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JDPA

Journal of Dermatology for Physician Assistants

Official Journal of the Society of Dermatology Physician Assistants

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Journal of Dermatology for Physician Assistants

The official journal of the Society of Dermatology Physician Assistants

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DIGITAL

The SDPA Board of Directors is pleased to announce the launch of SDPA Digital 2020!

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THANK YOU for your continued support and we look forward to having you join us online for **SDPA Digital 2020!**

Alleviate Your Stress by Giving to Others and Reap All the Benefits of "Helper's High"

It goes without saying that living through a pandemic has been a bit crazy. Okay, "a bit crazy" may be an understatement. We have been forced to accept drastic changes in both our personal and professional lives—two worlds that are now converging as we all continue to face the most unpredictable situations. Professionally, many individuals, including fellow physician assistants (PAs) have felt the strain of the pandemic through layoffs, furloughs, reduced work hours, and changes to contracts that often occur without benefit of negotiation. Health care providers continue to work long hours without proper personal protective equipment and others are cautiously navigating resumption of in-person patient visits. Personally, many are still feeling the impact of school closures, weighing childcare options that will provide the safest environment and ultimately wondering what, if anything, is in fact "safe." It is obvious that the impact of COVID-19 is far reaching, and as the fear of contracting the virus continues to loom in the back of our minds, another dangerous health threat is rising—our stress levels.

The American Psychological Association (APA) warns the negative mental health effects of the coronavirus will be serious and long-lasting, and recent data support this. In their annual poll Stress in America™, which was adapted this year to address the unique stressors of 2020 thus far and aptly subtitled, "Stress in the Time of COVID-19," the APA shows that not only are individuals experiencing considerable stress related to the coronavirus, they are also reporting higher levels of general stress. The jump in average reported stress levels from 2019 to 2020 marked the first significant increase since the survey began in 2007.

So, how can we cope with higher than average, sometimes off-the-chart levels of stress, and how can we alleviate it across different aspects of our daily lives? One word—give.

While everyone reacts differently to stressful situations and methods for finding relief are largely based on personal preference (i.e., not everyone finds that meditation, journaling, listening to music are the best pathways to stress relief), giving is a universal stress reliever backed by science. Being altruistic, whether it be giving your time, money, or energy to help others in need, can translate to real benefits for mind, body, and spirit. Research has shown that "gift-giving behavior" stimulates secretion of "feel good" chemicals in the brain, such as serotonin, dopamine, and oxytocin, leading to what is often referred to as "helper's high." Studies also show that doing good deeds, even small acts of kindness, such as holding the door for someone or donating goods, is associated with myriad potential health effects, including reduction in blood pressure, chronic pain, and depression. In addition, giving has the power to boost your sense of well-being, purpose, and personal satisfaction. All these benefits translate to potentially living a longer, happier life.

Opportunities to give are everywhere.

Monetary donations are always appreciated and can help charities achieve important missions. For instance, monetary contributions made to the Dermatology PA Foundation (DPAF), the official foundation of the Society of Dermatology Physician Assistants (SDPA), fund research, scholarships, educational activities, and philanthropy designed to improve the practice of dermatologic patient care by PAs and other medical professionals. Such organizations also offer ways in which to get involved through volunteering your time and expertise. As a Derm PA, you might consider volunteering at a free clinic performing skin cancer screenings or giving back to your profession by participating in a preceptorship, directly helping to training the next generation of physician assistants.

Look no further than your own neighborhood and circle of friends/family for even more opportunities to help others. Call or video chat with someone who might be feeling lonely. Ask a neighbor if you can give them a ride to or pick up some items at the grocery store. Suggest trading childcare duties with someone so you can each get out to get errands done efficiently. Some other ideas: Grow vegetables and give away the extra, foster animals for the local shelter, bake some cookies for a neighbor.

If all that still seems like too much considering your resources, then just give a smile (a full smile with the eyes so everyone knows you are smiling behind the mask). Compliments are free and can make someone's day. Tell a passerby you love their hair style, the color of that shirt, or that cool mask. It just feels so good to give from the heart. For our part, we will continue to deliver stellar content that enhances and celebrates the Derm PA profession.

I hope you enjoy this latest issue.

Regards,

Jennifer Winter, MSPAS, PA-C
JDPA Deputy Editor
jdpa@dermpa.org

ANNOUNCEMENTS…

Call for Contributors!

INTERESTED IN GETTING MORE INVOLVED IN THE PEER-REVIEW PROCESS?

JDPA is currently seeking applications for Department Editors and Editorial Advisors! Review responsibilities below and apply today!

Send your application to jdpa@dermpa.org

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Department Editors possess a high degree of expertise in their specialty and are appointed to ensure the journal is providing its readers with accurate coverage of their specialty. Department Editors may be called upon to solicit content on suitable topics for their respective departments, recommend reviewers, and complete formal peer-review on any submissions that fit under their department.

Primary Responsibilities.....

- ✓ Provide insight for department, suggesting specialty topics and potential authors.
- ✓ Peer-review all article submissions that fit within their department/area of expertise.
- ✓ Guide the Editor-in-Chief and Managing Editor in categorizing accepted content pieces into the journal's dedicated departments and/or article types.
- ✓ Act as an ambassador for the journal, continuously seeking new ways to enhance communication about the Derm PA profession to the readership and larger medical community.
- ✓ Generate ideas to further improve the volume and quality of submissions.
- ✓ Commission content and field submission enquiries as appropriate
- ✓ Write one special correspondence, "Message from the Department Editor," explaining the current state of the specialty, to be published in the journal.

Term Length.....2 Years

How to Apply: Send 1) a brief vision statement detailing how you hope to contribute in the desired position, 2) your areas of expertise ordered by preference; and 3) your current curriculum vitae

EDITORIAL ADVISORS

Relied upon to be JDPA's content referees, Editorial Advisors, also called "peer reviewers," play a key role in contributing to the quality, the value, and even the reputation of science published in the journal. Editorial Advisors are invited to join the Editorial Advisory Board by the Senior Editors and, upon acceptance, commit in advance to provide peer reviews for submissions that fall within their designated area of expertise.

Primary Responsibilities.....

- ✓ Peer review article submissions that fit within their area of expertise as assigned by the Managing Editor
- ✓ Assist the Senior Editors in decision making over issues such as plagiarism claims and incongruous reviews to reach final decisions.
- ✓ Act as an ambassador for the journal, continuously seeking new ways to enhance communication about the Derm PA profession to the readership and larger medical community.
- ✓ Generate ideas to further improve the volume and quality of submissions.
- ✓ Commission content and field submission enquiries as appropriate
- ✓ Identify topics for special issues and supplements, which they may guest edit.
- ✓ Submit one article for publication consideration during their term.

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Note: Department Editor and Editorial Advisor positions are volunteer; individuals will not be compensated monetarily.

LETTER TO THE EDITOR

Teledermatology during COVID-19 Allows Patient Connections and Continuity of Care

"Compassion is the greatest form of love humans have to offer." - Rachel Joy Scott

March 23, 2020:

As I signed into my first day of teledermatology from my small but quaint Manhattan apartment, in the middle of what would quickly become the epicenter of COVID-19, I did not know what to expect. In the week and a half leading up to this there was a palpable anxiety in the air due to a multitude of unknowns. So many of my colleagues were getting furloughed, working reduced hours, or given the choice of unemployment. My first day of telemedicine was a pleasant surprise. The very first patient was so extremely thankful and happy to be on a call with me and to be interacting in a time of social isolation that both of us were laughing by the end of the visit. Another patient and I shared tips on staying active and stress relief. I asked each of them about their mental health and vice versa. This seemed to happen repeatedly throughout the days and weeks to follow.

In a time where we have become so technologically advanced, in some ways we have all been so disconnected. I recall days in the office when I was seeing patients in busy Midtown Manhattan. I noticed so many of them staring into their phone screens, seemingly unphased that they were in a medical care setting, tethered to technology even while undergoing a procedure. Patients were often in a rush, managing the hustle and bustle of New York City and quickly stepping out for an appointment during their lunch break or squeezing it into their busy days. I recognize that technology has its benefits, but the unfortunate side effect of multi-tasking to stay constantly connected, from my observations, is, ironically, disconnection. When distracted by technology, people just aren't able to be fully present and give their full attention to personal interactions taking place.

As I went through my first day of telemedicine, I quickly felt the difference this pandemic has made. People were more compassionate. As a care provider, I found I had a little more time in my schedule to dedicate to remote appointments. I also noticed that patients, not as distracted by texts, emails, and social media pop ups on their phones, were more present. I had multiple conversations with patients throughout the day and noticed that each one included mutual, sincere expressions concern for how the other person was feeling. My patients were excited to be video chatting with me after spending days in isolation, especially those living alone in a city that thrives on social interaction. I found that the remote visits seemed to offer an extra outlet for in-person communication, a sufficient substitute during this unique and often lonely time. The benefit of technology usage in dermatology is that, since the skin is a visual organ, we can easily see and often evaluate conditions such as acne, eczema, pigmentation, rashes, and rosacea through pictures and video.

Of course, telemedicine cannot fully replace an in-person dermatology visit since most of what we do includes touching the affected area, seeing skin up close and many times, performing procedures. Now that I have been using this newer technology for a few months, I've identified some major takeaways as to how this will impact the future of our practice as well as how to make sure our patients are getting the best care possible.

Key Takeaways from TeleDermatology Visits in Pandemic Times

For the patient:

- Schedule the visit during a time you are likely to have minimal distractions
- Have a list of symptoms and, if possible, recent quality photos ready. These can be sent via an app or directly to the provider's email prior to the visit
- Be prepared to discuss your medical history and have a list of current medications handy
- Try to sit in the best lighting possible so the provider can see the area that is affected.
- Consider using a pharmacy that will ship medications directly to your home.
  - Previously only a service offered by specialty pharmacy, other pharmacies now ship prescriptions in response to COVID-19. Call your preferred pharmacy to ask if they offer delivery and don't forget to ask if there is an extra cost associated (e.g., shipping fee)
- Follow up with your provider if you have concerns after the visit. Make a follow-up teledermatology appointment if necessary.
- Remove makeup and tie back hair if affected area is on the face or neck
- Have all skincare products available or written down if you want to discuss a skincare routine
- Have a list of past treatments, making note of what products (prescription and over the counter [OTC]) did and did not seem to help in treating your condition or achieving other desired results

For the provider:

- Try to look at our response to delivering patient care during the COVID-19 pandemic as an opportunity that allows us to change the scope of our practice.

- Directing patients to use the clinic's remote care services could improve in clinic operations

- For example, conducting cosmetic informational consults over the phone and scheduling procedures ahead of time might help day-to-day patient care run more smoothly and efficiently.
  - Providing remote health services allows us to extend continuity of care to patients who find it inconvenient to travel to the office for an in-person appointment.
- For example, some patients live far from or have a difficult commute to the office location. Others are not able to break from work or other personal responsibilities to attend an appointment in person.
  - We can structure our days differently to provide optimal productivity based on patient needs
- Be aware of any issues that may arise with insurance coverage and prepare to handle them.
  - For example, put procedures in place with pharmacies regarding switching medications for coverage.
- Prepare to "see" your teledermatology patients as you would in clinic – thoroughly review the patient chart and check for any patient communication, such as e-mail or voicemail, prior to the scheduled appointment as this will help optimize time and care provided.

In closing, I see teledermatology as a way to connect with our patients during this time of social distancing and allow for continuity of care. As much as we all want to get back into the office, I think this option allows our patients to continue treatment with us. I believe that having this additional tool in our toolbox will only strengthen our abilities as providers and this will remain an option in the years to come. I hope you are experiencing the same laughter and compassionate banter with your patients via teledermatology that I have been enjoying.

