rebound, dependence, rosacea, red skin, red face, red scrotum, tachyphylaxis and status cosmeticus, perioral dermatitis, acneiform, and rosacea-like eruptions. The search strategy is outlined in Table I (available at http://www.jaad.org). References of key articles were hand searched to find additional articles.

All captured titles and abstracts were screened by 2 reviewers (T. H. and Y. A. L.). The remaining articles were studied by the same reviewers for relevance using inclusion exclusion criteria. Only studies that reported symptoms after withdrawal of TCS were included. Studies of adverse effects that occur during the use of TCS were not included.

Study selection criteria

Inclusion criteria.

1. Language: English.
2. Relevance: Articles must have described at least 1 case of steroid withdrawal as defined by the following criteria: (A) Cutaneous eruption that followed TCS use, which either appeared: (i) after discontinuation of TCS or (ii) when elevated doses and applications of TCS were needed to prevent it from appearing. (B) The eruption was localized to the site(s) of application (at least primarily). (C) Resolution of the eruption at some point after TCS cessation was considered contributory to the diagnosis.
3. Study design: Because of the anticipated low number of studies and lack of uniformity regarding disease definition, we elected to include all relevant published studies regardless of study design.

Exclusion criteria.

1. Lack of a clear temporal relationship among TCS use, TCS withdrawal, and the eruption.
2. Reviews or expert opinions that do not include specific case descriptions.
3. Lack of precise data (eg, exact number of patients with the syndrome in the report).

Data extraction

Two independent reviewers extracted the data of included studies onto an Excel (Microsoft, Redmond, WA) extraction data form, which includes the fields shown in Tables II to VI.

Quality assessment

At the individual study level, quality was evaluated according to the GRADE guidelines.[13] We defined the level of evidence (levels 1-4) supporting each article.[14]

Data synthesis

Data were combined at the aggregate level and evaluated using descriptive methods. The following outcomes were defined:

Primary outcome.

1. Clinical features of TCS withdrawal
   A. Patient factors: Age, gender, indication for TCS
   B. TCS factors: potency, duration of use
   C. Signs including morphology and location
   D. Symptoms

Secondary outcomes.

1. Histologic features of TCS withdrawal
2. Treatment
   A. Treatment modalities
   B. Response to treatment
   C. Duration of treatments

Table II. Studies included in the systematic review

	Authors	Year	Article type (No. of patients*)	Level of evidence	GRADE quality†
1	Sneddon[15]	1969	Case series (8)	4	Very low
2	Sneddon[16]	1969	Case report (1)	4	Very low
3	Weber[17]	1972	Case series (6)	4	Very low
4	Burry[18]	1973	Case series (2)	4	Very low
5	Leyden et al[19]	1974	Case series (10)	4	Very low
6	Stegman[20]	1974	Case report (1)	4	Very low
7	Kligman[21]	1976	Case series (3)	4	Very low
8	Urabe and Koda[22]	1976	Case series (25)	4	Very low
9	Wilkinson et al[23]	1979	Cross-sectional (259)	4	Very low
10	Franco and Weston[24]	1979	Case report (1)	4	Very low
11	Sheu and Chang[25]	1991	Case series (23)	4	Very low
12	Wells and Brodell[26]	1993	Case series (2)	4	Very low
13	Uehara et al[27]	1996	Case series (135)	4	Very low
14	Velangi et al[28]	1998	Case report (1)	4	Very low
15	Rapaport and Rapaport[29]	1999	Case series (100)	4	Very low
16	Rapaport and Rapaport[30]	1999	Case series (5)	4	Very low
17	Brodell and O'Brien[31]	1999	Case report (1)	4	Very low
18	Fukaya[32]	2000	Case report (1)	4	Very low
19	Goldman[33]	2001	Case report (3)	4	Very low
20	Pabby et al[34]	2003	Case report (1)	4	Very low
21	Rapaport and Lebwohl[35]	2003	Case series (10)	4	Very low
22	Zalaudek et al[36]	2005	Case report (1)	4	Very low
23	Rathi[37]	2006	Case series (5)	4	Very low
24	Chu et al[38]	2007	Case series‡ (40)	4	Very low
25	Abbas et al[39]	2008	Case series (9)	4	Very low
26	Liu and Du[40]	2008	Case series‡ (50)	4	Very low
27	Chen and Zirwas[41]	2009	Case report (1)	4	Very low
28	Lu et al[42]	2010	Case series (312)	4	Very low
29	Del Rosso[43]	2011	Case report (1)	4	Very low
30	Rathi and Kumrah[44]	2011	Case series (110)	4	Very low
31	Saraswat et al[45]	2011	Cross-sectional (65)	4	Very low
32	Zhang and Zhu[46]	2011	Case report (1)	4	Very low
33	Monroe et al[47]	2011	Case report (1)	4	Very low
34	Narang et al[48]	2013	Case series (12)	4	Very low
1206 total patients					

*No. of patients with topical corticosteroid withdrawal syndrome (not to the total No. of reported patients in publication).
†Quality of evidence in regard to topical corticosteroid withdrawal, not overall quality of evidence.
‡Before-after study.

