# Chicago Dermatological Society

# December 2007
# Monthly Educational Conference

## Program Information
## Continuing Medical Education Certification
## and
## Case Presentations

Wednesday, December 5, 2007

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

# Program

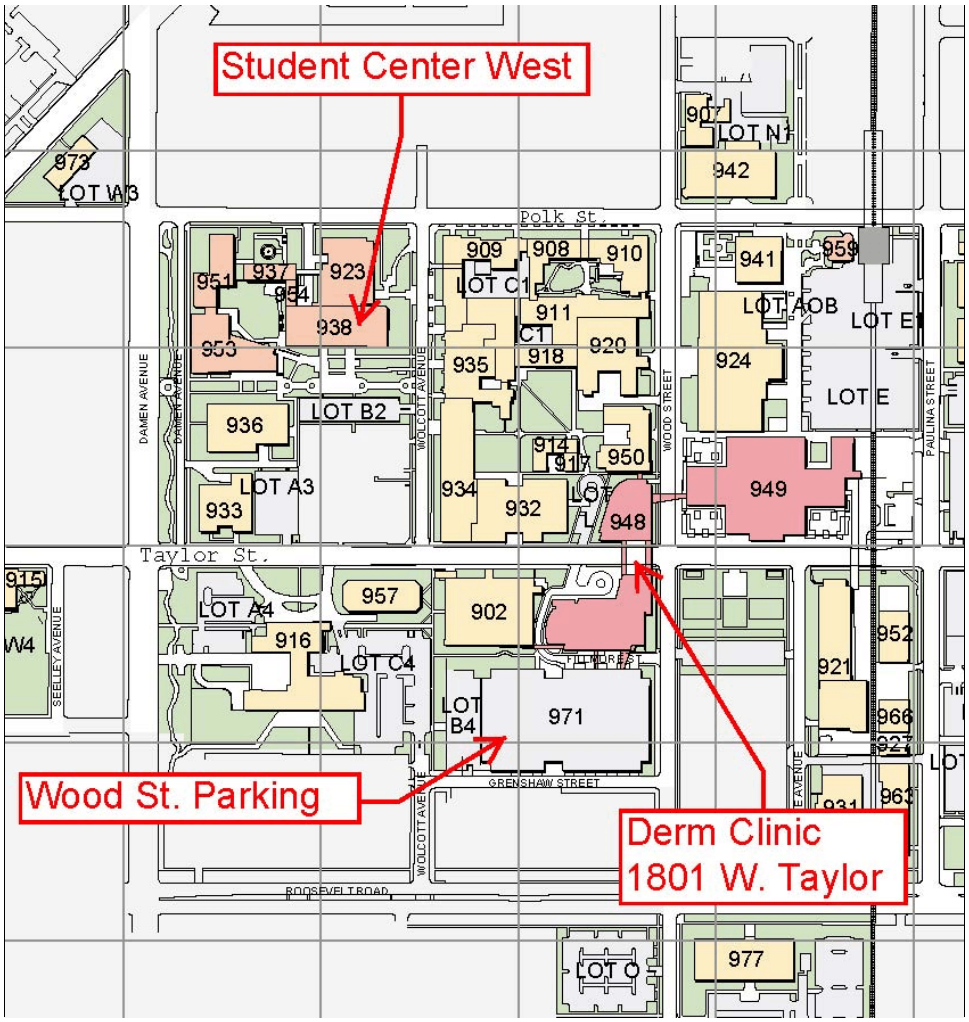
***Committees & Registration***

| | |
|---|---|
| 8:00 a.m. - 9:00 a.m. | IDS Board of Directors<br>*Room 216 AB - Student Center West* |
| 8:00 a.m. - 9:00 a.m. | CDS Finance Committee<br>*Room 213 AB - Student Center West* |
| 9:00 a.m. - 10:00 a.m. | CDS Plans & Policies Committee<br>*Room 213 AB - Student Center West* |

***Program Activities***

| | |
|---|---|
| 8:00 a.m. | Registration opens & continental breakfast<br>Pre-function area - Chicago Room A-C, Student Center West |
| 9:00 a.m. - 10:00 a.m. | Resident Lecture – *Chicago Room A-C, Student Center West*<br>UPDATE ON LP; WHAT ARE EM AND SJS; AND ERYTHRODERMA<br>Neal H. Shear, MD, FACP |
| 9:30 a.m. - 11:00 a.m. | Clinical Rounds |
| | Patient Viewing – *Dermatology Clinic, 1801 W. Taylor St., Suite 3E*<br>Slide Viewing – *Room 206 A/B, Student Center West* |
| 11:00 a.m. - 12:15 p.m. | General Session - *Chicago Room A-C, Student Center West* |
| 11:00 a.m. | CDS Business Meeting |
| 11:15 a.m. | Guest Lecture – DRUG REACTIONS: STILL A DIFFICULT PROBLEM<br>Neal H. Shear, MD, FACP |
| 12:15 p.m. - 1:00 p.m. | Luncheon |
| 1:00 p.m. - 2:30 p.m. | Case Discussions – *Chicago Room A-C, Student Center West* |
| 2:30 p.m. | Meeting adjourns |

## UIC Campus Map



# CME Information

**This activity is jointly sponsored by the Chicago Medical Society and the Chicago Dermatological Society.**

This activity has been planned and implemented in accordance with the Essentials Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Chicago Medical Society and the Chicago Dermatological Society. The Chicago Medical Society is accredited by the ACCME to provide continuing medical education for physicians. The Chicago Medical Society designates this educational activity for a maximum of four (4) *AMA PRA category 1 credits*™. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

*Commercial Support:* There are no educational grants associated with this meeting. One or more companies may pay a fee to be present as exhibitors. The program content is free from any commercial or corporate influence.

## Guest Speaker

Neal H. Shear, MD, FACP; Professor & Chief of Dermatology; University of Toronto Medical School; Toronto, Ontario, Canada
Dr. Neil Shear's main research interest is in idiosyncratic drug reactions that involve the skin. He has published more than 200 peer reviewed papers and numerous chapters and abstracts. He has diverse clinical interests. Dr. Shear earned a degree in Engineering Science from the University of Toronto in 1973 and received his medical degree from McMaster University in 1976. He completed training in both Internal Medicine and Dermatology, as well as a research fellowship in Clinical Pharmacology. He joined the staff at Toronto's Sunnybrook Hospital in 1984.

## Speaker CME Disclosure of Financial Interests

Dr. Shear has the following relationships: Telecris (C, S, I); Johnson & Johnson (C); Schering Plough (C,S); Abbott (C); and Glaxo Smith Kline (C, I).
*Key: C = consultant; S = speaker; I = investigator*

## CME Credit Documentation

Following the meeting, the Chicago Medical Society will send you a certificate documenting your attendance at this conference and the number of Category 1 CME credits you earned.
It is essential that you sign the CME sign-in sheet located at the Chicago Dermatological Society registration desk. Do so before you leave the conference! If you have any questions about your credits, please contact the Chicago Dermatological Society at 847/680-1666, or by email: RichardPaul@DLS.net

## Evaluation Forms

Please complete and return your meeting evaluation form. This feedback is an important part of the CME process and helps us to design programs in the future that better meet the needs of our members. Note that the form will be scanned by computer; keep your responses within the spaces provided, and avoid making any extraneous marks on the sheet. Thank you!

# University of Illinois at Chicago
# Department of Dermatology

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**Case # 1**

**Case Presented by Aleksandar L. Krunic M.D., Ph.D,
and Aaron S. Cetner M.D.**

**History of Present Illness:**
This 73 year-old Caucasian female presented in September 2006 for evaluation and treatment of recurrent, multifocal squamous cell carcinoma (SCC) of the scalp. She had been diagnosed three years previously at an outside institution. Initial therapy included surgical excision, followed by Mohs surgery for tumor recurrence. Subsequently, new multifocal tumors appeared over several months, necessitating nine individual Mohs surgeries. The patient was unable to tolerate a short course of either acitretin or isotretinoin. The patient was then treated with chemotherapy (cisplatin and 5-fluorouracil) with concurrent radiation in May 2004. She experienced recurrence in 2004 and underwent full-thickness debridement of the scalp and bilateral helices. PET and CT scans of the head and neck revealed no metastatic disease. In June 2006, the patient underwent scalp resection with split-thickness skin grafting for persistent lesions and exposed calvarium. An MRI revealed no metastatic or invasive disease. In September 2006, biopsy of a left pre-auricular nodule was consistent with keratoacanthoma.

**Past Medical History:**
Hypertension, hyperlipidemia, fracture of lumbar and thoracic vertebrae

**Medications:**
Lisinopril, atorvastatin, risedronate, citracal, ibuprofen

**Allergies:**
No known drug allergies

**Social History:**
The patient is retired. She smokes 1 pack of cigarettes per day and does not use alcohol.

**Review of Systems:**
Negative

**Physical Exam:**
At the time of presentation, examination revealed an area of exposed bone at the vertex scalp measuring 5 x 3.2 cm. Surrounding this was shiny, atrophic skin consistent with split-thickness skin graft, with superficial erosions surrounding the graft. At the graft periphery were discontinuous, raised, hyperkeratotic plaques and a crateriform nodule at the occipital scalp. There was no lymphadenopathy.

**Histopathology:**
Of 18 specimens from April 2005 to November 2006, 5 read as SCC were reviewed. There is a crateriform lesion with hyperkeratosis, parakeratosis, and scale crust. There is massive pseudoepitheliomatous hyperplasia of the epidermis with uniform nuclei. At the deepest portion of the hyperplastic epidermis, there is mild atypia with occasional mitoses. Dilated blood vessels and a perivascular infiltrate of lymphocytes and eosinophils are seen in the dermis.

**Diagnosis:**
Keratoacanthoma centrifugum marginatum

**Treatment and Course:**

The patient was started on 15 mg of oral methotrexate per week. To date, she has developed no new lesions, and existing lesions have regressed. The exposed calvarium at the vertex scalp has begun to heal. Oral methotrexate was recently discontinued after 6 months of therapy without any evidence of recurrence.

**Discussion:**

Keratoacanthoma centrifugum marginatum (KCM) is an uncommon variant of keratoacanthoma, characterized by progressive peripheral expansion and concomitant central clearing. It was first reported by Miedzinski and Kosakiewicz in 1962, and the term KCM was subsequently coined by Belisario in 1965. Like all keratoacanthomas, the etiology of KCM is uncertain, though heredity, sunlight, tar, pitch, tobacco, and even trauma have been identified as contributing factors. Although the role of human papilloma virus (HPV) in keratoacanthoma is controversial, only one study has examined this relationship with respect to KCM, with the detection of HPV type 6 and 11 within the lesion. In addition, mutations of the tumor suppressor gene p53 have been suggested in classic keratoacanthoma, as well as activation of the oncogene H-ras.

The differential diagnosis for KCM is broad, including deep fungal infection, mycobacterial infection, and halogenoderma. Like classical keratoacanthoma, it is most important prognostically to be able to distinguish KCM from squamous cell cancer (SCC). Clinically, the two entities may have some overlap, though findings more characteristic of KCM include rapid peripheral expansion of a hyperkeratotic, raised margin, concurrent central clearing, and formation of new keratoacanthomas at the periphery. Although the histopathology of KCM may resemble the crateriform lesions of classic keratoacanthoma, more often the picture is dominated by pseudoepitheliomatous hyperplasia and varying degrees of keratinization and cyst formation. Cytologic atypia is absent to mild, and mitotic figures are rare, in contrast to the more pleomorphic and aggressive appearance of SCC. Finally, although some early authors regarded KCM as a form of low grade SCC, there is no tendency to develop distant organ metastasis.

KCM responds to a number of treatments, including intralesional and oral methotrexate, topical 5-fluorocuracil, Mohs surgery, intralesional bleomycin, and oral retinoids. Epidermal growth factor receptor (EGFR) antagonists, such as cetuximab, are a potential, though as yet unreported therapeutic option given there effectiveness in squamous cell head and neck cancers.

**References:**


1. Belisario JC. Brief review of keratoacanthoma and description of keratoacanthoma centrifugum marginatum, another variety of keratoacanthoma. *Australas J Dermatol* 1965; 8: 65-72.
2. de la Torre C, et al. Keratoacanthoma centrifugum marginatum: treatment with intralesional bleomycin. *J Am Acad Dermatol* 1997; 37(6): 1010-1.
3. Divers AK, et al. Keratoacanthoma centrifugum marginatum: a diagnostic and therapeutic challenge. *Cutis* 2004; 73(4): 257-62.
4. Ogasawara Y, et al. A case of multiple keratoacanthoma centrifugum marginatum : response to oral etretinate. *J Amer Acad Dermatol* 2003;48(2):282-5.
5. Peteiro MC, et al. Keratoacanthoma centrifugum marginatum versus low-grade squamous cell carcinoma. *Dermatologica* 1985; 170(5): 221-4.
6. Yuge S, et al. Keratoacanthoma centrifugum marginatum: response to topical 5-fluorocuracil. *J Am Acad Dermatol* 2006; 54(5 Suppl): S218-9.

**Case # 2**

**Case Presented by Claudia Hernandez M.D.**
**and Monika Kiripolsky M.D.**

**History of Present Illness:**
This 25 year-old female presented with a five month history of tender open sores on both shins. The lesions were first noted shortly after she had a pedicure, which included a whirlpool foot soak. She reports having shaved her legs immediately before visiting a salon for the pedicure. The lesions first appeared as 'bumps' which then began to drain green pus and blood. Prior to presenting to UIC, the patient had undergone several skin biopsies as well as sequential wound and blood cultures. All results were negative or inconclusive. At the time of her initial visit to UIC, the patient was applying clobetasol 0.05% cream and fluocinonide 0.05% cream to skin lesions daily for two months, as well as undergoing daily vinegar-soaks without significant improvement. A course of doxycycline resulted in only minimal improvement.

**Past Medical & Surgical History:**
Cholelithiasis and subsequent cholecystectomy

**Medications:**
None

**Review of systems:**
She denied fevers, chills, fatigue, mental status changes, diarrhea, nausea, weight loss or ulcers elsewhere.

**Physical Examination:**
The patient had several 1- 4cm circular erythematous plaques with central ulcerations and serosanguinous crusting on both of her anterior tibial regions. Palpation of lesions yielded only minimal to no tenderness. The sites were not malodorous and the remainder of the skin exam was unremarkable.

**Laboratory Data:**
The following were positive or abnormal:
White blood cell count 16.7 k/uL (3.5-10.5), wound exudate and lesional tissue cultures grew *Pseudomonas aeruginosa (P. aeruginosa)* as well as few beta-hemolytic group B *Streptococci*

The following were negative or within normal limits:
Fungal culture (no yeast or fungi), basic metabolic panel, liver function tests, and complete blood count (except white blood cell count)

**Histopathology:**
5/07 Right leg: The epidermis shows irregular acanthosis and spongiosis. An increased number of fibroblasts are seen in the papillary and upper reticular dermis The capillaries are dilated. A granulomatous infiltrate is seen in the mid dermis; this infiltrate consists of aggregates of neutrophils, lymphocytes and epithelioid histiocytes. There is a scar in the lower dermis. Periodic acid schiff, Gomori's methenamine silver and Gram stains were negative.