Ami Dalal, MS, PA-C
Schweiger Dermatology Group
New York, New York

Ms. Dalal *is a certified physician assistant at Schweiger Dermatology Group in New York, New York. She has extensive training in medical dermatology, cosmetic dermatology, and laser surgery and has been practicing in medicine for over 13 years. She specializes in skin of color, hair loss, and anti-aging.*

Disclosures: *The author has disclosed no potential conflicts of interest, financial or otherwise, relating to the content of this article.*

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Call for Applications: DPAF 2020 Research Grant Program

Do you have a great research idea that would benefit dermatology education and/or clinical practice?

In conjunction with Sun Pharmaceutical Industries, The Dermatology PA Foundation (DPAF) is proud to announce the 2020 DPAF Physician Assistant Research Grant Program Funding Opportunity.

Have a Great Research Idea?

Follow these steps to turn your idea into a competitive grant applicaton!

The DPAF Physician Assistant Research Grant Program provides funding for research that examines the impact of dermatology PAs on patient outcomes and is consistent with at least one of DPAF's seven priority goals. The program is intended to increase scholarly activity among dermatology PAs and PA educators.

More information is available on the DPAF website. Applications are due October 1, 2020.

Have questions or unsure where to start?
Contact us at research.grants@dermpafoundation.org

CALENDAR OF EVENTS

2020

ALERT: Due to the coronavirus (COVID-19) pandemic, many medical organizations have made the difficult decision to cancel or postpone planned live events. Please refer to meeting host websites for more information.

AUGUST

A Virtual Day with Dermoscopy—Online Live CME Workshop *hosted by California Dermatology Physician Assistant Society (CDPAS)*
August 29, 2020
https://www.caldermpasociety.com/2020-dermoscopy-course-updated.html

SEPTEMBER

12th Annual Dermatology PEARLS—Virtual Online Live Conference *hosted by Georgia Dermatology Physician Assistants (GDPA)*
September 10-12, 2020
https://www.gadermpa.org/dermatology-pearls-conference

Skin of Color Update 2020—Live Virtual
September 12-13, 2020
https://skinofcolorupdate.com/

OCTOBER

"Keystone Dermatology Conference—Live and Virtual"
hosted by Pennsylvania Dermatology Physician Assistants (PDPA)
October 8-10, 2020
The Logan Hotel
Philadelphia, PA
https://www.padermpa.org/keystone-derm-2020.html

SDPA Annual Fall Dermatology Conference-- SDPA Digital 2020
October 29-November 1, 2020
http://www.dermpa.org

FROM THE PRESIDENT'S DESK:

Allowing Growth from the Changes that Surround Us

The past few months have taught me that the only thing constant is change. The COVID-19 pandemic has tested all of our limits. Many of you, like me, have become overnight homeschool teachers in addition to working full-time clinical hours. We have learned the basics of telemedicine and put them swiftly into practice. We have implemented recommended health and safety precautions in hopes of "flattening the curve." We have even witnessed a change in our words—"social distancing," "community spread," and "contact tracing," are all now part of our pandemic lexicon.

Life as we have known it has dramatically changed within a few short months. We have all been given a crash course in change. We have learned that the quicker we can adapt to change, the more resilient we become.

One example of adapting to drastic change can be seen in the community PAs who served and continue to serve on the frontlines amidst the pandemic. The SDPA has highlighted a few of our DermPA colleagues who had previous expertise in hospitalist medicine and chose to answer the call to be first responders in this pandemic. I want to take this moment to thank every healthcare provider, especially PAs, who provided and continue to provide aid in a time of crisis. I applaud you for meeting the challenge head on and answering with the courage to provide patient care in the most difficult circumstances.

As we approach the second half of the year, change continues to be a main theme in 2020, and the recent call for action to end racial injustices within our society is a welcome one. I want to acknowledge all the PAs who have stood together nationwide to participate in the White Coats for Black Lives (WC4BL) marches. Bringing awareness to racial injustices is an important first step on the road to racial equality. Racism has no place anywhere and I stand in solidarity against all racial injustices a nd inequalities.

We as a society have also adeptly adapted to change. Due to the ongoing COVID-19 pandemic, the Board of Directors recently decided to transform our in person Fall Conference to a digital format. While we had sincerely hoped to see you in Miami, the health and safety of all in attendance takes precedence. But make no mistake, we will still be delivering the same high-quality, interactive education for which we are known. Except this time, we will be utilizing an innovative virtual platform to deliver it. I welcome you to join us this year to experience "SDPA Digital."

In closing, I am reminded of the words of a well-known leadership author, John C. Maxwell, who said, "Change is inevitable, growth is optional." Let's join together and allow the change that surrounds us to grow us. Thank you for the opportunity to serve as your President. I look forward to the year ahead and all we can accomplish together for our patients and our profession.

With you and for you,

Archana Sangha, MMS, PA-C
President SDPA

Alopecia Areata: A Review of Clinical Presentation, Diagnosis, and Treatments

By Shelby Saltsman, PA-C and Mallory M. Aycock, MPA, PA-C

ABSTRACT

Alopecia areata (AA) is an autoimmune condition characterized by patchy hair loss, typically occurring in a circular pattern, that can affect the scalp, eyebrows, eyelashes, and body hair. AA is a highly unpredictable and variable condition that occurs in approximately two percent of the population. It can be associated with psychological distress in patients affected. Common treatments for AA include intralesional, topical, and systemic corticosteroids, topical immunotherapy, and a newer class of medications called Janus kinase (JAK) inhibitors. JAK inhibitors have shown promising results in clinical trials and represent an exciting development in the treatment for AA. This article reviews the clinical manifestations, diagnosis and monitoring, guidelines for management, and emerging pharmacologic treatment of AA.

» 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 July 2020. 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 post-test at https://www.dermpa.org/JDPA_Exams

Learning Objectives:

1. *Discuss the pathophysiology and incidence of alopecia areata.*
2. *Identify signs and symptoms of alopecia areata.*
3. *Discuss diagnostic tests, treatment options, and treatment efficacy for alopecia areata.*
4. *Review current research concerning the efficacy, safety, and feasibility of Janus kinase (JAK) inhibitors in the treatment of alopecia areata.*

INTRODUCTION

Alopecia areata (AA) is a T-cell mediated autoimmune disorder that causes patchy areas of recurrent, non-scarring hair loss and can affect the scalp, eyebrows, eyelashes, and body hair.[1] AA occurs in approximately two percent of the population, and the prevalence of AA is equal amongst all races and genders. Onset of AA typically occurs between ages 15 and 29, with onset after age 40 being uncommon.[1] The presence of AA carries an increased risk of associated thyroid disease, atopic dermatitis (AD), vitiligo, and systemic lupus erythematous.[1] AA is a highly unpredictable condition that can cause psychological distress to the patient. However, hair regrowth typically occurs within a year for most patients and less than 10 percent of patients experience extensive alopecia.[1]

PATHOPHYSIOLOGY

Sites of hair follicles in a healthy scalp have a low expression of major histocompatibility complex (MHC) Class I and Class II and decreased activity of a certain type of leukocyte called a natural killer (NK) cell.[1] These properties of the follicle sites, among other features, make them inherently exempt from the attack of the body's immune system. The regulation of immunity at the site of the hair follicle occurs through the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) signaling pathway, which comprises a cytokine receptor, JAK (an enzyme), and a signal transducer and activator of transcription (STAT).[1]

In patients with AA, there is a flaw in the signaling of the JAK-STAT pathway resulting in an increase in MHC Class I expression and/or a decrease in the suppression of NK cells that renders the hair follicle

susceptible to attack from the immune system.[1] Patients with AA have an increase in the level and activity of pro-inflammatory cytokines which has been demonstrated by the presence of increased interleukin-6 (IL-6), IL-15, IL-17, and interferon-gamma (IFN*γ*) levels in the serum of AA patients.[2] Patients with AA also show an overexpression of the JAK enzymes JAK1, JAK2, and JAK3 in scalp biopsies.[2]

CLINICAL PRESENTATION

AA presents as discrete patches of non-scarring hair loss typically located on the scalp, though it can occur on any hair-bearing site. Patients with active disease may have a positive "hair-pull test," typically at the periphery of the patch of hair loss, that shows "exclamation point" hairs.[3] The "hair-pull test" is performed by grasping and gently pulling 50 to 60 hairs in the affected area then counting the number of hairs that were removed from the scalp. If 10 percent or more (about 6) of the hairs were removed, then the test is considered positive.[4] Exclamation point hairs are tapered at the base closest to the hair follicle and are pathognomonic for the diagnosis of AA.[3] Patients with AA may also present with the "yellow dot sign," which represents dead keratinocytes in the hair follicle and can be considered the most sensitive and most common clinical characteristic of AA.[3] The center of these yellow dots typically contain dystrophic hairs that appear as black dots on trichoscopy.[3]

Typically, patients are asymptomatic. Some patients report scalp burning, stinging, or tingling on the scalp that precedes loss of hair.[5] Nail dystrophy is seen in 10 to 20 percent of patients with AA and corresponds to increased disease severity. Nail defects include nail pitting and fragility of the nail.[5]

DIAGNOSIS

AA can be diagnosed on the basis of clinical presentation and does not require a biopsy;[3] however, punch biopsies are often performed to confirm a diagnosis. Histopathological evaluation of a scalp biopsy in AA shows multiple features, including a peribulbar lymphocytic infiltrate, miniaturized hair follicles, peribulbar inflammation, fibrovascular stelae, and pigment casts, which represent malformed pieces of hair.[6,7] There is not one specific histopathologic feature that defines AA; instead, it is a constellation of possible features that leads the pathologist to the diagnosis. Often, the appearance of the specimen differs based on the phase of disease. The acute stage is characterized by increased bulbar lymphocytes encompassing terminal hair follicles and miniaturized follicles.[7] In the subacute stage, there is a decrease in the number of hairs in the anagen phase, which is the growth phase of the hair cycle.[7] There is also an increase of hairs in both the catagen and telogen phases, which are the transitional phase and resting phase of the hair cycle, respectively.[7] After active disease is over, biopsies show resolution of peribulbar inflammation and multiple hairs in the anagen phase, representing regrowth of new terminal hairs.[7]

Trichoscopy involves visualizing the scalp with dermoscopic views and can be done with a small handheld device called a dermatoscope. Trichoscopy can also be used to follow patients during treatment and assess response.[3] The Severity of Alopecia Tool (SALT) score can also be used to assess disease severity. This score is determined by dividing the scalp into four segments, each considered 25 percent of the scalp, and evaluating the percentage of hair loss in each area.[1]

TREATMENT

There are no United States Food and Drug Administration (FDA)-approved treatments for AA, though several treatment options are commonly used by clinicians. Intralesional steroid injections, typically with triamcinolone acetonide 2.5 mg/mL to 10 mg/mL, are the initial treatment intervention for AA.[8] Steroids are used to reduce inflammation at the site of the hair follicles in patients with AA.[8] Injections are typically given every 4 to 6 weeks and often take two or three treatments to begin observing a response.[8] Injections are typically avoided in young children under the age of 10 years old.[8]

Topical steroids are considered less effective than intralesional or systemic steroids, with only 30 to 50 percent of patients seeing clinical improvement with recommended use.[8] Typically, a class 1 steroid is used with or without occlusion to increase the level of scalp penetration.[8] Topical steroids work slowly and may take six months to see any improvement in hair regrowth. Furthermore, relapse rates of up to 63 percent have been reported in studies on topical steroid use in AA.[8]

The use of short courses of systemic steroids like prednisone are often used in cases of more severe AA but also show high rates of relapse after treatment cessation.[8] Systemic steroids have been shown to be much less effective in very severe forms of AA, such

as alopecia totalis (AT) or alopecia universalis (AU).[8] Additionally, due to the high number of serious adverse effects of long-term systemic steroid use, prednisone is not a reasonable long-term option for the treatment of AA.[8]

