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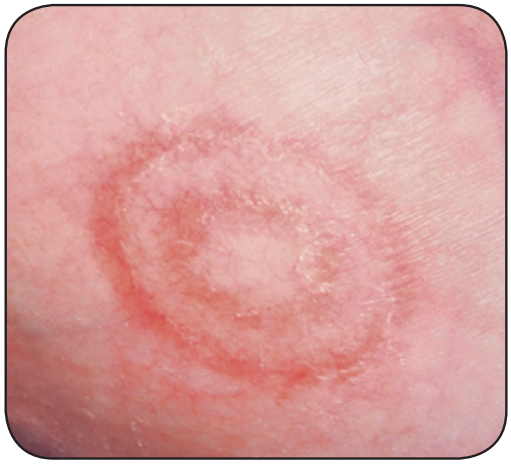
JDPA

Journal of Dermatology for Physician Assistants



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Official Journal of the Society of Dermatology Physician Assistants

INDICATION

ALTRENO™ (tretinoin) lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

IMPORTANT SAFETY INFORMATION

ALTRENO is for topical use only. Not for ophthalmic, oral, or intravaginal use.

Skin Irritation: Patients using ALTRENO may experience application site dryness, pain, erythema, irritation, and exfoliation. Depending upon the severity of these adverse reactions, instruct patients to use a moisturizer, reduce the frequency of the application of ALTRENO, or discontinue use. Avoid application of ALTRENO to eczematous or sunburned skin.

Ultraviolet Light and Environmental Exposure: Minimize unprotected exposure to ultraviolet light, including sunlight and sunlamps. Warn patients with frequent sun exposure and those with inherent sensitivity to sunlight to exercise caution. Use sunscreen and protective clothing over treated areas when exposure cannot be avoided.

Fish Allergies: ALTRENO contains soluble fish proteins. Use with caution in patients with known sensitivity or allergy to fish. Advise patients to contact their healthcare provider if they develop pruritus or urticaria.

Adverse Reactions: The most common adverse reactions in clinical trials were application site dryness (4%), pain (3%), erythema (2%), irritation (1%) and exfoliation (1%).

Nursing Women: It is not known whether topical administration of tretinoin could result in sufficient systemic absorption to produce detectable concentrations in human milk. The developmental health benefits of breastfeeding should be considered along with the mother's clinical need for ALTRENO and any potential adverse effects on the breastfed child from ALTRENO.

To report SUSPECTED ADVERSE REACTIONS, contact Customer Service at 1-800-321-4576 or the FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Please see Brief Summary of Prescribing Information on following pages.

References: 1. Altreno lotion [package insert]. Bridgewater, NJ: Ortho Dermatologics, a division of Valeant Pharmaceuticals North America LLC. **2.** Data on file. Ortho Dermatologics, a division of Valeant Pharmaceuticals North America LLC.

Altreno™
(tretinoin) Lotion, 0.05%

Ortho | Dermatologics

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use ALTRENO safely and effectively. See full prescribing information for ALTRENO.

ALTRENO™ (tretinoin) lotion, for topical use
Initial U.S. Approval: 1973

INDICATIONS AND USAGE

ALTRENO™ (tretinoin) lotion, 0.05% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Skin Irritation

Patients using ALTRENO may experience application site dryness, pain, erythema, irritation, and exfoliation. Depending upon the severity of these adverse reactions, instruct patients to use a moisturizer, reduce the frequency of the application of ALTRENO, or discontinue use. Avoid application of ALTRENO to eczematous or sunburned skin.

Ultraviolet Light and Environmental Exposure

Minimize unprotected exposure to ultraviolet light including sunlight and sunlamps during the use of ALTRENO. Warn patients who normally experience high levels of sun exposure and those with inherent sensitivity to sun to exercise caution. Use sunscreen products and protective clothing over treated areas when sun exposure cannot be avoided.

Fish Allergies

ALTRENO contains soluble fish proteins. Use with caution in patients with known sensitivity or allergy to fish. Advise patients to contact their healthcare provider if they develop pruritus or urticaria.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

In 2 randomized, double-blind, vehicle-controlled trials, subjects age 9 years and older applied ALTRENO or vehicle once daily for 12 weeks. The majority of subjects were White (74%) and female (55%). Approximately 47% were Hispanic/Latino and 45% were younger than 18 years of age. Adverse reactions reported by ≥1% of subjects treated with ALTRENO and more frequently than vehicle are summarized in Table 1.

Table 1: Adverse Reactions Reported by ≥1% of Subjects Treated with ALTRENO and More Frequently than Vehicle

Adverse Reactions n (%)		
	ALTRENO N=767	**Vehicle N=783**
Application site dryness	29 (4)	1 (<1)
Application site pain[1]	25 (3)	3 (<1)
Application site erythema	12 (2)	1 (<1)
Application site irritation	7 (1)	1 (<1)
Application site exfoliation	6 (1)	3 (<1)

[1]Application site pain defined as application site stinging, burning or pain.

Skin irritation was evaluated by active assessment of erythema, scaling, hypopigmentation, hyperpigmentation, itching, burning and stinging. The percentage of subjects who were assessed to have these signs and symptoms at any post baseline visit are summarized in Table 2.

Table 2: Application Site Tolerability Reactions at Any Post Baseline Visit

	ALTRENO N=760 Mild/Mod/Severe	**Vehicle N=782 Mild/Mod/Severe**
Erythema	51%	44%
Scaling	49%	30%
Hypopigmentation	12%	10%
Hyperpigmentation	35%	35%
Itching	35%	28%
Burning	30%	14%
Stinging	21%	8%

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Available data from published observational studies of topical tretinoin in pregnant women have not established a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. There are no data on ALTRENO use in pregnant women. The systemic levels following topical administration are lower than with administration of oral tretinoin; however, absorption of this product may result in fetal exposure. There are reports of major birth defects similar to those seen in infants exposed to oral retinoids, but these case reports do not establish a pattern or association with tretinoin-related embryopathy *(see Data)*.

Animal reproduction studies have not been conducted with ALTRENO. Topical administration of tretinoin in a different formulation to pregnant rats during organogenesis was associated with malformations (craniofacial abnormalities [hydrocephaly], asymmetrical thyroids, variations in ossification, and increased supernumerary ribs) at doses up to 0.5 mg tretinoin/kg/day, approximately 2 times the maximum recommended human dose (MRHD) based on body surface area (BSA) comparison and assuming 100% absorption. Oral administration of tretinoin to pregnant cynomolgus monkeys during organogenesis was associated with malformations at 10 mg/kg/day (approximately 100 times the MRHD based on BSA comparison and assuming 100% absorption) *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of major birth defects, loss, and other adverse outcomes. The background risk in the U.S. general population of major birth defects is 2 to 4% and of miscarriage is 15 to 20% of clinically recognized pregnancies.

Data

Human Data

While available studies cannot definitively establish the absence of risk, published data from multiple prospective controlled observational

studies on the use of topical tretinoin products during pregnancy have not identified an association with topical tretinoin and major birth defects or miscarriage. The available studies have methodologic limitations, including small sample size and in some cases, lack of physical exam by an expert in birth defects. There are published case reports of infants exposed to topical tretinoin during the first trimester that describe major birth defects similar to those seen in infants exposed to oral retinoids; however, no pattern of malformations has been identified and no causal association has been established in these cases. The significance of these spontaneous reports in terms of risk to the fetus is not known.

Animal Data

Tretinoin in a 0.05% gel formulation was topically administered to pregnant rats during organogenesis at doses of 0.1, 0.3 and 1 g/kg/day (0.05, 0.15, 0.5 mg tretinoin/kg/day). Possible tretinoin malformations (craniofacial abnormalities [hydrocephaly], asymmetrical thyroids, variations in ossification, and increased supernumerary ribs) were observed at maternal doses of 0.5 mg tretinoin/kg/day (approximately 2 times the MRHD based on BSA comparison and assuming 100% absorption). These findings were not observed in control animals. Other maternal and reproductive parameters in tretinoin-treated animals were not different from control. For purposes of comparison of the animal exposure to human exposure, the MRHD is defined as 4 g of ALTRENO applied daily to a 60-kg person.

Other topical tretinoin embryofetal development studies have generated equivocal results. There is evidence for malformations (shortened or kinked tail) after topical administration of tretinoin to pregnant Wistar rats during organogenesis at doses greater than 1 mg/kg/day (approximately 5 times the MRHD based on BSA comparison and assuming 100% absorption). Anomalies (humerus: short 13%, bent 6%, os parietal incompletely ossified 14%) have also been reported when 10 mg/kg/day (approximately 50 times the MRHD based on BSA comparison and assuming 100% absorption) was topically applied to pregnant rats during organogenesis. Supernumerary ribs have been a consistent finding in rat fetuses when pregnant rats were treated topically or orally with retinoids.

Oral administration of tretinoin during organogenesis has been shown to induce malformations in rats, mice, rabbits, hamsters, and nonhuman primates. Fetal malformations were observed when tretinoin was orally administered to pregnant Wistar rats during organogenesis at doses greater than 1 mg/kg/day (approximately 5 times the MRHD based on BSA comparison). In the cynomolgus monkey, fetal malformations were reported when an oral dose of 10 mg/kg/day was administered to pregnant monkeys during organogenesis (approximately 100 times the MRHD based on BSA comparison). No fetal malformations were observed at an oral dose of 5 mg/kg/day (approximately 50 times the MRHD based on BSA comparison). Increased skeletal variations were observed at all doses in this study and dose-related increases in embryo lethality and abortion were reported in this study. Similar results have also been reported in pigtail macaques.

Oral tretinoin has been shown to be fetotoxic in rats when administered at doses 10 times the MRHD based on BSA comparison. Topical tretinoin has been shown to be fetotoxic in rabbits when administered at doses 4 times the MRHD based on BSA comparison.

Lactation

Risk Summary

There are no data on the presence of tretinoin or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. It is not known whether topical administration of tretinoin could result in sufficient systemic absorption to produce detectable concentrations in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ALTRENO and any potential adverse effects on the breastfed child from ALTRENO.

Pediatric Use

Safety and effectiveness of ALTRENO for the topical treatment of acne vulgaris have been established in pediatric patients age 9 years to less than 17 years based on evidence from two multicenter, randomized, double-blind, parallel-group, vehicle-controlled, 12-week trials and an open-label pharmacokinetic study. A total of 318 pediatric subjects aged 9 to less than 17 years received ALTRENO in the clinical studies [see *Clinical Pharmacology* and *Clinical Studies* in full Prescribing Information].

The safety and effectiveness of ALTRENO in pediatric patients below the age of 9 years have not been established.

Geriatric Use

Clinical trials of ALTRENO did not include any subjects age 65 years and older to determine whether they respond differently from younger subjects.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

A 2-year dermal mouse carcinogenicity study was conducted with topical administration of 0.005%, 0.025% and 0.05% of a tretinoin gel formulation. Although no drug-related tumors were observed in surviving animals, the irritating nature of the drug product precluded daily dosing, confounding data interpretation and reducing the biological significance of these results.

Studies in hairless albino mice with a different formulation suggest that concurrent exposure to tretinoin may enhance the tumorigenic potential of carcinogenic doses of UVB and UVA light from a solar simulator. This effect was confirmed in a later study in pigmented mice, and dark pigmentation did not overcome the enhancement of photocarcinogenesis by 0.05% tretinoin. Although the significance of these studies to humans is not clear, patients should minimize exposure to sunlight or artificial ultraviolet irradiation sources.

The genotoxic potential of tretinoin was evaluated in an in vitro bacterial reversion test, an in vitro chromosomal aberration assay in human lymphocytes and an in vivo rat micronucleus assay. All tests were negative.

In dermal fertility studies of another tretinoin formulation in rats, slight (not statistically significant) decreases in sperm count and motility were seen at 0.5 mg/kg/day (approximately 2 times the MRHD based on BSA comparison and assuming 100% absorption), and slight (not statistically significant) increases in the number and percent of nonviable embryos in females treated with 0.25 mg/kg/day and above (approximately the MRHD based on BSA comparison and assuming 100% absorption) were observed.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Manufactured for:
Dow Pharmaceutical Sciences, a division of
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

By:
Valeant Pharmaceuticals International, Inc.
Laval, Quebec H7L 4A8, Canada

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This program is not yet approved for CME Credit. Conference organizers plan to request maximum of 25 hours (21maximum earnable by any attendee) of Category I CME Credit from AAPA.

We look forward to seeing you in Atlanta!

JDPA Journal of Dermatology for Physician Assistants

EDITORIAL MISSION: The JDPA is the official clinical journal of the Society of Dermatology Physician Assistants. The mission of the JDPA is to improve dermatological patient care by publishing the most innovative, timely, practice-proven educational information available for the physician assistant profession.

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GOING GREEN: Since its inception, the JDPA has utilized eco-friendly printing practices. The JDPA is printed on paper obtained from sustainable forests that meet strict environmental standards. Soy-based inks that have a low environmental impact are used during printing of the journal and the journal is printed using 100% renewable energy. SDPA members may join us in our efforts and opt to receive the JDPA in digital format.

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To read the JDPA publication's Ethics and Malpractice Statement, please visit www.jdpa.org/write.html.

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Traditions

As we approach the New Year, there tends to be a reflecting back and examining of the year we are about to leave behind, as well as a focus of attention on what goals or plans we might have in mind for the new and exciting year ahead. This retrospection and introspection is part of a yearly tradition many of us partake in. As I am reflecting on my past year, I realize that much of my life revolves around traditions, both with my family and in my career. My family has several traditions that are just second nature now. The thought of going through a year without certain traditions, quite honestly would make it feel so different. At times, we need to make adjustments and out of circumstance, cherished traditions give way to new ones, maybe even improved traditions. These traditions aren't necessarily major to dos, often they are little things that have become cherished and anticipated pieces of holidays, birthdays, vacations, and day-to-day routines and rituals. These little pieces have become engrained in major traditions and events for my family. They are what make certain events special. I am thankful for these memories and traditions. Even more so, I am thankful for the flexibility to not be afraid to be open enough to let new traditions sneak in every now and again. Being able to be open to new ideas and traditions makes it possible for new ones to form and join in the mix.

We experience traditions all the time as members of the SDPA and within our profession. Reflecting on the past year, it has occurred to me that attending the SDPA conferences has become part of my cherished and anticipated traditions. Around Halloween time, in the midst of all of my family's traditions, I know that I will be attending the SDPA Annual Fall Conference. I look forward to the familiar routine of arriving, gathering as a Society, collaborating with colleagues who have become friends, meeting new members, and being immersed in a culture of fellow dermatology PAs who want to further develop and grow themselves and our profession. The same anticipation and tradition is true for the Annual Summer Conference. The SDPA is a group that has grown and flourished because of its openness to be flexible and not be afraid of letting new traditions unfold. The SDPA has introduced new activities and features to their conferences through the years. Some of these new additions have been amazing and will continue to be part of the cherished traditions of conferences well into the future.

As I reflect on the past year and look ahead to the New Year, I am beyond grateful for the past thirteen years I have been a part of the SDPA. This Society is in a continued state of embracing tried and true tradition, all while keeping its eyes and minds open for new and innovative ways to grow, develop, and flourish as a Society, and as dermatology PAs. I look forward to being part of the cherished traditions and developing new traditions in this New Year ahead. I hope you can join the SDPA on this exciting adventure.

Travis Hayden, MPAS, PA-C
JDPA Editor in Chief
editor@jdpa.org

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CALENDAR OF EVENTS

2019

MARCH
77th AAD Annual Academy Meeting
March 1 - 5, 2019
Washington, DC

JUNE
SDPA Summer Dermatology Conference
June 5 - 9, 2019
Marriott Marquis
Washington, DC

JULY
AAD Summer Meeting
July 25 - 28, 2019
New York, NY

NOVEMBER
SDPA 17th Annual Fall Dermatology Conference
November 21 - 24, 2019
The Westin Kierland Resort & Spa
Scottsdale, AZ

2020

MAY
SDPA Annual Summer Dermatology Conference
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Hyatt Regency Denver at Colorado Convention Center
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FROM THE SDPA
NEWS & CURRENT AFFAIRS

Dear Colleagues,

Thank you to all of our members who attended the SDPA's 16th Annual Fall Conference in Orlando, Fl. We kicked off the conference with a festive Halloween themed reception. The Welcome took place at Universal Orlando Resort™/The Wizarding World of Harry Potter™ - Hogsmeade™ Event. The DPAF held their 3rd Annual Silent Auction, which was a great success raising $11,556.67 to benefit Camp Wonder. The members professional headshot studio was busy the entire conference. You should have already received the 2 complimentary retouched photos you chose. The "Mingle Zone" was a great place to recharge and engage. In addition to all of these amenities, there continued to be state of the art conference presentations. A heartfelt thank you to our Conference Committee for all of their behind the scenes work to make all of our conferences so successful.

Speaking of behind the scenes, the SDPA BOD recently voted in favor of hiring a PR firm. We hired JPA Health Communications. They will work closely with the BOD to assist us with monitoring social media involving dermatology PAs and developing the most effective approaches to educating and responding to any and all fronts involving the SDPA and our cherished profession. The SDPA leadership believes that providing accurate, timely, and educated responses to social media involving dermatology PAs will help keep our profession moving forward in a positive momentum. We are also working with the PR firm on a campaign to show how vital PAs are in decreasing patient wait times in dermatology. A special thanks to those who have already joined in our coalition advocacy group to include American Academy of PAs, National Eczema Association, National Alopecia Areata Foundation, Melanoma Research Alliance, AiM at Melanoma Foundation, Polka Dot Mama Melanoma Foundation, Derma Care Access Network, The American Health Quality Association, and Dermatology Nurses' Association. This is just the beginning, as the advocacy group continues to grow. I hope you all got a chance to see the spotlight videos, Your DermPA Can! as well as the dermatology PA patient interviews.