**Diagnosis:**
*Pseudomonas aeruginosa* pyoderma following a pedicure

**Treatment and Course:**
The patient began a five-day course of azithromycin prior to initial culture and sensitivity results. Once *P. aeruginosa* was identified as the infecting organism, a fourteen-day course of ciprofloxacin and twice daily gentamicin ointment to the lesions was initiated. After completing the full course of ciprofloxacin

and topical gentamicin, the patient noted only minimal improvement of her eruption. Culture sensitivities indicated that *P. aeruginosa* was susceptible to levofloxacin and a two week course was started. The ulcerations/erosions cleared completely, but with residual hyperpigmentation and scarring. Due to the patient's concern regarding the residual dyschromia and scarring, she has been applying retin-A 0.025% cream to the sites each night and is considering cosmetic consultations for scar treatment options.

**Discussion:**

*Pseudomonas* is a gram-negative, opportunistic, pathogenic rod. *Pseudomonas* often has a characteristic sweet odor and more than half of isolates produce pyocyanin, a blue-green pigment. *P. aeruginosa* is commonly isolated from swimming pools, whirlpools, hot tubs and saunas. It grows well in whirlpools due to the organism's rapid multiplication in high temperatures and its ability to withstand chlorine. Despite being ubiquitous in nature (also found in soil, plants and animals), it only rarely causes disease in healthy people. However, *Pseudomonas* is a common pathogen in immunosuppressed persons, as well as in those with nosocomial pneumonia, bacteremia and urinary tract infections. In cases of *Pseudomonas* not associated with immunocompromise, the infection is usually due to a loss of physical barrier function of the skin or mucus membranes. *P. aeruginosa* colonizes skin through hair follicles or micro-tears such as those caused by shaving. In 1976, the first reported whirlpool-acquired *Pseudomonas* infection was described; it was a pruritic, pustular eruption in patrons of a motel's whirlpool. Subsequent cases of whirlpool-acquired *Pseudomonas* have been reported to cause other infections, including otitis externa and urinary tract infections.

*P. aeruginosa* causes two distinct types of cutaneous eruptions, follicular-based papules (folliculitis) and painful plantar nodules ("hot foot syndrome"). A folliculitis subset known as "hot tub folliculitis" typically begins as pruritic, erythematous macules, progressing to papules and pustules, and resolves within 2-10 days. This subtype favors a "swimsuit distribution" due to *P. aeruginosa's* preference for warm, damp environments. Due to its self-limited nature, most cases of *Pseudomonas* folliculitis go unreported.

Skin infections following pedicures have been well-documented, especially those due to non-tuberculous strains of *Mycobacteria* (i.e. *M. fortuitum* and *M. mageritense*). Like *P. aeruginosa*, *M. fortuitum* had previously been identified in nosocomial infections associated with surgical or clinical devices with contaminated water supplies. However, a literature search failed to uncover any prior reports of cutaneous infection by *P. aeruginosa* acquired via exposure to a pedicure footbath. The California Department of Public Health found that 97% of cultured nail salon footbaths grew non-tuberculous *Mycobacteria*. Due to its high prevalence yet low incidence of reported cutaneous infections, non-tuberculous *Mycobacteria* (and *P. aeruginosa*) must have a predilection for causing cutaneous disease in people with certain yet to be identified risk factors. Shaving with razor blades has been postulated to be a risk, as epidermal micro-trauma from shaving is a potential portal for infection.

Regardless of the microbe, the most significant risk factor for whirlpool acquired infections is improper disinfection of the whirlpool. The Environmental Protection Agency recommends that pedicure footbaths should be disinfected after each client, as well as each night. The disinfectant must be a product that protects against *Staphylococcus aureus*, *P. aeruginosa*, and *Salmonella enterica*.

**References:**


1. Environmental Protection Agency. Recommended Cleaning and Disinfection Procedures for Foot Spa Basins in Salons. (Accessed 10/07 online at http://www.epa.gov/pesticides/factsheets/footspa_disinfection.htm).
2. Ratnam et al. Whirlpool-associated folliculitis caused by *Pseudomonas aeruginosa*: report of an outbreak and review. *J Clin Microbio* 1986; 23(3): 655-9.
3. Redbord K, et al. Atypical Mycobacterium furunculosis occurring after pedicures. *J Am Acad Dermatol* 2006; 54(3):520-4.
4. Washburn J et al. *Pseudomonas aeruginosa* rash associated with a whirlpool. *J Am Med Assoc* 1976; 235(20): 2205-7.
5. Winthrop K, et al. An outbreak of *Mycobacterial* furunculosis associated with footbaths at a nail salon. *N Eng J Med 2002;* 346: 1366-71.

**Case # 3**

**Case Presented by Iris Aronson M.D.**
**and Amber Stevenson M.D.**

**History of Present Illness:**
This is a 56 year-old African American man who initially presented in 2004 for evaluation of a recurrent diffuse vegetative dermatitis with ulcerations. Lesions started 4 years prior to presentation and the patient described that lesions began as pea-sized, hyperpigmented, non-tender nodules that would progressively become ulcerative, vegetative and extremely malodorous over a period of several months. Occasionally new lesions would develop in areas of trauma. This has been a chronic condition since it started, without any period of complete clearance.

**Past Medical History:**
Diabetes mellitus II, hypertension, pulmonary hypertension, polyclonal gammopathy suggestive of liver disease, end stage renal disease on hemodialysis, liver cirrhosis due to alcohol abuse, gout, prior colon resection for diverticulitis, history of infection of hemodialysis catheter

**Medications:**
Lansoprazole, sevelamer, bumetanide, renal multivitamin, allopurinol, cinalcet, diazepam, epoetin alfa, tramadol

**Allergies:**
No known drug allergies

**Physical Examination on presentation in 2004:**
His face showed scattered verrucous plaques. Over his chest and abdomen were multiple well-healed surgical scars and scattered verrucous plaques on an erythematous base, some with purulent drainage. His back showed scattered hyperpigmented macules, papules and inflammatory nodules. His arms and legs had many superficial ulcerations with overlying yellow crust as well as scattered firm verrucous plaques, some with purulent and hemorrhagic drainage.

**Laboratory Data:**
The following were positive or abnormal:
Potassium 5.4mmol/L (3.5-5.3), calcium 7.5mg/dL (8.6-10.6), blood urea nitrogen 47mg/dL (6-20), creatinine 10.4mg/dL (0.5-1.5), alkaline phosphatase 170 u/L (40-125), aspartate aminotransferase 76 u/L (10-40), albumin 1.2g/dL (3.4-5), hemoglobin 8.4g/dL (13.2-18), erythrocyte sedimentation rate 132mm/hr (0-10), IgG 4780 mg/dL (768-1632), and iodine total 109mg/dL; Aerobic bacterial tissue cultures: coagulase negative *Staphylococcus aureus*, *Corynebacterium*, Group B *Streptococcus*, Methicillin-resistant *Staphylococcus aureus;* SPEP = decreased albumin. Increased beta region with beta-gamma bridging suggestive of liver disease or polyclonal IgA. Slight restriction within the polyclonal increase in the gamma region; polyclonal increase in IgG and IgA, no monoclonal proteins seen.

The following were negative or within normal limits:
Hepatitis C, hepatitis B, rapid plasma reagin, bromide level, IgM, IgA, white blood cell count, fungal and acid-fast cultures, GGT, protein, and total bilirubin

**Histopathology:**
Right back, Right Arm: The epidermis shows pseudoepitheliomatous hyperplasia. Large aggregates of neutrophils and nuclear dust forming abscesses are observed throughout the dermis. There is also a dense infiltrate of lymphocytes, histiocytes and many plasma cells. There are an increased number of stromal fibroblasts with focal fibrosis as well as an increased number of capillaries. The dermal stroma is edematous. Russell bodies and diffuse hemorrhage with hemosiderin pigment were also observed in

additional biopsy specimens. PAS and GMS stains are negative for hyphae, but GMS stain shows a subepidermal abscess. Direct immunofluorescence from 10/04 was compatible with dermatitis.

Abdomen: The skin shows diffuse necrosis with neutrophils, nuclear dust, fibrin and hemolyzed red blood cells. Multiple clusters of bacteria are observed

**Diagnosis:**
Superficial pyoderma

**Treatment and Course:**
At presentation, the patient had failed treatment with dapsone, prednisone, cyclophosphamide and isotretinoin. Pulse cyclophosphamide initially induced improvement, but the patient subsequently developed worsening of lesions. Tacrolimus ointment gave mild improvement, but due to high cost was discontinued. After failure of anti-inflammatory and immunosuppressive agents, positive bacterial cultures, and discovery the patient was not bathing except for rare sponge cleansing in order to avoid getting his dialysis catheter wet, he was instructed to bathe with liquid antibacterial soap twice daily. Multiple courses of antibiotics were started, initially seeing improvement with ciprofloxacin, and most recently amoxicillin clavulanate as per infectious disease recommendations in 2/05. With this approach, the patient has decreased cutaneous pain and near disappearance of his skin lesions.

**Discussion:**
A broad differential diagnosis has been considered in this patient. His initial diagnosis when he presented was vegetative pyoderma gangrenosum (PG) associated with monoclonal gammopathy of undetermined significance, although serum electrophoresis did not show monoclonal gammopathy. His biopsies were consistent with PG, however he failed to appropriately respond to immunosuppressive agents. There is a variant of PG known as superficial granulomatous pyoderma that is clinically more consistent with the chronic course of ulcerations and the extensive vegetative margins in this patient. This variant is usually not associated with systemic disease. There have been documented cases, however, in patients with chronic renal failure on dialysis. Superficial pyoderma is also usually more responsive to treatment, although difficult cases may eventually respond to intravenous immunoglobulin therapy or cyclosporine.

Pemphigus vegetans and iododerma are also in the differential; however, DIF results and histopathology were not consistent with either diagnosis. An infectious etiology has also been considered; however, there have not been consistent results indicating a specific diagnosis. Clinically his lesions are suggestive of a deep fungal infection, but cultures and fungal stains have never been positive. Lesions are also suggestive of botryomycosis, but the associated granular bodies have not been seen on pathology.

The most likely underlying etiology of this unusual pyoderma is some form of an immunologic abnormality with an inability to handle superficial cutaneous bacterial infections. There are previous reports of a patient with similar symptoms (superficial pyoderma gangrenosum-like lesions) who had an associated leukocyte adhesion molecule deficiency due to an abnormality in CD18. Patients with leukocyte adhesion defects and also murine models with CD18 abnormalities develop spontaneous skin ulcerations and erosions on a chronic basis.

**References:**

1. Dobson CM. Parslew RA. Evans S. Superficial granulomatous pyoderma treated with intravenous immunoglobulin. *J Am Acad Dermatol* 2003; 48 (3): 456-460.
2. Goto M et al. Vegetative pyoderma gangrenosum in chronic renal failure. *Br J Dermatol* 2002; 146 (1): 141.
3. Lachapelle J, Marot L, Jablanska S. Superficial granulomatous pyoderma gangrenosum of the face successfully treated with Cyclosporine: a long-term follow-up. *Dermatology* 2001; 202: 155-7.
4. Schauffetter-Kochanek K, et al. Spontanous skin ulceration and defective T-cell function in CD18-null mice. *J Exp Med* 1998 July 6; 188 (1): 119-31.

**Case # 4**

**Case Presented by Iris Aronson M.D., David Fretzin M.D., and Rikk Lynn M.D.**

**History of Present Illness:**
This 74 year-old man presented with a five month history of blistering lesions involving his head, trunk and mouth in November 2003. The biopsy was consistent with pemphigus vulgaris. He was initially started on mycophenalate mofetil and prednisone. Due to various complications, prednisone was tapered and intravenous immunoglobulin (IVIG) infusions were started as steroid sparing treatment. Despite this regimen, he continued to have worsening of his disease. In addition to recurring blisters, he began developing multiple vegetative lesions. Dapsone therapy was added to his regimen with little improvement at maximum doses. The patient did not wish to start cyclophosphamide secondary to potential malignancy side effects and he also had contraindications to azathioprine treatment. In November 2006 he stopped all immunosuppressive agents except low dose prednisone and began a rituximab and IVIG treatment protocol as outlined below. The patient achieved full remission and has been off all treatments without any recurrence of disease.

**Past Medical History:**
Cerebrovascular accident, diabetes mellitus, hypertension, hyperlipidemia, osteoporosis, glaucoma, hypothyroidism

**Medications:**
Rituximab, IVIG, alendronate, glyburide/metformin, simvastatin, levothyroxine, metoprolol, aspirin, losartan/hydrochlorothiazide, timolol ophthalmic, brimonidine, nifedipine, insulin

**Allergies:**
No known drug allergies

**Review of systems:**
Patient's fatigue, muscle weakness and chilled sensation improved slightly. There have been no recent infections. The patient denied fevers, night sweats, insomnia, abdominal pain, nausea, vomiting, or diarrhea. The patient denied any vision changes.

**Physical Examination:**
There are some mildly crusted, flat-topped plaques on the frontal scalp and healing erosions on the nasal ala. The ears, back, arms and legs show healed pink patches with mild scale. There is a large erythematous to brown vegetative plaque with some crusting on the chest.

**Diagnostic Procedures and Tests:**
IIF: 11/2003 1:160 - on monkey esophagus, rat bladder negative
11/2006 1:640 - severe flare, rituximab/IVIG therapy started
12/2006 1:160 - completed 6 rituximab infusions and 2 plasmapheresis treatments
02/2007 1:40 - patient in full remission

**Histopathology:**
4/05 The epidermis shows hyperkeratosis with scale-crust, acanthosis, and suprabasal separation. The acantholytic cells are seen within the intraepidermal vesicle. A dense lymphocytic infiltrate is observed in the perivascular area. Occasional neutrophils and nuclear dust are seen.

**Diagnosis:**
Pemphigus vulgaris

**Treatment and Course:**
On 11/2006 the patient stopped all immunosuppressive agents except low dose prednisone and began rituximab infusions once weekly for three weeks followed by an IVIG infusion on the fourth week. In mid-treatment the patient had a severe reactivation of lesions with extensive blisters. Two sequential plasmapheresis treatments were used, immediately followed by intravenous methylprednisolone 60 mg. The rituximab/IVIG month long cycle was repeated once and was finally followed by an addition of once monthly infusion of rituximab and IVIG for four months (see Reference 1). The patient achieved full remission and has been off all pemphigus vulgaris treatments without any recurrence of disease. The patient is presented for clinical interest and discussion of new treatment options for patients with pemphigus vulgaris resistant to standard cytotoxic agents and steroid medications.

**Discussion:**
The term pemphigus describes a group of chronic blistering skin diseases in which autoantibodies are directed against the cell surface of keratinocytes resulting in the loss of cell-cell adhesion. Pemphigus can be divided into three major forms: pemphigus vulgaris (PV), pemphigus foliaceus and paraneoplastic pemphigus. Essentially all patients with PV develop painful erosions of the oral mucosa.

