Chicago Dermatological Society

Monthly Educational Conference

Program Information
CME Certification
and
Case Presentations

Wednesday, April 12, 2017
Gleacher Center – Chicago, IL

Conference Host:
Stroger Hospital of Cook County
Division of Dermatology
Chicago, Illinois

Program

Host: Stroger/Cook County Hospital

Conference Location

Gleacher Conference Center
450 N. Cityfront Plaza Dr., Chicago

All meeting activities take place on the 6th Floor of the Gleacher Center.

8:00 a.m.	**Registration & Continental Breakfast with Exhibitors** *6th Floor Lobby and Room 600*
8:30 a.m. - 10:00 a.m.	**Clinical Rounds** Posters – *Room 602/604 (available throughout the morning)* Slide viewing – *Room 608 (available throughout the morning)*
9:00 a.m. - 10:00 a.m.	**Resident/Basic Science Lecture** – *Room 621* "Skin Manifestations of Rheumatic Disease: Recognition and Treatment" *Jan Dutz, MD, FRCPC*
10:00 a.m. - 10:30 a.m.	**Break and Visit with Exhibitors** – *Room 600*
10:30 a.m. - 12:15 p.m.	**Resident Case Presentations & Discussion** **MOC Self-Assessment Questions** *Room 621*
12:15 p.m. - 12:45 p.m.	**Box Lunches & visit with exhibitors** *Room 600*
12:45 p.m. - 1:00 p.m.	**CDS Business Meeting** *Room 621*
1:00 p.m. - 2:00 p.m.	**General Session** – *Room 621* *BARSKY LECTURE*: "Autoinflammation and Primary Immunodeficiency in Adults - a Rheum Derm Perspective" *Jan Dutz, MD, FRCPC*
2:00 p.m.	**Meeting adjourns**

Mark the Date!

Next CDS monthly meeting – Wednesday, May 10, 2017 at the Gleacher Center

President's Conference and Annual Awards Luncheon – Wednesday, June 7, 2017 at the Stephens Convention Center in Rosemont

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

Guest Speaker

JAN DUTZ, MD, FRCPC

Professor, Department of Dermatology and Skin Science, University of British Columbia Vancouver, BC, Canada

Delivering the Sidney Barsky Lecture

Dr. Dutz is a Professor at the University of British Columbia and a scientist with the Child and Family Research Institute and the Vancouver Coastal Health Research Institute. He received his MD degree from Queen's University (1983), and continued with postgraduate training with a residency in internal medicine and rheumatology fellowship at the University of Toronto, and a residency in dermatology at the University of British Columbia.

Dr. Dutz has been the recipient of numerous honors and grants for research and investigation, and has co-authored over 50 scientific journal publications and 50 journal abstracts, as well as several chapters in books. His practice includes a Connective Tissue Disease clinic, and he is one of a few physicians in North America to be board certified and maintain active clinical interest in both Rheumatology and Dermatology. He has been awarded for his teaching and in the connections he brings to linking basic science discoveries and clinical dermatology. His current interests are skin immunization, melanoma, diabetes, and alopecia areata.

Dr. Dutz is the Coordinator of Resident Research for the UBC Department of Dermatology and Skin Science, and the focus of his laboratory has an independent laboratory is to study the skin immune system and its participation in autoimmune disease.

CME Information

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 1903 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 2016/17 series of meetings, the participant should be able to:

1. Discuss key factors in the diagnosis and treatment for viral diseases and bacterial infections.
2. Describe the manifestation of skin cancers and the efficacy of treatments available to the dermatologist.
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 4.5 *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. Note - You may complete the paper version of the evaluation form or submit your evaluation online.

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.

Today's guest speaker, Dr. Jan Dutz, has disclosed the following potential conflicts of interest: Consulting fees - Janssen-Ortho, Abbvie, Amgen, Leo Pharma, Celgene, Lilly, Novartis, Cipher, Pfizer; Speakers Bureau - Janssen-Ortho, Abbvie, Amgen, Leo Pharma, Celgene, Novartis. None of the planning committee members have any conflicts of interest to disclose.

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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.

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*Protocol to be posted same-day on the CDS website

Key locations: ears, nose **CASE 1**

Presented by Sangeetha Venkatarajan MD, and Shilpa Mehta MD

History of Present Illness

A 59-year-old African American woman presented with a two-year history of recurrent episodes of ear swelling, redness, and pain. Since onset, she has had four similar episodes, with each lasting about two weeks. These episodes were associated with fever, and resolved spontaneously.

Additionally, she reported developing hoarseness about six years ago, which was followed by recurrent episodes of nasal pain five years ago. She also complained of numbness and tingling in her feet that radiated to the legs for the last one year. No other family members had similar findings.

Past Medical History

Asthma, osteoarthritis

Social History

She is a former smoker with a five pack-year history. Negative for illicit drug use.

Medications

Sulfamethoxazole/trimethoprim, fluticasone propionate nasal spray, albuterol, beclomethasone, ergocalciferol, folic acid, loratadine, pantoprazole, thiamine

Review of Systems

Positive for bilateral knee pain
Negative for ear discharge, hearing loss, tinnitus, eye pain, eye discharge, chest pain, dyspnea, headaches, dizziness

Physical Exam

Ears: Thickened and deformed pinnae with sparing of the lobules
Nose: Saddle nose deformity

Laboratory Data

CBC with differential	Within normal limits	
Urinalysis	Within normal limits	
SPEP/serum immunofixation	Within normal limits	
Serum creatinine	0.7 mg/dL	[0.6-1.4 mg/dL]
CRP	0.19 mg/dL	[0.0-0.50 mg/dL]
ESR	4 mm/hr	[0-33 mm/hr]
Rheumatoid factor	<20 IU/mL	[<20 IU/mL]
ANA	Negative	
p-ANCA	Negative	
c-ANCA	Negative	
RPR	Negative	
Collagen type 2 antibodies	42.3 EU/mL	[Negative <20, Equivocal 20-25]

Imaging
Chest X-ray: unremarkable

CT, soft tissue/neck (2014): persistent soft tissue thickening in the retrolaryngeal hypopharynx near the pharyngoesophageal junction with narrowing of the trachea. Stable erosive changes of the cricoid cartilage.

Stress echocardiogram: no evidence of ischemia, valvular abnormalities or dysfunction

Diagnosis
Relapsing polychondritis

Treatment and Course
The patient was initially treated with an oral prednisone taper but she discontinued treatment after a few doses due to insomnia. She is currently undergoing work-up for peripheral neuropathy. The plan is to start colchicine for recurrent auricular chondritis.

Discussion
Relapsing polychondritis (RP) is a rare multisystemic autoimmune disorder that affects proteoglycan-rich structures and cartilaginous tissues, including the ears, nose, larynx, tracheobronchial tree, and cardiovascular system. The estimated incidence is 3.5 cases per million. It usually occurs in middle-aged patients with an average age of 50 years. The disease affects men and women equally.

The pathophysiology of RP remains unknown. An autoimmune etiology for RP is supported by frequent association with other autoimmune disorders, effectiveness of immunosuppressive therapy, infiltration of cartilaginous structures by CD4+ T lymphocytes, and presence of autoantibodies directed against several types of collagen and cartilage proteins. Other autoimmune disorders, myelodysplasia, and systemic inflammatory conditions are found in 25-30% of adult patients with RP.