Education is of upmost importance to the SDPA. We are pleased to announce one of the remaining two modules, Module 6, of the Diplomate Fellowship Program is now available! After completing Module 6, "Papulosquamous Eruptions and Eczematous Dermatosis," learners can expect to walk away with knowledge and understanding of: atopic dermatitis and other eczematous eruptions, irritant and allergic contact dermatitis, lichenoid dermatoses, other papulosquamous disorders, regional dermatoses, psoriasis and psoriatic arthritis. This module contains 6 sections in total and will provide 5.5 hours of Category I CME and costs $38.50. Log in to the SDPA Learning Center to learn more and get started! The remaining module (Module 21) is expected to be released soon... stay tuned!

Please don't forget to mark your calendars for the special 25th SDPA anniversary celebration planned during the SDPA Annual Summer Conference June 5-9, 2019 in Washington, DC. The 25th anniversary of the founding of the SDPA will take place in 2019. We've come a long way since 1994 when founder, Joe Monroe and a small group of PAs came up with the idea to begin the SDPA. Please join us on June 5, 2019, preceding the SDPA summer conference as we climb the political ladder and advocate for dermatology PAs for Capital Hill Day in Washington, D.C. The determined efforts of the SDPA has grown the society into the largest and most advanced PA specialty organization in the nation. Come join us for what will be a great celebration of all of our leaders and members past and present! I am looking forward to another year filled with continued progress and achievements for the SDPA and the dermatology PA profession.

Sincerely,

Joleen M. Volz

Joleen M. Volz, MPAS, PA-C, DFAAPA
SDPA President

Dermatology Market Watch

Ortho Dermatologics Announces Launch of JubliApp™

Mobile App Designed to Help Patients Adhere to Treatment with Jublia® for Toenail Fungus

Ortho Dermatologics recently announced the launch of JubliApp™ mobile app designed to help encourage patients to adhere to treatment with Jublia® (efinaconazole 10% topical solution), a topical azole used to treat fungal infections of the toenails.

JubliApp™ was designed to help patients reach their treatment goals through their daily administration of Jublia. The app offers treatment reminders, efficacy tracking, and a game to keep patients engaged while the daily application is drying, helping to make the 48-week long therapy less intimidating. JubliAppTM also has several other key features to keep patients on track with their treatment, including:

- Reminding patients on a daily basis to apply the treatment and notifying them on a monthly basis when they will need to refill their prescription
- Taking and comparing side-by-side photos of toenails to track the results of the treatment over time; patients can also share the photos with their healthcare professional to monitor progress
- Identifying which toenails have been affected by toenail fungus
- Ensuring patients allow the daily treatment the time needed to dry by encouraging them to play the Mission Plu-Toe game after application—then notifying them when drying time is up
- Sharing weekly progress reports, which track whether the patient applied the daily treatment, played the game, or took a photo of the affected toenails

To download the app, visit the App Store on an iOS device or Google Play on an Android mobile device and search "JubliApp" or "Jublia" and click "Get" to download.


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Certification Review

All Those Things Inside the Skin You Might Have Forgotten

By James A. Van Rhee, MS, PA-C

Are you recertifying soon? Start your board review early. Each issue of the JDPA features one board question accompanied by a brief explanation of the answer along with any pertinent test taking tips. Best of luck!

QUESTION: A 25-year-old female, with a history of mitral valve prolapse with moderate regurgitation, presents with a temperature of 102.4° F. On further questioning she states one week ago she had a cystoscopy performed for a history of hematuria. She denies any recent dental work. On exam her heart rate is 110/minute. Cardiac examination reveals regular rhythm, no gallops are noted, and a grade IV/VI systolic murmur is noted. One month ago in the office her murmur was rated as II/VI. Which of the following is the next best step in the evaluation of this patient?

A. Obtain an echocardiogram
B. Obtain a spiral CT scan
C. Draw blood cultures
D. Perform an EKG
E. Start ampicillin

EXPLANATION: This patient presents with the classic presentation of endocarditis. The history of a cardiac murmur and recent invasive procedure are risk factors for the development of endocarditis. Symptoms include a new or changing cardiac murmur, Janeway lesions, Roth spots, splinter hemorrhages, and Osler nodules. The test of choice for diagnosing endocarditis is obtaining blood cultures. Cultures will identify the infectious organism and direct antibiotic therapy is indicated. While an echocardiogram may be obtained and may identify valvular vegetations, it will not identify the infectious agent. A spiral CT scan and EKG will not aid in the diagnosis of endocarditis. Starting an antibiotic prior to obtaining cultures may delay the identification of the infectious agent.

The correct answer is C.

James A. Van Rhee, MS, PA-C, *is the Program Director for the Yale University School of Medicine Physician Assistant Online Program. Mr. Van Rhee has been involved in physician assistant education for over 20 years. He has served as project director and test item writer for the Physician Assistant Education Association's (PAEA) Physician Assistant Clinical Knowledge Rating Assessment Tool (PACKRAT) and is the author of the Physician Assistant: Certification and Re-certification Review Book, published by Elsevier. For the last fifteen years he has been course director and presenter of the Physician Assistant Board Review, which is now being produced live online by Kaplan Medical.*

SAVE THE DATE

Pre-Conference: June 5, 2019
Conference: June 6-9, 2019

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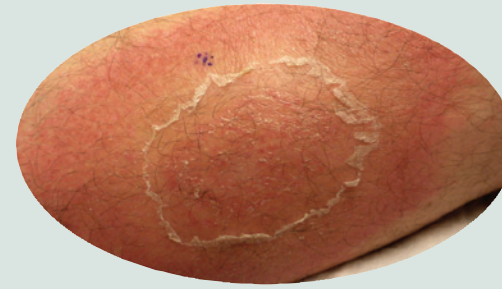
Erythema Annulare Centrifugum
A Review of its Etiology, Epidemiology, and Management

By John Burns, MSPA, PA-C

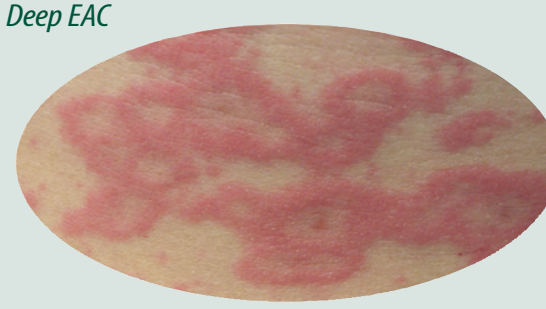
From nomenclature to treatment, since its description by Darier in 1916 erythema annulare centrifugum (EAC) has been a point of dermatologic contention.[1] A diagnosis of exclusion, EAC is not a disease per say, but an immunological expression manifested as annular, erythematous, plaques.[2] The presence or absence of "trailing scale" permits EAC to be subcategorized into superficial EAC or deep EAC. If a plaque has scale that lags behind its erythema then the superficial prefix is used and if scale is absent then the deep prefix is used, refer to Figure 1.[3]

Figure 1:

Superficial EAC



Deep EAC



Both types can be readily differentiated from one another by histologic examination with only occasional overlap.1 Histologic attributes of the two presentations are readily suggested by their clinical appearance. Weyers et al retrospectively examined fifty cases of superficial EAC and thirty-two cases of deep EAC.[1] As one would expect from its clinical appearance, eighty percent of superficial EAC cases demonstrated spongiosis, sixty-six percent of cases parakeratosis, and fifty percent crusts. All cases of deep EAC showed no spongiosis, three percent showed parakeratosis, and none showed crusts. All cases of superficial EAC demonstrated a superficial, lymphocytic, infiltrate and all cases of deep EAC showed a deep, lymphocytic, infiltrate. The hallmark finding of EAC, lymphocytic perivascular cuffing, was present in only one of the fifty cases of superficial EAC and in twenty-two of the thirty-two deep EAC cases.

Purported stimuli of both types of EAC have included medications, pregnancy, malignancy, foods, bacterial infections, viral infections, and autoimmune

» **CME**

This program has been reviewed and is approved for a maximum of .5 hours of AAPA Category I CME credit by the Physician Assistant Review Panel.

Approval is valid for 1 year from the issue date of December 2018. Participants may submit the self-assessment exam at any time during that period.

This program was planned in accordance with AAPA's CME Standards for Enduring Material Programs and for Commercial Support of Enduring Material Programs.

SDPA members may access the posttest at www.jdpa.org

Learning Objectives:

1. *Understand how erythema annulare centrifugum (EAC) is an immunologic response manifested in the skin to multiple antigens.*
2. *Review the typical presentation for EAC, occurring primarily in middle-aged adults, lasting for at least one year, and may or may not be symptomatic.*
3. *Review the existing recommendations for the evaluation of patients with EAC (based largely on case reports and retrospective case studies - no formal guidelines exist).*
4. *Discuss the absence of any evidenced based guidelines for the treatment of EAC (treatment should focus on the identification of EAC's triggers).*

conditions.[3] It has been suggested that deep EAC is not an entity per say, but simply another figurate erythema such as tumid lupus or cutaneous Lyme disease.[1,2]

Despite the number of figurate erythemas there is a lack of direct information regarding their annular nature. Stone in 1989 purposed the annular phenomenon is due to a hypersensitive immune system and "connective tissue-active peptides." Further study of this process under this terminology is not readily evident in the medical literature.[4]

Many treatments for EAC have been proposed throughout the medical literature. Currently a structured treatment approach for EAC remains unavailable, but the overarching theme reported throughout the medical literature is to remove or treat its cause.[5]

GOALS

The objectives of this review were to explore the available medical literature on EAC in hopes of better understanding its clinical nature, to discern whether additional testing should be performed following a diagnosis of EAC, and to try to establish treatment options.

METHODOLOGY

A literature search was performed using PubMed with keyword phrases obtained from the retrospective study on EAC performed by White and Perry including: "erythema annulare centrifugum," "figurate erythema," "gyrate erythema," "erythema perstans." [6] To be included within this review, a case report must have contained a clinical description fitting EAC and be accompanied by congruent histology. Retrospective studies were also evaluated in the preparation of this review, but were not required to meet the previous two criteria due to the inherent nature of retrospective studies and the lack of studies on the subject. A total of two hundred thirty-six citations were obtained of which eight-seven were procurable for review. Of these eighty-seven articles, forty-seven case reports fit the aforementioned criteria and there were five retrospective studies. To maximize the output of the review of these studies the creation of two groups for statistical comparison was considered. The first group would have consisted of the case reports and the second group the cases from the retrospective studies. This was not performed due to the potential for reporting bias. Subjective comparisons between these two groups were made both out of categorical simplicity and the lack of an alternate mechanism for the author.

The most recent editions of six major dermatologic texts were also consulted in the preparation of this article including: Dermatology, Andrew's Disease of the Skin, Fitzpatrick's Dermatology in General Medicine, General Dermatology, Dermatologic Signs of Systemic Disease, and Treatment of Skin Disease: Comprehensive Therapeutic Strategies.[3, 7-11]

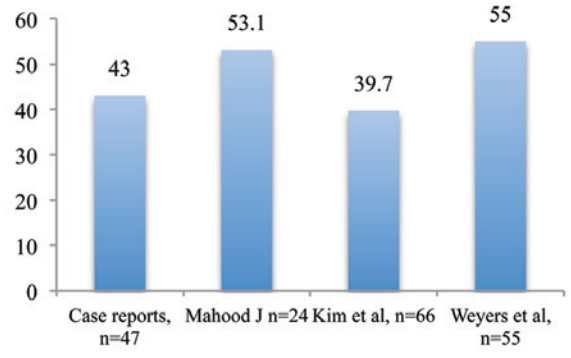
STUDY LIMITATIONS

One limitation of this study was the inability to obtain all 236 articles noted in the initial search query due to the inherent cost of interlibrary loan for a private practitioner; two state medical centers and a state medical resource consortium were used to obtain the reviewed articles. Another limitation of this review was the lack of available prospective studies on EAC leaving only case reports and retrospective studies available for review.

RESULTS

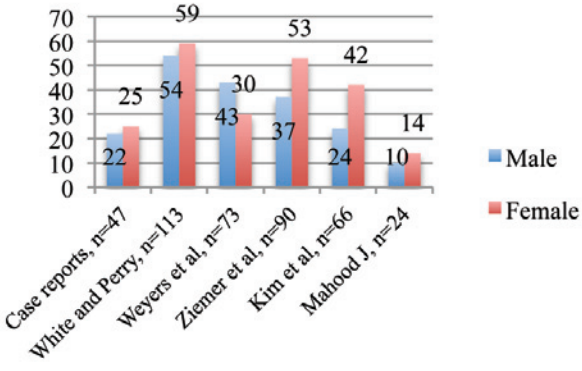
Figures 2 through 5 contain demographic and descriptive data for the forty-seven case reports and five retrospective studies.[1,2,6,12-58]

Figure 2: *Average Patient Age in Years*[a]



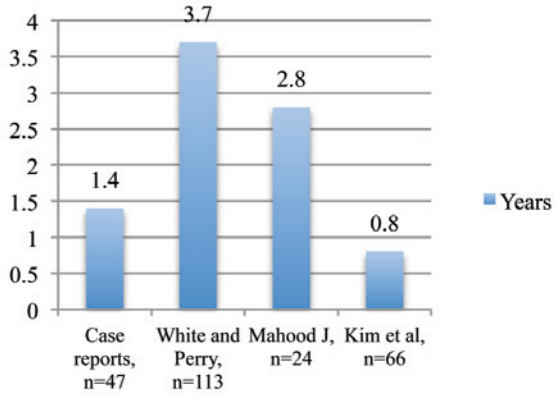
[a]*Data derived from case reports*[12-56]*, Mahood J*[57]*, Kim et al*[58]*, and Weyers et al*[1]

Figure 3: *Number of Male and Female Patients*[a]



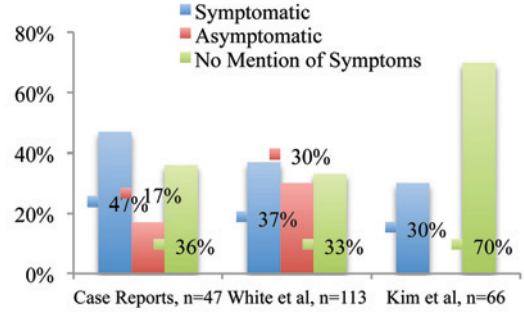
[a]*Data derived from case reports*[12-56]*, White and Perry* [6]*,Weyers et al*[1]*, Ziemer et al*[2]
Kim et al[58]*, Mahood J*[57]

Figure 4: *EAC Duration at Time of Diagnosis*[a]



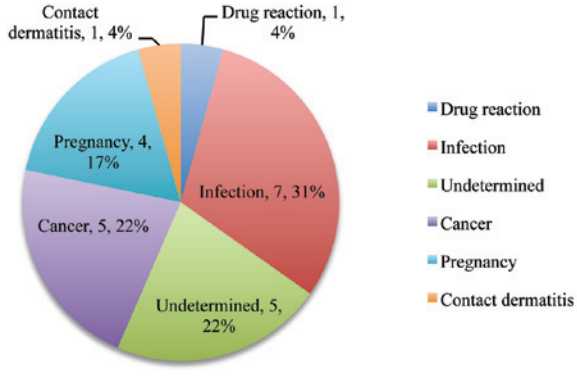
[a]*Data derived from case reports*[12-56], *White and Perry* [6], *Mahood J*[57], *Kim et al*[58]

Figure 5: *Rate of Symptoms in EAC Patients*[a]



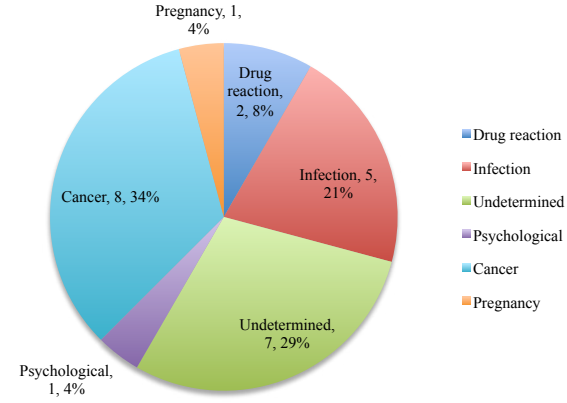
[a]*Data derived from case reports*[12-56], *White and Perry*[6], *Kim et al*[58]

Figure 6: *Etiologies for Twenty-three Cases of Superficial EAC*[a]



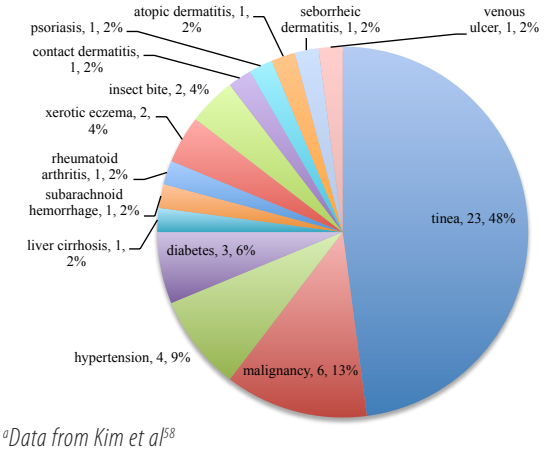
[a]*Data derived from case reports* [12,14,16-19,22,26,27,33,34,37,39,42,43,46,48,49,51,54,55,56]

Figure 7: *Etiologies for Twenty-four Cases of Deep EAC*[a]



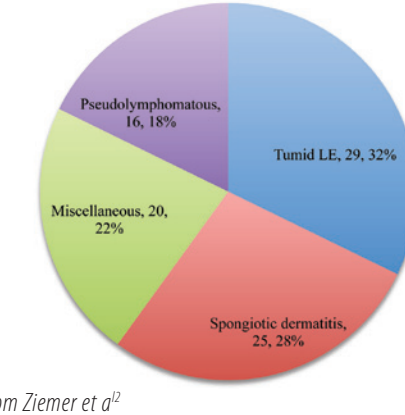
[a]*Data derived from case reports*[5,13,15,20,21,23,24,25,28-32,35,36,38,40,41,44,45,47,50,52,53]

Figure 8: *Associations of Sixty-six Cases of EAC*[a]



[a]*Data from Kim et al*[58]

Figure 9: *Histologic Categorization of 90 EAC Cases*[a]



[a]*Data from Ziemer et al*[12]

From this data one can assume that a patient diagnosed with EAC will likely be middle aged, either sex, symptomatic, and have the condition for close to 1 year; superficial and deep EAC patients from the case reports were combined here to reflect the retrospective studies which did not separate their cases.