With topical and intralesional steroid use, the patient must be monitored for the development of adverse effects, including skin atrophy, hypopigmentation, striae, telangiectasias, folliculitis, and steroid-induced acne.[8] Systemic steroids have higher risks of more serious side effects such as hyperglycemia, diabetes, hypertension, weight gain, insomnia, avascular necrosis, and mood changes.[8]

Topical minoxidil 5% is typically used as an adjunct therapy for AA and should not be considered as an option for monotherapy.[8] Minoxidil works to promote growth of the hair that has not been lost in the disease process, however, it can take six months or more before any results are observed.[8] Potential side effects include irritation and allergic reaction.[8]

Topical sensitizers such as diphenylcyclopropenone (DPCP) or anthralin are typically used in refractory cases of AA.[8] DPCP works by creating an allergic response on the skin that initiates an immune response and results in hair regrowth.[8] Studies show roughly 60 percent of patients respond to treatment with DPCP. Cessation of treatment can result in return of hair loss.[8] Adverse effects of DPCP include severe reactions that involve blistering, vesicles, lymphadenopathy, and alteration in skin pigmentation.[8] Anthralin is a topical that can be used in AA to create an irritant dermatitis to stimulate hair regrowth.[8] However, studies on the efficacy of anthralin treatment on AA show a wide variation in proposed responses that range from 25 to 75 percent.[8]

Literature suggests serum levels of vitamin D are lower in patients with AA.[9] Furthermore, patients who have had AA for a longer period of time had significantly lower serum levels of vitamin D and were more likely to be diagnosed with vitamin D deficiency.[9] Treatment of AA with topical calcipotriol, a vitamin D analogue, has shown efficacy as an alternative treatment for mild to moderate AA.[10]

JAK inhibitors are a new development in the future of AA treatment. JAK inhibitors work by inhibiting different JAK enzymes, including JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2). This group of tyrosine kinases play a role in signal transmission needed for immune cell function, making them key players in a variety of autoimmune conditions, including AA.[1] JAK inhibitors that are currently being studied for use in AA include ruxolitinib, tofacitinib, and baricitinib. Treatment with oral ruxolitinib resulted in 75 percent of participants achieving the primary outcome of 50-percent regrowth. Those that were responders also exhibited a 92-percent reduction in hair loss from baseline and regrowth was seen as soon as four weeks after initiation of treatment.[11] Treatment of AA with oral tofacitinib citrate resulted in best responses in those with "shorter duration of disease and histological peribulbar inflammation on pretreatment scalp biopsies."[12] Oral preparations of JAK inhibitors have shown much more promising effects on hair regrowth than topical preparations.[1] The adverse effects of oral JAK inhibitor treatment of AA in clinical studies have overall been mild and brief, with the most common complication being an upper respiratory infection.[1] Studies have shown that termination of treatment typically results in recurrence of hair loss, although shedding often does not reach baseline levels. This may indicate that treatment of AA with JAK inhibitors would need to be lifelong, though these data do not yet exist.[1] Overall, JAK inhibitors are a promising development in AA treatment considering there have been no FDA-approved treatments to date.

Scalp prostheses, such as toppers and wigs, can be used to hide hair loss in patients with AA who do not respond adequately to treatment. Oral disease-modifying antirheumatic drugs (DMARDS) such as methotrexate, sulfasalazine, and cyclosporine have been used to treat AA effectively in some patients.[8] Platelet-rich plasma (PRP) injections are a newer treatment option that have shown some improvement in hair regrowth in AA. However, the high cost burden of this procedure is a considerable barrier to treatment for many patients.[8] Furthermore, the majority of studies have focused on the effectiveness of PRP injections on androgenetic alopecia, not autoimmune-related hair loss such as AA.[8]

PROGNOSIS

There is variation in the prognosis of AA, as it is a very unpredictable disease that may progress, recur, or never recur after a single episode. A poor prognosis is associated with nail abnormalities, young age of onset, extensive hair loss, and the existence of comorbid autoimmune disease.[8] Overall, studies show anywhere from 40 to 70 percent of patients with AA in the limited-patch stage will have full hair regrowth.[8]

Patients with severe forms of AA such as AU and AT have been shown to have a full hair growth rate of only 17.1 percent after being followed for 10 or more years after onset of hair loss. Rates of cosmetically acceptable hair regrowth in the same study were slightly more favorable, with a total of 24.2 percent of patients achieving this outcome.[13]

The prevalence of anxiety and depression has been found to be higher among patients with AA when compared to controls.[14] This is an important consideration for clinicians who are treating individuals with AA. Many resources are available for those suffering from AA, including the National Alopecia Areata Foundation. There is no cure for alopecia areata.

CONCLUSION

AA is an unpredictable autoimmune condition that causes hair loss and affects people of all ages, sexes, and races. Alopecia areata results in intense emotional distress in the individuals and loved ones of those impacted by this disease. Modern medical advancements, including the use of JAK inhibitors, will hopefully enable providers to treat patients with AA much more effectively in the future.

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JDPA Grand Rounds

Seeing the big picture in a case of an "itchy rash and sore throat"

By Cynthia Faires Griffith, MPAS, PA-C and Sarah Jane Whinery, MPAS, PA-C

Abstract:

In this grand-rounds style presentation and discussion, readers are challenged to evaluate a clinical vignette and, based on the information provided, guess the diagnosis. The clinical vignette described here is from a real-world case seen at UT Southwestern Medical Center in Dallas, Texas.

The authors describe the case of a 37-year-old man who has sex with men who presented to a dermatology office with a skin rash. Prior to presenting to dermatology, the patient reported being treated by his primary care provider for a painless, nonpruritic rash that appeared on his trunk and back extending on the arms. He was prescribed oral prednisone for five days for presumed contact dermatitis. Two weeks later, the patient returned to his primary care provider reporting that the existing rash had worsened, spread to his legs and ankles, and was now pruritic. He also had new onset of sore throat. The patient's physical examination at dermatology revealed pink to erythematous urticarial, oval macules and papules on the chest with no involvement of the palms or soles. Physical exam also revealed neither lymphadenopathy nor oropharyngeal erythema, cobblestoning, exudate, or lesions. A biopsy of a representative lesion from the patient's right flank was done and was found to be sparse superficial infiltrate of lymphocytes and plasma cells. An immunohistochemical stain for *Treponema palladium* showed spirochetes in the epidermis and Periodic acid–Schiff staining revealed no fungal elements.

Clinical Vignette

A 37-year-old man who has sex with men presented to his primary care physician (PCP) with new onset of rash that started after the patient began wearing a new shirt with high-end fabric without pre-washing the shirt. The rash was described as painless and nonpruritic and was visible on the trunk and back, extending on the arms on the medial more than inner surface *(Figure 1 and Figure 2).* The patient did not use any new detergents or soaps that might have caused a skin rash. Aside from a friend visiting the patient's home with a dog and a cat, no pet exposures and no previous allergies to pets were reported. The patient did not present with and denied experiencing fever, chills, and lymphadenopathy.

Figure 1

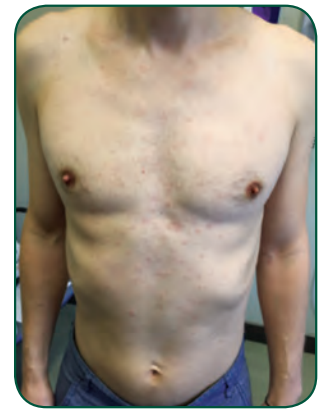
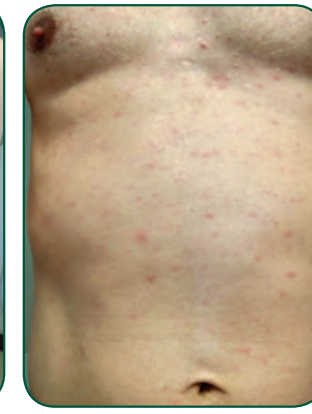


Figure 2



He was prescribed oral prednisone for five days for presumed contact dermatitis. Two weeks later, the patient returned to his PCP reporting that the existing rash had worsened. The rash had spread to his legs and ankles and was now pruritic. He also had new onset of sore throat that started approximately two weeks after the rash first appeared. He had diffuse muscle soreness for two days. He took over-the-counter ibuprofen and found it was semi-effective in treating the soreness. He reported a low-grade fever which maxed out at 99.5 °F. He initially suspected that the sore throat was from the change of weather. He tried using throat numbing spray, which he found to be ineffective in relieving the sore throat. He did not have a cough or sputum production. Along with complete medical history examined during the patient's visit with dermatology, reported symptoms included decreased appetite, weakness, malaise/fatigue, and muscle weakness.

The patient's physical examination at dermatology revealed pink to erythematous urticarial, oval macules and papules on the chest with no involvement of the palms or soles. Physical exam also revealed neither lymphadenopathy nor oropharyngeal erythema, cobblestoning, exudate, or lesions.

JDPA Grand Rounds QUIZ:

1. What is the most likely diagnosis for the cutaneous lesions described above?

A. Pityriasis rosea

B. Hand, foot and mouth disease

C. Scarlet Fever
D. Syphilis

2. Match the causative agent to the diagnosis

A. Spirochete	1. Scarlet Fever
B. Group A streptococcus	2. Syphilis
C. Coxsackievirus A16	3. Pityriasis Rosea
D. Herpesviruses 6 and 7	4. Hand Foot and Mouth disease

3. What are the other findings associated with this diagnosis?

A. Ear infections, throat abscesses, and pneumonia
B. Hair loss, neurologic changes
C. Painful, red, blister-like lesions on the tongue, gums and inside of the cheeks
D. No other findings associated with this diagnosis

Diagnosis

A biopsy of a representative lesion from the patient's right flank was done and was found to be sparse superficial infiltrate of lymphocytes and plasma cells. An immunohistochemical stain for *Treponema palladium* shows spirochetes in the epidermis. Periodic acid–Schiff (PAS) revealed no fungal elements.

We concluded that the patient's clinical picture and biopsy were compatible with the diagnosis of secondary syphilis. This case highlights clinical manifestations, diagnoses, and treatment considerations for this historic condition.

Keywords

Dermatology grand rounds, case report, secondary syphilis, pruritus, sore throat, differential diagnosis

Discussion

Syphilis is an infection cause by the bacterium *Treponema palladium,* an organism that was first identified in 1905. It is too slender to be visualized on direct microscopy, but it can be seen with dark field microscopy. It is shaped like a corkscrew.

Rates in the United States. In the later 1980s and early 1990s, there was a mini epidemic of early syphilis that produced cases higher than any time since the introduction of penicillin in 1943. The cases peaked in 1990 at 20.3 cases per 100,000 but subsequently fell 90 percent to a new low in 2000, and there were thoughts that syphilis could be eradicated.[1] However, the cases of primary and secondary syphilis increased and continued to increase every year from 2000 to 2018. By 2018, the overall number of reported primary and secondary syphilis cases was 35,063, which is the highest rate reported since 1993.[2] This rise was attributed to methamphetamine drug use and increased cases among men who have sex with men.

Transmission. Syphilis is a sexually transmitted disease. Transmission occurs by skin-to-skin contact with a syphilitic lesion called a chancre. T. palladium can also cross the placenta in a pregnant woman with syphilis, transmitting the infection to the fetus.

Clinical Manifestations & the Four Stages of Syphilis. The clinical manifestations depend on the stage of the disease.