RP typically presents with sudden-onset chondritis of the ears, nose, and laryngobronchial tree. The most common manifestation is sudden-onset of auricular chondritis, which occurs in 90% of patients. Nasal cartilage chondritis occurs in 60% of patients and results in a saddle nose deformity in 29% of patients. Laryngobronchial tree chondritis can result in dry cough, hoarseness, and pain at the proximal trachea and larynx. Articular involvement is the second most frequent clinical feature, and usually involves the wrists, knees, metacarpophalangeal, and proximal interphalangeal joints. It is usually an asymmetric, migratory, non-erosive, and intermittent oligo- or polyarthritis. Patients can additionally present with constitutional symptoms such as fever, fatigue, and malaise.

Ophthalmological involvement has been reported in 20-60% of patients, and common manifestations include episcleritis, scleritis, and conjunctivitis. Skin manifestations are more frequently seen with concomitant myelodysplastic syndrome, and affect about one-third of the patients. Common dermatologic manifestations include oral aphthosis, nodules, purpura, papules, sterile pustules, superficial phlebitis, livedo reticularis, limb ulcerations, distal necrosis, neutrophilic dermatoses, and angioedema.

The most common causes of death in RP are respiratory and cardiac complications. Strictures, mucosal edema, and cartilage collapse may lead to fatal airway obstruction. Cardiac complications include valvular impairment, coronary artery vasculitis, conduction disturbances, and pericarditis. Central and peripheral nervous system involvement is uncommon and occurs in approximately 3% of cases. Manifestations are

heterogeneous and include vasculitis, headache, seizures, hemiplegia, cerebral aneurysms, mixed motor sensory neuropathy, and mononeuritis multiplex.

The most common laboratory findings are non-specific changes in the levels of acute-phase reactants, especially serum C-reactive protein. The presence of serum autoantibodies (collagen type II, IX, X, XI, matrillin-1, cartilage oligomeric matrix proteins) are of poor diagnostic value since they are found in a limited number of patients and are not specific to RP. Serum collagen type II antibodies have a low sensitivity and specificity, and are found in approximately 30% of patients with RP.

The diagnosis of RP is mainly based on clinical evidence and imaging studies. A biopsy of the injured cartilage can be helpful in making the diagnosis. McAdams et al. provided clinical criteria for the diagnosis of RP. These diagnostic criteria were later modified by Damiani et al. and Michet et al. While the latest criteria require histological confirmation in at least one site, most experts believe that a biopsy is not necessary in patients with classic clinical presentation. When a biopsy is performed, the easiest site to access is the outer ear, and should be performed during an episode of acute chondritis.

Diagnostic Criteria:

Michet et al.	Proven inflammation in two out of three cartilages: auricular, nasal, and laryngotracheal, OR
	Proven inflammation in one of the above + two other signs: ocular inflammation, hearing loss, vestibular dysfunction, or seronegative inflammatory arthritis

There are no standardized therapeutic guidelines for RP due to the rarity of this disease. Therapeutic options for mild disease include nonsteroidal anti-inflammatory drugs, dapsone, or colchicine. Severe cases require high-dose or pulsed high-dose corticosteroids. Corticosteroid-sparing agents such as azathioprine, methotrexate, cyclosporine, and anti-TNF agents may be given. Surgical procedures such as stenting, airway dilatation, tracheostomy, laser extirpation, and laryngotracheal reconstruction can help with the management of airway lesions.

References

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CASE 2

Presented by Katie Manno MD, and David C Reid MD

A 38-year-old woman presented with a pruritic eruption for one week.

UNKNOWN

Key locations: intertriginous areas **CASE 3A**

Presented by Maria Yaldo MD, David C Reid MD, Kubinne Kim MD, and Shilpa Mehta MD

History of Present Illness
A 57-year-old black woman presented with a one-year history of a pruritic rash underneath the breasts. The eruption progressed over time to involve her chest and left axilla. The patient reported that the lesions were exacerbated by heat and sweat. She also noted the affected areas were malodorous. She had tried topical miconazole cream with minimal improvement. The patient denied history of similar lesions in adolescence or early adulthood.

Past Medical History
Hypertension, hyperlipidema, hyperthyroidism, and congestive heart failure

Medications
Furosemide, hydralazine, enalapril, carvedilol, aspirin, atorvastatin, methimazole

Family History
No known history of skin conditions

Social History
No tobacco, drug, or alcohol use

Physical Exam

Skin:	Left axilla and inframammary folds with hundreds of grouped, scaly, reddish-brown papules with erosions
Nails:	Left 5th fingernail with V-shaped nicking Right 4th fingernail with a small V-shaped nick and alternating red/white bands

Histopathology
Punch biopsy, central chest: intraepidermal focus of acantholysis in the suprabasilar layer with few dyskeratotic cells

Diagnosis
Darier disease (keratosis follicularis)

Treatment and Course
The patient was prescribed tretinoin 0.025% cream to use every other night to the affected areas, alternating with triamcinolone 0.1% ointment. She noted minimal improvement and was unfortunately lost to follow up.

Key locations: intertriginous areas **CASE 3B**

History of Present Illness
A 56-year-old man presented with pruritic and painful lesions involving the axillae, back, and central chest for several years. She had frequent remissions and exacerbations worsened with heat and moisture. Previous treatments included two courses of fluconazole 200 mg daily for seven days and dilute bleach baths with minimal improvement.

Past Medical History
None

Medications
None

Family History
Hailey-Hailey disease in his sister, mother, and grandmother

Social History
40 pack-year history of smoking
No alcohol or illicit drug use

Physical Exam

Central back:	Circinate plaques with erosions and crusting
Axilla:	Erythematous, macerated plaques with fissures
Chest:	1-3 mm scattered red, scaly papules and erosions, few larger erythematous plaques in the center about 1 cm in size

Histopathology
Punch biopsy, left inferior axilla: full thickness intra-epidermal acantholysis with minimal dyskeratosis

Diagnosis
Hailey-Hailey disease (familial benign chronic pemphigus)

Treatment and Course
The patient initially presented with exacerbation of disease, and he was started on a prednisone taper that was stopped due to worsening pain. He was then given a trial of doxycycline 100mg twice daily, topical tretinoin 0.025% cream, and triamcinolone 0.1% ointment twice daily. At follow-up, the patient had stopped using the topical treatments as he did not note any improvement. Further treatment with doxycycline 100mg twice daily yielded no additional benefit.

Key locations: intertriginous areas **CASE 3C**

History of Present Illness
A 32-year-old woman presented with "dark spots" on her neck, axillae, and inframammary folds for several years. She described occasional irritation when she wore necklaces, but she was otherwise asymptomatic. Six months prior, she developed new lesions involving the groin. Previous treatment included beclomethasone one year prior to presentation, but this was discontinued due to development of striae.

Past Medical History
None

Medications
None

Family history
No known history of skin conditions

Social History
No tobacco, drug, or alcohol use

Physical Exam
Neck, inframammary folds, axillae, inner thighs: Several 2-3 mm, hyperpigmented, flat papules and reticulated hyperpigmented patches

Histopathology
Punch biopsy, left inframammary fold: epidermal thinning, basilar melanosis, and finger-like rete ridges. Minimal superficial patchy pigment incontinence and overlying mild orthokeratosis.

Diagnosis
Dowling-Degos disease (reticulate pigmented anomaly of the flexures)

Treatment and Course
The patient was started on hydroquinone 3% solution for hyperpigmentation and pimecrolimus 1% cream as needed for irritation twice daily with minimal improvement.