Table 1: Descriptive Characteristics of Drug Induced EAC[a]

# of drug induced cases of EAC	Time to resolution of EAC following drug cessation	Time from introduction of the drug to appearance of EAC	Number of cases with histology being compatible with EAC	Eosinophils noted on histology
n=3	10–14 days	3 days to 9 months	4	None

[a] Data from [13,15,43]

Purported etiologies and associations for the forty-seven case reports and two of the retrospective cohorts evaluated in the preparation of this manuscript are displayed in **Figures 6-9.**[2,58]

Despite larger sample sizes, evaluated retrospective studies failed to provide detailed information regarding individual cases and their courses. Case reports did provide this detail and the following paragraphs highlight this. **Table 1** contains clinically pertinent information regarding cases of drug induced EAC.

Based on these cases, histology for drug induced EAC is no different than EAC not caused by a medication and cannot be relied upon to differentiate the two; drug reactions and EAC share similar features histologically. These results suggest that drug induced EAC should resolve fairly quickly following cessation of the causative agent, but discerning the medication trigger based on time of its initiation may prove difficult.

Infections purported to cause EAC described in the case report literature include: pseudomonal sepsis, herpes zoster, HIV, Pedicuolsis pubis, Candida albicans of the intestine, urinary tract infection caused by Escherichia coli, molluscum contagiosum.[20,21,33,39,46,49,51,54] Of particular interest are the three cases of EAC reported to be the result of underlying Candida albicans infections. Two of the cases were diagnosed by stool culture and one was in a child with thrush; the article containing the two cases with positive stool cultures makes no mention of what prompted a search for candida in the stool and it should be remembered that Candida albicans is not uncommonly encountered in the gastrointestinal tract.[49,46,49] However, these three patients completely responded to antifungal treatment within 2 weeks and in these cases histology from the skin eruption was reported to either be consistent with EAC or the histologic description was consistent with EAC.[46,49] Purposed relationships between inflammatory skin disorders and infection are not uncommon including a relationship between psoriasis and Candida albicans; in a murine

Table 2: Demographic and Clinical Data for Cases of Pregnancy Induced EAC[a]

Case report:	Trimester of pregnancy	Involved the trunk	Involved the extremities	Superficial EAC	Deep EAC	Resolved	Pregnancy	Histology
Dogan[29]	1st	1	1		1	36th week of pregnancy	1st	Mild epidermal parakeratosis and spongiosis. Dense perivascular lymphocytic infiltrate and a few eosinophils in the upper dermis. No direct immunofluorescence (DIF) was performed
Rosina et al[42]	3rd		1	1		1 month after delivery	1st	Spongiosis associated with parakeratosis in the epidermis and a dense perivascular lymphocytic infiltrate in the upper dermis. DIF was negative
Choonhakarn and Seramethakun[48]	3rd	1	1	1		3 days after delivery	1st	Dense perivascular lymphocytic infiltrate in the upper dermis. DIF was negative
Fuentelsaz et al[14]	1st	1	1	1		3 days after delivery	No mention	Lymphohistiocytic infiltrate superficial with spongiosis and focal parakeratosis.
Senel and Gulec[26]	2nd	1	1	1		33 week of pregnancy	1st	Mild hyperkeratosis, mild focal parakeratosis, spongiosis in the epidermis, and partially well demarcated perivascular lymphocytic infiltrate in a sleeve with arrangement in superficial dermis.

[a] Data from [14,26,29,42,48]

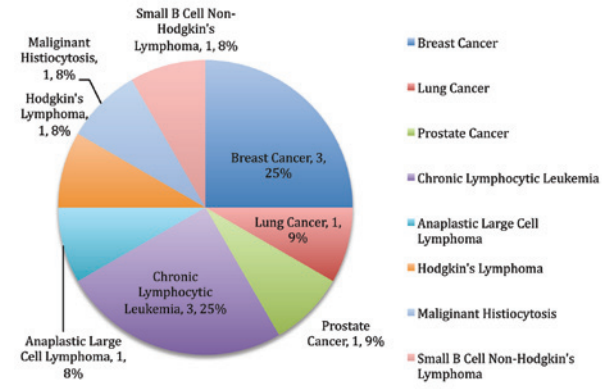
model, Candida albicans was shown to increase both IL-17 and IL-23 in colonized gastric and oral tissues.[59,60] It should be noted that cases of EAC treated with oral antifungals have failed antifungal treatment.[15]

Five case reports describing EAC occurring during pregnancy were located in the preparation of this review.[14,26,29,42,48] Clinically and histologically discerning whether these cases of EAC are not variations of pruritic urticarial papules and plaques of pregnancy (PUPPP) also known as polymorphic eruption of pregnancy (PEP) is difficult due to their similar nature.[1,61] **Table 2** *(See Page 19.)* contains the demographic and clinical data for these five cases.

Noteworthy attributes of these case reports include: **1.** Two of the cases of EAC occurred during the first trimester, unusual for PEP though the remaining cases occurred during the 2nd and 3rd trimester, typical of PEP; **2.** Four of the five cases were nulliparous females, the fifth case failed to report the pregnancy status of the patient, and this would be typical for PEP; **3.** All cases resolved either shortly before delivery or shortly thereafter, another commonality of PEP. No adverse events for either the mother or child were reported in these five case reports. Like EAC the exact biologic mechanism of PEP is unrealized.

Concern has been expressed that EAC may represent a harbinger of malignancy though which EAC patients should be screened and how this should be performed is undetermined.[62] Thirteen of the case reports evaluated in this study suggested cancer as the etiology of EAC *(refer to Figure 10)* and eight of these cases met at least 1 of Curth's criteria[12,17,23,24,25,27,30,31,32,38,45,55,56]; Curth's criteria are used to evaluate a potential relationship between a skin disease and a malignancy (refer to Table 3).[10] Curth's criteria are mentioned throughout the literature and in leading dermatology texts, though how the criteria should be applied and what emphasis should be placed on any one particular criterion is lacking.[3,10] **Table 4** contains demographic and descriptive data for these thirteen patients.

Figure 10: *Types of Cancer and Their Numbers Found in Reviewed Case Reports*[a]



[a]*Data derived from* [12,17,23,24,25,27,30,31,32,38,45,55,56]

Table 3: Curth's Criteria[a]

1. There is a genetic link between a malignancy and a skin disease.
2. Case controlled studies have proven an association between a malignancy and a skin disease.
3. A malignancy and skin disease occur at the same time.
4. A skin disease and a malignancy share an analogous course; treatment of the malignancy results in resolve of the skin disease and its recurrence is heralded by the skin disease.
5. A tumor cell type or site is associated with a specific skin disease
* Not all of the criteria must be present to suggest an association between a cutaneous disease and a malignancy.

[a] Adapted from Skin Signs of Internal Malignancy[10]

Five of the thirteen case reports evaluated in the preparation of this article that met at least 1 of Curth's criteria were classified as superficial EAC1[2,17,27,55,56] and the remaining eight cases were classified as deep EAC.[12,17,22,24,25,27,30,31,32,38,45,55,56]

Table 4: Demographic and Descriptive Data for EAC Cases Contributed to Malignancy[a]

n=	Mean patient age in years, median age, & age ranges	Sex	Number of cases of EAC Diagnosed simultaneously with malignancy	Number of EAC cases resolved with treatment of malignancy	Number of solid tumor malignancies	Number of hematologic malignancies
13	54 years, 53 years, 21-74 years	5 male, 8 female	5	6	5	8

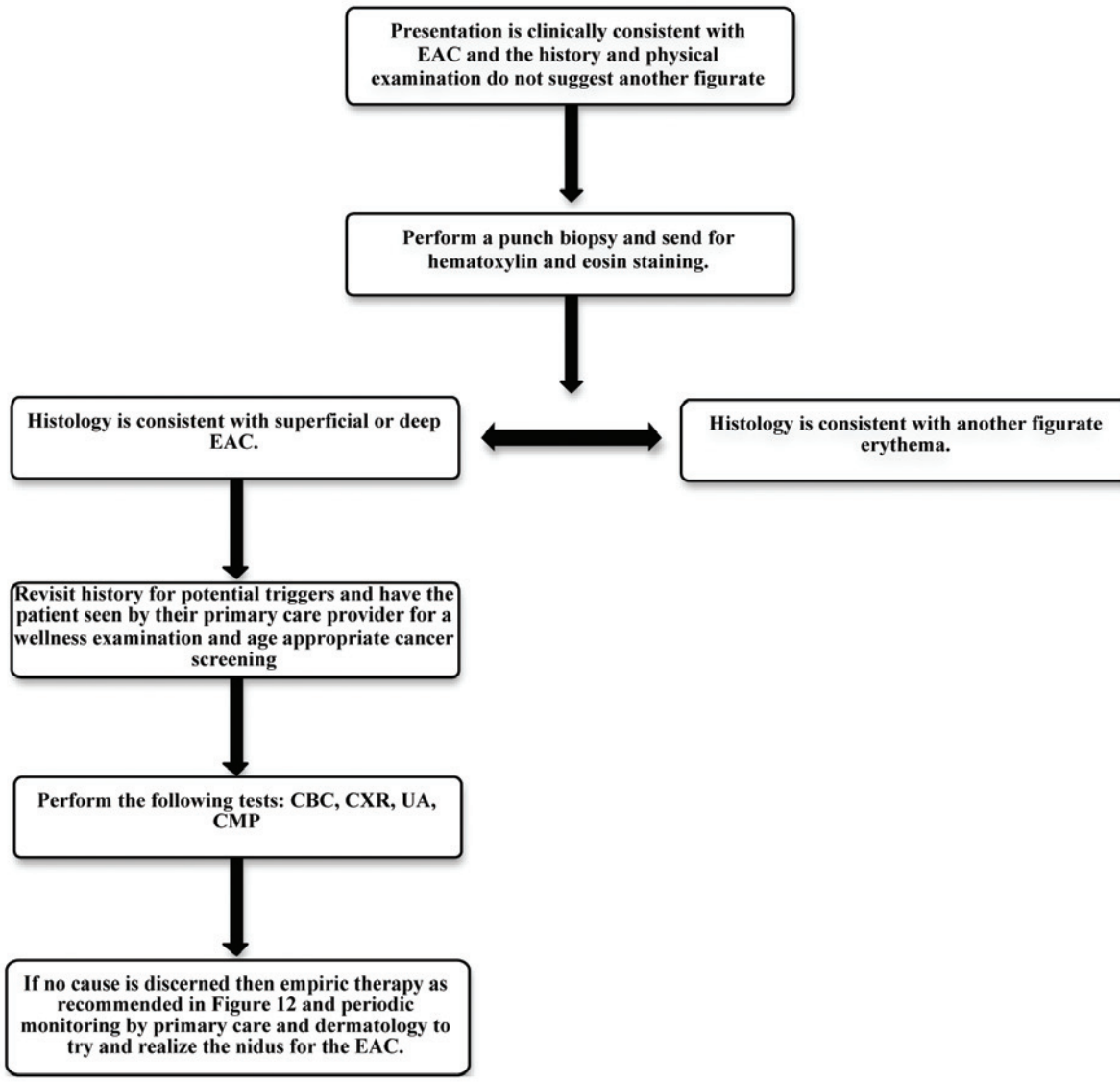
[a] Data from [12,17,23,24,25,27,30,31,32,38,45,55,56]

In only five of these thirteen cases did laboratory, radiological exam, physical examination, and routine follow-up prompted by EAC result in the diagnosis of malignancy.[17,27,30,31,55] Procedures that led to the diagnosis of malignancy included: chest x-ray, CBC, general physical examination, routine follow-up. Of the five retrospective studies evaluated in the preparation of this article, none provided specific recommendations for the evaluation of malignancy in EAC patients.[1,2,6,57,58] In the retrospective study conducted by Mahood, none of the 24 patients with EAC were diagnosed with a malignancy despite an average follow-up time of 5.9 years.[57] In their review of ninety cases of EAC, Zeimer et al do not mention malignancy; this article's purpose was an attempt to histologically categorize EAC.[2] Kim et al describe six out of sixty-six patients with EAC who suffered from malignancy including: acute myeloid leukemia, lung cancer, acute lymphocytic leukemia, non-Hodgkin's lymphoma, rectal cancer, and hepatocellular carcinoma.[58] They do not mention whether the patient's EAC responded to treatment of the malignancy or the number of cases whose EAC presented at the same time as the malignancy; two patients are reported to have had their malignancy diagnosed prior to their EAC. White and Perry reported on one hundred thirteen cases of EAC out of which seven also had a diagnosis of malignancy.6 Only three of these cases shared a time frame suggesting a causal relationship; a psoriasis control group showed a similar incidence of malignancy. They concluded that if EAC is an indicator of malignancy the incidence is low. Weyers et al reported on seventy-three cases of EAC and six of these patients had a history of malignancy.1 They felt these neoplasms were unrelated to their skin disease. Five out of the six dermatologic texts evaluated in the preparation of this article mention the potential for EAC to be a sign of malignancy, but only Regula and Anderson provide specifics regarding laboratory and radiological examinations; they not delineate which tests are being used to discern the presence of malignancy except for the ordering of a serum (SPEP) and urine (UPEP) protein electrophoresis.[3,5,7,5,8,10] Based on the available literature it seems plausible that EAC could be triggered by an underlying malignancy. How frequently this occurs and basis for differentiation of these cases from other cases of EAC remains undetermined.

The broad collection of etiologies shown by these groups of patients and the lack of any identifiable trigger in the twenty-four EAC patients described by Mahood and the one hundred thirteen patients described by White and Perry reinforce the idea that EAC represents an immunologic reactive process.[6,57] Unfortunately this provides little aid in the clinical decision to either recommend or not recommend further evaluation of patients who present with EAC. Thirty-nine of the forty-seven reviewed case reports make no mention of whether patients with EAC should be evaluated for an underlying etiology.[12-16,18-24,26,28,29,31-37,39,41-50,52,54-62] Seven of the reviewed case reports recommended evaluation for potential etiologies of EAC though provide no specific guidelines.[17,25,27,30,38,40,53] Only one case report provides guidelines in regard to clinical evaluation and that is to evaluate for a urinary tract infection.51 None of the retrospective studies evaluated offer any specific guidelines on evaluation of EAC patients.[1,2,6,57,58] Only one of the six dermatologic texts examined provides specific recommendations on the evaluation of EAC. Regula and Anderson recommend the following evaluations be performed in all patients: 4 mm punch biopsy, full skin examination for potential skin infections, potassium hydroxide examination (KOH) or culture of suspected EAC lesions, Wood's lamp examination, complete blood cell count (CBC), liver function test (LFT), urinalysis (UA) , and chest x-ray (CXR).[5] They recommend an antinuclear antibody test (ANA), thyroid stimulation hormone test (TSH), human immunodeficiency virus test (HIV), intradermal trichophyton or candidal skin injection and tuberculin test, malignancy work up including an serum and urine protein electrophoresis (SPEP/UPEP) if clinically indicated. It is noteworthy that if the recommendations provided by Regula and Anderson were applied to the examined case reports only the following tests would have been useful in the evaluation of those patients: 4 mm punch biopsy, CBC, UA, CXR.5 Burgdorf in Fitzpatrick's Dermatology in General Medicine recommends "It is better to view EAC as idiopathic" and James, Berger, Elston in Andrew's Diseases of the Skin report "The majority of cases are idiopathic."[7,8] Espana in Dermatology reports that "Most patients with EAC do not have an underlying disorder that can be identified, nor can the onset, fluctuations, or duration be related to a specific antigen."[3] Of course the clinically disturbing nature, chronicity, and lack of satisfactory treatments for EAC leave clinicians pressured to attempt to discern an underlying etiology and provide treatment. What the author considers a reasonable approach to EAC based on the examined literature is shown in **Figure 11.** *(See Page 22.)*

Treatment of EAC should focus on discerning its cause. Selection of treatments for EAC without an apparent etiology is difficult due to the lack of information on the subject. **Figure 12** *(See Page 23.)* contains an algorithm for the treatment of patients with

Figure 11: *Methodology for the Evaluation of EAC*



EAC without an established etiology. It is based on individual case reports where resolution was obtained with a treatment; the algorithm was arranged based on the convenience and potential side effect profiles of the treatments.[12,16,18,32,33,36,44,46,49,50,52,53] Due to these treatments being based on individual case reports, exact dosage and length of usage is uncertain and should be conservative and grounded in labeled usage

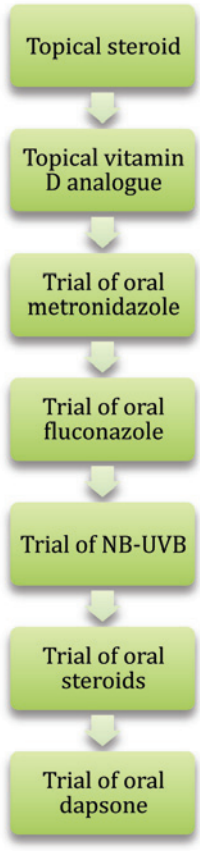
CONCLUSION

EAC is a member of the figurate erythemas, a diagnosis of exclusion, and a cutaneous expression of the body's immune system to a multitude of antigens. Case reports and retrospective analysis fail to provide evidence-based guidelines for the evaluation and treatment of EAC. Evaluation and treatment of EAC patients should focus on discerning an underlying nidus though this may not always be possible and EAC patients should be apprised of this.

