CURRENT CONCEPTS IN DERMATOLOGY

DANIEL LADD, D.O., FAOCD
JOHN MINNI, D.O., FAOCD

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Continuing Medical Education Statements

This activity will change your practice and improve patient outcomes!

AOA Statement:
The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians. This activity anticipates being approved for 28 hours of AOA Category 1-A credit pending approval by the AOA CCME and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity. October 25 - 28, 2017

AAD Statement:
The American Osteopathic College of Dermatology Current Concepts in Dermatology (Program #698100) is recognized by the American Academy of Dermatology for 28 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology's Continuing Medical Education Award. October 25 - 28, 2017

ACCME Statement:
The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. October 25 - 28, 2017
American Osteopathic College of Dermatology
Mission Statement &
Continuing Medical Education Needs Assessment

The Continuing Medical Education Program of the American Osteopathic College of Dermatology will support, enhance and advance new models of academic excellence and community health care.

The mission of the American Osteopathic College of Dermatology is to create innovative education, support, and opportunities in dermatology that promote excellence in patient care and community health through advocacy, consciousness, inclusivity, and osteopathy.

Purpose
The purpose of the CME program is to provide AOA-accredited continuing medical education activities to inform the dermatologist physician. The program will provide a mechanism by which its constituents can improve competency, maintain board certification and cultivate lifelong learning. CME will provide physicians with the opportunity to further develop their knowledge through individual and group learning activities. The Continuing Medical Education Committee will monitor the quality of all programs conducted by the AOCD.

Accreditation:
The AOCD is accredited by the American Osteopathic Association. This activity anticipates being approved for 28 hours of AOA Category 1-A credit pending approval by the AOA CCME.

The American Osteopathic College of Dermatology Current Concepts in Dermatology (Program #698100) is recognized by the American Academy of Dermatology for 28 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology's Continuing Medical Education Award.

The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

This meeting will provide a diversified CME presentation focusing on the art and science of dermatology. Information will be presented through lectures and scientific paper presentations. The activity actively encourages members to develop enduring materials as an evolving tool for continuing education. The College is committed to exploring the development of its capacity to expand resources in other educational techniques, including Web-based activities and point-of-care technologies.

Commercial Support Disclosure
AOCD CME will identify relevant financial relationships prior to awarding AOA Category 1A and/or AMA PRA Category 1 Credit™ for CME activities. All persons in a position to influence or control CME content (course directors, program planning committee members, speakers, authors and staff) will complete a standardized disclosure form. Information about funding will be requested to identify CME activities at higher risk for commercial bias.

All AOCD CME activities will be evaluated by learners and possibly peer reviewers to determine if the content was free of commercial bias. All those identified as having influence and/or control of CME content perceived as either manifesting conflicts of interest or being biased may be disqualified from consideration as resources (planning group member, authors, faculty, etc) in subsequent CME activities.

Learners will be provided with information on identified COI from any of the above categories of persons that affect the content of CME, and that information will be positioned in course materials such that it is read by learners prior to the execution of the CME activity. Speakers for the AOCD will be required to provide disclosure information to meeting attendees during their introduction of their topic. Additionally, disclosure statements are provided in the program schedule given to each meeting attendee and is available online at www.aocd.org.

In accordance with the ACCME’s Standards for Commercial Support of Continuing Medical Education, the Policy on Collection of Financial Relationships and Resolution of Conflicts of Interest (COI) exists to provide guidance for staff, instructors, planners, reviewers and managers of CME activities sponsored by The American Osteopathic College of Dermatology, (AOCD). This policy addresses the underlying philosophy of disclosure to learners,
mechanisms to collect disclosure information and the parties from whom financial disclosure shall be collected, the mechanisms to resolve COI, and requirements to make disclosure to learners prior to the start of an activity.

**Professional Practice Gap Statement:**
Physicians need to understand, update and manage changes in dermatology in order to provide optimal patient care. Dermatologists in private practice may not have immediate access to new updates in therapies and treatments. This activity will help to close gaps in physician’s areas of MACRA/MIPS, communication with patients, therapeutic updates, melanoma updates, dermoscopy, psoriasis updates, Hansen’s disease, pediatric dermatology and hair loss.

**Expected Outcomes:**
As a result of participation in the AOCD/CME activity, practicing clinicians will improve competency; maintain specialty board certification; and cultivate lifelong learning. It is expected that attendees of this meeting will improve their diagnostic competence regarding a wide range of dermatologic conditions. In addition to increased diagnostic competence, enhanced concepts of therapy and treatment in dermatologic care will be gained for implementation in everyday practice.

- Attendees will learn practical tips useful in dermatologic surgery.
- Attendees will learn techniques that increase patient safety and comfort.
- Attendees will learn techniques used to treat BAP-oma.
- Attendees will gain an understanding of and be able to identify the various causes and etiology of hair loss.
- Attendees will learn the key histological features of common and uncommon skin conditions.
- Attendees will learn traditional medical treatments for dermatological conditions and non-traditional treatments.
- Attendees will review the basic concepts of osteopathic philosophy and learn its application to dermatology.
- Attendees will learn treatment protocols for uncomplicated leprosy, prevention of disability and management of the immunological reactions.
- Attendees will gain an understanding of how to select patients for radiation therapy compared with other skin cancer treatment modalities.
- Attendees will be able to recognize clinical patterns of cutaneous disease.
- Attendees will be able to treat skin diseases while also coordinating care with appropriate specialists.
- Attendees will gain an understanding of the Quality Payment Program included in the MACRA legislations.

The overall result being improved physician/provider performance and increased positive patient outcomes.

These objectives will be achieved in a setting which is evidence-based, culturally sensitive and free of commercial bias. The AOCD is committed to the practice of continuing program improvement. The AOCD will actively explore new educational technologies, develop collaborative relationships with other CME providers and seek to build the capacity to evaluate competency-based outcomes among the clinicians we serve. CME will provide physicians with the opportunity to further develop their knowledge through individual and group learning activities.

**Needs Assessments:**
The activity was developed based upon the needs of physicians within the association identified through:
- An evaluation/survey provided to meeting participants at both our annual and midyear meeting
- Consensus of faculty members within a department or service area
- New advances in dermatologic treatment identified in major publications or research studies
- New methods of diagnosis or treatment
- Availability of new medication(s) or indication(s)
- Development of new technology
- Acquisition of new facilities or equipment
- Input from experts regarding advances in medical knowledge
- Legislative, regulatory, or organizational changes effecting patient care
- Epidemiological data
- Quality assurance/audit data
- Statistics infection control data
- Surgical procedures statistics
- Journal articles/literature citations

The AOCD Continuing Medical Education Committee works to assure the inclusion of appropriate Osteopathic content in the Continuing Medical Education activities presented by AOCD, and to assure that the Continuing Medical Education Programs of the AOCD will achieve the stated objectives of each meeting in a setting which is evidence-based, culturally sensitive and free of commercial bias.
The Continuing Medical Education Committee of the AOCD will monitor the quality of all activities conducted.

**Content Areas:**
The AOCD approves the CME activities based upon needs assessment data to ensure that all offerings present current, up to date and cutting edge information. Specific areas of emphasis include, new advances in dermatologic treatment, new methods of diagnosis or treatment, availability of new medication(s) or indication(s), development of new technology, advances in medical knowledge and legislative, regulatory, or organizational changes effecting patient care. The Osteopathic Core Competencies of Osteopathic Philosophy, Principles, Practice and Manipulative Medicine, Medical Knowledge, Patient Care, Interpersonal and Communication Skills, Professionalism, Practice-Based Learning and Improvement and System-Based Practice will also be incorporated into all CME activities.

**Target Audience:**
The primary target audience of the CME activities conducted by the AOCD are the dermatologist physician members. The College also serves community physicians, volunteer clinical faculty, academic clinicians and students affiliated with the AOCD. The activity will also actively seek to broaden its audience through developing affiliations with CME providers on the national level.

**Faculty Disclosure:**
As a sponsor accredited by the AOA, it is the policy of the AOCD to require the disclosure of anyone who is in a position to control the content of an educational activity. All relevant financial relationships with any commercial interests and/or manufacturers must be disclosed.

**Disclosure of Commercial Support of CME:**
As you undoubtedly know from the national media, there has been much discussion concerning the relationships between CME sponsors, faculty and commercial companies providing support of CME.

Both the American Osteopathic Association and the Committee on Continuing Medical Education have adopted regulations for ethical actions in this area which the American Osteopathic College of Dermatology endorse and have adopted for all our educational activities.

Please be assured that having an affiliation with a company does not imply in any way that something is wrong or improper; however, we want to inform attendees that such a relationship exists.

Should you have any questions regarding the facilities, handouts, activity content, or concerns about CME compliance with the AOA “Uniform Guidelines,” feel free to contact the AOCD representative:

Marsha A. Wise, BS  
Executive Director  
P.O. Box 7525  
Kirksville, MO 63501  
660-665-2184  
800-449-2623

Unresolved issues regarding compliance with the AOA “Uniform Guidelines” can be brought to the attention of the AOA Division of CME by calling: 800-621-1773, or by writing:

AOA CME Office  
142 East Ontario Street  
Chicago, IL 60611
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Meeting Faculty & Needs Assessments

Daniel Ladd, DO, FAOCD
Program Chair

Dr. Daniel Ladd, is the Medical Director and Founder of Tru-Skin™ Dermatology in Austin, Texas. He earned his B.A. from the University of Texas at Austin and received his medical degree from Des Moines University in 1999. He completed his dermatology residency at the Northeast Regional Medical Center in Kirksville, Missouri in conjunction with the Dermatology Institute of North Texas in 2004. In addition to being board-certified in general and cosmetic dermatology, Dr. Ladd is also board-certified in Mohs micrographic surgery.

He is a member of the American Academy of Dermatology, American Osteopathic College of Dermatology, the American Society of Dermatologic Surgeons and the American Society of Cosmetic Dermatology and Aesthetic Surgery, as well as a Member of the American Society of Mohs Surgery. Dr. Ladd is a lifetime member of the Skin Cancer Foundation’s Amonette Circle, an elite group of the country’s foremost dermatologists and Mohs surgeons who have made a commitment to skin cancer education and prevention.

Disclosures: Physician Training: Sensus Healthcare; Medical Officer/Minority Shareholder: SkinCure Oncology; Director, Officer or Employee of: Shade Project; Spouse is Director, Officer or Employee of: Shade Project

John Minni, DO, FAOCD
Program Chair

Dr. John Minni is board-certified in dermatology. He graduated, with honors, from Nova Southeastern College of Osteopathic Medicine in Fort Lauderdale, FL. He completed his internship at Union Hospital/St. Barnabas Healthcare System in New Jersey. He then returned to Florida and completed both family medicine and dermatology residencies at Columbia Hospital and the VA Medical Center in West Palm Beach, FL. Dr. Minni also served as chief resident in dermatology. Between residencies, Dr. Minni practiced family medicine at the Palm Beach County Health Department, while training residents, interns and medical students. Prior to medical school, Dr. Minni attended the University of Notre Dame as a Notre Dame Scholar and graduated with honors with a B.S. in biology.

Disclosures: Speaker: Abbvie, Janssen, Promius, Leo, Novartis, Galderma

Sanjiv Agarwala, MD

Sanjiv Agarwala, MD, is the chief of medical oncology and hematology at St. Luke’s Cancer Center and professor of medicine at Temple University School of Medicine, in Philadelphia, PA. Dr. Agarwala is nationally and internationally recognized as an expert in the research and treatment of melanoma and immunotherapy of cancer and has presented and led numerous conferences and meetings across the globe.

Dr. Agarwala received his undergraduate education and medical degree from Bombay University. He completed his medical training through residencies and fellowships at the University of Bombay in India, Otago University in New Zealand and the University of Pittsburgh in Pennsylvania.

Dr. Agarwala has written and contributed to over 200 publications and book chapters on melanoma, immunoncology and other research areas. He is board certified in oncology and hematology and is as an active member of several professional and scientific societies, such as the American Association for Cancer Research, the American Society of Clinical Oncology, the European Society of Medical Oncology, and the Society for Melanoma Research.

Dr. Agarwala has been principal investigator for multiple clinical trials involving immunotherapy and targeted therapy for melanoma, renal cancer and other malignancies. He has received several honors, including listings as one of America’s top doctors for cancer and best doctors in the United States.

Updated Medical Treatment for Melanoma
Objectives:
1. Update on new information and studies
2. Update on new therapies
3. New detection techniques
Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new technology

References:

Core Competencies: 2, 3, 6

Disclosures: No disclosures provided by speaker

Sanjiv Agarwala, MD
Ashfaq A. Marghoob, MD
Merrick I. Ross, MD
Edward H. Yob, DO, FAOCD (Moderator)

Case Studies in Melanoma: An Interactive Panel
This lecture will be an interactive discussion of complex melanoma patients with a panel of experts and the attendees.

Objectives:
1. Review and discuss of complex melanoma patients from a diagnostic standpoint
2. Review and discuss treatment alternatives in treating complex melanoma patients
3. Invite audience participation through discuss of complex cases from the practice

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)

References:

Core Competencies: 2, 3, 4, 6

Ali Banki, DO, FAOCD
Dr. Ali Banki is a board-certified dermatologist runs a solo practice in Glastonbury, CT and is a Clinical Associate of Dermatology at University of Connecticut School of Medicine, as well as attending dermatologist at Saint Francis Hospital and Medical Center in Hartford, CT.

In 1998, Dr. Banki graduated from the University of Connecticut, summa cum laude, with a degree in physiology and neurobiology, earned through the honors program. After completing his undergraduate degree, he participated in a research team involved in developing new methods in the treatment of multiple sclerosis. This experience ultimately resulted in a publication within a leading journal. A second research project at the University of Connecticut Health Center in the Department of Immunology was completed in the following year. In 2001, a year-long Pathology Fellowship at the University of Connecticut School of Medicine allowed him to gain vast knowledge and experience in all aspects of systemic pathology, including both gross and microscopic methods.

Dr. Banki received his medical degree from the New York College of Osteopathic Medicine in 2006, finishing at the top of his class with multiple honors recognitions in various fields. After graduation, he attended the New York Saint Barnabas residency program in dermatology, where he successfully completed his chief residency year in 2010. Here, he was awarded first place for his Intendis research paper, an award given annually for the top research paper by a
dermatology resident nationwide. He has also published in several dermatology journals, dermatology textbooks and has also presented nationally at dermatology meetings.

He is a member of the American Academy of Dermatology and the Connecticut Dermatology & Dermatological Surgery Society. Dr. Banki is also on the editorial board for the Journal of American Osteopathic College of Dermatology.

