Dermatomyositis: Clinical Pearls From the Dermatology–Rheumatology Clinic
Ruth Ann Vleugels, MD, MPH

Introduction. Dr. Vleugels focused on skin-limited—amyopathic—dermatomyositis (DM), a diagnosis that may frequently be missed given the lack of muscle disease and the fact that skin biopsy findings are indistinguishable from those of lupus erythematosus. Yet making this diagnosis early “has a significant impact on patients’ lives.” Vleugels treats approximately 200 such patients, adding several new patients each month.

Case 1. The patient was hospitalized with shortness of breath, thought to be a pulmonary infection that progressively worsened. When dermatology was called several days later, a diagnosis of amyopathic DM was made. The patient had midfacial erythema involving the nasolabial folds, erythema and edema of the upper eyelid margin (heliotrope eruption), and Gottron’s papules on the knuckles with classic psoriasiform scaling. Unfortunately, he passed away from fulminant lung disease in association with amyopathic DM, highlighting the critical point that patients with skin-limited DM may have lung disease even in the absence of muscle involvement. Thus all adult patients with DM require screening with pulmonary function tests (PFTs) with diffusion capacity of carbon monoxide (DLCO).

Case 2. The patient arrived from rheumatology diagnosed with arthritis and vasculitis impairing the use of her hands. Her exam, however, displayed ulcerations over the Gottron’s papules and elbows, tender palmar papules, alopecia, and arthritis, enabling a diagnosis of anti-melanoma differentiation-associated protein (MDA-5)-associated DM. The characteristic ulcerations result from vasculopathy. Recognizing this cutaneous phenotype—described by Dr. David Fiorentino—is critical, as therapy should be aimed at the underlying vasculopathy in addition to using the immunosuppressive therapy needed to treat the DM. These patients—at high risk for morbidity and mortality from interstitial lung disease—require close follow-up with PFTs with DLCO every 3–6 months.
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Case 3. Vleugels described the absence of an association to malignancy in juvenile DM, contrasting this to adult patients in whom thorough malignancy screening should be completed. Their risk of malignancy is considered elevated for the first 3–5 years following disease onset. Although there are no standard screening guidelines, many experts recommend: baseline blood work, stool occult blood and age-appropriate endoscopy, CA-19-9, and CT of the chest, abdomen, and pelvis. Women also need a Pap smear, CA-125, mammogram, and transvaginal pelvic ultrasound.

MDA-5-associated Dermatomyositis

Evaluation

- Routine studies
  - CBC, CMP, TSH, UA
  - Stool occult blood testing
  - Gastrointestinal endoscopy (age-appropriate)
  - Women—Papanicolaou smear, CA-125
  - CA-19-9
  - PFTs (with diffusion studies)
  - EKG
  - Esophageal studies, eg, barium swallow, manometry
- Radiographic examination
  - CT chest/abdomen/pelvis
  - Women—transvaginal pelvic ultrasound, mammography
- Full physical exam with internist yearly
- Risk remains elevated for 3–5 years

Therapy: Cutaneous DM

- Don’t forget to treat pruritus
- Photoprotection
  - Behavior, sunscreens, protective clothing
  - Consider vitamin D status
- Topicals
  - Corticosteroids, tacrolimus
- Systemic agents
  - Antimalarials; consider in combination
  - Methotrexate, mycophenolate mofetil, IVIG
  - Azathioprine, thalidomide, dapsone, RTX, etc.

Case 4. Vleugels discussed the case of a young woman with severe, intensely pruritic, recalcitrant disease to review treatment options for cutaneous DM. Photoprotective clothing and wide-brimmed hats are critical. Topical steroids are adjunctive rather than a primary treatment. Antimalarials can be helpful, but approximately one-third of DM patients develop a drug eruption to hydroxychloroquine and a pretreatment warning is beneficial. Many patients with cutaneous DM need therapy beyond antimalarials; the most frequently used are methotrexate, mycophenolate mofetil, and intravenous immunoglobulin (IVIG). Although treatment data for recalcitrant cutaneous DM supports IVIG as likely the most beneficial therapy, its use is limited due to its cost. Vleugels and colleagues recently reported a novel series of patients with refractory cutaneous DM who responded to tofacitinib.

Treating to Target in Psoriasis

Junko Takeshita, MD, PhD

Introduction. Treating to target involves treating a chronic disease to achieve a prespecified response. It has been part of cardiovascular medicine for many years, eg, treating hypertensive patients to attain a target blood pressure, or diabetics to an HbA1c target. Data support targets in some instances (eg, stricter control of type 1 and type 2 diabetes improves outcomes), but not others (eg, in specific type 2 diabetes populations, intensive glucose-lowering therapy is associated with increased mortality), and certain targets—such as lipid levels—have become controversial, but the overall concept is firm. Dr. Takeshita explained that the treat to target concept is being considered in dermatology, in part because our medical system is moving toward a pay-for-performance basis, and in
part because the emergence of an increasing number of highly effective treatments—as for psoriasis—is finally beginning to make treating to target an attainable goal.

**Preparations for psoriasis.** Treat to target requires appropriate endpoint targets. Although clinical trials in psoriasis have conventionally defined efficacy as achieving a PASI 75, the newer biologics make achieving PASI 90 or 100 (or almost clear or clear endpoints) increasingly possible. Should we change our gold standard of therapeutic efficacy? And does a target of clear skin have a different impact than almost clear skin? And more—should the chosen treatment endpoints be defined by PASI (often too time-consuming for the clinical setting), by the Physician Global Assessment (PGA), or by a patient quality-of-life (QOL) assessment such as the DLQI (Dermatology Life Quality Index)? Takeshita offered the PGA as an instrument that is feasible in the clinical setting, and described the significant difference in patient impact she found between those who had clear vs almost clear skin. 20% of almost clear patients met the DLQI criteria for the need to change treatment as suggested by European guidelines, compared to just 2% of clear patients. And patients with almost clear skin were 60% more likely to report no impact of their psoriasis on their QOL. Data from a phase II brodalumab trial for psoriasis showed similar findings.

**Take-home points.** In the clinical setting, we found that reaching clear vs almost clear skin holds meaningful differences for patients. But before determining that we should target the stricter endpoint of clear skin, larger studies are necessary, and we need to assess the potential side effects and costs that may be associated with stricter disease control.

### Patients With Clear Skin:

Lower DLQI scores more likely to report no effect on quality of life

<table>
<thead>
<tr>
<th>DLQI bands, N (%)</th>
<th>Clear</th>
<th>Almost Clear</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No effect (0–1)</td>
<td>74 (76)</td>
<td>194 (44)</td>
<td>&lt;0.001</td>
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<tr>
<td>Small effect (2–5)</td>
<td>21 (22)</td>
<td>160 (36)</td>
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<tr>
<td>Moderate effect (6–10)</td>
<td>1 (1)</td>
<td>56 (13)</td>
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<tr>
<td>Very large effect (11–20)</td>
<td>1 (1)</td>
<td>22 (5)</td>
<td></td>
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<tr>
<td>Extremely large effect (21–30)</td>
<td>0 (0)</td>
<td>7 (2)</td>
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### Clinical Context:

**20% of almost clear patients meet criteria for treatment change**

<table>
<thead>
<tr>
<th>DLQI</th>
<th>Clear</th>
<th>Almost Clear</th>
<th>P Value</th>
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<tbody>
<tr>
<td>≥ Moderate effect, N(%)</td>
<td>2 (2)</td>
<td>85 (20)</td>
<td>&lt;0.001</td>
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### Dermatology Conundrums From the Annals of the CDC

**Boris D. Lushniak, MD, MPH, RADM**

**The MMWR.** The CDC’s Morbidity and Mortality Weekly Report keeps dermatologists on the forefront of what is going on in the world of public health in ways that can enhance our patient awareness. Dr. Lushniak provided illustrative examples.

