# Chicago Dermatological Society

# October 2018 Educational Conference

Program & Speaker Information
CME Certification
Case Presentations
*David Fretzin Lecture*

Wednesday, October 17, 2018
Gleacher Center
Chicago, IL

*Conference Host*
Department of Dermatology
University of Illinois at Chicago
Chicago, Illinois

# Program

***Host: University of Illinois at Chicago***
*Wednesday, October 17, 2018*
*Gleacher Center, Chicago*

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| 8:00 a.m. | **Registration & Continental Breakfast with Exhibitors**<br>*All activities will take place on the 6th Floor of the Gleacher Center* |
| 9:00 a.m. - 10:30 a.m. | **Clinical Rounds**<br>Slide viewing/posters |
| 9:00 a.m. - 10:00 a.m. | **Basic Science/Residents Lecture**<br>"A Guided Tour of the Electromagnetic Spectrum"<br>*Harvey Lui, MD* |
| 10:00 a.m. - 10:30 a.m. | **Break and Visit with Exhibitors** |
| 10:30 a.m. - 12:15 p.m. | • **"In Memoriam"**<br>• **Resident Case Presentations & Discussion; MOC Self-Assessment Questions** |
| 12:15 p.m. - 12:45 p.m. | • **Box Lunches & visit with exhibitors**<br>• **Medical Student Mentoring Lunch** - Room 602 |
| 12:55 p.m. - 1:00 p.m. | **CDS Business Meeting** |
| 1:00 p.m. - 2:00 p.m. | **General Session**<br>FRETZIN LECTURE - "New Insights in Photomedicine"<br>*Harvey Lui, MD* |
| 2:00 p.m. | **Meeting adjourns** |

***Mark the Date!***
Next CDS monthly meeting – Hosted by Northwestern University
Wednesday, November 14th; Gleacher Center, Chicago

Watch for details on the CDS website: www.ChicagoDerm.org
Save time and money – consider registering online!

# Guest Speaker

## HARVEY LUI, MD

### Head of the Department of Dermatology and Skin Science; University of British Columbia Vancouver, BC, Canada

Dr. Lui has been the Medical Director of The Skin Care Centre, the Lions Laser Skin Centre, and the Psoriasis & Phototherapy Clinic since 1994. He is also the Head of the Department of Dermatology and Skin Science at the University of British Columbia. After receiving his Bachelor of Science, Medical Degree, and Dermatology specialization from the University of British Columbia, Dr. Lui was a Clinical Fellow at the Massachusetts General Hospital, Harvard Medical School. He is a member of the American Board of Dermatology and the American Society for Laser Medicine and Surgery. Along with his duties at The Skin Care Centre and UBC, he is also on staff at the BC Cancer Agency and the BC Children's Hospital.

Dr. Lui has been the principal investigator in more than 35 research projects, has published more than 70 journal articles and more than 80 abstracts, is the chair or moderator of many dermatological conferences, and is an editor and reviewer for several international dermatology journals. He also is the current Director of the CIHR Skin Research Training Centre and the VGH Photomedicine Institute. His clinical and research interests include lasers, photomedicine, psoriasis, vitiligo, and dermatologic education.

# CME Information

10.17.2017

This educational activity is jointly provided by the Chicago Dermatological Society in partnership with the Indiana Academy of Ophthalmology

**Overview**

The Chicago Dermatological Society was established in 1901 and has strived to provide meaningful educational opportunities to dermatologists in the Chicago area for more than a century. Guest speakers from across the country share their expertise with CDS members, as well as residents in training medical students doing their dermatology rotation. CDS schedules six day-long meetings each year which are "hosted" by one of the dermatology residency programs in the city. In addition to two lectures given by the guest speaker, the residents of the host institution present cases which are offered for audience discussion. In addition, live patients, posters and microscopic slides prepared by the residents are made available during the "clinical rounds" portion of the meeting. CDS also offers a session that qualifies for "Maintenance of Certification" self-assessment questions under the auspices of the American Board of Dermatology.

**Target Audience**

This activity has been designed to meet the educational needs of dermatologists. CDS members, residents in training and medical students engaged in their dermatology rotation are invited to attend.

**Learning Objectives**

At the conclusion of the 2018/19 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for various diseases and conditions of the skin, including use of new or emerging medication options.
2. Describe the surgical techniques for treatment of skin cancers and for cosmetic purposes.
3. List the therapeutic options available to the dermatologist for a variety of skin diseases, both medical and surgical, and discuss how new emerging treatments can be successfully incorporated into a dermatology practice.

**Physician Accreditation Statement**

This activity is planned and implemented by Indiana Academy of Ophthalmology (IAO) and the Chicago Dermatological Society. IAO is accredited by the Indiana State Medical Association to provide continuing education for physicians.

***Credit Designation for Physicians*** – IAO designates this live activity for a maximum of 4.75 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**Attendees are required to submit a CME claim form upon departure from the conference. Please leave your form, along with the evaluation form, at the registration table when you leave the meeting. Thank you for your attention to this important item.**

**Disclosure of Conflicts of Interest**

The IAO and CDS require instructors, planners, managers and other individuals and their spouse/life partner who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified conflicts of interest are thoroughly vetted by IAO and CDS for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis for content, and appropriateness of patient care recommendations. All speakers are asked to follow the "first slide" rule to repeat their conflict of interest disclosures during their talk.

The guest speaker, Harvey Lui, MD, has disclosed the following potential conflicts of interest: Grants/Research Support - Johnson & Johnson, Pfizer, Novartis; Speakers Bureau - Novartis; Ownership interest or shareholder - Replicel Life Sciences, Lumen Health Innovations; Royalty/Patent Holder - Elsevier. None of the planning committee members have any relevant conflicts of interest to disclose.

*Continued next page*

**Contact Information**

For information about the physician accreditation of this program please contact the CDS administrative office at: 847-680-1666; email: Rich@RichardPaulAssociates.com

**Americans with Disabilities Act**

In compliance with the Americans with Disabilities Act, we will make every reasonable effort to accommodate your request. For any special requests, contact CDS at: Rich@RichardPaulAssociates.com

**Disclaimer**

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed in this activity should not be used by clinicians without evaluation of patient conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

**Dislosure of Unlabeled Use**

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

**Chicago Dermatological Society**
**Patient Privacy and HIPAA Compliance**

*APPROVED*
*June 3, 2015*

## Purpose

The purpose of this policy is to reaffirm the intent of the Chicago Dermatological Society (CDS) to appropriately safeguard patient privacy with respect to CDS conferences, publications and its website, and also to adhere to HIPAA requirements. All CDS members are expected to be aware of and conform to all regulations concerning patient privacy when attending a conference or utilizing any materials produced by CDS which contains any form of patient information which could be considered to be Protected Health Information.

## Background

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its implementing regulations restrict health care providers and others to use and disclose protected health information (PHI). Protected health information means information that is created or received by an entity and relates to the past, present, or future physical or mental health condition of a patient; the provision of health care to a patient; or the past, present, or future payment for the provision of health care to a patient; and that identifies the patient or for which there is a reasonable basis to believe the information can be used to identify the patient. Protected health information includes information of persons living or deceased.

Some examples of PHI are:
- Patient's medical record number
- Patient's demographic information (e.g. address, telephone number)
- Information doctors, nurses and other health care providers put in a patient's medical record
- Identifiable images of the patient
- Conversations a provider has about a patient's care or treatment with nurses and others
- Information about a patient in a provider's computer system or a health insurer's computer system
- Billing information about a patient at a clinic
- Any health information that can lead to the identity of an individual or the contents of the information can be used to make a reasonable assumption as to the identity of the individual

## Policy

The CDS takes seriously compliance with HIPAA regulations and safeguards concerning protected health information. Accordingly, the Chicago Dermatological Society has adopted the following provisions:

1. Case descriptions included in clinical conference "protocol books" and posters may not include information that could potentially identify a particular patient.