He is active within the community in educating skin cancer awareness and the importance of skin cancer screenings. He periodically devotes time to the education of residents in training by lecturing at the University of Connecticut and New York Saint Barnabas Dermatology Programs. He regularly attends national dermatology meetings and continually keeps updated through current leading dermatology journals and publications.

Clinical and Dermoscopic Characteristics of Desmoplastic and Amelanotic Melanomas
This session will help dermatologists to gain a better understanding of amelanotic and desmoplastic melanomas. It will consists of the following two sessions: 1. Review of key clinical and dermoscopic features as well as differential diagnosis and pathogenesis of these neoplasms. 2. Surgical and non-surgical treatments for desmoplastic melanoma will be discussed.

Objectives:
1. Summarize key vascular dermoscopic morphologies associated with melanomas as well as some of benign and malignant melanocytic and non-melanocytic lesions.
2. Recognize key clinical features of amelanotic and desmoplastic melanomas
3. Recognize key dermoscopic features of amelanotic and desmoplastic melanomas

Needs:
1. New methods of diagnosis or treatment
2. Advances in medical knowledge

References:

Core Competencies: 1, 2, 3, 4, 5, 6, 7

Disclosures: No disclosures provided by speaker

Neal Bhatia, MD
Dr. Neal Bhatia is a leading dermatologist in Southern California, providing patients in and around San Diego with the skilled, individualized care they need for skin and nail diseases and cosmetic concerns. With extensive skill and experience in treating a wide range of dermatologic issues, Dr. Bhatia is skilled at diagnosing common and uncommon skin diseases and conditions and in determining the ideal treatment for the best response and results for all skin types. At his practice in San Diego, he provides an array of services including state-of-the-art treatments for acne, psoriasis, rosacea, skin cancer and more.

Skin Cancer Horse
This lecture will provide photographic evidence and compilation of data of latest updates in management, chemoprevention, and photoprotection.

Objectives:
1. Understand and apply mechanisms of action of currently available therapies to the modification of the disease process contributing to actinic keratosis formation
2. Manage and optimize anticipated local skin reactions associated with topical therapies
3. Explain and define the role of combination therapies in clinical practice
Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis and treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge

References:

Core Competencies: 2, 3, 6, 7

Disclosures: Advisor, Consultant, Investigator, Speaker: Abbvie, Activis, Allergan, Aqua, Bayer, Biofrontera, BiopharmX, Castle, Cipher, Dermira, Encore, Exeltis, Ferndale, Foamix, Galderma, Intraderm, ISDIN, LaRoche-Posay, Leo, Novan, Novartis, PharmaDerm, Pfizer, Promius, Regeneron, Sanofi, SunPharma, Valeant

Neal Bhatia, MD
Mark Kaufmann, MD
Andrea Murina, MD
Lisa Swanson, MD

**Bureaucracy and Burnout Panel**
This is an interactive panel discussion among members of the AAD Board of Directors and leaders of the AOCD as well as the audience to review the current state of dermatology and collaboration between the organizations.

Objectives:
1. Identify current threats to patient safety and the growth of dermatology
2. Review plans of action from the AAD, AOCD, and other societies within organized dermatology as well as efforts to collaborate
3. Discuss current and future issues facing training new dermatologists to face the challenges of scope of practice

Needs:
1. Legislative, regulatory, or organizational changes effecting patient care

Reference:

Core Competencies: 5, 7

**Lloyd Cleaver, DO, FAOCD**
Dr. Lloyd Cleaver, DO founded the Cleaver Dermatology Clinic in 1986. Dr. Cleaver completed his internship and residency at the Navy Regional Medical Center in San Diego, CA. He is a graduate of Kirksville College of Osteopathic Medicine. He is also a board-certified dermatologist, Fellow of American Osteopathic College of Dermatology and board-certified in Mohs micrographic surgery.

A leader in medical education, Dr. Cleaver is a Professor of Dermatology at the Kirksville College of Osteopathic Medicine/A.T. Still University and Assistant Dean of Continuing Medical Education at the Kirksville Osteopathic Medical Center/A.T. Still University. He serves as Vice Chair for the Certification Committee of American Osteopathic Association and has been Vice Chair and is currently Secretary to the American Osteopathic Board of Dermatology. He is a Past President of the Kirksville Osteopathic Alumni Association and a Past President of American Osteopathic College of Dermatology.
Osteopathic Continuous Certification Update

Objectives:
1. Understanding of the OCC process that ensures osteopathic physicians are current in their specialty
2. Understanding of the five components of OCC which include: Unrestricted License, Lifelong Learning, Cognitive Assessment, Practice Performance, and Continuous AOA Membership

Needs:
1. Ensuring college membership
2. Understand new requirements for accreditation
3. Maintenance of our board certification

References:

Core Competencies: 1, 3, 5, 6

Disclosures: No disclosures provided by speaker

Steve Feldman, MD
Chronic skin diseases have a huge impact on patients’ lives. We can help make great improvements in our patients’ lives, if they will use the medicine we prescribe. That’s a big if. Dr. Steven Feldman has opened our understanding of adherence issues in the treatment of psoriasis, atopic dermatitis and acne. He is author of over 700 MEDLINE-referenced publications and serves as editor of the Journal of Dermatological Treatment.

Dr. Feldman is a board-certified dermatologist and dermatopathologist. He is Professor of Dermatology, Pathology and Public Health Sciences at the Wake Forest University School of Medicine in North Carolina. He earned his M.D. and PhD degrees from Duke University in Durham, NC, and then completed a dermatology residency at the University of North Carolina at Chapel Hill and his dermatopathology residency at the Medical University of South Carolina, in Charleston.

Adherence to Treatment
Poor adherence to treatment is nearly ubiquitous. Poor treatment outcomes and many other puzzling dermatologic phenomena are mediated by poor use of medication. This session describes how well people use their medications, relying on evidence obtained using objective electronic monitors. Practical ways to improve patients’ use of medications will be discussed. These measures can help dramatically improve outcomes of treatment for patients with many chronic skin diseases including acne, atopic dermatitis, and psoriasis.

Objectives:
1. Describe ways to manage difficult to treat psoriasis
2. Describe how well (poorly) patients use dermatological treatment
3. List ways to improve patients’ use of medications

Needs:
1. New methods of diagnosis and treatment
2. Development of new technology
3. Advances in medical knowledge

References:

Core Competencies: 2, 3, 4, 5, 7
**Capt. John Figarola, MA, LOTR, CHT**

Captain John Figarola is the director of the Rehabilitation and Education Services Department at the National Hansen’s Disease Programs located in Baton Rouge, LA. He is a Board Certified Hand Therapist with over 25 years of experience managing the neuropathic hand, teaching and consulting on the prevention of disability in leprosy. His career in the U.S. Public Health Service has been dedicated to improving the lives of people coping with deformities and disabilities secondary to leprosy. Captain Figarola received a Master of Arts in Occupational Therapy from Texas Woman’s University and a Bachelor of Science in Occupational Therapy from Louisiana State University.

Disclosures: No disclosures provided by speaker

**Barbara Stryjewska, MD**

Dr. Barbara Stryjewska obtained her medical doctorate in 1977 from the Jagiellonian University School of Medicine in Krakow, Poland. After completing her residency in Radiation Oncology, she served as an attending on the Oncology service at the Centre of Oncology at the Curie Memorial Institute in Krakow until her immigration to the United States in 1988, when she retrained in family medicine at St. Joseph’s Medical Center in Yonkers, NY.

She served as a primary care provider in Baton Rouge, LA until 2002, when she assumed the position of Medical Officer for the National Hansen’s Disease Clinical Center, the only facility in the United States solely devoted to the treatment of leprosy.

In addition to her duties coordinating the overall care of Hansen’s disease patients, Dr. Stryjewska also provides consulting support to physicians and health departments around the country and regularly leads educational seminars on the medical, surgical, and therapeutic management of leprosy. She was invited to lecture at the, Emory, NIH in Bethesda and Harvard Medical School in Boston. In summer 2013 and 2015 she conducted Leprosy Workshop in Kosrae, Yap, Chuuk, Pohnpei (Federated States of Micronesia), Republic of Marshall Islands, Republic of Palau and American Territories in Guam and in American Samoa.

Disclosures: No disclosures provided by speaker

**Richard Truman, Ph.D**

Dr. Richard Truman has more than 30 years of experience in leprosy research and has lead numerous national and international study groups. He is the former Chief of the Laboratory Research Branch of the National Hansen’s Disease Program, and Principal Investigator of the Leprosy Research Support program of the National Institutes of Allergy and Infectious Disease. With his recent retirement from the U.S. Public Health Service, Dr. Truman now serves as an Adjunct Professor of Epidemiology at the Louisiana State University School of Veterinary Medicine.

Dr. Truman's primary research interests involve elucidation of leprosy transmission networks and the role of zoonotic reservoirs in perpetuating leprosy. He is an expert on animal disease modeling and molecular techniques used to monitor genetic variation in leprosy bacilli, diagnose the infection and assess drug susceptibility of various clinical isolates.

Disclosures: Stock: Celgene, Inc.; Research Grant: IDRI, LLC

**Hansen’s Disease in the United States Today**

This presentation will include leprosy cases in the United States. The unique clinical features of leprosy, the cardinal signs and the criteria for a presumptive diagnosis. The importance of early diagnosis and treatment to prevent disability. A treatment protocol for uncomplicated leprosy and frequent immunological complications of leprosy that can result in morbidity and disability.
Objectives:
1. Participants will learn the unique clinical features of leprosy, the cardinal signs and the criteria for a presumptive diagnosis
2. Participants will learn about frequent immunological complications of leprosy resulting in morbidity and disability
3. Participants will learn treatment protocols for uncomplicated leprosy, prevention of disability and management of the immunological reactions

Needs:
1. Advances in medical knowledge

References:

Core Competencies: 2, 3

Brad Glick, DO, FAOCD
Dr. Brad P. Glick, is a board-certified dermatologist and dermatologic surgeon practicing in Margate and Wellington, FL. Dr. Glick graduated from Emory University with a B.A. in chemistry and received his M.P.H. from the Emory University School of Public Health. He earned his D.O. degree with honors at Nova Southeastern University. His internship in internal medicine was performed at South Broward Hospital and his residency in family medicine was performed at Wellington Regional Medical Center and the Palm Beach County Public Health Unit in West Palm Beach, FL. Dr. Glick's dermatology residency training was performed at the Greater Miami Skin and Laser Center at Mount Sinai Medical Center, Miami Beach, FL, where he earned certificates in dermatologic, Mohs micrographic and laser surgery. Dr. Glick is a Diplomate of the American Osteopathic Board of Dermatology, American Osteopathic Board of Family Practice and National Board of Osteopathic Medical Examiners.

Dr. Glick has served as the Director of Dermatology Residency Training at Wellington Regional Medical Center and is the current director at Larkin Community Hospital/Palm Springs. He is Assistant Clinical Professor of Dermatology at the Herbert Wertheim College of Medicine at Florida International University. Dr. Glick has authored numerous publications including journal articles and textbook chapters. Dr. Glick is the Past President of the American Osteopathic College of Dermatology, President of the Foundation for Osteopathic Dermatology and Past President of the Broward County Dermatologic Society.

Psoriasis
Objectives:
1. Properly define psoriasis as a systemic disease
2. Identify specific comorbid conditions associated with psoriasis
3. Understand the current treatment algorithm for the management of psoriasis
4. Understand the mechanism of action of the latest psoriasis therapies

Needs:
1. New advances in dermatologic treatment
2. Availability of new medication(s) or indication(s)
3. Advances in medical knowledge

References:

Core Competencies: 2, 3, 4, 5, 6, 7

Disclosures: Speaker: Lilly, Abbvie, Jansen, Pfizer, Sanofi/Genzyme-Regeneron, Novartis; Advisor: Lilly
Dale Han, MD
Dale Han, MD, FACS is an Assistant Professor of Surgery in the Section of Surgical Oncology at Yale University. His clinical practice focuses on the treatment of melanoma and sarcoma. He earned his undergraduate and medical degrees through the Scholars for Medicine combined medical program at SUNY at Stony Brook. He completed his general surgery residency at the Hospital of the University of Pennsylvania and subsequently completed a surgical oncology fellowship at the Moffitt Cancer Center. He also completed post-doctoral research fellowships in surgical oncology at the Hospital of the University of Pennsylvania and at the Moffitt Cancer Center. His research interests are in clinical outcomes in patients with melanoma and sarcoma.

Desmoplastic Melanoma: Surgical Management and Adjuvant Therapy
This lecture will give an overview of the histologic subtypes of desmoplastic melanoma and will review treatment of primary disease, indications for sentinel lymph node biopsy and treatment of nodal disease, and adjuvant treatment options for desmoplastic melanoma.

Objective:
1. Review histologic subtypes of desmoplastic melanoma and treatment of primary disease
2. Review indications for sentinel lymph node biopsy and treatment of nodal disease for desmoplastic melanoma
3. Review adjuvant treatment options for desmoplastic melanoma

Needs:
1. Advances in medical knowledge

References:

Disclosures: No disclosures provided by speaker

David Herold, MD
Dr. David Herold is one of the few board-certified radiation oncologists in the country to have specialized in the treatment of skin cancer using therapeutic radiation. He has practiced both in general and specialty radiation oncology in Palm Beach County since 1999 and has served for over a decade as the Medical Director of Jupiter Medical Center Department of Radiation Oncology and the Palm Beach Cancer Institute - Center for Radiation Oncology.

Dr. Herold attained his undergraduate degree from Cornell University in Ithaca, NY. Prior to medical school, he spent a year studying psychology and neurophysiology at Oxford University in England. He attended the University College of Medicine in Gainesville, FL and completed his internship in internal medicine at Northwestern University – Evanston Hospital in Evanston, IL. Dr. Herold completed his radiation oncology residency training at the prestigious Fox Chase Cancer Center in Philadelphia, PA. He spent time during residency training to learn specialized radiation techniques with experts at MD Anderson Cancer Center in Houston, TX and Thomas Jefferson University Hospital and Children’s Hospital of Pennsylvania in Philadelphia. After serving as chief resident at Fox Chase Cancer Center, he began working in private practice at Jupiter Medical Center. Over the next fifteen years he established countless radiation oncology programs, protocols and treatment plans and diligently cared for hundreds of cancer patients. Dr. Herold pioneered the skin cancer program at Jupiter Medical Center and was responsible for all aspects of the radiation oncology program. He has refined the management of skin cancer treatment using advanced radiation techniques.

The Art of Radiotherapy in Skin Cancer Management
This lecture will begin with a history of the role of radiation in the dermatology office then discuss patient selection, treatment options and outline technologies currently available to deliver treatment in an office setting.