Discussion
Intertriginous dermatoses encompass a wide spectrum of cutaneous diseases ranging from common entities, such as intertrigo, to uncommon and rare disorders, such as Dowling-Degos disease. Often, it is difficult to clinically discern intertriginous dermatoses, as lesions are often macerated or superinfected due to repetitive friction in the body folds.

Darier disease (keratosis follicularis) and Hailey-Hailey disease (familial benign chronic pemphigus) are within the category of intertriginous dermatoses and are often misdiagnosed until a skin biopsy is performed. Both are autosomal dominant disorders characterized by mutations leading to calcium dysregulation. Darier disease is caused by a mutation in the ATP2A2 gene, whereas Hailey-Hailey disease is due to a mutation in the ATP2C1 gene. Both usually present between the second and third decade, although they can also present later in adulthood. Clinically, greasy, keratotic papules in a seborrheic distribution tend to favor Darier disease, while lesions of Hailey-Hailey present

as superficial vesicles and bullae that frequently rupture to form moist eroded plaques. Both disorders worsen with heat, sweat, or occlusion, and frequently have an associated malodor. Associated nail findings typical of Darier disease include V-shaped nicking, subungual hyperkeratosis, and longitudinal red and white lines, while longitudinal leukonychia can be seen in both disorders. Darier disease is also associated with palmoplantar punctate keratoses, flat-topped, skin-colored papules on the dorsal hands and feet, and whitish papules on the oral mucosa. Both diseases can have complications such as bacterial or fungal superinfection, Kaposi's varicelliform eruption, and rarely squamous cell carcinomas.

Histopathology further helps differentiate the two disorders. Darier disease shows a focus of suprabasilar clefting with numerous dyskeratotic cells, including the characteristic corps ronds and grains. Hailey-Hailey has less dyskeratosis and classically features full-thickness epidermal acantholysis creating a 'dilapidated brick wall' appearance. Very rarely, corps ronds and grains may be seen. Although pathology may provide clues to the diagnosis, it is best to use clinical correlation, as there is no specific finding on histopathology that can reliably distinguish the two entities.

Intertriginous dermatoses with primarily pigmentary anomalies can also present a diagnostic dilemma. Dowling-Degos disease (DDD), also known as reticulate pigmented anomaly of the flexures, is a rare, autosomal dominant disease. It has variable penetrance characterized by reticulated or spotted hyperpigmentation in intertriginous areas due to loss–of-function mutations in the gene encoding keratin 5. Keratin 5 plays a role in melanosome trafficking. Presentation usually occurs in the third and fourth decade of life and is slowly progressive. Other associated findings include scattered comedo-like lesions, follicular hyperkeratotic papules, and pitted, perioral scars. There have also been associated reports of hidradenitis suppurativa, keratoacanthomas, and squamous cell carcinoma. Histopathology typically reveals downward elongations of the rete ridges in a reticulated pattern with hyperpigmentation in the basal layer. The latter findings with acantholysis is suggestive of Galli-Galli disease, which has been described as a rare variant of DDD.

A more common intertriginous dermatosis, acanthosis nigricans, lies in the differential of DDD. Acanthosis nigricans can be clinically discerned as it typically presents with velvety hyperpigmented plaques, as opposed to the flattened, or minimally keratotic, reticulate lesions of DDD. Histologically, there is hyperpigmentation of the basal layer in both disorders; however, acanthosis nigricans has hyperkeratosis and papillomatosis, which is not seen in Dowling-Degos. Another clinical differential of DDD includes lichen planus pigmentosus-inversus, a rare variant of lichen planus with less than 40 reported cases in the literature. Typically, lichen planus pigmentosus-inversus presents with asymptomatic or mildly pruritic hyperpigmented, dark-brown macules or patches in intertriginous areas. Common histopathologic features include an atrophic epidermis, lichenoid inflammation with lymphocytes and histiocytes, and pigmentary incontinence in the superficial dermis, which differentiates it from DDD. An additional pigmentary reticulated disorder that may be difficult to differentiate from DDD is reticulate acropigmentation of Kitamura. This entity is an autosomal dominant disease that presents in the first or second decade of life with a reticulate, slightly depressed, freckle-like pigmentation. Although lesions may include body folds, they are typically isolated to the dorsal hands and feet. Other clinical findings include palmoplantar pits and a characteristic break in dermatoglyphics, which can help distinguish it from DDD. Because histopathology exhibits features similar to DDD, some experts believe that these two entities may represent a single complex disease with different phenotypic expression.

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Key locations: chest, back, face **CASE 4A**

Presented by Anand Haryani MD, Victoria Angelova MD, Warren Piette MD, and David C Reid MD

History of Present Illness
A 68-year-old man presented to the emergency department for multiple tender skin growths, which he first noticed three months prior. The lesions were located on his face, chest, abdomen, back, and groin. The patient was unable to provide any definitive information on the evolution of these lesions, and he had no previous medical evaluation.

Past Medical History
Hypertension

Medications
None

Social History
Smokes tobacco (1-2 packs/day)
Alcohol abuse

Review of Systems
Positive for fatigue, decreased appetite, weight loss (10 lbs. over 2 months), difficulty swallowing, and hoarseness of voice
Negative for fevers, chills, shortness of breath, nausea, vomiting, and diarrhea

Physical Exam

Vitals:	Afebrile
Skin:	Chest, back, abdomen, face, groin with several large (4-6 cm), tender, erythematous, subcutaneous nodules with prominent telangiectasias, and exophytic erythematous nodules with central ulceration

Histopathology
Incisional skin biopsy, right back: diffuse dermal proliferation of small cells composed of bland-appearing nests and cords. Mitotic figures with pleomorphism, uniform cells with a high nucleus-to-cytoplasm ratio, rare prominent nucleoli. Tumor strongly immunoreactive for CD56, synaptophysin, chromogranin, and neuron specific enolase with weakly positive TTF-1. Keratin stains including Ber-EP4, CK8/18, keratin Oscar, and AE1/AE3 strongly positive. Cytokeratins CK5/6, CK7, and CK20 negative. Immunohistochemistry panel confirmed the neuroendocrine differentiation of the tumor.

Supraglottic biopsy: neuroendocrine carcinoma

Diagnosis
Cutaneous metastatic neuroendocrine carcinoma with supraglottic primary

Treatment and Course
The patient was started on octreotide, but he continued to decline during his hospital stay. After several discussions with the family, he was discharged to a hospice facility.

Key locations: abdomen, thighs **CASE 4B**

History of Present Illness
A 65-year-old Hispanic woman with a history of recurrent cervical cancer, diabetes mellitus, and hypertension presented to the emergency room with "bumps on the abdomen and thighs" for three weeks. She had tried hydrocortisone 1% cream without improvement. Associated symptoms included pain of the skin and swelling of the legs. There were no aggravating or alleviating factors.

Past Medical History
Hypertension, diabetes mellitus, and cervical cancer (diagnosed 6/2011) with recurrence in 2014 in the cervix and lymph nodes

Medications
Furosemide, metformin, amlodipine, enalapril, atorvastatin, and occasional insulin use

Social History
No alcohol use, illicit drug use, or tobacco use

Review of Systems
Positive for fatigue, decreased appetite, and weight loss (10 lbs. over 2 months)
Negative for fevers, chills, shortness of breath, nausea, vomiting, and diarrhea

Physical Exam

Vitals:	Afebrile
Skin:	Lower abdomen to anterior thighs with several 1-3 mm erythematous, pearly papules, occasionally grouped in 2-3 papule clusters; no central umbilication, no vesicles Vulva unaffected

Histopathology
Punch biopsy, left abdomen: metastatic squamous cell carcinoma, morphologically similar to the patient's known cervical primary. Staining for p16 strongly positive with focal weak nuclear staining of p63. Tumor cells present within the lymphatic channels, which were highlighted with a CD31 stain.