In general, immunosuppressive agents such as prednisone, azathioprine, and cyclophosphamide may result in control of the disease and an increased percentage of clinical remissions. Remissions, and even cures, are seen with cyclophosphamide, but its profile of complications is more extensive and severe and is therefore utilized less commonly. Mycopohenolate mofetil (MM), an effective immunosuppressive agent, has increasingly been used as first line treatment for bullous diseases because of its better safety profile. MM is not effective in all pemphigus patients, therefore, other therapies are used in addition to or in place of MM in partially responsive patients. High dose IVIG has been used as an additional therapy for resistant disease. Though its mechanism of action has yet to be elucidated, it has been a useful adjunctive steroid sparing therapy in bullous disorders. It is not a curative treatment and some patients have had flares while on IVIG. Plasmapheresis is useful for quickly reducing the titers of circulating autoantibodies and should be considered for severe pemphigus if the disease is unresponsive to a combination of prednisone and immunosuppressive agents. Concomitant immunosuppression with corticosteroids and cytotoxic agents prevents a post-plasmapheresis rebound increase in the production of autoantibody. High-dose IVIG may be another option for post plasmapheresis treatment to decrease the rebound phenomenon.

Ahmed et al recently described a new treatment option for unresponsive PV with rituximab and IVIG therapy which showed remission in the majority of treated patients. The treatment course consisted of rituximab infusions once weekly for 3 weeks and then IVIG on the fourth week. This cycle was repeated once more and then followed by monthly infusions of rituximab and IVIG for 4 additional months. If necessary, this regimen was followed by 2 additional IVIG infusions. In the study, 9 of 11 patients had rapid resolution of their lesions and achieved clinical remission lasting 22 to 37 months. All immunosuppressive therapy, including prednisone, was discontinued before ending rituximab treatment in all patients. Two patients were treated with rituximab only during recurrences and had sustained remissions. Side effects usually associated with rituximab, including infections, were not observed. There have been additional studies investigating the use of rituximab treatment without IVIG. Two studies to date showed effective remission in patients with severe PV with 1 cycle of 4 treatments of rituximab.
Further investigation is needed to determine if IVIG is necessary during rituximab therapy to prevent infections.

**References:**

1. Ahmed AR, et al. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. *N Engl J Med.* 2006; 355: 1772-1779.
2. Diaz LA. Rituximab and pemphigus—a therapeutic advance. *N Engl J Med* 2007; 357: 605-607.
3. Cianchini G, et al. Treatment of severe pemphigus with rituximab. *Arch Dermatol* 2007; 143:1033-1038.

**Case # 5**

**Case Presented by Iris Aronson M.D.**
**and Deborah Marble M.D.**

**History of Present Illness:**
This is a 45 year-old female who presented to our clinic with a 9 month history of red papules around her eyes. Originally she had only a few lesions, but they increased in number over time. At the time of presentation patient was taking hydroxychloroquine 200mg twice daily and using clocortolone pivalate cream to lesions daily. The patient noted that the papules were smaller on this regimen, but that she was still getting new lesions and old lesions were not clearing completely. The patient had failed many other medication trials including: metronidazole cream 1%, tetracycline 500mg twice daily, erythromycin 333mg twice daily for 10days, triamcinolone cream 0.1%, benzoyl peroxide/clindamycin gel, two doses of fluconazole 150mg, and doxycycline 75mg twice daily.

**Past Medical History:**
Anemia

**Medications:**
Hydroxychloroquine 200mg twice daily and clocortolone pivalate cream

**Allergies:**
No known drug allergies

**Family History:**
No history of autoimmune or other skin disorders

**Social History:**
Lives with her husband and daughter, denies smoking, and occasionally drinks alcohol

**Review of Systems:**
Negative for shortness of breath, pain, fatigue, muscle weakness or visual changes

**Physical Examination:**
The patient had multiple 2-5mm reddish brown papules on bilateral zygomatic cheeks, temples and directly superior to eyebrows

**Laboratory Data:**
The following were positive or abnormal:
Hemoglobin 7.9 g/dl (12-16), hematocrit 26 g/dl (36-45.6), mean corpuscular volume 60 fl (84-99)

The following were negative or within normal limits:
Angiotensin-converting enzyme level, white blood cell count, liver function tests, basic metabolic panel

**Diagnostic Procedures and Tests:**
1/07 Chest X-ray within normal limits

**Histopathology:**
1/07 Right and left zygoma: The epidermis is flattened. In the upper dermis there is granulomatous infiltrate consisting of epithelial cells surrounded by lymphocytes. Occasional langhans giant cells are observed. Most of the granulomas have a periadnexal location.

**Diagnosis:**
Lupus miliaris disseminatus faciei

**Treatment and Course:**
Patient is presently being continued on hydroxychloroquine 200mg twice daily due to slight improvement of the lesions while on this medication.

**Discussion:**
Lupus miliaris disseminatus faciei, also known as acne agminata or acnitis, is a granulomatous process that affects mainly the periorbital area. Clinically the disease presents with flesh-colored to reddish brown discrete dome-shaped papules and nodules, mostly on the central face, with a predilection for the eyelids. The lesions are non-tender and usually symmetric. On diascopy, lesions appear yellow-brown. On histopathology the lesions show epithelioid granulomas with central necrosis.

Originally the disease was thought to be a cutaneous expression of tuberculosis, but this is no longer thought to be the case. Some authors believe it is a distinct form of granulomatous rosacea, while others suspect it to be a type of cutaneous sarcoidosis. In general patients do not exhibit common signs of rosacea including flushing, telangiectasias and erythematous papules and pustules.

Lupus miliaris disseminatus faciei is most common in young adults and is equal in both genders. It is inconsistently responsive to tetracyclines and oral steroids. There are small case studies that report effective treatment with dapsone 50mg daily or 1450nm diode laser. The disease usually follows a self-limited course, but results in ice-pick scarring.

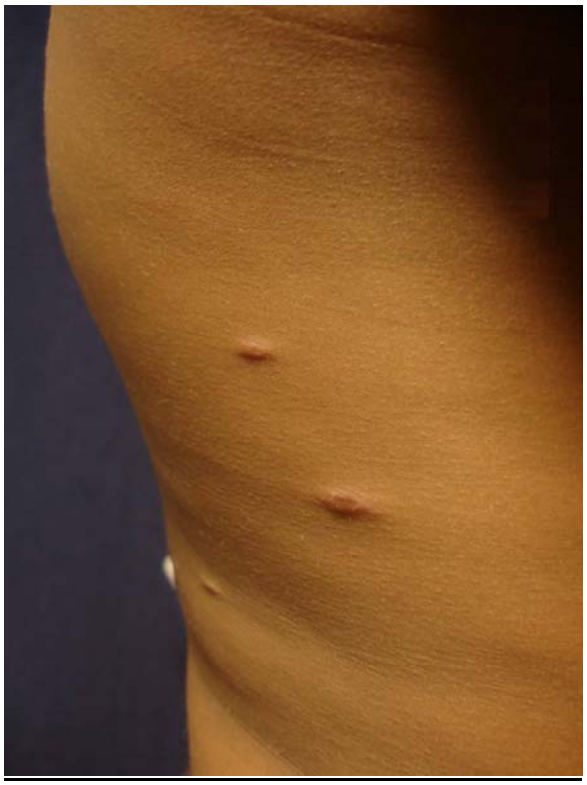
**References:**

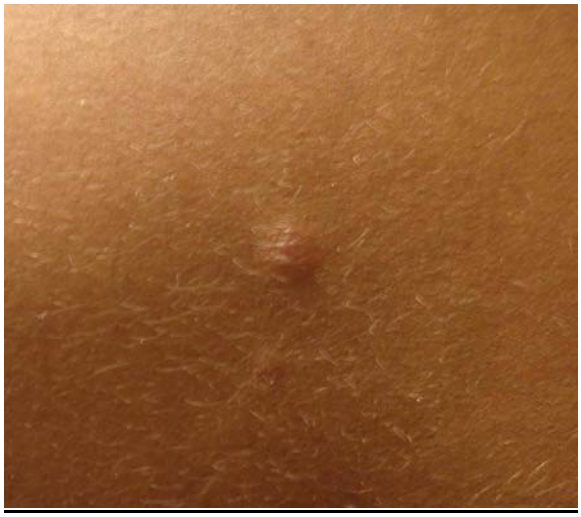
1. Hodak E et al. Lupus miliaris disseminatus faciei-the DNA of Mycobacterium tuberculosis is not detectable in active lesions by polymerase chain reaction. *Br J of Derm* 1997; 137: 614-619.
2. Jih M et al. Lupus miliaris disseminatus faciei: treatment with the 1450-nm diode laser. *Arch Dermatol* 2005; 141:143-145.
3. Skowron F et al. FIGURE: Facial idiopathic granulomas with regressive evolution. *Dermatol* 2000; 201: 287-289.
4. Van de Scheur et al. Lupus miliaris disseminatus faciei: A distinctive rosacea-like syndrome and not a granulomatous rosacea. *Dermatol* 2003; 206: 120-123.

**Case # 6**

**Case Presented by James Feinberg M.D., J.D.**
**and Sima Jain M.D.**

**UNKNOWN CASE**





**Case # 7**

**Case Presented by Sophie Worobec M.D.**
**and Caroline Schmitt M.D.**

**History of Present Illness:**
This 40 year-old woman with Crohn's disease presented with a 2 month history of nonhealing, painful ulcers on the left lower leg. Prior to onset of these ulcers, she had been hospitalized for an abscess with surrounding cellulitis of the same area and was treated with intravenous piperacillin-tazobactam followed by oral amoxicillin-clavulanate. Although she had initially experienced some improvement, there was subsequent progressive ulceration on the anteromedial left lower leg. A culture of the purulent drainage of the ulcer had grown *Pseudomonas aeruginosa* and *Citrobacter freundii*. Her treatment regimen at time of presentation consisted of broad spectrum oral antibiotics, clotrimazole-betamethasone cream to the ulcer borders, whirlpool therapy, and papain-urea ointment-impregnated dressings.

**Past Medical History & Surgical History:**
Crohn's disease, exploratory fistulectomy, recurrent leg ulcers

**Medications:**
Prednisone 30 mg daily, mesalamine, hydrocodone/acetaminophen, clindamycin, ciprofloxacin

**Allergies:**
No known drug allergies

**Family History:**
Diabetes, colitis

**Social History:**
Smokes 1.5 packs per day, denies alcohol intake, is on disability

**Physical Examination:**
On the left leg, overlying the anterior tibia and extending continuously onto the medial calf, was a large ulcer with an irregular, slightly raised, blue-red border and an erythematous base with purulent and hemorrhagic exudate. Superiorly the border was undermined.

**Laboratory Data:**
The following were abnormal:
White blood cell count 21.7 k/ul (3.5-10.5) with an absolute neutrophil count 18.2 k/ul (1.3-7.5)

The following were negative or within normal limits:
Hemoglobin, platelet count, complete metabolic panel, methemoglobin, anticardiolipin antibodies, wound gram stain with cultures for fungi, bacteria, and acid fast bacilli.

**Diagnostic Procedures and Test:**
Bone scan negative for osteomyelitis, PPD negative

**Histopathology:**
The epidermis is acanthotic with focal pseudoepitheliomatous hyperplasia. There is a dense perivascular infiltrate consisting of lymphocytes, plasma cells, and neutrophils. The papillary dermis is edematous and there are increased numbers of blood vessels with extravasated red blood cells. Fibrotic change is noted in the mid to lower dermis.

**Diagnosis:**
Pyoderma gangrenosum

**Treatment and Course:**

Initial therapy consisted of dapsone which, along with azathioprine and prednisone prescribed by gastroenterology, led to ulcer size stabilization without regression. Amoxicillin-clavulanate was added for polymicrobial positive bacterial cultures and the patient was counseled in smoking cessation. Cyclosporine was initiated, but within weeks there was ulcer progression with increased pain and malodorous discharge. The patient was then admitted for an infliximab infusion, which she tolerated well. Within two weeks there was ulcer size and depth diminution, with beefy red granulation tissue noted at the base. Due to elevation of liver transaminases, cyclosporine was discontinued, with subsequent liver function test normalization. Continued ulcer regression was noted with infliximab infusions every 1-2 months; azathioprine was discontinued and prednisone was tapered to zero. Complete healing was achieved at 16 months.

**Discussion:**

Pyoderma gangrenosum (PG) is a rapidly evolving noninfectious inflammatory ulcerative disease associated with inflammatory bowel disease (IBD) in 36-50% of cases. Initially PG was reported to be more frequent in the ulcerative colitis (UC) subset of IBD patients, but now the incidences are approximately equal for UC and Crohn's disease. Pathogenesis is thought to stem from dysregulation of the T-cell response with production of TNF-α and "neutrophil tracking" as well as immune complex-mediated neutrophilic vascular reactions. The diagnosis is clinical, with histology primarily serving to rule out Wegener's granulomatosis, infection, lymphoma, polyarteritis nodosa, and antiphospholipid antibody syndrome.

Therapies for PG are varied. In a 2005 evidence-based review of the literature, systemic treatment with corticosteroids and cyclosporine was deemed first-line therapy. Other efficacious treatments have included thalidomide, mycophenolate mofetil, tacrolimus, dapsone, antibiotics, and azathioprine, although there are no prospective randomized controlled trials for any of these therapies.

Infliximab is a chimeric mouse-human monoclonal antibody that neutralizes TNF-α. The fact that PG lesions are responsive to infliximab was first reported in the gastroenterologic literature, as patients who were being treated with this medication for IBD also showed improvement in PG lesions. In a retrospective study by Reguerio, 13 IBD patients (12 of whom had Crohn's) showed complete healing of their PG lesions with monthly infliximab 5mg/kg infusions. The rapidity of clearance was inversely correlated with ulcer area, with the largest ulcer (14 cm diameter) healing in 210 days. Four patients who had recurrence cleared with reinstitution of the medication. Sapienza reported 4 female adult patients with active fistulizing Crohn's and PG who rapidly cleared with one or two infliximab 5mg/kg infusions, although ulcer size was not specified. Because of these and other studies, infliximab is now considered a first-line therapy for IBD-associated PG. The presumed mechanism of action is blunting of the TNF-α-induced proinflammatory cascade with suppression of neutrophil infiltration and tissue destruction. There have recently been reports of idiopathic PG dramatically improving on infliximab, as well as PG clearance in a child with PAPA syndrome (pyogenic sterile arthritis, PG, and acne). Thus, infliximab may also be an effective therapy for non-IBD associated PG.

**References:**


1. Dini V, et al. Improvement of idiopathic pyoderma gangrenosum during treatment with anti-tumor necrosis alfa monoclonal antibody. *Int J Low Extrem Wounds* 2007; 6(2): 108-13.
2. Reguerio M, et al. Infliximab for treatment of pyoderma gangrenosum associated with inflammatory bowel disease. *Am J Gastroenterol* 2003; 98( 8): 1821-6.
3. Reichrath J, et al. Treatment recommendations for pyoderma gangrenosum: an evidence-based review of the literature based on more than 250 patients. *J Am Acad Dermatol* 2005; 53(2): 273-83.
4. Sapienza MS, et al. Treatment of pyoderma gangrenosum with infliximab in Crohn's disease. *Dig Dis Sci* 2004; 49(9): 1454-7.
5. Stichweh DS, et al. Dramatic improvement of pyoderma gangrenosum with infliximab in a patient with PAPA syndrome. *Pediatr Dermatol* 2005; 22(3): 262-5.