Objectives:
1. Review the historic role of radiation therapy in the field of dermatology
2. Understand how to select patients for radiation therapy compared with other skin cancer treatment modalities
3. Discuss currently available technologies to deliver radiation therapy in a dermatology office setting

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new technology
4. Advances in medical knowledge
5. Legislative, regulatory, or organizational changes effecting patient care

References:
1. NCCN Guidelines for BCC and SCC Management (www.NCCN.ORG/PROFESSIONALS/PHYSICIAN).

Core Competencies: 2, 3, 6

Disclosures: Honorarium: South Beach Symposium

Kate Holcomb, MD
Kate Holcomb, MD, FAAD, graduated from Tulane University School of Medicine in 2004 with the Mark Gibbs III graduation award. She was chief resident in dermatology at Saint Luke’s-Roosevelt Hospital Mount Sinai. During residency, Dr. Holcomb received the American Society of Dermatologic Surgeons Resident Scholarship two years in a row and the American Academy of Dermatology International Society Annual Meeting Travel Grant to Scotland. She served in the U.S. Navy to fulfill her commitment for the Health Professions Scholarship Program, working as a clinical professor and staff dermatologist for the National Capital Consortium Dermatology Residency at Walter Reed Army Medical Center in Washington, D.C. and the National Naval Medical Center in Bethesda, MD. She completed her service in 2012 and received an honorable discharge as a lieutenant commander.

Dr. Holcomb is a clinical assistant professor of dermatology at Tulane University School of Medicine since 2014 where she supervises the dermatology residents in cosmetic clinic. She also teaches the family medicine residents at East Jefferson Hospital. She actively participates in clinical studies on FDA clinical trials, as well as cosmetic products and procedures. She opened her own office, Pure Dermatology, in March 2017.

Dr. Holcomb is a member of the American Academy of Dermatology, American Society of Dermatologic Surgeons, American Acne and Rosacea Society, Skin of Color Society, North American Contact Dermatitis Society, Louisiana Dermatological Society and Women’s Dermatologic Society for which she has served on a number of committees.

How to Turn Your Acne, Rosacea, and Skin Checks into a Robust Aesthetic Business
This lecture is designed to encourage fellow dermatologists to offer products for sale in their practice to enhance their patient outcomes by having more control over the patient’s full skin regimen. This lecture is also designed to encourage those considering adopting aesthetic procedures that it can be done at any stage of practice.

Objectives:
1. Present reasons why we as dermatologists are the experts in all facets of skincare, including non-prescription topicals and aesthetic treatments
2. Suggest options for dispensing products in your office
3. Present methods of incorporating aesthetic procedures into your practice

Needs:
1. Availability of new medication(s) or indication(s)
2. Legislative, regulatory, or organizational changes effecting patient care

References:

**Core Competencies:** 3, 4, 5, 6

**Disclosures:** Speaker: Allergan, Galderma; Research Grant: Galderma

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**Mark Kaufmann, MD**

Mark Kaufmann, MD is a board-certified dermatologist and dermatologic surgeon. After graduating Alpha Omega Alpha from NYU’s School of Medicine, Dr. Kaufmann trained at the Hospital of the University of Pennsylvania, and the Albert Einstein College of Medicine, where he served as chief resident. He then completed a fellowship in dermatologic cosmetic surgery.

For the past 23 years, Dr. Kaufmann has been practicing all aspects of dermatology, and has been featured on Good Morning America, the New York Times, Wall Street Journal, and has appeared in Good Housekeeping and Shape magazines. He has published articles in both the Journal of the American Academy of Dermatology, as well as the Archives of Dermatology. He serves as an Associate Clinical Professor of Dermatology at the Mount Sinai School of Medicine, where he teaches residents in-training dermatologic surgery.

Dr. Kaufmann frequently lectures nationally and has been invited to be on the faculty for the annual meeting of the American Academy of Dermatology for the last eleven years. He also serves as a contributing editor, and is on the editorial boards of several dermatology journals. Dr. Kaufmann also sits on several committees for the American Academy of Dermatology and was recently elected to serve on the Board of Directors of the American Academy of Dermatology.

Dr. Kaufmann has been recognized as one of America’s Top Dermatologists by the Consumers’ Research Council of America, and is also a New York Superdoctor, as listed in a New York Times magazine supplement feature.

**Holy MACRA! Avoiding MIPS Penalties**

This lecture will provide attendees with a better understanding of the direction of healthcare reform, to review the important aspects of the MACRA legislation, and to learn how to easily avoid any MIPS penalties this year.

**Objectives:**
1. Understand the basis for healthcare reform
2. Understand the Quality Payment Program included in the MACRA legislation
3. Learn how to avoid MIPS penalties

**Needs:**
1. Development of new technology
2. Legislative, regulatory, or organizational changes effecting patient care

**References:**
1. Medicare Program, Merit-Based Payment System (MIPS) and Alternative Payment Model (AMP) Incentive Under the Physician Fee Schedule and Criteria for Physician-Focused Payment Models, 81 FR 77008. (final Rule Nov. 4, 2016).

**Core Competencies:** 3, 6, 7

**Disclosures:** Stock: Modernizing Medicine, Inc.

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**Ashfaq A. Marghoob, MD**

Dr. Ashfaq A. Marghoob is a board-certified dermatologist specializing in the diagnosis and treatment of cancers of the skin. He is the director of the Memorial Sloan-Kettering regional skin cancer clinic located in Hauppauge, Long Island. In addition to consulting and treating patients on Long Island, he also sees patients at the Memorial Sloan-Kettering outpatient facility in Manhattan.
Although, providing the best care possible for patients is his primary objective, he remains committed to education and research. Dr. Marghoob's belief is that improved efforts in educating physicians and the public regarding the importance of early skin cancer detection will translate into lives saved. His clinical research has led to the publication of numerous peer reviewed manuscripts and book chapters on topics related to skin cancer with an emphasis on melanoma, acquired melanocytic nevi, congenital melanocytic nevi and basal cell carcinoma. The focus of much of his research is on early recognition of skin cancer by utilizing imaging instruments such as photography, dermoscopy and reflectance confocal microscopy. He continuously explores the importance and significance of the clinical and dermoscopic morphology of cutaneous lesions. Although his research efforts are primarily focused on discovering ways to improve clinician diagnostic accuracy, he remains engaged in research aimed at deciphering the natural biology of nevi and melanoma with a particular interest in nevogenesis and melanomagenesis. Dr. Marghoob frequently lectures on all of the aforementioned topics both nationally and internationally.

**Dermoscopy Simplified: The TADA Algorithm**

This lecture will review a simplified method of using Dermoscopy to help diagnose skin cancer.

**Objectives:**

1. Recognize the key features to help diagnose seborrheic keratosis, angiomas and dermatofibromas with dermoscopy
2. Acknowledge the importance of entropy (distribution of colors and structures) in diagnosing skin cancer
3. Recognize and define the key dermoscopy features of malignancy

**Needs:**

1. New methods of diagnosis or treatment

**References:**

3. Wang SQ, et al; Differences in Dermoscopic Images from Non polarized Dermoscope; *Dermatologic Surgery* 2008; 34;1389-1395.

**Core Competencies:** 2, 3

**Disclosures: No disclosures provided by speaker**

**Tulane University Panel**

**Andrea Murina, MD**

Dr. Murina is board-certified in dermatology by the American Board of Dermatology. Dr. Murina completed her residency at Tulane University School of Medicine. She joined the faculty at Tulane University School of Medicine in 2012 where she practices general dermatology and participates in residency education.

**Disclosures: Speaker: Celgene, Abbvie, Novartis; Advisory Board: Celgene**

**Brittany Oswald Stumpf, MD**

Dr. Brittany Stumpf is board-certified in dermatology by the American Board of Dermatology. Dr. Stumpf completed her residency at Tulane University School of Medicine. She joined the faculty at Tulane University School of Medicine in 2009 where she practices general dermatology and participates in residency education.

**Disclosures: No disclosures provided by speaker**

**Laura Williams, MD**

Dr. Laura Williams, a board-certified dermatologist. She currently serves as a faculty member at Tulane University Medical School after working in a busy private practice in New Orleans for 12 years and recent work at St. Thomas Community Health Center. Dr. Williams received her undergraduate degree at Dartmouth College and returned to her native New Orleans for medical school and residency at Louisiana State University Health Sciences Center. She has a general dermatology practice treating patients of all ages with psoriasis, eczema, skin cancer, acne and other less common skin conditions. When not working, Dr. Williams enjoys spending time with her husband and three daughters, as well as gardening and playing tennis.

**Disclosures: No disclosures provided by speaker**
**Cases from the Crescent City: Dermatology Self-Assessment**

This session features case-based challenges and will involve assessment questions to test medical knowledge. The speakers will present diverse cases of skin disease with focus on clinical findings, histopathology, evaluation, diagnosis, and treatment.

**Objectives:**
1. Recognize clinical patterns of cutaneous disease
2. Utilize appropriate diagnostic tools and additional testing in the evaluation of internal disease
3. Treat skin diseases while also coordinating care with appropriate specialists

**Needs:**
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Advances in medical knowledge

**References:**

**Core Competencies:** 2, 3, 6

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**Michael Nowak, MD**

Dr. Michael Nowak is board-certified in anatomic and clinical pathology and dermatopathology. Dr. Nowak earned a Bachelor of Science degree from Xavier University, followed by a medical degree from Wright State University. After completion of an internship in internal medicine, he served as chief resident and cancer fellow at Western Reserve Care System where he completed a residency in anatomic and clinical pathology. Dr. Nowak finished his training in Providence, RI at Brown University, where he completed fellowship training in dermatology and dermatopathology.

After his training, Dr. Nowak joined Palm Beach Dermatology in 1999. He organized the development and staffing of Palm Beach Dermatology’s CLIA-certified diagnostic dermatopathology laboratory, where he serves as Medical Director. The laboratory is equipped with the latest technology and staffed with five ASCP-certified and state-licensed technologists who specialize in dermatology samples.

Dr. Nowak has authored over 15 articles in major medical journals on a variety of subjects including malignant melanoma, extramammary Paget’s disease, generalized pruritis and infectious diseases of the skin. He is also a member of the medical staff at Columbia Hospital in West Palm Beach, FL, where he conducts weekly teaching sessions with dermatology residents and has been awarded “Dermatology Attending of the Year” by his peers at the hospital. He is also a reviewer for the journal titled the *Physician and Sports Medicine*, and is on the editorial board for the journal *Postgraduate Medicine*. Resident lectures and review of journal articles ensures that Dr. Nowak stays current with the latest advances in the science of dermatopathology. Dr. Nowak’s practice is dedicated to the evaluation and diagnosis of skin pathology samples.

**BAP-oma and Beyond**

**Objectives:**
1. Discussion regarding the treatment of Bap-oma
2. Understanding the methods of diagnosis of Bap-oma
3. Discuss concepts and techniques used to treat Bap-oma

**Needs:**
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new technology
4. Advances in medical knowledge

**References:**

Core Competencies: 2, 3, 4, 6

Disclosures: Stock Holder: Modernizing Medicine

Nicole Rogers, MD
Dr. Nicole Rogers is a fellowship-trained hair transplant surgeon and board-certified dermatologist. She and her team of highly trained technicians have successfully treated hundreds of patients with hair loss using the most cutting-edge techniques. She graduated with honors from Harvard University and moved to New Orleans to attend Tulane Medical School. As a dermatology resident at Tulane she was chief resident and helped rebuild the training program after hurricane Katrina. She spent a year-long fellowship studying hair transplantation in Manhattan before returning to New Orleans to practice.

Dr. Rogers has written and spoken extensively about surgical and medical treatments for hair loss, including contemporary techniques in hair transplantation, minoxidil, finasteride, and the use of low-level light therapy for hair growth. She has co-edited two textbooks on hair transplantation, and has written numerous chapters for other textbooks on hair loss and hair transplantation. Since starting practice, she has been featured in television, radio, newspaper, internet, and magazine reports discussing surgical, medical, and cosmetic approaches to thinning hair.

Dr. Rogers is the recent Past President of the Louisiana Dermatologic Society. She is also an Assistant Clinical Professor at Tulane’s Department of Dermatology, where she teaches the residents about hair and scalp disorders. She is a contributing editor for the Journal of Dermatologic Surgery, and serves advisory roles for the International Society of Hair Restoration Surgery, the Cicatricial Alopecia Research Foundation and the Louisiana State Board of Electrolysis Examiners. She has a passion for treating all forms of hair loss using the most up-to-date medical and surgical techniques.

Updates in the Medical & Surgical Treatment of Hair Loss

Objectives:
1. Understand and identify the various causes and etiology of hair loss
2. Understand and identify treatments and/or therapies for hair loss
3. Understand and determine hair transplantation as a treatment for hair loss and when it is appropriate

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) and indication(s)

References:
1. 4th ed. Hair Transplantation, Unger, pgs. 516-524.
2. 5th ed. Hair Transplantation, Unger, pg. 37.
3. ISHRS.org, hair foundation.org.

Core Competencies: 2, 3, 4, 5, 6

Disclosures: No disclosures provided by speaker

Les B. Rosen, MD
Dr. Les Rosen is a board-certified dermatopathologist, who has been practicing dermatopathology for 30 years. He is nationally recognized as one of the top dermatopathologist in the country. He completed his dermatopathology fellowship and anatomic and clinical pathology residency both at Mount Sinai Medical Center in Miami Beach, FL and received his medical degree from the State University of New York Downstate in Brooklyn, NY.

Dr. Rosen is actively involved in resident training. He teaches monthly to the residents at the University of Miami, Louisiana State University and Tulane University to help in their dermatopathology training, as well as other regional review courses in Florida and Oregon. This covers programs in Pennsylvania, Ohio, Indiana and Illinois.
This lecture will review dermatopathology topics and case discussions.

Objectives:
1. Review the fundamentals of dermatopathology
2. Discuss the key histological features of common and uncommon skin conditions
3. Demonstrate the relationship between the clinician and dermatopathologist

Needs:
1. New methods of diagnosis or treatment

References:

Core Competencies: 2, 3

Disclosures: No disclosures provided by speaker

Merrick I. Ross, MD
Merrick I. Ross, MD, is Professor of Surgery and Chief of the Melanoma Section in the Department of Surgical Oncology at the University of Texas M.D. Anderson Cancer Center in Houston, Texas.

He received his medical degree from the University of Illinois School of Medicine in Chicago, completed a residency in general surgery at the University of Illinois Affiliated Hospitals in Chicago, and was administrative chief resident at the University of Illinois Department of Surgery. Additionally, Dr. Ross served a research fellowship at Scripps Clinic and Research Institute in La Jolla, CA, and completed both an administrative and a surgical oncology fellowship at the University of Texas M.D. Anderson Cancer Center.