REFERENCES:

1. Weyers W, Diaz-Cascajo C, and Weyers I. Erythema annulare centrifugum: results of a clinicopathologic study of 73 patients. Am J Dermatpathol. 2003;25(6):451-462.
2. Ziemer M, Eisendle K, and Zelger B. New concepts on erythema annulare centrifugum: a clinical reaction pattern that does not represent a specific clinicopathologic entity. Br J Dermatol. 2009;160(1): 119-26.
3. Espana A. Figurate Erythemas. In: Bolognia J, Jorizzo J, Schaffer J. Dermatology. 3rd ed. London, England: Elsevier Saunders; 2012.
4. Stone O. A mechanism of peripheral spread or localization of inflammatory

Figure 12: *Therapeutic Ladder for Treatment of Idiopathic EAC*[a]



[a]*Data derived from*[12,16,18,32,33,36,44,46,49,50,52,53]

reactions-role of the localized ground substance adaptive phenomenon. Med Hypotheses. 1989 Jul;29(3):167-9.

5. Regula C, Anderson B. Erythema Annulare Centrifugum. In: Lebwohl M, Heymann W, Berth-Jones J, et al. Treatment of Skin Disease: Comprehensive Therapeutic Strategies. 4th ed. Edinburgh, England. Elsevier Saunders; 2014.
6. White J, Perry H. Erythema perstans. Br J Derm. 1969;3: 641-51.
7. James W, Berger T, Elston D. Erythema and Urticaria. In: James W, Berger T, Elston D. Andrews' Diseases of the Skin: Clinical Dermatology. 12th ed. Philadelphia, PA: Elsevier; 2016.
8. Burgdorf, W. Erythema Annulare Centrifugum and Other Figurate Erythemas. In: Goldsmith L, Katz S, Gilchrest B, Paller A, Leffell D, and Wolff K. Fitpatrick's Dermatology in General Medicine. 8th ed. New York, NY: McGraw-Hill; 2012.
9. Schwarzenberger K, Werchniak A, and Ko C. General Dermatology. London, England: Elsevier Saunders; 2009.
10. Cowen E, Callen J. Skin signs of internal malignancy. In: Callen J, Jorizzo J, Zone J, Piette W, Rosenbach M, Vleugels R,eds. Dermatologic Signs of Systemic Disease. 5th ed. Edinburgh, London: Elsevier; 2016: 131-140.
11. Lebwohl M, Heymann W, Berth-Jones J, et al. Treatment of Skin Disease: Comprehensive Therapeutic Strategies. 4th ed. Edinburgh, England. Elsevier Saunders; 2014.
12. Gudi V, Armour A, and Burden A. Erythema annulare centrifugum associated with disseminated prostatic carcinoma. Acta Derm Venereol. 2002;82(4):306-7.
13. Gonul M, Cakmak S, Ozcan N, Oguz I, and Ozhamam E. Erythema annulare centrifugum due to pegylated interferon-α-2a plus ribavirin combination therapy in a patient with chronic hepatitis c virus infection.
14. Fuentelsaz V, Corredera C, Ara M, and Carapeto FJ.Pregnancy-related erythema annulare centrifugum. Actas Dermosifiliogr. 2011 Jan;102(1):66-8.
15. Mendes-Bastos P, Coelho-Macias V, Moraes-Fontes MF, Milheiro A, Rodrigues AM, and Cardoso J. Erythema annulare centrifugum during rituximab treatment for autoimmune haemolytic anaemia. J Eur Acad Dermatol Venereol. 2014 Aug;28(8):1125-7.
16. Coronel-Perez I, Morillo-Andujar M. Erythema annulare centrifugum responding to natural ultraviolet light. Actas Dermosifiliogr. 2010 Mar;101(2):177-8.
17. Atalay AA, Abuaf OK, and Dogan B. Squamous cell lung carcinoma presenting with erythema annulare centrifugum. Acta Dermatovenerol Croat. 2013;21(1):56-8.
18. De Marchi S, Cecchin E, and De Marchi SU. Erythema annulare centrifugum. Am J Med Sci. 2014 May;347(5):414.
19. Samycia M, Salopek TG. Erythema annulare centrifugum in a patient with crohn disease. J Cutan Med Surg. 2012 Nov-Dec;16(6):442-4.
20. Kavurt S, Aydemir O, Celik U, Bas AY, and Demirel N. Erythema annulare centrifugum as the presenting sign of Pseudomonas aeruginosa sepsis in a newborn. Eur J Pediatr. 2013 Jun;172(6):847-9.
21. Ohmori S, Sugita K, Ikenouchi-Sugita A, and Nakamura M. Erythema annulare centrifugum associated with herpes zoster. J UOEH. 2012 Sep 1;34(3):225-9.
22. Chou WT, Tsai TF. Recurrent erythema annulare centrifugum during ustekinumab treatment in a psoriatic patient. Acta Derm Venereol. 2013 Mar 27;93(2):208-9.
23. Ko WC, You WC. Erythema annulare centrifugum developed post-breast cancer surgery. J Dermatol. 2011 Sep;38(9):920-22.
24. Tageja N, Giorgadze T, and Zonder J. Dermatological complications following initiation of lenalidomide in a patient with chronic lymphocytic leukaemia. Intern Med J. 2011 Mar;41(3):286-8.
25. Dourmishev LA, Gergovska MJ, Nikolova KK, and Balabanova MB.

Erythema annulare centrifugum in a patient operated on for breast carcinoma. Acta Dermatovenerol Croat. 2010;18(4):264-6.

26. Senel E, Gulec AT. Erythema annulare centrifugum in pregnancy. Indian J Dermatol. 2010;55(1):120-1.
27. Carlesimo M, Fidanza L, Mari E, Pranteda G, Cacchi C, Veggia B, Cox MC, and Camplone G. Erythema annulare centrifugum associated with mantle b-cell non-Hodgkin's lymphoma. Acta Derm Venereol. 2009;89(3):319-20.
28. Ibrahim SF, Pryor J, Tausk FA. Stress-induced erythema annulare centrifugum.

Dermatol Online J. 2009 Apr 15;15(4):15

29. Dogan G. Pregnancy as a possible etiologic factor in erythema annulare centrifugum. Am J Clin Dermatol. 2009;10(1):33-5.
30. Panasiti V, Devirgiliis V, Curzio M, Rossi M, Roberti V, Bottoni U, and Calvieri S. Erythema annulare centrifugum as the presenting sign of

breast carcinoma. J Eur Acad Dermatol Venereol. 2009 Mar;23(3):318-20.
31. Helbling I, Walewska R, Dyer MJ, Bamford M, and Harman KE. Erythema annulare centrifugum associated with chronic lymphocytic leukaemia. Br J Dermatol. 2007 Nov;157(5):1044-5
32. Stokkermans-Dubois J, Beylot-Barry M, Vergier B, Bouabdallah K, and Doutre MS. Erythema annulare centrifugum revealing chronic lymphocytic leukaemia. Br J Dermatol. 2007 Nov;157(5):1045-7.
33. González-Vela MC, González-López MA, Val-Bernal JF, Echevarría S, and Arce FP, Fernández-Llaca H. Erythema annulare centrifugum in a HIV-positive patient. Int J Dermatol. 2006 Dec;45(12):1423-5.
34. Sambucety PS, Agapito PG, and Prieto MA. Contact erythema annulare centrifugum. Contact Dermatitis. 2006 Nov;55(5):309-10.
35. Lee HW, Lee DK, Rhee DY, Chang SE, Choi JH, Moon KC, and Koh JK. Erythema annulare centrifugum following herpes zoster infection: Wolf's isotopic response? Br J Dermatol. 2005 Dec;153(6):1241-3.
36. De Aloe G, Rubegni P, Risulo M, Sbano P, Poggiali S, Fimiani M. Erythema annulare centrifugum successfully treated with metronidazole. Clin Exp Dermatol. 2005 Sep;30(5):583-4.
37. Gulati S, Mathur P, Saini D, Mannan R, and Kalra V.
Erythema annulare centrifugum with autoimmune hepatitis. Indian J Pediatr. 2004 Jun;71(6):541-2
38. Gündeşlioğlu AO, Ertaş NM, Celebioğlu S, and Hücümenoglu S. Erythema annulare centrifugum: an unusual presentation for acute leukemia. Plast Reconstr Surg. 2004 Feb;113(2):798-9.
39. Bessis D, Chraibi H, Guillot B, and Guilhou JJ. Erythema annulare centrifugum induced by generalized Phthirus pubis infestation. Br J Dermatol. 2003 Dec;149(6):1291.
40. Ioannidou D, Krasagakis K, Stefanidou M, Tosca A. Erythema annulare centrifugum and osteoarthritis treated with hyaluronic acid. Clin Exp Dermatol. 2002 Nov;27(8):720-2.
41. Bottoni U, Innocenzi D, Bonaccorsi P, Carlesimo M, Faina P, Richetta A, Cugini P, and Calvieri S. Erythema annulare centrifugum: report of a case with neonatal onset. J Eur Acad Dermatol Venereol. 2002 Sep;16(5):500-3.
42. Rosina P, D'Onghia FS, and Barba A. Erythema annulare centrifugum and pregnancy. Int J Dermatol. 2002 Aug;41(8):516-7.
43. Kuroda K, Yabunami H, and Hisanaga Y. Etizolam-induced superficial erythema annulare centrifugum. Clin Exp Dermatol. 2002 Jan;27(1):34-6.
44. Gniadecki R. Calcipotriol for erythema annulare centrifugum. Br J Dermatol. 2002 Feb;146(2):317-9
45. Ural AU, Ozcan A, Avcu F, Kaptan K, Taştan B, Beyan C, and Yalçin A. Erythema annulare centrifugum as the presenting sign of CD 30 positive anaplastic large cell lymphoma--association with disease activity. Haematologia (Budap). 2001;31(1):81-4.
46. Alex MP, Mohan L, Singh KK, and Mukhiya RD. Erythema annulare centrifugum due to candida infection. Indian J Dermatol Venereol Leprol. 1999 Nov-Dec;65(6):283-4.
47. Garty B. Erythema annulare centrifugum in a patient with polyglandular autoimmune disease type 1. Cutis. 1998 Nov;62(5):231-2.
48. Choonhakarn C, Seramethakun P. Erythema annulare centrifugum associated with pregnancy. Acta Derm Venereol. 1998 May;78(3):237-8.
49. Schmid MH, Wollenberg A, Sander CA, and Bieber T. Erythema annulare centrifugum and intestinal Candida albicans infection--coincidence or connection? Acta Derm Venereol. 1997 Jan;77(1):93-4.
50. Roy AK, Ghosh SK. Erythema annulare centrifugum. Indian J Dermatol Venereol Leprol. 1996 Nov-Dec;62(6):377-8.
51. Borbujo J, de Miguel C, Lopez A, de Lucas R, and Casado M. Erythema annulare centrifugum and Escherichia coli urinary infection. Lancet. 1996 Mar 30;347(9005):897-8.
52. Sankar R. Erythema annulare centrifugum responding to dapsone. Indian J Dermatol Venereol Leprol. 1995 Nov-Dec;61(6):385-6
53. Altomare GF, Capella GL, and Frigerio E. Sarcoidosis presenting as erythema annulare centrifugum. Clin Exp Dermatol. 1995 Nov;20(6):502-3
54. Furue M, Akasu R, Ohtake N, and Tamaki K. Erythema annulare centrifugum induced by molluscum contagiosum. Br J Dermatol. 1993 Nov;129(5):646-7.
55. Yaniv R, Shpielberg O, Shpiro D, Feinstein A, Ben-Bassat I.
Erythema annulare centrifugum as the presenting sign of Hodgkin's disease.
Int J Dermatol. 1993 Jan;32(1):59-61.
56. Dodd HJ, Kirby JD, Chambers TJ, and Stansfeld AG. Erythema annulare centrifugum and malignant histiocytosis--report of a case. Clin Exp Dermatol. 1984 Nov;9(6):608-135.
57. Mahood J. Erythema annulare centrifugum: a review of 24 cases with special reference to its association with underlying disease. 1983 Jul;8(4):383-7.
58. Kim KJ, Chang SE, Choi JH, Sung KJ, Moon KC, and Koh JK. Clinicopathologic analysis of 66 cases of erythema annulare centrifugum. J Dermatol. 2002 Feb;29(2):61-7.
59. Fry L, Baker B. Triggering psoriasis: the role of infections and medications. 2007 Nov-Dec;25:606-615.
60. Kumamoto C. Inflammation and gastrointestinal Candida colonization. 2011 Aug;14(4):386-391.
61. Roth M. Pregnancy Dermatoses: diagnosis, management, and controversies. Am J Clin Dermatol. 2011Feb; 12(1):25-41.
62. Chodkiewicz H, Cohen P. Paraneoplastic erythema annulare centrifugum eruption: Peace. 2012 Aug;13(4):239-246.

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From The Patient's Perspective

Victoria Gibbs: The long road to diagnosis

Lupus Foundation of America

I remember like it was yesterday, "It looks like you have lupus."

After hearing my doctor utter these words, I cried. Following that, with a flood of tears streaming down my face, I asked, "Is my hair going to keep falling out?" Both the doctor and my father smiled, she responded, "most likely for now." My life changed immediately at that moment. I barely knew what lupus was, but I knew that I didn't want to have it.

The months leading up to my diagnosis were painstakingly difficult. At the time, I was training for the National Yoga Asana Championship and was pushing my body to new levels. I was in the yoga studio six or seven days a week, taking bikram yoga, and rehearsing my competition routine diligently both before and after class. In the beginning, I felt good, I thought I was invincible. During that time, I was working for a hedge fund, in the office Monday to Friday from 8:30AM to 6PM.

"I thought I was invincible."

At the end of my work day, I'd rush to the yoga studio for class, and end my day with a 90-minute commute back home to Huntington, Long Island. I was having dinner at 10PM, in bed by midnight, and up at 6AM to do it all over again. I would spend four hours both Saturday and Sunday training for this competition and I thought I had it all under control.

It was finally in March, after coming back from a weeklong stay in Puerto Rico that I noticed something unusual. I had gotten a severe sunburn. I never had one before but the sun was so strong in Puerto Rico that I thought nothing of it. I continued my daily work and yoga routine and finally in April, I caught a cold that never went away. I took time off from work thinking that all I needed was rest.

I had never slept so much in my life. I went to an Urgent Care facility and they diagnosed me with the flu. I left with no medication and was told to keep resting. All the rest in the world wasn't helping. I reluctantly cut back on my yoga training because I simply didn't have the energy or the strength to take class or even worse, train for my competition.

In the following weeks my face exploded and I had what sounded like tuberculosis. I went back to a different Urgent Care facility and they told me I had the mumps. That didn't seem likely because I was vaccinated as a child but I didn't argue with them. My colleagues advised me to stay home and rest. At that time I was working about half of the week and sleeping the rest of the time. I was devastated, it was now early May and my competition was two weeks away. I could barely move but I pushed through. I had worked so hard for this competition and after placing

second in the New York regional, nothing was going to prevent me from competing.

Despite my determination, I felt terrible. I took one last yoga class the week before the competition which was May 20th and figured that more rest would get me through. Two days prior to my departure I noticed that I had several white spots in my mouth and my throat was burning. I couldn't comfortably get any food down and was in extreme discomfort. I pushed it aside, purchased throat medication, and kept on going. Things came to a halt the weekend of my competition in Jackson Hole, Wyoming. I could barely drag myself out of bed; I had an insane fever, and started noticing these painful blood blisters on my fingers. When it came time to compete my body literally collapsed underneath me. I didn't perform up to expectation and was extremely disappointed. Overall, the experience was terrible. I came back to New York and didn't step foot again into the yoga studio. I went back to work and was barely surviving. I began getting these awful migraines every time I looked at the computer screen.

"My body literally collapsed underneath me."

I realized things were getting bad when my ex-boyfriend would call me at work and I didn't recognize his voice or his number. He urgently encouraged me to leave work; I was now becoming a danger to myself. In a cloud of confusion he forced me to go back to an Urgent Care facility near his home and there they finally gave me steroids and encouraged me to see my regular physician.

My parents live in Montgomery, NJ and I didn't have the strength or the energy to commute from Long Island, where I resided with my aunt. At this point, it was June and my health was deteriorating rapidly. It came to the point where I realized that I was in serious danger. I was no longer recognizing familiar faces, voices, or places. I'd be at work and not know who my colleagues were, couldn't remember where I worked or what floor I worked on. I could barely figure out when I got to the train station, and once I got there, I'd spend almost 45 minutes walking in circles around the parking garage trying to find my car. It was at my parent's insistence that I finally went home to Montgomery. It was a miracle that I even got home but once I arrived on my 31st birthday, little did I know I would be spending the entire summer there.

"I barely knew what lupus was, but I knew that I didn't want to have it."

The doctors' appointments began immediately. At that point, I barely knew where I was or what was going on. My motor skills had declined significantly, I could barely walk without holding onto someone or something, I couldn't feed myself, I was experiencing severe night sweats, my hair was falling out in chunks, my fingers were covered in blood blisters, also known as Raynaud's disease. I had high fevers, my mouth ulcers had taken on a life of their own, my taste buds were no longer functioning, and all I wanted to do was sleep.