Biopsy, cervix: poorly differentiated squamous cell carcinoma

Diagnosis
Cutaneous metastasis of cervical cancer

Treatment and Course
The patient was treated with combination chemotherapy by oncology with noted improvement of her cutaneous metastases. However, recent CT scan demonstrated omental carcinomatosis suggesting progression of disease.

Key locations: neck, chest **CASE 4C**

History of Present Illness
A 71-year-old man presented to the emergency room with neck swelling that began six months prior. Initially, the swelling was limited to the submental area, which he attributed to an accidental fall. The patient then developed additional facial and hand swelling. He saw two physicians and was given antibiotics and anti-histamines without improvement. His family members noted worsening of the swelling, which prompted this emergency room visit. One month prior to presentation, he noticed a new pink nodule on his left eyelid, and soon thereafter noted a pink nodule on his left arm.
He had no pain or pruritus in the affected areas, but described new hoarseness and snoring.

Past Medical History
None

Medications
None

Social History
Previous tobacco use and alcohol use
No illicit drug use

Review of Systems
Positive for weight loss (5-7 lbs. over the past 6 months)
Negative for fevers, chills, nausea, vomiting, and diarrhea

Physical Exam

Vitals:	Afebrile
Skin:	Anterior and bilateral neck with thick, erythematous, symmetric, firm plaques with overlying peau d'orange appearance Central upper chest with an erythematous patch with surrounding telangiectasia Left upper arm with ill-defined, pink, edematous papules and plaques, of which the largest lesion was 3 cm in size and firm
Lymph nodes:	Prominent inguinal and axillary lymphadenopathy

Histopathology
Punch biopsy, left upper arm: dermal periadnexal infiltrates of atypical lymphocytes admixed with few eosinophils, histiocytes, and rare plasma cells. The deep portion of the specimen largely necrotic with expanding perivascular atypical lymphoid infiltrates. Reed-Sternberg cells present. Immunohistochemistry panel positive for CD30, CD20, and PAX5. Staining for Epstein-Barr virus strongly positive. Lymphoid infiltrate composed of predominately T-cells, expressing CD3, CD5, and CD7 with more CD4 positive cells compared to CD8 positive cells. Transcription factor BOB-1 not expressed. Large cells negative for CD45 and CD21.

Core biopsy, lymph node: classical Hodgkin lymphoma, nodular sclerosis type, CD20-positive

Diagnosis
Cutaneous involvement of Hodgkin lymphoma

Treatment and Course
The patient completed six cycles of combination chemotherapy with complete remission noted on PET scans.

Discussion
Cutaneous metastatic disease occurs in 0.7% to 9.0% of all patients with cancer. The relative frequencies of cutaneous metastases are similar to those of the primary cancers. Primary cancers of the breast, colon, and melanoma are the most common to metastasize to skin in women, and cancers of the lung, colon, and melanoma are the most common in men. Additionally, cutaneous metastatic disease presenting as the first sign of internal cancer is most commonly seen in cancers of the lung, kidney, and ovary. In many cases, these metastases represent an opportunity to detect a potentially treatable cancer, update the tumor stage, and modify therapy.

The mechanism of metastasis can be viewed as a sequence of steps: detachment from the primary tumor, invasion, intravasation into a blood or lymphatic vessel, circulation, stasis within the vessel, extravasation, invasion into tissue, and proliferation at the metastatic site. These provide three basic patterns of distribution of metastases: mechanical tumor stasis (anatomic proximity and lymphatic drainage), site specific (selective attachment of tumor cells to a specific organ), and nonselective (independent of mechanical and organ-specific factors). Other physical factors may be important in determining the location of cutaneous metastases, such as body segmental temperature and the connectivity of the venous system. Cutaneous tumors have been thought to signify secondary metastases of metastases, especially from cancers of the lung and liver, potentially accounting for the ominous significance of several tumors metastasizing to the skin.

Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasias identified primarily through their common features: capability of secreting hormones, neurotransmitters, neuromodulators, and neuropeptides. The presumed precursor cells, neuroendocrine cells, are found in all solid organs, skin, and mucosae, allowing for tumors to arise from several locations. An approximate incidence rate of 1-2 new cases per 100,000 inhabitants per year has been reported in data from the US and Europe, representing 0.5% of all malignancies. The most common primary site is the gastrointenstial tract (62%), followed by the appendix (27%), lungs (23%), and the small intestine (15%). Twelve percent of patients present with metastases from an unknown primary site.

As a group, NETs metastasize in 30% of cases, signaling a worse prognosis. Most commonly, NETs travel to the lymph nodes, liver, and lung. Cutaneous metastases are considered rare, with a total of 31 cases reported. Data suggest a slight increase in prevalence in men (16/31), with a mean age of 55 years at the time of diagnosis. Generally, lesions reported were single or multiple nodules, non-ulcerated, painless, slow growing, and ranging from 0.5 to 2.5 cm in diameter. In most cases, the scalp and trunk were involved. The overall prognosis for metastatic NEC to any location is poor, with a five-year survival rate of 19%. However, resection of the primary site can increase disease-free survival and allow for appropriate chemotherapy.

Hematogenous spread of cervical cancer is uncommon, presenting either in advanced stage disease or a recurrence. In these situations, it is often localized in the liver, lung,

and bone, in decreasing order of frequency. Even in the late stages of disease, cutaneous metastasis from carcinoma of the cervix is rare, with an incidence of less than 2 %. In a review of 190 patients with cervical cancer, Imachi *et al*. reported 15 patients developed skin metastasis. The incidence of skin metastasis varied according to the initial tumor stage: 0.8 % in stage I, 1.2 % in stage II, 1.2 % in stage III, and 4.8 % in stage IV. The incidence of skin metastasis seemed to be higher in patients with adenocarcinoma and undifferentiated carcinoma than in patients with squamous cell carcinoma. On macroscopic examination, three common patterns of skin metastasis, such as nodules, plaques, and inflammatory telangiectatic lesions, have been reported. Lesions may be single or multiple. The prognosis is considered grave after the diagnosis of skin metastasis. The main treatment for these patients has been extirpation of the skin lesion followed by radiotherapy.

The incidence of cutaneous involvement of Hodgkin lymphoma was recently estimated to be between 0.5% and 3.4%; a reduction compared to the early 20th century. Improved therapy, particularly the use of stem cell transplantation, has been the major contributor in the steady decline. When cutaneous involvement does develop, it tends to be in the setting of advanced disease (generally Stage IV disease) and is a poor prognostic sign.