**MMWR 2/22/13.** In December 2012, Washington DC dermatologist Dr. Scott Norton saw 3 premature infants in the neonatal ICU with cholestasis and prolonged parenteral nutrition, all presenting with diaper dermatitis, perioral erosions, and bullae on dorsal hands and feet. Norton discovered that his hospital’s pharmacy had recently exhausted its supplies of injectable zinc. These infants were diagnosed with zinc deficiency dermatitis, but action did not stop there. The CDC and the American Academy of Pediatrics were informed, and by January 22, 17 hospitals in 10 states had reported this shortage and steps were taken to fill the zinc gap.

**MMWR 5/19/09.** A previously healthy 20-year-old member of the military was admitted to the hospital with fever, headache, and leukopenia and diagnosed with acute myelogenous leukemia. This patient had received the smallpox vaccination 2 weeks earlier, a live vaccine still administered using scarification technique. Lushniak described the evolution of his initial lesion before and after hospitalization, and the highly challenging and complex treatments required for his progressive vaccinia (vaccinia gangrenosum). For any patient presenting with unique lesions, ask about military involvement and recent immunization history.

**MMWR 5/18/07.** This case involved household transmission of the vaccinia virus from a military smallpox vaccinee (with a history of childhood eczema) to his 28-month-old son with eczema and resulting eczema vaccinatum. The father had visited his family after his deployment was delayed. Several weeks later the 28-month-old was hospitalized with severe eczema, failure to thrive, fever, and a generalized papular and vesicular rash on his face, neck, and upper extremities. Environmental swabbing at home showed the vaccinia virus everywhere, including on the baby’s belongings.

**MMWR 4/12/13.** The varicella vaccine introduced in 1995 dramatically reduced annual hospitalizations and deaths, but
between 2002 and 2007 there were 112 deaths, primarily in healthy unvaccinated people. Lushnia described a nonvaccinated healthy 15-year-old who died of pneumonia and septic shock 21 days after hospital admission, underlining the importance of the initial and follow-up immunizations.

**MMWR—**

**Morbidity and Mortality Weekly Report**

- The CDC’s primary voice for scientific publication of timely, reliable, authoritative, accurate, objective, and useful science-based public health information and recommendations to those in need of the information
- http://www.cdc.gov/mmwr
- *Public health: The science and art of preventing disease, prolonging life, and promoting health through the organized efforts and informed choices of society, organizations public and private, communities, and individuals. (CEA Winslow, 1920)*

**Chronic GVHD: What the Dermatologist Needs to Know**

**Edward Cowen, MD**

**Introduction.** Roughly 50% of bone marrow transplant patients develop chronic GVHD (cGVHD), which is far more complex and poorly understood than acute disease. Acute GVHD reflects T-cell alloreactivity; cGVHD also involves B cells and autoantibodies, affecting nearly every organ system with manifestations mimicking autoimmune diseases (Sjögren’s disease, systemic sclerosis) although without autoantibody specificity. The skin is often the most commonly affected organ system, and sclerotic skin changes—Dr. Cowen’s focus—hold the most concerning potential impact (after bronchiolitis obliterans). Dermatologists bring unique knowledge that can be critical to patient care. We “should certainly be involved at the diagnostic stage, and I think we can partner in management”—including discussing the importance of systemic treatment for aggressive disease.

**Predictive.** Up to 50% of patients with a full match from a sibling donor are at risk for cGVHD. At highest risk are males transplanted from a female donor, especially one who has had children, especially males. Cowen found a female donor in all 15 transplant recipients (male and female) he studied with post-transplant alopecia areata or vitiligo.

**Cutaneous manifestations.** Certain skin features are diagnostic when they appear after transplant: poikilodermatous, lichen planus-like changes, lichen sclerosus-like changes, morphea-like sclerosis, scleroderma-like sclerosis, and eosinophilic fasciitis-like changes. Others require a skin biopsy or other organ system involvement to make a diagnosis of cGVHD. Nondiagnostic features,

**Diagnostic Dermatologic Criteria**

Sufficient to establish cutaneous cGVHD diagnosis in the appropriate clinical setting

- Poikilodermatous
- Lichen planus-like features
- Lichen sclerosus-like features
- Morphea-like sclerosis
- Scleroderma-like sclerosis
- Eosinophilic fasciitis-like features

**Distinctive Dermatologic Criteria**

Feature of cGVHD, but insufficient alone to establish diagnosis

- Depigmentation
- New onset scarring or non-scarring scalp alopecia
- Scaling, papulosquamous scalp lesions
- Nail dystrophy
  - Longitudinal ridging, splitting, brittleness
  - Onycholysis
  - Pterygium unguis
  - Anonychia


**Planned Giving to the DF:**

**Future Support of Your Chosen Specialty**

A recent national physicians survey* shows dermatology as providing the highest level of general career satisfaction in medicine. It also identifies the primary source of this satisfaction—the ability to provide the highest levels of patient care.

Maintaining the specialty’s ability to provide cutting edge treatments and therapies relies on continued research progress in understanding and caring for the skin. Contributions to the DF ensure the career-launching research funding essential to keeping the specialty strong. To help extend this legacy of progress, consider adding a bequest to the DF in your will.

Contact your attorney or financial advisor to determine your most beneficial bequest option. Be sure to identify the Foundation, a 501(c)3 organization, as the gift recipient in your will or other instrument. Please note that only monetary donations can be accepted. Should you have any questions, contact Sandra Benz, Executive Director, at 847-328-2256.

*Medscape Dermatologists Compensation Report 2016
including ichthyosiform GVHD, are “very easy to miss” especially in patients with very dry skin after chemotherapy. Vulvovaginal disease is very common in the cGVHD setting, yet is often missed because transplant physicians typically do not examine this area or ask the necessary questions.

Sclerotic manifestations. Cowen calls deeper manifestations “sclerotic GVHD,” a highly polymorphous category that includes skin changes resembling lichen sclerosus, morphea, scleroderma, or eosinophilic fasciitis. He highlighted the important differences from the autoimmune disease of scleroderma, and emphasized the need “to touch and pinch the patient’s skin to determine where involvement starts and stops.” Fasciitis is more common than reported, particularly difficult to treat, tends to be the most disabling—and is thus crucial to prevent or halt early. Cowen’s group found that total body irradiation in pretransplant conditioning regimens elevates sclerosis risk often months and even years later.

Management and therapy. Determining whether skin fibrosis and other manifestations are active or not “is one of the most difficult things I encounter” when there is no overlying epidermal GVHD. Cowen discussed disease flares and emphasized the need to be extremely alert “to subtle new signs of deeper seated involvement or fasciitis.” The first early fibrotic signs commonly appear in the waistband area, under the brassiere band, in areas of repeated needle sticks, and at port sites. Cowen provided guidance for skin-directed therapies and systemic management, and salvage therapy for patients who have failed steroids and their calcineurin

### cGVHD: A Polymorphous Skin Disorder

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<th>Epidermal cGVHD</th>
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<td>Lichen planus-like</td>
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<td>Papulosquamous</td>
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<td>Ichthyosiform</td>
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<td>Poikiloderma</td>
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<td>Keratosis pilaris-like</td>
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<td>Acral erythema</td>
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<th>Dermal cGVHD</th>
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<tr>
<td>Lichen sclerosus-like</td>
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<td>Morphea</td>
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<td>Scleroderma</td>
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<th>Subcutaneous cGVHD</th>
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<tr>
<td>Subcutaneous sclerosis</td>
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<td>Fasciitis</td>
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### Save the Date—Sunday Evening, March 5

**Annual Leadership Gala**

Each year, the Dermatology Foundation’s Annual Leadership Gala recognizes those who are dedicated to the future of dermatology: members of the DF’s Leaders Society, Annenberg Circle, AC Sustaining, and Fitzpatrick Legacy Fund. The Gala honoring 2016 members will be held on March 5, 2017 from 7:30–9 pm at Orlando’s Orchid Garden. This memorable venue—graced with stained glass windows and marble—was inspired by New Orleans courtyards.