Finally, my rheumatologist diagnosed me with lupus. Two nights later, I got a fever of 105. My parents couldn't lower the temperature and dragged me screaming to the emergency room. After being admitted, they ran a battery of tests on me. I was poked and prodded at for an entire week, it was confirmed that I had lupus. The real recovery process was about to begin.

I took off the entire summer from work, yoga, and everything. For the first time in my life I had to selfishly focus on myself. I did the best I could to handle my current situation with grace but when you are going through all of those changes physically, mentally, and emotionally, life becomes challenging. The amount of times that I would say, "I'm fine," when really, I felt like I was dying inside. The reality of being on a significant amount of daily medication itself was overwhelming. Overall, I couldn't have gotten through the initial stages of my recovery without the love and support of my family and close friends.

"The good news is that being diagnosed with lupus wasn't the end of the world, but rather a new beginning."

The good news is that being diagnosed with lupus wasn't the end of the world, but rather a new beginning. It's amazing when I look back and think about how I feel now versus before all of this began, when I thought I was feeling good. While I'm not 100% and still working to gain strength and stamina, I feel significantly better than I have in the last five years. I know that everything is going to be all right.

If you are struggling with mysterious symptoms and suspect that it might be lupus, there are several things that you can do – educate yourself about lupus, communicate with your doctor, and see a rheumatologist.

Journal Club: *Practice Changing Articles for Dermatology PAs*

Patterns of Infiltration and Local Recurrences of Various Types of Cutaneous Sarcomas Following Three-Dimensional Histology.

J Dtsch Dermatol Ges. 2018 Dec;16(12):1434-1442. doi: 10.1111/ddg.13708.

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Background

Cutaneous sarcomas are rare and characterized by pathogenetic heterogeneity. Knowledge about local infiltration patterns and recurrence rates may be useful in improving patient care and outcomes. The objective of the present study was to compare these two characteristics in sarcomas that had been treated using the identical surgical procedure.

Patients and Methods

Between 2006-2010, 84 patients with various types of sarcoma underwent surgery followed by three-dimensional histology. Tumor entities included dermatofibrosarcoma protuberans (DFSP, 54 patients), leiomyosarcoma (ten patients), rhabdomyosarcoma (one patient), angiosarcoma (seven patients) as well as atypical fibroxanthoma (AFX, three patients) and cutaneous undifferentiated pleomorphic sarcoma (UPS, nine patients). Median follow-up was four years (range: 2-6 years).

Results

Local recurrence rates among patients with primary DFSP were 2.2 %. All patients undergoing re-excision were subsequently tumor free. Patients with leiomyosarcoma, rhabdomyosarcoma, AFX, and cutaneous UPS experienced no local recurrence; however, one individual developed in-transit metastasis (UPS) (8.3 %). Three patients with angiosarcoma developed local recurrence (43 %), two of whom remained tumor free following re-excision. Two angiosarcoma patients died from distant metastases (29 %). Both DFSP and especially angiosarcoma lesions exhibited extensive subclinical growth.

Conclusion

Recurrence rates of cutaneous sarcomas following three-dimensional histology are low. Local recurrences are readily manageable by re-excision. Angiosarcoma is characterized by extensive superficial growth, aggressive biological behavior, and predominantly hematogenous spread.

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Journal clubs are a great way to review and critically evaluate the most current literature impacting the practice of dermatology. For PAs who are new to the practice of dermatology, journal clubs can assist them to become more familiar with advanced medical literature and improve their understanding of current issues within the field. The articles selected for the JDPA Journal Club are meant to be shared and discussed with your colleagues, peers, and collaborating physicians. If you have any articles to recommend for the JDPA Journal Club, please email them to editor@jdpa.org.

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ILUMYA™ (tildrakizumab-asmn) is an interleukin-23 antagonist indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

A NEW IL-23 INHIBITOR[1]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ILUMYA is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Cases of angioedema and urticaria occurred in ILUMYA-treated subjects in clinical trials. If a serious allergic reaction occurs, discontinue ILUMYA immediately and initiate appropriate therapy.

Infections

ILUMYA may increase the risk of infection. Treatment with ILUMYA should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated.

Consider the risks and benefits of treatment prior to prescribing ILUMYA in patients with a chronic infection or a history of recurrent infection. Instruct patients receiving ILUMYA to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection, or is not responding to standard therapy, closely monitor and consider discontinuation of ILUMYA until the infection resolves.

Pretreatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA. Do not administer ILUMYA to patients with active TB infection. Initiate treatment of latent TB prior to administering ILUMYA. Consider anti-TB therapy prior to initiation of ILUMYA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving ILUMYA should be monitored closely for signs and symptoms of active TB during and after treatment.

Immunizations

Prior to initiating therapy with ILUMYA, consider completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with ILUMYA should not receive live vaccines.

Adverse Reactions

The most common (≥1%) adverse reactions associated with ILUMYA treatment that were more frequent than in the placebo group are upper respiratory infections, injection-site reactions, and diarrhea.

Please see brief summary of Full Prescribing Information on next page or visit ILUMYApro.com for Full Prescribing Information.

Reference: 1. ILUMYA™ [package insert]. Princeton, NJ: Sun Pharmaceuticals, Inc.

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Brief Summary of Prescribing Information for ILUMYA™ (tildrakizumab-asmn)
ILUMYA™ (tildrakizumab-asmn) injection, for subcutaneous use
See package insert for full Prescribing Information

INDICATIONS AND USAGE ILUMYA™ is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

CONTRAINDICATIONS
ILUMYA is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients *[see Warnings and Precautions]*.

WARNINGS AND PRECAUTIONS
Hypersensitivity: Cases of angioedema and urticaria occurred in ILUMYA treated subjects in clinical trials. If a serious hypersensitivity reaction occurs, discontinue ILUMYA immediately and initiate appropriate therapy *[see Adverse Reactions]*.

Infections: ILUMYA may increase the risk of infection. Although infections were slightly more common in the ILUMYA group (23%), the difference in frequency of infections between the ILUMYA group and the placebo group was less than 1% during the placebo-controlled period. However, subjects with active infections or a history of recurrent infections were not included in clinical trials. Upper respiratory infections occurred more frequently in the ILUMYA group than in the placebo group *[see Adverse Reactions]*.

The rates of serious infections for the ILUMYA group and the placebo group were ≤0.3%. Treatment with ILUMYA should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing ILUMYA. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the patient closely and consider discontinuation of ILUMYA until the infection resolves *[see Adverse Reactions]*.

Pretreatment Evaluation for Tuberculosis: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA. Initiate treatment of latent TB prior to administering ILUMYA. In clinical trials, of 55 subjects with latent TB who were concurrently treated with ILUMYA and appropriate TB prophylaxis, no subjects developed active TB (during the mean follow-up of 56.5 weeks). One other subject developed TB while receiving ILUMYA. Monitor patients for signs and symptoms of active TB during and after ILUMYA treatment. Consider anti-TB therapy prior to initiation of ILUMYA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Do not administer ILUMYA to patients with active TB infection.

Immunizations: Prior to initiating therapy with ILUMYA, consider completion of all age appropriate immunizations according to current immunization guidelines. Avoid the use of live vaccines in patients treated with ILUMYA. No data are available on the response to live or inactive vaccines.

ADVERSE REACTIONS
The following serious adverse reactions are discussed elsewhere in the labeling:
Hypersensitivity Reactions *[see Warnings and Precautions]*
Infections *[see Warnings and Precautions]*

Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials, a total of 1994 subjects with plaque psoriasis were treated with ILUMYA, of which 1083 subjects were treated with ILUMYA 100 mg. Of these, 672 subjects were exposed for at least 12 months, 587 for 18 months, and 469 for 24 months.

Data from three placebo-controlled trials (Trials 1, 2, and 3) in 705 subjects (mean age 46 years, 71% males, 81% white) were pooled to evaluate the safety of ILUMYA (100 mg administered subcutaneously at Weeks 0 and 4, followed by every 12 weeks [Q12W]) *[see Clinical Studies]*.

Placebo-Controlled Period (Weeks 0-16 of Trial 1 and Weeks 0-12 of Trials 2 and 3)
In the placebo-controlled period of Trials 1, 2, and 3 in the 100 mg group, adverse events occurred in 48.2% of subjects in the ILUMYA group compared to 53.8% of subjects in the placebo group. The rates of serious adverse events were 1.4% in the ILUMYA group and 1.7% in the placebo group.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the ILUMYA group than in the placebo group.

Table 1: Adverse Reactions Occurring in ≥1% of Subjects in the ILUMYA Group and More Frequently than in the Placebo Group in the Plaque Psoriasis Trials 1, 2, and 3

Adverse Reaction	ILUMYA 100 mg (N=705) N (%)	Placebo (N=355) N (%)
Upper respiratory infections*	98 (14)	41 (12)
Injection site reactions†	24 (3)	7 (2)
Diarrhea	13 (2)	5 (1)

* Upper respiratory infections include nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, and pharyngitis.

† Injection site reactions include injection site urticaria, pruritus, pain, reaction, erythema, inflammation, edema, swelling, bruising, hematoma, and hemorrhage.

During the placebo-controlled period of Trials 1, 2, and 3, adverse reactions that occurred at rates less than 1% but greater than 0.1% in the ILUMYA group and at a higher rate than in the placebo group included dizziness and pain in extremity.

Specific Adverse Reactions
Hypersensitivity Reactions
Cases of angioedema and urticaria occurred in ILUMYA-treated subjects in clinical trials *[see Warnings and Precautions]*.

Infections
Infections were slightly more common in the ILUMYA group. The difference in frequency of infections between the ILUMYA group (23%) and the placebo group was less than 1% during the placebo-controlled period. The most common (≥1%) infections were upper respiratory infections. The rates of severe infections for the ILUMYA group and the placebo group were ≤0.3%.

Safety Through Week 52/64
Through Week 52 (Trials 1 and 3) and Week 64 (Trial 2), no new adverse reactions were identified with ILUMYA use and the frequency of the adverse reactions was similar to that observed during the placebo-controlled period.

Immunogenicity
As with all therapeutic proteins there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of incidence of antibodies to tildrakizumab in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

Up to Week 64, approximately 6.5% of subjects treated with ILUMYA 100 mg developed antibodies to tildrakizumab. Of the subjects who developed antibodies to tildrakizumab, approximately 40% (2.5% of all subjects receiving ILUMYA) had antibodies that were classified as neutralizing. Development of neutralizing antibodies to tildrakizumab was associated with lower serum tildrakizumab concentrations and reduced efficacy.

DRUG INTERACTIONS
Live Vaccinations
Avoid use of live vaccines in patients treated with ILUMYA *[see Warnings and Precautions]*.

USE IN SPECIFIC POPULATIONS
Pregnancy: Risk Summary
Limited available data with ILUMYA use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. Human IgG is known to cross the placental barrier; therefore, ILUMYA may be transferred from the mother to the fetus. An embryofetal developmental study conducted with tildrakizumab in pregnant monkeys revealed no treatment-related effects to the developing fetus when tildrakizumab was administered subcutaneously during organogenesis to near parturition at doses up to 159 times the maximum recommended human dose (MRHD). When dosing was continued until parturition, a small increase in neonatal death was observed at 59 times the MRHD *[see Data]*. The clinical significance of this nonclinical finding is unknown.

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data: *Animal Data*

In an embryofetal developmental study, subcutaneous doses up to 300 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks during organogenesis to gestation day 118 (22 days from parturition). No maternal or embryofetal toxicities were observed at doses up to 300 mg/kg (159 times the MRHD of 100 mg, based on AUC comparison). Tildrakizumab crossed the placenta in monkeys.

In a pre- and postnatal developmental study, subcutaneous doses up to 100 mg/kg tildrakizumab were administered to pregnant cynomolgus monkeys once every two weeks from gestation day 50 to parturition. Neonatal deaths occurred in the offspring of one control monkey, two monkeys at 10 mg/kg dose (6 times the MRHD based on AUC comparison), and four monkeys at 100 mg/kg dose (59 times the MRHD based on AUC comparison). The clinical significance of these nonclinical findings is unknown. No tildrakizumab-related adverse effects were noted in the remaining infants from birth through 6 months of age.

Lactation: Risk Summary
There are no data on the presence of tildrakizumab in human milk, the effects on the breastfed infant, or the effects on milk production. Human IgG is known to be present in human milk. Tildrakizumab was detected in the milk of monkeys *[see Data]*.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ILUMYA and any potential adverse effects on the breastfed child from ILUMYA or from the underlying maternal condition.

Pediatric Use: Safety and effectiveness of ILUMYA in pediatric patients (<18 years of age) have not been established.

Geriatric Use: A total of 1083 subjects were exposed to ILUMYA 100 mg during Phase 2 and 3 trials. A total of 92 subjects were 65 years or older, and 17 subjects were 75 years or older. Although no differences in safety or efficacy were observed between older and younger subjects, the number of subjects aged 65 and over is not sufficient to determine whether they respond differently from younger subjects.

OVERDOSAGE: In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and administer appropriate symptomatic treatment immediately.

PATIENT COUNSELING INFORMATION: Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide).

Instruct patients and/or caregivers to read the Medication Guide before starting ILUMYA therapy and to reread the Medication Guide each time the prescription is renewed. Advise patients of the potential benefits and risks of ILUMYA.

Hypersensitivity
Advise patients to seek immediate medical attention if they experience any symptoms of serious hypersensitivity reactions *[see Warnings and Precautions]*.

Infections
Instruct patients of the importance of communicating any history of infections to the doctor and contacting their doctor if they develop any symptoms of infection *[see Warnings and Precautions]*.

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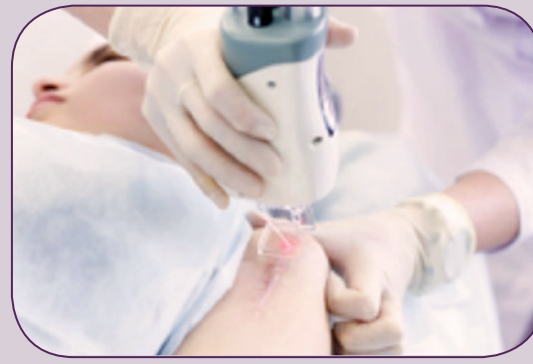
Dermcast.tv Blog - *Do Lasers Really Minimize Scar Formation?*

By Martha L. Sikes, MS, RPh, PA-C

In order to reduce or minimize scar formation, some clinicians have begun using lasers on an incision or wound within three months after injury. This method, which is attempting to target the early wound-healing process, has been used with some success, but there was no systematic review of whether the practice is recommended.



A recent systematic review evaluated the clinical evidence for early laser intervention to reduce scar formation in studies where laser treatment was introduced in the early stages of wound healing. The authors identified twenty-five studies, most of which were controlled studies, and were able to compare laser treatment to untreated control scars. Most of the studies investigated laser treatments applied to surgical scars, but the review also included one study on burn scars and one study on surgical or traumatic scars.

When lasers were applied immediately after or during wound closure, the intervention was applied to the inflammation stage of wound healing. In this case, three of four studies on laser use in this stage found significant improvement on treated scars compared to untreated.

The next stage of wound healing is the proliferation stage, which mainly starts at the time of suture removal. Six of the sixteen studies at this stage found significant improvement in major clinical outcome on laser-treated scars. The final stage of wound healing, which occurs three weeks to two years after injury is known as remodeling. Five studies looked at laser use during this stage and significant improvement in clinical outcome was seen in two of the studies.

Overall, the authors note that in general, the twenty-five included studies were of limited methodological quality and that limitation should be considered. However, the review suggests that laser-treated wounds and scars showed benefit from laser intervention. The authors state that more rigorous studies are needed.

Dermcast.tv Blog Post: August 1, 2018
Source: Wiley Online
Adapted from the original article.

Dermcast.tv is the official online media resource of the SDPA and is your free source for the latest SDPA-related audio podcasts, current dermatology news and research, and videos featuring thought-leaders, procedures, conference highlights, and much more. In addition, Dermcast is the #1 dermatology-related podcast on iTunes! To read more Dermcast.tv Blogs and/or to follow the next live blog from an upcoming SDPA dermatology conference, please visit the Dermcast.tv website at www.dermcast.tv and subscribe today.

How to Clean Your Makeup Brushes

By Annie Chiu, MD

According to dermatologists from the American Academy of Dermatology, dirty makeup brushes can wreak havoc on the skin. In addition to collecting product residue, dirt and oil, makeup brushes are a breeding ground for bacteria. This could compromise your complexion, in the form of acne breakouts and rashes, as well as your health, they say.

"Dirty makeup brushes can irritate your skin and cause an infection, such as fungal infections, E. coli, or a staph infection - the latter of which can be very serious," says board-certified dermatologist Annie Chiu, MD, FAAD, who maintains a private practice in Redondo Beach, California. "To protect your skin and kill any harmful bacteria that lingers in your makeup brushes, it's a good idea to wash your brushes every 7 to 10 days."

To clean your makeup brushes, Dr. Chiu recommends the following tips:

1. Rinse the tips of your brushes under lukewarm, running water to remove residual makeup. Only rinse the tip, as submerging the whole brush head will eventually dissolve the glue that connects the brush head to the handle.
2. Fill a bowl with lukewarm water and a tablespoon of either gentle shampoo or clarifying shampoo. Using plain soap and water can dry out the bristles.
3. Swirl each brush tip in the bowl. For a good lather, you can also massage each brush tip in the palm of your hand.
4. Rinse the brush tips under running water.
5. Continue shampooing and rinsing each brush until the water runs clear from the brush.
6. Squeeze out excess moisture with a clean, dry paper towel.
7. Lay your brushes flat to dry on a towel with the tips hanging off the edge of the counter. Do not dry your brushes upright in a container, as this will cause the water to run down the brushes, loosening the glue that connects the brush head with the handle.