Primary syphilis. The initial clinical manifestation is a chancre. The median incubation period before a chancre appears is 21 days (range of 3 to 90 days) from initial exposure.[3] A chancre appears at the site of exposure as painless papule that then ulcerates. There can be associated mild to moderate regional lymphadenopathy. Chancres, often unnoticed by patients, are self-limited and can heal spontaneously 3 to 6 weeks from emergence.

Secondary syphilis. Within 2 to 3 months or less, approximately 25 percent of untreated infections develop secondary syphilis.[4] This stage of syphilis has a wide variety of signs and symptoms, including constitutional, weight loss, fever, headache, malaise, sore throat, lymphadenopathy, gastrointestinal, hepatitis, musculoskeletal, renal, and ocular *(see Table 1).*

It is during this stage that the patient can develop symmetric pink, sometimes-subtle, macules and papules that can be scaly and appear on the trunk. This was the presentation in our patient *(Figure 1, 2).* Secondary syphilis also characteristically affects the palms and soles, however not in our patient. During this stage, patients can also present with a moth-eaten noncicatricial alopecia on the occipital scalp.

Untreated patients in early-stage syphilis can experience relapsing symptoms for up to five years.[4]

Tertiary syphilis. Approximately 25 to 40 percent of patients with untreated syphilis develop late disease. The timetable for presentation ranges from 1 to 30 years after exposure/infection. Clinical manifestations include cardiovascular, central nervous system, or gummatous (i.e., granulomatous) disease of the skin, subcutaneous tissues, bones, and organs.

Latent syphilis. Latent syphilis is positive serologic testing in the absence of symptoms.

Diagnostic Testing. There are two types of serologic testing for syphilis: Nontreponemal and treponemal.

Nontreponemal testing. Nontreponemal tests look at serum reactivity to cardiolipin-cholesterol-lectin antigen. While treponemal tests look for antibodies to the spirochete, nontreponemal tests detect biomarkers of cell damage done by the spirochetes. This is a nonspecific/indirect test that requires confirmation testing as it is not definitive. These types of serologic tests were previously used as screening tools due to low cost, ease of performance. Three nontreponemal tests are available in the United States:

• Rapid Plasma Regain (RPR)

Table 1

Secondary Syphilis Clinical Manifestations	
Generalized	Fever, headache, malaise, anorexia, sore throat, myalgias, weight loss, lymphadenopathy
Dermatologic	Diffuse symmetric pink macules and papules sometimes scaly Moth eaten alopecia on the scalp, eyebrows, beard
Gastrointestinal	GI tract ulcerations
Musculoskeletal	Synovitis, osteitis, periostitis
Renal	Mild transient albuminuria, nephrotic syndrome, acute renal failure, acute nephritis with hypertension
Neurologic/ocular	Headache, meningitis, stroke, uveitis, visual changes

- Venereal Disease Research Laboratory (VDRL)
- Toluidine Red Unheated Serum Test (TRUST)

These tests are qualitative meaning they measure the amount of immunoglobulin M (IgM) and immunoglobulin G (IgG), that are made by the body in response to cell damage early in infection as a crude marker of activity of infection. Positive tests are reported as a titer of antibodies in the serum. Titers will decrease over time regardless of treatment, but effective treatment accelerates the antibody decline. These titers are followed after treatment as a measure of therapeutic response.

Treponemal testing. Historically treponemal tests have been more expensive and difficult to perform than nontreponemal tests. As a result, treponemal tests have been used as a confirmatory rather than screening test for syphilis. However, more recently, treponemal tests have been simplified, automated, cheaper, and thus used more as an initial screening test for the syphilis infection. Specific treponemal tests include the following:

- Fluorescent treponemal antibody absorption (FTA-ABS)
- Microhemagglutination test for antibodies to T. pallidum (MHA-TP)
- T. pallidum particle agglutination assay (TPPA)
- T. pallidum enzyme immunoassay (TP-EIA)
- Chemiluminescence immunoassay (CIA)

These tests are qualitative meaning they are either reported as reactive or nonreactive. These tests are also usually positive for life and therefore not beneficial in diagnosis of syphilis in a patient with prior treated disease.

Testing limitations. Serologic testing to diagnose syphilis should include a treponemal and nontreponemal test. Use of one type of test (treponemal or nontreponemal) is typically not definitive for diagnosis, particularly the nontreponemal tests, which can show false-positive or false-negative results. Nontreponemal testing resulting in false-positive reaction has been associated with pregnancy, acute febrile illness, recent immunization, lupus, chronic liver disease, human immunodeficiency virus (HIV), and intravenous illegal drug use.[5] A false-negative nontreponemal test result can also occur as this relies on the humoral immune response, which can be compromised in patients with advanced immunosuppression or those in early or late stages of syphilis infection. For patients who present early in the course of disease (e.g., when ulcer and rash first emerge), serologic testing may be negative. If there is a high clinical suspicion for syphilis, presumptive treatment should be administered and then repeat serologic testing should be performed in 2 to 4 weeks. In late-stage syphilis, the nontreponemal tests can be falsely negative as the test can become nonreactive over time. False-positive treponemal tests can be seen with other spirochetal infection, malaria, and leprosy.6 If a diagnosis of neurosyphilis is being considered, additional testing of the patient's cerebrospinal fluid (CSF) should be performed.

Test Result Interpretations. ***Positive nontreponemal/positive treponemal test.*** A positive nontreponemal/positive treponemal test is reflective of a true-positive result and thus supports syphilis diagnosis. For patients without a history of syphilis, this is consistent with new infection and should be treated. If the patient has a history of past infection with syphilis, then the clinician should look at the nontreponemal titer. If this is elevated four times greater than post treatment titer (using the same nontreponemal test), then it is likely new infection.[9]

Positive nontreponemal/negative treponemal test. A positive nontreponemal/negative treponemal test outcome for syphilis is considered a false-positive result. The nontreponemal test will tend to be positive with a low titer in this case and this supports the false-positive conclusion. As stated previously, these false positives in the testing section are common with pregnancy, acute febrile illness, recent immunization, lupus, chronic liver disease, human immunodeficiency virus (HIV), and intravenous illegal drug use.[5]

Positive treponemal/negative nontreponemal test. A positive treponemal/negative nontreponemal test outcome is often an indicator of past incidences of syphilis that were successfully treated. If the patient has a history of treatment for syphilis infection, then no further evaluation or treatment is required unless there is concern for re-exposure. However, if the patient does not have a history of treated syphilis infection, current incidence could be either early- or late-stage syphilis when nontreponemal tests are nonreactive (i.e., false

negative). If the history and clinical presentation support early syphilis, treatment and continued monitoring of titers is prudent. If patient has symptoms of late syphilis, then further work up like lumbar puncture to evaluate for neurosyphilis are indicated. If no signs/symptoms are present, it is recommended that the clinician retest with a different treponemal test as another positive treponemal test result is consistent with the diagnosis of latent syphilis. A negative treponemal test at this late stage means that a false positive treponemal result was potentially caused by a different infection, such as malaria, leprosy, or other spirochete infection.[9]

Treatment

Penicillin. Benzathine penicillin G (BPG) administered by intramuscular (IM) injection is the treatment of choice for all stages of syphilis. If the patient is penicillin allergic, the recommended course of action is as follows: test for penicillin allergy and/or rechallenge with penicillin, desensitize to penicillin if allergy present, or use alternative agent with close post-treatment monitoring. Treatment for primary and secondary syphilis is a single dose of 2.4 million U of BPG IM; tertiary syphilis treatment regimen is three weekly doses of 2.4 million U of BPG IM.[7]

Alternative treatments. Alternatives treatments to penicillin along with recommended dosage include doxycycline (100 mg twice daily for 14 days), ceftriaxone (1 to 2 grams daily IM or IV for 10 to 14 days), tetracycline (500 mg four times daily for 14 days), and amoxicillin (3 grams with probenecid 500 mg, both given twice daily for 14 days).[7]

Treatment response is monitored by serologic re-testing. In general, a nontreponemal test result showing a four-fold decrease from original titers at 6 and 12 months and in tertiary syphilis 24 months indicate a positive response to treatment.

Clinical Vignette Continued

Treatment Course & Response. The patient was put on pre-exposure prophylaxis (PrEP) for HIV prevention and continues to be followed by infectious disease. Thirteen months before presenting at dermatology, a screening syphilis treponemal antibody test (TP Ab) showed a negative result. At that time, testing to detect presence of gonorrhea/chlamydia and HIV were also all negative. Seven months presenting to dermatology with the rash, he reported known exposure to syphilis, and, at that time, a urine test revealed the presence of T. pallidum antibodies. The patient's *T. pallidum* particle agglutination assay (treponemal test) was positive, though he had a negative RPR. The RPR was tested again two and four months later and remained negative. The patient reported penicillin allergy and was therefore treated with doxycycline 100 mg twice daily for 14 days. His RPR titer did not become positive during that time. He was sent for penicillin allergy confirmation/rechallenge and results showed he did not have a penicillin allergy. Two months later, he presented with worsening of the initial rash and dermatology proceeded with a biopsy. The skin biopsy confirmed a diagnosis of secondary syphilis. The patient's RPR was retested and was 1:128, indicating that the nontreponemal test supported the skin biopsy diagnosis of syphilis. He was treated with penicillin G 2.4 million U IM injection split dosed to 1.2 million U administered per buttock. Two months later, his RPR was 1:256 and he was treated with another round of penicillin G (2.4 million U split dosed to 1.2 million U administered per buttock). One month later, his RPR was 1:16. Three months later, RPR decreased to 1:4, signaling that the treatment of the syphilis was successful.

Clinical Aside

1. This patient never reported a chancre. Since chancres can be painless, occur in locations that make them difficult to notice (e.g., the vagina or anus), and heal without treatment in 3 to 6 weeks, they can easily go unnoticed by the patient. However, the absence of chancre(s) does not rule out the possibility of syphilis infection.

Syphilis: A Historical Aside

Origin. One popular hypothesis on the origin of syphilis states that the navigators in Christopher Columbus's fleet brought the affliction back to Europe on their return form the New World in 1493.

Famous Cases. Writers Oscar Wilde and Leo Tolstoy, philosopher Friedrich Nietzsche, painter Vincent van Gogh, composer Ludwig van Beethoven, Adolf Hitler, Al Capone, were among historical figures diagnosed or strongly suspecting of suffering with syphilis.

Treatment Evolution. Before penicillin was discovered and became the main treatment of syphilis, widely utilized remedies were largely ineffective and painful. Early treatments for syphilis included botanical concoctions made from the guaiac tree, also known as sasafras or willow and the administration of mercury in often toxic doses.

From M Tampa, I Sarbu, C Matei, V Benea, SR Georgescu. Brief history of syphilis. J Med Life. 2014 Mar 15; 7(1): 4–10. PMID: 24653750

2. This patient's clinical presentation was consistent with pityriasis rosea. Pityriasis rosea is a common erythemato-squamous dermatosis that is among the differential diagnoses for secondary syphilis. When pityriasis rosea is suspected, the treating clinician should order RPR or VDRL testing to rule out secondary syphilis diagnoses.

3. This patient's history showed positive treponemal test and persistently negative RPR for seven months before his rash presented. Prior to presenting at his PCP for a skin rash, the patient was treated with doxycycline 100 mg twice daily for 14 days for presumed syphilis diagnosis as he had a known exposure to syphilis, positive treponemal test, negative nontreponemal test, and no history of syphilis diagnosis/treatment. As his RPR never increased to show a positive result, it is possible that his clinical team concluded sufficient treatment the doxycycline regimen. We know from the final diagnosis of secondary syphilis that the patient could have been either insufficiently treated with the doxycycline or re-infected, thus causing symptoms and a different RPR result (positive) months later. This underscores the importance of diligence in continued monitoring of the RPR titers after treatment. After this patient's treatment with penicillin, his RPR continued to rise and he was given another dose of penicillin.