3. Evaluation for exclusion of alternate diagnoses (eg, patch testing, phototesting)
4. Nomenclature

RESULTS

The search yielded a total of 294 articles. After 2 independent reviewers screened titles and abstracts, 123 articles remained. Review of the references of key articles for relevant articles added 69 additional citations. A total of 192 full-text articles were then evaluated applying the inclusion/exclusion criteria. The review included 34 studies for analysis (Fig 1 and Table II), with the oldest article published in 1969 and the most recent in 2013. The level of evidence and study quality were consistent throughout the studies and identified as being a lower level of evidence (level 4). All studies were ranked as very low quality according to the GRADE guidelines.[13]

Primary outcome—clinical features

Patient factors. The majority of patients with manifestations of TCS withdrawal were women (81%) who had used TCS on their face (97%). The primary indication for the initial use of TCS was atopic dermatitis in 33.3% followed by cosmetic use and pigmentary disorders in 14.3% and a variety of other conditions (Table III).

TCS factors. The majority of the described patients were using either mid- or high-potency TCS (98.6%). Data regarding frequency of use were

Table III. Patient and steroid characteristics of topical corticosteroid withdrawal

Feature (No. of patients)*	All	Erythematoedematous	Papulopustular
	No. of patients (%)		
Gender	(n = 1085)	(n = 263)	(n = 446)
Female	879 (81)	158 (60)	394 (88.3)
Age, y	(n = 963)	(n = 128)	(n = 456)
<18	69 (7.1)	0	41 (8.9)
>18	894 (92.8)	128 (100)	415 (91)
Indication for TCS use	(n = 752)	(n = 263)	(n = 273)
Atopic dermatitis	251 (33.3)	210 (79.8)	7 (2.5)
Cosmetic use and pigmentary disorders	121 (16.0)	4 (1.5)	111 (40.6)
Facial rash, red scrotum	105 (13.9)	17 (6.4)	93 (34)
Seborrheic dermatitis, pityriasis simplex	72 (9.5)	26 (9.8)	20 (7.3)
Acne	69 (9.1)	4 (1.5)	22 (8)
Other†	65 (8.6)	2 (0.7)	5 (1.8)
Rosacea	44 (5.8)	0	12 (4.3)
Perioral dermatitis	21 (2.7)	0	3 (1)
Location of TCS use‡	(n = 1147)	(n = 194)	(n = 472)
Face	1113 (97)	184 (94.8)	469 (99.3)
Genital	27 (2.3)	6 (3)	1 (0.2)
Other§	7 (0.6)	4 (2)	2 (0.4)
TCS potency//	(n = 364)	(n = 67)	(n = 297)
Low	5 (1.3)	4 (5.9)	1 (0.3)
Mid	134 (36.8)	26 (38.8)	107 (36)
High	225 (61.8)	37 (55.2)	189 (63.6)
Frequency of use	(n = 40)	(n = 10)	(n = 14)
Continuous daily use	40 (100)	10 (100)	14 (100)
Duration of use, mo	(n = 210)	(n = 187)	(n = 29)
<1	7 (3.3)	7 (3.7)	0
1-3	7 (3.3)	7 (3.7)	1 (3.4)
>3-6	2 (0.9)	0	2 (6.8)
>6-12	12 (5.7)	10 (5.3)	7 (24.1)
>12	179 (85.2)	163 (87.1)	19 (65.5)

TCS, Topical corticosteroid.

*No. of patients with reported data for the specified feature. If partial or imprecise data were reported, we estimated the data to the best of our understanding.

†Seasonal, eyelid, contact, hand eczema, lichen simplex chronicus, winter itch, solar dermatitis, pityriasis alba, scaling, tinea, intertrigo, post-sunburn, vitiligo, *herpes simplex virus* infection, folliculitis, urticarial.

‡In 31 patients the eruptions expanded beyond the application site (initial sites: 29 facial, 1 genital, 1 forearm).

§n = 1 for each: perianal; arms; back of hands; right forearm; legs; erythroderma.

//TCS potency was defined as follows: low = class 6-7; medium = class 4-5; high = class 1-3. Potency descriptions (eg, medium strength) without specified formulations were included. The last applied formulation is the one depicted in the table.

limited. Only 1 study clearly specified the frequency of use in the patients with steroid withdrawal. This study of 40 patients reported that all patients with TCS withdrawal had been using TCS daily.[38] Data regarding duration of use were reported in 14 studies (210 total patients) and 85.2% reported their use for more than 12 months.