Dr. Ross is well-published in medical literature and lectures extensively both domestically and abroad. He has also been the recipient of various awards, including the Charles M. McBride Distinguished Professorship in Surgical Oncology.

Surgical Approach to Melanoma

Objectives:
1. Update on different surgical approaches in the treatment of melanoma
2. Recognize the use of different surgical techniques in the treatment of melanoma

Needs:
1. New methods of diagnosis or treatment
2. Advances in medical knowledge

References:

Core Competencies: 2, 3, 5, 6

Disclosures: Ad Board Member: Merck, Amgen, GSK; Consultant: GSK; Speaker: Proventus
Suzanne Sirota Rozenberg, DO, FAOCD

Dr. Suzanne Sirota Rozenberg is a board-certified dermatologist practicing in Woodmere, NY. She earned her Doctor of Osteopathic Medicine degree at New York College of Osteopathic Medicine in 1988. After medical school, she completed both an internship and residency in family practice at Peninsula Hospital Center in Far Rockaway, NY, in 1992. She has been board certified in family medicine since then. She then practiced for the next ten years with her brother and father. From 2002-2005, she trained in the dermatology residency program at St. John's Episcopal Hospital in Far Rockaway, where she now serves as Program Director. She served as Associate Director of Medical Education from 2005-2012. She is a Clinical Associate Professor at TouroCOM and LECOM. She has a full-time dermatology practice as well.

Dr. Rozenberg’s memberships include the AOA, ACOFP, AOCD and AAD. She is a Past President of the AOCD and the ACOFP-NYS Chapter. She served on the AOCD Board of Trustees from 2008-2015, holding the positions of Trustee, Vice President and President. She represents the AOCD on the Program and Trainee Review Council of the AOA. She has been the AOCD Delegate and the New York State Delegate to the AOA House of Delegates. She has served on the AOCD Education Evaluating Committee since 2009. For her years of service to the AOCD, Dr. Rozenberg has earned the title of Fellow of Distinction. She is a member of the AAD Ad Hoc Task Force for Osteopathic Dermatology Recognition and an NBOME POCKET member. Dr. Rozenberg lectures locally and nationally, speaking at meetings of the AOCD, EROC, ROC-NY and the New York State Chapter of ACOFP. In addition to dermatology, she is board-certified in family practice and sclerotherapy.

Disclosures: Speaker: Valeant

Amy Spizuoco, DO, FAOCD

Dr. Amy Spizuoco is a board-certified dermatologist and dermatopathologist. She received her Bachelor of Arts at SUNY Binghamton with a double major in Italian and biology. She earned her medical degree at New York College of Osteopathic Medicine. She completed a medical internship at Lutheran Medical Center. She then went on to Alta Dermatology Residency Program in Mesa, AZ, where she spent a year researching reflectance confocal microscopy and subsequently completed her dermatology residency, serving as chief resident her final year. During residency she received training at the Mayo Clinic Scottsdale, as well as Phoenix Children’s Hospital. After residency, Dr. Spizuoco completed a fellowship in dermatopathology. Currently, Dr. Spizuoco is a member of the American Academy of Dermatology, the American Osteopathic College of Dermatology, the American Society for Dermatopathology, the American Society of Mohs Surgery, the American Society for Dermatologic Surgery, the New York State Osteopathic Medical Society, the Women's Dermatologic Society and the Dermatologic Society of Greater New York.

Disclosures: Speaker: Pfizer

The 5th Dimension: All Inclusive Aspects of Osteopathic Medicine in Dermatology

This lecture will be case based studies.

Objectives:
1. Review traditional medical treatments for dermatological conditions and non-traditional treatments
2. Review the basic concepts of osteopathic philosophy and its application to dermatology
3. Enhance the complete and multifactorial approach to dermatology

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge

Reference:

Core Competencies: 1, 2, 3, 4, 5, 6
Sean Stephenson, DO, FAOCD
Dr. Sean Stephenson is a board-certified dermatologist and dermatopathologist. Dr. Stephenson received his Bachelor of Business Administration degree from the University of Michigan, graduating magna cum laude. He earned his medical degree from Michigan State University College of Osteopathic Medicine. He completed a traditional rotating internship at University Hospital Health Systems in Richmond Heights, OH. Dr. Stephenson completed his residency in dermatology at O’Bleness Memorial Hospital in Athens, OH. Following his dermatology residency, Dr. Stephenson completed a dermatopathology fellowship at the Ackerman Academy of Dermatopathology in New York, NY.

Select Dermatopathology Topics for the Practicing Dermatologist
The lecture will be covering topics that are pertinent to the practicing dermatologist.

Objectives:
1. Discuss changes to the new AJCC staging guidelines for Melanoma
2. Discuss the genetics and genetic testing of melanocytic neoplasms
3. Discuss the controversy of re-excising dysplastic nevi

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Advances in medical knowledge

References:

Core Competencies: 2, 3, 6

Disclosures: Off-Label or Investigational Use: Melanoma Decision Rx, Serum S100B

Lisa Swanson, MD
Dr. Swanson is a board-certified dermatologist. She was born in New Orleans, LA and raised in Scottsdale, AZ. She attended college at the University of Colorado at Boulder, graduating with honors as an English major. After that, she obtained her medical degree from Tulane University School of Medicine in New Orleans. She performed her internship at Mayo Clinic in Scottsdale, AZ and went on to complete her dermatology residency at Mayo Clinic in Rochester, MN. She completed a fellowship in pediatric dermatology at Phoenix Children’s Hospital in Arizona.

Feel the Burnout
The lecture will cover burnout in all facets – What it is, why it happens, and how to manage it.

Objectives:
1. Understand why burnout happens
2. Understand what burnout is
3. Understand how to manage/prevent burnout

Needs:
1. Advances in medical knowledge
2. Legislative, regulatory, or organizational changes effecting patient care

References:
Core Competencies: 2, 3, 4, 5, 6, 7

**Updates in Pediatric Dermatology**
This lecture will provide synopsis of what is new in the diagnosis & treatment of kids with skin disease.

**Objectives:**
1. Understand the impact of atopic dermatitis and ways to manage it
2. Learn about new treatments for pediatric dermatology issues
3. Know how to manage common pediatric dermatology conditions

**Needs:**
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)
4. Advances in medical knowledge
5. Legislative, regulatory, or organizational changes effecting patient care

**References:**

Core Competencies: 2, 3, 4, 5, 6, 7

*Disclosures: Speaker: Amgen, Promius, Aqua, Valeant, Bayer; Advisory Board: Sanofi-Regeneron, Allergan*

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**Edward H. Yob, DO, FAOCD**
Dr. Edward Yob is board certified by the American Osteopathic Board of Dermatology in dermatology with a certificate of added qualification in Mohs micrographic surgery. Dr. Edward Yob received his medical degree from the Philadelphia College of Osteopathic Medicine and completed his residencies at the United States Air Force Regional Hospital and Boston University/New England Medical Center.

His practice is limited to the diagnosis and treatment of skin cancers. He is a clinical associate professor at the University of Oklahoma Health Sciences Center, Department of Dermatology.

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**Practical Pearls in Dermatologic Surgery**
This lecture will content will consist of a collection of tips and pearls useful in the practice of dermatologic surgery.

**Objectives:**
1. Encourage discussion on practical tips useful in dermatologic surgery
2. Renew tips used to aid the dermatology surgeon in treatment of patients
3. Discuss concepts and techniques that increase patient safety and comfort

**Needs:**
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Availability of new medication(s) or indication(s)

**References:**

Core Competencies: 2, 3, 4, 6

*Disclosures: No disclosures provided by speaker*
Wednesday, October 25, 2017

8:00 a.m. - 12:00 p.m.  Exhibitor Set Up
9:00 a.m. - 12:00 p.m.  Board of Trustees Meeting
12:00 p.m. - 1:00 p.m.  Registration/Lunch
1:00 p.m. - 2:00 p.m.  *Practical Pearls in Dermatologic Surgery*  
Edward H. Yob, DO, FAOCD
2:00 p.m. - 3:00 p.m.  *Osteopathic Continuous Certification Update*  
Lloyd Cleaver, DO, FAOCD
3:00 p.m. - 5:00 p.m.  *Dermatopathology Jeopardy*  
Les B. Rosen, MD, Dermpath Diagnostics
Thursday, October 26, 2017

6:30 a.m. - 7:30 a.m.  
*Introducing the First-In-Class Novel Biologic That Selectively Blocks Interleukin-23*  
Erin Boh, MD, PhD  
Janssen Biotech, Inc. Product Theater (No CME Awarded)

7:30 a.m. - 8:00 a.m.  
Morning Coffee with Exhibitors

8:00 a.m. - 9:00 a.m.  
*Updates in the Medical & Surgical Treatment of Hair Loss*  
Nicole Rogers, MD

9:00 a.m. - 10:00 a.m. 
*How to Turn Your Acne, Rosacea, and Skin Checks into a Robust Aesthetic Business*  
Kate Holcomb, MD

10:00 a.m. - 10:30 a.m.  
Break with Exhibitors

10:30 a.m. - 12:30 p.m.  
*The 5th Dimension: All Inclusive Aspects of Osteopathic Medicine in Dermatology*  
Suzanne Sirota Rozenberg, DO, FAOCD & Amy Spizuoco, DO, FAOCD

12:30 p.m. - 1:30 p.m.  
*Clinical Insights on Taltz*  
Bradley Glick, DO, MPH, FAOCD  
Lilly USA, LLC Product Theater (No CME Awarded)

1:30 p.m. - 4:30 p.m.  
*Hansen's Disease in the United States Today*  
Capt. John Figarola, MA, LOTR, CHT; Barbara M. Stryjewska, MD & Richard W. Truman, Ph.D

5:00 p.m.  
Reception
How to turn your Acne, Rosacea, and Skin Checks into a Robust Aesthetic Business

Kate Zibilich Holcomb
Pure Dermatology, Metairie Louisiana
Assistant Clinical Professor Dermatology, Tulane University School of Medicine
Assistant Clinical Professor Family Medicine, East Jefferson General Hospital

AOCD October 26, 2017

Disclosures
- Allergan: Speaker, advisory board
- Galderma: Investigator, speaker, advisory board
- Cutera: Speaker

ASDS Consumer Survey 2017
- The percent of consumers considering a cosmetic medical procedures has doubled in the last five years.
- 7/10 respondents said they are considering a cosmetic treatment
- Dermatologists ranked as the No.1 Influencer on the decision to have a cosmetic procedure each year.
  - Dermatologist 50%
  - Friends: 49%
  - Primary Care Physician: 34%

- Injectables and laser treatments continue to increase 2-4% since 2015
- EXCEPTIONS
  - Laser Hair Removal
  - Non-dissolvable fillers (PLLA, CaHA, etc.)

Statistics on Acne
- 40-50 million Americans
- 1 out of 3 women in 30’s
- 1 out of 4 women in 40’s
- #1 complaint in skin of color, #2 in Caucasians
- 13 products tried before coming to dermatologist

Statistics on Rosacea
- 16 million Americans
- 45% in 30’s and 40’s
- >50% over 50
- EOB United health

- Cash pay alternatives for medical derm

- Finding happiness and pleasure in our work

**Steps to developing 6 P's**

- Perfect
- Participate
- Products
- Purge
- Partner
- Promote

**Perfect**

- Aesthetics is an art
- Delegation removes EXPERT!
- We have years of training on anatomy and subtle skin changes
- We are the major influencers of patients in making a decision about treatments
Participate

- Patients want to know your experience
  - Your network
- Office staff are best advertisement and support
- Treating patients not friends
  - Photos
  - Expand social circle

Products

- Too many choices for patients
- They are coming to us for guidance
- Control of outcomes

Purge

- Comparison of tiered pricing
- Products that don’t move
- Poor support
- Single company OK

Partner

- Local vs. national companies
- Events
- Samples
- Help selling
- Speaking/Ad boards

Promote

- Branding
- Social media
- Advertising by area
- Teaching and lecturing

Personal Growth

- Perfect
- Participate
- Products
- Purge
- Partner
- Promote
Thank you!
A Multifactorial Case-Based Approach to Medical Dermatology

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Objectives

- Comprehensive approach to Medical Dermatology
- Review Osteopathic Tenets and Philosophy
- Review Case-Based approach to Medical Dermatology
- Review current medical treatments
- Review multifactorial modalities to treatment

Osteopathy in Dermatology

Cases

- Burning mouth syndrome
- Herpes Zoster
- Post herpetic neuralgia
- Notalgia Paresthetica
- Brachioradialis pruritis
- Vulvodynia
- Lipodermatosclerosis
- Elephantiasis Nostra Verrucosa
- Stasis Dermatitis
- Hyperhidrosis

Burning mouth syndrome

- Chronic pain syndrome characterized by burning or stinging feeling affecting the oral mucosa in the absence of clinically detectable signs.
- Triad: chronic, unremitting pain, dysgeusia and xerostomia.
- Current treatments include antidepressants, antipsychotics, antiepileptics and analgesics.
- Trigeminal nerve dysfunction or hypo-functioning of the PNS may be possible areas of treatment.