4. This patient reported a penicillin allergy. Reported penicillin allergy has been found to be associated with a 14-percent increased risk of death due to inadequate antibiotic treatment. When allergy tested, 95 percent of adults with a recorded penicillin allergy are found to be penicillin tolerant when re-tested/re-challenged.[8]

JDPA Grand Rounds Quiz Answer Key:
1) D; 2) A,2; B,1; C,4; D,3; 3) B

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The official journal of the Society of Dermatology Physician Assistants

JOURNAL OVERVIEW

The *Journal of Dermatology for Physician Assistants* (*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 being accepted for publication. Manuscripts submitted for publication are reviewed with the understanding that they are original and have neither been submitted elsewhere nor are being considered by other journals. Electronic submissions are accepted and should be sent to jdpa@dermpa.org.

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The *Journal of Dermatology for Physician Assistants* (*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.

Manuscripts that meet our editorial purpose include, but are not limited to, original research pertaining to the field of dermatology and/or physician assistant education and practice, review articles on dermatological conditions and their treatments, case reports and studies, clinical pearls related to surgical and/or cosmetic procedures, commentaries on published literature, opinion essays on current issues, and letters to the editor.

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The main departments featured in *JDPA* are as follows:

- Clinical Dermatology
- Cosmetic Dermatology
- Dermatology PA News & Notes
- Professional Development
- Surgical Dermatology

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Reference Formatting Guide

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Journal article with more than 5 authors
Lim HW, Collins SAB, Resneck JS Jr, et al. The burden of skin disease in the United States. *J Am Acad Dermatol*. 2017 May;76(5):958-972.e2. Epub 2017 Mar 1.

Authored book
Griskey RG. *Transport Phenomena and Unit Operations*. Hoboken, NJ: John Wiley & Sons, Inc.; 2005.

Edited book
Cleophas TJ. *SPSS for Starters and 2nd Levelers*. 2nd ed. 2016. (Zwinderman AH, ed.). Cham: Springer International Publishing; 2016.

Book chapter
Worbs T, Förster R. T Cell Migration Dynamics Within Lymph Nodes During Steady State: An Overview of Extracellular and Intracellular Factors Influencing the Basal Intranodal T Cell Motility. In: Dustin M, McGavern D, eds. *Visualizing Immunity. Current Topics in Microbiology and Immunology*. Berlin, Heidelberg: Springer; 2009:71-105.

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Melanona and Parkinson's Disease Treatment

Francesca Wolfe, PA-C and Kiera Kelleher, BS

ABSTRACT

Many studies have established a lower overall cancer risk in people with Parkinson's disease; however, the occurrence of melanoma is higher in patients with PD than in the general population. The relationship is reciprocal; patients with melanoma are at increased risk for Parkinson's disease. Here, we describe the case of a patient who developed multiple malignant melanomas after being on a combination of medications used to treat Parkinson's disease and discuss the relationship between major drugs used in the treatment of Parkinson's disease and the development of malignant melanoma.

KEYWORDS

Parkinson's disease, melanoma, treatment, rasagiline, levodopa, carbidopa

INTRODUCTION

Parkinson's disease (PD), a progressive movement disorder that affects the nervous system, is prevalent, affecting more than 10 million people worldwide and around 1 million in the United States. Increasing age remains the largest risk factor in developing PD, and about one percent of the elderly population, defined as individuals 60 years of age or older, live with PD in the United States. Although many studies have established a lower overall cancer risk in people with PD, the risk of melanoma is higher in patients with PD than in the general population, and vice versa.[1] In fact, researchers have observed a two-fold increased risk of developing malignant melanoma in individuals with PD compared with the general population.[2] While epidemiological studies have evaluated the association between PD and melanoma, there is still more to discover.

As of recent years, one major area of study has focused on the connection between malignant melanoma and medications used to treat PD. The most frequently used medication for the treatment of PD symptoms is the combination levodopa-carbidopa. Speculation surrounding levodopa's role in increased risk of melanoma first started in the 1960s, when some reports linked an occurrence of malignant melanoma with the use of this medication. Studies have since been inconclusive, demonstrating that the occurrence with malignant melanoma and levodopa was coincidental versus causal.[3,4] Rasagaline, approved for the treatment of PD symptoms in 2005, has also been speculated in the occurrence of PD and malignant melanoma, however, limited data exist to determine a causal or coincidental relationship. Here, we present a case summary of a woman with PD who developed multiple malignant melanomas while being treated with a combination of rasagiline and levodopa-carbidopa.

CASE REPORT

A 76-year-old Caucasian woman, Fitzpatrick skin phototype (FSPT) III, with an average number of nevi, no previous history of melanoma, or family history of melanoma, was first examined in May 2016 for a skin cancer screening. The woman reported a history of moderate sun exposure as an adolescent, having suffered several sunburns, however, reported no blistering sunburns. At the time of the screening, the woman had already been diagnosed with PD, which was being treated with a combination of rasagiline and levodopa-carbidopa.

During her first screening in May 2016, she was diagnosed with her first malignant melanoma. The melanoma was located on her right clavicular neck, superficial spreading type, with a Breslow depth of 0.3 mm, Clark's level II, stage pT1a and was successfully treated by a wide local excision. In January 2017, she was diagnosed with her second malignant melanoma during a routine skin examination. Her second superficial spreading melanoma was located on her left pretibial region, with a Breslow depth of 0.63 mm, Clark's level II, stage pT1a and was also treated successfully by a wide local excision. After developing two malignant melanomas in less than a one-year time frame, her surgical oncologist suggested to discontinue rasagiline, but remain on levodopa-carbidopa.

In January 2019, after remaining off rasagiline for two years, she developed her third malignant melanoma. This melanoma was a malignant melanoma in situ located on the right upper back and was successfully treated by wide local excision. In April 2019, she then developed her fourth malignant melanoma. This melanoma was a malignant melanoma in situ, lentigo maligna type located on her left nasal ala, treated successfully by Mohs surgery. None of the melanoma diagnoses required sentinel lymph node mapping. The woman did not receive genetic testing and continues to receive skin cancer screenings every four months.

DISCUSSION

PD and Melanoma Co-occurrence.

Pathophysiology. The synthesis of dopamine and melanin occurs on a shared biochemical pathway. Tyrosine is oxidized by the enzyme tyrosinase and is converted to levodopa which is converted to the neurotransmitter dopamine by decarboxylation. Tyrosinase is bifunctional and also converts levodopa to dopaquinone, which, when oxidizes, forms the pigment melanin the same pigment produced by melanocytes.[5] Increasing dopamine is the goal of PD treatments like rasagiline and levodopa. Investigators have questioned if increasing the production of exogenous dopamine through a synthetic pathway would therefore also increase the production of melanin leading to recurrent melanoma in those with a positive history or increase patients' risk for a primary melanoma.[5]

Melanoma in patients with PD on levodopa. In 1972, more than a decade following the introduction and utilization of levodopa for treatment of PD symptoms, Skibba et al reported a case of cutaneous melanoma in a patient with PD on levodopa treatment.[6] The patient was a 50-year old man already diagnosed with PD when a melanoma in his left scapular area appeared before he started levodopa treatment. The melanoma was excised and there was no evidence of metastasis. He was started on levodopa in September of 1971 and four months later was diagnosed with recurrent melanoma in the surgical site. Levodopa was discontinued that month. More cases of melanoma occurring in patients with PD taking levodopa followed, prompting the United States Food and Drug Administration (FDA) to require that levodopa package inserts contain an advisory and recommend regular monitoring for melanomas while on treatment.

Further discussion in the form of research letters exchanged in the *Journal of the American Medical Association (JAMA)* addressed these cases. The authors ultimately agreed that the medical field should take a cautious approach until there was clear epidemiological evidence regarding risk of melanoma progression associated with the use of levodopa.[7] A large Danish cohort study provided that evidence; however its main conclusion was that the increase rate of malignant melanoma was unrelated to the treatment with levodopa. In a study of more than 14,000 patients diagnosed with PD, researchers found that the incidence of melanoma was doubled that of the general population.[2] They also found a significant fourfold to fivefold increase in the risk for melanoma in patients with idiopathic PD compared to other patients. Although further research has been conducted, studies have largely been inconclusive, demonstrating that the occurrence with malignant melanoma and levodopa was coincidental versus causal. However, research continues to support increased melanoma screening in patients with PD.[4]

Melanoma in patients with PD on rasagiline. Rasagiline is a selective and irreversible monoamine oxidase inhibitor (MAOI), particularly targeting monoamine oxidase B (MAO-B). By irreversibly binding to MAO-B, rasagiline prevents the breakdown of dopamine and its precursor levodopa.[8]

During the clinical trials for rasagiline, one of the adverse side effects reported was the development of malignant melanoma. Due to this and the already known connection between PD and melanoma, the medication administered a warning of possibly developing melanoma and the need for frequent skin cancer screenings. These warnings were supported by the findings of the PRESTO study, randomized placebo-controlled trial clinical trial in which three new cases of melanoma were diagnosed among 472 levodopa-treated patients with PD and motor fluctuations after starting rasagiline. Another clinical trial, called the TEMPO trial, was a randomized, multicenter, placebo controlled, double-blind study where patients were given different dosages of rasagiline. This study included 404 patients and was conducted over a six-month period where patients were randomly assigned to rasagiline 1 mg/daily, rasagiline 2 mg/daily, or placebo group. After beginning the trial, three patients in the part of the rasagiline 2 mg/daily group developed melanoma.[8]

Epidemiology of Melanoma and PD.

As more research becomes available, the newly observed positive association between malignant melanoma and PD has continued to gather significant attention. Previous studies showed that patients living with PD had a decreased risk of developing fatal cancer than the general population, hinting that PD, like Alzheimer's and Huntington's disease, may offer some type of protection against certain types of cancer.[9] However, researchers have observed that patients with PD are at a substantially higher risk of developing malignant melanoma (Hazard ratio [HR]:2.75; 95% Confidence interval [CI], 1.35-5.59). In one large-scale study, being diagnosed with melanoma was found to be associated with a 50-percent increased risk of later developing PD, whereas a diagnosis of PD demonstrated a two-fold increased risk of later developing melanoma. Not only are individuals with PD at an increased risk of developing malignant melanoma, they have an increased mortality from melanoma.[10] Other studies have found that individuals with a family history were twice as likely to develop PD, compared to individuals who reported no family history of melanoma.[10]

One case reported in the literature, similar to the one we described previously, posed a causal relationship

...Continued on Page 28

From The Patient's Perspective

Mother and Son Conquer the Visible and Invisible Challenges of Ichthyosis with Strong Will, Determination, and Support

By Kelsey Julian

When my son Ian was born, I had no idea what it meant to be diagnosed with ichthyosis, a genetic skin disorder characterized by dry, scaling skin. As a new mom, I couldn't help but wonder how this might impact his life and the day-to-day routine of caring for my child. During his infant and toddler years, we were living in South Eastern New Mexico and the dryness in the air was having a severe impact on Ian's skin. Every aspect of his care had to be considered and, unfortunately, that meant a lot of trial and error. We were struggling with his skin regimen, especially finding diapers that didn`t cause awful rashes. Ian would constantly get methicillin-resistant *Staphylococcus aureus* (MRSA) in the diaper area and the routine skin care and dealing with infections was beginning to drain me.

Foundation for Ichthyosis & Related Skin Types

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The Foundation for Ichthyosis & Related Skin Types, Inc, exists to improve lives and seek cures for those affected by ichthyosis and related skin types. Stay tuned, in the coming months we will relaunch our tele-ichthyosis site where medical professionals can submit cases and receive coordinated feedback from our expert physicians. It will be available on www.teleichthyosis.org coming soon!

Please visit www.firstskinfoundation.org to learn more.