The clinical descriptions of cutaneous involvement of Hodgkin lymphoma (painless, erythematous papules and nodules that frequently become ulcerated) have been consistent throughout case reports and time. Although cutaneous involvement of Hodgkin lymphoma tends to present with distinct lesions, it still must be histologically and immunohistochemically distinguished from infection, graft-versus-host disease, the nonspecific skin conditions that accompany Hodgkin lymphoma, and other lymphoid proliferations, particularly mycosis fungoides, lymphomatoid papulosis, anaplastic large cell lymphoma, and granulomatous slack skin disease. All of these can be associated with systemic lymphoma. In addition, nonspecific cutaneous manifestations are common, with between 3% and 50% of patients experiencing pruritus and associated prurigo, as well as acquired ichthyosis. The most frequent mode of spread from systemic Hodgkin lymphoma to the skin seems to be retrograde from the affected nodes, as most of the reported cases occur over areas of skin drained by affected lymph nodes, such as the chest and axilla. Although the incidence of cutaneous involvement of Hodgkin lymphoma is declining, it still can occur, even in treated patients or those who have minimal systemic disease. Discovering cutaneous involvement may result in earlier therapeutic intervention or may signal the need for more aggressive therapy in a patient with established systemic disease currently undergoing treatment.

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Key locations: lips, mouth, hands **CASE 5**

Presented by Tarana Mohammadi MD, and Kubinne Kim MD

History of Present Illness
A 7-year-old boy with a history of atopic dermatitis presented to the dermatology clinic with a pruritic rash.

Past Medical History
Atopic dermatitis

Medications
Triamcinolone 0.1% ointment, hydrocortisone 1% ointment

Social History
Normal growth and development, meeting appropriate pediatric milestones

Review of Systems
Negative for weight loss, fatigue, abdominal pain, nausea, vomiting, melena, and hematochezia
Positive for sleep disturbance

Physical Exam

Lips/oral mucosa:	10's of dark brown-black, 1-3 mm macules
Neck/upper back:	Ill-defined pink and hyperpigmented scaly plaques
Palmar fingers:	About 5 brown macules
Trunk:	Diffuse follicular prominence and xerosis

Laboratory Data
The following labs were remarkable/abnormal:

STK11 gene	Positive 5'UTR_EX1 deletion

Diagnosis
Peutz-Jeghers syndrome

Treatment and Course
The flare of atopic dermatitis was treated with topical steroids and emollients with improvement in the eczematous plaques on the neck and back. On exam, the patient was noted to have numerous pigmented macules on the lips, buccal mucosa, gingiva, and acral surfaces. Upon further history, the patient's mother had similar dense dark macules on the perioral skin, oral mucosa, palms and palmar fingers, and she reported a family history of such in her sister and father. Her sister died at age 42 from an unknown gynecologic cancer and father died at age 52 from colon cancer. The patient's exam findings and history prompted evaluation with genetics, which confirmed a diagnosis of Peutz-Jeghers syndrome.

Discussion
Peutz-Jeghers syndrome (PJS) is characterized by hamartomatous polyps in the gastrointestinal tract, mucocutaneous pigmentation, and an increased risk of cancer. The prevalence of PJS is estimated to be between 1 in 8,300 and 1 in 280,000 births. It is an autosomal dominant disorder most commonly due to germline mutations in the serine/threonine-protein kinase 11 (STK11) gene (also known as the LKB1 gene). This

serine-threonine kinase is important in second messenger signal transduction, modulation of cellular proliferation, and control of cell polarity. This mutation is detected in 50-80% of families with PJS. The syndrome has a penetrance of greater than 90% by age 30.

The characteristic dermatologic feature of PJS is mucocutaneous pigmented macules. These range from one to five millimeters and are brown or blue-gray. Melanotic macules most commonly appear on the lips and perioral area (94%), palms (74%), buccal mucosa (66%), and soles (62%). They may also be seen on the nose, perianal area, and genitals, and rarely in the intestines. Mucocutaneous pigmentation usually occurs during the first one to two years of life, increases in size and number over the ensuing years, and is reported to fade after puberty except for buccal mucosal lesions.

Gastrointestinal hamartomatous polyps most commonly occur in the small intestine, but can also be found in the stomach and colon. Polyps develop in the first decade of life. Patients may become symptomatic by age ten. PJS can present with intestinal obstruction caused by intussusception with up to 69% of patients experiencing an intussusception during their lifetime. Patients may also present with abdominal pain second to intestinal occlusion by a polyp or a polyp infarction, or rectal bleeding caused by polyp ulceration. On histology, polyps contain a unique arborizing smooth muscle core. The overlying epithelium appears normal on endoscopy. Patients may have one to more than twenty such hamartomatous polyps that can vary in size. The hamartomas are generally considered to lack premalignant potential.

Patients with PJS are at an increased risk for gastrointestinal and non-gastrointestinal malignancies. Estimates for the lifetime risk of any cancer vary widely, but have been reported between 37 and 93%, with an average age of 42 years at diagnosis. The most common sites are colorectal followed by breast, stomach, small bowel, and pancreas.

A diagnosis of PJS requires one of the following features:

- Two or more histologically confirmed Peutz-Jeghers polyps
- Any number of Peutz-Jeghers polyps detected in an individual who has a family history of PJS in a close relative
- Characteristic mucocutaneous pigmentation in an individual who has a family history of PJS in a close relative
- Any number of Peutz-Jeghers polyps in an individual who also has characteristic mucocutaneous pigmentation

Patients meeting these clinical criteria should undergo genetic testing to confirm the diagnosis and to counsel at-risk family members about cancer screening.

Cancer screening recommendations in PJS have been issued by several groups and are based largely on expert opinion and observational data. Although various societies have slightly different recommendations, all PJS patients require multidisciplinary care and longitudinal surveillance. Routine monitoring involves regular complete blood counts to look for anemia secondary to occult gastrointestinal bleeding. Esophagogastro-duodenoscopy, video capsule endoscopy, and colonoscopy are recommended starting at age eight. Based on findings, these tests can be repeated every three years (if polyps are found) or again at age 18 (if no polyps are found). Testicular exams and exams for signs of feminization should be performed from birth though teenage years to screen for Sertoli cell tumors in males. Females should have annual pap smears starting at age 21 to screen for adenocarcinoma of the uterine cervix as well as pelvic or transvaginal ultrasound starting at age 21 to screen for endometrial and ovarian cancer. They should also start monthly breast self-examinations at age 18 years and annual breast MRI and/or mammography starting at age 25 years to screen for breast cancer.

Pancreatic cancer screening may be completed with MRI or endoscopic ultrasound every one to two years starting at age 30 years. Genetic counseling should also be offered.

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Key location: chest **CASE 6**

Presented by Mariam Mafee MD, and Warren Piette MD

History of Present Illness
A 38-year-old man with nevoid basal cell carcinoma syndrome (Gorlin syndrome) was admitted for work-up of left upper abdominal pain radiating to the back. Dermatology was consulted for a large ulceration on the chest, which had been present for over 10 years. The lesion was biopsied eight years ago at another institution, and was consistent with an infiltrative basal cell carcinoma (BCC).

Two years prior to presentation, the patient was following with an outside dermatologist, and was on vismodegib 150mg daily. The patient decided to discontinue the vismodegib due to severe muscle spasms. He subsequently lost his health insurance, and had not seen a dermatologist since stopping treatment.