"At a time when skin infections are on the rise, never share your makeup brushes with anyone else and wash them often," says Dr. Chiu. "If you suspect that your makeup is causing acne breakouts or other skin irritation, make an appointment to see a board-certified dermatologist."

These tips are demonstrated in "How to Clean Your Makeup Brushes," a video posted to the AAD website and YouTube channel. This video is part of the AAD's "Video of the Month" series, which offers tips people can use to properly care for their skin, hair and nails. A new video in the series posts to the AAD website and YouTube channel each month.

Annie Chiu, MD *is a Board-Certified Dermatologist practicing in the Beach Cities area of Los Angeles who received her Medical Degree from Stanford University. She obtained her Bachelors of Science from UC Berkeley, where she graduated with top honors and was a University Medal finalist. She is the founder and owner of her private practice, The Derm Institute.*

Dr. Annie Chiu recognizes that healthy, beautiful skin should be attainable for every patient. She specializes in artful, subtle cosmetic rejuvenation with multiple techniques including Botox, fillers, Sculptra, peels, lasers, and tailored cosmeceuticals. Dr. Chiu currently participates in clinical trials for injectables.

Dr. Chiu lectures and teaches advanced cosmetic procedures and techniques throughout the country and internationally. She is currently a consultant, trainer and speaker for Allergan, Galderma, Merz, as well as various energy based device companies. She has also participated in multiple trials on acne, Botox, photoaging, and eczema. She is the author of numerous publications, book chapters, and review articles. Dr. Chiu is also often a media expert for editors and TV Shows alike, appearing on shows such as The Doctors, and was named a "Skin Genius" by Elle Magazine.

Dr. Chiu is also actively involved in the American Academy of Dermatology, American Society of Dermatologic Surgeons, and Women's Dermatologic Society. She serves on the AAD Future Leaders Panel, Patient Advocacy Taskforce, Public Education Committee and Chairs the ASDS Product and Service Development Workgroup, is a member of the Development and Industry Advisory Council and Social Media Task Force. She believes strongly in patient advocacy and outreach, organizing community awareness and empowering patients through confidence in their appearance.

Dermcast.tv Blog

How Safe and Effective are 5ARI to Treat Alopecia?

By Martha L. Sikes, MS, RPh, PA-C

Frontal fibrosing alopecia (FFA) causes hair loss near the front of the head, and causes scarring due to inflammation as the hair follicles are destroyed. This condition, which mostly affects postmenopausal women, is challenging to treat, and studies have examined the off-label use of 5-alpha-reductase inhibitors (5ARI) as a possible option for more severe cases.

A recent review looked at the available literature to determine how effective and safe 5ARI may be for this use. The authors were able to identify 14 studies that used either finasteride or dutasteride to treat FFA. Between these studies, a total of 121 patients were on finasteride, and 149 patients were on dutasteride. Adverse effects of 5ARI were described in five articles, which involved a total of 79 patients. The authors graded the quality of evidence presented in each studies in accordance with the American College of Physicians (ACP) outcome study grading system where grade 1 represents the highest-quality evidence and grade 4 represents very low quality and/or insufficient evidence to suggest efficacy.

The review showed that no study achieved the top grade, but there were two that met the standard of moderate quality of evidence for efficacy. This included a multicenter retrospective review on 355 patients with FFA where 111 of the patients were treated with 5ARI. Patients showed improvement or stabilization when treated with 5ARI in combination, but only 15% showed improvement when used as a mono-therapy.

As for safety, the review showed that the level of evidence for the risks and safety of 5ARI in women is very low. Most studies did not report the risks and safety aspects of this medication.

The authors state that while this review demonstrated that FFA patients treated with 5ARI could achieve either disease stability or reduction in the rate of progression, but there is a need for a well-designed randomized, double-blind, controlled study to reinforce the role of 5ARI as one of treatment tools for FFA.

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Source: Wiley Online
Adapted from the original article

Dermcast.tv is the official online media resource of the SDPA and is your free source for the latest SDPA-related audio podcasts, current dermatology news and research, and videos featuring thought-leaders, procedures, conference highlights, and much more. In addition, Dermcast is the #1 dermatology-related podcast on iTunes! To read more Dermcast.tv Blogs and/or to follow the next live blog from an upcoming SDPA dermatology conference, please visit the Dermcast.tv website at www.dermcast.tv and subscribe today.

NOTES from your Office Manager

The Proper Use of Patient Portals

THE RISK:

Patient portals are an effective tool to actively engage patients in their care to improve health outcomes. However, healthcare professionals must be aware of the potential risks presented by this technology. Some of these risks include: reliance on the patient portal as a sole method of patient communication; patient transmission of urgent/emergent messages via the portal; the posting of critical diagnostic results prior to provider discussions with patients; and possible security breaches resulting in HIPAA violations. Implementing appropriate policies and procedures in the use of portals will enhance patient communication and mitigate liability risks for the practice.

RECOMMENDATIONS:

1. Develop comprehensive patient portal policies which include:
   - patient username and password requirements (minimum number of characters including capitals and non-alphabet characters);
   - a privacy/confidentiality statement on all outgoing messages;
   - encryption updates;
   - account lockout after a specified number of failed login attempts;
   - a mechanism to ensure termination of user access when indicated (e.g., the patient leaves the practice, death, inappropriate use of the portal, etc.);
   - timeframes for responding to patient communication;
   - designated responsibility for replying to patients when the primary provider is not available;
   - utilizing a two patient identifier system for importation of diagnostic studies into the patient portal;
   - monitoring patient access to posted diagnostic results;
   - a follow-up system for patients that do not access the portal; and
   - a mechanism to notify patients if the portal is not functioning properly. A notification should be placed on the practice's website, and also included on any prerecorded telephone message.
2. Advise patients of the reporting mechanism for:
   - email address changes;
   - questions regarding portal use;
   - potential errors in their information; and
   - suspected breaches of privacy.
3. Providers should not use the portal as the means to communicate critical/significant diagnostic results. Diagnostic results should not be posted to the portal until this communication occurs.
4. Instruct patients that the portal is not to be used to evaluate and treat new problems.
5. Utilize a disclaimer on the portal that clearly states it is not to be used for emergencies/urgent problems and include instructions for patients to call 911 or go to the nearest emergency department.
6. Consider the use of a patient portal user agreement that:
   - defines the information patients may access (e.g., appointments, medication refills and referral requests, form downloads, routine appointment reminders, and laboratory reports);
   - prohibits requests for narcotic medication refills;
   - states that the patient portal is the only permissible method of electronic communication with the practice; and
   - includes the disclaimer statement regarding urgent/emergent/new problems.
7. Have staff educate patients regarding the use of the portal and the contents of the portal user agreement upon patient sign-up and as necessary.

Outside & Inside the 9 to 5...

Jessy Ayala MS, PA-C

The Dermatology PA Foundation (DPAF) is thrilled to be able to continue to make monetary contributions to Camp Wonder as well as to be able to send dermatology PAs to serve as medical volunteers at the summer camp. One of our recently selected volunteers, Jessy Ayala, MPAS, PA-C, attended Camp Wonder as a volunteer this past Summer 2018. Mr. Ayala shares with us now his thoughts on what motivated him to apply as a Camp Wonder volunteer.

I have been in practice for over sixteen years. My first six years was a tenure in emergency medicine and for the last eleven years I have been practicing in the field of dermatology. When I first graduated PA school seventeen years ago, I was excited to start volunteering. My first attempt to do so though was met with rejection. I reached out to the Operation Smile foundation to start helping others and unfortunately found out that they did not accept PAs at the time.

Jessy Ayala, MS, PA-C

I would not be deterred. In 2017 I was fortunate to serve on a dermatology humanitarian mission called Passion to Heal that was based in Kenya. This mission trip helped to reinforce the concept of team spirit and altruism. I stay in regular touch with some of the dermatology members of this trip (PAs and MDs), many of whom I now consider my lifetime friends. This mission trip was a life changing experience for me and it is what prompted me to apply for the DPAF Camp Wonder mission. My time spent in Africa with the Passion to Heal trip helped me to realize that my skills are needed outside of the private clinic setting.

Prior to my trip, I believed that Camp Wonder would be a fun but challenging experience. I anticipated that the campers would have chronic and severe skin conditions that would test my knowledge base. My previous volunteer trip lacked true access to new age pharmaceutical drugs due to its remote region in the world. Since Camp Wonder is based out of the United States, I expected to have medical resources readily available during my time at camp.

Having completed my volunteer experience at camp, my perception of Camp Wonder has completely changed. I now know that Camp Wonder annually creates a safe haven for over 80 children with severe and life threatening conditions such as epidermolysis bullosa (EB). From the moment the campers walk through the door, the ample medical and volunteer staff attend to their every need. Campers are checked in, screened for head lice, and then have a thorough history taken by a dermatology resident. They are then shown to their cabin by the nursing team. During the week we were encouraged to interact and have fun with the campers. Some of these fun activities included rock climbing, zip lining, carnival night, and prom night.

On my third day, I was assigned to a dressing change for a child with EB. This would change my life forever. Prior to this experience, I had never seen the skin of a patient who has

EB without dressings. My patient was 16-year old male who had the height and stature of an 8-year old. Typical dressing changes for him can range anywhere from 1.5 - 2 hours, including removing old dressing, bathing, and reapplying a new dressing. The special dressings that are used are called Mepilex and Mepitel. These dressings draw out fluid and are used in combination with vast amounts of Aquaphor. This camper's dressing changes occur three times a week. This provided me with a small glimpse into some of the lifelong care needed for children with this condition. My experience at Camp Wonder has reinforced my drive towards humanitarianism. I look forward to continuing to dedicate time in my life to help others that are less fortunate.

Volunteering has renewed my sense of commitment to dermatology and the medical profession as a whole. After my first volunteer trip, I have made a commitment to myself to volunteer once a year on medical humanitarian missions and I will be applying in the future to Camp Discovery (a dermatology summer camp sponsored by the AAD). It would be my highest recommendation for any dermatology PA who is considering to start doing some volunteer work to apply for the DPAF Camp Wonder or Passion to Heal programs.

Jessy Ayala, MS, PA-C *is a practicing dermatology PA and the Director of Clinical Operations at Westchester Dermatology Center. He enjoys lecturing across the nation on various general dermatology diseases, including acne, rosacea, and psoriasis. With more than a decade of experience, Jessy also serves as a dermatology preceptor for PA students from Marist College and Touro College. He brings his passion and commitment to patient care through community service and volunteer work.*

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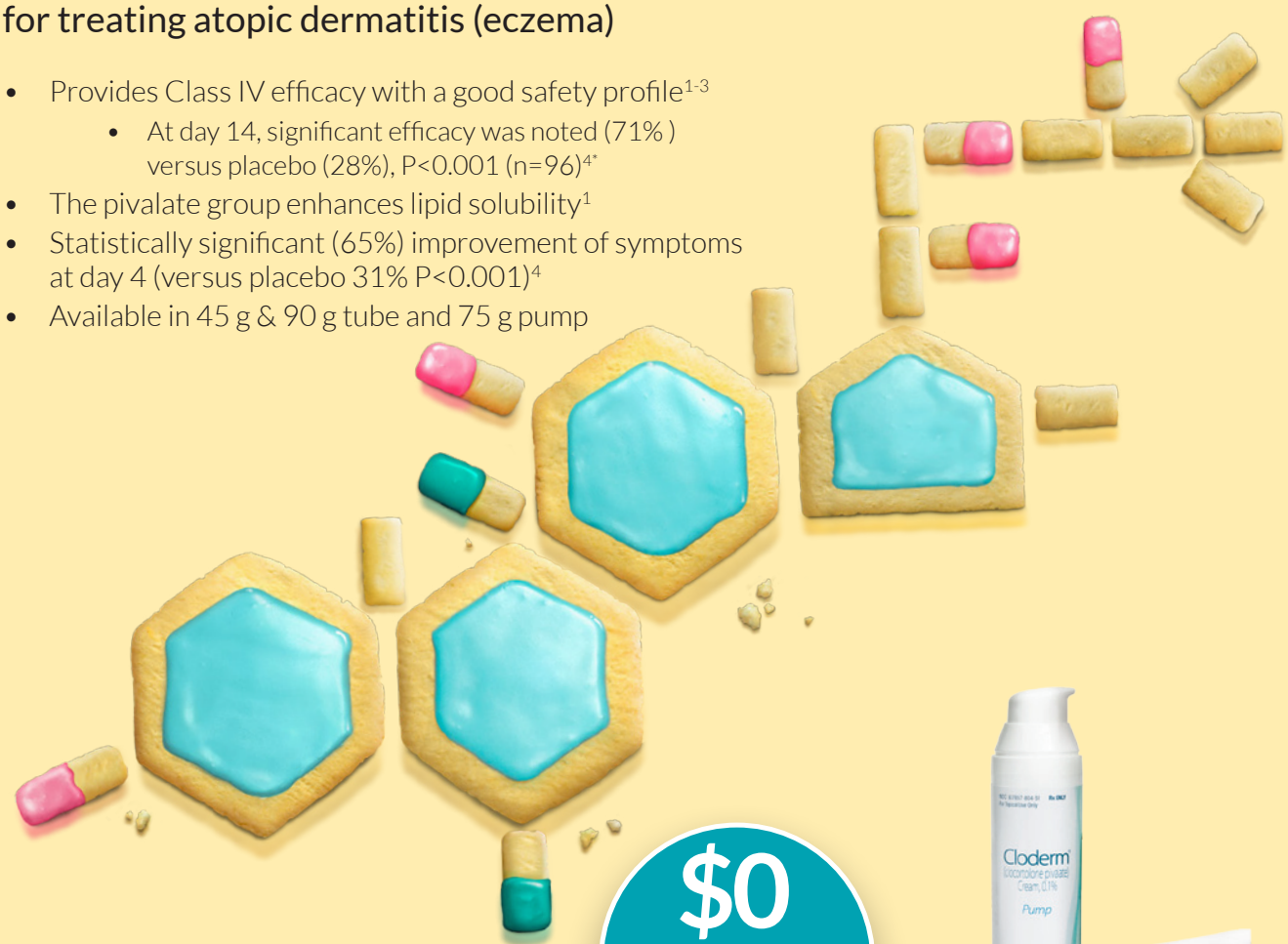

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References: 1. Bikowski J, Pillai R, Shroot B. The position not the presence of the halogen in corticosteroids influences potency and side effects. J Drugs Dermatol. 2006;5(2):125-130. **2.** Del Rosso J, Friedlander SF. Corticosteroids: options in the era of steroid-sparing therapy. J Am Acad Dermatol. 2005;53(1 Suppl 1):S50-58. **3.** US Food and Drug Administration NDA 017765. Promius Pharma, LLC, Princeton, NJ: Aug 1977. **4.** Rosenthal AL. Clocortolone pivalate: a paired comparison clinical trial of a new topical steroid in eczema/atopic dermatitis. Cutis. 1980;25(1):96-98. J Am Acad Dermatol. 2005;53(1 Suppl 1):S50-58. 3. US Food and Drug Administration NDA 017765. Promius Pharma, LLC, Princeton, NJ: Aug 1977.

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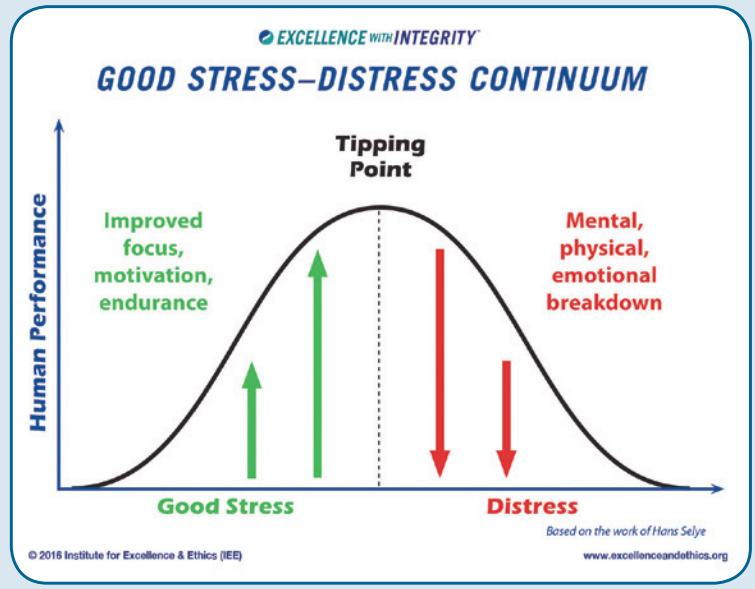
Workplace Excellence

Manage Stress; Become Your Personal Best

By Matthew Davidson, PhD

In my work as President of the Institute for Excellence & Ethics (IEE) I have had the opportunity to work with diverse individuals and organizations in their quest to achieve excellence. This column dedicated to workplace excellence explores the organizational, interpersonal, and ethical issues that contribute to (or detract from) individual or organizational excellence within the physician assistant profession. If you have any workplace topics you would like to see covered in the JDPA please feel free to share them with us. Email editor@jdpa.org with any topic ideas or questions concerning the workplace.

Helen Keller famously said, "Character cannot be developed in ease and quiet. Only through experience of trial and suffering can the soul be strengthened, ambition inspired, and success achieved." ONLY through trial and suffering - what a powerful truth about the development of character. Unless or until we experience adversity, hardship, disappointment, our character is not put to the test. Until it is put to the test, it doesn't fully develop. Some have argued that "sports don't develop character, they reveal it." I would actually say that whether we're talking sports or anything else that puts our character to the test, it simultaneously DEVELOPS and REVEALS our character. I might break under the strain of some adversity, and this may reveal the current capacity of my character, but as a result of this experience I may also grow and develop and be stronger in the future as a result.