I eventually learned that Calmoseptine® Ointment created the best barrier to protect his skin from diaper rashes and using dye- and fragrance-free diapers also helped. In the warmer months, allowing him to go without a diaper when MRSA was not present kept him healthy too. In my attempt to find the best products and strategies for keeping him comfortable, I quickly discovered that Aquaphor® Healing Ointment worked in improving his skin and was essential to his care regimen. I would go through almost two jars of it per week. We ended up moving from New Mexico to my hometown in Texas and while this change in environment helped to decrease the amount needed to manage the ichthyosis, the financial burden of it all was noticeable, especially during those early days.

Ian was around one year old when I saw a pediatric dermatologist. She told me about the Foundation for Ichthyosis & Related Skin Types (FIRST) and encouraged us to research it. I am so thankful she did because that is when I felt the floodgates of support open. If it wasn't for FIRST, I would have never known about the wealth of resources available, like a program offered by the manufacturers of Aquaphor that sent care packages to families who use large amounts of their products due to chronic skin issues. Qualifying for this program was truly a weight lifted off our shoulders. I remember getting our first case in the mail. It felt like Christmas. When I saw how many containers were in the box, I wept tears of joy.

Looking back, I realize that the challenges of managing ichthyosis extended beyond Ian's skin regimen. He was considered underweight, an issue brought up to us by pediatricians and professionals from The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). We were trying everything to help him grow at a healthy rate and keep his skin under control, so it was frustrating to receive criticism from medical professionals and others outside of my circle. When out in public, complete strangers would comment about him being tiny for his age, suggesting that I should feed him more and asked why I allowed him to get so badly sunburned. Sometimes I wanted to scream, "It's ichthyosis, look it up!"

Though he protested and squirmed like most toddlers do, Ian was surprisingly tolerant of the extensive skin care routine and never showed a desire to scratch or rub off his lotions and creams. Maybe he associated early on that the lotions made his skin feel better or more comfortable. I'm not sure. I did find that applying the ointment at night, although not necessarily the most effective strategy, was extremely important. Nighttime required a heavier application due to clothes and blankets rubbing against the skin. Another consideration in his care was potential mess and stains created by using such a large amount of skin creams. I found that fleece was the most forgiving material and stocked up on inexpensive jammies at Walmart® and re-sale shops.

"I used to think having ichthyosis would prevent Ian from being able to do "normal" childhood activities like playing outdoors and learning sports. As he grew up, his strong will and determined spirit showed me how wrong I was."

We did have a season where his skin went through some changes. When Ian was four-years old, his skin changed and became drier, more sensitive, and more inflamed than before. One night after a bath, I was applying ointment and he was crying. He slapped my hand and screamed, "Why do you like hurting me? It burns, mommy. Please stop!" My heart sank. I called in reinforcement and excused myself to my bedroom for a heartfelt cry. I had no idea how to explain to a 4-year old that when I apply skin products, it is out of the deepest love and care. I knew the burning was momentary and long-term effects of not applying those products would cost much more pain and aggravation than a few moments of burning. But again, how do you get a four-year old to understand that? Thankfully, we moved past it. His skin improved and I never had to experience that situation again.

Even though on the surface Ian's case is much milder than others of ichthyosis, he struggles tremendously with heat and cold intolerance. This is because individuals with ichthyosis do not sweat normally. The condition does not allow their sweat to reach the surface of their skin and cool them effectively. In very hot and humid weather they are at risk for overheating, heat exhaustion, and heat stroke, so we had to work hard to keep him comfortable and look for any warning signs.

Ian was around three years old when we received a gift that made it possible for him to enjoy the outdoors—a cooling vest. Some dear friends learned that Ian overheated the previous summer during Memorial Weekend when the high was only 76° F. This couple didn`t want him to go through another summer of having to stay indoors all the time. I would have never known about the cooling vest. Receiving the cooling vest opened so many doors of opportunities for Ian to participate in outdoor activities—going to the park and participating in things like zoo trips, Easter egg hunts, school field trips. He was even able to take part in recess and physical education class.

Since those difficult infant and toddler years, I've slowly been able to take a back seat and allow Ian to be responsible for managing his skin care routine. When

he is really dry, he will ask for help getting his back or other areas of concern. Ian fully understands ichthyosis and the importance of keeping up with care. He lets me know when he is getting low on products and when he finds something that works well. Right now, his favorite products are Hempz Moisturizing lotion and Sweet Girl Farm Tallow Butter, which is made right here in Forney, Texas. He also understands he is at risk for overheating during exercise if he does not have his cooling vest and that clothing plays a role in keeping him comfortable. Now that he is a preteen, he mostly wears jersey net shorts, white cotton undershirts, and fleece pajama pants during the winter.

I used to think having ichthyosis would prevent Ian from being able to do "normal" childhood activities like playing outdoors and learning sports. As he grew up, his strong will and determined spirit showed me how wrong I was. We just celebrated Ian's 12th birthday and, if we stay on track, he will be going for his black belt, which signifies mastery of the fundamentals of Taekwondo. We are so thankful to have found FIRST as their resources and support have eased so much of the visible and invisible burdens of growing up with ichthyosis.

Melanona and Parkinson's Disease Treatment ...Continued from Page 24

between levodopa and rasagiline therapy and the appearance of melanoma. Garrido et al described the case of an 81-year-old Caucasian woman with PD who, like our patient, developed melanoma lentigo maligna type on her right cheek after being treated with rasagiline and levodopa-carbidopa for 18 months. The subject, also like our patient, reported no history of sunburns and no family history of melanoma.[11]

CONCLUSION

Although case reports are not conclusive evidence, a growing incidence of melanoma in patients with PD being treated with carbidopa-levodopa and rasagline can be observed in the literature. Within the first year of melanoma diagnosis, the association between PD and melanoma is very high (standardized incidence ratio: 2.35) and decreases in subsequent periods.[7] This supports the evidence that the association is not due to PD treatment, but perhaps another pre-existing causal or confounding factor.

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Cutaneous COVID: Reviewing Cutaneous Morphology Observed in COVID-19

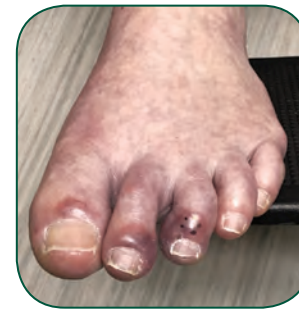
By Lauren M. Madigan MD, and Rosemary DeShazo, MD

Five Clinical Patterns Associated with Skin Manifestations and a Diagnosis of COVID-19 in Adults Results from a Rapid Prospective Nationwide Consensus Study in Spain (N=375)[1]	
Acral areas of violaceous erythema and edema ***(pseudo-chilblain)***	So-called "COVID Toes"
	Affects a younger population
	May be associated with itching or pain
	Potentially a delayed manifestation of less severe disease
	Exact relationship to infection has yet to be established
	Self-limited, but prolonged cases have been reported
Vesicular eruptions	Small, monomorphic vesicles with a predilection for the trunk
	Observed in middle-aged patients with active infection
	Associated with a disease course of intermediate severity
	Resolves over approximately 7-10 days
Urticarial lesions	Either true hives or persistent, urticarial lesions
	Predominantly truncal or diffuse
	Observed in middle-aged patients with active infection
	Similar overall course to the maculopapular group
	Resolves over approximately 7-10 days
	Itch is common
Other maculopapular eruptions ***(Majority of cases)***	BROAD DEFINITION *Encompasses exanthems, papulosquamous lesions, petechial eruptions, Grover's-like lesions, flexural eruptions, targetoid lesions*
	Observed in middle-aged patients with active infection
	Similar overall course to the urticarial group and less severe as those with livedo/necrosis
Livedo or necrosis ***(Less common)***	Purpuric lesions suggestive of vascular occlusion
	Affected cohort was older than others and followed a more severe course
	An important sign of systemic coagulopathy
	Higher associated mortality

Table adapted from Galván Casas C, Català A, Carretero Hernández G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases Br J Dermatol. 2020 Apr 29 : 10. doi: 10.1111/bjd.19163 [Epub ahead of print]

Introduction

Since the emergence of SARS-CoV-2, the virus that causes COVID-19, we have learned more about how it spreads, how it can be prevented, and how it presents in an infected patient. With patients reporting a wide range of symptoms, illness severity, and duration, much research has focused on the more unique and defined characteristics of the infection. Aside from symptoms that are common with other illnesses and oftentimes indistinguishable from those caused by influenza, studies show that patients diagnosed with COVID-19 can experience new loss of taste or smell and gastrointestinal symptoms in addition to the signature set of symptoms reported—fever or chills, cough, shortness of breath or difficulty breathing, and sore throat. As the world investigates the intricacies of the virus, it is crucial that we examine how it affects every organ system. Research across disciplines continues to give us a fuller picture of the scope of this illness and with more reports of skin manifestations of COVID-19, the field of dermatology has become an important area of interest. Reviewing cutaneous morphology observed during the COVID-19 pandemic will help increase awareness and knowledge among health care providers of "cutaneous COVID." As with all fields, our understanding of these presentations is constantly evolving.



"COVID toes"

Editor's Note: All reference material cited were the most current at the time of publication. The information and reference material listed in this feature were compiled from Grand Rounds presentations given by the authors' at the University of Utah. All reference material cited were the most current at time of publication.

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NOTES from your Office Manager

The Proper Use of Scribes

The Risk: As the use of electronic health records (EHRs) has become widespread, documentation practices and workflow patterns have changed significantly and have added to a growing clinical and administrative workload. The use of this technology has increased the amount of time necessary to complete medical record documentation and order entry.

One way that physicians have chosen to address these issues is through the use of scribes. Scribes originated in the fast-paced clinical setting of the emergency department (ED) as a way to reduce the time physicians needed to spend documenting care in an electronic format. The use of scribes has expanded from these roots in the ED to numerous other clinical settings. Scribes perform EHR data entry under the direct supervision of a licensed professional, freeing the physician or other provider to spend more time directly interacting with the patient.

As unlicensed members of the healthcare team, the recruitment, training and supervision of scribes is paramount in managing their use in all clinical settings. Whether you are currently using scribes in your practice, or are considering employing them, the following recommendations may be useful in evaluating your program or determining strategies for implementation.

Recommendations:

1. Use documentation policies for your organization that comply with regulatory requirements. In addition, practices should monitor federal, state and regulatory changes to maintain compliance with these guidelines.

2. Develop a written job description for scribes that outlines required qualifications and competencies, including proficiency with your EHR system and medical terminology. Clearly delineate job responsibilities.

3. Provide orientation that includes, but is not limited to, HIPAA, privacy regulations, organizational policies, and patient rights.

4. Scribes should not perform any clinical functions or provide any direct patient care (unless they are otherwise a licensed healthcare provider such as an LPN or RN.)

This includes:

- acting independently;
- touching patients;
- handling bodily fluids or specimens;
- translating for a patient;
- interpreting any information; and
- conducting other duties while acting as a scribe.

5. Scribes should be assigned their own unique user ID/password credentials to access the EHR system. All entries to the record made by a scribe must be while logged in with their own password and user ID. In the event a licensed clinical staff member functions as a scribe, they must have two separate user IDs and passwords and use them accordingly.

6. Introduce the scribe to the patient and give the patient the opportunity to decline having the scribe present during the examination.

7. The primary responsibility of the scribe should be to document the clinical encounter, including the history of present illness, a review of systems, the physical exam, and the assessment and plan, as presented by the provider. Scribes may also create pending orders as dictated by the provider. Providers must review and complete all medical orders.

8. All information entered into a medical record by a scribe must include:

- the name of the patient and the provider providing care;
- the date and time; and
- authentication.