Just for Young Leaders

The DF is grateful for the support of Leaders Society members who have joined within five years of completing their residency—the Foundation’s Young Leaders. In honor of their early career commitment, the DF will hold its second Young Leaders Pre-Gala, beginning at 6:15 pm. Last year’s event was met with warm enthusiasm and enabled new dermatologists and DF Leaders to share their interests with peers from across the country.

Be sure to save the date and look for your invitations or visit dermatologyfoundation.org for more details.

*The Young Leader Pre-Gala and Leadership Gala are made possible by corporate sponsorships.*
inhibitor. He reviewed up-and-coming treatments, especially JAK/STAT inhibitors “very impressive results in early reports.”

**Resources.** Dermatologists who want to learn more about managing these patients are invited to join his cGVHD listserv. “Dermatologists could really benefit this field by being more involved with research and clinical trials.”

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**Contact Information**

- cowene@mail.nih.gov 301-496-4299
- GVHD Derm/Onc listserv
  - Ed Cowen/Jen Huang (Boston Children’s)
- Patient support/education websites
  - Bethematch.org
  - BMThinonet.org
- Clinical trials: www.clinicaltrials.gov
  - NIH: GVHD Natural History, oral clobetasol, pomalidomide, baracitinib
  - NIH patient recruitment office (800) 411-1222 prpl@mail.cc.nih.gov

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**KEYNOTE ADDRESS**

Anger, Frustration, and Imbalance in the Life of a Physician

*Suzanne M. Olbricht, MD*

**Background.** Dr. Olbricht likes to subtitle this talk *Practicing Medicine in the Age of Anxiety*, and it is a challenging and omnipresent reality that began to preoccupy her roughly 10 years ago. Official concern with physician unhappiness and burnout has emerged during this time, and spurred studies among different groups. Olbricht summarized results, highlighting factors that contribute to this problem and those that facilitate the opposite—the ability to experience pleasure, satisfaction, and value as a physician.

**A personal “before” and “after.”** Olbricht prefaced her discussion by narrating 3 highly distressing incidents that had occurred in her office in the past. One was losing a biopsy specimen during an unusually rushed day. Another involved the inadvertent use of contaminated instruments on a day of sudden staff shortages and patient overload. The third was an on-the-job injury in a highly time-pressured environment when “the nurse running around with me gave me the handle of a disposable blade in a way I didn’t usually use it.” The blade ended up in Olbricht’s hand and left her with a permanently numb finger. Olbricht has developed rules to help prevent the high-stress environments that allowed these distressing incidents to occur.

**Literature.** The *MEMO* (Minimize Error, Maximize Outcome) Project in Great Britain initially surveyed 420 physicians there and identified causes of acute stress, causes of chronic stress, and specific job-related stressors. 61% of this physician group found work stressful, 27% reported burnout symptoms, and 31% anticipated leaving their job in 2 years. “The likelihood of making errors in patient care was associated with a stressful organizational climate...”

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**MEMO Project**

- 420 physicians
- 61% stressful work, 27% burnout symptoms, 31% will likely leave job in 2 yrs
- Chaotic office strongly associated with stress
- Lack of quality emphasis associated with past errors
- Lack of emphasis on information/communication correlated with future errors
- Lack of trust in organization associated with intent to leave

**CONCLUSION:** “Likelihood of making errors is associated with organizational climate and office environment.”

1. Obtain good information systems
2. Promote culture of quality
3. Improve hectic environments


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**DF Welcomes New Young Leaders**

The DF Board of Trustees greatly appreciates the foresight and generosity of the following Young Leaders, who joined the Leaders Society within five years of completing residency. They made this early-career decision in 2016, joining a like-minded group of 74 young colleagues. Their annual commitment of $1,500 enables each of them to help further every aspect of dermatology and patient care.

**Arizona**

Matthew Beal, MD

**California**

Katrina E. Abuabara, MD

Tina Bhutanl, MD

Marlys S. Fassett, MD, PhD

Nina Hansra, MD

Amanda K. Raymond, MD

**Colorado**

Kelly Morrissey Williams, MD

**Florida**

Elias E. Ayli, DO

Rodolfo Chirinos, MD

**Louisiana**

Elizabeth Clemons, MD

**Minnesota**

Leah M. Schammel, DO

**New York**

Peter Saitta, DO

Melanie Warycha, MD

**Pennsylvania**

Robert Micheletti, MD

Evan Piette, MD

**Utah**

Adam Taintor, MD

**Canada**

Allison Sutton, MD

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**As of September 14, 2016**
Stiefel Scholar Awardee Published in Science: Engineered T Cells Destroy Pemphigus B cells

Dr. Payne, Associate Professor of Dermatology at the University of Pennsylvania, received DF awards at critical junctures in her academic and research careers. The 2006 DF Career Development Award and Research Grant for continuing her postdoctoral study of pemphigus autoantibodies was “key to my transition from postdoctoral researcher to tenure track faculty, and it supported me until my NIH K08 award was funded.” The midcareer 2015 Charles and Daneen Stiefel Scholar Award in Autoimmune Diseases was essential to advancing her career and the research progress resulting in this early-stage pemphigus therapy.

“I am indebted to the Stiefels and the Dermatology Foundation for supporting the basic science research into mechanisms of disease in pemphigus that facilitated the translational work in this study,” Dr. Payne emphasizes. “This is an example of how focused study of a rare but well-defined disease has the potential to identify novel strategies to treat many other autoimmune diseases.”

A main focus in Dr. Payne’s lab has been targeted therapy, finding a way to eliminate the autoantibodies—and only those autoantibodies—that recognize and destroy Dsg3 (desmoglein 3), a molecule critical to cell adhesion in the skin and mucous membranes. Current treatment generally suppresses the immune response, with serious side effects. Successful targeted therapy of pemphigus could ultimately transform the therapeutic strategies for autoimmune diseases in general. Working with cancer immunologist Michael C. Milone, MD, PhD, Dr. Payne adapted a targeted cancer treatment to pemphigus. They found success in the culture dish and then mice.

Their research—already called a breakthrough by some scientists—appeared in the July 1 issue of Science, one of the world’s top academic journals publishing important original scientific research. Dr. Payne and her colleagues were inspired by the clinical success of therapy using T cells with antigen receptors that have been engineered to incorporate an antibody fragment that targets a distinctive antigen on the cancer cell. Then these chimeric antigen receptor T cells (CAR-T cells) are able to recognize and kill the cancer cells carrying this unique cancer cell antigen. Dr. Payne and Dr. Milone engineered T-cell receptors to recognize specifically, and exclusively, B cells producing antibodies against Dsg3. They call this CAAR-T therapy: chimeric autoantibody receptor T cells. When given to diseased mice, their CAAR-T cells cleared the disease.

Showing that these cells kill only the disease-specific B cells “suggests their potential for long-term disease control and possible cure,” Dr. Payne says. This innovative therapeutic strategy avoids the risks of general immunosuppression, and can likely be applied to other autoantibody-mediated diseases. Diseases involving multiple autoantigens could be treated with appropriate combinations of CAARs. Their next step is “to cure dogs with pemphigus,” Dr. Payne says. Dogs are one of the few species besides humans that naturally develop this disease, and demonstrating that CAAR-T cells are effective in dogs “would break down barriers for future human trials.”


and office environment.” The current MEMO Project, studying 372 physicians at 92 clinics in New York City, sorted them by the degree of institutional pressure to use electronic medical records (EMR). “Time pressure was felt most severely among physicians in high EMR functions, and this was most closely correlated with burnout and the intent to leave practice.”