Signs. Data on signs were able to be extracted from 1141 patients in this category; not all articles included each of the clinical features (Table IV). The most common sign was erythema (92.3%). One article (n = 100 patients) described a sharp cutoff between red and normal-appearing skin that often ran down the mid to outer cheeks whereas the nose and the ears remained clear, referred to as the "headlight" sign.[29] Papules ± nodules and pustules were reported in half of the patients.

Symptoms. The most frequently reported symptoms were burning/stinging, exacerbation with heat or sun, pruritus, pain, and facial hot flashes.

Subtypes. Clinical features and patient factors are described in Tables III and IV. Three articles were excluded from this subanalysis because the data could not be extracted by subtype,[40,42] and 1 because it did not describe clinical features.[45] In a post hoc analysis of the data, 2 morphologically distinct subtypes emerged: (1) a papulopustular

Table IV. Clinical features of topical corticosteroid withdrawal

Feature (No. of patients)*	All	Erythematoedematous	Papulopustular
	No. (%)		
Onset of symptoms upon withdrawal†	(n = 151)	(n = 104)	(n = 11)
24-48 hr	3 (1.9)	0	2 (18.1)
48-96 hr	27 (17.8)	1 (0.9)	0
4-14 d	20 (13.2)	2 (1.9)	9 (81.8)
14-21 d	100 (66.2)	100 (96.1)	0
Symptoms	(n = 761)	(n = 280)	(n = 378)
Burning/stinging	499 (65.5)	265 (94.6)	134 (35.4)
Exacerbation with heat or sun	477 (62.6)	2 (0.7)	113 (29.8)
Pruritus	346 (45.4)	139 (49.6)	88 (23.2)
Pain	284 (37.3)	27 (9.6)	1 (0.2)
Facial hot flashes	256 (33.6)	0	0
Diminished tolerance for lubrication	100 (13.1)	100 (35.7)	0
Tightness	32 (4.2)	0	32 (8.4)
Hyperesthesia	1 (0.1)	1 (0.3)	0
Signs	(n = 1141)	(n = 307)	(n = 472)
Erythema	1054 (92.3)	291 (94.7)	415 (87.9)
Papules ± nodules	703 (61.6)	135 (43.9)	379 (80.2)
Pustules	532 (46.6)	26 (8.4)	369 (78.1)
Swelling/edema	495 (43.3)	119 (38.7)	14 (2.9)
Dryness/friable/cracked skin	472 (41.3)	39 (12.7)	102 (21.6)
Telangiectasia	402 (35.2)	10 (3.2)	61 (12.9)
Desquamation/peeling	381 (33.3)	128 (41.6)	0
Scaling	155 (13.5)	154 (50.1)	1 (0.2)
Other‡	79 (6.9)	31(10.9)	35 (7.4)
Vesicles/oozing/crusting	12 (1.0)	9 (2.9)	2 (0.4)

*No. of patients with reported data for the specified feature. If partial or imprecise data were reported, we estimated the data to the best of our understanding.
†One patient reported symptom onset after 21 d.
‡Hyperpigmentation, atrophy, striae, increased hair growth, blackheads.

variant (52.1%) (Fig 2) and (2) an erythematoedematous variant (47.9%) (Fig 3). These 2 entities are seen in the photographs from 2 patients recently evaluated by the authors (Figs 2 and 3).

Of patients with the erythematoedematous type, 90% had an underlying primary eczematous skin condition such as atopic dermatitis and seborrheic dermatitis, whereas the majority of patients with the papulopustular type used TCS for cosmetic use or an acneiform disorder.

Clinical signs and symptoms differed between the 2 types with some overlap (Table IV). In the erythematoedematous variant, the most commonly reported signs were erythema, scaling, papules ± nodules, desquamation/peeling, and swelling/edema. The most commonly reported symptoms were burning/stinging (94.6%), pruritus, pain, and diminished tolerance for emollients. The papulopustular variant may be distinguished from the erythematoedematous variant by the prominent features of pustules, papules ± nodules, and less frequently edema and burning/stinging.

Secondary outcomes

Reported treatments. Almost all authors recommended discontinuing the use of TCS (95.5%). The papulopustular subgroup was more frequently treated with oral antibiotics whereas the erythematoedematous variant reported the use of antihistamines, ice/cool compresses, and psychological support.