Current Medical Treatment

- Tricyclic antidepressants
- Benzodiazepines
- Anticonvulsants
- Capsaicin
Pemphigus Vulgaris

Mucocele

Cheilitis
OMT

- Sphenopalatine ganglion release – using Myofascial release

Herpes Zoster Infection

- Viral infection due to Varicella Zoster Virus (HHV3)
- Airborne droplets are the usual route of transmission
- The incubation ranges from 11-20 days
- The virus replicates in the affected dorsal root ganglion and produces painful ganglionitis. Neuron inflammation and necrosis can result in a severe neuralgia that intensifies as the virus spreads down the sensory nerve.
- Typically resolves without sequelae; however, the most common complication is post-herpetic neuralgia that persist after the skin lesions have healed.
VZV clinical findings

**Herpes Zoster**
- Vesicular
- Ballooning degeneration
- Acantholysis
- Slate grey nuclei
- Homogenous/Eosinophilic cytoplasm

**3 Ms**
- Molding
- Multinucleation
- Margination
- Intranuclear inclusion bodies

Clinical findings related to dermatome involved

**Hutchinson's sign**

**Ramsay Hunt Syndrome**

**Cervical spine**

**Thoracic spine**

**Lumbar spine**

**Folliculitis**
- Superficial and deep infiltrate
- Bottom heavy
- Necrotic follicle
Current pharmacologic therapy

- Antiviral agents
  - Acyclovir, valcyclovir, Famcyclovir
- Oral corticosteroids
- Anti-inflammatory agents
  - Oral and topical options
- Opioids
- Botulinum Toxin injections
- Complementary treatment including honey, capsaicin, and lidocaine
- Anti-depressants
  - Tricyclic, anticonvulsants,
OMT in VZV
- Can be use as adjuvant therapy after acute phase to help prevent post herpetic neuralgia
- Suboccipital decompression to normalize the PNS
- Muscle energy to upper thoracic and cervical regions
- Rib raising to normalize the sympathetic nerves

Brachioradial Pruritus
- Neurogenic pruritic condition between the wrist and elbows
- Unknown etiology
- Unilateral or bilateral excoriations
- Common in fair skinned, affluent, and middle-aged people in sunny climates
- Scratching makes the symptoms worse
- Exacerbated by sun exposure
- Ice packs usually helps the itch

Brachioradial Pruritus treatment
- Cervical nerve block
- Acupuncture
- Injections with botulinum toxin A
- Topical mixture of amitriptyline hydrochloride 1.0% ketamine hydrochloride 0.5% and vanicream applied 2-3 times per day
- Aprepitant, a neurokinin-1 inhibitor

OMT
- Patients have altered sensation in the distribution of the posterior cutaneous nerve of the arm that supplies the skin over the brachioradialis muscle
- Corresponds to C5-C8
- Presence of a cervical rib or cervical nerve root impingement may contribute to altered cutaneous sensation
- Treatment of cervical arthritis and cervical spine manipulation provides relief
OMM techniques

Muscle energy

Counterstrain

- Tender point arises when abnormal muscle tone is maintained through an inappropriate strain reflex.
- Passively placing the patient into a position of ease, allows for resetting of the neural components involved in the strain reflex.
- Normal resting tone is achieved, resulting in balance in the muscular system, skeletal system, neural and vascular systems.

Counterstrain points

Notalgia Paresthetica

- Uncommon pruritic condition seen most commonly in middle aged women
- Unknown etiology
- Affecting mainly the interscapular region (especially the T2-T6 dermatomes)
- OMT may decrease the sensation of neuropathic pain/itch

Notalgia Paresthetica

Complementary Treatments

Successful Treatment of Notalgia Paresthetica With Botulinum Toxin Type A

Pamela Kischer Weinfield, MD

OMM techniques

Treatments include:
- Muscle energy
- HVLA
- Chapman’s points
- Counterstrain

Macular Amyloid

Chapman’s Points

Vulvodynia
- Burning vulvar discomfort, with increased pelvic floor muscle tonicity
- Irritation, itching, pain, rawness, allodynia, hyperalgesia, and dyspareunia
- Possible due to nerve compression and/or myofascial hypertonicity
- DNA polymorphisms, peripheral and central neuropathic processes, nerve compression, increased density of C-afferent nociceptive fibers in the vestibular mucosa as possible pathogenesis.

Treatment options
- Topical medications such as lidocaine ointment
- Drug therapy: pain relievers, antidepressants, or anticonvulsants
- Biofeedback therapy
- Physical therapy to strengthen the pelvic floor musculature
- Injections of steroids or anesthetics
- Surgery to remove the affected skin and tissue in localized areas
- Relaxation techniques, massage therapy, homeopathy, acupuncture.

Syphilis
Condyoma Accuminata

Verruciform Xanthoma

Verruciform Xanthoma

Verruciform Xanthoma

Bowenoid Papulosis

Bowenoid Papulosis
**Bowenoid Papulosis**

**OMT**
- Trigger points of the levator ani muscles
- Pelvic diaphragm release
- Counterstrain

**Stasis Dermatitis**
- Common condition seen in older patients with cardiac insufficiency and venous incompetence
- Due to gravity and increased hydrostatic pressure leading to leaky vessels
- Hemosiderin deposits in the skin of lower extremities causing hyperpigmentation
- Lymphatic pump/effleurage may decrease edema and thus improve condition and decrease the incidence of venous stasis ulcers
Stasis Dermatitis

- Marked edema of affected extremity secondary to severe lymphadema or venous insufficiency
- Results in cutaneous changes: hyperkeratotic verrucous plaques
- Treatment is challenging
- Patients benefit from lymphatic pumping and effleurage

Osteopathic manipulation in Elephantiasis Nostras Verrucosa

Medical management
- Support stockings (knee high, 20-30 mmHg pressure)
- Leg elevation
- Topical steroids
- Compresses if weeping
- Unna boot
- Surgery

Erythema Nodosum
Lipodermatosclerosis

- Also known as sclerosing panniculitis
- Acute phase – painful, symmetric, red to purple, poorly demarcated, indurated plaques in a stocking like distribution.
- Exact pathogenesis remains unknown, possible static blood in lobular capillaries ultimately leading to pannicular ischemia, fat necrosis and fibrosis.
- Tx similar to stasis dermatitis, can add manual stretching to help the fibrosis

DDX

- Morphea profunda
- Scleroderma
- Acrodermatitis chronica atrophicans

Medical Management

- Compression therapy
- Stanozolol
- Pentoxifylline
- Superficial venous surgery
- Antibiotics
- ILK
- Foam sclerotherapy
- Danazol
Complementary therapies


Refractory lipodermatosclerosis treated with intralles platelet-rich plasma.

Jeong KH, Shin MK, Kmn Ni.
Hyperhidrosis

- Affects 0.6 to 1% of western population
- Excessive function of the sweat control system typically affecting palms, axilla and soles
- Primary
- Secondary
  - Cancer, endocrine dysfunction, infections and medications
- OMM Findings:
  - T2-T3 dysfunction

Pathogenesis

Current treatment options

- Topical aluminum chloride hexahydrate
- Topical anticholinergics
- Oral anticholinergics
- Iontophoresis
- Botulinum A neurotoxin
- Liposuction and surgical excision (axilla)
- Sympathectomy

OMT

- Rib raising
- Occipital release
- Cranial manipulation
Rib raising technique

Conclusions

- Multifactorial approach to medical dermatology
- Think “outside the box”
- Osteopathic manipulation has definite benefits to dermatology patients

References:

14. Weinfield PK. Successful treatment of Notalgia Paresthetica with botulinum toxin type A. The Cutting Edge. 2007; August
6:30 a.m. - 7:30 a.m.  
Cosentyx® (secukinumab): A Comprehensive Approach to Treating Moderate to Severe Plaque Psoriasis  
Dr. Eric William Baum  
Novartis Product Theater (No CME Awarded)

7:30 a.m. - 8:00 a.m.  
Morning Coffee with Exhibitors

7:30 a.m. - 8:00 a.m.  
CLIA Proficiency Exam  
Gregory Papadeas, DO, FAOCD

8:00 a.m. - 9:00 a.m.  
The Art of Radiotherapy in Skin Cancer Management  
David Herold, MD

9:00 a.m. - 11:00 a.m.  
Cases from the Crescent City: Dermatology Self-Assessment  
Tulane University Panel  
Andrea Murina, MD; Brittany Oswald Stumpf, MD & Laura Williams, MD

11:00 a.m. - 12:00 p.m.  
Feel the Burnout  
Lisa Swanson, MD

12:00 p.m. - 12:30 p.m.  
Break with Exhibitors

12:30 p.m. - 1:30 p.m.  
A Novel Nonsteroidal Topical Prescription for Mild-to-Moderate Atopic Dermatitis  
Bradley Glick, DO, MPH, FAOCD  
Pfizer Product Theater (No CME Awarded)

1:30 p.m. - 2:30 p.m.  
Adherence to Treatment  
Steve Feldman, MD

2:30 p.m. - 3:00 p.m.  
Break with Exhibitors

3:00 p.m. - 4:00 p.m.  
Skin Cancer Horse  
Neal Bhatia, MD

4:00 p.m. - 5:00 p.m.  
Holy MACRA! Avoiding MIPS Penalties  
Mark Kaufmann, MD

5:00 p.m. - 6:00 p.m.  
Bureaucracy and Burnout Panel  
Neal Bhatia, MD; Mark Kaufmann, MD; Andrea Murina, MD & Lisa Swanson, MD
Cases from the Crescent City
Andrea Murina MD FAAD
Associate Professor of Dermatology
Tulane University School of Medicine

DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY
Andrea Murina MD FAAD

DISCLOSURES
Celgene: Advisory Board – Honoraria
Abbvie, Celgene, Novartis- Speaker – Honoraria
Regeneron: Investigator – Grants

How to respond
• Text messaging:
  TEXT
  To phone number: 22333
  Message: ANDREAMURINA104 OR
  • Online
  • Join the poll @ pollev.com/andreamurina104

TEST QUESTION
1. The most likely diagnosis is:
   • The most likely diagnosis is:
     A. Disseminated gonorrhea
     B. Meningococcemia
     C. Erythema multiforme
     D. Rocky Mountain Spotted fever
     E. Syphilis
1 Disseminated gonorrhea

- The answer is disseminated gonorrhea.
- Hematologic spread of the N. gonorrhea causes:
  - arthritis-dermatitis syndrome or
  - localized septic purulent arthritis without skin lesions.

Louisiana Dermatological Society Meeting: New Orleans, April 16, 2016

Disseminated Gonorrhea

- Diagnosis: Culture from the primary infected mucosal site: urethra, cervix, oropharynx, or rectum.
- Cultures of the joints, skin lesions, and blood are less likely to isolate the bacteria.
- Tx: Ceftriaxone 1 g IM or IV every 24 hours PLUS Azithromycin 1 g orally in a single dose then oral agent x 7 days


Louisiana: 1st (221.1 per 100,000 persons).

2

A 44-year-old male with history of renal transplant complains of new onset skin colored growths on his face and hands. Histopathology shows a bluish and bubbly cytoplasm. His skin condition increases his risk of which of the following cutaneous infections?

a. Candida
b. Epstein Barr virus
c. Herpes virus
d. Human papilloma virus
e. Molluscum contagiosum

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d. Human papilloma virus
e. Molluscum contagiosum
Epidermodysplasia Verruciformis (EDV)

- The answer is D, human papilloma virus (HPV).
- The genetic defect in EDV is caused by a truncating mutation in the genes EVER1 and EVER2.
- This allows beta-HPV types, which lack E5, to become pathogenic.
- H&E: keratinocytes have large perinuclear halos and blue-gray cytoplasm.

Histopathology

- A 53-year-old female presented with a 5-year history of skin lesions that have been slowly spreading and increasing in size. Review of systems was positive for weight loss, chronic fatigue, and lower extremity weakness.
- Punch biopsies were performed and the histopathology and Fite stain are shown above. This disease is associated with:
  - A. Abnormal chest x-ray
  - B. Atypical lymphocytes on flow cytometry
  - C. Decreased sensation in the lower extremities
  - D. Elevated aldolase levels
  - E. Joint pains in the hands and feet

Lepromatous leprosy

- The answer is C, decreased pain sensation in the lower extremities.
- Infection caused by Mycobacterium leprae.
- Peripheral nerve damage is one of the most common findings.

Cuataneous Leprosy

- Tuberculoid (paucibacillary)
  - Asymmetric
  - Few hyperpigmented or hypopigmented macules with loss of sensation
  - Swelling of peripheral nerves
- Lepromatous (multibacillary)
  - Symmetrical
  - Multiple skin lesions: nodules, plaques
  - Nasal mucosa involvement: congestion, nosebleeds
  - Anesthesia in a stocking-glove distribution
Leprosy in the US

• 178 new cases reported in 2015
• 72 percent (129) of new cases were reported by Arkansas, California, Florida, Hawaii, Louisiana, New York and Texas
• Diagnosis: Skin or nerve biopsy

A 25-year-old otherwise healthy woman presents with a two-week history of painful nodules on her lower leg, as shown in the image below.

She mentions that lesions developed several days after receiving a pedicure.

Which of the following Mycobacterial species do you suspect caused this infection?

a. M. leprae
b. M. ulcerans
c. M. kansasii
d. M. fortuitum
e. M. bovis

Cutaneous Mycobacteria

The answer is D. M. fortuitum.

The occurrence of rapidly growing mycobacterial infections after nail salon pedicures has been well documented in the literature.

• Mycobacterium fortuitum
• Mycobacterium chelonae

Skin microtrauma due to shaving has been identified as a risk factor for disease.

• Tattooing is another risk for exposure.


A 23 year old male with past medical history of HIV is evaluated for papules on the face for 3 months. They are non pruritic and asymptomatic. What is the most likely causative organism?

A. Herpes simplex virus
B. Varicella virus
C. Parapox virus
D. Propionibacterium acnes
E. Malassezia furfur

The answer is C parapox virus (MC) in an HIV patient.

In patients with HIV, MC can indicate advancing immunosuppression and can be difficult to treat.
5  Herpes simplex

- The answer is D, Valacyclovir.
- The patient was confirmed to have an atypical presentation of HSV-2 infection.
- In patients with low CD4 counts, vesicles can be transient, leaving ulcerated, crusted and necrotic lesions.
- Pain, active vesicular border and a scalloped periphery are clues to HSV infection.
- The presence of multinucleated keratinocytes on histopathology are the key to the diagnosis of herpes infection.


Louisiana Dermatological Society Meeting September 2015.

7

- A 47 year old male with HIV/AIDS (CD4 count-3) presents to the ED with an ulcer on the penis and scattered umbilicated papules on the face, trunk and extremities with hemorrhagic and necrotic centers.
- There is a penile ulcer and several white papules on the penile shaft. You perform a KOH and biopsy of the penile ulcer. What is your diagnosis?
What is your diagnosis?

a. Blastomycosis
b. Cryptococcus neoformans
c. Histoplasma capsulatum
d. Molluscum contagiosum
e. Treponema Pallidum

The answer is B, Cryptococcus neoformans.

The patient had disseminated Cryptococcus, which is an opportunistic infection that can involve the CNS, bone, and visceral organs.

It is the fourth most common opportunistic infection in AIDS patients (CD4 counts <100).

Cutaneous manifestations of infection vary from molluscum contagiosum like papules, ulcerations, cellulitis, and herpetiform lesions.

Diagnosis:
- Culture of CSF, sputum, urine, and blood
- Fixed tissue staining
  • Mucicarmine
  • Fontana-Masson
- Serum and CSF testing for cryptococcal antigen

Tx: Flucyosine + Fluconazole

A 44-year-old male is evaluated in your clinic for a 2-day history of pruritic rash on the face, chest, and back. The patient reports generalized malaise and subjective fevers and chills overnight. Photograph of the patient is shown. Of the following, the most appropriate in-office test to perform is:

A. Aerobic culture
B. Gram stain
C. KOH prep
D. Scabies prep
E. Tzanck smear

The best answer is E, Tzanck smear.