A study of Canadian family physicians found 25% planning to leave their practice within 5 years and 43% content with their professional lives, ultimately identifying factors correlated with job dissatisfaction as well as those that correlated with job satisfaction.

Olbricht also noted that “we are living in a time of unprecedented and stressful change. The way we practiced medicine 5 years ago is no longer the way we practice now.” And she noted that the intrusion of regulatory elements into our offices now to ensure the quality of patient care produces a stressful sense of uncertainty.

Burnout. A recent study on physician burnout found the highest rate in family practice (35%), followed by surgeons (45%) and then other specialties (around 35%). “To me, even one-third of us having some form of burnout qualifies as an epidemic. Burnout is important for us to recognize, not just in our personal care but in the care we give our patients.” Burnout diminishes quality of care—which includes increased errors—and has also increased the suicide rate among physicians. And if one-third of physicians decide to leave medicine, “then who is going to take care of us as we get older?”

Coping strategies. Olbricht’s favorite article—published more than 20 years ago—identified medical students who coped more effectively with stress, and how they did it. Disengagement strategies (social withdrawal, drinking, drugs) do not work. Engagement strategies—involving problem-solving, seeking social support, talking about one’s feelings, and cognitive restructuring—are productive.
Olbright’s rules for effective stress management. She emphasizes cognitive restructuring—a dedicated effort to modify one’s perspective—and articulates goals for achieving this. 1. Because change is part of life, accept it and try to find some value in it. 2. Multi-tasking is unavoidable, so we have to accept it. 3. Procrastination is not a moral sin, but tends to accompany perfectionism. Work at it: try to tackle off-putting tasks early in the day, do the most onerous first, and cut large ones up into small ones. 4. You have to be who you are. 5. Step outside the walled city by taking on new challenges. 6. Take care of yourself physically and otherwise. 7. Spend time with people who share your enthusiasms. 8. There are some people you should not spend time with at all, eg, complainers. 9. Outdoor space—whether real, photographed, or painted—lowers stress hormones. 10. Be grateful for what you have, and focus on what it gives you, not on what it does not.

Job Satisfaction Correlated With:
- Strongly value my relationships with my patients—85% (frequently)
- Participation in CME—80%
- Active review of workload and scheduling—57%
- Discuss issues and problems with staff—57%
- Use other nonphysician HP regularly in practice—57%
- Consistent in setting limits to my practice—42%
- Difficult tasks = Opportunities to learn and develop my skills—40%

Note: People scoring lowest in these scales are most of the 25% who would anticipate leaving practice


Burnout vs Resilience

“physician resilience...the ability to invest personal resources in a way that initiates positive resources spirals in spite of stressful working conditions.”


Disengagement Strategies
- Wishful thinking
- Problem avoidance

Engagement Strategies
- Self-criticism
- Social withdrawal
- Problem-solving
- Social support
- Express emotions
- Cognitive-restructuring

MINI-SYMPOSIUM: POLICY, ETHICS, AND THE LAW

Images & Mirages: Woe Be the Educator

Abel Torres, MD, JD

Introduction. We deal with images regularly when we educate and communicate. Recognizing the important issues that arise when we use them in different contexts will help us be better communicators and learn how to protect ourselves. Dr. Torres discussed the images and information we share—of ourselves on social media, of patients in a variety of contexts and purposes, and those taken from work others have produced. His goal was to provide awareness of central concepts, emphasizing the need for individual research when applying them.

Social Media. Torres cautioned strongly that medical students and physicians must respect the acutely negative potential from professional behavior on Twitter, Facebook, Instagram, etc. One study of the first day’s numerous Tweets from 260 brand new physician users identified 3% of posts as unprofessional. This included profanity, violations of patient privacy, sexually explicit material, and discriminatory statements. Individual-identifying information was common. In a survey of medical school deans regarding Facebook use by medical students, 60% reported incidents of students posting unprofessional behavior. 13% involved HIPAA violations of patient confidentiality. Remember—what happens online remains there forever, and can ruin or diminish a medical career. Make your profile private, use all privacy settings, observe regulatory restrictions, and then post carefully and protectively.

HIPAA. HIPAA continually evolves, and we must keep up with the changes. Torres described two rules recently published by the U.S. Department of Health and Human Services. The privacy rule protects written information, and sets standards in terms of individually identifiable information, spelling out limits on the disclosures one can make. The security rule, which protects electronically recorded patient information, requires protective safeguards. Personally identifiable health information (PHI) comprises all of a patient’s personal health information created by a covered entity (physician as well as institution), held in any form, that can possibly identify the individual. This includes photos of individuals associated with the patient. Although text messages have the same impli-

PHI: Protected Health Information
- Created by a covered entity
- Identifies the individual the information concerns, or a reasonable basis exists to believe it can be used to identify the individual
- Held in any form or media—electronic, paper, or oral
- Includes an individual’s past, present, or future physical or mental health or condition
- It does not include records subject to, or defined in, the Family Educational Rights and Privacy Act, 20 U.S.C. §1232g or employment records
- Photographs of relatives, employers, and household members are PHI
  – unless the photograph has no identifying feature
  – and has no written information containing PHI
- The same holds for written information transmitted electronically, such as email and text messages
- PHI does not include the use or disclosure of de-identified health information:
  – all specified identifiers of the individual and of the individual’s relatives, household members, and employers have been removed
  – thus it cannot directly identify, or provide a reasonable basis for identifying, the individual
emphasize moisturization

Good education, cheerleading, and close follow-up

It’s best never to store, maintain, display, or otherwise
A pplies to all health plans, healthcare clearinghouses, Measures to protect the privacy of a subset of records—

Consider daily massage with the oils

These measures ensure the integrity, confidentiality, and security of “electronically protected health information” (e-PHI), ie, all individually identifiable health information

Applies to all health plans, healthcare clearinghouses, and healthcare providers—the “covered entities”—who transmit health information in electronic form

Photos—Authorization and Masking

• Photographs containing PHI cannot be used in external settings (such as conferences and seminars), or taken with one when leaving the institution, unless specifically authorized by the patient

• A clinician can mask identifying features in a photograph before displaying it at meetings

• Be aware that as files are moved, photographs can easily become unmasked, even unintentionally

• It’s best never to store, maintain, display, or otherwise use photographs containing PHI without written authorization from the patient

Case 1: Atopic dermatitis. A 9-month-old girl came in with a 7-month history of AD, constantly scratching and with badly disrupted sleep. Severity had increased despite topical steroids and antibiotics, and her agitated mother insisted on “natural.” Lio explained that an acupuncture study from nephrology (patients with uremic pruritus) “is what got me excited about the possibility of alternatives in AD.” Itch scores had dropped rapidly and dramatically for patients given acupuncture 3x/week (using the Large Intestine 11 point, LI11), while scores for sham-treated patients were unchanged. Lio substituted massage of LI11 with an acupressure bead for needles to treat children, and pilot study results surprised him. Adding it to standard of care (which control patients received) reduced itch significantly and lichenification somewhat, creating a helpful bedtime ritual with adolescent patients. Lio discussed the anti-inflammatory, emollient, barrier repair, water retention, and sepsis-reducing properties (in premature infants) of sunflower seed oil. Topical coconut oil—virgin, cold-processed—rich in medium-chain fatty acids, significantly outperforms mineral oil’s emollient actions and has antimicrobial benefits. Massage reduces anxiety, redness, lichenification, excoriation, and pruritus. Topical vitamin B12 is anti-inflammatory. (A compounding pharmacy mixes cobalamin powder with a simple base.) Probiotics improve gut mucosal permeability, which otherwise worsens with worsening skin disease. For this patient: Lio initially focused on moisturizing—massaging on a sunflower-coconut oil mixture after bathing, then a moisturizer—and dilute bleach baths. As the skin improved, the mother accepted a brief burst of fluconazole and, as improvement continued, she accepted incorporation of a conventional regimen. (Lio has published an evidence-based review of complementary and alternative medicine for AD: http://www.ncbi.nlm.nih.gov/pubmed/27388911.)