Histologic features of TCS withdrawal. The most common histologic findings in the erythematoedematous subtype were a thinned epidermis, spongiosis, a thin or absent granular layer, numerous dilated vessels in the dermis, sparse perivascular infiltrate, prominent sebaceous glands surrounded by inflammatory cells, and degeneration of collagen.[15,35,48] One article reported that of 41 cases that presented with a red face, 36 displayed histologic features of chronic eczema with superimposed steroid rosacea-like changes, and 5 patients had chronic eczematous features alone.[27]

The papulopustular subtype displays findings common to rosacea such as a perifollicular or

Table V. Treatment options

Treatment (No. of patients)*	All	Erythematoedematous	Papulopustular
Treatment	No. (%) (n = 713)	No. (%) (n = 306)	No. (%) (n = 360)
Discontinue the use of TCS	681 (95.5)	275 (89.8)	356 (98.8)
Doxycycline, tetracycline, erythromycin	240 (33.6)	26 (8.4)	164 (45.5)
Antihistamines	151 (21.1)	101 (33)	0
Psychological support	150 (21)	100 (32.7)	0
Short-term oral steroids, tapering down use of TCS and topical anti-inflammatories†	135 (18.9)	135 (44.3)	0
Ice and cool compresses	103 (14.4)	102 (33.4)	1 (0.2)
Avoid sun exposure	50 (7.0)	0	0
Calcineurin inhibitors	47 (6.5)	2 (0.3)	45 (12.5)
Low-potency TCS	30 (4.2)	2 (0.6)	28 (7.7)
Analgesics, tranquilizers, pregabalin, amitriptyline	14 (1.9)	14 (4.5)	0
Other: Fat-free powder suspension, soothing creams, burrows soaks, baths, oatmeal lotion, povidone iodine, zinc oxide	14 (1.9)	10 (3.2)	8 (2.2)
Topical antibiotics, benzoyl peroxide	6 (0.8)	0	6 (1.6)
UVA/UVB	1 (0.1)	0	1 (0.2)
Isotretinoin	1 (0.1)		

TCS, Topical corticosteroid; *UV*, ultraviolet.
*No. of patients with reported data for the specified feature. If partial or imprecise data were reported, we estimated the data to the best of our understanding.
†A recommendation from 1 article with 135 patients.[27]

Table VI. Time to complete or partial clearance

Feature (No. of patients)*	No. (%)
Duration and response to treatment, mo (n = 254)†	
0-3	195 (76.7)
3.1-6	32 (12.5)
6.1-12	14 (5.5)
>12.1	13 (5.1)

*No. of patients with reported data for the specified feature. If partial or imprecise data were reported we estimated the data to the best of our understanding.
†Additional information on duration and response to treatment, n = 10 responded in 6-28 wk,[19] n = 100 responded in 6 mo to 3 y.[29]

granulomatous infiltrate with neutrophils and lymphocytes, dilated vessels in the dermis, and degeneration of collagen fibers.[22,23,27,36]

Evaluation for exclusion of alternate diagnoses (eg, patch testing, phototesting). The majority of patients were not reported as being patch tested. A total of 6 articles reported patch testing[23,27,29,30,35,48] and of those, 1 received photo patch testing.[27] One of the articles was excluded from analysis because the author did not specify the number of positive and negative results.[29] A total of 177 patients with clinical symptoms of withdrawal were patch tested. Of these, 143 were negative and 33 were positive. Of the positives, 10 were not found to be relevant, and 23 patients were positive to allergens that they applied to their face, including TCS, topical nonsteroidal anti-inflammatory drugs, moisturizers, and cosmetics.

Nomenclature. Using our a priori definition of TCS withdrawal, the following names listed were used to describe this entity: facial corticosteroid addictive dermatitis, red skin syndrome, topical corticosteroid—induced rosacea-like dermatitis, steroid addiction syndrome, steroid withdrawal syndrome, steroid dermatitis, post-laser peel erythema, status cosmeticus, red scrotum syndrome, chronic actinic dermatitis, anal atrophoderma, chronic eczema, corticosteroid addiction, light-sensitive seborrheid, perioral dermatitis, rosacea-like dermatitis, steroid-rosacea, and steroid dermatitis resembling rosacea.

DISCUSSION

TCS withdrawal (addiction) appears to be a clinical adverse effect distinct from other well-described TCS adverse effects. Our review indicates that TCS withdrawal results from prolonged, inappropriate, and frequent use of moderate- to high-potency TCS primarily on the face and genital area in most cases. Women are a population particularly at risk; only 69 (7.1%) cases were reported in patients 18 years of age and younger, of which only 0.3% were reported younger than 3 years. Burning and stinging are the most frequently reported symptoms with erythema being the most common sign. Signs and symptoms occur days to weeks after TCS discontinuation. More data