2. Photos of patients will not be published in clinical conference handout materials, including the protocol book.

3. To the extent possible, posters, slide presentations and videos displayed at CDS clinical conferences should avoid using photos that display a patient's full face or other features that could identify a particular patient. When a full-face photo must be used for clinical/educational reasons, the photo must be altered as much as possible to disguise the identity of the patient.

4. At all times, all attendees of CDS clinical conferences must adhere to appropriate behavior that respects the patient's right to privacy. Taking personal photos of posters or other displays, images included in general session lectures/presentations, and live patients at CDS conferences is strictly prohibited. Making audio recordings of any session at a CDS conference also is prohibited.

5. Attendees may not share materials distributed by CDS as part of the clinical conference or on its website with others who are not participating in the conference or who are not members of the CDS.

6. It is the responsibility of the "host" department partnering with CDS for a clinical conference to obtain all appropriate patient waivers and/or informed consent regarding the patient's participation in the CDS conference, including presentation of their case and display of posters or photos.

7. CDS will include a copy of its patient privacy policy in every meeting packet, and it will display a poster reiterating this policy at the entrance to live patient and poster viewing areas.

## Dr. Sophie Marie Worobec, MD

October 19, 1948 – July 12, 2018

Sophie Marie Worobec, BS 1970, MD 1973, died July 12, 2018 at age 69. She and a twin brother, Thomas George, were born in Manhattan, NY to a refugee Ukrainian family on Oct. 19, 1948. As infants they lived with their parents on the Lower East Side with a 10 year older brother, Roman. Their family had arrived as Displaced Persons post World War II just months earlier, having been being sponsored by their father's brother, Jack (Jakiv) Worobec . The family was also, after Jack's death, taken in by Jack's widow Mary (Marina). They lived in a tiny 3rd floor tenement apartment in the East Village. One luxury their mother allowed herself was a diaper service. During this time, their father, who had been a TB specialist in Europe, studied to learn English, get his NY State medical license and complete his American training in pulmonary medicine. After two years the family moved to an area outside of Shawnee, Oklahoma and lived in government housing on an Indian Reservation right next to a TB Sanatorium. Sophie loved that during her early years in Oklahoma, she was able to run freely from morning until early evening with her twin brother, Thomas, and a collie named Daisy throughout grassy fields, coming home mainly for meals. At age five, the family moved to Chicago. It was a shock that now, living in a rental apartment, it was only on special trips to public parks, that she was free to run on the grass. Walking on privately owned lawns was forbidden. But walking in back alleys and sidewalks was allowed. Unless, of course, it was a "dangerous area." But the city's shoreline, central public library, museums and Art Institute held a world of fascinating finds. Sophie did all her schooling in Chicago, first at Catholic schools, then at the University of Illinois, receiving her BS at age 21 and MD at age 24, and becoming a dermatologist at age 28.

Sophie was board certified in dermatology and dermatopathology. She worked in private practice for 5 years from 1977 to 1982, both in Bolingbrook IL and Downers Grove, IL. She also taught at Cook County Hospital in the occupational medicine department after finishing her dermatology residency in 1977. She became an Associate Professor of Clinical Dermatology in the College of Medicine at Chicago in 1988, and then again from 1999 to the present. She was instrumental in first obtaining federal funding for the Regional Hansen's Disease Clinic at the COM at Chicago in 1982 and served as its Director for six years. She also worked at Johnson and Johnson in Raritan, NJ from 1988 to 1992 in Clinical research and medical affairs, Kaiser Permanente in Los Angeles Sunset Medical Center 1992-1993, and the University of Rochester from July 1993 to c. August 1999. She worked in the field of contact dermatitis from 1973 until 2013, and she directed the Cutaneous Lymphomas and Related Diseases Clinic at UIC COM 1999 to the present. She received Discovery Award from the Robert Wood Johnson Pharmaceutical Research Institute in Raritan, NJ in 1991; the Chicago Dermatological Society's Founder's Award in 2005, and was named to Best Doctors in America from 2009 through 2016. She served as President of the Buffalo-Rochester Dermatological Society from 1997-1998.

Despite having a benign spinal cord tumor diagnosed and decompressed at age 29, Sophie worked a hectic life as a full time doctor for 43 years, until age 67. In the midst of this, at age 34, she had a daughter. Dr. Sophie was very proud that her daughter Adrienne also became a medical doctor and chose hematology and oncology as her specialty.

Upon her semi-retirement in Jan 1, 2016, Sophie had a chance to more leisurely enjoy her family, friends, good food, music, movies, television, a little travel, language lessons, a little homemaking and books. Survivors include husband John Gregory Victor, two brothers, Thomas and Roman (Trina); daughter Adrienne Irene Victor (Derrick Taylor), granddaughter Cassandra Lynn Taylor, grandson Aiden Grant Taylor, nieces Sophia Catherine Worobec, Sarah Kaiman, Danielle Victor Calloway, Kendall Rose Victor,

and nephews Henry, Thomas and David Worobec , Jeffrey Kaiman, and Bobby, Collin, Quentin and Cameron Victor.

## Tributes from CDS Members

"Will truly miss Dr. Worobec. She was a very friendly, supportive colleague who really cared about our Chicago Dermatological Society and our community of dermatologists. She definitely left her mark as a great clinician and teacher with generations of dermatology residents both inside and outside the University of Illinois program. I really appreciated her warm collegiality and friendship and support as a CDS officer and throughout my career. She really embodied the concept of not only being an outstanding dermatologist; but adding to our specialty and leaving a legacy for the future." - Dr. Jeffrey S. Altman

"Dr. Worobec demonstrated the importance of forging a strong physician-patient relationship. In today's environment of short patient encounters and maximizing our schedules, Dr. Worobec taught me to always take the time to talk and listen with the patient. She cared deeply for her patients, both to help them medically but also to get to know them as people and individuals." - Anonymous

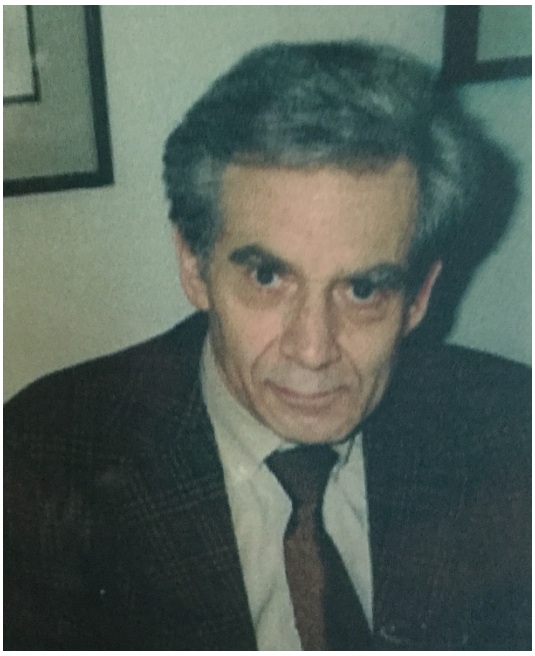
"Dr. Worobec was a truly compassionate physician and person. Working with and her and training from her always reminded me to slow down and think about the whole patient, maybe not only his or her skin. She made every effort to become close to her patients; she tried learning Spanish to communicate better, she constantly asked about those in our lives, new nieces, etc. I don't know of many physicians who cared as much as she did.

We worked for months on a textbook chapter and with each phase she made a point to tell me what a great job I was doing, it meant so much to me but what was so amazing was how it meant something to her to tell me that I knew I was doing well, to share that feeling with me. She was direct and productive with her feedback always with the hopes of making us the best dermatologists possible.

