

**A case for case reports: A retrospective evaluation of the case reports published in the *Journal of the American Academy of Dermatology* in 2000**



*To the Editor:* In 2015, the *Journal of American Academy of Dermatology (JAAD)* stopped printing case reports, transitioning their publication into a case reports–only online journal titled *JAAD Case Reports*. This change was supported by arguments that case reports reduce the impact factor of *JAAD* and are “less valid” than other study types. By moving these case reports to *JAAD Case Reports*, their circulation has decreased 15-fold despite their popularity among *JAAD* readers.<sup>1,2</sup> We evaluated this by reviewing the impact and validity of case reports published in *JAAD* from January to December 2000. This study was adapted from Venning’s landmark study on drug reaction “first alerts.”<sup>3</sup>

Overall, we identified 159 articles. We separated these articles into reports of (1) unique clinical findings (116 of 159), (2) new conditions (3 of 159), (3) drugs’ adverse effects (21 of 159), and (4) new treatment modalities (19 of 159) (Tables I to IV). For information on reports of rare cases and/or unique

clinical findings of known conditions, see Table I (available at <https://data.mendeley.com/datasets/ydn9xjvh93/1>). To assess the relevance of these case reports, we analyzed their impact and validity. On average, they were each cited approximately 34 times, with new treatments cited most frequently (~49 times). This is half as frequently as prospective, retrospective, and basic science studies and one-tenth as frequently as CME articles (Table V).

We then assessed the validity of reports of unique clinical findings, new conditions, and drug adverse effects. Of the 116 unique clinical findings reported, 100 were subsequently reported again. Notable findings include autosomal recessive reticulate acropigmentation of Dohi, for which the underlying mutation has subsequently been identified.

Three new conditions were described: acral peeling skin syndrome and RACAND syndrome [Raynaud phenomena (R), anticentromere antibodies (ACA), and necrosis of digits (ND)] have subsequently been confirmed as distinct entities; computer palms is likely an occupational contact dermatoses.

Drug reactions were initially divided into first alerts (11 of 21) and previously described reactions

**Table II.** Reports of new conditions

Condition	Unique finding	Cases, n	Additional cases documented (Y/N)	Citations, n	URL
Acral peeling skin syndrome	Case unique because of isolation of disease on the hands and feet. Reportedly never previously documented. Subsequent research has identified the causative mutation, showing that this is distinct from continuous peeling skin syndrome.	1	Y	43	<a href="https://www.jaad.org/article/S0190-9622(00)23324-0/fulltext">https://www.jaad.org/article/S0190-9622(00)23324-0/fulltext</a>
Computer palms	Unique because patients with the same occupation and same baseline rash on hands. Reportedly never previously documented.	2	N Possibly grouped as an occupational contact dermatitis?	34	<a href="https://www.jaad.org/article/S0190-9622(00)90306-2/fulltext">https://www.jaad.org/article/S0190-9622(00)90306-2/fulltext</a>
Raynaud phenomenon (proposed RACAND syndrome)	Occurred in a triad with anticentromere antibodies and necrosis of finger digits without sclerodactyly and sclerosis.	4	Y Confirmed the existence of RACAND syndrome.	16	<a href="https://www.jaad.org/article/S0190-9622(00)21579-X/abstract">https://www.jaad.org/article/S0190-9622(00)21579-X/abstract</a>

N, No; RACAND, Raynaud phenomena (R), anticentromere antibodies (ACA), and necrosis of digits (ND); URL, uniform resource locator; Y, yes.