Pink papules and vesicles of various stages.

On Tzanck smear, the characteristic finding for herpetic infections is acantholytic and multinucleated keratinocytes.

In one study, the sensitivity and specificity of this cytologic finding for herpetic infections were 84.7% and 100%, respectively.

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9. What is the best next test?

A. Skin culture
B. Pharyngeal culture
C. Patch test
D. KOH prep
E. Scabies prep

9. Staphylococcal Scalded Skin Syndrome
- Tender flaccid bullae
- Hematogenous spread of exfoliative toxin (ETA and ETB) which cleave desmoglein 1
- Leads to disruption at the granular layer
- Positive cultures come from conjunctiva, oropharynx, feces
- Treat with Dicloxacillin, Cephalexin

10. A 72 year old female with a history of CLL status post stem cell transplant is evaluated for this lesion on the right thigh. Biopsies for H&E are show. What is the most likely diagnosis?
A. Bullous pemphigoid
B. Calciphylaxis
C. Bullous impetigo
D. Mucormycosis
E. Vibrio vulnificus

11. Cutaneous Mucormycosis
- Rhizops, Mucor, Absidia
- Characterized by necrotic skin lesions
- Risk factors are diabetes mellitus and immunosuppression
- Broad non septate hyphae with 90° branching
- Primary infection: direct inoculation
  - patients with burns or other forms of local skin trauma.
- Secondary cutaneous: hematogenous spread
  - painful cellulitis to an ulcer with black eschar.

11. This skin disease often involves:
11. This skin disease often involves:
A. Brain
B. Eyes
C. Kidneys
D. Muscle
E. Salivary glands

Dermatomyositis

• The answer is muscle.
• The photographs show a patient with dermatomyositis.
• Autoimmune connective tissue disease that can present as a proximal extensor inflammatory myopathy.

Key Points to Dx:
- Photo-Distribution
- Poikiloderma
- Heliotrope
- Gottron’s
- Mottled Pigmentation
- Cuticular Dystrophy

12. This 68-year-old male with a past medical history of polycythemia vera for 15 years presents with a new onset rash. Which drug is responsible for his skin eruption?

Drug induced dermatomyositis

• The answer is hydroxyurea, which a known cause of drug induced dermatomyositis.
• Others are phenytoin, penicillamine, statins, phenylbutazone, tegafur, and TNF alpha inhibitors.

This 20-year-old female is evaluated in your office for this new rash on the trunk and extremities.

Histopathology shows urticarial vasculitis.

She has a low CH50 and low C1q.

Which disease is most likely related?

a. Allergic rhinitis
b. Crohn's disease
c. Dermatomyositis
d. Systemic lupus erythematosus
e. Ulcerative colitis

The answer is Systemic lupus erythematosus.

Hypocomplementemic urticarial vasculitis (HUV) is associated with systemic symptoms including:

- musculoskeletal,
- pulmonary,
- ocular,
- renal manifestations,

Associated disease include:

- SLE,
- Sjogren's syndrome,
- celiac disease,
- rheumatoid arthritis,
- autoimmune thyroiditis, and
- Type 1 diabetes mellitus.

Williams, J et al. Anaphylaxis and urticaria. Immunology and Allergy Clinics of North America. 35 (1); 199 -219


Type of Chronic Cutaneous Lupus

- Acute CLE: Butterfly rash
- Subacute CLE: Polyscopic plaques / papulosquamous papulisform
- Chronic CLE: Discoid, chilblain, nodul, panniculitis

Subacute Cutaneous Lupus
A 45-year-old female is in your office to establish dermatologic care. She has a long history of Raynaud’s phenomenon. About 10 years ago she developed ulcers on the distal fingertips and has had resorption of 2 of her fingertips. This year, she has noticed gradual difficulty in swallowing solids, and has noticed changes in the skin around her mouth. Her ANA is positive 1:160 and she also has a positive scl-70. The scl-70 autoantibody is suggestive of the following diagnosis:

- Diffuse systemic sclerosis
- CREST syndrome
- Limited systemic sclerosis
- Lupus erythematosus
- Mixed connective tissue disease

• The answer is A diffuse systemic sclerosis.
• The scl-70 auto-antibody corresponds to topoisomerase I.
• It is associated with diffuse systemic sclerosis and in particular lung fibrosis.
• This test is highly specific (>99.5% in some studies) but only moderately sensitive (20-50%).

![Discoid Lupus Erythematosus](image1)

![Other](image2)

![Work up for Cutaneous Lupus](image3)

![Diffuse systemic sclerosis](image4)
How to tell the difference

Limited Cutaneous Systemic Sclerosis
- Raynaud’s
- + centromere

Diffuse Cutaneous Systemic Sclerosis
- Interstitial lung disease
- Esophageal dysmotility
- Pulmonary artery hypertension

Facial involvement
- Raynaud’s
- Digital resorption
- Renal crisis
- + Scl70
- + RNA polymerase III

Sclerodactyly

Nail changes

Calcinosis

Telangiectasias

+ANA

15. What is the diagnosis?
A. Tinea corporis
B. Blastomycosis
C. Mycosis Fungoides
D. Bowen’s disease
E. Sarcoidosis

16. 74-year-old African American female presents with a one-year history of generalized rash which consists of numerous 1-3mm papules over the face, chest, arms, abdomen, and upper thighs. Histopathology is shown. What is the next best step in diagnosis?

Large Cell Transformation of Mycosis Fungoides
- 20-50% of advanced MF
- Histopathological transformation of neoplastic small lymphocytes to a large cell phenotype.
- Associated with a poor prognosis

- Pulitzer et al. Pathology, 2014; 46(7):610-616
16. What is the next best step in diagnosis?
A. Ophthalmic exam
B. CT head and neck
C. Chest X ray
D. Peripheral blood smear
E. Serum protein electrophoresis

- The best answer is E, serum protein electrophoresis.
- The photograph and histopathology demonstrate scleromyxedema.
- Histopathology: mucin deposition, fibroblasts, and fibrosis.
- Highly associated with a monoclonal gammopathy—
  —CHECK SPEP!

Extracutaneous manifestations of Scleromyxedema
- dermato-neuro syndrome
- peripheral neuropathy
  - arthralgias
- cardiac involvement

17. WHAT IS YOUR DIAGNOSIS?
A. Lupus erythematosus
B. Mucormycosis
C. Mycosis fungoides
D. Sarcoidosis
E. Rosacea

- The answer is D, sarcoidosis.
- Increased incidence in African Americans
- Red-brown or violaceous papules and plaques

Cutaneous Sarcoidosis
18. Which systemic manifestation is associated with lupus pernio?
A. Heart conduction defects
B. Lung involvement
C. Migrating polyarteritis
D. Nephropathy
E. Parotid gland enlargement

The answer is B, lung involvement.
Lupus pernio is associated with lung and laryngeal involvement.

19. The diagnosis is:
A. Bullous lupus erythematosus
B. Bullous pemphigoid
C. Epidermolysis bullosa acquisita
D. Pemphigus foliaceus
E. Pemphigus vulgaris

The answer is A. bullous pemphigoid.
Histopathology = subepidermal blister.
Collagen IV stain = blister above the collagen IV stained areas.
– level of the blister occurs at the lamina lucida.
The most common neoplasm associated with this patient's condition is:

A. Castleman's disease
B. Chronic myelogenous leukemia
C. Non-Hodgkin's lymphoma
D. Sarcoma
E. Thymoma

The answer is C. Non-Hodgkin's lymphoma.

Paraneoplastic pemphigus is an autoimmune suprabasilar blistering disorder seen in association with malignancy. The most characteristic clinical feature is intractable hemorrhagic stomatitis, often extending to the vermilion border and resistant to therapy.
A 52 year old male complains of painful lesions on the scalp and back for over 1 year. On examination he has several tender shallow erosions with scale on the scalp, neck, chest and back. He denies the presence of oral or genital ulceration. Histopathology is shown. This patient likely has antibodies to:
A. Hepatitis C
B. Desmoglein 1
C. Desmoglein 3
D. Anti nuclear
E. Collagen VII

The correct answer is B desmoglein 1 antibodies. The diagnosis is pemphigus foliaceus which is characterized by autoantibodies that target the intercellular adhesion protein desmoglein 1. This causes acantholysis and subcorneal blisters that rupture easily leaving erosions and scale.


22. WHAT IS YOUR DIAGNOSIS?
A. Ocular rosacea
B. Allergic contact dermatitis
C. Cicatricial pemphigoid
D. Angioedema
WHAT IS THE PROTEIN TARGET IN THIS DISEASE?
A. Bullous pemphigoid antigen 1
B. Collagen VII
C. β4 integrin
D. desmoglein

Ocular Cicatricial Pemphigoid
• Autoantibodies to the β4 subunit of α6β4 integrin is specific for the ocular predominant disease
• Other forms of cicatricial pemphigoid can involve laminin or BP180
• Starts as a chronic conjunctivitis (inflammation) that leads to progressive scar tissue formation.
• Trichiasis, entropion are common and lead to corneal trauma and blindness

The most likely diagnosis is:
A. Cicatricial pemphigoid
B. Erythema multiforme
C. Lichen planus
D. Pemphigus Foliaceus
E. Pemphigus Vulgaris

The answer is pemphigus vulgaris.
• Antibodies to intracellular keratinocyte adhesion protein desmoglein 3
• Oral erosions, buccal and palatine, often the presenting symptoms.
• DIF: intercellular IgG and C3 deposition, primarily in lower epidermis.

Louisiana Dermatological Society Meeting, New Orleans, September 17, 2016

UNUSUAL CLINICAL PRESENTATION:
- Isolated crusted plaque on face or scalp
- Paronychia
- Foot ulcers
- Diphtheritic eczema
- Macroglossia

Thank you!
• amurina@tulane.edu
Cases from the Crescent City

Brittany Stumpf, MD
Assistant Professor
Department of Dermatology
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Disclosure

- Investigator: Regeneron, Novartis

- What is the most likely diagnosis?
  a. Chronic cutaneous lupus
  b. Cutaneous sarcoidosis
  c. Demodex folliculitis
  d. Perioral dermatitis
  e. Rosacea

- The answer is B, cutaneous sarcoidosis.
- This is a case of lupus pernio which presents as indurated, lumpy, violaceous lesions on the nose, cheeks, lips, and ears (areas most affected by cold = pernio).
- This variant is more frequently associated with cystic lesions in the distal phalanges.
- Lupus Pernio has a high predictive value for:
  - pulmonary involvement (75%)
  - involvement of the nasal and oral mucosa, larynx and pharynx, salivary glands, tongue, and tonsils (50%)


Sarcoidosis

- Bimodal onset:
  - 1/3 patients with systemic sarcoidosis will develop skin lesions.
- Commonly presents: red-brown papules/plaques
- Mimicker: hypopigmented, SQ nodules, ichthyosiform, alopecia, verrucous plaques, erythema multiforme

This is a 59 y/o lady previously treated for renal cell carcinoma and breast cancer presenting for asymptomatic erythematous scaly plaques over the bilateral axilla for 10 years progressing to involve the back and the thighs. Patient also started to have new skin colored nodules over the nose, eyelids and fingers.
• What is the most likely diagnosis?
  a. Rosacea
  b. Demodex folliculitis
  c. Psoriasis
  d. CTCL
  e. Perioral dermatitis

answer is d, CTCL

• Primary cutaneous CD8+ small/medium-sized pleomorphic T-cell lymphoma is a rare type of cutaneous T-cell lymphoma that usually affects the head and neck area with an indolent course however it can be more widespread. (1) Granulomatous morphology is an unusual histopathologic pattern that has been described with many cutaneous T-cell lymphomas mainly mycosis fungoides however it is rarely described with CD8+ small/medium-sized pleomorphic T-cell lymphoma. (3)
• Biopsy of nasal bridge showed CD8+ small/medium pleomorphic primary cutaneous T-cell lymphoma with prominent granulomatous inflammation.
• Biopsy of the axilla was consistent with Mycosis fungoides with positive T-cell rearrangement. No internal involvement was found.
• Presence or absence of granulomatous pattern doesn’t affect the prognosis nor the treatment of cutaneous T-cell lymphoma. (4)

• 31 year old M with HIV presents with a chief complaint of 6 m h/o worsening bilateral lower extremity edema.
  • It has progressed to the point that patient can no longer walk. He denies any history of heart failure, hepatic insufficiency or renal insufficiency.
  • Over same time period he developed asymptomatic brown/purple plaques and nodules on his arms, legs and back.
  • ROS: +fatigue, wt gain, leg swelling
  • PE: 4+ pitting edema; scattered violaceous papules, plaques and nodules on all extremities and trunk, with lower extremities more involved than elsewhere
  • LYMHP: no palpable LAD

The diagnosis is:
A. Bacillary angiomatosis
B. Herpes simplex
C. Kaposi’s sarcoma
D. Merkel cell carcinoma
E. Nodular amyloidosis
Kaposi’s Sarcoma

- It is the most common tumor in HIV-infected patients and is an AIDS defining illness.
- The patient’s CD4 count is considered to be the most important factor in tumor development, which explains why a rise in combination antiretroviral therapy has correlated with a decline in the incidence of AIDS related KS.
- Lymphedema is classically associated with a non-AIDS-related variant called classical KS, it can be seen in the AIDS-related type.
- The edema most likely results from a combination of vascular obstruction caused by tumor-related lymphadenopathy and the associated increased cytokine production, which increases the permeability of lymphatic vessels.

AIDS-Related Kaposi’s Sarcoma

- The characteristic findings are whorled spindle-cells, leukocytic infiltration, and neovascularization of small blood vessels.
- KS associated with HHV-8/Kaposi’s sarcoma-associated herpes virus (KSHV)
- There is a staging system for AIDS-related KS that sorts a patient into prognostic categories based on the extent of the tumor (including associated lymphedema), immune status (as determined by the CD4 count), and severity of systemic illness. Patients may be screened for visceral involvement with a stool occult blood test and a chest x-ray for pulmonary lesions, but these manifestations are less common among AIDS-related KS.