She took such joy in spending time with her patients. She never cared about being behind in clinic if the patient truly needed the attention. She approached each patient as a *person* and addressed him or her with open mind and heart. I currently have patients tell me that they used to see "Sophie" and what a wonderful person she was. Commenting on her as a person far exceeds comments on her dermatologic skills, showing what truly stays with patients over time. I have learned so much from Dr. Worobec, and as a current academic faculty member, I hope to leave a legacy as profound and significant as the one that Dr. Worobec has left. She is admirable in so many ways, and the things she has taught her many residents will survive indefinitely." – Dr. Eden Lake

"Dr. Worobec was a close friend and colleague of many years duration who possessed a generous spirit and keen intellect. Her passing leaves a large void in all our lives." – Dr. Carlotta Hill

"What was special about Sophie? I have known her since 1979.
She was always knowledgeable and her opinion was sought not only on clinical matters but also her intellect and non-biased thought processes were an invaluable asset for analyzing papers and research projects. In meetings she was attentive and would make incisive and relevant comments. Her understanding of and experience with dermatological conditions especially Hansen's disease, contact dermatitis, and cutaneous lymphoma was invaluable. As a person she was resilient, focused and on track. As a friend she was solid, reliable and steadfastly there." – Dr. Anne Laumann



## Dr. Hans van den Broek, MD

December 20, 1932 - September 13, 2018

Dr. Hans van den Broek was an Assistant Professor of Dermatology at UIC and Chief of Dermatology at Hines VA Hospital from 1977 - 1989. He was an excellent and compassionate physician; an outstanding teacher and role model; a knowledgeable and collegial colleague; and a kind, caring, and true friend.

After leaving Chicago, Dr. van den Broek joined the faculty at the University of New York at Buffalo where he assumed responsibility as Chief of Dermatology at the Buffalo VA Hospital. At both institutions, he was especially fond of his residents and always served as an excellent role model; he was their mentor and their friend. As his former residents will attest, his stern demeanor gave way to a dry sense of humor after the work was done for the day. Once the residents got to know him, they always had a soft spot in their hearts for him.

Dr. van den Broek was born and raised in The Hague, and graduated from the University of Leiden in the Netherlands. He did postgraduate training in Internal Medicine at Montefiore Medical Center in New York City. He completed a Cardiology Fellowship at Hahnemann University Hospital in Philadelphia where he was subsequently on the faculty for ten years as an Interventional Cardiologist. During that time he was exposed to Dermatology and decided to make a career switch.
After completing his Dermatology training at Hahnemann, he joined the faculty at UIC in 1977. He was triple boarded in Internal Medicine, Cardiology, and Dermatology. The residents always knew to whom to turn for answers to difficult medical problems.

Following his retirement in 2005, he pursued his long time interests in Medieval Philosophy and Medieval History earning two Masters' Degrees, one in each area, from the University of New York at Buffalo. He found his greatest joy in his pursuit of nature photography. He saw and appreciated the awe inspiring beauty of nature and was able to share the beauty he found with those fortunate enough to see the photographs that he created.

He is survived by his brother Carl, Carl's daughter Marjolein, and Carl's son Marc.

We remember and honor Dr. Hans van den Broek - an exemplary physician, an outstanding teacher, our esteemed colleague, our dear friend.

Virginia C. Fiedler, MD
Professor Emerita and Former Head
Department of Dermatology, UIC

*Photographs by Hans van den Broek, MD*

# University of Illinois at Chicago
# Department of Dermatology

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Olivia Lai, MD
Regina O'Brien, MD

**First Year**
Jacob Charny, MD
Thomas Klis, MD
Owen Kramer, MD
Krishna Patel, MD

# Table of Contents

**Case Presented by Artem Sergeyenko, MD**
**and Michelle Bain, MD**

**History of Present Illness:**
A 67 year old male presented to the hospital for subarachnoid hemorrhage and was incidentally noted to have heavy scaling on the bilateral lower extremities. The patient was non-conversant at time of consultation, but the daughter provided history at bedside. The patient had always worn long-sleeved clothing and pants, thus no one had seen his skin in many years. It was unclear how long scaling had been present.

**Past Medical and Surgical History:**
Congestive heart failure, type 2 diabetes mellitus, hypertension, and schizophrenia

**Medications:**
Risperidone, carvedilol, sertraline, aspirin, isosorbide mononitrate, doxazosin, enalapril, hydralazine, furosemide, and atorvastatin

**Allergies:**
None

**Family History:**
Family history was notable for eczema in distant relatives, but negative for comparable conditions.

**Review of systems:**
The patient was non-conversant and unable to provide a review of systems.

**Physical Examination:**
The anterior chest, abdomen, lateral arms, and forearms have many large, exophytic brown papules and plate-like scaling. The anterior legs and feet are extensively covered with coalescing, hyperkeratotic plaques and papules with scattered verrucous brown papules on the dorsal aspects of the feet bilaterally.

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**Histopathology:**
Left foot, skin: Low power view shows a patchy diminished granular cell layer beneath an extensive, dense compact orthokeratotic column of hyperkeratosis. Higher power view of the abnormal granular cell layer shows expanded granular cells that retain a normal nuclear to cytoplasm ratio. This view highlights the contrast between the normal edge of skin and abnormal center containing enlarged atypical cells and diminished granular cell layer. Immunohistochemical staining with cytokeratin markers AE1/3, 5/6, and 19, showed normal, positive uptake.

**Genetic Testing:**
DNA sequencing for an ichthyosis gene panel revealed a c.1121G>A transition in exon 10 of the steroid sulfatase (STS) gene

**Diagnosis:**
X-linked Ichthyosis

**Treatment and Course:**
Topical keratolytics were recommended for the patient and genetic counselling was suggested for his family members. Due to the comorbidities associated with the patient's subarachnoid hemorrhage, the patient was discharged to a rehabilitation facility and was subsequently lost to follow-up.

**Discussion:**
X-linked ichthyosis (XLI) is a congenital skin disorder first classified in 1965 by Dr. Wells and Dr. Kerr. It belongs to a heterogenous group of acquired and congenital disorders of keratinization that manifest with hyperkeratosis, xerosis, and scaling. With a prevalence of 1 in 6000 males, XLI is the second most common type of ichthyosis. Although XLI occurs almost exclusively in males, females can be carriers and may rarely exhibit skin manifestations.

The disorder is caused by a mutation or deletion in the steroid sulfatase (STS) gene on the X chromosome. Absence of STS activity results in the accumulation of cholesterol sulfate in the stratum corneum, which leads to corneocyte cohesion, hyperkeratosis, and impaired skin permeability.

X-linked ichthyosis usually presents in the first six months of life with generalized desquamation and xerosis that then progresses to fine scaling of the trunk and extremities. Over time, scales often become coarser and darker affecting the lateral face, axillae, and neck almost universally, while typically sparing the palms, soles, mid-face, antecubital, and popliteal fossae. Extracutaneous manifestations of XLI include comma shaped corneal opacities, hypogonadism, cryptorchidism, as well as an increased risk of testicular cancer. Female carriers may have prolonged labor of the affected child.

Due to similarity in presentation to other ichthyoses, such as ichthyosis vulgaris and lamellar ichthyosis, genetic analysis should be used to distinguish XLI from potential mimickers, and should be considered in all patients with an atypical presentation. After diagnosis of XLI, prompt symptomatic treatment, genetic counseling, and work-up for extracutaneous manifestations should be performed.

**Essential Lesson:**
- X-Linked Ichthyosis is the second most common type of ichthyosis.
- It occurs due to a mutation in the steroid sulfatase gene.
- X-linked ichthyosis may be associated with hypogonadism, testicular cancer, corneal opacities, and prolonged labor in female carriers.

**References:**


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2. Brookes KJ, et al. Polymorphisms of the steroid sulfatase (STS) gene are associated with attention deficit hyperactivity disorder and influence brain tissue mRNA expression. *Am J Med Genet Part B Neuropsychiatr Genet* 2010;153(8):1417-1424.
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4. Fernandes NF, et al. X-linked ichthyosis: An oculocutaneous genodermatosis. *J Am Acad Dermatol* 2010;62(3):480-485.
5. Hernandez A. X-linked ichthyosis: an update. *Br J Dermatol* 1999;141(4):617-27.
6. Kent L, et al. X-linked ichthyosis (steroid sulfatase deficiency) is associated with increased risk of attention deficit hyperactivity disorder, autism and social communication deficits. *J Med Genet* 2008;45(8):519-24.
7. Marukian NV., Choate KA. Recent advances in understanding ichthyosis pathogenesis. *F1000Res* 2016;5(0):1497.
8. Wells RS, Kerr CB. Genetic classification of ichthyosis. *Arch Dermatol* 1965;92(1):1-6. http://dx.doi.org/10.1001/archderm.1965.01600130007001.