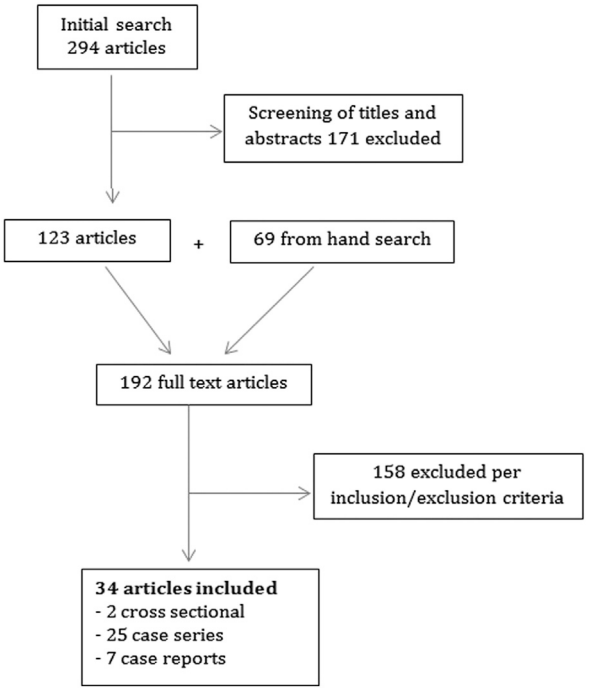

Fig 1. Flowchart of article selection.

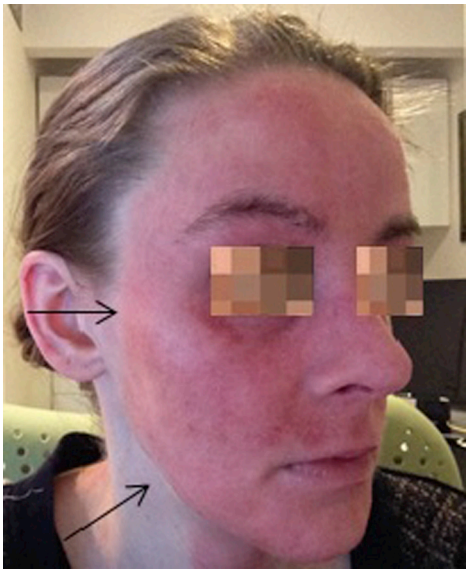

Fig 2. Erythematoedematous subtype of steroid withdrawal syndrome. Edema and erythema with a sharp cutoff (*arrows*) line between red and normal-looking skin. The patient reported a burning sensation.

are needed regarding the frequency and duration of use that predisposes to this condition. Further, there are no data regarding the prevalence of this condition. It is also unclear whether children are actually less likely to develop this disorder or that cases of TCS withdrawal in the pediatric population are underreported.

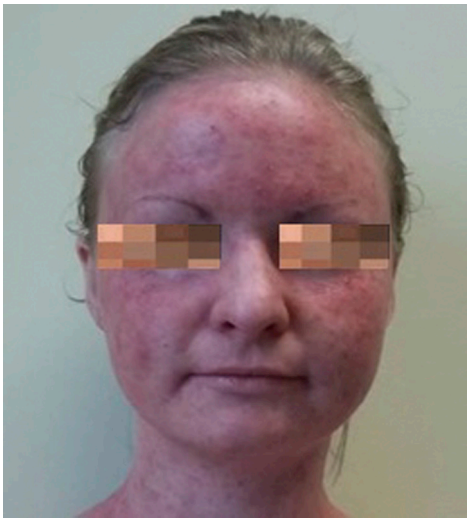

Fig 3. Papulopustular subtype of steroid withdrawal syndrome. Erythema, papules, and pustules.

In general, TCS withdrawal can be divided into 2 distinct morphologic syndromes: papulopustular and erythematoedematous. The erythematoedematous type develops more frequently in patients who have underlying chronic eczematous conditions such as atopic dermatitis and seborrheic dermatitis; is characterized by erythema, scaling, and edema; and is generally accompanied by a burning sensation. The papulopustular type is more common in patients who are using TCS for pigmentary disorders or acneiform conditions. The papulopustular withdrawal subtype is more likely in patients who develop steroid rosacea, but this is not a prerequisite condition for this subtype. The papulopustular variant can be differentiated from the erythematoedematous subtype by the prominent features of pustules and papules, along with erythema, but less frequently swelling, edema, burning, and stinging.

Although our data identified 2 relatively specific withdrawal phenotypes, the diagnosis of steroid withdrawal could overlap with other clinical entities such as allergic contact dermatitis. Patch testing may be warranted because of the possibility of allergic contact dermatitis to the steroid molecule itself or a cream excipient. In addition to allergic contact dermatitis, a flareup of the underlying inflammatory condition or skin infection may also be considered. Confusing the signs and symptoms of atopic dermatitis for steroid withdrawal could lead to unnecessary withholding of needed anti-inflammatory therapy. Extrapolating from our review, a clinician should favor TCS withdrawal over a flareup of the underlying atopic dermatitis if the following features are present: (1) burning is the prominent symptom, (2) confluent erythema occurs within days to weeks of TCS discontinuation, and

(3) a history of frequent, prolonged TCS use on the face or genital region. Histology is nonspecific, thus of no help differentiating between atopic dermatitis and steroid withdrawal. The rosacea that follows TCS use may have overlapping mild clinical features that may be a prodrome of the papulopustular variant.