<table>
<thead>
<tr>
<th>Kaposi’s Sarcoma Subtype</th>
<th>Epidemiology</th>
<th>Clinical Features</th>
<th>Behavior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical</td>
<td>Older males, Mediterranean or Ashkenazi Jewish origin</td>
<td>Skin of lower extremities</td>
<td>Indolent, risk of developing non-Hodgkin lymphoma, second malignancy</td>
</tr>
<tr>
<td>African/Endemic</td>
<td>Mid-age African adults/kids</td>
<td>Multiple skin tumors</td>
<td>Progressive</td>
</tr>
<tr>
<td>AIDS associated</td>
<td>Mostly homosexual males and IV drug users</td>
<td>Disseminated mucocutaneous and visceral involvement</td>
<td>Aggressive, lesions may regress or flare with start of antiretroviral treatment</td>
</tr>
<tr>
<td>Iatrogenic/Organ transplantation</td>
<td>Immunosuppressed individual other than AIDS associated</td>
<td>Localized or disseminated mucocutaneous involvement</td>
<td>Variable, may regress with discontinuation of immunosuppression</td>
</tr>
</tbody>
</table>

- What is the most likely diagnosis?
  a. Contact dermatitis
  b. Guttate psoriasis
  c. Pityriasis rosea
  d. Secondary syphilis
  e. Tinea corporis

- The answer is C, pityriasis rosea.
  - The largest plaque shown is the herald patch or initial lesion, which is a pink to salmon-colored patch or plaque with slightly raised margin.
  - Following the appearance of the herald patch, symmetrical lesions appear with longitudinal axes following the Langer lines of the trunk.
  - HHV-6, HHV-7 more recent focus association

- Pityriasis Rosea-like Drug eruption: ACE inhibitors, metronidazole, isotretinoin, imatinib, clonidine, gold, arsenic, bismuth, omeprazole, etanercept, triplelennamine, ketotifen, salcarsan, BCG vaccine
  - Drug induced PR is slower to resolve than idiopathic form.

• Which biologic agent blocks the interleukin-4 receptor?
  a. Dupilumab
  b. Guselkumab
  c. Secukinumab
  d. Tocilizumab
  e. Ustekinumab

  The answer is A, Dupilumab.
  The anti-interleukin-4 receptor (IL-4R) antibody dupilumab inhibits signaling via IL-4 and IL-13 on immune cells.
  Guselkumab is an IL-23 inhibitor.
  Secukinumab is an IL-17A inhibitor.
  Tocilizumab is a IL-6 inhibitor.
  Ustekinumab is an IL-12 and IL-23 inhibitor.
  Tsianakas A. et al. Dupilumab: a milestone in the treatment of atopic dermatitis

Cytokine Activation in AD Skin


• This 11 year old patient is brought in by his mother for worsening eczema. The patient has been well controlled with emollients and topical steroids in the past.
• His mother is concerned because there are some new bumps near his eye that have come up over the past few days.
• They are mildly pruritic and minimally painful.
• The patient denies changes in vision or photophobia.

What the best choice of treatment?
  a. Cephalexin
  b. Desonide
  c. Doxycycline
  d. Imiquimod
  e. Valacyclovir

  The answer is E Valacyclovir.
  The diagnosis is eczema herpeticum.
  AD patients are especially susceptible to cutaneous bacterial and viral infections, and may develop severe or fatal herpes simplex virus infection or eczema herpeticum, requiring intensive antiviral therapy.
  Decreased filaggrin and decreased production of antimicrobial peptides may have pathogenic role.
  Leung DY. Why is eczema herpeticum unexpectedly rare? Antiviral Res. 2013; 98 (2); 153-7

Atopic Dermatitis: Pathogenesis

• Genes
  – Altered protein expression in epidermis: i.e. filaggrin
  – Proteins with immunologic function not specific to the skin: i.e. IL-4, IL-5

• Epidermal Dysfunction
  – Lipid defects
  – Tight junction defects

• Immune Dysregulation
  – Th2 predominant cytokine profile: IL-4, IL-5, IL-13
  – IL-22 increased in lesional skin

• Pruritus
  – Persistent and severe in AD
  – Currently elucidating mechanisms: role of IL-31
• Th17 cells produce:
  a. IFN-gamma
  b. IL-13
  c. IL-17
  d. IL-4
  e. IL-5

• The answer is c, IL-17.
  • The Th17 cells produce IL-17, IL-22 and TNF-alpha.
  • Other cell types that produce IL-17: mast cells, neutrophils and macrophages.

• Patients with genetic deficits in the IL-17 pathway have had impaired mucocutaneous immune response to which microorganism?
  a. Candida albicans
  b. Malassezia furfur
  c. Mycobacterium marinum
  d. Salmonella enterica
  e. Streptococcus pyogenes

• The answer is Candida albicans.
  • Genetic defects resulting in IL-17 pathway deficiencies have been associated with impaired mucocutaneous immune responses, particularly against Candida albicans and Staphylococcus aureus.
  – However, the immune responses to both of these pathogens are complex and not mediated exclusively by the IL-pathway.
  – Most of these patients had genetic defects that affected other immune pathways including the Th1 pathway and IL-22.
  – In the trials for the new IL-17 inhibitors, small percentages of patients experienced neutropenia, which was generally mild to moderate (2 cases of grade-3 neutropenia in the study of brodalumab)
  – but there was no evidence for increased risk of opportunistic infections or mucocutaneous candidiasis.

• This disease can flare during treatment with secukinumab:
  a. Ankylosing spondylitis
  b. Atopic dermatitis
  c. Crohn’s disease
  d. Psoriatic arthritis
  e. Rheumatoid arthritis

• The answer is Crohn’s disease.
  • When Secukinumab was tested in patients with Crohn’s disease, the patients in the treatment group had a lack of therapeutic effect and an increased risk of adverse events.
  • Secukinumab has shown favorable results in the treatment of ankylosing spondylitis and psoriatic arthritis.

• Which genetic syndrome is associated with an inability to mount a Th17 immune response?
  a. Bloom syndrome  
  b. Dyskeratosis congenita  
  c. Fanconi syndrome  
  d. Hyper IgE syndrome  
  e. Wiskott-Aldrich syndrome

• The answer is Hyper IgE syndrome.  
  • Patients with hyper-IgE syndrome (Job's syndrome) have been shown to have defects in Th17 cells (which produce IL-17 and -22), but not Th1 cells (which produce IFN-γ).
  • These patients are prone to chronic S. aureus abscesses, chronic candidiasis, and pulmonary infections.


• Bloom syndrome is associated with immune deficiency involving low levels of IgM and IgA.
  • Defect BLM gene: functions in unwinding DNA and genomic stability
  • Increased malignancies: esp leukemia/lymphomas

• Dyskeratosis congenita is not associated with cutaneous infections.
  • Defect DKC1 gene: dyskerin gene interacts with telomerase enzyme
  • Bone marrow dysfunction: anemias, leukopenia, thrombocytopenia,pancytopenia
  • Predisposition to malignancies: H&N SCC, leukemia, Hodgkin lymphoma

• Fanconi syndrome is not associated with cutaneous infections.
  • Bone marrow dysfunction: anemias, thrombocytopenia, pancytopenia
  • Predisposition to malignancies: muscosal SCC,AML, hepatocellular ca, incr risk breast and pancreatic ca.

• Wiskott-Aldrich is associated with increased risk of sinus and ear infections
  • WASP gene mutation, WASP expressed in ALL hematopoetic cell lineages
  • Low serum IgM, IgG2, elevated IgA, IgE, IgD
  • Hepatosplenomegaly, lymphadenopathy, autoimmune disorders common
  • 25% develop lymphomas

What is the best initial treatment?
  A. Corticosteroids  
  B. Cyclosporine  
  C. Methotrexate  
  D. Mycophenolate mofetil  
  E. Tacrolimus

• The answer is A. corticosteroids.
  • Acute graft versus host disease (GVHD) occurs due to recognition of host tissues as foreign by immunocompetent donor cells.
  • The three main features of acute GVHD are skin eruption, diarrhea, and bilirubin elevation.
  • 3 organs systems affected: skin, GI, liver
  • Systemic corticosteroids for both acute and chronic GVHD are the gold standard, but less than 50% of patients with have a sustained response to steroids and will need secondary therapy.

### Risk Factors for GVHD

<table>
<thead>
<tr>
<th>Donor</th>
<th>Recipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA incompatibility with recipient</td>
<td>Age (older &gt; middle &gt; pediatric)</td>
</tr>
<tr>
<td>Unrelated</td>
<td>Stem cell source</td>
</tr>
<tr>
<td>Female (esp multiparous) with male recipient</td>
<td>Peripheral &gt; bone marrow &gt; chord</td>
</tr>
</tbody>
</table>

| Other | Myeloablative conditioning regimen [higher rate aGVHD] |

### GVHD

**Acute**
- Morbilliform with acral predilection
- Can affect GI tract and Liver

**Chronic: Polymorphous Condition**
- Lichen planus-like
- Lichen sclerosus-like
- Morphea-like
- Poliosis
- Scleroderma-like
- SQ: Fasciitis
- Oral: Keratotic plaques, LP-like lesions
- Restriction of oral opening from sclerosis
- Genital: LP-like; Vaginal scarring/stenosis
- Less specific: nail changes, alopecias, xerostomia, mucositis, mucocele, ichthyosis, edema, bullae, morbilliform

### Stage Classification of GVHD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Skin</th>
<th>Liver</th>
<th>Gut</th>
<th>Grade</th>
<th>Histologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;25% BSA</td>
<td>2-3 mg/dl</td>
<td>Nausea or 500-1000 mg/dl</td>
<td>I</td>
<td>Focal basovascular changes</td>
</tr>
<tr>
<td>2</td>
<td>25-50% BSA</td>
<td>3-6 mg/dl</td>
<td>1000-1500 mg/dl</td>
<td>II</td>
<td>I + epidermal necrotic keratinocytes and/or perifollicular or dermal lymphocytic infiltrate</td>
</tr>
<tr>
<td>3</td>
<td>&gt;50% BSA</td>
<td>6-15 mg/dl</td>
<td>&gt;1500 mg/dl</td>
<td>III</td>
<td>II + cloeth/microvessel</td>
</tr>
<tr>
<td>4</td>
<td>Erythroderma with bullae</td>
<td>&gt;15 mg/dl</td>
<td>Severe abdominal pain +/- ileus</td>
<td>IV</td>
<td>III + large areas of epidermal sloughing</td>
</tr>
</tbody>
</table>

### Pathology of Grover’s Disease

- **Grover’s disease** is a transient or persistent, monomorphous, papulovesicular, asymptomatic or pruritic eruption classified as non-familial acantholytic disorder.
- It is more common in middle age and elderly men.
- The etiology is unknown, but excessive UV exposure, heat, sweating, and ionizing radiation are linked to the disease.
- Darier’s disease and Hailey Hailey are similar acantholytic disorders that are hereditary.
- These diseases also can involve intertriginous areas and the neck.
- Colonie et al. Mckee’s Pathology of the Skin. 4th ed. Chapter 5 pages 151-179

### 60 year old male with history of itchy crops of red papules and vesicles. There is no significant family history of similar rash.

Pathology shows focal acantholytic dyskeratosis. The diagnosis is:

A. Allergic contact dermatitis
B. Darier’s disease
C. Grover’s disease
D. Hailey Hailey disease
E. Lymphomatoid papulosis

**This finding is most commonly associated with:**

A. gout
B. lupus erythematosus
C. psoriasis
D. rheumatoid arthritis
E. scleroderma
The correct answer is C psoriasis.

- This photograph shows a telescoping digit which is a result of progressive erosive disease and osteolysis caused by psoriatic arthritis (PsA).
- It is also called the “opera glass hand.”
- Up to 57% of psoriatic arthritis patients have erosive disease and functional disability occurs in 11-19% of patients.
- Rheumatoid arthritis tends to affect the same joint in all of the digits, whereas PsA is more likely to affect all of the joints in any one digit.
- Gout is associated with gouty arthritis which causes limited joint mobility.
- Scleroderma is associated with ventral pterygium of the nails, Raynaud’s phenomenon and scoliosis.
- Lupus erythematosus is associated with tortuous capillary loops of the nail fold and Raynaud’s phenomenon.

You are consulted in the Emergency Department for a 15-year-old female who presented with a 3 day history of flu-like symptoms and painful blisters on the face for the past 24 hours. She has a history of depression, ADHD, asthma. Which drug is the most likely cause?

a. Fluoxetine
b. Lamotrigine
c. Lithium
d. Methylphenidate
e. Montelukast

The answer is B lamotrigine.
The patient developed Stevens-Johnson syndrome SJS secondary to Lamotrigine.
50% of all SJS cases are due to drug exposure, and usually take 1-3 weeks of starting the drug to appear.
The anticonvulsant class of medications are high risk for causing SJS.
Lamotrigine is a commonly used mood stabilizer and anti-convulsant.
The risk of SJS is increased when Lamotrigine is used with Valproate.
The frequency of SJS and TEN in patients treated with lamotrigine is:
- 1:1000 adults
- 3:1000 children.

Skin Lesions: dusky macules with or without epidermal detachment; macular atypical targets; bullae
<10% BSA detachment
Affecting trunk and face
Severe mucosal involvement
Systemic symptoms
May progress to TEN
Drug induced, occasionally mycoplasma pneumoniae, rarely immunizations

What is the best treatment option?
a. Hydrocortisone cream
b. Doxycycline
c. Prednisone
d. Menadione
e. Mupirocin ointment
• This 60-year-old male has severe reaction to cetuximab being used for colorectal cancer.
• The papules are tender and pruritic.
• What is the best treatment option?
  a. Hydrocortisone cream
  b. Doxycycline
  c. Prednisone
  d. Menadione
  e. Mupirocin ointment

  The answer is B, Doxycycline.
  Cetuximab is EGFR antagonist
  Grade 2 and 3 eruptions (≥10-30% BSA, tenderness, pruritus, and/or superinfection) often require systemic treatment.
  Tetracyclines are considered first-line agents and are likely active through their antiinflammatory properties.
  Given the higher prevalence of bacterial superinfection with Staphylococcus species than in acne vulgaris, -cyclines likely also play an antimicrobial role.


A 23 year old female presents to clinic for a brown spot on the right eyelid that appeared 2 weeks ago. It is asymptomatic. She has never had a similar rash on any other areas. She requests medication to fade the area. What is the most likely diagnosis?

A. Contact dermatitis
B. Congenital nevus
C. Erythema dyschromicum perstans
D. Fixed drug eruption
E. Lichen planus

  The answer is D Fixed drug eruption.
  The patient had a fixed drug eruption to Naproxen.
  Fixed drug eruptions typically occur within 1-2 weeks of exposure to a drug.
  Round erythematous violaceous hyperpigmented or targetoid lesions can recur in the same location, usually within 24 hours of the second exposure.
  There is a predilection for the lips, face, hands, feet and genitalia.
  The most common causes are sulfa medications, pseudoephedrine, NSAIDs, barbituates, tetracycline and carbamazepine
A 31-year-old pregnant female at 18 weeks gestational age presents to clinic with a 1-week history of these painful lesions on the legs. She reports associated fevers and malaise for the past 1 week. You decided to perform a biopsy. What is the most likely pattern seen on histopathology?