9. Providers must review the scribe's documentation and verify the entry. An attestation statement should include:

- affirmation of the provider's presence during the time the encounter was entered;
- confirmation that the provider reviewed the information and verified its accuracy; and
- authentication, including date, time, name and credentials.

10. Perform regular audits/assessments of the scribe's documentation and provide constructive feedback for performance improvement, as indicated.

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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: Diuretics are often used in the treatment of hypertension. Thiazide diuretics are considered first-line treatment for many patients with hypertension. Which of the following locations within the nephron is the site of action of the thiazide diuretics?

A. Cortical collecting tubule
B. Distal convoluted tubule
C. Collecting duct
D. Loop of Henle

EXPLANATION: The distal convoluted tubule functions include the active reabsorption of filtered sodium and chloride and calcium under the control of parathyroid hormone; is the site of action of the thiazide diuretics. The cortical collecting tubule functions to reabsorb sodium coupled with potassium and hydrogen secretion; is the site of action of the potassium-sparing diuretics. The collecting duct functions to reabsorption of water under vasopressin control; is the site of action of osmotic agents and antidiuretic hormone (ADH) antagonists. The loop of Henle thin descending limb is involved with the passive reabsorption of water and is the site of action of osmotic agents; the thick ascending limb is involved with the active reabsorption of filtered sodium, potassium, and chloride and is the site of action of the loop diuretics.

The correct answer is B.

James A. Van Rhee, MS, PA-C, *is the Program Director for the Yale University School of Medicine Physician Associate 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). He is the author of the Physician Assistant: Certification and Re-certification Review Book and Consulting Editor of Physician Assistant Clinics, both published by Elsevier. For the last 15 years he has been course director and presenter of the Physician Assistant Board Review, produced live online by Kaplan Medical.*

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Listening To Patients
The Corona Kid

By Alan Rockoff, MD

The first installment of this column was obsolete on arrival. It referred to walking abroad at midday, with no mention of masks and social distancing. The whole thing was so February 2020.

My last day in the office was in mid-March. Friday the 13th.

For a few weeks I've been seeing patients remotely. I pitched telemedicine to an HMO about 30 years ago. I was hardly an innovator. Researchers had already shown the practical use of remote dermatology by then, using stored and forwarded images.

What I had in mind was visits by patients in nursing homes or too sick at home to come in. It always bothered me to see very aged and infirm patients brought to the office at great inconvenience and expense for what often turned out to be problems like xerosis or eczema that could have been managed quite well remotely.

The HMO never got back to me, though. There were too many hurdles, mostly bureaucratic rather than medical. Would insurance pay? What about consent? Malpractice? It has been interesting to watch the current crisis sweep away the inertia of such obstacles, including licensure considerations (seeing patients across state lines for cutaneous purposes). People get around to fixing the roof when it's pouring. Perhaps next time there will be tests, masks, respirators. Perhaps.

Seeing patients remotely has acquainted me with all the technical headaches everyone stuck at home talks and jokes about: Balky transmission (What did you say after, "and then the blood…..""?); patients who can't figure out how to log on, or start the video, or unmute themselves, and so on and on. Picture resolution is not great, as anyone knows from watching TV newscasters interview talking heads who are stuck at home.

I was never all that image-conscious, but my beard has grown fuller and my hair unkempter. Even though I sit at my desk, I do take care to keep my trousers on. Not taking any chances.

Everyone agonizes over what the "new normal" may be. Will people come back to doctors' offices? Will practices survive economically if many patients don't come back? Stay tuned. For a long time.

Mostly, though, remote visits seem to work. Helped if necessary by better-resolution emailed photos, one can make useful decisions, including which lesions can wait for in-person evaluation, until….

…Until what? In an effort to keep this column up-to-the-nanosecond, I am writing it as many countries tentatively "open up". Careful analysis of the knowledge behind this world-wide project shows…not much. It seems to come down to some educated guesswork about what might work and what the risks might be, which leads to advice that differs widely from state to state and country to country. It's as if people everywhere just decided that locking everyone down is a real drag, is financially ruinous, has a duration both uncertain and longer than most people and governments think they can handle, so let's get out there and "be careful," whatever that is said to mean.

And the risks? Well, more people will get sick and some will die. How many "extra" deaths are ethically acceptable? Thoughtful people are working on that. They'll get back sometime to

those who are still around to hear them.

I don't blame anyone for our staggering ignorance about this terrifying new reality. But absorbing the ignorance in real time is not edifying.

I have nothing but sympathy for those who are not emeritus, who have departments to run, practices to sustain, families to feed. I didn't ask to be born 73 years ago, and take no credit for the honor. So much of what happens to us depends on when and where we were born, two factors for which we deserve absolutely no credit. Having no better choice, we do the best we can.

Meantime, I am in a "high-risk" category. If I were obese, I could try to lose weight. But my risk factor is age, which tends not to decline. Risk-wise, there is just one way to exit my group.

So I don't expect to get back to the office anytime soon. To paraphrase a comedian who shall remain nameless: I don't want to live on in the hearts of men. I want to live on in my house.

Alan Rockoff, MD, *practices dermatology in Boston, Massachusetts. He graduated with his medical degree in 1972 from the Albert Einstein College of Medicine in Bronx, New York and then completed a pediatric internship and residency at Bronx Municipal Hospital Center in Bronx, New York. Continuing his education, Dr. Rockoff completed a dermatology residency program at the combined program at Boston University and Tufts University in Boston, Massachusetts. 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 more than 35 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 numerous 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.

This column first appeared as a commentary on MDedge® Dermatology/Dermatology News.
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Diseases of the Tongue; Some Unusual Lesions and Disorders †

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Many lesions and disorders of the oral cavity may affect the tongue as well. On the other hand, some lesions have a strong preference for occurrence on the tongue or may be even limited to the tongue. A selection of both categories will be discussed, emphasizing the diagnostic and management aspects.

Lymphangioma is a developmental disorder that arises at a young age. The clinical presentation is more or less diagnostic. Nevertheless, the taking of a biopsy is recommended. Treatment possibilities are limited, except for small lesions that may be removed without causing much morbidity.

Geographic tongue is not so much a rare lesion, but probably often remains undiagnosed by clinicians, particularly when occurring in children *(Figure 1)*. A rare phenomenon is the occurrence of geographic tonguelike lesion elsewhere in the mouth, being referred to as ectopic geographic tongue or geographic stomatitis. There are no possibilities to cure geographic tongue and the disease may last lifelong.

Median rhomboid glossitis is usually easy to diagnose based on clinical features alone. If a biopsy is taken, it should be realized that the pathologist may be challenged by the presence of elongated rete ridges that may mimic squamous cell carcinoma. Treatment is only indicated in case of symptoms and consists of elimination of possible causative factors, e.g., tobacco habits and the use of corticoid inhalation spray for pulmonary disease and the use of topical antifungals. In rare instances a Kaposi sarcoma may arise in the foramen cecum area, somewhat mimicking median rhomboid glossitis. It should be realized that Kaposi sarcoma (KS) may be the first manifestation of an underlying HIV-infection. At the same time, oral KS has been reported in immunocompetent patients.[1]

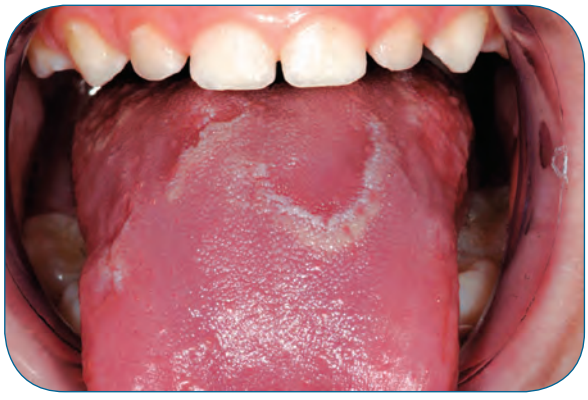

Figure 1. Geographic tongue in a 3-year-old boy.

Lingual papillitis is a poorly understood inflammation of the fungiform papillae, showing a quite distinct clinical picture. Lingual papillitis is usually self-healing ('Transient lingual papillitis').[2]

A persistent ulcer on the dorsum of the tongue may have a specific cause, e.g., syphilis I. The occurrence of a squamous cell carcinoma at that particular site is rare. A rather rare entity, mainly occurring on the tongue, is traumatic ulcerative granuloma with stromal eosinophilia (TUGSE). The histopathologic features are quite diagnostic. Occasionally, CD30 positive lymphocytes may indicate a peculiar type of T-cell lymphoma. In such cases the patient should be staged for possible involvement elsewhere in the body.[3]

A ***granular cell tumor*** may occur everywhere in the body but has a strong preference for the mouth, particularly for the tongue. The diagnosis is based on histopathologic aspect. A well-known pitfall is the occurrence of pseudoepitheliomatous hyperplasia of the overlying epithelium, that may be misdiagnosed as squamous cell carcinoma.

Lymphoid (follicular) hyperplasia may occur

on the borders of the tongue at the junction of the anterior part ('oral tongue') and the base of the tongue.[4] There is usually a bilateral presentation of slightly swollen, soft elastic mucosa. Symptoms are usually absent and in such event a biopsy nor follow-up is indicated. In symptomatic cases, particularly when unilateral, the possibility of a squamous cell carcinoma should be considered.

A range of lesions and conditions may present as bilateral white changes at the borders of the tongue *(Table 1)*. These lesions can sometimes be diagnosed based on the presence of similar lesions elsewhere in the oral cavity, e.g., morsicatio, but others may require a biopsy *(Figure 2)*. This is particularly true when hairy leukoplakia is suspected in a patient with a negative medical history. The histopathologic features, including positivity of an Epstein Barr Virus (EBV) immunohistochemical stain, are diagnostic. Although hairy leukoplakia is mainly known as manifestation of an underlying HIV-infection, also other causes of immunosuppression may result in this lesion.

Table 1. Differential diagnosis of bilateral white lesions of the tongue *(in alphabetical order).*

Candidiasis, hyperplastic
Hairy leukoplakia
Leukoplakia ('true')
Lichen planus
Morsicatio
Pachyonychia congenita
Syphilis, second stage
White sponge nevus

In the second stage of syphilis multiple white lesions ('plaques muceuses') may occur in the oral mucosa, often of the tongue. Another manifestation may be the occurrence of red, patchy and sometimes aphthouslike changes of the oral mucosa, particularly on the dorsal surface of the tongue. Such lesions may follow a recurrent pattern. A suspected diagnosis of syphilis should be confirmed by serological tests.

A rather unusual tumor, often benign and more or less limited to the anterior tongue, is the ectomesenchymal chondromyxoid tumor. The clinical presentation of the tumor is not characteristic, just being a non-ulcerative firm elastic swelling with

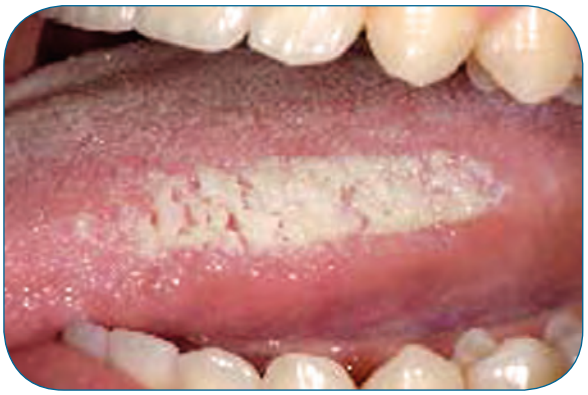

Figure 2. Verrucous lesion, bilateral, on the border of the tongue, being caused by morsicatio.

an intact mucosal surface. Since its first description in the nineties of the last century less than fifty cases have been reported. The challenge is with the histopathologic interpretation, including the use of various immunohistochemical stains. The tumor may be wrongly diagnosed, e.g., as a salivary gland tumor or a (rhabdomyo)sarcoma.[5]

Conflicts of Interest: The author declares no conflict of interest.