Our review was unable to identify a clearly effective management strategy. We found that steroid discontinuation and supportive care (eg, cool compresses, psychological support) were the primary management strategies used for this condition. Because of the violent rebound that may occur upon steroid discontinuation, some authors recommend the use of an oral steroid combined with a "safe" TCS (negative on patch testing).[35] It is unclear if either a tapering off of TCS or immediate discontinuation has any added benefits. There were no reports regarding the use of calcineurin inhibitors or systemic immunosuppressants for this condition.

In conclusion, our review found TCS withdrawal to be an adverse effect that generally occurs with the inappropriate prolonged frequent use of high-potency TCS. Clinicians and patients should be aware of this entity and the predisposing factors. Patients should be counseled regarding the risks, including TCS withdrawal, from prolonged daily use of TCS beyond their approved indication. Physicians must avoid inappropriate overprescribing and lax monitoring of refills. This risk of developing TCS withdrawal, however, should not prevent the appropriate treatment of patients with chronic inflammatory skin disease. The concern for developing steroid addiction has been recognized as 1 cause of failed therapy, especially for atopic dermatitis.[10] Recent clinical guidelines found TCS, when used appropriately, remain key to the successful short-term (and long-term) management of atopic dermatitis.[1,3,4,6,9] Because of the low quality of evidence, variability in the extent of data, and lack of studies using rigorous methodology, well-designed, prospective studies are needed to better understand and define this entity.

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REFERENCES

1. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis, section 1: diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70:338-351.
2. Leung TNH, Chow CM, Chow MPY, et al. Clinical guidelines on management of atopic dermatitis in children. *Hong Kong J Paediatr*. 2013;18:96-104.
3. Garnacho-Saucedo G, Salido-Vallejo R, Moreno-Giménez JC. Atopic dermatitis: update and proposed management algorithm. *Actas Dermosifiliogr*. 2013;104:4-16.
4. Proudfoot LE, Powell AM, Ayis S, et al. The European treatment of severe atopic eczema in children taskforce (TREAT) survey. *Br J Dermatol*. 2013;169:901-909.
5. Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. *J Allergy Clin Immunol*. 2013;131:295-299.e27.
6. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis, section 2: management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71:116-132.
7. Anvar M, Lohrasb MH, Javadpour A. Effect of convenient dermatologic intervention on quality of life in patients with chronic eczematous dermatitis. *Iran J Psychiatr Behav Sci*. 2010;4:47-50.
8. Maroti M, Ulff E, Wijma B. Quality of life before and 6 weeks after treatment in a dermatological outpatient treatment unit. *J Eur Acad Dermatol Venereol*. 2006;20:1081-1085.
9. Samarasekera EJ, Sawyer L, Wonderling D, Tucker R, Smith CH. Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses. *Br J Dermatol*. 2013;168:954-967.
10. Aubert-Wastiaux H, Moret L, Le Rhun A, et al. Topical corticosteroid phobia in atopic dermatitis: a study of its nature, origins and frequency. *Br J Dermatol*. 2011;165:808-814.
11. Aubert H, Barbarot S. Non adherence and topical steroids. *Ann Dermatol Venereol*. 2012;139(Suppl):S7-S12.
12. Hanifin JM, Cooper KD, Ho VC, et al. Guidelines of care for atopic dermatitis. *J Am Acad Dermatol*. 2004;50:391-404.
13. Schünemann H, Hill S, Guyatt G, Akl EA, Ahmed F. The GRADE approach and Bradford Hill's criteria for causation. *J Epidemiol Community Health*. 2011;65:392-395.
14. Howick J. Oxford center for evidence-based medicine: levels of evidence. Available from: URL: http://www.cebm.net/?o=1025. Accessed February 20, 2013.
15. Sneddon I. Adverse effect of topical fluorinated corticosteroids in rosacea. *Br Med J*. 1969;1:671-673.
16. Sneddon I. Iatrogenic dermatitis. *Br Med J*. 1969;4:49.
17. Weber G. Rosacea-like dermatitis: contraindication or intolerance reaction to strong steroids. *Br J Dermatol*. 1972;86:253-259.
18. Burry JN. Topical drug addiction: adverse effects of fluorinated corticosteroid creams and ointments. *Med J Aust*. 1973;1:393-396.
19. Leyden JJ, Thew M, Kligman AM. Steroid rosacea. *Arch Dermatol*. 1974;110:619-622.
20. Stegman SJ. Pustular dermatosis on withdrawal of topically applied steroids [letter]. *Arch Dermatol*. 1974;109:100.
21. Kligman AM. Topical steroid addicts [letter]. *J Am Med Assoc*. 1976;235:1550.
22. Urabe H, Koda H. Perioral dermatitis and rosacea like dermatitis: clinical features and treatment. *Dermatologica*. 1976;152(Suppl):155-160.
23. Wilkinson DS, Kirton V, Wilkinson JD. Perioral dermatitis: a 12-year review. *Br J Dermatol*. 1979;101:245-257.
24. Franco HL, Weston WL. Steroid rosacea in children. *Pediatrics*. 1979;64:36-38.
25. Sheu HM, Chang CH. Alterations in water content of the stratum corneum following long-term topical corticosteroids. *J Formos Med Assoc*. 1991;90:664-669.
26. Wells K, Brodell RT. Topical corticosteroid 'addiction': a cause of perioral dermatitis. *Postgrad Med*. 1993;93:225-230.
27. Uehara M, Omoto M, Sugiura H. Diagnosis and management of the red face syndrome. *Dermatol Ther*. 1996;1:19-23.