Character is often defined as "values in action." At IEE we talk about the importance of BOTH performance character and moral character. Performance character consists of those values in action - such as effort, self-discipline, and perseverance - that enable us to do our best in any performance environment. Moral character refers to those values needed for successful relationships and ethical behavior such as fairness, honesty, respect, and humility.

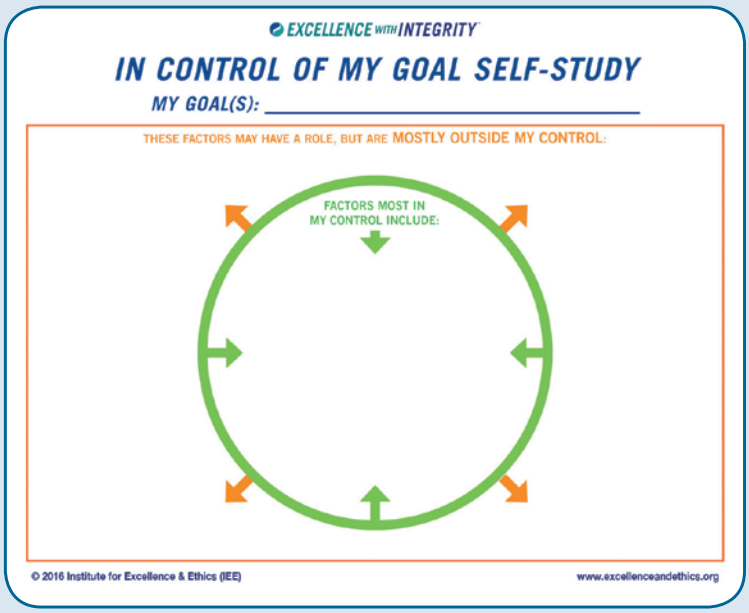
It's the "in action" piece that is often neglected in the development of character, and that's the wisdom at the core of the Helen Keller quote: it is WHEN and IF you put a value into action that character is developed and revealed. Think about character as a muscle: all muscles have a certain strength capacity. The way a muscle's capacity is developed is by putting it under stress, by working it out. We understand and accept this truth when it comes to our minds and our bodies, but we often think you're born with your character muscles or that you inherit them. Sure, just like our other muscles, we're all born with certain character gifts or strengths, some of which are a genetic gift of sorts. However, just like any other natural ability, it's only through hard work and

deliberate practice that we maximize the potential of our natural abilities.

Bottom line: character is a muscle that must be worked, must be put into action. Our character muscles are not unlike the muscles of our mind: there's book smarts and then there's street smarts. When it comes to character, lots of us are book smart. We have knowledge about character, what it is and why it's important. That's not unimportant, but it's the street smarts about character that Helen Keller is talking about. Street smarts come from putting your character muscles to the test in the real world challenges - and not simply the ones we choose, but also the ones that choose us. Doing what you don't want to do, when you don't want to do it; doing what life demands of you, even if you wouldn't choose this path, that's when the street smarts of character are really put to the test.

Stress - Life's All-Natural Character Development Supplement

Our character muscle is an interesting muscle in that it is a muscle that is put to the test whenever we put any other muscle to the test. Trying to learn something will test our willpower, attitude, and effort; it will also test our humility and honesty. Any intellectual, physical, emotional or spiritual muscle activates or puts stress on our character muscle.



When it comes to muscle development, it's stress that leads to growth. Too little, and muscles remain weak; too much, and muscles get injured. Just the right amount of stress and you get optimal muscle development. Below is what we call the Good Stress-Distress Continuum.

Research shows that the experience of stress actually improves human performance, including focus, motivation, and endurance. This is what coaches/supervisors are doing when they create a practice/training experience designed to push athletes/staff members mentally and physically. However, there is a tipping point where good stress becomes distress and where we begin to experience physical and emotional breakdown. In sport and life, our ability to manage stress is essential. When you manage stress well, you find ways to remain grateful, mindful and joyful, even when your struggles are difficult and painful. On the one hand we often do not like to work out our character muscles (who really likes adversity, right?); on the other hand, we often forget that like any other muscle, your character muscle gets tired too. This explains in part why after being responsible and disciplined on your diet all day long, you binge at ten at night and eat a bag of chips! It also explains why we make bad ethical decisions when we're under great stress.

Like a good strength and conditioning coach in the weight room, the best coaches,

supervisers, and fellow staff members (and friends) help to "spot you," helping to allow just the right amount needed for the circumstance and given your particular capabilities and/or sensibilities. Too much or too little, and sooner or later you enter distress either from weakness or from overuse. In our efforts to manage our stress we will need to use lots of different strategies. Different times in our life, different situations, different personalities and preferences all mean that no one strategy will work for everyone. However, there are certain responses to stress that almost always lead to MORE stress.

We want to be careful to avoid STRESS MULITPLIERS, like worrying about how we compare to others; hiding struggles or weaknesses; being embarrassed if our product or performance isn't perfect; or not asking for help. You'll notice that lots of these "stress multipliers" are also connected to character weaknesses, like bad pride, lack of humility, etc. So it's a circular relationship of sorts: character weaknesses cause more stress; the additional stress tends to overtax and then reveal our character weaknesses.

Mindset and Focus - The Hidden Driver of Excellence

Through his experience in extreme adversity, Holocaust survivor, Viktor Frankl, identified what he referred to as, "The last of the human freedoms, to choose one's attitude, to choose one's own way." In essence, it's our mindset and what we choose to focus on that provides us the greatest character strength, and stress management technique. In his book entitled, Focus, Daniel Goleman argues that focus is, "the hidden driver of excellence." He also notes that today we are a distracted, burned out, and stressed out population, constantly striving for the next thing, worrying about the past, and obsessing about the future. Our mindset, what we focus on, and how we reframe challenging situations as growth opportunities is one of the essential qualities of great performers in every walk of life. No matter what happens, good or bad, we still have the power to choose our focus, how we approach the challenge, and how we respond.

FOCUS - On What's In Your Control

Focus is a hidden driver of excellence, precisely because it is often hidden from the things we commonly think about being in our control to develop. For any goal that you might have in life, any goal whatsoever, there are things you can control and things you cannot.

Joseph Campbell said, "The cave you fear to enter holds the treasure you seek." We are often afraid of the adversity and challenges we face; ironically, it's in and through the things we most fear, life's challenges and adversities, and in pursuit of noble goals that we find the hidden treasure that lies within our character muscles. But it's not enough to simply think about these things, we have to put them into action. Developing the value of focus requires putting it into action consistently so that it becomes a habit. What are some optimal performance indicators of focus?

1. Focus on what's in your control
2. Work hard and smart
3. Build on your strengths
4. Strengthen (but DON'T obsess about) your weaknesses
5. Be radically grateful for everything - for the opportunity, for your strengths, for your challenges
6. DON'T whine, complain, or make excuses or blame outside factors for your struggles
7. Avoid perfectionism and fear of failure
8. Be open to suggestions for improvement
9. Seek external help and support as needed

When you face trial and hardship (and it's not if) but when, these are the things on which to focus. If these become your habits, they become your character; and this strength of character will ensure that your "soul be strengthened, your ambition inspired, and your success achieved."

Matthew L. Davidson, Ph.D. is the Founder, President, and Director of Education for the Institute for Excellence & Ethics (IEE), a 501(c)3 nonprofit corporation dedicated to helping individuals and organizations achieve excellence. He is a National Spokesperson for the Business Bureau National Center for Character Ethics. The IEE specializes in the development and dissemination of research-based tools for developing the culture and competencies of excellence and ethics in schools, athletics, the workplace, and the home; this is done through professional development workshops & academies, teaching & learning resources, assessment, and consulting services. He is a frequent national presenter and is available for keynote lectures, professional development, retreats, and organizational consulting. He has indicated no relationships to disclose relating to the content of this article. For additional information or to contact the IEE, please visit www.excellenceandethics.org.

Listening To Patients

The Flight Attendant Said My Leg Was Going to Fall Off

By Alan Rockoff, MD

Henry came in leaning on a cane. He rolled up his trousers and showed me his shins, both red and scaly. That's not an infection," I told him, "just a kind of eczema caused by poor circulation. It often comes with age." I recommended a cortisone cream to get rid of the symptoms of itch and scale.

"I'm a diabetic, you know," Henry said. He told me the name of the doctor at a diabetes clinic who had referred him. "I was taking a plane trip two weeks ago, a little after this rash first came in," he said. "A flight attendant passed by, saw that my pants legs were rolled up a little, and said, "I used to be a nurse. You have cellulitis."

"I understand," I said to Henry. "So because you have diabetes, what the flight attendant said worried you, because an infection like cellulitis could lead to your losing your leg."

"Yes," said Henry.

"That's why I started off by saying that what you have is not infected," I told him. "For one thing, cellulitis happens only on one leg and gets worse fast. It doesn't affect both legs and then just hang around and itch a little. A lot of people with this common kind of circulation-related rash worry that bad things will happen to their leg, but especially if they're diabetic. They hear that they may have cellulitis from friends, sometimes even from doctors. Not many hear it from a flight attendant."

Stories like Henry's (they come up often) point to several lessons that are not on the standard medical curriculum:

- To know what people are truly worried about, you can't just go by what they tell you (the "Chief Complaint"). Henry didn't care about the itch. He was afraid of amputation. Really.
- If you convince people that their symptoms don't matter, you may not even have to treat them. Now that Henry is no longer concerned that he'll lose his leg, he'll probably stop using the cream in two days. In my experience, men can be like that.
- Even native speakers may not understand medical talk, despite being spoken to in plain English. When the flight attendant told Henry he had "cellulitis," Henry knew he had something bad, but not what kind of bad. So even though I began by saying, "This is not an infection," he didn't pick up that I was being reassuring about exactly what was worrying him.
- It is very easy for medical people to make patients feel worse without really trying. You can't blame the flight attendant/nurse for not knowing that Henry didn't have a bacterial infection. She was not really examining him, and a glance at legs squeezed between airline seats is not much of an examination anyway. What she was really implying was, "You'd better have that checked out," which was not bad advice.

There are, of course issues that go beyond causing unnecessary worry. Nobody wants to miss a cellulitis, but practitioners do patients no favors by admitting and treating them for "bilateral cellulitis" with IV antibiotics that don't

make them better, because all they have is stasis eczema. But that's a talk for another time.

In the meantime, the flight attendant told Henry, quite properly, to get his leg checked out. What Henry heard was, "You're going to get gangrene and lose your leg."

Not quite what you want from the Friendly Skies.

Alan Rockoff, MD *practices dermatology in Boston, MA. He graduated with his medical degree in 1972 from the Albert Einstein College of Medicine in New York and then completed a pediatric internship and residency at Bronx Municipal Hospital Center. Continuing his education, Dr. Rockoff completed a dermatology residency program at the combined program at Boston University and Tufts University. Dr. Rockoff is a Clinical Assistant Professor of Dermatology at Tufts University School of Medicine. He has taught senior medical students and other trainees for over thirty-five years.*

Dr. Rockoff has been named one of Boston's Top Doctors by Boston Magazine for five years. Dr. Rockoff is board certified by the American Board of Pediatrics and the American Board of Dermatology. Dr. Rockoff is a Fellow of the American Academy of Dermatology and a member of the Massachusetts Medical Society and the Massachusetts Academy of Dermatology.

Dr. Rockoff's publications have appeared in a number of journals. He writes a monthly column for his dermatologic colleagues in Dermatology News as well as a blog for the magazine Psychology Today. His first book, "Under My Skin: A Dermatologist Looks at His Profession and His Patients" is available on Amazon and is his second book, "Act Like a Doctor, Think Like a Patient: Teaching Patient-focused Medicine" is available on Amazon and at Barnes and Noble.

From the Desk of...

Jennifer Winter, MSPAS, PA-C

Optimal Team Practice

The physician assistant (PA) profession has been around for 50 years and PAs are found in all areas of medicine including dermatology. Envisioned to address a shortage of physicians and based on the fast-track training of physicians during World War II, this profession started with former military medics who had a lot of experience, but no civilian opportunities to use that experience.

PAs are trained in the medical model and originally worked with physicians out of necessity. It was a new profession that needed to be nurtured and those early folks had to prove that they could take care of patients safely with their abbreviated training. Fifty years later medicine has evolved more than anyone could have imagined, and the PA profession has indeed proven to be a success. After learning the basics during training, PAs continue to learn in the clinic and hospital just the way residents learn and practice, alongside physicians.

Physicians who needed to increase access to care for patients turned to PAs to address that need. They created a team that worked together for the benefit of the patient. Medicine has become so specialized that team practice is the norm and solo practitioners are becoming rare. As physicians are increasingly employees rather than practice owners, they have less control over hiring decisions about team members such as PAs. Those decisions are being made by administrators, who may not understand the training of PAs and their long-standing team approach to medicine and who see only the barriers and paperwork that are required to hire PAs vs. other providers. This results in fewer PAs being hired and the profession is now at risk, especially at large hospital systems.

It is those barriers that PAs are seeking to break down in order to continue to have a viable profession. In dermatology, the trend toward corporate practice has been slower than many other specialties, but it is growing. PAs have trouble volunteering and providing care in areas where there are no physicians because of state laws that have not kept up with the changes in the way medical care is provided. Patients have lost access to care when a supervising physician has retired, died, or become unable to practice leaving a PA unable to continue based on current laws.

Because these concerns affect PAs in general, dermatology PAs also support reducing the legal barriers to practice. Optimal Team Practice or OTP, is an idea whose time has come. OTP is a policy adopted by the American Academy of Physician Assistants with a broad vision of the future of the profession. OTP calls for laws and regulations that authorize PAs to practice without an agreement with a specific physician. This removes the physician from the liability for the care the PA provides and places that responsibility back on the individual PA.

The idea behind OTP is not to seek solo independent practice, frankly even physicians are less likely to be independent these days, but to have the decisions about how much autonomy a PA will have made at the practice level rather than the state level. The level of autonomy will vary depending on the experience and training of the PA and the type of patients being cared for.

PAs do not want to change the current PA role, working with physicians, which is well established after 50 years. We value our relationship with physicians, greatly respect their depth of knowledge and training, and wish to continue that partnership. PAs will remain legally and ethically obligated to consult with and refer patients to physicians based on the needs of the patient.

PAs need OTP to remain a viable profession and continue to provide quality care to our patients. We appreciate your support. This is a complex issue; if you would like additional information or clarification, please feel free to contact me directly at sdpa@dermpa.org.

Jennifer Winter, MPAS, PA-C *is in practice in Olympia, Washington. She is a past President of the Society of Dermatology Physician Assistants and serves as the current Chair of the Public Education Committee.*

Originally published in The Dermatologist, August 16, 2018

Collaborating Physician **CORNER**

Dermatologists, Skin Cancer Survivors Tell "Skin Cancer, Take a Hike!"

Twelve skin cancer advocates trek remote Alaska to raise awareness, funds for skin cancer prevention and detection

Skin cancer is the most common cancer in the United States, affecting one in five Americans in their lifetime. To help raise awareness of skin cancer prevention and detection, 12 dermatologists, skin cancer survivors, and their family and friends told "Skin Cancer, Take a Hike!" during a four-day trek through remote Alaska. Starting Sunday, July 15, the hikers trekked more than 20 miles along Alaska's Denali and Foraker mountains to raise funds for the American Academy of Dermatology's SPOT Skin Cancer™ campaign. Proceeds raised through Skin Cancer, Take a Hike!™ will support community outreach programs and services, including free skin cancer screenings, shade structures where children learn and play, and sunscreen dispensers in public pools and parks.

"As a dermatologist and skin cancer survivor myself, this is a cause that is very near and dear to my heart," said board-certified dermatologist Ellen Marmur, MD, FAAD, associate clinical professor, Icahn School of Medicine at Mount Sinai, who is leading the team of hikers. "Skin cancer affects more Americans than any other cancer, yet most cases are preventable by seeking shade, wearing protective clothing, and generously applying sunscreen before going outdoors. In addition, everyone should check their skin regularly and call a board-certified dermatologist if they notice any new or suspicious spots or any spots that are changing, itching or bleeding."

It is estimated that more than 9,500 people are diagnosed with skin cancer every day. While skin cancer is highly treatable when diagnosed early, it can be deadly. On average, one American dies from melanoma, the deadliest form of skin cancer, every hour.

Skin Cancer, Take a Hike!™ began in 2014 when Dr. Marmur and eleven others impacted by skin cancer climbed to the top of Mount Kilimanjaro to raise money for skin cancer awareness. Since then, Skin Cancer, Take a Hike!™ has grown to include six fundraising events throughout the country and has raised more than $800,000. This year's events are generously supported by national sponsors, including Coppertone, Endo Pharmaceuticals and EltaMD, Inc.

"I learned the hard way how to be vigilant about sun protection, and I want to prevent other families from experiencing the same," said Dr. Marmur. "Join us in the fight against skin cancer by supporting this hike. Your support will help save lives by funding skin cancer prevention and detection programs and supporting our vision of a world without skin cancer."

Skin Cancer, Take a Hike!™ is part of the Academy's SPOT Skin Cancer™ campaign to reduce mortality from and the incidence of skin cancer through public awareness, community outreach programs and services, and advocacy that promote the prevention, detection and care of skin cancer. Thanks to the campaign's dedicated hikers and donors, the AAD's SPOT Skin Cancer™ campaign has provided more than 2.7 million free skin cancer screenings, built more than 350 shade structures, and installed 52 sunscreen dispensers in public pools and parks.