**Case Presented by Regina O'Brien, MD**
**and Maria Tsoukas MD, PhD**

## UNKNOWN

A 54 year old Caucasian male presented to dermatology for a lump on his left lower cheek slowly growing for five months.

**Case 3**

**Case Presented by Krishna Patel, MD,**
**James Feinberg, MD, JD, MPH, and Lawrence Chan, MD**

**History of Present Illness:**
A 61 year old African American female presented with a one-month history of painful nodules on the extremities and trunk. The nodules appeared suddenly, grew rapidly in size, and had no associated drainage. The patient also noted an occasional cough, shortness of breath, and night sweats prior to the onset of her cutaneous lesions. No new medications or interventions were initiated prior to symptom development.

**Past Medical History:**
Sjogren's disease, anterior uveitis, and IgG4 associated autoimmune pancreatitis

**Medications:**
Rituximab infusions, hydroxychloroquine, prednisone, methotrexate, and folic acid

**Allergies:**
Iodine

**Family History:**
No history of skin cancer or skin conditions. The patient has a daughter with multiple myeloma.

**Review of systems:**
The patient reported an intentional 50 pound weight loss over the past year. She also reported longstanding arthralgia, mouth sores, eye pain, photosensitivity, eye redness, and eye dryness. New symptoms included night sweats, chills, cough, and dyspnea. The patient denied weakness, fatigue, hemoptysis, or pruritus.

**Physical Examination:**
The patient has firm, slightly tender subcutaneous nodules, ranging from 3 to 5 cm in size, on the forearms, legs, chest, and back. A larger 7 cm subcutaneous nodule is on the abdomen with an overlying ring of erythema. Faint mottled hyperpigmentation and a few erosions are noted on the shins, along with +1 pitting edema of the lower extremities.

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**Laboratory Data:**
The following were positive or abnormal:
*Antinuclear antibody 1:160 (<1:40)*
*SSA 79 EU (0-19)*
*Anti-ribonucleoprotein 32.76 EU (0-19)*
*Rheumatoid factor 20.4 IU/mL (0-15)*

The following were negative or within normal limits:
Complete blood count, complete metabolic panel, SSB, cyclic citrullinated peptide antibody, anti-Smith antibody, C3, C4, CH50, anti-dsDNA antibody, HLA B27, Quantiferon gold, ACE level, and hepatitis panel.

**Diagnostic Procedures and Tests:**

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|---|---|
| 10/10 | X-ray, Chest: No abnormalities. |
| 10/10 | Pulmonary Function Testing: Normal diffusing capacity of the lung for carbon monoxide. |
| 11/15 | Computed Tomography, Chest: Non-specific bilateral hilar adenopathy, ground glass opacities, and bilateral basilar infiltrates. |

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**Histopathology:**
Right forearm, skin: Granulomatous dermatitis and panniculitis marked by multiple discrete non-caseating granulomas composed of epithelioid histiocytes, with multinucleated giant cells surrounded by fibrosis involving the deep dermis and subcutis. The periodic acid-Schiff and acid-fast bacilli stains are negative for microorganisms.

**Diagnosis:**
Darier-Roussy Sarcoidosis

**Treatment and Course:**
The patient's prednisone dose was increased from 7 to 20 mg daily. Plaquenil was continued at 200 mg twice daily and methotrexate at 20 mg weekly. Within one month, no new lesions were noted and by three months, all existing lesions were flattened with residual mild post-inflammatory hyperpigmentation. The patient also reported a reduction in dyspnea and night sweats. Prednisone was tapered to 12.5 mg daily after three months, and the patient is currently on 3 mg daily approximately one year later. Ophthalmology noted that her anterior uveitis was likely associated with the new diagnosis of sarcoidosis. Rheumatology transitioned the patient from rituximab to infliximab infusions for management of Sjogren's syndrome and anterior uveitis due to persistent symptoms. Pulmonology recommended repeat computed tomography scan of the chest. The scan showed improvement in the ground glass opacities, resolution of hilar adenopathy, and no new lung nodules or consolidation.

**Discussion:**
Darier-Roussy sarcoidosis is a rare form of sarcoidosis with involvement of the deep subcutaneous tissue. The disease has a female predilection with a peak incidence in the fourth decade of life. Typical cutaneous findings include the presence of painless, firm mobile nodules, without overlying epidermal involvement. The nodules are mostly frequently found on the extremities (78.8%), trunk (28%), buttocks (10%), and forehead (5%). Clinical presentation may mimic erythema nodosum and tuberculosis.

The diagnosis is made by biopsy, with pathology showing noninfectious epithelioid granulomas with multi-nucleated giant cells involving the deep reticular dermis and panniculus. Subcutaneous sarcoidosis represents 1.4 - 6.0% of all sarcoidosis cases and the prevalence in patients with systemic disease is 4.3 - 12.1%. It may sometimes present as the initial manifestation of systemic sarcoidosis. These patients may have less severe systemic disease, but will often have associated hilar adenopathy, so pulmonary evaluation is recommended.

Oral glucocorticoids are the mainstay of treatment for subcutaneous sarcoidosis. Prednisone, 20 - 40 mg daily with taper, as well as weight-based dosing methods for prednisone, have both been described. Responses are typically noted four to eight weeks after initiation of therapy. The most common steroid sparing drug used is hydroxychloroquine. Second line medications include methotrexate, clofazimine, thalidomide, dapsone, potassium iodide, and minocycline.

Herein, we present a patient with a rare variant of sarcoidosis. Patients with subcutaneous sarcoidosis should undergo evaluation for systemic involvement. A thorough infectious work-up should also be performed to rule out an infectious etiology such as tuberculosis.

**Essential Lesson:**

- Darier-Roussy sarcoidosis is a rare form of sarcoidosis involving the deep subcutaneous tissue that usually presents with painless, firm mobile nodules without overlying epidermal involvement.
- Hilar adenopathy is the most common systemic finding.
- Subcutaneous sarcoidosis typically responds well to treatment with oral gluococorticoids and hydroxychloroquine is the most commonly used steroid sparing agent.

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**Case Presented by Kurt Ashack, MD**
**and Carlotta Hill, MD**

**History of Present Illness:**
A 29 year old man from Hyderabad, India presented with 18 months of progressive numbness and tingling in his lower extremities. He immigrated to the United States three years prior. He denied a family history of Hansen's disease as well as contact with armadillos or persons with the disease. A neurologist initially diagnosed and treated a vitamin B12 and thiamine deficiency. Additionally, the neurologist ordered two electromyography tests, without a nerve conduction velocity test, that were inconclusive.

In January of this year the patient visited India where he developed a rash on his legs, which spread to his hands and arms. The rash was described as red, raised, and asymptomatic. He consulted a physician there who did a biopsy that was "positive" for acid-fast bacilli. In March, a physician in India started him on rifampin 600 mg once a month, dapsone 100 mg daily, and clofazimine 100 mg every other day. Several weeks into treatment he noted ulcerations in areas previously involved with the rash and was given unknown antibiotics for ten days. He presented to our dermatology clinic for further management.

**Past Medical History:**
None

**Medications:**
Rifampin 600 mg monthly, dapsone 100 mg daily, clofazimine 100 mg every other day

**Allergies:**
No known drug allergies

**Family History:**
No history of Hansen's disease or other skin disorders

**Social History:**
He is married and has one child. He immigrated to the US three years ago from Hyderabad, India. He denies any tobacco, alcohol intake, or illicit drug use.

**Review of systems:**
The patient complained of edema of the extremities as well as paresthesias in his feet and in the first three fingers of his left hand. He denied fevers, chills, weight loss, pain, or pruritus.