28. Velangi SS, Humphreys F, Beveridge GW. Periocular dermatitis associated with the prolonged use of a steroid eye ointment. *Clin Exp Dermatol*. 1998;23:297-298.
29. Rapaport MJ, Rapaport V. Eyelid dermatitis to red face syndrome to cure: clinical experience in 100 cases. *J Am Acad Dermatol*. 1999;41:435-442.
30. Rapaport MJ, Rapaport V. Prolonged erythema after facial laser resurfacing or phenol peel secondary to corticosteroid addiction. *Dermatol Surg*. 1999;25:781-785.
31. Brodell RT, O'Brien MJ Jr. Topical corticosteroid-induced acne: three treatment strategies to break the 'addiction' cycle. *Postgrad Med*. 1999;106:225-229.
32. Fukaya M. Improvement of atopic dermatitis after discontinuation of topical corticosteroid treatment. *Arch Dermatol*. 2000;136:679-680.
33. Goldman D. Tacrolimus ointment for the treatment of steroid-induced rosacea: a preliminary report. *J Am Acad Dermatol*. 2001;44:995-998.
34. Pabby A, An KP, Laws RA. Combination therapy of tetracycline and tacrolimus resulting in rapid resolution of steroid-induced periocular rosacea. *Cutis*. 2003;72:141-142.
35. Rapaport MJ, Lebwohl M. Corticosteroid addiction and withdrawal in the atopic: the red burning skin syndrome. *Clin Dermatol*. 2003;21:201-214.
36. Zalaudek I, Di Stefani A, Ferrara G, Argenziano G. Childhood granulomatous periorificial dermatitis: a controversial disease. *J Dtsch Dermatol Ges*. 2005;3:252-255.
37. Rathi S. Abuse of topical steroid as cosmetic cream: a social background of steroid dermatitis. *Indian J Dermatol*. 2006;51:154-155.
38. Chu CY. An open-label pilot study to evaluate the safety and efficacy of topically applied pimecrolimus cream for the treatment of steroid-induced rosacea-like eruption. *J Eur Acad Dermatol Venereol*. 2007;21:484-490.
39. Abbas O, Kibbi AG, Chedraoui A, Ghosn S. Red scrotum syndrome: successful treatment with oral doxycycline. *J Dermatolog Treat*. 2008;19:1-2.
40. Liu ZH, Du XH. Quality of life in patients with facial steroid dermatitis before and after treatment. *J Eur Acad Dermatol Venereol*. 2008;22:663-669.
41. Chen AY, Zirwas MJ. Steroid-induced rosacealike dermatitis: case report and review of the literature. *Cutis*. 2009;83:198-204.
42. Lu H, Xiao T, Lu B, et al. Facial corticosteroid addictive dermatitis in Guiyang City, China. *Clin Exp Dermatol*. 2010;35:618-620.
43. Del Rosso JQ. Management of papulopustular rosacea and perioral dermatitis with emphasis on iatrogenic causation or exacerbation of inflammatory facial dermatoses use of doxycycline-modified release 40mg capsule once daily in combination with properly selected skin care as an effective therapeutic approach. *J Clin Aesthet Dermatol*. 2011;4:20-30.
44. Rathi SK, Kumrah L. Topical corticosteroid-induced rosacea-like dermatitis: a clinical study of 110 cases. *Indian J Dermatol Venereol Leprol*. 2011;77:42-46.
45. Saraswat A, Lahiri K, Chatterjee M, et al. Topical corticosteroid abuse on the face: a prospective, multicenter study of dermatology outpatients. *Indian J Dermatol Venereol Leprol*. 2011;77:160-166.
46. Zhang R, Zhu W. Coexistence of dermatosis neglecta, facial seborrheic dermatitis, and corticosteroid-dependent dermatitis in a 21-year-old woman. *Am J Clin Dermatol*. 2011;12:347-348.
47. Monroe JR. What caused this woman's addiction to steroids? *JAAPA* 2011;24:20.
48. Narang T, Kumaran MS, Dogra S, Saikia UN, Kumar B. Red scrotum syndrome: idiopathic neurovascular phenomenon or steroid addiction? *Sexual Health* 2013;10:452-455.