Treat AD—Consider:

• Emphasize moisturization and protecting the skin—sunflower seed oil
  – Topical application increases synthesis of ceramides and has direct emollient and barrier-repair properties
  – Also has anti-inflammatory properties, possibly via PPAr-α activation

• Discuss coconut oil (virgin cold-pressed) as an antibacterial possibility
  – Decreases SCORAD more effectively than mineral oil
  – Decreases staph colonization

• Consider daily massage with the oils

• Consider acupressure trial (in older children)
  – Can reduce VAS score by >25%

• Good education, cheerleading, and close follow-up

Case 2: Acne. A 17-year-old adolescent girl with a 2-year history of breakouts on her chin and jawline and increased facial hair had failed a range of topicals. She refused antibiotics, and also spironolactone for what Lio called a textbook case of hormonal-type acne. Lio’s roster of evidence-based alternatives includes tea tree oil, equivalent in efficacy to 5% benzoyl peroxide, with slower onset. Spearmint tea “is fascinating,” an antiandrogen shown in PCOS patients to reduce free and total testosterone, and raise LH and...
Treating Acne—Consider:

- Trial of tea tree oil topically
  - Equal efficacy to topical 5% benzoyl peroxide, slower onset
- Spearmint tea twice daily (herbal tea)
- Niacinamide +/− Zinc gluconate supplementation
  - Improvement reported after 4 weeks
  - Topical niacinamide equal in efficacy to topical clindamycin
- A physical modality:
  - PDT
  - Blue light/red light alone
  - Chemical peels
  - Extractions
  - Other lasers and light sources

Vascular Anomalies—Evolving Evidence: Impact on Clinical Practice

Maria C. Garzon, MD

Introduction. Vascular anomalies are now categorized into three groups: vascular tumors, malformations, and—recently added— provisionally unclassified. Dr. Garzon focused her talk on the malformations, with updates on advances in understanding and treatment that directly affect clinical practice. All medications noted are off-label.

Port-wine stain (PWS). These capillary malformations occur in ~3/1,000 children. A critical paper in 2013 described the central importance of somatic activating mutations in the GNAQ gene (guanine nucleotide-binding protein subunit alpha Q) in both Sturge-Weber syndrome (SWS) and isolated PWS. GNAQ mutations impact the developing vasculature, and the hypothesis is that SWS with skin, CNS, and eye involvement reflects a mutation that occurred early in development. Recognizing that facial PWS follow the embryonic vasculature pattern, and not the trigeminal nerve pattern, has altered conventional thought on the basis for identifying PWS patients at the highest risk for association with SWS. Recognizing the true risk pattern early now enables prevention of ophthalmologic complications. Garzon mentioned the ongoing discussion of early medical management for children at risk for seizures. She cited a recently published algorithm for guiding the next steps for patients with facial PWS (see R. Waelchli et al. Br J Dermatol. 2014;171:861–7).

Overgrowth syndromes. Despite their clinically heterogeneous nature, many overgrowth syndromes are associated with genes in the PIK3CA-AKT (phosphatidylinositol-3 kinase) pathway. These conditions are associated with hemihypertrophy, soft tissue growth, vascular and skeletal anomalies, epidermal nevi, and variable neurodevelopmental deficits. Some carry a malignancy risk. PIK3CA-related overgrowth spectrum (PROS) is the proposed new name for these rare, challenging conditions. PIK3CA is very important in cell signaling and development, and affects the mTOR pathway downstream, a “master switch” for cell growth and angiogenesis. Venous malformations have been associated with activating mutations in the TEK gene (which encodes endothelial cell tyrosine kinase receptor TIE2), but recent research has found that venous malformations may also be associated with somatic mutations in PIK3CA. Because many vascular malformations represent mosaic conditions, testing and arriving at a diagnosis can be challenging. A collaborative multicenter study is underway to
better understand the genetics, clinical features, and prognosis of these disorders. Ten years ago, “I could not conceive of being able to treat a malformation with a medication,” but identifying mTOR’s role has changed this. Garzon discussed the off-label use of the mTOR inhibitor sirolimus—standardly used to prevent rejection in transplant patients—for treating these complex vascular anomalies. She also emphasized the very high risk for thromboembolic disease when these patients undergo surgical procedures. Patients with these complex disorders need to be managed by a team including hematology and oncology.

How I Think About the Impact of New Scientific Findings on Development of New Treatments for Hair Loss

George Cotsarelis, MD

Introduction. Dr. Cotsarelis noted that “the hair follicle is a very unusual organ, because it cycles.” He profiled alterations in this cycle involved in hair loss and noted factors that can cause alterations. Cotsarelis also profiled several genes with important roles in hair growth and loss. Understanding the hair follicle cycle and the effect of genes on the cycle provides a foundation to recognize the potential relevance of emerging discoveries on the development of new treatments.

Hair cycle basics. Anagen is the growth period. “Nature puts great effort into controlling its duration,” as this determines hair length and the percentage of follicles in telogen. Cells in the bulb rapidly proliferate and generate the multiple layers of the new hair shaft, then stop dividing and undergo apoptosis. This pushes the hair follicle into catagen in which the cells move up into the dermal papilla, the only part of the follicle that survives. Then it transitions to telogen, a quiescent period normally involving ~7% of follicles at any given time. Telogen follicles contain only the bulge—home of the SCs (stem cells)—and a secondary germ adjacent to the dermal papilla below. ~1% of telogen hairs are shed daily during exogen. After the appropriate time in telogen the SCs activate and enter anagen to form a new lower hair follicle and entirely new hair shaft.

Alopecias. In androgenetic alopecia (AA) hair follicles gradually miniaturize, becoming microscopic as the anagen phase shortens and thus increases the percentage of follicles in telogen. Testosterone, which is converted to the more active dihydrotestosterone by the enzyme 5-alpha reductase type II (inhibited by finasteride), drives this miniaturization. Cotsarelis discussed different types and causes of telogen effluvium (excess hair shedding), all reflecting hair follicles forced to enter exogen prematurely. Abnormalities can also occur during catagen. Mutations in the hairless gene result in deformed hair follicles unable to cycle at all once the birth hair has fallen out.

Port-Wine Stains

• Many are associated with activating mutations in GNAQ
  – Sturge-Weber Syndrome
  – Isolated PWS
• Somatic activating mutations in GNAQ
  – Impact developing vasculature (skin, eye, CNS)
  – Activation of ERK pathway leads to altered blood vessel development?
• Hypothesized:
  – Earlier mutation → SWS
  – Cell of origin remains unknown
• Why is this important?
  – Early recognition of at-risk infants
  – Urgent ophthalmologic evaluation
  – Possible “feed and wrap” option for brain MR
  – Early diagnosis
  – Prevention of ophthalmologic complications
  – Ongoing discussion among experts of treatment of CNS disease
    – Possible aspirin therapy?
    – Presymptomatic anticonvulsant therapy?