**Case # 8**

**Case Presented by by Aleksandar Krunic M.D., Ph.D, Neil Peters M.D., Taraneh Firoozi M.D., Helen Chen M.D.,
and Platina Coy Gershtenson, M.D.**

**History of Present Illness:**
This 31 year-old female presented with a 14 year history of multiple asymptomatic lesions limited to the outer portion of her right hip. The individual lesions slowly increased in size and number over time, but did not disseminate. The patient was referred for surgical consultation since the biopsy performed in an outside institution was suggestive of dermatofibrosarcoma protuberans.

**Past Medical History:**
Seasonal allergies and gastroesophageal reflux disorder

**Medications:**
Lansoprazole and loratadine

**Allergies:**
No known drug allergies

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

**Review of systems:**
The patient denies any fevers, chills, night sweats, weight loss or joint pains.

**Physical Examination:**
The patient has a 21 cm x 22 cm plaque on her right outer hip consisting of a cluster of small 5-10 mm hyperpigmented to violaceous dermal papules. There is no regional lymphadenopathy.

**Laboratory Data/Diagnostic Procedures and Tests:**
None

**Histopathology:**

7/07 Right hip: The epidermis shows hyperkeratosis and acanthosis with broad rete ridges. The basal cell layer is hypermelanotic. Melanin pigment is seen in upper dermal melanophages. Within the mid to lower dermis there is an infiltrate of cells with spindle shaped and stellate nuclei. There is evidence of collagen trapping. There are occasional multinucleated giant cells. The subcutaneous fat is not involved. No nuclear atypia is noted and no mitoses are seen. CD34 stain is positive in endothelial cells and some of the tumor cells. Tumor cells are positive for vimentin and negative for S100, Ki67, CD68, EMA, AE1/3 and actin.

8/07 Right thigh: There is a mid dermal plate-like infiltrate of spindled cells with uniform nuclei. There is collagen trapping at the periphery. No tumor is seen in the subcutaneous tissue. Collagen trapping is noted at the periphery of the tumor. Elastic fibers are diminished. Masson trichrome stain reveals a collagenous stroma. CD34 is negative and Factor XIIIa is positive. Tumor cells are negative for CD68.

**Diagnosis:**
Multiple clustered dermatofibroma

**Treatment and Course:**
The patient has had not treatment to date. The patient is presented for discussion of diagnosis.

**Discussion:**
Dermatofibroma (DF), or histiocytoma, is a common benign cutaneous lesion that typically presents as a reddish-brown papule or nodule most commonly on the lower extremities of middle-aged women. There are many clinical variants including giant DF, eruptive DF, atrophic DF, atypical polypoid DF and subcutaneous fibrous histiocytoma. Histologically, DF variants include cellular benign fibrous histiocytoma, aneurysmal benign fibrous histiocytoma, atypical benign fibrous histiocytoma and epithelioid benign fibrous histiocytoma. Multiple dermatofibroma is a rare entity in which more than fifteen lesions occur. Disseminated DF has been described in patients with both normal and altered immune function and has been reported in association with human immunodeficiency virus infection, myasthenia gravis, atopic dermatitis, systemic lupus erythematosus and diabetes.

Multiple clustered dermatofibroma (MCDF) is a very rare variant with less than ten reports in the literature. In the majority of cases, the lesions occurred on the lower extremity in females. One reported case was congenital. Clinically, MCDF appears as a well-demarcated, reddish- to brown group of papules arranged in a large plaque. The lesions are asymptomatic or initially present with mild pruritus, and tend to stabilize in size after several years. All MCDF reports thus far have occurred in the setting of healthy persons. Onset tends to be in the first, second or third decade with initial increase in size and number over a period of years. There have been no reports of malignant transformation or metastatic disease. The histology is consistent with a common DF. In all cases reported to date in which immunohistochemistry was implemented, Factor XIIIa was positive and CD34 was negative.

The differential diagnosis of MCDF includes dermatofibrosarcoma protuberans (DFSP), atypical fibroxanthoma, xanthoma, dermatomyofibroma, nodular fasciitis, leiomyoma, dermatofibrosis lenticularis disseminata and congenital nevus with fibrosis. Differential diagnosis between DF and DFSP may sometimes be difficult. Traditionally, CD34 and Factor XIIIa have been used to differentiate between DF and DFSP, with CD34 positive in DFSP and Factor XIIIa positive in DF. However, CD34 positivity is reported in up to 20% of dermatofibromas. Stromelysin-3 (ST3) has recently been reported as a new more specific immunohistochemical marker that is positive in DF and negative in DFSP.

We believe our case is an example of multiple clustered dermatofibroma. We diagnosed MCDF based on the long history, superficial type of proliferation, decreased cellularity, less storiform architecture and absence of nuclear atypia. We present this case for clinical interest especially in light of the difficulties with histological diagnosis between DF and DFSP.

**References:**

1. Heenan PJ. Tumors of Fibrous Tissue Involving the Skin *in* Lever's Histopathology of the Skin, Ninth Edition. Elder DE editor in chief. Philadelphia: Lippincott Williams & Wilkins, 2005: p979-1013.
2. Hueso L, Sanmartin O, Alfaro-Rubio A, et al. Giant Dermatofibroma: Case Report and Review of the Literature. *Actas Dermosifitlogr* 2007; 98:121-124.
3. Kim HJ, Lee LY, Kim YJ, et al. Stromelysin-3 expression in the differential diagnosis of dermatofibroma and dermatofibrosarcoma protuberans: comparison with factor XIIIa and CD34. *British Journal of Dermatology* 2007; 157:319-324.
4. Soleto R, Yanguas I, Saracibar N and Goday JJ. Histiocytofibromes multiples groupes: A propos d'un cas avec etude immunohistochimique. *Ann. Dermatol. Venereol* 1994; 121: 482-484.
5. Soon SL, Howard AK and Washington CV. Multiple, Clustered Dermatofibroma: A Rare Clinical Variant of Dermatofibroma. *J Cutan Med Surg* 2003; 7(6):455-457.
6. Unamuno P.D., Carames Y, Fernandez-Lopez E, et al. Congenital multiple clustered dermatofibroma. *Br J Dermatol* 2000; 142: 1040-1043.

**Case # 9**

**Case Presented by Aleksander Krunic M.D., Ph.D, Sophie Worobec M.D., and Tarun Kukreja M.D.**

**History of Present Illness:**
This 56 year-old female presented with a several year history of pruritic lesions involving her abdomen, chest, back, arms, and legs. They first began as a few itchy bumps, which gradually increased in number and size. The initial clinical diagnosis was suggestive of prurigo nodularis, but the patient failed to improve on high potency topical steroids and topical calcipotriol.

Two lesions were then biopsied and reported as verruca vulgaris, leading to treatment with imiquimod cream with no improvement. Subsequent biopsies taken were consistent with verrucae, but on re-review of pathology there was concern that many of the lesions could be consistent with keratoacanthoma.

**Past Medical History:**
Primary hyperparathyroidism treated with parathyroidectomy in June of 2005, hypertension

**Medications:**
Allegra, acitretin, hydrochlorothiazide, atenolol, ibuprofen as needed

**Review of systems:**
Negative

**Physical Examination:**
The patient has numerous hyperkeratotic, hyperpigmented large ~1cm dome shaped papules on her trunk, back, arms, legs, dorsal hands, dorsal feet, and helices of ears. Many lesions demonstrate central invagination and are filled with keratin.

**Laboratory Data:**
The following were negative or within normal limits:
Complete blood count, liver function tests, complete metabolic panel, T and B cell markers, anti-nuclear antibody, human immunodeficiency virus (HIV), hepatitis panels, lipid panel, thyroid panel, parathyroid hormone level

**Histopathology:**
3/05 Immunohistochemical staining for human papillomavirus is negative. The epidermis shows marked hyperkeratosis with focal parakeratosis and central crater formation. Keratinocytes are pale. Granular layer is thickened with course keratohyaline granules. Dense upper dermal infiltrate of lymphohistiocytic cells with no significant nuclear atypia and no dyskeratotic cells.

**Diagnosis:**
Keratoacanthoma-like prurigo nodularis

**Treatment and Course:**
Based on the clinical appearance and the pathology revealing a possibility of multiple keratoacanthomas and non-responsiveness to imiquimod and liquid nitrogen, the patient was treated for the possibility of a rare variant of prurigo nodularis of the keratoacanthoma-like type. She has been recently started on 25mg of acitretin daily with significant improvement in the number and size of the lesions.

Our patient was non-responsive to treatment of her lesions as verrucae. In addition, no human papillomavirus (HPV) was found on in-situ hybridization of her lesions. Our differential diagnosis then included a rare variant of prurigo nodularis that has been described in the literature that histologically resembles keratoacanthoma (KA), multiple nonfamilial acquired keratoacanthomas, and verrucae. Given the clinical appearance of prurigo nodularis and the pathology being read as both keratoacanthoma and verruca, we decided to start therapy with acitretin 25mg daily as it has been used to treat verrucae, prurigo nodularis, and keratoacanthomas with success.

**Discussion:**
Prurigo nodularis usually presents as multiple pruritic nodules on the extremities, especially the legs. When lesions are fully developed, they can become verrucous. The itching is usually confined to the lesions themselves, and the pruritus usually worsens when the patients are under stress. The cause is unknown, with many factors contributing to this including atopic dermatitis, anemia, HIV, pregnancy, renal failure, lymphoproliferative diseases, and insect bites. Systemic retinoids such as acitretin may reduce the size of the nodules and the severity of the itch. The exact mechanism of action for acitretin is not known. One possible explanation is altered gene expression through binding to nuclear retinoic acid receptors (RARs) causing changes in protein synthesis. Although acitretin binds to all three classes of RARs (alpha, beta, and gamma receptors), it binds selectively to beta and gamma receptors to modify gene expression.

Retinoids exert a wide range of effects on cells including the regulation of growth and differentiation, along with possibly being an immunomodulater. An inverse relationship was observed between concentrations of retinoids and HPV deoxyribonucleic acid within infected epithelial cells suggesting an effect on viral replication. Oral retinoids have also been used with dramatic clinical improvement in the management of extensive warts.

Although our patient did not have HPV on in-situ hybridization of her lesions, HPV has also been detected in immunocompromised and immunocompetent patients with multiple keratoacanthomas. Several DNA serotypes have been detected in 50% of patients with KA, including HPV types 5, 6, 9, 10, 14, 19, 20, 21, 38, 49, and 80. The specific role of HPV in KA pathogenesis is still poorly understood.

**References:**

1. Kocsard D, Palmer G, Constance TJ. Multiple Keratoacanthoma-like Neurodermatitis Nodularis. *Australas J Dermatol* 1972; 13(3): 100-4
2. Choi YL, Lee KJ, Kim WS, Lee DY, Lee JH, Lee ES, Yang JM. Treatment of extensive and recalcitrant viral warts with acitretin. *Int J Dermatol* 2006; 45(4): 480-2.
3. Karraa A, Khachemoune A. Keratoacanthoma: a tumor in search of a classification. *Int J Dermatol* 2007; 46(7): 671-8.

**Case # 10**

**Case Presented by Iris K. Aronson M.D.**
**and Sabrina Guillen Fabi M.D.**

***Patient A***

**History of Present Illness:**

This 6 year-old Hispanic girl presented in early August 2007 with a 7 month history of a intensely pruritic cutaneous eruption that began on her fingers and gradually involved her arms, buttocks, legs, and face. The patient's parents noticed sunlight exacerbated the rash. The patient denied any muscle pain at rest, but did admit to pain and difficulty when combing her hair or walking up stairs.

In April 2007, cetirizine 1mg daily was initiated by her primary doctor and the patient was referred to Rheumatology. There was concern that the patient was erythrodermic and the patient was referred to our clinic for evaluation. In the interim, the patient's primary doctor added hydrocortisone 2.5% ointment twice a day, as adjunctive treatment for the patient's pruritic cutaneous eruption.

**Past Medical History:**

None

**Medications:**

Hydrocortisone 2.5% ointment, cetirizine 1mg daily

**Allergies:**

No known drug allergies

**Family History**

No history of skin disease or autoimmune disease

**Review of systems:**

Positive for occasional fevers and girdle muscle pain when combing her hair or climbing stairs. Negative for fatigue, chills, sweats, weight loss, dysphagia, shortness of breath, chest pain, hematuria, joint pain, or muscle pain at rest.

**Physical Examination:**

The exam was remarkable for a periorbital heliotrope flush, extending superiorly to involve the forehead and inferiorly to involve the bridge of the nose and the malar area bilaterally. The nape of the neck, extensor surfaces of the arms, buttocks, and proximal legs, most notably over that lateral aspects of the thighs, demonstrated violaceous patches. The hands exhibited flat topped, pink, polygonal shiny papules over the knuckles.

**Laboratory Data:**

06/29/07: lactate dehydrogenase 284 (90-180), creatine kinase 101 u/L (20-185)**,** aldolase 7.9 u/L (3-12), erythrocyte sedimentation rate 15 mm/hr (0-13), anti-nuclear antibody titer 1:160; anti-RNP, anti-smith, SS-A IgG, SS-B IgG, anti-dsDNA, C3, C4, and urine analysis all within normal limits
08/28/07: lactate dehydrogenase 560 (90-180), creatine kinase 190 u/L (20-185)**,** aldolase 24.4 u/L (3-12), erythrocyte sedimentation rate 59 mm/hr (0-13); Complete blood count within normal limits
10/19/07: lactate dehydrogenase 241 (90-180), creatine kinase 40 u/L (20-185)**,** aldolase 7.5 u/L (3-12), erythrocyte sedimentation rate 27 mm/hr (0-13); Complete blood count within normal limits

**Diagnostic Procedures and Tests:**
08/20/07 Nerve conduction studies of the right sural and ulnar sensory, and right peroneal and ulnar motor responses were normal. The right ulnar F wave latency was normal, F wave latency of the right peroneal was unobtainable. Electromyography of selected muscles of the right lower extremity was performed. Spontaneous activity in the forms of positive waves and fibrillations was present in the right tibialis anterior. Voluntary contraction of the right tibialis anterior elicited polyphasic motor unit action potentials that are of short duration. Recruitment pattern was normal in all muscles tested. This study was interpreted as abnormal, with the right tibialis anterior demonstrating necrotizing myopathy.

**Diagnosis:**
Juvenile Dermatomyositis (JDM)

**Treatment and Course:**
Based on these results, the patient was started on prednisolone 30mg (1mg/kg) daily and strict sun protection was advised. Within 2 months the patient's rash began to clear, although still demonstrating significant photosensitivity, and her proximal muscle weakness improved. Tapering of prednisolone by 0.1mg/kg per month was initiated, and the patient is presently on prednisolone 24mg (0.8mg/kg) daily with notable improvement and no complications.