**Physical Examination:**
The patient has several erythematous, slightly indurated, and hyperkeratotic plaques and patches on both upper and lower extremities, on the dorsal hands and feet, and on the lower back and abdomen. Within these plaques are multiple ulcerations with irregular borders on the medial right leg, anterior left lower leg, and left lateral lower leg lacking purulent drainage or surrounding erythema. A similar ulcer with a hyperpigmented rim and extensive granulation tissue is noted on the right palm. The left second and third fingers have two hypopigmented patches from previous burns and the first, second, and third fingers are tapered proximally to distally. Mild hypothenar atrophy of the left hand is also noted. The right ulnar nerve is enlarged and tender to palpation. There is edema of the lower extremities and the hands.

**Laboratory Data:**
The following were positive or abnormal:
*Hemoglobin: 11.7 g/dL (13.2-18.0)*
*Hematocrit: 36.1% (38.0-55.0)*
*Red blood cell distribution width: 15.1% (11.6-15.0)*
*Absolute lymphocytes: 1.2 k/uL (1.3-4.2)*
*Glucose-6-phosphate dehydrogenase: 18.9 U/g Hb (9.9-16.6)*
*Urinalysis: 3 red blood cells per high power field (0-2)*

The following were negative or within normal limits:
Acute hepatitis panel, Quantiferon gold, C-reactive protein, comprehensive metabolic panel, and the remainder of the complete blood cell count.

**Microbiology:**
6/17: Superficial wound culture positive for Staphylococcus aureus, Escherichia coli, and Enterobacter cloacae/complex

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**Histopathology:**
Left upper arm, skin: Sections reveal a slightly acanthotic epidermis. A chronic inflammatory infiltrate consisting of disorganized aggregates of histiocytes with interspersed lymphocytes replaces 30-40% of the dermis and extends into the subcutaneous tissue. Collections of large multinucleated giant cells are present within the aggregates. The infiltrates surround small vessels, dermal appendageal structures, and rare cutaneous nerves. Fite stains reveal scattered intact acid-fast bacilli within histiocytes and within a cutaneous nerve twig.

Molecular studies: Positive PCR for Mycobacterium leprae

Bacterial index: 2-3+

**Diagnosis:**
Hansen's disease, multibacillary, borderline, active, with type I (reversal) reaction

**Treatment and Course:**
The patient was started on prednisone taper, 40 mg daily for one week, 30 mg for two weeks, and then 20 mg daily for one month. He was continued on rifampin, dapsone, and clofazimine. Vitamin D and calcium supplements were recommended while he was taking prednisone. The patient was also started on doxycycline 100 mg twice daily for ten days given the positive wound culture. Additionally, physical and occupational therapy evaluated the patient and he received diabetic boots given the extent of his peripheral neuropathy. At a one month follow-up visit, the patient's lesions improved with flattening and hyperpigmentation of the plaques as well as reduction in both the size of the ulcers and the extent of edema of the extremities. He was continued on a slow taper of prednisone over the next ten weeks.

**Discussion:**
Leprosy is a chronic, infectious disease caused by Mycobacterium leprae that mainly affects the peripheral nervous system and skin. Currently, leprosy is classified based on clinical features, histopathology, bacterial load, and the degree of the cell-mediated immune response. Based on these criteria, five classifications exist: Tuberculoid leprosy (TT), borderline tuberculoid (BT), borderline-borderline (BB), borderline lepromatous (BL), and lepromatous (LL). An indeterminate (I) type of leprosy also exists which may evolve into any of the above.

Additionally, patients with leprosy are also classified based on bacterial load, or index, defined as the average number of bacilli per microscopic field using an oil-immersion objective. Patients with a bacterial index less than 2+ are considered paucibacillary and multibacillary if the bacterial index is equal to 2+ or higher. This classification helps determine the therapeutic regimen for the patient.

Borderline-borderline leprosy, the classification of our patient, is a rare subtype and the most unstable, meaning it can downgrade toward the resistant LL form or upgrade toward a more favorable prognostic group within the leprosy spectrum. Clinically, lesions in the BB group favor a “swiss cheese” appearance. They contain a hypochromic center, a well-defined inner border, and a vaguely defined outer border. Plaques are often indurated. Nerve involvement varies among patients.

A unique presentation of leprosy, more common among borderline subtypes, is a type 1 leprosy reaction, also known as a reversal reaction. This occurs when a heightened cellular immune response occurs against Mycobacterium leprae antigens. It can occur gradually before, during, or after receiving multidrug therapy, and can last for weeks to months.

Diagnosis of a type 1 reaction is often made clinically, as laboratory tests and histopathology are of limited help. Patients with a type 1 reaction often present with induration and erythema of existing lesions. Occasionally, as in our patient, ulcerations can occur in areas of involved skin. Acral and facial edema, and worsening of neuritis are additional features. Without treatment, patients may develop permanent nerve damage and possibly resultant paralysis.

Aside from BL patients having a 30 - 50% risk of a type 1 reaction, other factors thought to increase the risk of a type 1 reaction include concurrent infection, stress, trauma, use of oral contraceptives, increasing age, and extensive disease. Roche et al. also showed that patients with an elevated IgM anti-phenolic-glycolipid-1 antibody and lepromin positivity were at increased risk of developing a type 1 reaction.

When a type 1 reaction occurs, prednisone administered concomitantly with the traditional multidrug therapy (rifampin, dapsone, and clofazimine) is the standard of care. A starting dose of 40 to 60 mg of prednisone daily is recommended. Naafs et al. pooled all data from the All Africa Leprosy and Rehabilitation Training Centre from 1968 to 1974, and 1974 on, along with data from the World Health Organization from 1994 to 1995, and concluded that prednisolone at a starting dose of 0.5 to 1.0 mg/kg could be administered daily until the reaction settles. Once this occurs, prednisolone should be tapered slowly, remaining greater than 0.25 mg/kg/day for at least three to six months, and then tapered off completely. If oral steroids are contraindicated, cyclosporine or azathioprine may be used, but these drugs are less effective.

Herein, we present a patient with an uncommon type of BB/BL leprosy who developed a type 1 reaction that responded favorably to oral prednisone. We also highlight the cutaneous presentation of reversal reactions so as to facilitate prompt recognition of this condition and prevent permanent loss of nerve function.

**Essential Lesson:**

- Leprosy is a chronic, infectious disease caused by Mycobacterium leprae that usually targets the peripheral nervous system and skin.
- There are five types of leprosy: TL, BT, BB, BL, and LL. An Indeterminate type also exists.
- BB is an uncommon type of leprosy and is highly unstable.
- Type 1 reversal reactions commonly occur in borderline leprosy patients, and present with worsening of skin lesions, ulcerations, and progressive neuritis.
- Prednisone is the mainstay of treatment for type 1 reactions and it is imperative that it is initiated rapidly given the grave consequences of the progressive neuritis.

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**Case 5**

**Case Presented by Jeremiah Au, MD**
**and Amy Flischel, MD**

## UNKNOWN

A 37 year old male military recruit presented to the dermatology clinic for a pruritic rash on his chest, abdomen, and back for one week.

**Case Presented by Thomas Klis, MD,**
**Marylee Braniecki, MD, and Iris K Aronson, MD**

**History of Present Illness:**
A 27 year old female transferred to the University of Illinois, Chicago, Hospital from an outside hospital where she had presented with painful lesions on her arms, legs, and buttocks. The nodules on her buttocks had been incised and drained, and she was given methylprednisolone and ampicillin-sulbactam without improvement. The majority of the nodules had resolved over the previous week, leaving bruising and some ulcerations. She reported having constant pain and swelling over her upper and lower extremities. Some of the nodules had overlying blisters on initial presentation. A punch biopsy performed at an outside hospital was too superficial for a conclusive diagnosis.

**Past Medical History:**
None

**Medications:**
None

**Allergies:**
Cephalexin and hydromorphone

**Family History:**
No family history of skin conditions, autoimmune, or genetic diseases

**Social History:**
Patient is a current smoker but denies any illicit drug use.

**Review of systems:**
The patient complained of mild constipation. She denied any fevers, lethargy, confusion, chills, nausea, vomiting, abdominal pain, night sweats, weight loss, or joint pains.