PIK3CA-Related Overgrowth Spectrum: PROS

Formal diagnostic criteria proposed

• CLOVES
• Klippel-Trenaunay-CLVM
• Hemimegalencephaly/Megalencephaly-CM
• Fibroadipose overgrowth
• Facial infiltrating lipomatosis
• Hemi hyperplasia multiple lipomatosis (HHML)
• Macrodactyly
• Skin Conditions
  – Epidermal nevi
  – Seborrheic keratoses
  – Benign lichenoid keratoses


Telogen Effluvium: 5 types

Premature Telogen—premature anagen to telogen conversion; perhaps most common; due to fever, meds, etc.

Delayed Telogen—prolonged anagen, eg, post-partum effluvium

Premature Exogen—rapid onset; club hairs shed prematurely and synchronously due to precipitating event, eg minoxidil

Shortened Anagen—chronic telogen effluvium?

Prolonged Telogen—telogen follicles accumulate, then enter exogen synchronously; possible precipitators are pronounced changes in light cycle (seasonal, or due to travel), and malnutrition

Documented

Speculative


(Continued on page 15)
JUBLIA®
(efinaconazole)
Topical Solution 10%

ONYCHOMYCOsis*
STEALING THE SHOW?

FIGHT IT
AT THE SITE OF INFECTION

*For the treatment of onychomycosis of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.

JUBLIA allows some patients to have clearer toenails grow back. Individual results may vary.

INDICATION
JUBLIA (efinaconazole) topical solution, 10% is indicated for the topical treatment of onychomycosis (tinea unguium) of the toenail(s) due to Trichophyton rubrum and Trichophyton mentagrophytes.

IMPORTANT SAFETY INFORMATION
• JUBLIA is for topical use only and is not for oral, ophthalmic, or intravaginal use.
• Patients should be instructed to contact their health care professional if a reaction suggesting sensitivity or severe irritation occurs.
• The most common adverse reactions (incidence >1%) were (vs vehicle): ingrown toenail (2.3% vs 0.7%), application-site dermatitis (2.2% vs 0.2%), application-site vesicles (1.6% vs 0%), and application-site pain (1.1% vs 0.2%).
• JUBLIA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus, and should be used with caution in nursing women. The safety and effectiveness in pediatric patients have not been established.

Please see Brief Summary of full Prescribing Information on the adjacent page.
JUBLIA safely and effectively. See full prescribing information for JUBLIA.

This Brief Summary does not include all the information needed to use JUBLIA. See full prescribing information for JUBLIA.

**INDICATIONS AND USAGE**
JUBLIA (efinacozonazole) topical solution, 10% is an azole antifungal indicated for the topical treatment of onychomycosis of the toenail(s) due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.

**DOSE AND ADMINISTRATION**
Apply JUBLIA to affected toenails once daily for 48 weeks, using the integrated flow-through brush applicator. When applying JUBLIA, ensure the toenail, the toenail folds, toenail bed, hyponychium, and the undersurface of the toenail plate, are completely covered.

JUBLIA is for topical use only and not for oral, ophthalmic, or intravaginal use.

**CONTRAINDICATIONS**
None.

**ADVERSE REACTIONS**

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

In two clinical trials, 1227 subjects were treated with JUBLIA, 1161 for at least 24 weeks and 780 for 48 weeks. Adverse reactions reported within 48 weeks of treatment and in at least 1% of subjects treated with JUBLIA and those reported in subjects treated with the vehicle are presented in Table 1.

**Table 1: Adverse Reactions Reported by at Least 1% of Subjects Treated for up to 48 Weeks**

<table>
<thead>
<tr>
<th>Adverse Event, n (%)</th>
<th>JUBLIA N = 1227</th>
<th>Vehicle N = 413</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingrown toenail</td>
<td>28 (2.3%)</td>
<td>3 (0.7%)</td>
</tr>
<tr>
<td>Application site dermatitis</td>
<td>27 (2.2%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Application site vesicles</td>
<td>20 (1.6%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Application site pain</td>
<td>13 (1.1%)</td>
<td>1 (0.2%)</td>
</tr>
</tbody>
</table>

**DRUG INTERACTIONS**
In vitro studies have shown that JUBLIA, at therapeutic concentrations, neither inhibits nor induces cytochrome P450 (CYP450) enzymes.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Pregnancy Category C

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

Systemic embryofetal development studies were conducted in rats and rabbits. Subcutaneous doses of 2, 10 and 50 mg/kg/day efinacozonazole were administered during the period of organogenesis (gestational days 6-16) to pregnant female rats. In the presence of maternal toxicity, embryofetal toxicity (increased embryofetal deaths, decreased number of live fetuses, and placental effects) was noted at 50 mg/kg/day (559 times the Maximum Recommended Human Dose (MRHD) based on Area Under the Curve (AUC) comparisons). No embryofetal toxicity was noted at 10 mg/kg/day (112 times the MRHD based on AUC comparisons). No malformations were observed at 50 mg/kg/day (559 times the MRHD based on AUC comparisons).

Subcutaneous doses of 1, 5, and 10 mg/kg/day efinacozonazole were administered during the period of organogenesis (gestational days 6-19) to pregnant female rabbits. In the presence of maternal toxicity, there was no embryofetal toxicity or malformations at 10 mg/kg/day (154 times the MRHD based on AUC comparisons).

In a pre- and post-natal development study in rats, subcutaneous doses of 1, 5 and 25 mg/kg/day efinacozonazole were administered from the beginning of organogenesis (gestation day 6) through the end of lactation (lactation day 20). In the presence of maternal toxicity, embryofetal toxicity (increased prenatal pup mortality, reduced live litter sizes and increased postnatal pup mortality) was noted at 25 mg/kg/day. No embryofetal toxicity was noted at 5 mg/kg/day (17 times the MRHD based on AUC comparisons). No effects on postnatal development were noted at 25 mg/kg/day (89 times the MRHD based on AUC comparisons).

**Pediatric Use**
Safety and effectiveness of JUBLIA in pediatric subjects have not been established.

**Geriatric Use**

Of the total number of subjects in clinical trials of JUBLIA, 11.3% were 65 and over, while none were 75 and over. No overall differences in safety and effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and the younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

**NONCLINICAL TOXICOLOGY**

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

A 2-year dermal carcinogenicity study in mice was conducted with daily topical administration of 3%, 10% and 30% efinacozonazole solution. Severe irritation was noted at the treatment site in all dose groups, which was attributed to the vehicle and confounded the interpretation of skin effects by efinacozonazole. The high dose group was terminated at week 34 due to severe skin reactions. No drug-related neoplasms were noted at doses up to 10% efinacozonazole solution (248 times the MRHD based on AUC comparisons).

Efinacozonazole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and Chinese hamster lung cell chromosome aberration assay) and one in vivo genotoxicity test (mouse peripheral reticulocyte micronucleus assay).

No effects on fertility were observed in male and female rats that were administered subcutaneous doses up to 25 mg/kg/day efinacozonazole (279 times the MRHD based on AUC comparisons) prior to and during early pregnancy. Efinacozonazole delayed the estrous cycle in females at 25 mg/kg/day but not at 5 mg/kg/day (56 times MRHD based on AUC comparisons).

**PATIENT COUNSELING INFORMATION**
See FDA-Approved Patient Labeling (Patient Information).

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

Manufactured by:
Kaken Pharmaceutical Co. Ltd., Shizuoka, Japan

Product of Japan

U.S. Patents 8,039,494; 7,214,506

Based on 9391902
**Important genes.** *Sonic hedgehog,* known for its involvement in basal cell carcinoma, is also important for hair follicle growth. Mouse knockouts grow tiny hair follicle structures, and applying hedgehog agonist to the dorsal skin of a mouse with hair follicles in telogen converts telogen follicles to anagen. *β-catenin,* a powerful transcription factor required for hair growth, also turns resting follicles into growing ones. A mouse missing beta-catenin lacks hair, but overexpressing beta-catenin can generate dramatically excessive hair growth and induce pilomatrixomas. Genes controlling the phenotype of the hair have also been identified, both in dogs (E. Cadieu et al. *Science.* 209;326:150–3) and humans (Y.G. Kamberov et al. *Cell.* 2013;152:691–702).