Review of Systems
Positive for eight-pound weight loss over three weeks
Negative for fever, chills, and night sweats

Past Medical History
Gorlin syndrome: first BCC at age 22, several subsequent BCCs (treated with surgery, ED&C, and vismodegib), odontogenic cyst removed at age 17, bifid rib, pectus excavatum

Medications
None

Social History
Smokes tobacco (1/2 pack per day)
Previously worked outside in construction for eight years

Physical Exam

General:	Pain with any movement of upper body
Scalp, face, back:	Numerous 2-3 mm light-brown, thin papules
Left nasal sidewall:	1x1 cm ulceration with pearly, pink, rolled borders
Philtrum:	4x4 mm erosion with pink, rolled borders
Central chest:	10x6 cm irregular ulceration with hemorrhagic crust and firm, pink cicatrix at left lateral border

Laboratory Data
The following labs were remarkable/abnormal:

WBC	2.8	[4.4 - 10.6 k/uL]
Hemoglobin	6.9	[12.9 - 16.9 g/dL]
Platelets	81	[161 - 369 k/uL]
LDH	465	[85 - 210 U/L]
PTCH1 mutation	Positive	

Radiology
CT, chest/abdomen: pectus excavatum, right fourth bifid rib, diffuse patchy sclerosis of the vertebra, ribs, and sternum concerning for metastatic disease

Histopathology

Bone marrow biopsy, right posterior iliac crest: marrow tissue is replaced by fibrotic stroma and nests of neoplastic basaloid cells, which stain for Ber-EP4. Stains for EMA, CK7, PSA were negative.

Diagnosis

Metastatic basal cell carcinoma to the bone marrow in a patient with Gorlin syndrome

Treatment and Course

The patient was started on vismodegib 150mg daily. He continued to have significant back pain, therefore, oncology decided to radiate the lumbar spine for palliation. Although radiation is known to increase risk for cutaneous BCC in Gorlin syndrome, radiation was administered to target the vertebra with minimal exposure to the skin. Since starting vismodegib several lesions, including the one on his chest, have decreased in size. His white blood cell counts, hemoglobin, and platelet counts were trending up and had reached a normal range. However, his most recent counts have decreased to below normal.

Discussion

Metastatic BCC is extremely rare with an incidence of less than 0.55%. Risk factors for metastasis include: male gender, location of the primary tumor on the head and neck, history of recurrence, and history of ionizing radiation. Size and duration of the primary tumor is also associated with a risk for metastasis. Snow et al. reported an incidence of 2% if the primary lesion was greater than 3 cm; the median interval from onset of primary tumor to metastasis was 12 years. Other studies have reported a median interval of nine years. Tumor subtype may also play a role, as morpheaform and basosquamous subtypes are most commonly implicated.

Basal cell carcinoma can metastasize by lymphatic or hematogenous spread. Metastasis to the lymph nodes is the most common presentation, followed by lung and bone. Bone invasion is often reported as sclerotic lesions on imaging. Invasion of the bone marrow resulting in cytopenias is especially rare. The first reported case was published in 1968, and since then there have been six additional reported cases. Our patient would be the first case report of bone marrow invasion in a patient with Gorlin syndrome. Mean survival of metastatic BCC ranges from 8 months to 3.6 years. Lymphatic spread portends a better prognosis than hematogenous spread.

Given that metastatic BCC is extremely rare, there are no standard guidelines for therapy. In the past, patients have been treated with radiation and/or chemotherapy. Cisplatin has been reported to be somewhat effective, and was previously the most common agent used for treatment. The discovery of the hedgehog pathway and its relation to BCCs has led to the development of targeted therapy with smoothened inhibitors, such as vismodegib and sonidegib. Vismodegib was approved for metastatic BCC and locally advanced BCC in 2012. The ERIVANCE trial reported a 30% overall response rate in metastatic BCC with vismodegib, which was defined as at least a 30% decrease in the sum of the longest diameter of target lesions. A systematic review reported a 33.6% partial response rate in metastatic BCC, while complete response was seen in 3.9% of cases. Sonidegib was approved in 2015 for locally advanced BCC, but is not FDA approved for metastatic BCC.

Common side effects of vismodegib that may affect tolerance include muscle cramps, alopecia, dysgeusia and fatigue. Our patient discontinued vismodegib in the past due to muscle cramps, but currently is tolerating this medication.

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Key location: lower lip **CASE 7A**

Presented by Barry Ladizinski MD, MPH, MBA, Warren Piette MD, & David C Reid MD

History of Present Illness
A 23-year-old otherwise healthy man presented with a painful plaque on the lower lip. He previously snipped a "pimple" with a blade that was used for woodwork, and he then developed the current lesion, which grew over the past seven months. He denies recent travel or sick contacts. He does not own any pets.

Past Medical History
None

Medications
None

Social History
Construction worker

Review of Systems
Negative for fever, weight loss, cough, dyspnea

Physical Exam

Inferior lip:	Vermillion and cutaneous lip with circumscribed, erythematous, heme-crusted, verrucous plaque with rolled, indurated borders

Laboratory Data
The following labs were unremarkable:

CBC	Within normal limits
HIV	Negative
Syphilis EIA	Negative

Histopathology
Punch biopsy, inferior cutaneous lip: verrucous hyperplasia with rare budding yeasts, morphologically consistent with *blastomyces*

Microbiology
Tissue fungal culture, inferior cutaneous lip: *blastomyces dermatitidis*

Radiology
Chest X-ray: no infiltrate

Diagnosis
Primary cutaneous blastomycosis

Treatment and Course
He was started on oral itraconazole 200 mg daily for three days, followed by 200 mg twice daily. There was significant reduction in lesion thickness after two weeks of therapy. The patient was subsequently lost to follow-up.

Key location: right neck **CASE 7B**

History of Present Illness
A 53-year-old man with well-controlled diabetes presented with a slowly progressive, asymptomatic growth on the right neck. He previously snipped a "skin tag" with a nail clipper, and he then developed additional lesions, which grew over the following eight months. He works as a taxi driver and resides from Pakistan, but he has not returned for over 20 years. He does not own any pets and denies sick contacts.

Past Medical History
Diabetes mellitus

Medications
Metformin

Review of Systems
Negative for fever, weight loss, cough, dyspnea

Physical Exam
Right neck: Two malodorous, circumscribed, erythematous, heme-crusted, verrucous plaques with rolled, indurated borders

Laboratory Data
The following labs were unremarkable:

CBC	Within normal limits
HIV	Negative
Syphilis screening by EIA	Negative

Histopathology
Punch biopsy, right neck: pseudoepitheliomatous hyperplasia with intraepidermal neutrophilic abscesses and granulomatous inflammation. Grocott methenamine silver (GMS), periodic acid-schiff (PAS), and mucicarmine highlight broad-based budding organisms, morphologically consistent with *blastomyces*.

Microbiology
Tissue fungal culture, right neck: *blastomyces dermatitidis*

Radiology
Chest X-ray: no infiltrate

Diagnosis
Primary cutaneous versus disseminated blastomycosis

Treatment and Course
He was started on oral itraconazole 200 mg daily for three days, followed by 200 mg twice daily, which was continued for six months. There was a remarkable reduction in lesion thickness following two weeks of therapy and complete clearance on six-month follow-up.

Key locations: face, trunk, extremities **CASE 7C**

History of Present Illness
A 44-year-old otherwise healthy man presented with a diffuse, asymptomatic eruption. He previously soaked his feet in a Millennium Park fountain and then noticed a small red bump on the left leg, which was accompanied by fevers, cough, and vomiting for one week. During the next six months, he developed over 200 lesions covering most of his body. He is from Mexico but has not traveled back in the past ten years. He does not own any pets and denies sick contacts.