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Dermatology Market Watch

Sarna® Sensitive Lotion Awarded National Eczema Association (NEA) Seal of Acceptance™

Sarna® Sensitive Lotion, a steroid-free anti-itch moisturizer manufactured by Crown Laboratories, has been awarded the National Eczema Association (NEA) Seal of Acceptance™. Crown will begin to incorporate the NEA's Seal of Acceptance™ in product packaging, digital, and print communications. In addition to being steroid-free, Sarna Sensitive Lotion is fragrance, dye, and paraben free, Sarna Sensitive Lotion's 1% pramoxine hydrochloride (external analgesic) formulation was found to be safe and effective for daily use. To learn more about Sarna Sensitive Lotion, visit Sarnalotion.com.

About National Eczema Association's Seal of Acceptance. NEA's Seal of Acceptance helps individuals recognize products that are suitable for care of eczema or sensitive skin. Products eligible for the Seal of Acceptance™ are those that have been created or intended for use by persons with eczema or severe sensitive skin conditions and that have satisfied the Seal of Acceptance™ criteria, which includes the review of testing data on sensitivity, safety and toxicity, as well as ingredients, content, and formulation data.

NEA accepts applications from products in the following categories:

- Cleansers
- Clothing and Fabrics
- Disposable Wipes
- Hair Care products
- Household Products
- Moisturizers
- OTC drugs
- Sunscreens

More Resources from NEA. For the full directory of products with the NEA Seal of Acceptance, visit https://nationaleczema.org/eczema-products/. To date, the directory contains 221 products, and is searchable by category, age, and brand. Check out NEA's website https://nationaleczema.org/ for other resources, such as downloadable and printable patient fact sheets on common eczema triggers, care tips for eczema and atopic dermatitis, prescription treatment guide, and even a bleach bath recipe card.

Highlights from the Society for Pediatric Dermatology 45th Annual Meeting: Abeona Therapeutics Announces Two Presentations Related to its Recessive Dystrophic Epidermolysis Bullosa Clinical Program

Abeona Therapeutics Inc., a clinical-stage biopharmaceutical company developing gene and cell therapies for serious diseases, announced that two poster presentations related to its clinical program for recessive dystrophic epidermolysis bullosa (RDEB) were featured at the Society for Pediatric Dermatology (SPD) 45th Annual Meeting, which was presented virtually July 10-12, 2020 with session recordings available through December 31, 2020.

The first poster includes a detailed analysis of patients with RDEB in the EB-101 Phase 1/2a trial showing that wound healing following EB-101 treatment was associated with improved long-term pain relief. A separate poster provides insights on the significant disease burden associated with RDEB, highlighting data from a literature review on the clinical characteristics, humanistic consequences, and economic impact of living with RDEB on patients and their families.

EB-101 Treatment of Large, Chronic Wounds Is Associated with Durable Healing and Pain Reduction in Patients with Recessive Dystrophic Epidermolysis Bullosa (RDEB)

Jean Tang, MD, PhD, Professor of Dermatology, Stanford University Medical Center and Principal Investigator of the EB-101 pivotal Phase 3 VIITALTM study, presented long-term outcomes following EB-101 treatment for large, chronic wounds in patients with RDEB. EB-101 treatment resulted in considerable and durable reduction in wound burden in the range of three to five years in a Phase 1/2a study. Wound healing of 50% or greater following EB-101 treatment was associated with no pain at treated sites at three years, four years and five years post-treatment, compared with presence of pain in 53% of wound sites at baseline. The ongoing VIITALTM study will further characterize the relationship between reduction of wound burden and pain relief following EB-101 treatment.

The Full Burden of Recessive Dystrophic Epidermolysis Bullosa (RDEB)

M. Peter Marinkovich, MD, Bullous Disease Clinic Director, Stanford University Medical Center, and Investigator in the VIITALTM study, presented findings from a literature review of 65 studies that provide new insights on the disease burden from the perspective of patients with RDEB and their families. Key observations of the clinical, humanistic and economic burden of RDEB include:

- Large, chronic wounds comprise a major clinical burden of RDEB and are correlated with pain.
- Many patients experience anxiety and depression.
- Parents of children with RDEB reported negative effects on their relationship, choosing to not have more children.
- 50% of U.S. families characterized the economic impact of managing RDEB as "high" or "severe."

About Recessive Dystrophic Epidermolysis Bullosa. Recessive dystrophic epidermolysis bullosa (RDEB) is a rare connective tissue disorder characterized by severe skin wounds that cause pain and can lead to systemic complications impacting the length and quality of life. People with RDEB have a defect in the COL7A1 gene, leaving them unable to produce functioning type VII collagen, which is necessary to anchor the dermal and epidermal layers of the skin. There is currently no approved treatment for RDEB.

More information on the clinical trials of EB-101 can be found at https://www.abeonatherapeutics.com/clinical-trials/rdeb and http://www.ClinicalTrials.gov

(Identifier: NCT04227106).

Arcutis Enrolls Last Patient in Phase 2b Clinical Trial Evaluating ARQ-154 (Topical Roflumilast Foam) as a Potential Treatment for Scalp Psoriasis

Arcutis Biotherapeutics, Inc., a late-stage biopharmaceutical company focused on developing and commercializing treatments for unmet needs in immune-mediated dermatological diseases and conditions, or immuno-dermatology, announced the completion of enrollment of the Phase 2b clinical trial evaluating ARQ-154 (topical roflumilast foam) as a potential treatment for scalp psoriasis. Roflumilast foam is a once-daily topical foam formulation of a highly potent and selective phosphodiesterase type 4 inhibitor (PDE4 inhibitor) that Arcutis Biotherapeutics, Inc. is developing particularly to treat inflammatory dermatoses in hair-bearing areas of the body such as the scalp.

Roflumilast foam is a topical foam formulation of a highly potent and selective PDE4 inhibitor (roflumilast). Roflumilast has been approved by the U.S. Food and Drug Administration (FDA) for systemic treatment to reduce the risk of exacerbations of chronic obstructive pulmonary disease (COPD) since 2011. Roflumilast has shown greater potency (25 to 300 fold) than the two other FDA-approved PDE4 inhibitors. PDE4 is an intracellular enzyme that increases the production of pro-inflammatory mediators and decreases production of anti-inflammatory mediators and has been implicated in a wide range of inflammatory diseases including psoriasis, eczema, and COPD. PDE4 is an established target in dermatology, and other PDE4 inhibitors have been approved by the FDA for the topical treatment of atopic dermatitis or the systemic treatment of plaque psoriasis.

The Phase 2b trial in scalp psoriasis is an eight-week, multi-center, multi-national, double blind, vehicle-controlled, study of the safety and efficacy of topical roflumilast foam 0.3% administered once-daily in approximately 300 adult and adolescent patients with plaque psoriasis that includes plaques on the scalp. The primary endpoint of the trial is achievement of an Investigator Global Assessment score of 'clear' or 'almost clear' plus a 2-grade improvement from baseline on the scalp (S-IGA) at Week 8. Multiple secondary endpoints will also be evaluated.

About Scalp Psoriasis

Scalp psoriasis is a manifestation of plaque psoriasis characterized by raised, red areas of skin ("plaques") covered with a silver or white scale that occurs in the hair-bearing area of the scalp and sometimes extending to the forehead, back of the neck, or behind or inside the ears. Patients with scalp psoriasis commonly have plaques on other areas of the body as well. Nearly half of the estimated 8.6 million Americans with psoriasis have involvement of the scalp. Scalp psoriasis plaques are identical to psoriatic plaques on other areas of the body, however topical treatment of scalp plaques is complicated by the difficulty of delivering topical drugs under the hair and onto the skin. As with psoriatic plaques on other parts of the body, psoriasis on the scalp is often itchy and is sometimes painful. Scalp psoriasis can also be associated with hair loss, likely due to damage to the hair from excessive scratching, rubbing, or combing of the affected area.

To access full study details, visit http://www.ClinicalTrials.gov and search NCT04128007; Safety and Efficacy of ARQ-154 Foam in Adolescent and Adult Subjects With Scalp and Body Psoriasis

Dermatology Market Watch

Nevisense Systems Point-of-care Technology for Detection of Melanoma Installed at Advanced Dermatology and Cosmetic Surgery Group in Florida

ADCS's *Windmere Location First of Several Sites Planned to Offer Technology*

SciBase Holding AB (SciBase), developer of augmented intelligence-based solutions for skin disorders, recently announced the installation of the Nevisense Systems at the Advanced Dermatology and Cosmetics Surgery (ADCS) Windermere, Florida location led by Dr. Bill Steffes. Based in Maitland, Florida, ADCS is the largest dermatology practice in the country with over 150 sites of care located across 14 states. Windmere is the first of several sites planned to offer Nevisense this year.

Nevisense is based on a method called Electrical Impedance Spectroscopy (EIS), which uses the varying electrical properties of human tissue to categorize cellular structures and thereby detect malignancies and abnormalities. A risk score is determined on a scale where 0 to 3 strongly indicates a benign lesion, and a score of 4 to10 represents the degree of atypia in the tissue indicating the risk of melanoma. The Nevisense 3.0, the third generation of the system, was approved by the US Food and Drug Administration (FDA) in May 2020. The update allows more pigmented skin lesions to be examined on one patient session (from 10 to up to 20).

For more information, access the full press releases at www.scibase.com and www.advancedderm.com

On International Kissing Day, the Restylane® Brand Shares First-of-its-Kind Phase IV Kissability Study Results Showing Both Subject and Partner Satisfaction with Restylane® Kysse

On International Kissing Day, July 6, 2020, the Restylane® brand announced results of a first-of-its-kind phase IV, Kissability study for injectable hyaluronic acid (HA) lip filler Restylane® Kysse, which evaluated not only subject satisfaction but, for the first time, partner satisfaction following treatment.

In the Kissability study, all subjects (100%) and a majority of their partners (90%) were satisfied with their lips after Restylane Kysse treatment, with most partners (73%) reporting a more kissable and natural feel.[1*] Following approval by the U.S. Food and Drug Administration (FDA) earlier this year, Restylane Kysse is the latest addition to the Restylane family of HA dermal fillers portfolio by Galderma Laboratories, L.P.

For more information on the Restylane Brand, including Restylane Kysse, visit https://www.restylaneusa.com/

1 Data on File, 05DF1807 Clinical Study Report. Fort Worth, TX: Galderma Laboratories, L.P., 2020.

** In a phase IV clinical study, 59 subjects were treated with Restylane Kysse in the lips (n=19) or Restylane Kysse in the lips in combination with either Restylane Refyne (n=21) or Restylane Defyne (n=37) in the NLFs or MLs.*

Ortho Dermatologics Launches Arazlo™ (tazarotene) Lotion, 0.045%, in the United States

Ortho | Dermatologics

Bausch Health Companies Inc. and its dermatology business, Ortho Dermatologics recently announced that Arazlo™ (tazarotene) Lotion, 0.045%, indicated for the topical treatment of acne vulgaris in patients nine years of age and older, is now available commercially to health care professionals in the United States.

The FDA approval for Arazlo Lotion, 0.045%, in December 2019 was based on data from two Phase 3 multicenter, randomized, double- blind, vehicle-controlled clinical trials in 1,614 patients with moderate to severe acne. In both Phase 3 studies, all primary efficacy endpoints were met with statistical significance (p<.001). ARAZLO was also shown to be generally well-tolerated in the clinical study population.[1]

For more information, visit the Arazlo Health Care Provider website at https://www.arazlo.com/hcp/

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