***Patient B***
**History of Present Illness:**
This 39 year-old African American woman presented to our clinic in December 2006 with an approximately 2 year history of an asymptomatic cutaneous eruption that began on her abdomen and rapidly progressed to involve her back, legs, and face. The patient noticed sunlight exacerbated the rash. The patient denied ever having any muscle pain at rest or difficulty when getting out of a chair, combing her hair or walking up stairs. Direct immunofluorescence and biopsies performed at an outside institution in April 2006 were read as interface dermatitis consistent with a connective tissue disease, namely dermatomyositis. Given her lack of muscle symptoms in conjunction with initially normal muscle enzyme serology, the patient was diagnosed with amyopathic dermatomyositis. Therapy was initiated, including hydrocortisone probutate 0.1% daily to her face and clobetasol propionate 0.05% daily to her body, which the patient noted improvement from. The patient was also started on hydroxychloroquine 200mg twice daily. Subsequent electromyography showed bilateral ulnar mononeuropathy at the elbows and delays in sensory responses only of both median nerves at the wrists, and radiographs demonstrated mild calcific tendinosis of the left common extensor tendon, and right flexor tendon origin. The patient presented to us for further evaluation and treatment.

**Past Medical History:**
Gastroesophageal reflux disorder, seasonal allergies

**Medications:**
Hydrocortisone probutate 0.1%, clobetasol propionate 0.05%, hydroxychloroquine sulfate 200mg twice daily, cetirizine

**Allergies:**
No known drug allergies

**Family History**
No history of skin disease, autoimmune disease, or malignancy

**Social History**
Denies tobacco use or alcohol intake, works as a transportation manager for the CTA

**Review of systems:**
Negative for fevers, chills, sweats, weight loss, dysphagia, shortness of breath, chest pain, abdominal pain, hematuria, muscle pain at rest or with movement, or muscle weakness. Positive for fatigue, knee pain, color changes in her fingers with cold exposure, and paresthesias of the right $4^{th}$ and $5^{th}$ fingers.

**Physical Examination:**
The exam was remarkable for a mottled hyperpigmented patches over the forehead, nose, malar region, chin, nape of the neck, back, anterior thighs, and knees. The hands exhibited flat topped, pink, polygonal shiny atrophic plaques over the knuckles.

**Laboratory Data:**
The following tests were positive or abnormal:
Creatine kinase 330 u/L (20-185), anti-nuclear antibody titer 1:160, speckled, white blood cell count 3.4 k/uL (3.5-10.5), complete blood count differential: neutrophils 27.8% (35-75), monocytes 15.2% (2-12), absolute neutrophils 1 k/uL (1.3-7.5), CH50 147 U (60-144), aspartate aminotransferase 43 U/L (10-40), total bilirubin 1.6 mg/dL (0-1.2)

The following tests were negative or within normal limits:
Aldolase, anti-RNP, anti-smith, SS-A IgG, SS-B IgG, anti-dsDNA, anti-Scl 70 IgG, RF, anti-thyroid peroxidase IgG, C3, C4, anti-cardiolipin IgM, IgA, and IgG, erythrocyte sedimentation rate, c-reactive protein, complete blood count with differential (except white blood cell count, neutrophils %, monocytes %, and absolute neutrophils), liver function test (except aspartate aminotransferase and total bilirubin), CA-125, and urine analysis.

**Diagnosis:**
Dermatomyositis (DM)

**Treatment and Course:**
Under our care, strict sun protection was advised, topical therapy was initiated, including triamcinolone 0.1% ointment twice daily to her body, hydrocortisone 2.5% cream twice daily to her face, and hydroxychloroquine 200mg twice daily was continued. Further laboratory work up was performed, demonstrating abnormal muscle enzymes. Evaluation for internal malignancy, including ovarian ultrasound, mammography, chest x-ray, chest computed tomography, and three consecutive fecal occult blood tests, were negative. The patient was referred to Rheumatology and in January was started on azathioprine 50mg twice daily, but discontinued after two months because of worsening neutropenia. Mycophenolate mofetil 250mg twice daily was then initiated but discontinued four months into treatment because of severe neutropenia. A hematology consult was placed, but the patient has yet to follow up. Overall, the patient noted minimal improvement and continuous flares of her disease, including erythema and ulceration of her skin, while on oral therapy. The patient reported most notable improvement from topical therapy with triamcinolone 0.1% ointment and hydrocortisone 2.5% cream. The patient recently sustained a motor vehicle accident, in fracturing multiple bones and subsequently experiencing significant flare up of her disease. While hospitalized, all treatments except hydroxychloroquine 200mg twice daily were discontinued, and the patient was started on prednisone 20mg daily with normalization of her muscle enzyme serology.

**Discussion:**
Dermatomyositis (DM) is a rare, chronic, multisystem idiopathic inflammatory myopathy that primarily involves skin and muscles, but can affect the gastrointestinal tract, pulmonary and cardiac systems. There is a bimodal distribution in disease onset, with most presenting in the fifth to seventh decades of life and the remainder presenting in childhood.

Juvenile dermatomyositis is defined as onset of disease before the age of 18 years of age. Two childhood variants exist. Brunsting type is typically steroid responsive, with an indolent course of progressive weakness and calcinosis. A fulminant course is seen in Banker type, which is not responsive to steroids, and is characterized by rapid onset of muscle weakness, with vasculitis of the muscles and gastrointestinal tract, resulting in high death rates.

Bohan and Peter proposed a set of criteria to aid in the diagnosis and classification of DM and polymyositis, despite the probably different pathogenesis of the two myopathies. A patient has definite DM, if they have the characteristic cutaneous findings and 3 of 4 of the following criteria: symmetric proximal muscle weakness, elevated muscle-derived enzymes, muscle histopathologic findings, and electromyographic changes characteristic of an inflammatory myopathy. Probable DM and possible DM are defined by having 2 of the 4 criteria or 1 of the 4 criteria, respectively, with presence of compatible cutaneous disease. Although Bohan and colleagues noted that skin lesions can precede the development of myositis, sometimes for up to 2 years, it is also common for muscle inflammation to be present but asymptomatic. This demonstrates the importance of obtaining a good clinical history at every visit to assess for muscle involvement, as well as performing serial muscle enzyme serology, even when initial laboratory data proves inconclusive. A small subset of patients never develop muscle weakness or muscle enzyme abnormalities, despite having prominent cutaneous changes, and they are classified as having amyopathic dermatomyositis.

A wide variety of malignancies have been reported in patients with DM, more commonly occurring in adults, and seldomly associated in cases of JDM, although cases have been reported. Malignant disease may occur before the onset, concurrently with myositis, or after the onset of DM. Therefore an assessment of malignant disease should be done in all adult patients, and selected on the basis of the patient's age and sex. Assessment of malignancy should be repeated if new symptoms arise, or yearly for the first 3 years after diagnosis. Calcinosis is a frequent complication of DM in children and adolescents, less commonly in adults, and is related to severity and duration of disease. Calcinosis may involve intermuscular fascial planes, be subcutaneous or dermal. This complication can be further compounded by ulcerations and cellulitis.

Oral corticosteroid therapy is the mainstay of treatment for juvenile and adult onset DM with active muscle disease. Approximately 25% of patients with DM will not respond to systemic corticosteroids and 25-50% will develop substantial steroid-related side-effects. In which case, steroid-sparing agents such as methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, chlorambucil, or cyclosporine may be effective in inducing or maintaining remission. In cases recalcitrant to these above mentioned treatments, response has been shown with pulse methylprednisolone, high-dose intravenous immunoglobulin therapy, etanercept, infliximab, and rituximab.

In cases without muscle involvement (DM sine myositis) or in cutaneous flares of DM, skin lesions may respond to systemic corticosteroid therapy however this form of therapy is not warranted because of lack of predictability and failure of cutaneous disease to involute despite remission of myositis. Some evidence suggests methotrexate, mycophenolate mofetil and intravenous immunoglobulin therapy, may be beneficial. But treatment options remain limited. Although cutaneous disease may be less important in patients with severe myositis, in many patients, like with ours, the cutaneous involvement may become the most important part of their disease.

**References:**


1. Callen JP, Wortmann, RL. Dermatomyositis. *Clin Dermatol* 2006; 24: 363-373.
2. Callen JP. Dermatomyositis. *Lancet* 2000; 355: 53-57.
3. Jordan JR, et al. Spontaneously remitting dermatomyositis. *J Eur Acad Derm Venereol* 2004; 18(4): 495-498.
4. Peloro TM, et al. Juvenile Dermatomyositis: A retrospective review of a 30-year experience. *J Am Acad Dermatol* 2001; 45(1): 28-34.

**Case # 11**

**Case Presented by Iris Aronson M.D.**
**and Deborah Marble M.D.**

**History of Present Illness:**
This 38 year-old female presented with a life-long history of hypertrophy and nodular vascular proliferation of her right arm as well as her right hemi-thorax. The patient notes intermittent pain localized to the nodular lesions. She has had symptoms since birth and was given a diagnosis at age 15. Prior to presenting to our clinic, the patient had tried compression therapy without improvement in the frequency or severity of her intermittent pain. She follows up regularly with vascular surgery, but no surgical procedures have been performed as she has yet to have demonstrated any vascular lesions concerning to them. The patient says that she was told she was not a candidate for surgery due to the large size of her lesions.

**Past Medical History:**
Psoriasis, migraines, seasonal allergies

**Medications:**
Sumatriptan succinate, fexofenidine, calcipotriene/betamethasone diproprionate ointment

**Allergies:**
No known drug allergies

**Family History:**
Her father has psoriasis. No family members have similar hypertrophic/vascular abnormalities.

**Physical Examination:**
The patient's right arm, right hand, and right hemi-thorax have near complete involvement with numerous large bluish-purple varicosities and nodules. There is associated hypertrophy of the tissue. There are no stasis changes or ulcers

**Diagnostic Procedures and Tests:**
1984 MRI showed a diffusely infiltrative lesion involving the muscle of the posterolateral aspect of the right neck, the posterolateral aspect of the right thorax and the right anterolateral aspect of the abdominal wall. The lesion extended into right arm, with the most marked involvement being seen within the right forearm. There were similar lesions on the abdominal wall extending down to 4 to 5 centimeters above the iliac crest. These results were consistent with a diagnosis of Klippel-Trenaunay syndrome.

**Diagnosis:**
Klippel-Trenaunay syndrome

**Treatment and Course:**
The patient was treated with compression therapy, but stopped due to discomfort and lack of improvement. She visited vascular surgery and was again told that she was not a candidate for surgery.

**Discussion:**

Klippel-Trenaunay syndrome, also known as angio-osteohypertrophy syndrome, consists of a triad of capillary malformations, varicose veins, and hypertrophy of bone and soft tissues. This syndrome is usually limited to one extremity. The leg is the most commonly affected site. It usually presents at birth with capillary malformations. The vascular malformations vary in depth and may affect areas other than the involved extremity. Involvement of internal organs may result in internal bleeding. If arterio-venous fistulas are present, they represent a greater morbidity and may ultimately result in high output cardiac failure. The primary process involved in Klippel-Trenaunay syndrome is hypertrophy of the limb, which is not due to lymphedema or stasis-induced changes.

Various possible etiologies for Klippel-Trenaunay syndrome have been proposed. One theory is that a spinal cord abnormality is involved, due to the dermatomal distribution of lesions. It has been proposed that tissue hypertrophy is due to vasoconstrictor paralysis, and that lesions result from an intrauterine injury to the sympathetic ganglion or to the interomediolateral tract. Somatic mutations that may be involved in vasculogenesis and angiogenesis during embryonic development have been documented in some cases.

Treatment is mainly symptomatic. Compression stockings are recommended to decrease edema in the affected limb. Surgery to correct limb length discrepancies may be undertaken. Venous stripping/sclerotherapy may be helpful in a select group of patients. Lasers have been used to treat the cutaneous vascular lesions.

**References:**


1. Garzon MC et al. Vascular malformations. Part II: associated syndromes. *J Am Acad Dermatol* 2007; 56(4): 541-64
2. Kihiczak G et al. Klippel-Trenaunay syndrome:A multisystem disorder possibly resulting from a pathogenic gene for vascular and tissue overgrowth. *Int J Dermatol* 2006;45: 883-90.

**Case # 12**

**Case Presented by James Feinberg M.D., J.D.,**
**and Monika Kiripolsky M.D.**

**History of Present Illness:**
This 52 year-old man presented with a three month history of a slowly enlarging, asymptomatic mass on the lateral aspect of his right thigh. The patient denied any preceding trauma to the site. He denied any lesional fluid drainage or inflammation. It had never been pruritic or tender. The patient's internist initially felt that the mass was an abscess and subsequently started him on cephalexin. However, the mass did not change after completion of this seven day course of antibiotics, and the patient was referred to dermatology for further diagnosis and treatment.

**Past Medical History:**
Hepatitis C with cirrhosis, bipolar disorder, idiopathic thrombocytopenic purpura with platelet counts ranging in the low 50's over the preceding few months

**Medications:**
Gabapentin, clonazepam, risperidone, and multivitamins

**Social History:**
The patient is a Vietnam veteran with no known exposure to Agent Orange. He does admit to extensive sun exposure and smokes a pack of cigarettes per day.

**Review of Systems:**
The patient stated that he had an asymptomatic 'lump' in his right groin; he felt this groin mass might be growing. He denied any weight loss, anorexia, night sweats, fevers, epistaxis, hematochezia, melena, easy bruising, bone pain, leg swelling, or leg tenderness.

**Physical Examination:**
The patient had a 5 cm x 4.2 cm firm subcutaneous mass on the lateral aspect of his right upper thigh. The mass was violaceous, non-fluctuant, non-pulsatile, and non-tender to deep palpation. The mass did not feel warmer than surrounding skin and there was no overlying punctum. In his right inguinal fossa was an approximately 4 cm non-tender, firm, non-mobile nodule. No cervical, axillary, popliteal, or left inguinal lymphadenopathy was appreciated.

**Diagnostic Procedures and Test:**
10/07 Chest radiograph: within normal limits
10/07 CT of pelvis with and without contrast: There are enlarged right-sided obturator and external iliac lymph nodes. Inguinal nodes vary from 1.8 cm to 6.3 cm. There is hepatosplenomegaly. There are neither focal liver abnormalities nor osseous metastases.
10/07 CT of thorax with and without contrast: There is an enlarged non-calcified lymph node in the mediastinal azygo-esophageal recess. There is splenomegaly and a nodular surface of the liver, consistent with lymphomatous involvement or cirrhosis. The lungs are clear.
10/07 MRI of right lower extremity with and without contrast: There is a 2.8 cm x 2.4 cm x 1.8cm lobulated mass with patchy enhancement along the lateral aspect of the thigh in the subcutaneous tissue. There is induration around the mass. There is no involvement of the bones.

**Histopathology:**
9/07 Right lateral thigh: The epidermis is somewhat acanthotic. There is a perivascular and periadnexal lymphoplasmacytic infiltrate. In the deep dermis, a neoplastic infiltrate is seen

consisting of numerous cells with basophilic nuclei and small amounts of cytoplasm. Mitoses are numerous. The nuclei show marked atypia and pleomorphism. Pyknotic nuclei and degenerated cells are numerous. Large areas of necrosis are seen within the tumor. The following stains are positive: keratin (AE 1/3), cytokeratin 20 and synaptophysin. Chromogranin is weakly positive. The tumor is negative for the following stains: thyroid transcription factor, leukocyte common antigen and keratin 7.