### Keeping Up With Psoriasis Comorbidities

**Introduction.** Before discussing some of the more newly documented psoriasis comorbidities, Dr. Takeshita summarized the past 10 years of psoriasis comorbidity research. She focused on the increased risk of cardiovascular disease among people with psoriasis and the fact that cardiovascular disease is the primary cause of mortality, particularly among those with severe psoriasis, “helping us understand that psoriasis is more than just a skin disease.” Then Takeshita discussed the next most common causes of mortality in this psoriasis subgroup—the more recently identified risks for serious infection (requiring hospitalization), malignancy, and chronic kidney disease—that have emerged from studies using the population-based electronic medical record database in the UK. Although we need to improve our understanding and characterization of these risks and separate out disease vs treatment-induced effects, this new knowledge immediately affects our clinical practice.

**Possible biology.** There are many threads to sort out. Psoriasis is associated with other comorbid diseases and behavioral factors—obesity, diabetes, smoking, and drinking—that can increase risk for developing infection, malignancy, and kidney disease. Then there are treatment effects. Nephrotoxic drugs may contribute to kidney disease, and immunosuppressive effects of both older drugs and newer biologics may induce infections and malignancies. Lastly, the underlying immune dysfunction and systemic inflammation associated with psoriasis may also play roles, and it is important for us to determine if psoriasis itself has an independent association with these three comorbidities.

**Infection risk.** Lower respiratory infections are most common, followed by skin and soft tissue infections and upper respiratory infections. Focusing on pneumonia requiring hospitalization, subanalyses of data including direct measures of psoriasis severity (body surface area involvement) suggest that disease severity may be partially driving this. In our practice: it is important for psoriasis patients, especially those on immunosuppressive treatments, to remain up to date with recommended vaccinations. “We cannot simply rely on primary care physicians to keep our psoriasis patients up to date. We must talk with patients about this.” Annual inactivated flu vaccine and both the prevnar and pneumovax pneumonia vaccines are particularly relevant. Avoid live vaccines in those who are immunosuppressed.

**Malignancy risk.** The increased overall risk of any cancer (excluding nonmelanoma skin cancer) was small but statistically significant, especially for lymphoma (particularly CTCL). Those receiving treatment for severe psoriasis were at greatest risk. Increased risks of lung cancer (after controlling for smoking) and nonmelanoma skin cancer were also found. In our practice: have a low threshold to biopsy patients whose psoriasis or treatment response is atypical, to make sure that psoriasis is the true diagnosis. Encourage patients, especially those on immunosuppres-

### Infection, Malignancy, and Kidney Disease—important causes of mortality in psoriasis patients treated for severe disease

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Hazard Ratio (95% CI)</th>
<th>Absolute Risk*</th>
<th>Excess Risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Cardiovascular Disease</td>
<td>1.57 (1.26–1.96)</td>
<td>61.9</td>
<td>3.5</td>
</tr>
<tr>
<td>2. Infection</td>
<td>1.65 (1.26–2.18)</td>
<td>40.1</td>
<td>2.6</td>
</tr>
<tr>
<td>3. Malignancy</td>
<td>1.41 (1.07–1.86)</td>
<td>39.0</td>
<td>1.6</td>
</tr>
<tr>
<td>4. Kidney Disease</td>
<td>4.37 (2.24–8.53)</td>
<td>3.5</td>
<td>1.2</td>
</tr>
</tbody>
</table>

*Deaths per 1,000 patient-years


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**Clinical Implications—Severe Psoriasis and….**

**Infection**

- Vaccination for:
  - Influenza yearly (inactivated)
  - Pneumonia
    - CDC recommends pneumonia vaccination for all adults ages 19–64 with immunocompromising conditions and for all adults >65
    - PCV13 (Prevnar) and PPSV23 (Pneumovax)
  - Zoster (age >60): live vaccine not recommended while on immunosuppressive therapy
  - Hepatitis B
  - HPV (ages 11–26; may start age 9)

**Cancer**

- Biopsy patients with atypical features of psoriasis and/or those not responding to treatment
- Encourage patients to stay up to date on age-appropriate cancer screening
  - Cervical: pap smear (q 3 yrs ages 21–65)
  - Breast: mammography (q 2 yrs ages 50–74)
  - Colon: (50–75) fecal occult blood testing (FOBT) q yr, flex sig q5 yrs + FOBT q3 yrs, colonoscopy q10 yrs
  - Lung: annual low-dose CT screening for 55–80 with ≥30 pack-year history or current smoker or quit within 15 yrs
  - Large, long-term follow-up studies needed to determine cancer risk with psoriasis treatments

**Kidney Disease**

- Consider closer monitoring for renal insufficiency with BSA >3%: urinalysis, creatinine, blood urea nitrogen
- Caution with potentially nephrotoxic medications
- Additional studies to confirm and further characterize these findings

[http://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html](http://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html)
Psoriasis is independently associated with comorbid diseases beyond cardiometabolic disease.

- Serious infections: upper and lower respiratory infection, skin/soft tissue infections
- Malignancies: lymphoma, lung, NMSC
- Chronic kidney disease
- Comorbidities of psoriasis have important clinical implications in providing comprehensive care for patients.
- Additional studies needed to further characterize psoriasis comorbidities and impact of psoriasis therapies.

**Summary**

- Psoriasis is independently associated with comorbid diseases beyond cardiometabolic disease.
- Serious infections: upper and lower respiratory infection, skin/soft tissue infections
- Malignancies: lymphoma, lung, NMSC
- Chronic kidney disease
- Comorbidities of psoriasis have important clinical implications in providing comprehensive care for patients.
- Additional studies needed to further characterize psoriasis comorbidities and impact of psoriasis therapies.

**Harnessing UV Light to Soften Fibrotic Skin**

**Sewon Kang, MD**

**Introduction.** Dr. Kang’s therapeutic use of ultraviolet (UV) light to reduce fibrotic changes in skin was sparked by learning—during his group’s study of photoaging—that a measurable increase in collagen breakdown occurs even in sun-protected skin following a single UV exposure. Kang set the stage by describing the balance between collagen synthesis and breakdown in normal skin and the pathologic collagen excess in fibrotic skin.

**Normal and fibrotic skin.** Kang described the multistep process of collagen synthesis in the dermis of healthy skin-protected skin, resulting in fibrils that are enzymatically cross-linked in the extracellular space to provide strong and resilient skin. Synthesis is balanced by dermal remodeling, in which these tough collagen macromolecules are broken down by matrix-degrading metalloproteinases (MMPs)—collagenase (which begins the degradation), then gelatinase and stromelysin. Fibrotic skin contains excessive collagen because the patient is overproducing procollagen and/or destroying too little of it. And at a gross histologic level, all fibrotic skin shares a highly similar appearance—an excessively compact dermal matrix—regardless of the underlying pathophysiology. Kang’s novel therapy addresses this imbalance rather than the specific pathophysiology causing it.