Past Medical History
None

Medications
None

Social History
Construction worker

Review of Systems
Negative for fever, rigors, weight loss, cough, dyspnea, hemoptysis

Physical Exam

Face/trunk/extremities:	Approximately 200 scattered, circumscribed, erythematous, heme-crusted, verrucous plaques with rolled, indurated borders

Laboratory Data
The following labs were unremarkable:

CBC	Within normal limits
HIV	Negative
Syphilis screening by EIA	Negative

Histopathology
Punch biopsy, right arm: pseudoepitheliomatous hyperplasia with intraepidermal neutrophilic abscesses and granulomatous inflammation. GMS, PAS, and mucicarmine highlight broad-based budding organisms morphologically consistent with *blastomyces.*

Microbiology
Tissue fungal culture, right arm: no growth

Radiology
Chest X-ray: no infiltrate

Diagnosis
Disseminated blastomycosis

Treatment and Course
He was started on oral itraconazole 200 mg daily for three days, followed by 200 mg twice daily, which will be continued for six to twelve months. A significant reduction in thickness of all lesions was noted following two weeks of therapy.

Discussion

Blastomycosis, also known as North American blastomycosis and Chicago disease, is a systemic pyogranulomatous infection caused by *blastomyces dermatitidis* or *blastomyces gilchristii*; the latter is a recently recognized species that may be associated with more severe pulmonary disease. These organisms are typically found in soil and animal habitats in states bordering the Great Lakes, the Ohio River basin, and the Mississippi River. Soil exposure is the most commonly reported risk factor, and most studies do not demonstrate significant associations with sex, age, occupation, or season. Outbreaks of blastomycosis are often associated with close proximity to waterways or major highway developments.

Infection occurs following inhalation of non-pathologic *blastomyces* conidia, which are either phagocytized or converted to pathogenic yeast forms in tissue. Primary pulmonary infection is the most common presentation, with 20 to 80% of patients developing secondary cutaneous disease. Of note, most patients have asymptomatic or subclinical disease, frequently delaying diagnosis and treatment. Disseminated blastomycosis occurs secondary to hematogenous spread from the lungs. The skin is the most commonly affected organ, followed by the skeletal system (presenting as osteomyelitis), genitourinary tract, and central nervous system.

Primary cutaneous infection, also known as Gilchrist disease, is fairly rare, and due to direct inoculation of the organism. Primary cutaneous infection is usually observed in laboratory or morgue workers, and less frequently in dog handlers following a bite or scratch. Other reported cases of direct inoculation include grain elevator door-related trauma, sawhorse-related injury, tree bark trauma, gardening, and lancing of a bullous pemphigoid bulla. The median incubation period for primary cutaneous disease is about two weeks, which is shorter than the four to six-week incubation period for disseminated disease.

Blastomycosis is diagnosed via visualization of broad-based, budding yeast forms in sputum/tissue culture or histopathology, or detection of fungal antigens in serum or urine. There is currently no cutaneous or serologic test to distinguish primary cutaneous blastomycosis from secondary cutaneous disease. Culture of *blastomyces* demonstrates white, fluffy colonies and small round conidia on conidiophores at 25 degrees Celsius (room temperature) and budding yeast forms at 37 degrees Celsius (body temperature). Histopathology shows pseudoepitheliomatous hyperplasia, suppurative and granulomatous inflammation, and round yeast forms with broad-based budding and thick double-contoured cell walls. Fungal organisms can be highlighted with many stains, such as PAS, GMS, mucicarmine, or methanamine silver.

Based on recommendations from the 2008 Infectious Diseases Society of America guidelines, mild to moderate pulmonary or disseminated disease (excluding CNS involvement) is treated with itraconazole 200 mg orally every eight hours for three days, followed by itraconazole 200 mg twice daily for 6-12 months. Moderately severe to severe pulmonary or disseminated disease is treated with the lipid formulation of amphotericin B 3-5 mg/kg every 24 hours or amphotericin B deoxycholate 0.7-1 mg/kg every 24 hours for one to two weeks, followed by itraconazole 200 mg every 12 hours for 6-12 months. Itraconazole is typically well-tolerated, and potential adverse effects include hepatotoxicity, hypokalemia, pedal edema, and, rarely, heart failure. Lipid formulations of amphotericin B have decreased nephrotoxicity and increased CNS penetration compared to the non-lipidized form.

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Key locations: full body **CASE 8**

Presented by Divya Sachdev MD, and Vidya Shivakumar MD

History of Present Illness

A 35-year-old Indonesian man developed sore throat, fever, cough, nasal congestion, and generalized weakness two to three days after arriving to the United States. Three days later, he developed a rash on his face and neck that rapidly spread to the rest of his body. After visiting an urgent care, amoxicillin-clavulanate was prescribed; however, he did not improve and was admitted to Stroger Hospital shortly thereafter for further work-up. He denied sick contacts, but had briefly visited a health care facility in Indonesia for work a few weeks prior.

Past Medical History

Asthma
Typhoid fever

Medications

Albuterol PRN

Social History

Patient was born and raised in Indonesia and works as an accountant. He is heterosexual and monogamous with one female partner. He abstains from tobacco, illicit drugs, or alcohol consumption. His immunization status is unknown.

Review of Systems

Positive for abdominal pain, fever, chills, diarrhea, nausea, vomiting, sore throat, and myalgias

Physical Exam

Vitals:	T 103.1°F, BP 144/87, HR 116, RR 18, SaO2 95% RA
Skin:	Diffuse, erythematous, coalescing macules and papules
Intraoral:	Buccal mucosa with linear shaggy plaques and 2-3 white papules adjacent to right 1st molar

Laboratory Data

The following labs were remarkable/abnormal:

WBC	10.5	[4.4-10.6 k/uL]
AST	223	[0-40 U/L]
ALT	289	[5-35 U/L]

Infectious studies

Blood cultures	negative
Syphilis EIA	negative
HIV PCR	negative
HBVsAg	negative
HCV Ab	negative
Parvo B19 IgM/IgG	negative
Rubella IgG	positive
Rubella IgM	negative
Measles IgG negative	negative
Measles IgM	positive (1:80)

Diagnosis
Measles

Treatment and Course
The patient was kept under droplet and airborne precautions and treated with supportive care. He was discharged after four days in good condition.

Discussion
Measles is caused by a single-stranded RNA virus that is a member of Paramyxoviridae family. The virus gains entry by respiratory mucosa and incubates for seven to twenty-one days and is considered highly contagious. This is followed by a prodrome for two to four days, and then an exanthem for five to seven days. The morbilliform rash usually appears fourteen days after the person is exposed to a contagious source, and an infected individual is communicable for four days prior to and four days after onset of rash. The entire course of measles on average lasts seven to ten days in a healthy immunocompetent person.

Diagnosis can be made clinically or serologically. Midway through the prodrome – which consists of fever, malaise, cough, coryza, and conjunctivitis—a pathognomonic feature, known as Koplik spots, may develop on the buccal mucosa near the second molars. These lesions are characterized by gray-white papules and typically resolve by onset of rash. The rash begins as red macules and papules that appear on the forehead, hairline, and behind the ears and then spreads to trunk and extremities in a cephalocaudal distribution. Cervical lymphadenopathy and pharyngitis can also accompany the cutaneous exanthem stage.