**Table III.** Drug adverse effects

Drug name	Reaction	Cases, n	Verification	Subsequent reports/studies	Citations, n	URL
Hirudo medicinalis	Pseudolymphocyte formation	1	First alert Obviously valid Based on the fact that lesions were located only at sites of leech therapy	Multiple case reports	29	<a href="https://www.jaad.org/article/S0190-9622(00)49506-X/abstract">https://www.jaad.org/article/S0190-9622(00)49506-X/abstract</a>
D-Penicillamine	Pemphigus vulgaris	1	Has been well described in the past, with $\geq 100$ cases described Discontinuation of therapy allowed the patient to eventually reach remission after period of worsening	Multiple case reports, including 2 from a cohort of 1209 patients with pemphigus	32	<a href="https://www.jaad.org/article/S0190-9622(00)70124-1/abstract">https://www.jaad.org/article/S0190-9622(00)70124-1/abstract</a>
Stomahesive paste (Stomahesive paste, specifically)	Peristomal allergic contact dermatitis	1	1 previous case described Verified through patch testing	Multiple case reports, some referring specifically to Stomahesive paste	22	<a href="http://www.jaad.org/article/S0190-9622(02)70043-1/fulltext">http://www.jaad.org/article/S0190-9622(02)70043-1/fulltext</a>
Actinomycin plus vincristine	Persistent serpentine supragenous hyperpigmented eruption Eccrine neutrophilic hidradenitis on skin biopsy specimen	1	First alert Obviously Valid Based on the fact that the reaction was at the delivery site and arose only hours after	1 similar reaction with docetaxel, another with 5-fluorouracil	20	<a href="https://www.jaad.org/article/S0190-9622(00)85668-6/fulltext">https://www.jaad.org/article/S0190-9622(00)85668-6/fulltext</a>
Medroxyprogesterone acetate	Pigmented purpuric eruption	1	Not a first alert; several prior case reports Skin cleared after cessation of injections. No rechallenge	A subsequent case report	29	<a href="http://www.jaad.org/article/S0190-9622(00)04068-8/fulltext">http://www.jaad.org/article/S0190-9622(00)04068-8/fulltext</a>
Immunosuppression (cyclosporine presumed)	Pilomatrix dysplasia	1	Not a first alert Assumed because of prior reports of use of cyclosporine with follicular problems and inability to find other causes	1 case report following Discovery in 2010 of a virus associated with trichodysplasia spinulosa in immunosuppressed patients	31	<a href="https://www.jaad.org/article/S0190-9622(00)22410-9/fulltext">https://www.jaad.org/article/S0190-9622(00)22410-9/fulltext</a>

Protease inhibitors	Angiolipomatosis	3	First alert Meeting reasonable criteria of validity Based on the fact that protease inhibitors have known side effects of lipodystrophy and a time relation similar to that of other reactions	Multiple case reports Cited in an article elucidating new lipid pathways of HIV	44	<a href="http://www.jaad.org/article/S0190-9622(00)90021-5/pdf">http://www.jaad.org/article/S0190-9622(00)90021-5/pdf</a>
Ticlopidine	Psoriasis improvement, agranulocytosis	3	First alert Meeting reasonable criteria of validity Based on regression of psoriasis with low WBC count and re-emergence after WBCs recovered when ticlopidine was stopped	Cited in multiple studies on pathogenesis in psoriasis	44	<a href="http://www.jaad.org/article/S0190-9622(00)69224-1/abstract">http://www.jaad.org/article/S0190-9622(00)69224-1/abstract</a>
Carbon dioxide laser	Spontaneous bullae	2	First alert Obviously valid Both occurred 19 d after laser treatment in same area of lower cheeks close to jaw	No further case reports made Known side effects include erythema, milia, HSV infection but no bullae	2	<a href="https://www.jaad.org/article/S0190-9622(00)70120-4/fulltext">https://www.jaad.org/article/S0190-9622(00)70120-4/fulltext</a>
Lamotrigine	Stevens-Johnson syndrome	1	Not a first alert Previous reports of lamotrigine use, especially with valproic acid Verified because of an increase in symptoms with increase in lamotrigine dosage and cessation after cessation of the drug	Demonstrated with lymphocytes in vivo before this case report Part of a large EuroSCAR study on the risks of newer drugs	63	<a href="http://www.jaad.org/article/S0190-9622(00)25312-7/abstract">http://www.jaad.org/article/S0190-9622(00)25312-7/abstract</a>
Busulfan, etoposide, and cyclophosphamide	Epidermal dysmaturation	1	Not a first alert Association based on a temporal association	Previously documented in case series	15	<a href="https://www.jaad.org/article/S0190-9622(00)49764-1/abstract">https://www.jaad.org/article/S0190-9622(00)49764-1/abstract</a>