**Photoaging, and the birth of an idea.** Kang and colleagues had found collagen breakdown in the dermis to be responsible for transforming skin exposed to the environment and solar radiation to an aged, wrinkled, photoaged phenotype. Alterations were primarily in the dermis. He discussed their observations of AP-1 (activated protein-1), which induces the MMPs. AP-1 is created from the union of 2 proteins. One, c-Fos, is normally present in the epidermis and dermis. c-Jun only appears a few hours after UV exposure, which is when these MMPs also appear. A single exposure of UV light not only increases collagen breakdown and reduces procollagen synthesis, but synthesis does not begin to resume for several days. Kang wanted to find out if UV exposure could be used to reduce the overpresence of collagen in fibrotic skin.

**A novel antifibrotic therapy.** The answer was yes—if the right wavelengths are used and adjustments are made for more pigmented skin. Both short (320 nm) and longer (360 nm) UV wavelengths are able to elevate MMPs in human skin after a single exposure. UVA1 (340–400 nm), far less likely to burn the skin, produces robust induction of MMPs in light skin but penetrates highly pigmented skin poorly. Using pure UVB light (280–320 nm) and increasing the dose overcomes the pigment barrier. When Kang et al. used this UVB source (3x/week vs sham treatment) in a split-scalp clinical trial in African-American patients with acne keloidalis nuchae, sham treatment made no change, but UBV induced improvements of 36% after 8 weeks, and 53% after 16 weeks. Similar treatment of scleroderma patients with UVA1 has softened the diseased skin reproducibly. “I think this could be a way to cause antifibrosis in patients with various fibrotic ailments.”

**UVB & Long UVA Induce Collagenase (MMP-1) mRNA in Human Skin In Vivo**

**High-Dose UVA1 Phototherapy**

- High-dose (130 J/cm²) superior to low-dose (20 J/cm²)
  - Stege et al., 1997 (Düsseldorf, Germany)
  - 10/10 scleroderma patients responded
  - Complete clearance in 4/10
- Our experience:
  - Modest softening in 9/12 patients treated with high-dose UVA1 (130 J/cm²) given 3x/wk
  - Modest softening in additional patients treated with other high-dose UVA1 regimens (eg, 1x/wk)

**UV Induction of MMP-1 mRNA in Dark vs Light Skin In Vivo**

- High-dose (130 J/cm²) superior to low-dose (20 J/cm²)
  - Stege et al., 1997 (Düsseldorf, Germany)
  - 10/10 scleroderma patients responded
  - Complete clearance in 4/10
- Our experience:
  - Modest softening in 9/12 patients treated with high-dose UVA1 (130 J/cm²) given 3x/wk
  - Modest softening in additional patients treated with other high-dose UVA1 regimens (eg, 1x/wk)
The Dermatology Foundation is grateful to the following corporations for their generous contributions last year. Their support furthers the DF’s mission to develop and retain tomorrow’s leaders in the specialty, enabling advancements in patient care.

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2017 Dermatology Foundation Research Funding
Crucial for the Advancement of the Specialty

The Dermatology Foundation plays an essential role in the scientific advancement of the specialty. By providing early career research funding, the DF ensures that promising, highly motivated investigators have the support they need to pursue new knowledge in all areas of dermatology. In an era of rapidly accelerating medical research costs and steep competition for funding, DF research support has become more important than ever.

Research Award Applications Due October 17, 2016

In keeping with its sole purpose—to help enable advancements in patient care—the Foundation is accepting applications for the 2017 funding year. Its nationally recognized Research Awards Program provides funding opportunities that are intended for those who most clearly show the potential and desire to make significant contributions to the future of dermatology. The program supports research in all areas of dermatology and cutaneous biology with multi-year career development awards, one-year fellowships, and grants. The new funding year begins July 1, 2017.

Career Development Awards (CDAs)

The nine CDA categories are intended to enable physician-scientists and investigators to transition from fellowship to established researcher. These highly competitive, effective awards provide an annual stipend of $55,000 for up to three years of support.

- Physician-Scientist CDA
- Clinical CDA in Dermatologic Surgery
- Clinical CDA in Health Care Policy/Public Health
- Dermatopathology Research CDA
- Science of Human Appearance CDA
- Women’s Health CDA
- Medical Dermatology CDA
- Pediatric Dermatology CDA
- Basic Science Research CDA

Fellowships

A one-year Dermatologist Investigator Research Fellowship is offered to individuals who have completed their residency training in dermatology; it provides a salary stipend of $30,000.

Research Grants

These one-year grants offer $20,000 in seed money for research projects in a variety of concentrations, including patient-directed investigation (translational studies with the potential for direct patient benefit), basic dermatologic research, and cutaneous biology.

APPLY NOW!

Research proposals accepted through October 17; funding year begins July 1, 2017.

Visit dermatologyfoundation.org/rap for everything you need:

- detailed eligibility criteria
- application instructions
- downloadable forms

Questions are welcome: 847.328.2256 or dfrap@dermatologyfoundation.org

2016 DF Clinical Symposia Faculty Disclosures (Part II)

# 2016 CLINICAL SYMPOSIA FACULTY
Proceedings—Part II

**George Cotsarelis, MD***  
*Professor and Chairman*  
Department of Dermatology, University of Pennsylvania

**Edward Cowen, MD**  
*Senior Clinician*  
Dermatology Branch, National Cancer Institute, NIH

**Maria C. Garzon, MD**  
*Professor*  
Department of Dermatology, Columbia University Medical Center, Director, Pediatric Dermatology, New York Presbyterian–Morgan Stanley, Children’s Hospital of New York

**Sewon Kang, MD***  
*Professor and Chairman*  
Department of Dermatology, Johns Hopkins University

**Peter A. Lio, MD**  
*Assistant Professor*  
Department of Dermatology, Northwestern University

**Boris D. Lushniak, MD, MPH, RADM, USPHS (Ret)**  
*Professor*  
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**Suzanne M. Olbricht, MD**  
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**Abel Torres, MD, JD**  
*Professor and Chair*  
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**Ruth Ann Vleugels, MD, MPH***  
*Associate Professor*  
Department of Dermatology, Brigham and Women’s Hospital, Harvard University

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**Educational Grant ($300,000)**

The DF is pleased to recognize Unilever for their support of the 2016 DF Clinical Symposia Resident Program.

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- Taro Pharmaceuticals U.S.A. Inc.
John C. Maize, Jr., MD, is passionate about his work as a medical dermatologist and dermatopathologist in his group practice in Charleston, South Carolina. He deeply enjoys his volunteer faculty appointment at the Medical University of South Carolina and the time dermatology residents spend in his practice.

Dr. Maize is also the dedicated and enthusiastic head of the Leaders Society campaign in his state. “The Dermatology Foundation is an organization I am drawn to and support. I tell everyone I’ve been an investor in the DF for the past 10 years. I’m investing in the furthering of dermatology for the benefit of myself and my patients—because we are supporting the future thought leaders who are going to drive our specialty forward.”

Dr. Maize fell in love with dermatology during a summer fellowship at the NIH that assigned him to Dr. Stephen Katz’s dermatology lab. “I entered medical school with an open mind, just trying to find my way,” he recalls. Dr. Maize was fascinated with what he learned from “some pretty hard-core scientists,” but it was his experiences at dermatology grand rounds that captured and inspired him. “There was a special confluence of training programs there that included the NIH, the Naval Hospital at Bethesda, and the Army Hospital. It was a very rich environment to see patients with rare and intriguing diseases, and the dermatologists there were all incredibly excited about what they do.”

Dr. Maize learned about the DF’s mission during his dermatopathology fellowship and time as faculty at the University of California, San Francisco. He became a Leaders Society member in 2007 and, since then, has maintained a strong commitment to the work of the Foundation. “The Dermatology Foundation is not just another charity. What we do daily is try to help our patients, and the DF is helping us do that better. We get back what we give—in a very tangible way.”

The DF is exceptionally grateful to its many volunteers who give generously of their time and inspiration to keep dermatology at the forefront of medicine.