Although measles is a clinical diagnosis, it is recommended to have laboratory confirmation. The measles-specific immunoglobulin M antibody assay is the test most often used and has almost a100% sensitivity if done two to three days after onset of the rash. This antibody generally disappears by four weeks. The downside to this test is that there may be false positives in the presence of other viral infections such as parvovirus B19 and rubella, as well as in the presence of rheumatoid factor. The measles Immunoglobulin G (IgG) antibody is present within seven to eight days of rash onset, and remains positive for life. At least a four-fold increase in measles IgG titers between the acute and convalescent phases is necessary to confirm the diagnosis. For immunocompromised patients, rapid polymerase chain is useful and the virus can be detected in various specimens within seven days of rash onset.

There is no specific antiviral treatment for measles. Management is supportive care as well as identifying and preventing complications. Those at risk of complications are children less than the age of five years, adults greater than twenty years old, immunocompromised individuals, pregnant women, and malnourished children. Complications are varied and include pneumonia, acute measles encephalitis, subacute sclerosing panencephalitis, otitis media, diarrhea, stomatitis, subclinical hepatitis, thrombocytopenia, appendicitis, ileocolitis, pericarditis, myocarditis, and hypocalcemia. One or two out of every one thousand children who become infected with measles will die from respiratory and CNS complications. The mortality rate from measles in the United States is two per one thousand patients or 0.2% based on 1985-1992 surveillance data. According to the World Health Organization and American Academy of Pediatrics, oral vitamin A is recommended for children with acute measles with the dosage varying based on age. This is especially important to avoid blindness, notably in Africa where measles accounts for a large proportion of preventable blindness. Post-exposure prophylaxis is indicated for those susceptible individuals who are not immune to

measles.

Measles is still a common disease around the world including areas such as Africa and Asia. According to the CDC, there are 20 million people affected worldwide yearly of whom 146,000 die. In the United States, measles was declared eliminated in 2000 as a result of the live measles vaccine, which was licensed in 1968; however, outbreaks still occur. In 2014, there was a record number of 667 cases of measles reported from 27 states, which was three times more than what was evident in 2013, and the majority of people who got measles had not been vaccinated. In 2015, the US had a large multi-state measles outbreak linked to Disney theme parks in Orange County, California. Recently, from January 1st to January 28th, 2017, 23 people from California, Colorado, Florida, New Jersey, New York, and Pennsylvania were reported to have measles. Those infected with measles were mostly unvaccinated and during this time anti-vaccination movements were ongoing due to the concern that vaccines were linked to autism. Although the national average of MMR vaccination coverage has been stable and as of 2013 was 91.9%, one out of 12 children will receive their first dose late, highlighting measles susceptibility across the country.

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Key locations: fingers **CASE 9**

Presented by Jackelyn Tanios MD, Jerry Feldman MD, and Kubinne Kim MD

History of Present Illness
A 62-year-old woman presented with a six-month history of painful nail growths of the left thumb and second digit. She reported a remote history of nail surgery on the right third through fifth digits, as well as the left second digit. On further questioning, she reported having a "blistering rash" as a newborn with residual light patches on her forearms. Like her father, she had many childhood dental procedures and has had chronic retinal problems. She denied any similar findings in her mother.

Past Medical History
Hypertension, osteoporosis

Medications
Losartan, alendronate

Social History
Worked for a phone company with substantial use of her fingers
Married without children

Review of Systems
Negative for weight loss, night sweats, or known HPV infection
Positive for pain of distal fingers

Physical Exam

HEENT:	Many teeth with crowns Strabismus
Skin/nails:	Left thumb and left second digit with distal swelling, hyperkeratosis, yellowing, and onycholysis of the nail plate with a subungual keratotic nodule Several additional nails with hyperkeratosis and distal onycholysis Bilateral forearms with reticulated, hypopigmented patches
Lymph nodes:	No axillary lymphadenopathy

Laboratory Data
The following labs were remarkable:
IKBKG gene deletion (NEMO) Positive

Histopathology
Excisional biopsy, left second finger nail bed: keratoacanthoma, cannot rule out minimal invasion (well-differentiated squamous cell carcinoma of keratoacanthoma type)

Re-excision, left second finger nail bed: keratoacanthoma, cannot rule out focal microinvasion (well-differentiated squamous cell carcinoma of keratoacanthoma type)

Left thumb nail bed excision: keratoacanthoma with possible focal microinvasion (well-differentiated squamous cell carcinoma of keratoacanthoma type)

Radiology
X-ray, left hand: bone mineral density appears diffusely diminished. Radiolucent osteolytic lesions noted in the distal first and second distal phalanges with surrounding focal periosteal reaction and focal soft tissue swelling. No acute fractures are identified.

Diagnosis
Subungual tumors in incontinentia pigmenti (STIP)

Treatment and Course
The patient was started on acitretin 25 mg, but was unable to tolerate this medication due to side effects. She was referred for Mohs surgery.

Discussion
Incontinentia pigmenti (IP) is an uncommon X-linked dominant genodermatosis that affects mostly females and is usually lethal in males *in utero*. The stages of IP progress from linear erythema and vesicles to verrucous linear plaques. Reticulate hyperpigmented streaks and swirls develop next with a predilection for the trunk and extremities, then fade by adolescence, leaving behind linear hypopigmented bands.

Although typically lethal in males, three potential mechanisms have been proposed to explain the rare survival of males carrying the NEMO mutation: abnormal karyotypes (47 XXY), somatic mosaicism, and hypomorphic mutations. A report of nine cases of IP in males with a review of the 64 previously reported cases showed that five patients had abnormal karyotypes. Of the remaining cases, the most likely explanation for the manifestations of IP in male patients was somatic mosaicism resulting from a postzygotic mutation.

The prevalence of nail dystrophy is unknown, with estimates ranging from as few as 7% to as many as 40% of all patients. Subungual and periungual keratotic tumors are rare and appear at a later stage, typically between puberty and the third decade. The tumors may regress spontaneously but usually continue to grow, causing pain and nail dystrophy. Subungual tumors in IP may be associated with destruction of the underlying phalanges. These lytic lesions may occur secondary to pressure necrosis from the overlying tumor or represent a primary bone manifestation of IP.

Clinically, the differential diagnosis of STIP includes keratoacanthoma (KA), verruca vulgaris, and squamous cell carcinoma (SCC). The distinguishing features of STIP from subungual KAs are the patient demographic (young women), the multiple recurring lesions over the course of several years, and the accompanying signs of IP. Subungual KAs and subungual SCCs are more frequent in older males and typically present as a single lesion. The bony erosions seen with STIP are more likely due to a pressure phenomenon rather than true neoplastic invasion of the underlying bone.

Conservative surgical excision and bone curettage is generally preferred as first line treatment. Because STIP is perceived as a benign subungual neoplasm, it is crucial to be aware of the association of these tumors with IP through a detailed clinical history, and to methodically review the histopathologic findings to exclude SCC, which can save the patient an unnecessarily aggressive surgical procedure including amputation. Previous publications indicate that these lesions follow a benign course clinically and that they do not recur after surgical excision.

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CASE 10

Presented by Evan Stokar MD, David C Reid MD, Jerry Feldman MD, & Joerg Albrecht MD

UNKNOWN

Patient A
A 66-year-old woman presented with an enlarging umbilical nodule that appeared three years after a laparoscopic cholecystectomy.

Patient B
A 50-year-old man presented with an asymptomatic, skin-colored umbilical nodule for four months.

Patient C
A 39-year-old healthy woman presented with a soft, compressible mass on her back that had been present for two years.

Patient D
An 81-year-old African American woman presented with a rapidly growing nodule on her left earlobe for one year.