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Table III. Cont'd

Drug name	Reaction	Cases, n	Verification	Subsequent reports/studies	Citations, n	URL
Conjugated estrogens	Acquired dermal melanocytosis	1	First alert Requiring verification Association based on a temporal association Evidence that estrogen receptors are important to dermal melanocyte proliferation	Additional reports of acquired dermal melanocytosis during pregnancy and after initiation of oral contraceptives are supportive	13	<a href="https://www.jaad.org/article/S0190-9622(00)89714-5/fulltext">https://www.jaad.org/article/S0190-9622(00)89714-5/fulltext</a>
All-trans retinoic acid	Scrotal ulceration	1	Not a first alert Association based on a temporal association 8 cases reported previously	Many additional reports of scrotal ulceration secondary to all-trans retinoic acid have been reported	31	<a href="https://www.jaad.org/article/S0190-9622(00)17358-X/abstract">https://www.jaad.org/article/S0190-9622(00)17358-X/abstract</a>
Interferon- $\alpha$	Capillaritis (lymphocytic vasculitis)		First alert Requiring verification Based on a temporal association (5 d after treatment) and biologic plausibility	Case series of 10 patients documenting relationship of HepC/B to capillaritis	22	<a href="https://www.jaad.org/article/S0190-9622(00)31957-0/abstract">https://www.jaad.org/article/S0190-9622(00)31957-0/abstract</a>
Blepharopigmentation with aluminum silicate	Delayed hypersensitivity granulomatous reaction	1	Based on a patch test reaction 8 d later Previously reported with tattoos	Multiple case reports. Cited in a large review of aluminum toxicity	25	<a href="http://www.jaad.org/article/S0190-9622(00)90264-0/fulltext">http://www.jaad.org/article/S0190-9622(00)90264-0/fulltext</a>
Danaparoid	Delayed hypersensitivity reaction	1	First alert Obviously valid Based on a temporal association and location of the rash Known reaction of heparin and LMWH and heparinoids	Multiple case reports	15	<a href="https://www.jaad.org/article/S0190-9622(00)04395-4/fulltext">https://www.jaad.org/article/S0190-9622(00)04395-4/fulltext</a>
Topical PUVA	Disseminated actinic prokeratosis	1	First alert Meeting reasonable criteria of validity Verified through resolution once PUVA has been discontinued	No further reports found on topical PUVA	34	<a href="http://www.jaad.org/article/S0190-9622(00)36209-0/fulltext">http://www.jaad.org/article/S0190-9622(00)36209-0/fulltext</a>

Vancomycin	Drug-induced linear IgA bullous dermatosis	1	Not a first alert Known drug cause, but did not blister on rechallenge	Multiple case reports	66	<a href="https://www.jaad.org/article/S0190-9622(00)90102-6/abstract">https://www.jaad.org/article/S0190-9622(00)90102-6/abstract</a>
Fluconazole	Fixed drug eruption	1	Not a first alert Confirmed with patch testing	Multiple case reports	35	<a href="https://www.jaad.org/article/S0190-9622(00)90262-7/fulltext">https://www.jaad.org/article/S0190-9622(00)90262-7/fulltext</a>
Polyoxyethylene laurylether	Follicular contact dermatitis	1	First alert Meeting reasonable criteria of validity Confirmed with patch testing	No further reports (seems to be an uncommonly used chemical?) Shown to form formaldehyde and peroxides by air oxidation	14	<a href="https://www.jaad.org/article/S0190-9622(00)90260-3/abstract">https://www.jaad.org/article/S0190-9622(00)90260-3/abstract</a>
Vitamin D <sub>3</sub>	Pseudoxanthoma elasticum exacerbation	1	First alert Requires verification Suggested by additional calcification during treatment	No further reports	14	<a href="https://www.jaad.org/article/S0190-9622(00)90189-0/fulltext">https://www.jaad.org/article/S0190-9622(00)90189-0/fulltext</a>

He4pC/B, Hepatitis C and/or B; HSV, herpes simplex virus; LMWH, low-molecular-weight heparin; PUVA, psoralen plus ultraviolet A; URL, uniform resource locator; WBC, white blood cell.