**Diagnosis:**
Merkel cell carcinoma with lymph node metastases; Stage III, T2N1M0

**Treatment and Course:**
The patient recently underwent a resection (via wide local excision) of the mass on his thigh as well as a right superficial inguinal lymph node dissection. Pathology results from the patient's recent lymph node dissection and mass excision are still pending. His post-operative course has been complicated by recurrent febrile episodes as well as development of cellulitis around his wound site. Once his pathology results return, the hematology oncology and radiation oncology teams will determine whether he will need adjuvant chemotherapy and/or radiation treatments.

**Discussion:**
Merkel cell carcinoma (MCC), also known as neuroendocrine carcinoma of the skin, is a rare and aggressive malignancy. MCC typically presents as a solitary, non-tender, firm, indurated dermal nodule, with an overlying slightly erythematous to deeply violaceous hue. Ulceration is uncommon. It frequently involves the regional lymph nodes at initial presentation (10-45% of cases). During the course of the disease, between 50-75% will develop regional lymph node metastases, and 50% will develop distant metastases. Like melanoma, MCC can progress rapidly.

Approximately 400 cases of MCC are reported each year in the United States, and it is a disease mostly occurring in elderly, white patients. Only 5% of cases occur in patients under age 50, the average age at diagnosis is 75 years, and whites have a 20-fold higher relative risk of developing MCC compared to blacks. Although MCC accounts for less than 1% of all cutaneous malignancies, its incidence appears to be rising over the past fifteen years.

The most common site for MCC is the periocular region, other areas of the head and neck, as well as the extremities. An immunosuppressed state as well as a history of methoxsalen and ultraviolet A treatment for psoriasis predisposes persons to developing MCC. The merkel cell has a mechanoreceptor function and is located within or near the basal layer of the epidermis, in close proximity to terminal axons.

Current treatment recommendations include wide local excision of the primary tumor (with 3 cm margins), with or without prophylactic complete lymph node dissection, as well as adjuvant radiotherapy and chemotherapy. Recurrence of MCC after primary tumor excision is relatively common, occurring in approximately 25-44% of patients; this is usually attributed to inadequate surgical margins. Sentinel lymph node biopsy as well as lymph node dissection procedures have not been found to confer an increased survival; these are mainly used for staging purposes and to predict risk of recurrence. MCC carries a poor prognosis, with an overall mortality rate of 25%.

**References:**

1. Haag M. et al. Merkel cell carcinoma. Diagnosis and treatment. *Dermatol Surg* 1995; 21(8): 669-83.
2. Hodgson N. Merkel cell carcinoma: changing incidence trends. *J Surg Oncol* 2005; 89(1): 1-4.
3. Nghiem P. et al. Merkel cell (cutaneous neuroendocrine) carcinoma. In: Sober A, Haluska F, eds.: *Skin Cancer.* Hamilton, Ontario: BC Decker Inc. 2001; 127-141.
4. Ratner D. et al. Merkel cell carcinoma. *J Am Acad Dermatol* 1993; 29(2): 143-56.
5. Yiengpruksawan A. et al. Merkel cell carcinoma. Prognosis and management. *Arch Surg* 1991; 126(12): 1514-9.

**Case # 13**

**Case presented by Claudia Hernandez M.D.**
**and Sima Jain M.D.**

**History of Present Illness:**
This 32 year-old male presented to our clinic with a six month history of bilateral foot swelling, pain, and redness. The erythema and pain were initially noted approximately six to seven months prior to presentation, but the patient attributed these symptoms to an increased amount of physical activity. He continued to experience intermittent pain over the ensuing months which increased until he had difficulty walking. The erythema and edema of his feet were also noted to worsen during this time. He denied having undergone any acute trauma to his feet prior to presentation.

**Past Medical History:**
None

**Medications:**
None

**Review of systems:**
He denied weight loss, fevers, chills, malaise, nausea, or abdominal pain.

**Physical Examination:**
The patient had approximately seven annular purpuric plaques overlying the medial aspects of both feet. Pitting edema over the ankles and toes were noted, as well as tenderness to palpation.

**Laboratory Data:**
Human immunodeficiency virus (HIV) antibody screen: positive
CD4 count: 121 cells/$mm^3$ (500-1500)

**Diagnostic Procedures and Tests:**
3/07 CT of the chest/pelvis/abdomen with and without contrast: No evidence of suspicious focal mass, metastatic disease or adenopathy.

**Histopathology:**
02/07 The epidermis is thickened. There is an increased number of blood vessels in a lobular formation, many of which are irregularly shaped with collapsed walls. The endothelial cells have hyperchromatic and enlarged nuclei. The neoplasm has a periadnexal distribution. Extravasated red blood cells are seen with scattered adjacent areas of hemosiderin.

**Diagnosis:**
Kaposi's sarcoma

**Treatment and course:**
The patient was found to be HIV positive. Highly active retroviral therapy (HAART), which included tenofovir, lopinovir, ritonavir, and emtricitabine, was initiated by the infectious disease service. His lesions began to recede within weeks of starting therapy, and he is now able to walk comfortably.

**Discussion:**

Kaposi's sarcoma (KS) is a multisystem vascular neoplasia characterized by mucocutaneous violaceous lesions and edema, with the potential to involve nearly any organ. The entity received little attention until it became an epidemic in male homosexuals and was recognized as an acquired immune deficiency syndrome (AIDS) defining disease. Five types of KS are recognized: 1) classic KS, an indolent disease seen primarily in middle-aged men of Southeastern and Eastern European origin; 2) African endemic or cutaneous KS, a locally aggressive process affecting middle-aged Africans; 3) African lymphadenopathic KS, an aggressive disease of the young, mainly children under the age of ten; 4) KS in immunosuppressed pts; 5) AIDS-related KS. The latter subtype is most commonly seen in HIV patients with low CD4 T cell counts, usually less than 500 cells/$mm^3$ (500-1500).

Clinical features in AIDS-related KS are variable and depend on the stage of the disease. Some patients may have a single cutaneous lesion, while others have disseminated disease. Twenty-five percent of AIDS-related KS patients have cutaneous involvement alone, and approximately 30% have only visceral disease. The most frequent sites of visceral involvement are the gastrointestinal tract, lymph nodes, and lungs. Lesions range from faint erythematous to purpuric macules, papules, plaques to purpuric-black tumors and nodules preferentially affecting the hard palate, penis, trunk, lower legs and soles. Lower extremity lesions may be accompanied by edema causing moderate to severe pain.

KS is manifested by a proliferation of abnormal vascular endothelial cells, and the histopathological appearance varies with the stage of the lesion. Early lesions demonstrate irregularly shaped, angulated ectatic vessels with scattered lymphocytes and plasma cells. The endothelial cells of the capillaries are large and protrude into the lumen. Later lesions show proliferation of vessels around preexisting vessels, which can extend into the vascular space forming a promontory sign. Plaque stage and nodular stage lesions contain spindle cells that form intersecting fascicles, separated by characteristic slit-like spaces containing erythrocytes, which may replace dermal collagen. Mitotic figures and pleomorphism are typically absent. The differential diagnosis varies with the stage of KS and includes the following: angiosarcoma, microvenular hemangioma, hobnail hemangioma, spindle cell hemangioma, benign lymphangiomatosis, and kaposiform hemangioendothelioma.

Treatments for KS include local excision, alitretinoin gel, radiation, cryotherapy, laser therapy, thalidomide, intralesional chemotherapy and interferon. Highly active antiretroviral therapy (HAART) has reduced the incidence of Kaposi's sarcoma in HIV infected patients by ten fold. This regimen results in the involution of KS lesions in about 50% of patients after six months of therapy. Thus, HAART should be the initial management in patients with mild to moderate disease.

**References:**


1. Jessop S. HIV-Associated Kaposi's Sarcoma. *Dermatol Clin* 2006; 24: 509-20.
2. Bolognia JL, Jorizzo JL, Rapini RP. *Dermatology* 2003; 1830-1833.
3. Al Zolibani A. Primary palmoplantar Kaposi's sarcoma: an unusual presentation. *Skinmed* 2006; 5 (5): 248-49.
4. Rubegni, P. Thalidomide in the treatment of Kaposi's sarcoma. *Dermatology* 2007; 215 (3): 240-4.

**Case # 14**

**Case Presented by Claudia Hernandez M.D.**
**and Aaron Cetner M.D.**

**History of Present Illness:**
This 38 year-old African American male presented with a long history of subcutaneous cysts on his chest, abdomen, back, upper and lower extremities. The cysts began to erupt at 14 years of age and subsequently spread. The cysts are usually asymptomatic but some may intermittently flare and rupture, exuding an odorless "cheesy" discharge. The patient has never undergone any medical therapy or surgical procedures for this condition. He denies any systemic symptoms associated with flares of the cysts. None of his family members are affected.

**Past Medical History:**
None

**Medications:**
None

**Allergies:**
No known drug allergies

**Family and Social History:**
The patient has no family history of skin disease. He works as a security guard, only occasionally drinks alcohol, and does not use tobacco.

**Review of Systems:**
Negative

**Physical Exam**
On the patient's chest, abdomen, back, and his proximal upper as well as lower extremities are numerous subcutaneous flesh-colored to yellowish cystic nodules. The nodules range in size from 2mm to 1.5 cm. He has several fluctuant cysts on his back. His face, groin, and distal extremities are spared.

**Histopathology**
01/07 Left arm: The epidermis is normal. Portions of a cyst containing fragmented keratinous material are seen in the dermis. The cyst wall is composed of stratified squamous epithelium, appears corrugated, and is lined by an eosinophilic cuticle on its luminal aspect. A mature sebaceous gland is in the vicinity of the cyst wall.

**Diagnosis:**
Steatocystoma multiplex

**Treatment and Course:**
The patient was offered isotretinoin therapy, as well as surgical excision of the fluctuant painful lesions. He was advised that extensive improvement would be unlikely, given the severity of his presentation. The patient has continued to decline treatment to date.

**Discussion:**

Steatocystoma multiplex (SM) is characterized by multiple, asymptomatic, slow-growing, yellow to flesh-colored cysts, ranging in diameter from millimeters to 2-3 centimeters. Cysts are located principally on the neck, trunk, axillae, and proximal extremities. However, there are also reports of localized variants affecting acral sites, the scalp, or the face. The overlying epidermis is typically normal, without evidence of a central punctum. The cyst contents may be either clear or oily, with white to yellow cheesy material. Onset pf SM is typically in adolescence or early adult life, though onset at birth or in late adulthood has been reported.

SM is classically inherited in an autosomal dominant manner. However, sporadic cases have also been reported. Analysis of cytokeratin expression in the cyst wall demonstrates cytokeratin 14 in the basal to prebasal layers, and cytokeratin 17 in the suprabasal layers. The cysts are thus likely derived from either transformed sebaceous ducts or cells differentiating towards those in the sebaceous ducts. Mutations that affect the helix boundary motifs of the keratin 17 structural protein (which is critical for the assembly of intermediate filaments) have been identified in inherited, although not sporadic, cases of SM. Keratin 17 is expressed in the outer root sheath of the hair follicle, sebaceous glands, and nail beds. Of note, mutations in keratin 17 are also associated with Pachonychia Congenita Type II (Jackson-Lawler Syndrome). Furthermore, identical keratin 17 mutations have produced phenotypes consistent with either SM or Pachonychia Congenita Type II in different families.

Treatment options for SM may be destructive, medical, or surgical. Destructive therapies include CO2 laser and cryodestruction, though both yield results that are subject to recurrence. Oral antibiotics do not seem to affect the course of this disease. Treatment with isotretinoin seems to affect only suppurative lesions, while leaving the non-suppurative cysts unaffected. Several reports have documented long term remission, while others note recurrence after discontinuation of isotretinoin. Various surgical modalities to treat lesions of SM include cyst drainage as well as the removal of the cyst wall. Several reported surgical techniques include: 1) Needle aspiration of the cyst contents; 2) Incision of the cyst with a scalpel blade, followed by evacuation of the contents as well as the cyst wall with a mosquito hemostat; and 3) Removal of the cyst wall with a vascular vein hook.

**References:**


1. Apaydin R, et al. Steatocystoma multiplex suppurativum: oral isotretinoin treatment combined with cryotherapy. *Australias J Dermatol* 2000; 41(2): 98-100.
2. Chu DH. Steatocystoma multiplex. *Dermatol Online J* 2003; 9(4): 18.
3. Covello SP, et al. Keratin 17 mutations cause either steatocystoma multiplex or pachonychia congenita type 2. *Br J Dermatol* 1998;139(3): 475-80.
4. Kaya TI, et al. A simple surgical technique for the treatment of steatocystoma multiplex. *Int J Dermatol* 2001; 40(12): 785-8.
5. Kurokawa I, et al. Cytokeratin expression in steatocystoma, multiplex. *Br J Dermatol* 2002;146(3): 534-6.
6. Mortazavi H, et al. Localized forms of steatocystoma multiplex: case report and review of the literature. *Dermatol Online J* 2005; 11(1): 22.
7. Rossi R, et al. CO2 laser therapy in a case of steatocystoma multiplex with prominent nodules on the face and neck. *Int J Dermatol* 2003; 42(4): 302-4.
8. Schmook T, Burg G, Hafner J. Surgical pearl: mini-incisions for the extraction of steatocystoma multiplex. *J Am Acad Dermatol* 2001; 44(6): 1041-2.

**Case # 15**

**Case Presented by Claudia Hernandez M.D.**
**and Platina Coy Gershtenson M.D.**

**History of Present Illness:**
This 75 year-old African American female with psoriasis presented with an eight month history of diffuse progressive leukoderma on her trunk, face and extremities. The pigmentary changes began two weeks after discontinuation of narrow band UVB phototherapy for psoriasis. She received eighteen treatments over nine weeks (2,230mJ total) which were discontinued due to tachycardia, chills and stinging after each phototherapy session. The patient and her family attributed the depigmentation to narrow band UVB therapy. Further review of her medical records revealed that an area dermatologist had prescribed a compounded ointment of 1% phenol, 0.2% menthol, liquor carbonis detergens and 4% betamethasone diproprionate, which was applied twice daily for the nine weeks during her phototherapy.

**Past Medical History:**
Psoriasis, hypertension, glaucoma, congestive heart failure, anemia

**Medications:**
Triamcinolone 0.1% cream twice daily, hydroxyzine, econazole cream, travoprost, cosopt, ferrous sulfate, hydrochlorothiazide, potassium, metoprolol, hydrocodone, ciprofloxacin, vitamin B12 injections

**Allergies:**
Ampicillin

**Family History:**
Son with mild psoriasis

**Review of Systems:**
The patient complains of fevers, chills, nausea, night sweats, insomnia, generalized weakness, weight loss, malaise, anorexia, dysuria and chronic shortness of breath.

**Physical Examination:**
The patient has extensive large irregular hypo- and depigmented non-scaly patches on her face, neck, trunk and extremities. Several patches have slight scale and mild erythema. She has extensive diffuse non-scarring alopecia. Her bilateral lower legs are significantly edematous.