**Physical Examination:**
The patient appears in no apparent distress and is alert and oriented to person, place, and time. Examination of the upper extremities reveals 3+ pitting edema and scattered firm nodules with overlying purpura. On the lower extremities, there are a moderate number of coalescing purpura and 3+ pitting edema. The left posterior calf has a 6 cm eroded nodule with an overlying ecchymosis. Her mucous membranes are clear. There is no evidence of lymphadenopathy or hepatosplenomegaly. At the time of initial presentation, the patient's chest, abdomen, and back were uninvolved.

**Laboratory Data:**
The following were positive or abnormal:
*Creatinine: 2.06 mg/dL (0.4-1.20)*
*Blood urea nitrogen: 86 mg/dL (4-20)*
*Lactic acid: 3.0 mmol/L (0.5-2)*
*AST: 89 u/L (10-40)*
*ALT: 66 u/L (10-40)*
*White blood cell count: 36 k/uL (3.9-12)*
*Hemoglobin: 9.7 g/L (11-16)*
*Alpha-1 antitrypsin level: 70 mg/dL (100-300)*

The following were negative or within normal limits:
Antinuclear antibody, antibodies to dsDNA, ssDNA, Smith, SSA, SSB, and histone; C-ANCA, P-ANCA, ESR, total bilirubin, direct bilirubin, alkaline phosphatase, platelets, serum protein electrophoresis; serum studies for Herpes simplex virus, Parvovirus, Cytomegalovirus and Epstein Barr virus; blood cultures for bacteria and fungi.

**Diagnostic Procedures and Tests:**
01/18 Computed Tomography, Abdomen and Pelvis: Moderate amount of abdominal and pelvic simple free fluid, diffuse colonic wall thickening, and pericolonic inflammatory change most compatible with colitis.
01/18 Chest X-Ray: Bilateral pleural effusions with superimposed atelectasis, right greater than left.
01/18 Abdominal Ultrasound: Normal size spleen, unremarkable, mild echogenicity of liver.

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**Histopathology:**
01/03/18 Left arm, skin: Subcutaneous fat shows foci of histiocytic engulfment of neutrophilic nuclear debris forming "bean bag' cells, with positive staining for CD68. Findings consistent with cytophagic histiocytic panniculitis, which may be secondary to possibly progressing lymphoid malignancy, connective tissue disorder, or an infection.

01/26/18 Left back, skin: Mixed lobular and septal neutrophilic panniculitis, with a predominance of neutrophils within the inflammatory infiltrate. High power reveals liquefactive fat necrosis with nuclear debris and absent elastic fibers. No changes of vasculitis are present in the subcutis. Bacterial and viral stains are negative and there is no calcification in the vascular walls of the subcutis.

**Genetic Testing:**
Alpha-1 antitrypsin genotyping: Homozygous for Z deficiency allele

**Diagnosis:**
Alpha-1 antitrypsin deficiency panniculitis, initially presenting with cytophagic histiocytic panniculitis

**Treatment and Course:**
The patient presented initially with painful nodules on her arms and legs and was given methylprednisolone and antibiotics. She subsequently developed abdominal pain. CT studies and exploratory laparotomy showed a perforated bowel, and an ostomy was performed. With the initial diagnosis of cytophagic histiocytic panniculitis (CHP), cyclosporine, plasmapheresis and intravenous immunoglobulin (IVIG) were given without improvement. A second biopsy was

performed, which revealed findings suspicious for alpha-1 antitrypsin deficiency (A1AT). After A1AT studies showed the patient to have ZZ homozygous A1AT deficiency, the previous treatment was tapered and she was started on A1AT augmentation therapy, Prolastin, at a dose of 60 mg/kg once weekly. Due to her continued deterioration, the dose was increased to twice weekly infusions at 120 mg/kg. Further consultation with A1AT specialists led to addition of dapsone 150 mg daily.

Despite these measures, the patient's clinical condition continued to deteriorate, and she returned to the operating room for a subtotal colectomy. The surgeon had commented that the abdominal tissue practically dissolved at her touch. The patient's hospital course was further complicated by development of sepsis (with positive blood culture growth of Candida) and disseminated intravascular coagulation. Massive transfusion protocol and vasopressors were initiated. Due to her worsening condition, the family elected to withdraw care and the patient expired after a hospital stay spanning over a month. Upon post-mortem autopsy, the patient's lungs showed right lower lobe with hemorrhagic necrosis and fungi. Only minimal emphysematous changes were seen on a microscopic level. The liver was fatty with hepatotosteatotic microvesicular and macrovesicular changes. Extensive generalized adipocytic autolysis was noted, including enzymatic degradation of visceral fat with secondary bacterial and fungal colonization.

**Discussion:**

The association of panniculitis and alpha-1 antitrypsin (A1AT) deficiency is rare, developing in 0.1% of patients with A1AT deficiency. Overall, about 100 cases have been reported in the literature. The panniculitis associated with A1AT deficiency of the homozygous ZZ variant tends to be relapsing and widely disseminated, with new lesions appearing as old ones resolve. The nodules can appear on any part of the body but are most frequent on the proximal parts of the extremities, the buttocks, and the ventral side of the trunk. Ulceration with drainage of oily, serosanguineous fluid from larger lesions has been described in many cases. A1AT panniculitis histopathology typically shows a lobular panniculitis but septal involvement may be seen. In early stages, neutrophils are interstitially arranged between collagen bundles of the deep reticular dermis, followed by a neutrophilic mixed panniculitis with lobular necrosis.

In some instances, the panniculitis can become severe, especially if necrotizing and/or infected. Life-threatening cases and death from panniculitis have been reported, including two patients seen at Loyola University at Maywood in the 1970s, which shows that the association between A1AT deficiency and panniculitis is unlikely to be accidental and that marked decrease in A1AT levels associated with panniculitis may be fatal. Another more recent case last year from Germany showed a patient with the ZZ mutation presenting with a severe, episodic panniculitis of the upper legs. Necrosis of the fatty tissue and a suspected superinfection led to amputation of one leg. Yet another case in the German literature showed a patient with the heterozygous PiMZ genotype develop a fatal necrotizing panniculitis associated with A1AT deficiency that appeared clinically like pyoderma gangrenosum. Patients with panniculitis, due to any reason where there is inflammation of the fat, may have gastrointestinal abnormalities as well, including bowel perforation, as in our patient's case. This has been shown by Aronson et al., in which post mortem evaluations showed panniculitis patients with gastrointestinal wall inflammation, including four who developed abdominal emergencies with bowel perforation.

Cytophagic histiocytosis may be seen in rare hematologic malignancies, inflammatory states, and infections. However, cytophagic histiocytosis is not a well-known histological finding in A1AT panniculitis. In the rare case of severe A1AT panniculitis, this can be explained by the polymerization of the defective A1AT molecule, which accumulates in the neutrophils,

histiocytes, and possibly adipocytes that eventually leads to cellular apoptosis and extracellular A1AT polymers, which are then phagocytosed. Thus, a plausible explanation for the observed cytophagic histiocytosis in A1AT panniculitis is that it is likely a reactive process in which the cellular debris has recruited phagocytic histiocytes. In addition, reviews on the inflammatory role of adipose tissue show that adipocytes are innate immune cells and adipocytokines are involved in primary inflammatory processes and diseases. Thus, A1AT polymers, which have been detected in affected skin, have proinflammatory and chemotactic effects which augment the inflammatory cascade initiated by the adipocytes.

Several therapies for A1AT deficiency panniculitis have been tried over the years, with the most successful being intravenous A1AT infusions. The treatment is given in doses of 60 –120 mg/kg once weekly, with higher doses being used for patients with pulmonary or hepatic disease. However, this replacement therapy is off-label use for treatment of cutaneous symptoms in most countries. A1AT infusion treatments are extremely expensive, costing $143 per 1 gram vial. Dapsone has been effectively used in numerous cases. Typically, dapsone doses of 50 – 150 mg daily were administered. The drug interferes with the action of myeloperoxidase and thus preserves the already limited amount of A1AT available to modulate the reactivity of inflammatory cells. A1AT deficiency panniculitis can be refractory to therapy and require commercial purified A1AT infusions. Early identification of A1AT deficiency, especially of the homozygous ZZ type, may help prevent development of complications such as COPD, cirrhosis, and progression of severe panniculitis.