(10 of 21). First alerts were further stratified as (1) obviously valid (4 of 11), meaning that they were either immediate reactions or drug delivery site reactions; (2) meeting reasonable criteria of validity (4 of 11), meaning predictable on the basis of known class reaction or pharmacodynamics or occurrence of a positive rechallenge reaction; and (3) requiring subsequent verification (3 of 11), meaning that supporting evidence included temporal association and a positive dechallenge reaction only. Only 1 first alert appeared to be a “false alarm” with no additional confirmatory reports. Notable first alerts included the association of ticlodipine-induced leukopenia with psoriasis improvement, which was subsequently used to elucidate the pathogenesis of psoriasis.

In all, 19 new treatment modalities were proposed. The impact of these is highlighted by cases of topical tacrolimus for ichthyosis linearis circumflexa, intravenous immunoglobulin for scleromyxedema, and ultraviolet A1 for chronic sclerodermic graft-versus-host disease. All have subsequently become mainstream therapies.

These findings suggest that case reports provide a quick way to disseminate novel observations so that these observations can spur “more-scientific” studies. Furthermore, the impact of case reports exceeds their rate of citation, as many observations initially described in case reports are subsequently incorporated into mainstream dermatology. Dermatology is advanced by the publication of case reports, and encouraging our JAAD readers to seek out *JAAD Case Reports* as regularly as they read *JAAD* would maximize the readership of exceptional studies and enhance patient care.

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**Table IV.** New treatment modalities

Treatment modality	Condition of interest	Cases, n	Subsequent reports	Citations, n	URL
Wide surgical excision (Failure with electrosection, pulsed laser, radiograph)	Cutaneous verruciform xanthoma	1	Multiple case reports on penis 10 case series on vulvular verruciform xanthoma (8 had surgical excision) 1 DNA study of NSDHL No studies documenting treatment	46	<a href="https://www.jaad.org/article/S0190-9622(00)90108-7/fulltext">https://www.jaad.org/article/S0190-9622(00)90108-7/fulltext</a>
High-dose erythropoietin and small-volume phlebotomy	Porphyria cutanea tarda with renal failure	1	Four prior case reports Only 1 subsequent case report	54	<a href="https://www.jaad.org/article/S0190-9622(00)90179-8/fulltext">https://www.jaad.org/article/S0190-9622(00)90179-8/fulltext</a>
Mycophenolate mofetil	Pemphigus foliaceus	1	1 case series study of 12 cases Multiple case reports	44	<a href="https://www.jaad.org/article/S0190-9622(00)90231-7/abstract">https://www.jaad.org/article/S0190-9622(00)90231-7/abstract</a>
Topical tacrolimus	Pyoderma gangrenosum	1	Part of a 350-patient case review finding topical tacrolimus evidence level B (n = 34) Studies demonstrating systemic absorption	50	<a href="http://www.jaad.org/article/S0190-9622(00)70126-5/fulltext">http://www.jaad.org/article/S0190-9622(00)70126-5/fulltext</a>
Isotretinoin	IgA pemphigus of subcorneal pustular dermatosis type	1	1 case with isotretinoin Multiple cases with acitretin	41	<a href="https://www.jaad.org/article/S0190-9622(00)70111-3/abstract">https://www.jaad.org/article/S0190-9622(00)70111-3/abstract</a>
IVIg	Scleromyxedema	2	A 10-case series with successful treatment in 8 cases Multiple other case reports Unclear mechanism	105	<a href="http://www.jaad.org/article/S0190-9622(15)00270-4/abstract">http://www.jaad.org/article/S0190-9622(15)00270-4/abstract</a>
Tretinoin and 5-FU	Noninflamed linear verrucous epidermal nevus	1	Used once in the past 1 further case report using isotretinoin Most case reports now focus on laser treatments	53	<a href="http://www.jaad.org/article/S0190-9622(00)23586-X/abstract">http://www.jaad.org/article/S0190-9622(00)23586-X/abstract</a>
Tazarotene gel	keratoderma blennorrhagicum	1	No other reports	6	<a href="http://www.jaad.org/article/S0190-9622(00)62891-8/abstract">http://www.jaad.org/article/S0190-9622(00)62891-8/abstract</a>
Q-switched ruby laser	Nonmelanotic hyperpigmentation	2	1 case series showing effectiveness in bleaching treatment with tretinoin and hydroquinone 1 report used for postsclerotherapy hyperpigmentation 1 retrospective study showing effectiveness in nevus of Ota	14	<a href="https://www.jaad.org/article/S0190-9622(00)08497-8/abstract">https://www.jaad.org/article/S0190-9622(00)08497-8/abstract</a>