In addition to the Alaska trek, Skin Cancer, Take a Hike!™ included five other fundraising hikes in 2018:

- Elk Grove Village, Ill.
- Atlanta, Ga.
- Phoenix, Ariz.
- Orange County, Calif.
- Las Vegas, Nev.

The hikes attract adults and families who are active in outdoor activities and excited to promote sun safety and skin cancer awareness in their communities.

To learn more about Skin Cancer, Take a Hike!™ or to donate, visit www.aad.org/SCTAH.

JDPA Journal of Dermatology for Physician Assistants

INFORMATION FOR AUTHORS – The JDPA is a peer-reviewed publication that delivers innovative clinical, surgical, cosmetic, and professional content exclusively for dermatology PAs. Submissions to the JDPA are peer-reviewed by a panel of experienced dermatology PAs, educational PAs, and dermatologists before articles are accepted for publication.

Manuscripts submitted for publication will be reviewed with the understanding that they are original and have not been submitted elsewhere nor are being considered by other journals. Electronic submissions are accepted and should be sent to editor@jdpa.org.

The five main sections featured in each issue of the JDPA are listed below along with a brief description of the various topics that authors can contribute to. Regardless of the section, all articles must follow the following criteria:

- ***Formatting*** - Times New Roman font, 12 point, double-spaced, left aligned.
- ***Article Order*** - Title, Author(s), Author bios (including disclosures), Text of Article, References, Tables, and Figures
- ***Reference Citations*** - Utilize the AMA Manual of Style, 10th Edition.

DERMATOLOGY PA NEWS AND NOTES

Feature Articles

Write a review about a new or innovative dermatological procedure, device, and/or approach to patient care (500-1000 words).

From The Desk Of…

Write an opinion essay sharing your insight regarding a current "hot item" issue *(e.g., specialty PA credentialing, dermatology access to care, supervising physician relationships, etc.)* or any other topic regarding the field of dermatology (250-1000 words).

CLINICAL DERMATOLOGY

CME articles

Content should be specific to the field of dermatology following any of the following formats:

Study – Original research (clinical or basic science).
Professional issues or health policy papers.
Review – Scholarly review of a topic.

Content length:

6 pages (requires 4 self-assessment Q&A) = .5hr of Cat. I CME.
12 pages (requires 8 self-assessment Q&A) = 1hr of Cat. I CME.

Article should include written learning objectives (3-4 required).

Dermatology Case Report

Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).

Journal Club: Dermatology PA Perspectives

Write a review of an already published article from an established dermatology journal *(e.g., JAAD, Cos Dermatol, Dermatol Surg, etc.),* summarizing the practical thoughts and clinical issues (250-1000 words).

From the Patient's Perspective

Patients' stories published in their own words. JDPA staff can even assist patients with writing their stories (250-1000 words).

Clinical Snapshots

Write a brief written description and clinical facts about an interesting cutaneous anomaly (250-500 words).

Drugs in Dermatology

Write about the current information regarding a particular dermatological medication, drug interaction, or medication side effect/adverse reaction (250-1000 words).

Dermatology Evidence-Based Medicine (derm EBM)

Write a brief, evidence-based assessment of the one or two most relevant studies retrieved to answer a focused clinical question that may have arisen from a real-life situation. A derm EBM is not a comprehensive review of a subject or a synthesis of all the available knowledge (500–1500 words).

SURGICAL DERMATOLOGY

Feature Articles

Write a review about a new or innovative surgical procedure, device, and/or approach to patient care (500-1000 words).

Surgical Wisdom

Write a brief article on a fact or pearl for the surgical setting (250-500 words).

Surgical Dermatology Case Report

Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).

Journal Club: Dermatology PA Perspectives

Write a review of an already published article from an established dermatology journal *(e.g., JAAD, Cos Dermatol, Dermatol Surg, etc.),* summarizing the practical thoughts and clinical issues (250-1000 words).

COSMETIC DERMATOLOGY

Feature Articles

Write a review about a new or innovative cosmetic procedure, device, and/or approach to patient care (500-1000 words).

Cosmetic Pearls

Write a brief article on a fact or pearl for the cosmetic setting (250-500 words).

Cosmetic Dermatology Case Report

Write a report and discuss a case(s) that illustrate an important or interesting observation (500-1500 words).

Journal Club: Dermatology PA Perspectives

Write a review of an already published article from an established dermatology journal *(e.g., JAAD, Cos Dermatol, Dermatol Surg, etc.),* summarizing the practical thoughts and clinical issues (250-1000 words).

PROFESSIONAL DEVELOPMENT

Feature Articles

Write an article that explores the professional issues dermatology PAs face such as reimbursement, education, medical trends, contracts, office management, etc. (500-1500 words).

Outside & Inside the 9 to 5

Allow us to share your story of the good work that you do either outside or inside your practice of dermatology. You can write this article yourself or the JDPA staff can interview you to write the article (250-1000 words). **Notes From Your Office Manager**
Write a brief article on a fact or pearl for the office setting (250-500 words).

Judicial and Ethical Affairs

Write an article that explores the complex or multifaceted ethical or judicial professional issues that affect the practice of dermatology for PAs (250-1000 words).

To read the JDPA publication's Ethics and Malpractice Statement, please visit www.jdpa.org/write.html.

ADVERTISER INDEX

For more information on advertising opportunities in the JDPA, please log on to www.jdpa.org

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use RETIN-A MICRO safely and effectively. See full prescribing information for RETIN-A MICRO.

RETIN-A MICRO® (tretinoin) gel microsphere, 0.1%, 0.08%, 0.06% and 0.04%, for topical use
Initial U.S. Approval: 1971

INDICATIONS AND USAGE
Retin-A Micro® is a retinoid indicated for topical application in the treatment of acne vulgaris.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Local Irritation
The skin of certain individuals may become excessively dry, red, swollen, or blistered.

Tretinoin has been reported to cause severe irritation on eczematous skin and should be used with utmost caution in patients with this condition.

If the degree of irritation warrants, patients should be directed to temporarily reduce the amount or frequency of application of the medication, discontinue use temporarily, or discontinue use all together. Efficacy at reduced frequencies of application has not been established. If a reaction suggesting sensitivity occurs, use of the medication should be discontinued.

To help limit skin irritation, patients must

- wash the treated skin gently, using a mild, non-medicated soap, and pat it dry, and
- avoid washing the treated skin too often or scrubbing it hard when washing.

Patients should apply a topical moisturizer if dryness is bothersome.

Exposure to Ultraviolet Light or Weather Extremes
Unprotected exposure to sunlight, including sunlamps (UV light) should be avoided or minimized during the use of Retin-A Micro and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight as a result of the use of tretinoin. Patients who may be required to have extended periods of UV exposure (e.g., due to occupation or sports), or those with inherent sensitivity to the sun, or those using medications that cause photosensitivity, should exercise particular caution. Use of sunscreen products (SPF 15 or higher) and protective clothing over treated areas are recommended when exposure cannot be avoided *[see Nonclinical Toxicology]*.

Weather extremes, such as wind or cold, also may be irritating to tretinoin-treated skin.

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Clinical Trials in Subjects with Acne
In separate clinical trials for each concentration, acne subjects treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1% or 0.04%, over the twelve-week period showed that cutaneous irritation scores for erythema, peeling, dryness, burning/stinging, or itching peaked during the initial two weeks of therapy, decreasing thereafter.

Approximately half of the subjects treated with Retin-A Micro, 0.04%, had cutaneous irritation at Week 2. Of those subjects who did experience cutaneous side effects, most had signs or symptoms that were mild in severity (severity was ranked on a 4-point ordinal scale: 0=none, 1=mild, 2=moderate, and 3=severe). Less than 10% of patients experienced moderate cutaneous irritation and there was no severe irritation at Week 2.

In trials of Retin-A Micro (tretinoin) Gel microsphere, 0.04%, throughout the treatment period the majority of subjects experienced some degree of irritation (mild, moderate, or severe) with 1% (2/225) of subjects having scores indicative of a severe irritation; 1.3% (3/225) of subjects treated with Retin-A Micro (tretinoin) Gel microsphere, 0.04%, discontinued treatment due to irritation, which included dryness in one patient and peeling and urticaria in another.

In trials of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, no more than 3% of subjects had cutaneous irritation scores indicative of severe irritation; 6% (14/224) of subjects treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, discontinued treatment due to irritation. Of these 14 subjects, four had severe irritation after 3 to 5 days of treatment, with blistering in one subject.

In a double-blind trial with 156 acne subjects comparing 12 weeks of treatment with Retin-A Micro (tretinoin) Gel, 0.04% or 0.1%, (78 subjects each group), the most frequently reported adverse events affected the skin and subcutaneous tissue (15.4% in the 0.04% group, and 20.5% in the 0.1% group). The most prevalent of the dermatologic adverse events in the 0.04% group was skin irritation (6.4%); and in the 0.1% group skin burning (7.7%), erythema (5.1%), skin irritation (3.8%), and dermatitis (3.8%). Most adverse events were of mild intensity (63.4%), and 34.4% were moderate. One subject in each group had adverse events characterized as severe, neither were dermatologic findings and neither was characterized as related to drug by the investigator.

Trials in Subjects without Acne
In a half-face comparison trial conducted for up to 14 days in women with sensitive skin, but without acne, Retin-A Micro (tretinoin) Gel microsphere, 0.1%, was statistically less irritating than tretinoin cream, 0.1%. In addition, a cumulative 21-day irritation evaluation in subjects with normal skin showed that Retin-A Micro (tretinoin) Gel microsphere, 0.1%, had a lower irritation profile than tretinoin cream, 0.1%. The clinical significance of these irritation studies for patients with acne is not established. Comparable effectiveness of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, and tretinoin cream, 0.1%, has not been established. The lower irritancy of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, in subjects without acne may be attributable to the properties of its vehicle. The contribution of decreased irritancy by the MICROSPONGE System has not been established. No irritation trials have been performed to compare Retin-A Micro (tretinoin) Gel microsphere, 0.04%, with either Retin-A Micro (tretinoin) Gel microsphere, 0.1%, or tretinoin cream, 0.1%.

Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Retin-A Micro Gel. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Temporary hyper- or hypopigmentation has been reported with repeated application of tretinoin.

USE IN SPECIFIC POPULATIONS
Pregnancy
Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Retin-A Micro should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Thirty human cases of temporally associated congenital malformations have been reported during two decades of clinical use of tretinoin products. Although no definite pattern of teratogenicity and no causal association has been established from these cases, five of the reports describe the rare birth defect category holoprosencephaly (defects associated with incomplete midline development of the forebrain). The significance of these spontaneous reports in terms of risk to the fetus is not known.

For purposes of comparison of the animal exposure to systemic human exposure, the MRHD applied topically is defined as 1 gram of Retin-A Micro (tretinoin) Gel microsphere, 0.1%, applied daily to a 60 kg person (0.017 mg tretinoin/kg body weight).

Pregnant rats were treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, at daily dermal doses of 0.5 to 1.0 mg/kg/day tretinoin on gestation days 6-15. Alterations were seen in vertebrae and ribs of offspring at 5 to 10 times the MRHD based on the body surface area (BSA) comparison.

Pregnant New Zealand White rabbits were treated with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, at daily dermal doses of 0.2, 0.5, and 1.0 mg/kg/day tretinoin on gestation days 7-19. Doses were administered topically for 24 hours a day while wearing Elizabethan collars to prevent ingestion of the drug. Increased incidences of certain alterations, including domed head and hydrocephaly, typical of retinoid-induced fetal malformations in this species, were observed at 0.5 and 1.0 mg/kg/day. Similar malformations were not observed at 0.2 mg/kg/day, 4 times the MRHD based on BSA comparison. Other pregnant rabbits exposed topically for six hours per day to 0.5 or 1.0 mg/kg/day tretinoin while restrained in stocks to prevent ingestion, did not show any malformations at doses up to 19 times (1.0 mg/kg/day) the MRHD based on BSA comparison, but fetal resorptions were increased at 0.5 mg/kg (10 times the MRHD based on BSA comparison).

Oral tretinoin has been shown to cause malformations in rats, mice, rabbits, hamsters, and nonhuman primates.

Tretinoin induced fetal malformations in Wistar rats when given orally at doses greater than 1 mg/kg/day (10 times the MRHD based on BSA comparison). In the cynomolgus monkey, fetal malformations were reported for doses of 10 mg/kg/day but none were observed at 5 mg/kg/day (95 times the MRHD based on BSA comparison), although increased skeletal variations were observed at all doses. Dose-related increases in embryolethality and abortion also were reported. Similar results have also been reported in pigtail macaques.

In oral peri- and postnatal development studies in rats with tretinoin, decreased survival of neonates and growth retardation were observed at doses in excess of 2 mg/kg/day (19 times the MRHD based on BSA comparison).

Nonteratogenic effects on fetus
Oral tretinoin has been shown to be fetotoxic in rats when administered at doses 24 times the MRHD based on BSA comparison.

Topical tretinoin has been shown to be fetotoxic in rabbits when administered at doses 10 times the MRHD based on BSA comparison.

Nursing Mothers
It is not known whether tretinoin and/or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Retin-A Micro is administered to a nursing woman.

Pediatric Use
Safety and effectiveness in children below the age of 12 have not been established.

Geriatric Use
Safety and effectiveness in a geriatric population have not been established. Clinical trials of Retin-A Micro (tretinoin) Gel microsphere, 0.1% and 0.04%, did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger subjects.

OVERDOSAGE
Oral ingestion of large amounts of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Dermal carcinogenicity testing has not been performed with Retin-A Micro (tretinoin) Gel microsphere, 0.1%, 0.08%, 0.06% or 0.04%.

In a 91-week dermal study in which CD-1 mice were administered 0.017% and 0.035% formulations of tretinoin, cutaneous squamous cell carcinomas and papillomas in the treatment area were observed in some female mice. These concentrations are near the tretinoin concentration of the 0.04% and 0.1% clinical formulations. A dose-related incidence of liver tumors in male mice was observed at those same doses. The maximum systemic doses associated with the administered 0.017% and 0.035% formulations are 0.5 and 1.0 mg/kg/day tretinoin, respectively. These doses are two and four times the MRHD based on BSA comparison.

The biological significance of these findings is not clear because they occurred at doses that exceeded the dermal maximally tolerated dose of tretinoin and because they were within the background natural occurrence rate for these tumors in this strain of mice.

There was no evidence of carcinogenic potential when 0.025 mg/kg/day of tretinoin was administered topically to mice (0.1 times the MRHD based on BSA comparison). Studies in hairless albino mice suggest that concurrent exposure to tretinoin may enhance the tumorigenic potential of carcinogenic doses of UVB and UVA light from a solar simulator. This effect has been confirmed in a later study in pigmented mice, and dark pigmentation did not overcome the enhancement of photocarcinogenesis by 0.05% tretinoin. Although the significance of these studies to humans is not clear, patients should minimize exposure to sunlight or artificial ultraviolet irradiation sources *[see Warnings and Precautions]*.

The genotoxic potential of tretinoin was evaluated in the Ames assay and in the in vivo mouse micronucleus assay, both of which were negative.

The components of the microspheres have shown potential for genetic toxicity and fetal malformation. EGDMA, a component of the excipient acrylates copolymer, was positive for induction of structural chromosomal aberrations in the in vitro chromosomal aberration assay in mammalian cells in the absence of metabolic activation, and negative for genetic toxicity in the Ames assay, and the in vivo mouse micronucleus assay.

In oral fertility studies in rats with tretinoin, the no-observable effect level was 2 mg/kg/day (19 times the MRHD based on BSA comparison).

PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Patient Information).

Manufactured for:
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

By:
Valeant Pharmaceuticals International, Inc.
Laval, Quebec H7L 4A8, Canada

Based on 9612500 October 2017 RAM.0025.USA.17

MORE PATIENTS THAN EVER. RETIN-A MICRO 0.06% gives you more treatment options for your patients, with microsphere technology and pump-controlled dosing.[1]

SEE TOLERABILITY AND EFFICACY RESULTS AT **RETINAMICRO.COM**

INDICATION

RETIN-A MICRO (tretinoin gel) microsphere is indicated for topical application in the treatment of acne vulgaris.

IMPORTANT SAFETY INFORMATION

- The skin of certain individuals may become excessively dry, red, swollen or blistered during the use of RETIN-A MICRO.
- Tretinoin has been reported to cause severe irritation on eczematous skin and should be used with utmost caution in patients with this condition.
- If warranted, patients should temporarily reduce the amount or frequency of application, or discontinue use temporarily or altogether. If a reaction suggesting sensitivity occurs, use should be discontinued.
- Unprotected exposure to sunlight, including sunlamps, should be minimized during the use of RETIN-A MICRO, and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight with the use of tretinoin.
- Patients should be encouraged to use a sunscreen with a SPF of 15 or higher and protective clothing over treated areas when exposure cannot be avoided.
- Weather extremes, such as wind or cold, also may be irritating to patients under treatment with tretinoin.
- The most common adverse events are mild to moderate irritation (erythema, peeling, dryness, burning/stinging, or itching of the skin).
- RETIN-A MICRO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus, and caution should be exercised in prescribing for nursing mothers. Safety and efficacy in patients under 12 have not been established.

To report SUSPECTED ADVERSE REACTIONS, contact Ortho Dermatologics at 1-800-321-4576 or FDA at 1-800-FDA-1088 or visit www.fda.gov/medwatch.

Please see Brief Summary of full Prescribing Information on the following page.

Reference: 1. Retin-A Micro Gel Package Insert. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC.

Ortho | Dermatologics

RETIN-A MICRO®
(tretinoin) Gel microsphere
0.06% / 0.08%