**Laboratory Data:**
The following were positive or abnormal:
Hemoglobin 10.6 g/dL (12-16), hematocrit 35.6 g/dL (36-45.6), neutrophils 71% (33-69), lymphocytes 13% (20-55), aspartate aminotransferase 58 u/L (8-39), alkaline phosphatase 367 u/L (38-126)

The following were negative or within normal limits:
Basic metabolic panel, thyroid stimulating hormone, leukocyte count, anti-nuclear antibody, selenium

**Histopathology:**
8/06 Arm: The epidermis shows psoriasiform changes. There is an upper dermal perivascular lymphoplasmocytic infiltrate and pigment drop with melanophages. Occasional eosinophils are seen. The melan A stain shows absence of melanocytes.

11/03 Leg: The epidermis shows psoriasiform hyperplasia with lack of granular cell layer and rare Munro microabscesses. There is overlying hyperkeratosis with alternating parakeratosis. There

is vertical streaking of collagen in the papillary dermis with pigment incontinence. Periodic acid schiff stain is negative for fungi.

**Diagnosis:**
Contact leukoderma after application of a phenol ointment

**Treatment and Course:**
After her initial presentation, the patient was hospitalized twice for malaise, weakness and anorexia. Despite numerous efforts to locate her, the patient has been lost to follow-up.

**Discussion:**
Vitiligo is an acquired depigmenting disorder caused by loss of melanocytes. Contact vitiligo is triggered by a chemical exposure. The vast majority of chemical inducers include aromatic or aliphatic derivatives of phenols and catechols. Interestingly, topical phenol is used as a treatment in several dermatoses including melasma and psoriasis. Phenol is readily absorbed through the skin and can cause numerous systemic toxicities including cardiac arrhythmias, hepatotoxicity, nephrotoxicity, gastrointestional irritation and metabolic acidosis. Local effects include erythema, painless blanching, skin necrosis and leukoderma. The extent of phenol absorption is dependent on total body surface area exposed and not the concentration of the phenol solution. Several mechanisms of phenol induced vitiligo-like leukoderma have been proposed. Phenol is structurally similar to tyrosine and competes for tyrosinase in the melanin synthesis pathway producing cytotoxic intermediates that eventuate in cell death via peroxidation of cell membranes. Alternatively, melanocyte-specific enzyme tyrosinase-related protein-1 (Tyrp1) catalyzes phenol compounds into oxygen radicals, which induce cytotoxicity via cell damage and oxidative stress.

The practice of treating psoriasis with topical phenol spans many decades. Accordingly, phenol is an ingredient in some commonly used products such as P&S liquid and shampoo. Although the mechanism of action in psoriasis is not fully understood, recent studies by Hsu et al demonstrated that human psoriatic tissues lack normal expression of caspase 14, a protein associated with normal epithelial cell differentiation. Application of epigallocatechin gallate (EGCG), a green tea polyphenol (GTP), induced caspase 14 expression in tissue culture of normal human epidermal keratinocytes. Similarly, topical application of 0.5% GTPs significantly reduced psoriatic symptoms in the flaky skin mouse model.

Narrow band UVB is an immune modulating therapy which has been reported to suppress contact hypersensitivity (CHS) responses to chemical haptens via secretion of IL-10 which down regulates the CHS response. Topical application of EGCG prior to UV exposure, however, has been shown to result in lower levels of IL-10 in a mouse model; this is proposed as a mechanism by which EGCG prevents UVB-induced immune suppression. Our patient was likely sensitized to phenol during its topical application, although this was not immediately apparent as the concurrent narrow band UVB treatments activated melanogenesis and thus prevented depigmentation.

**References:**

1. Boissy RE and Manga P. On the etiology of contact/occupational vitiligo. *Pigment Cell Res* 2004; 17: 208-214.
2. Fisher AA. Irritant and toxic reactions to phenol in topical medications. *Cutis* 1980; 26: 363-364, 390-392.
3. Gupta AK, Gover MD, Nouri K and Taylor S. The treatment of melasma: A review of clinical trials. *J Am Acad Dermatol* 2006; 55(6): 1048-1065.
4. Hsu S, Dickinson D, Borke J, et al. Green tea polyphenol induces caspace 14 in epidermal keratinocytes via MAPK pathways and reduces psoriasiform lesions in the flaky skin mouse model. *Experimental Dermatology* 2007; 16: 678-684.
5. Katiyar SK. UV-induced immune suppression and photocarcinogenesis: Chemoprevention by dietary botanical agents. *Cancer Letters* 2007; 255: 1-11.
6. Manga P, Sheyn D, Yang F, et al. A role for tyrosinase-related protein 1 in 4-*tert*-Butylphenol-Induced toxicity in melanocytes. *AJP* 2006; 169(5): 1652-1662.

**Case # 16**

**Case Presented by Michelle Bain M.D.**
**and Tanya Bulj M.D.**

**History of Present Illness:**
This 16 year-old male presented to our clinic for evaluation of a growth on the right posterior shoulder that initially appeared at 1 year of age. Surgical excision was performed at that time, with apparent resolution of the lesion. However, at age 15, a recurrence was noted at the prior surgical site. Initially, this appeared as a small, painless nodule that progressively increased in size, which had been stable in diameter for the past several months prior to presentation. He denied any pain on light palpation, but he did admit to discomfort if the site was traumatized.

**Past Medical History:**
None

**Medications:**
None

**Allergies:**
No known drug allergies

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

**Social History:**
The patient is in 10th grade, and lives with his parents

**Review of systems:**
Negative

**Physical Examination:**
A 2.4 x 2.4 cm soft, bluish-purple, dome-shaped nodule is seen on the right upper back, overlying the scapula. Surrounding the nodule are several skin colored to slightly hyperpigmented, glossy, flat-topped papules.

**Laboratory Data:**
The following were negative or within normal limits:
Complete blood count with differential and comprehensive metabolic panel

**Diagnostic Procedures and Test:**
6/07 MRI of the right upper extremity with and without contrast: An enhancing subcutaneous mass invades the skin but does not involve the deeper soft tissues. This lesion could represent a benign or malignant mesenchymal tumor. Consider such entities as subcutaneous nodular fasciitis, granuloma annulare, epithelioid sarcoma, dermatofibrosarcoma protuberans, fibrous histiocytoma as well as lymphoma.

**Histopathology:**
4/07 Right upper back: Several subepidermal vascular spaces contain homogeneous eosinophilic material mixed with lymphocytes and cellular debris. In the deeper dermis, there is proliferation of capillaries and venules with various-sized lumina lined by prominent endothelial cells. Within

several lumina, there is an endovascular papillary proliferation lined by endothelial cells. Some of the larger blood vessels are occluded by thrombi. There is an infiltrate of lymphocytes in upper dermis.

**Diagnosis:**
Masson's tumor with lymphangioma circumscriptum

**Treatment and Course:**
Wide local excision and closure by tissue rearrangement was performed on 10/9/07 without complication by the surgical oncology and plastic surgery services. The patient's recovery has been uneventful.

**Discussion:**
Masson's tumor is also known as intravascular papillary endothelial hyperplasia (PEH), vegetant intravascular hemangioendothelioma, and intravascular angiomatosis. This uncommon entity consists of a benign proliferation of endothelial cells arising within normal blood vessels or vascular entities including hemangiomas, angiokeratomas, pyogenic granulomas, lymphangiomas, venous lakes, capillary aneurysms, as well as phlebectasias and hematomas. Lesions predominate on the extremities, with a predilection for the fingers. Males are affected more often than females, with no age preference.

Masson first described this entity in a 68-year-old man with a painful hemorrhoid that could not be reduced. He observed microscopically that the internal lining of the large veins contained papillae, covered by endothelium. These papillae enlarged to form polypoid projections or vegetations. The blood could not circulate except through tiny spaces, and finally a thrombus formed.

The proliferation of endothelial cells is typically confined to one or more vascular lumina that have been occluded by thrombosis. In fully developed lesions, numerous papillated structures lined by a single layer of plump endothelial cells extend from the wall into the lumina of the affected structure. The papillary growth pattern and prominent endothelium can simulate the growth pattern of a well-differentiated angiosarcoma, but the sharp circumscription, intravascular location, lack of pleomorphism and mitotic figures, and the absence of a dissecting pattern into adjacent tissue allow differentiation of these two entities. Immunohistochemical studies have documented the endothelial derivation of the cells lining the papillations, and ultrastructurally the lesion resembles granulation tissue.

PEH is not a specific entity, rather it is a histopathologic pattern that can be found in different vascular proliferations. Currently, PEH is considered to be a reactive hyperplastic process of endothelial cells that develops in response to intravascular thrombosis, with subsequent organization of the thrombus. Occasionally no thrombus is found, leading some authors to suggest that PEH is a primary process with possible secondary thrombus formation. However, in lesions lacking thrombus, it seems most likely that the endothelial hyperplasia has simply persisted after the thrombus has disappeared.

PEH can be classified into three types: a pure or primary form that arises *de novo* in dilated vascular spaces; a mixed type (secondary or reactive) due to focal change in a pre-existing vascular lesion (hemangioma, pyogenic granuloma or vascular malformation); and rarely, in an extra-vascular location as a result of organization of a hematoma. Because PEH lacks specific clinical findings, diagnosis relies on microscopic examination. Simple excision is curative, with a low rate of recurrence.

**References:**

1. Requena L, Sangueza OP. Cutaneous vascular proliferations. Part II. Hyperplasias and benign neoplasms. *J Am Acad of Dermatol* 1997; 37(6): 887-922
2. Reed CN, et al. Intravascular papillary endothelial hyperplasia: multiple lesions simulating Kaposi's sarcoma. *J Am Acad Dermatol* 1984; 10: 110–13.
3. Steffen C. The man behind the eponym: C.L. Masson. *Am. J. Dermatopathol* 2003; 25(1): 71–6.

**Case # 17**

**Case Presented by Sophie Worobec M.D.**
**Tanya Bulj M.D.**

**History of Present Illness:**
This is 53 year-old African American woman with a history of discoid lupus erythematosus and rheumatoid arthritis presented to our clinic in 2005 for evaluation of painful leg ulcers. Examination of the extremities revealed multiple punched-out ulcers and hyperpigmented plaques that were exquisitely tender. The patient had experienced multiple hospitalizations related to her leg ulcers. The patient had also been evaluated by the hematology service for chronic but stable leukopenia and a low CD4 count that was thought to be related to her connective tissue diseases.

**Past Medical History:**
Rheumatoid arthritis, discoid lupus erythematosus, hysterectomy, and bilateral salpingoophorectomy

**Medications:**
Prednisone, hydroxychloroquine, salsalate, diclofenac, valsartan, ketoconazole shampoo, betamethasone diproprionate ointment, risedronate sodium, calcium with vitamin D, hydroxyzine, hydrocodone bitartrate and acetaminophen

**Allergies:**
No known drug allergies

**Family History:**
Mother with diabetes mellitus, hypertension and thyroidectomy; father with hypertension

**Social History:**
The patient is currently on disability. She quit smoking in 2005, and denies alcohol use

**Review of systems:**
Significant for numbness of the lateral thighs and burning of the soles of the feet

**Physical Examination:**
On initial presentation the patient had scattered, ill-defined hyperpigmented macules and patches on the nasal bridge, ears, chin, jaw, shoulders, arms, and upper back. Examination of the hands revealed swan-neck deformity of several digits with ulnar deviation. Large hyperpigmented patches and several punched out ulcers were seen on the legs. The largest ulcer was over the right medial malleolus, with fibrinous granulation tissue at the base, and no discharge or surrounding erythema. There was no splenomegaly.

**Laboratory Data:**
The following were abnormal:
White blood cell count 3.1 k/uL (3.5-10.5) and absolute lymphocyte count of 0.8 k/uL (1.2-4.0)

The following were negative or within normal limits:
Comprehensive metabolic panel, complement levels, anti-nuclear antibody panel

**Diagnostic Procedures and Test:**
Doppler exam of the lower extremities was negative for deep venous thrombosis
Ankle brachial index was approximately 0.85 bilaterally

**Histopathology:**
Right thigh: The epidermis is thinned with flattened rete ridges. There is focal vacuolar degeneration of the basal cell layer with pigment incontinence. Capillaries show fibrinoid necrosis with thrombi and

nuclear dust. The dermis is necrotic adjacent to involved blood vessels. The necrosis extends into adipose tissue.

**Diagnosis:**
Rheumatoid vasculitis

**Treatment and Course:**
The patient was treated in the past with etanercept, methotrexate, salsalate, predinisone and hydroxychloroquine. Most recently she had two infusions of rituximab and has had marked improvement since these infusions. Currently, she is being treated with hydroxychloroquine, salsalate, diclofenac, and a tapering course of prednisone. Overall her ulcers have almost healed.

**Discussion:**
Patients with rheumatoid arthritis (RA) are predisposed to developing chronic leg ulcers. The etiology is frequently multifactorial, but often associated with vasculitis and venous insufficiency. The incidence of leg ulceration in patients with RA is 10%. In about 55% of RA patients, vasculitis is manifest on biopsy samples of leg ulcers.

Rheumatoid vasculitis (RV) is an inflammatory condition of the small and medium-sized vessels that affects a subset of patients with established RA. It has a vast array of clinical manifestations with a predilection for the skin (peripheral gangrene, deep cutaneous ulcers) and the peripheral nervous system (mononeuritis multiplex). Because of the lack of specific signs and symptoms, the diagnosis relies on the exclusion of other causes of similar lesions and, ideally, on the histopathological demonstration of necrotizing vasculitis. Ulcers caused by vasculitis are often described as extremely painful.

The differential diagnosis of RV leg ulcers includes pyoderma gangrenosum, systemic lupus erythematosus (SLE), wegener's granulomatosis, erythema elevatum diutinum and others. NSAIDs, cyclophosphamide, chlorambucil, methotrexate, and cyclosporine have all been reported to be effective in the treatment of necrotizing vasculitis. In a report by Schneider et al, approximately 66% of patients had stabilization or improvement with a regimen of NSAIDs for pure sensory neuropathy or digital lesions and penicillamine, cytotoxic agents, or plasmapheresis for mononeuritis, gangrene, or leg ulcers.

Edwards et al conducted a randomized, double-blind, controlled study in 161 patients who had active rheumatoid arthritis despite treatment with methotrexate. In these patients a single course of two infusions of rituximab (anti CD20 monoclonal antibody, 1000mg on days 1 and 15), alone or in combination with either cyclophosphamide or with continued methotrexate provided significant improvement (50%) in disease symptoms at both weeks 24 and 48.

In our case, due to persistent leukopenia which was attributed to patient's connective tissue disease, she was not a good candidate for cyclophosphamide. The patient developed a drug reaction to etanercept, but responded well to treatment with rituximab (1000 mg infusion on days 1 and 15) with complete resolution of her leg ulcers.

**References:**

1. Sayah A, English JV. Rheumatoid arthritis: A review of the cutaneous manifestations. *J Am Acad Dermatol* 2005; 53: 191-209.
2. Edwards et al. Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. *N Engl J Med* 2004; 350: 2572-81
3. Schneider, H.A. et al. Rheumatoid vasculitis: experience with 13 patients and review of the literature. *Semin Arthritis Rheum* 1985; 14: 280-6
4. Fauci A.S. et al. Cyclophosphamide therapy of severe systemic necrotizing vasculitis. *N Engl J Med* 1979; 301: 235-8.