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**Table IV.** Cont'd

Treatment modality	Condition of interest	Cases, n	Subsequent reports	Citations, n	URL
Flashlamp-pumped pulsed-dye laser at 585 nm	Subungual hemangioma	1	No further reports of subungual treatments 1 long-term evaluation of 617 cases of childhood hemangioma treatment in childhood showed excellent results Another study of 165 children showed ineffective for hemangiomas with deep component	10	<a href="https://www.jaad.org/article/S0190-9622(00)70193-9/fulltext">https://www.jaad.org/article/S0190-9622(00)70193-9/fulltext</a>
Er:YAG laser	Birt-Hogg-Dubé syndrome	1	Multiple further case reports	36	<a href="http://www.jaad.org/article/S0190-9622(00)64041-0/abstract">http://www.jaad.org/article/S0190-9622(00)64041-0/abstract</a>
Pore strips	Nevus comedonicus	2	No further reports using pore strips Some reports using lasers	17	<a href="https://www.jaad.org/article/S0190-9622(00)85920-4/pdf">https://www.jaad.org/article/S0190-9622(00)85920-4/pdf</a>
UVA irradiation	Solar urticaria	3	Multiple other case reports 1 case report with UVB Cited in large paper recommending H1 as first-line treatment	95	<a href="https://www.jaad.org/article/0190-9622(93)70190-5/fulltext">https://www.jaad.org/article/0190-9622(93)70190-5/fulltext</a>
Topical tacrolimus	Ichthyosis linearis circumflexa	1	Multiple case reports 1 case series of 4 patients Studies demonstrating systemic absorption	71	<a href="https://www.jaad.org/article/S0190-9622(00)90234-2/abstract">https://www.jaad.org/article/S0190-9622(00)90234-2/abstract</a>
UVA1	Chronic sclerodermic graft versus host disease	1	Multiple case series including a total of $\geq 21$ patients UVA level C-1 recommendation with III-1 level evidence in GVH disease consensus article	86	<a href="https://www.jaad.org/article/S0190-9622(00)90023-9/fulltext">https://www.jaad.org/article/S0190-9622(00)90023-9/fulltext</a>
High-dose cyclophosphamide	Pemphigus vulgaris	1	In 1 article, said to be usable in refractory cases Shown to be effective in severe autoimmune diseases such as SLE	61	<a href="https://www.jaad.org/article/S0190-9622(03)01471-3/fulltext">https://www.jaad.org/article/S0190-9622(03)01471-3/fulltext</a>
Pentoxifylline	Kimura disease	1	No further reports of treatment with pentoxifylline	56	<a href="http://www.jaad.org/article/S0190-9622(00)84625-3/abstract">http://www.jaad.org/article/S0190-9622(00)84625-3/abstract</a>