**Essential Lesson:**

- A1AT deficiency panniculitis is an extremely rare and underdiagnosed entity, and there is a paucity of data on its treatment. Panniculitis may be the initial manifestation of this disorder caused by extracellular deposition of abnormal polymers in fat with a subsequent inflammatory reaction.
- Cytophagic histiocytic panniculitis (CHP) is a rare panniculitis, which shows lymphocytic and histiocytic infiltration of adipose tissue with cytophagocytosis. It may be seen in association with various disorders including viral infections (e.g. Epstein Barr virus), fungal infections (e.g. Histoplasmosis), connective tissues diseases, malignancies, and A1AT panniculitis.

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**Case Presented by Jacob W. Charny, MD**
**and Michelle Bain, MD**

**History of Present Illness:**
3 year old identical female triplets (patients 1, 2, and 3) were referred to dermatology from primary care for skin changes that had been present since birth. The parents noted that each child was born with a similar asymptomatic red lacey rash on the lower extremities, abdomen, chest, and upper extremities. The rashes were more pronounced with crying, but were always present. The rashes have not spread and have faded gradually over time.

**Past Medical & Surgical History:**
Patients 1, 2, and 3: Premature birth at 31 weeks via cesarean section, followed by 38 days spent in the neonatal intensive care unit without complications

Patient 1: Right Achilles tendon contracture status post z-lengthening surgery complicated by gross motor delay, bilateral diplegia, hyperopic astigmatism and intermittent exotropia with corrective glasses, speech delay and mild developmental delay

Patient 2: Mild developmental delay, speech delay

Patient 3: Mild developmental delay, speech delay

**Medications:**
None

**Allergies:**
No known drug allergies

**Family History:**
No family history of similar skin conditions, developmental delay or macrocephaly

**Review of systems:**
The family denied any limb swelling or atrophy, seizures, or behavioral changes.

**Physical Examination:**
Patients 1, 2, and 3 each similarly have diffuse erythematous blanching reticulated patches, most prominently on the lower extremities and with more subtle involvement of the chest, abdomen, and upper extremities. The extremities are warm with intact distal pulses. There are no ulcerations.

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**Laboratory Data:**
The following were negative or within normal limits:
Patients 1, 2, 3: Complete blood cell counts with differential and screening lead levels

**Diagnostic Procedures and Tests:**

Patient 1:

| | |
|---|---|
| 07/15 | Magnetic Resonance Imaging, Brain: Age appropriate and unremarkable. |
| 11/17 | X-ray, Pelvis: Normal hip joints. |
| | X-ray, Right leg: No evidence of intrinsic bone or joint pathology. |
| | X-ray, Bilateral Feet: Grossly normal left and right feet. |

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**Diagnosis:**

Cutis Marmorata Telangiectatica Congenita

**Treatment and Course:**

The family was educated and reassured that the cutaneous manifestations of Cutis Marmorata Telangiectatica Congenita should continue to improve with time and no treatment is indicated. The patients were encouraged to continue follow-up with orthopedic surgery, neurology, and ophthalmology. As all three triplets were affected, genetic testing was recommended.

**Discussion:**

Approximately 300 cases of cutis marmorata telangiectatica congenita (CMTC) have been reported in the literature, but the frequency, sex predominance, and pathogenesis remain unknown. The condition most commonly affects the limbs, particularly the legs, with the face and trunk less frequently affected. In 2009, Kienast and Hoeger put forth a set of diagnostic criteria for CMTC. Major criteria include: congenital reticular (marmorated) erythema, absence of venectasia, and unresponsiveness to local warming. Minor criteria include: fading of erythema within two years, port-wine stain, telangiectasia, ulceration, and/or atrophy of affected areas. According to the authors, three major and two minor criteria are sufficient to diagnose CMTC. The proposed criteria have not yet been validated.

Associated orthopedic, ocular, and neurologic diseases have been reported in patients with CMTC. Body asymmetry, typically presenting as limb-length discrepancy due to asymmetric limb hypoplasia or hyperplasia, is the most common extracutaneous abnormality with reported prevalence ranging from 33% to 68% of cases. It is uncertain whether the various other abnormalities reported in patients with CMTC are incidental or associated with the disease. Reported skeletal problems include tendonitis stenosans, syndactyly, hip dysplasia, cleft palate, and clubfoot. Associated ocular disorders include congenital glaucoma (15 cases) and congenital retinal detachment. Finally, neurologic disorders have been reported in 14% of cases according to one review. Abnormalities include developmental delay, neonatal hypotonia, psychomotor retardation, and seizures. Patients with neurologic findings may have a form of CMTC called macrocephaly-CMTC syndrome.

Most cases occur sporadically, but there are rare reports of familial cases. In these cases, CMTC appears to have an autosomal dominant mode of inheritance. Some patients with CMTC also have megalencephaly–capillary malformations associated with mosaic mutations in *PIK3CA*. Moreover, a homozygous nonsense mutation in *ARL6IP6* has been identified in a single case as a potential cause for the syndromic form of CMTC. The involvement of *ARL6IP6* in CMTC remains to be confirmed and replicated. Finally, CMTC has not been associated with low gestational age. Only six other cases of CMTC in preterm infants have been described (average gestational age: 32.8 weeks). While cutaneous manifestations typically fade over time, intense pulsed light therapy proved curative in a single case of persistent skin involvement.

Our case of identical triplets exhibiting similar lesions strongly suggests a pre-zygotic genetic etiology of the disease – whether inherited or sporadically occurring in a single germ cell. It would be highly unlikely for the mutation to arise de novo after the zygote split into three embryos. Given the patients' extracutaneous comorbidities, the three patients presented emphasize the importance of early referral to specialist care in cases of CMTC. Further studies will help elucidate the underlying genetic and environmental factors associated with this disease, as well as the associated anomalies requiring monitoring.

**Essential Lesson:**

- Pre-zygotic genetic mutations can lead to CMTC, and have been associated with abnormalities in PIK3CA and ARL6IP6 genes.
- Cutaneous involvement in patients with CMTC generally improves over time without treatment.
- Limb-length discrepancy is the most common extracutaneous manifestation of CMTC, however, a variety of orthopedic, ophthalmologic, and/or neurologic sequelae have been reported, necessitating multidisciplinary care.

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**Case Presented by Mark Juhl, MD,**
**Maria Tsoukas, MD, PhD, and Milena Lyon, MD**

## FAST BREAK

An 83 year old Hispanic female presented to the dermatology clinic with a left foot wound slowly growing for two years.

**Case 9**

**Case Presented by Lorelei DiTommaso, MD, MPH**
**and Vassilios Dimitropoulos, MD**

**History of Present Illness:**
An 81 year old Black male presented with a longstanding growth on the inner arch of his right foot of approximately 40 years. In the preceding year, the lesion intermittently bled and doubled in size, which interfered with his ability to ambulate.

**Past Medical History:**
No past medical history

**Medications:**
None

**Social History:**
The patient is a retired veteran and he denied smoking, alcohol intake, or illicit drug use.

**Review of systems:**
The patient denied any limb swelling, fatigue, unintentional weight loss, headaches, shortness of breath, abdominal pain, or other cutaneous lesions.

**Physical Examination:**
On the right plantar foot there is a 3.2 cm x 2.7 cm exophytic erythematous eroded plaque draining sanguineous fluid. There is no right lower extremity edema. No lymph nodes or right lower extremity masses are palpated.

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**Diagnostic Procedures and Tests:**
01/18 Computed Tomography with Contrast, Right Lower Extremity and Pelvis: No local invasion of the bone and no metastasis to the regional lymph nodes.