Table I. Search strategy

Database: Ovid MEDLINE and Ovid old MEDLINE <1946 to April week 3 2014>	
1	exp Drug Tolerance/(19987)
2	exp Glucocorticoids/(161109)
3	administration, topical/or administration, cutaneous/(46716)
4	1 and 2 and 3 (39)
5	red face syndrome.mp. (1)
6	exp Adrenal Cortex Hormones/ad, ae, po, tu, to [Administration & Dosage, Adverse Effects, Poisoning, Therapeutic Use, Toxicity] (157765)
7	exp administration, cutaneous/(14925)
8	1 and 6 and 7 (4)
9	((escalat$ or increas$ or more) adj5 (dose$ or dosag$ or amount$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (158833)
10	6 and 7 and 9 (4)
11	((steroid$ or glucocorticoid$) adj5 addict$ adj7 (topical$ or (adminst$ adj3 (skin or derm$)))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (1)
12	corticosteroid addiction.ti. (4)
13	((develop$ or experienc$ or becom$ or became) adj3 (tolera$ or intoler$) adj7 ((skin or derm$ or cutaneous$ or topical$) adj3 (steroid$ or corticosteroid$ or glucocorticoid$))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
14	((abus$ or overus$ or overutili$) adj7 ((skin or derm$ or cutaneous$ or topical$) adj3 (steroid$ or corticosteroid$ or glucocorticoid$))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (31)
15	((addict$ or compulsi$ or withdraw$ or toler$ or intoler$ or habit$) adj7 ((skin or derm$ or cutaneous$ or topical$) adj3 (steroid$ or corticosteroid$ or glucocorticoid$))).mp. (86)
16	((fear$ or phobi$$ or irrational$ or reject$ or non-complian$ or noncomplian$) adj7 ((skin or derm$ or cutaneous$ or topical$) adj3 (steroid$ or corticosteroid$ or glucocorticoid$))).mp. (63)
17	14 or 15 or 16 (176)
18	exp Skin Diseases/(808579)
19	exp Skin/(180033)
20	18 or 19 (928139)
21	17 and 20 (91)
22	(topical$ adj7 (steroid$ or corticosteroid$ or glucocorticoid$) adj7 rebound$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (10)
23	(atop$ adj5 (red or redness or redden$) adj5 (face or faces or facial$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (6)
24	((face or faces or facial$) adj7 (steroid$ or corticosteroid$ or glucocorticoid$) adj7 addict$ adj7 dermatit$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (3)
25	(indurat$ adj5 erythem$ adj5 (face or faces or facial$)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8)
26	((steroid$ or corticosteroid$ or glucocorticoid$) adj5 addict$ adj7 (rebound$ adj5 vasodil)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
27	((post or follow$ or subsequen$) adj5 (laser$ adj3 peel$) adj7 erythem$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (0)
28	status cosmeticus.mp. (4)
29	((red or redness or redden$) adj3 scrot$ adj5 syndrom$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (8)

Continued

Table I. Cont'd

Database: Ovid MEDLINE and Ovid old MEDLINE <1946 to April week 3 2014>	
30	((topical$ or skin or derma$ or cream$ or ointment$) adj5 (steroid$ or corticosteroid$ or glucocorticoid$) adj5 dependen$).mp. (39)
31	22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 (78)
32	4 or 5 or 8 or 10 or 11 or 12 or 17 or 21 or 31 (291)
33	exp Dermatitis, Perioral/(164)
34	((perioral$ or peri-oral$) adj3 dermatit$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier] (380)
35	2 and 34 (42)
36	6 and 34 (79)
37	35 or 36 (91)
38	exp Rosacea/(2176)
39	exp Rosacea/et, ep, ci (384)
40	2 and 39 (23)
41	6 and 39 (45)
42	40 or 41 (53)
43	exp acneiform eruptions/et, ep, ci (1958)
44	2 and 43 (80)
45	6 and 43 (123)
46	44 or 45 (136)
47	((steroid$ or corticosteroid$ or glucocorticoid$) adj5 (induc$ or generat$ or react$ or caus$ or etiolog$ or associat$) adj10 ((skin$ or derm$) adj5 (redness or redden$ or irritat$ or erupt$ or damag$ or advers$))).mp. (13)
48	((steroid$ or corticosteroid$ or glucocorticoid$) adj5 (induc$ or generat$ or react$ or caus$ or etiolog$ or associat$) adj10 (acne$ or pimple$ or comedo$ or dermatit$ or rosace$)).mp. (144)
49	47 or 48 (153)
50	limit 37 to English language (68)
51	limit 42 to English language (36)
52	limit 46 to English language (94)
53	limit 49 to English language (130)
54	50 or 51 or 52 or 53 (294)