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**Table IV.** Cont'd

Treatment modality	Condition of interest	Cases, n	Subsequent reports	Citations, n	URL
Cidofovir (same case as HPV 66 wart in a patient with HIV)	HPV verruca	1	Multiple studies showing effectiveness in studies of 14, 24, 30, and 47 patients Pilot study of topical cidofovir with 14 patients found that it was effective for refractory lesions	51	<a href="https://www.jaad.org/article/S0190-9622(00)53691-3/fulltext">https://www.jaad.org/article/S0190-9622(00)53691-3/fulltext</a>
Q-switched alexandrite and ruby laser	Imipramine-induced hyperpigmentation	1	Multiple case reports showing effectiveness of Q-switched alexandrite laser for causing hypopigmentation in various conditions Many showing effectiveness of Nd:YAG also	37	<a href="http://www.jaad.org/article/S0190-9622(00)28667-2/abstract">http://www.jaad.org/article/S0190-9622(00)28667-2/abstract</a>

*Er:YAG*, Erbium-doped yttrium-aluminum-garnet; *5-FU*, 5-fluorouracil; *GVH*, graft-versus-host; *HPV*, human papilloma virus; *IVIg*, intravenous immunoglobulin; *Nd:YAG*, neodymium-doped yttrium-aluminum-garnet; *NSDHL*, NAD(P) dependent steroid dehydrogenase-like; *SLE*, systemic lupus erythematosus; *URL*, uniform resource locator; *UVA*, ultraviolet A; *UVB*, ultraviolet B.

**Table V.** Citations by article type

Article type	Citations, n
Case reports	34
CME articles	346
Prospective studies	95.2
Retrospective studies	85.2
Basic science research	80.2

**REFERENCES**

- Pharma and Life Sciences Solutions. Journal of the American Academy of Dermatology. Journal detail Available at: <http://www.elsmediakits.com/us/journals/dermatology/journal-of-the-american-academy-of-dermatology/YMJD>. Accessed August 3, 2018.
- Pharma and Life Sciences Solutions. JAAD Case Reports. Journal detail Available at: <http://www.elsmediakits.com/us/journals/dermatology/jaad-case-reports/JDCR>. Accessed August 3, 2018.
- Venning G. Validity of anecdotal reports of suspected adverse drug reactions: the problem of false alarms. *Br Med J*. 1982;284:249-252.

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**Relative risk of microscopic colitis in dermatomyositis**

*To the Editor:* Chronic diarrhea, which is diagnosed when symptoms last 4 weeks or longer, is common in dermatomyositis and is attributable to many causes. Among the general population, 7.5% to 15% of chronic diarrhea is caused by microscopic colitis (MC), an idiopathic inflammatory colonic disease diagnosed by

colonoscopy that affects 107 to 219 individuals per 100,000.<sup>1-3</sup> Herein, we have investigated the association between MC and dermatomyositis.

This cohort study reviewed adult patients with dermatomyositis at the University of Pennsylvania between 2000 and 2017 (N = 644). Dermatomyositis subtype (classic dermatomyositis [CDM] vs clinically amyopathic [CADM]), highest antinuclear antibody (ANA) titer, myositis-specific antibody (MSA) and myositis-associated antibody (MAA) serologies, and gastroenterologic diagnoses were obtained by chart review. MC diagnosis required confirmatory colonic biopsy. Relative risks (RRs) were calculated against historic controls.<sup>1-6</sup> Statistical analyses were performed with Stata software (version 15.0, StataCorp LLC, College Station, TX). The University of Pennsylvania institutional review board approved this protocol (No. 828959).

Table I illustrates baseline characteristics and compares patients with MC to those without MC (non-MC). In all, 14 patients had colonic biopsy-confirmed MC. The median age at dermatomyositis onset was 49 years (interquartile range [IQR], 36.8-58 years). Patients with MC were more likely to be older, be white, and have CADM than patients with non-MC ( $P = .003$ ,  $P = .03$ , and  $P = .009$ , respectively). Most patients were female, with no sex differences observed ( $P = .14$ ). The median ANA titer was 1:80 (IQR <1:40-1:640