**Case # 18**

**Case Presented by Aleksandar Krunic M.D., Ph.D,**
**and Tarun Kukreja M.D.**

***Patient A***

**History of Present Illness:**

This 60 year-old man presented with whitish bumps on his scrotum since his thirties. The lesions are intermittently pruritic but are otherwise asymptomatic.

**Past Medical History:**

None

**Medications:**

None

**Review of systems:**

Negative

**Physical Examination:**

The patient has approximately twelve tan, 2-4 mm keratotic papules on the bilateral and anterior scrotum

**Laboratory Data:**

The following were negative or within normal limits:
Complete blood count, complete metabolic panel, hepatitis B and C, human immunodeficiency virus, rapid plasma reagin, chlamydia and neisseria.

**Histopathology:**

12/06 The sections show marked hyperkeratosis with orthokeratosis, papillomatosis, and acanthosis. The granular layer is thickened with course keratohyaline granules. There is separation and degeneration of cells in the granular layer. Necrotic keratinocytes are observed in the mid and upper epidermis. There is a mild perivascular lymphocytic infiltrate in the papillary dermis. Immunohistochemical stain for human papillomavirus is negative.

**Diagnosis:**

Epidermolytic Acanthoma

**Treatment and Course:**

The patients' lesions were treated with a cryoprobe applied directly to the lesions for 10 seconds for 1 or 2 freeze-thaw cycles. Over the course of a few treatments, the lesions are decreasing in number and size.

***Patient B***

**History of Present Illness:**

This 40 year-old man presented with whitish warty bumps on his scrotum for about six years. They are occasionally pruritic but are not otherwise bothersome.

**Past Medical History:**

Hypertension

**Medications:**

Quinapril, hydrochlorothiazide

**Review of systems:**
Negative

**Physical Examination:**
The patient has approximately fifteen, tan, 2-4 mm hyperkeratotic papules over all aspects of the scrotum

**Histopathology:**
12/06 The sections are tangentially cut. The epidermis shows acanthosis and hyperkeratosis with degeneration and pyknotic nuclei within the granular layer. Coarse keratohyaline granules are observed.

**Diagnosis:**
Epidermolytic Acanthoma

**Treatment and Course:**
The patient's lesions were treated using a cryoprobe applied directly to the lesions for 10 seconds for 1 or 2 freeze thaw cycles. Over the course of a few treatments, the lesions are decreasing in number and size.

**Discussion:**
Epidermolytic acanthoma is an uncommon benign tumor consisting of discrete keratotic papules that are usually asymptomatic. Two varieties exist: an isolated and a disseminated form, with both occurring any time during adulthood. The predilection for the scrotal area is rare, with only four cases described in the literature. The pathogenesis is unknown, although proposed etiologies UV light, trauma, and viruses such as human papillomavirus (HPV). Although it can clinically resemble verrucae, molecular studies have failed to detect HPV DNA in the lesions.

Both the solitary and disseminated forms present as keratotic papules with individual lesions generally less than 1cm in diameter. Isolated lesions may occur anywhere on the body, but the disseminated form has been described primarily on the back and perigenital regions.

While the lesions are benign, they may be cosmetically distressing for the patient. Treatment with destruction and excision have been reported to be successful. We present the first reported case in the literature of destruction of epidermolytic acanthomas with cryodestruction, a well tolerated and effective procedure.

**References:**

1. Banky JP, et al. Multiple scrotal epidermolytic acanthomas; secondary to trauma? *Clin Exp Dermatol* 2004; 29(5): 489-91.
2. Reguiai Z, et al. Multiple spreading epidermolytic acanthomas of the genital and perigenital skin. *Dermatology* 2005; 211(2): 152-4.
3. Sanchez-Carpintero I, et al. Disseminated epidermolytic acanthoma probably related to trauma. *Br J Dermatol* 1999; 141(4): 728-30.

**Case # 19**

**Case Presented by Sophie Worobec M.D.**
**and Rikk Lynn M.D.**

**History of Present Illness:**
This 38 year-old man was admitted to UIC in February, 2007 for fever, rigors, and recent onset of a rash. The patient had left an outside hospital against medical advice a few days prior after sustaining a subarachnoid hemorrhage in a motor vehicle accident. His course at the outside hospital was complicated by cervical osteomyelitis, brain abscess, and staphylococcal bacteremia. In addition, the patient had been started on phenytoin for seizure prophylaxis. The patient presented to UIC for evaluation of a new onset rash with diffuse desquamation, sparing the mucous membranes. On initial screening laboratories, the patient was noted to have marked hepatitis, acute renal failure, and eosinophilia.

**Past Medical History:**
Subarachnoid hemorrhage, C6 osteomyelitis, brain abscess, bronchitis

**Medications**:
Aztreonam, levaquin, vancomycin, clindamycin, acetaminophen, tramadol, phenytoin

**Allergies**:
Penicillin (develops an erythematous rash)

**Review of systems:**
Significant for fever, chills, lethargy, mild photophobia, sore throat, recent onset rash, and history of seizures status post motor vehicle accident. Negative for oral or nasal erosions and genital lesions.

**Physical Examination:**
Upon initial presentation the patient was supine in bed and noted to be shivering in bed. His face, neck, trunk, and extremities were erythrodermic with diffuse scaling. There was mild conjunctival injection but otherwise no mucous membrane involvement.

**Laboratory Data:**
The following were trends over the inpatient hospitalization (2/07-4/07):
Aspartate aminotransferase 191 u/L → 263 u/L → 21 u/L (10-40), alanine aminotransferase 392 u/L → 604 u/L → 21 u/L (10-50), alkanine phosphatase 98 u/L→ 177 u/L → 66 u/L (38-126), total bilirubin 9.2 mg/dL → 0.8 mg/dL (0-1.2), creatinine 3.8 mg/dL → 5.0 mg/dL → 1.0 mg/dL (0.4-1.2), absolute eosinophil count 2.2 k/uL → 3.3 k/uL → 0.4 k/uL (0.0-0.4)

**Histopathology:**
2/07 Right arm: The epidermis shows hyperkeratosis and parakeratosis with focal scale crust. There is irregular acanthosis with spongiosis. Necrotic keratinocytes are seen within the basal layer and the mid-epidermis. A perivascular infiltrate of lymphocytes and eosinophils is seen in the upper dermis, with exocytosis into the epidermis. Blood vessel walls show thickening, and extravasated red blood cells are seen.

**Diagnosis**:
Drug rash with eosinophilia and systemic symptoms (DRESS) syndrome

**Treatment and Course:**
The patient was started on intravenous steroids for suspected DRESS syndrome secondary to phenytoin, and initially showed marked improvement. Upon switching to oral steroids he had exacerbation of the rash with formation of large bullae over 30% of his body surface. He was subsequently transferred to an outside burn unit for suspected toxic epidermal necrolysis.

**Discussion**:
DRESS (drug rash with eosinophilia and systemic symptoms) syndrome has been proposed as a more specific term than hypersensitivity syndrome. The underlying mechanisms include specific alterations in the metabolism of particular drugs. For anticonvulsants, the inability to detoxify toxic arene oxide metabolites is likely a key factor. Cross reactivity in drug sensitivity between phenytoin, carbamazepine and phenobarbital is well documented. Other medications thought to cause DRESS syndrome include sulfasalazine, hydantoin, d-penicillamine, allopurinol, hydrochlorothiazide, abacavir, nevirapine and cyclosporine. More recently there have been reports of primary infection and reactivation of human herpesvirus six (HHV-6) infections as the cause of DRESS syndrome. These reports have recommended serologic testing for HHV-6 in suspected DRESS patients, though uncertainty about the link between these entities remains.

Clinically, the hypersensitivity syndrome develops between 2 to 6 weeks after the responsible drug is started. A fever and cutaneous eruption are the most common symptoms of DRESS syndrome, seen in 85% and 75% of cases, respectively. Cutaneous involvement usually begins as a morbilliform eruption, which later becomes edematous, often with a follicular accentuation. Additional manifestations include vesicles, tense bullae induced by dermal edema, follicular as well as non-follicular pustules, erythroderma and purpuric lesions. The face, upper trunk and extremities are usually the initial sites of involvement. Edema of the face is a frequent finding and is a hallmark of DRESS syndrome.

The most common site of visceral involvement is the liver. The hepatitis is sometimes fulminant and is responsible for the majority of deaths associated with this syndrome (10% of cases). Myocarditis, interstitial pneumonitis, interstitial nephritis, thyroiditis and even infiltration of the brain by eosinophils may be observed. The cutaneous and visceral involvement may persist for several weeks or months after drug withdrawal. Prominent eosinophilia is common and is a very characteristic feature of this syndrome. It is often accompanied by mononucleosis-like atypical lymphocytosis. Histologic examination of the skin demonstrates a dense lymphocytic infiltrate in the superficial dermis associated with eosinophils and dermal edema. If the rash persists, the dermal infiltrate may become quite dense, as in pseudolymphoma.

Early withdrawal of the offending drug is mandatory, but may not be sufficient for obtaining a rapid full recovery. Corticosteroids are the first line of therapy for DRESS syndrome. In milder cases, topical high-potency corticosteroids may be helpful for skin manifestations. Systemic corticosteroids are recommended for life-threatening involvement of the lung and heart because the inflammation is responsive to corticosteroids. The latter are not particularly useful for reversing kidney and/or liver disease. Relapse can occur when the dosage is tapered, and as a result, steroid therapy sometimes has to be maintained for several weeks and even months.

**References:**

1. Sullivan, JR, Shear, NH. The Drug Hypersensitivity Syndrome: What is the Pathogenesis? *Arch Dermatol* 2001; 137(3): 57-64.
2. Risa, Tamagawa-Mineoka, DRESS Syndrome Caused by Teicoplanin and Vancomycin, associated with reactivation of Human Herpesvirus-6. *Int J Dermatol* 2007; 46: 654-5.
3. Debarbieux, S. Drug hypersensitivity syndrome associated with a primary HHV-6 infection. *Ann of Derm Venerol* 2006; 133(2): 145-7.

**Case # 20**

**Case Presented by Carlotta Hill M.D.**
**and Caroline Schmitt M.D.**

**History of Present Illness:**
This 41 year-old Filipino man presented with a cutaneous eruption first noted at age 12. He reported acute onset of two coin-sized "red spots" on his face and back, with central numbness and occasional pruritus at the periphery. The patient did not seek treatment at symptom onset, and the lesions were stable for decades. Four years ago, he noticed similar lesions developing on his limbs, chest, back, and eventually his face and neck. The patient was treated with fluconazole for presumed tinea corporis without improvement.

**Past Medical History:**
Left foot drop since December of 2006, depression, recent cellulitis of the left foot

**Medication:**
Vitamin B and C complex, recently completed a 2 week course of cephalexin

**Allergies:**
No known drug allergies

**Family History:**
Heart disease, asthma

**Social History:**
Moved to the United States from the Philippines in 1992, manages and bartends at a bar, smokes 1 pack of cigarettes and drinks 2 alcoholic beverages per day

**Review of systems:**
Significant for anesthetic left foot and skin lesions

**Physical Examination:**
On the face, neck, trunk, and extremities are multiple anesthetic, annular erythematous plaques. The right ulnar nerve is boggy and enlarged. Overlying the left foot and ankle are diffuse hyperpigmented to violaceous patches. There is dependent edema and tenderness to palpation at the ankle. There is a 2 cm ulcer over the left lateral metatarsophalangeal joint and a supernumerary left toe. Strength testing is 0/5 on left foot dorsiflexion.

**Laboratory Data:**
The following were abnormal:
Aspartate aminotransferase 44 u/l (10-40), alanine aminotransferase 54 u/l (10-50), glucose-6-phosphate dehydrogenase level 1.2 u/gHgb (7-20.5)

The following were negative or within normal limits:
Complete blood cell count with differential, basic metabolic panel, and urinalysis

**Diagnostic Procedures and Test:**
Chest X-ray within normal limits

**Histopathology:**

04/07 Left forearm: On hematoxylin and eosin stain the epidermis is essentially normal. There are well-formed granulomatous inflammatory infiltrates seen at all levels of the dermis consisting of central epithelioid macrophages with a peripheral mantle of lymphocytes. The granulomas clearly involve nerve twigs and adnexal structures. On Fite stain there are rare intracellular acid-fast bacilli.

**Diagnosis:**

Hansen's disease, borderline tuberculoid on histology although clinically borderline lepromatous

**Treatment and Course:**

Therapies initiated included minocycline 100mg daily, ofloxacin 400mg monthly, and rifampin 600mg monthly, as dapsone was contraindicated. The patient was instructed to abstain from work as a bartender until 72 hours after treatment started and was referred for neurologic, ophthalmologic, and podiatric evaluation as well as physical and occupational therapy. Plaque regression was noted at follow-up.

**Discussion:**

Although Hansen's disease (HD) was targeted for elimination by the World Health Organization (WHO) by the year 2000, global prevalence is currently estimated at 0.4 million, with most patients living in India, sub-Saharan Africa, Latin America, and the Caribbean. In the US, 133 new patients, mostly immigrants, were reported to the National Hansen's Disease Registry in 2002. Overrepresented states include California, Hawaii, Texas, Louisiana, and New York.

*Mycobacterium leprae* bacillus causes a chronic granulomatous disease with variable cutaneous findings ranging from generalized lepromatous (LL) to localized tuberculoid (TL) leprosy, with corresponding histology showing multibacillary (MB) and paucibacillary (PB) disease, respectively. Aerosol transmission is suspected but contagiousness is low, and the reactional state and classification are determined by host immune response. Incubation periods average 3-5 years. Multiorgan involvement is possible, sparing only the brain, spinal cord, and lungs. Diagnostic criteria include anesthetic (usually hypopigmented, hyperpigmented, or erythematous) lesions, peripheral nerve hypertrophy, and acid-fast bacilli on smear or biopsy. Research is underway to create a sensitive and specific serologic assay capable of diagnosing leprosy months before clinical symptoms arise.

The global standard of care for HD is multidrug therapy (MDT) introduced by the WHO in 1982. For MB HD the adult regimen is rifampin 600mg once a month, dapsone 100mg daily, and clofazimine 300mg once a month and 50mg daily for one year. For PB HD the regimen is rifampin once a month and dapsone daily for six months. Single skin lesion PB HD is treated with a single dose of rifampin, ofloxacin 400mg, and minocycline 100mg. US recommendations differ, with daily rifampin for both MB and PB, for twice the duration. Relapse rate is approximately 1 in 100 after completion of MDT. Management may also include physical rehabilitation.

**References:**


1. Anderson H, et al. Hansen disease in the United States in the 21st century: a review of the literature. *Arch Pathol Lab Med.* 2007; 131(6): 982-6.
2. Duthie MS, et al. Leprosy diagnosis: early serological detection with protein antigens. Clin Vaccine Immunol. 2007 Sep 26 [Epub ahead of print]
3. Hortez, PJ, et al. Control of neglected tropical diseases. *N Engl J Med.* 2007; 357(10): 1018-27.
4. Sehgal VN, et al. The imperatives of leprosy treatment in the pre- and post-global leprosy elimination era: Appraisal of the changing scenario to current status. *J Dermatolog Treat*. 2007 May 21 [Epub ahead of print]
5. World Health Organization: http://www.who.int/lep/