**Histopathology:**
Right plantar foot, skin: The epidermis shows a proliferation of cords of anastomosing monomorphic hyperchromatic basophilic cells pushing inferiorly into the papillary dermis. Margins exhibit a pushing pattern. Numerous attempts of ductal formation are present throughout the lesion. There is cellular atypia marked by numerous mitoses, increased nuclear to cytoplasmic ratio, as well as the presence of large cells displaying irregular cellular contours and prominent nuclei.

**Diagnosis:**
Eccrine porocarcinoma

**Treatment and Course:**
The patient was treated with Mohs micrographic surgery in one stage. The post-surgical defect measured 3.6 cm x 3.1 cm, which was repaired with a rotation flap from adjacent skin of the medial foot. Physical examination has revealed no evidence of recurrence or lymph node metastasis six months post-operatively. The patient continues to follow for total body skin and lymph node examination every three months.

**Discussion:**

Eccrine porocarcinoma (EPC) is a rare cutaneous adnexal malignancy originating from the intraepidermal portion of the eccrine gland, the acrosyringium. A recent meta-analysis reports 453 cases in the literature as of 2016, though the exact prevalence is unknown and likely many cases go unreported. Unlike its benign counterpart, the poroma, which most commonly presents at sites of greatest eccrine gland density, such as the palms and soles, EPC has been most commonly reported on the head and neck, followed by the lower extremities. The average age at diagnosis is 67 years and the average duration of the neoplasm prior to diagnosis is 5.57 years, ranging from 4 days to 60 years. Given that many cases have noted a lesion of longstanding duration prior to diagnosis, many authors acknowledge that EPC may arise from a malignant change of a preceding poroma. The morphology of EPC varies widely. The most common presentations are a tumor or nodule (71.2%), followed by an ulcer (18.3%), plaque (9.8%), and less commonly, a swelling, keratotic papule, or pigmented lesion.

Histopathology is required for diagnosis. In general, a histopathological diagnosis of EPC can be made based on the findings of an invasive architectural pattern and/or significant cytologic atypia in a neoplasm showing eccrine differentiation, marked by characteristic poromatous basaloid epithelial cells separated by intercellular bridges and presence of ducts. At present, there are no definitively sensitive and specific tumor markers to identify the lesion. In a study comparing histologies of 39 cases of EPC to 28 cases of squamous cell carcinoma, the most specific immunohistochemical stain was found to be cytokeratin 19 (CK19, 82% for EPC) and most sensitive stain was carcinoembryonic antigen (CEA, 77% for EPC). A few case series have determined that histopathological features of EPC correlate with prognosis. Specifically, local recurrence was found to be associated with both infiltrative and pagetoid histological patterns, while both lymph node (LN) metastasis and death correlated with tumor depth > 7 mm, > 10 mitoses per high power field (HPF), infiltrative architecture, and lymphovascular invasion on histology.

Owing to its propensity to invade the lymphovascular system, EPC has been found to carry a significant risk of both local recurrence following primary excision as well as distant metastasis. Overall, 31% of cases have been reported to metastasize. The most common organs of involvement are lymph nodes (57.7%), lung (12.8%), liver (9%), brain (9%), skin (5.8%), bone (3.2%), disseminated cutaneous (1.3%), followed by breast (0.6%) and stomach (0.6%). When regional nodes are involved, the mortality rate is over 65%. One striking feature of EPC, which has been reported in various case reports, is that the neoplasm can produce lymphangitis carcinomatosa associated with massive lymphedema as well as disseminated cutaneous nodules following paths of lymphatic spread.

The prognosis of widespread metastatic EPC is generally fatal regardless of treatment. Therapeutic measures for advanced disease including chemotherapy, radiation, sentinel lymph node biopsy, and lymph node dissection are reported in case reports. As such, there is not sufficient evidence at present to measure the impact of these interventions on disease-specific survival and therefore to support their implementation. For localized disease, surgery may be curative if the tumor is excised in its entirety in a timely manner. However, both conventional and wide-local excisions have been associated with a relatively high number of local recurrences and post-operative regional LN metastasis, of approximately 20%. Though one study found less recurrences for excisions performed with > 2 cm margins compared to < 2 cm margins, there was no statistically significant difference. The case at present represents the 48th reported case of EPC treated with Mohs micrographic surgery (MMS). Of all EPC cases treated with MMS, there have been no cases of local recurrence, no disease-specific deaths, and two reports of subsequent LN metastasis, comprising 4.5% of all patients treated and

corresponding to an incidence of 14.2 cases per 1000 patient-years. We present this case to maintain an up-to-date analysis on the outcomes of MMS for EPC, as the advantages of MMS in its ability to provide a complete histopathological margin evaluation for this malignancy continue to be established in the literature.

**Essential Lesson:**

- EPC is a rare cutaneous malignancy originating from the acrosyringium of the eccrine gland that may behave aggressively.
- MMS is being increasingly implemented in the treatment of EPC with successful outcomes.
- Compared to standard excision, MMS is associated with less reported cases of local recurrence, regional node metastasis, distant metastasis, and disease-specific deaths.

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**Case 10**

**Case Presented by Owen Kramer, MD,**
**Marylee Braniecki, MD, and Michelle Bain, MD**

**History of Present Illness:**
A 7 year old Asian female was referred to dermatology for management of atopic dermatitis involving the flexures and hands. Her mother had tried several prescribed topicals for an unknown duration without success. As her atopic dermatitis began to fade with topical corticosteroids, a persistent pruritic rash on her right fifth digit remained. There was no history of trauma including no known arthropod bite.

**Past Medical History:**
Atopic dermatitis

**Medications:**
Unknown topicals

**Allergies:**
No known drug allergies

**Family History:**
No history of skin conditions

**Physical Examination:**
The patient has a reddish brown papule overlying a scaly patch on the dorsomedial aspect of the proximal right fifth digit. The patient also has follicular prominence on the chest and xerosis on the lower extremities.

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**Histopathology:**
Right fifth digit, skin: There is a dense dermal lymphoplasmacytic infiltrate with overlying epidermal attenuation. Immunohistochemical staining demonstrates a mix of T and B lymphocytes with a ratio close to 1:1. In situ hybridization for kappa and lambda light chains shows polyclonal uptake for both. Staining for Factor VIII highlights the vascular proliferation, and the endothelial cells are flattened in appearance.

**Diagnosis:**
Acral Pseudolymphomatous Angiokeratoma of Children (also known as Papular Angiolymphoid Hyperplasia)

**Treatment and Course:**
Fluocinonide 0.05% ointment was used twice daily for two months without improvement. Shave biopsy was then performed. Excision of the lesion was discussed, however the patient's parent elected for conservative treatment with topical corticosteroids.

**Discussion:**
Acral Pseudolymphomatous Angiokeratoma of Children (APACHE) was first described by Ramsay et al. in 1988. Since that time, 25 cases have been reported in the literature. It is a benign disorder classically characterized by erythematous to violaceous papules and small nodules in a unilateral acral distribution. It occurs mostly in children with a slight female

predominance, although rare occurrences on the trunk and in adults have been reported. It has therefore been proposed that the nomenclature of this entity be changed to a more inclusive term such as Papular Angiolymphoid Hyperplasia. Despite increased recognition of APACHE, its etiology remains unknown.

Immunohistochemical studies of APACHE reveal a polyclonal dense lymphoid infiltrate occupying the dermis, suggestive of a pseudolymphoma. Many cases also present with prominent and thickened capillaries, giving rise to debate amongst some authors about whether APACHE is truly a pseudolymphoma or rather a vascular malformation. Vascular prominence is not always present and may be a secondary proliferative process resulting from local hypoxia or cytokine infiltrate. Therefore, the theory of pseudolymphoma over vascular malformation has been generally accepted.

While treatment is primarily elective, it is also challenging. A trial of topical and intralesional corticosteroids may be initially successful, but generally lesions recur upon discontinuation of the medication. For this reason, if resolution is desired, then excision should be considered.

**Essential Lesson:**

- APACHE is a rare disorder classically seen in an acral distribution in children that presents histologically as a pseudolymphoma.
- Treatment of APACHE is challenging and often excision is the only curative modality.

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