- Eosinophilic spongiosis
- Leukocytoclastic vasculitis
- Lobular Panniculitis
- Septal Panniculitis
- Subepidermal blister

The answer is D septal panniculitis.

The photograph is a picture of erythema nodosum which is predominantly septal panniculitis with a predominance of lymphocytes.

- Predominant neutrophils and eosinophilic types have been reported.
- There is generally no vasculitis associated.
- The presence of thrombophelbitis has also been reported, but is not a classic finding.

Triggers:
- Pregnancy
- Drugs (oral contraceptives, aspirin, prazosin, gold, sulfonamides, bromide, and penicillins)
- Infections (streptococcal, tuberculosi, and hepatitis)

Calonje et al. McKee's Pathology of the Skin. 4th ed. 2012. pages 326-361

A 53-year-old woman, with history of inflammatory carcinoma of the left breast s/p mastectomy and radiation therapy in 2011, presented for initial evaluation of a concerning rash on her chest. Symptoms began gradually several months ago and involved the skin of the left breast and chest. She complained of redness, irritation, burning, pain, and stinging sensation in the affected areas. She is currently on Tamoxifen and Methotrexate. What is the diagnosis?

- Contact dermatitis
- Morphea
- Psoriasis
- Radiation recall dermatitis
- Recurrent breast cancer

The answer is radiation recall dermatitis.

Radiation recall dermatitis (RRD) is an acute inflammatory reaction at sites of previous irradiation after administration of a promoting agent.

DRUGS:
- Anthracyclines (doxorubicin)
- Taxanes (paclitaxel)
- Antimetabolites (gemcitabine)


Louisiana Dermatological Society Meeting, New Orleans, April 16, 2016

The most likely positive test is:

- Treponemal immunostain

This 35-year-old homeless male with history of IV drug abuse, Hepatitis C presents to clinic for rash on the trunk. The most likely positive test is:

- Anti-nuclear antibody
- Cryptococcal Ag
- Rheumatoid factor
- Rapid plasma reagin
- Scabies prep
The answer is rapid plasma reagin or RPR.
This is a case of lues maligna, a rare form of secondary syphilis.
Widespread pustules and nodules necrotic sharply demarcated ulcers
60x more likely in HIV/AIDS
Treatment: IV or IM Penicillin + corticosteroid to prevent Jarisch-Herxheimer reaction
Louisiana Dermatological Society Meeting, New Orleans, April 16, 2016

You see a 14 year old boy with history of Acute Lymphoblastic Leukemia in remission, and graft versus host disease. Which medication is the cause of this patient’s photodamage?

A. Methotrexate
B. Mycophenolate mofetil
C. Tacrolimus
D. Thalidomide
E. Voriconazole

The answer is Voriconazole.
The drug has been associated with phototoxicity presenting as a photodistributed eruption, photodamage or erythema.

Louisiana Dermatological Society Meeting March 7, 2015

A 57-year-old female with a past medical history of metastatic colon cancer, develops extremely painful hands and feet ten days after initiation of a new medication. Which drug is the most likely cause?
A. Ondansetron
B. Oxycodone
C. Regorafenib
D. Simvastatin
E. Verapamil

A 57-year-old female with a past medical history of metastatic colon cancer, develops extremely painful hands and feet ten days after initiation of a new medication.
• The answer is C. Regorafenib.
• The patient has **hand-foot skin reaction** (HFS), also known as palmo-plantar erythrodysesthesia.
• These reactions occur with the use of **multikinase inhibitor** chemotherapeutic agents, such as regorafenib.
• Other offenders: 5-FU, capecitabine, pegylated liposomal doxorubicin, and cytarabine.

* Louisiana Dermatological Society Meeting November 16, 2014

• This 40-year-old female complains of a rash since childhood on the trunk, arms and legs.
• It is asymptomatic and does not respond to topical steroids.
• What is your diagnosis?
  a. Id reaction
  b. Lichen nitidus
  c. Lichen planus
  d. Milia
  e. Molluscum contagiosum

• The answer is B, lichen nitidus.
• This woman had generalized lichen nitidus which was biopsy proven.
• Lichen nitidus is an uncommon idiopathic inflammatory cutaneous eruption first described by Pinkus in 1901.
  – Composed of multiple, small, discrete, glistening, flesh-colored to slightly pink papules that may occur anywhere on the skin;
  – however, the most common sites are the glans and shaft of the penis, genitalia, abdomen, and extremities.
• As in lichen planus, the Koebner phenomenon or isomorphic response is observed and is the hallmark of LN.
• The lesions are usually asymptomatic but may be mildly pruritic.

* Cho EB, Kim HY, Park EJ, Kwon IH, Kim KH, Kim KJ. Three cases of lichen nitidus associated with various cutaneous diseases. J Korean Dermatol - August 1, 2014; 51 (8); 699-701
Cases from the Crescent City

Laura Williams, MD
Tulane University School of Medicine
New Orleans, Louisiana

Conflict of interest:
I have nothing to disclose

Laura Williams, MD
Tulane University School of Medicine
New Orleans, Louisiana

1. Which patient is most likely to have psoriasis?

- The answer is E.
- Photo A shows longitudinal erythronychia and was in a patient with suspected Darier’s disease.
- Photo B shows sclerosis of the nail fold in a patient with systemic sclerosis.
- Photo C shows splinter hemorrhage which can be present in psoriasis but is not specific for psoriasis.
- Photo D shows nail dystrophy in a patient with a digital mucous cyst.
- Photo E shows distal onycholysis and nail pitting which is diagnostic for psoriasis.

2. What is your diagnosis?
   a. Brachyonychia
   b. Onychauxis
   c. Onychomadesis
   d. Onychoschizia
   e. Trachyonychia

- The answer is Onychomadesis.
  - Beau lines are transverse depressions on the back aspect of the nail plates.
  - Onychomadesis involves the complete separation and possible subsequent shedding of the nail plate and represents a more severe form of Beau lines.
    - Brachyonychia are racket nails or short nails, in which the length of the nail plate and nail bed is greater than the length.
    - Onychauxis is overgrowth and thickening of the nail plate.
    - Onychoschizia is plate-like splitting of the free edge of the nail.
    - Trachyonychia are longitudinal striations with a sandpaper appearance.

Onychomadesis

Post viral (HFMD), other infection, fever, systemic, nutritional, medication, SLE


3

- This 46-year-old patient presented to clinic with a rash that involved the trunk and extremities.
- Consider the appearance of nails.
- Which diagnosis will likely be found on histopathology?

a. Alternating orthokeratotic and parakeratosis
b. Full thickness epidermal separation
c. Lichenoid band of lymphocytes
d. Neutrophils in the stratum corneum
e. Subacute spongiotic dermatitis

- The answer is C, Lichenoid band of lymphocytes.
- This nail finding is pterygium and longitudinal ridging which are found in lichen planus.
  - Option A is consistent with pityriasis rubra pilaris
  - Option B is consistent with stevens johnson syndrome
  - Option D is consistent with psoriasis
  - Option E is consistent with various types of eczematous dermatitides

* Photo: Hutchinson’s Clinical Methods: An Integrated Approach to Clinical Practice, 2012;15, 333-347

4 This 46-year-old female is seen as a new patient for 1 year of hair loss and hair thinning in the right frontal hairline. The clinical and dermatoscopy photos of the scalp are shown. What is your diagnosis?

- This 46-year-old female is seen as a new patient for 1 year of hair loss and hair thinning in the right frontal hairline.
- The clinical and dermatoscopy photos of the scalp are shown.
- What is your diagnosis?
  - Central centrifugal cicatricial alopecia
  - Frontal fibrosing alopecia
  - Tinea capitis
  - Traction alopecia
  - Trichotillomania


4

- The answer is traction alopecia.
- Traction alopecia due to tight hairstyles is common in African American women.
- Dermatoscopy is very helpful to establish if the hairstyle is still causing traction as it shows hair casts around the hair shafts at the peripheral edges of the patches.
- These appear as cylindric structures that envelop the proximal portion of the hair shaft.
  - Central centrifugal cicatricial alopecia shows reduced hair density with hair shaft variability, pinpoint white dots, and peripilar white halos
  - Frontal fibrosing alopecia can show absence of follicular openings, cicatricial white patches, peripilar casts, blue-gray dots, and perifollicular erythema
  - Tinea capitis can produce comma hairs or corkscrew hairs
  - Trichotillomania can show black dots, yellow dots and broken hairs.
5

- What is the most likely diagnosis?
  a. Alopecia areata
  b. Discoid lupus
  c. Psoriasis
  d. Trichotillomania
  e. Secondary syphilis

5

- The answer is secondary syphilis.
- Temporary patchy alopecia can be associated with secondary syphilis.
- The "moth-eaten" pattern is the most common type and is considered a pathognomonic manifestation of secondary syphilis.
- The frequency of hair loss in secondary syphilis ranges from 2.9% to 7.9%.
- The precise pathogenesis is unknown.
- The alopecia usually resolves after 3 months after therapy.
  - Syphilitic alopecia can mimic alopecia areata both clinically and histopathologically.
  - Exclamation point hairs are present in alopecia areata but not in syphilis.
  - Trichotillomania can also present with several irregular patches, but there would be fewer patches than in this patient.
  - Discoid lesions in the scalp present as erythematous to violaceous plaques with scarring and depigmentation.
  - Scalp psoriasis can present with alopecia but will be associated with pityriasis with silvery scale.

6

This 56-year-old female complains of a patch of hair loss in the posterior scalp. Clinical and trichoscopy photos are shown above. What is your diagnosis?
A. Alopecia areata
B. Androgenetic alopecia
C. Lichen planopilaris
D. Tinea capitis
E. Trichotillomania

6

- The answer is A. alopecia areata.
- The most characteristic trichoscopic features according to the recent review of alopecia areata are:
  - yellow dots (63-94% of patients),
  - black dots (44-70%),
  - exclamation mark hairs (30-44%),
  - tapered hairs (12-42%),
  - broken hairs (45-58%),
  - vellus hairs (33-72%),

7

- What is your diagnosis?
  a. Allergic contact dermatitis
  b. Alopecia areata
  c. Frontal fibrosing alopecia
  d. Psoriasis
  e. Seborrheic dermatitis
7

- The answer is C, frontal fibrosing alopecia.
- This patient has biopsy proven frontal fibrosing alopecia.
- Frontal fibrosing alopecia is associated with:
  - progressive hair loss along the anterior hairline
  - significant perifollicular erythema and scale.
- A recent report highlighted the depression of the frontal veins as a new clinical sign of frontal fibrosing alopecia.

* Louisiana Dermatological Society Meeting: New Orleans April 18, 2015

8

You are evaluating a 56 year old female for this patch of alopecia in the frontal scalp. Biopsy is consistent with lichen planopilaris. The patient mentions other symptoms that are suggestive of Graham-Little-Piccardi-Lassueur Syndrome. Which areas of the body should you examine to determine if this is the correct diagnosis?

A. Axilla and eyebrows
B. Axilla and groin
C. Eyebrows and eyelashes
D. Eyebrows and groin
E. Forearms and groin


9

9. Which hair shaft abnormality is associated with this condition?

- The answer is B, Axilla and groin.
- Graham-Little-Piccardi-Lassueur Syndrome (GLPLS) is a variant of lichen planopilaris, associated with non-cicatricial alopecia of the axilla and groin.
- Pull test often reveals anagen hairs in GLPLS.
- It is more common in women, especially post-menopausal women.


9

- Which hair shaft abnormality is associated with this condition?
  A. Pili torti
  B. Pili trianguli et canaliculi
  C. Trichorrhexis nodosa
  D. Trichoschisis
  E. Trichothiodystrophy

- The answer is pili trianguli et canaliculi which occurs in uncombable hair syndrome.
- Known as spun glass hair, rare abnormality of hair shaft
- This disorder does not have increased hair fragility.
- The patients have course dry frizzy hair that develops in the first year of life.

* Louisiana Dermatological Society Meeting, New Orleans April 18, 2016
10. A 28 year old female is evaluated in clinic for pruritic bumps in the bilateral axilla as shown above. What type of previous treatment did this patient likely receive in the past?

A. Alexandrite laser  
B. Botulinum toxin injection  
C. Intralinesional triamcinolone injection  
D. ND:Yag laser  
E. Microwave thermolysis of eccrine glands

10. The correct answer is A, Alexandrite laser.  
- Fox Fordyce like disease has been reported following laser hair removal using the Alexandrite (755nm), intense pulsed light (810-945nm) and the Diode laser (800nm).  
- Fox Fordyce disease or apocrine millaria is characterized by multiple smooth skin colored to yellow dome shaped papules.  
- These lasers may induce damage to the follicular infundibulum which leads to altered keratinocytes forming keratin plug.

11. Polycystic ovarian syndrome is associated with:
   a. Alopecia areata  
   b. Clitoromegaly  
   c. Endometrial cancer  
   d. Galactorrhea  
   e. Type 1 diabetes mellitus

11. The answer is C, endometrial cancer.  
- Chronic anovulation in patients with PCOS predisposes patients to infertility and endometrial cancer.  
- The 3 main components are:
  - oligo- or anovulation
  - hyperandrogenism
  - polycystic ovaries
- Other important features include insulin resistance, obesity, cardiovascular disease, obstructive sleep apnea, nonalcoholic steatohepatitis, and psychiatric disease.  
- Cutaneous manifestations of polycystic ovary syndrome include signs of insulin resistance, such as:
  - acne
  - hirsutism
  - and signs of hyperandrogenism, such as thinning, acne, and hair loss.

[Check out the references for more detailed information.]
12. A 45-year-old African American female is evaluated for facial redness. She has no history of photosensitivity, joint pains, or oral ulcers. ANA is performed and is negative. Punch biopsy from the cheek shows perivascular and perifollicular infiltrates. Which additional histopathologic finding would suggest rosacea?

A. Demodex infestation  
B. Follicular plugging  
C. Mucin in the dermis  
D. Necrotic epidermal keratinocytes  
E. Perineural lymphocytic infiltrate

13. Which bacterium, cultured from a *Demodex folliculorum* mite, has been implicated in rosacea pathogenesis?

a. Bacillus  
   oloronicus  
   b. Chlamydia  
   c. Helicobacter  
   d. Propionibacterium acnes  
   e. Staphylococcus aureus

14. 50-year-old male is evaluated for facial flushing that is worse with anxiety, bending forward, and physical exertion. He admits to having occasional headaches, and diaphoresis. What is the next best test?

A. Abdominal CT  
B. Calcitonin level  
C. IgE level  
D. Urine 5-hydroxyindoleacetic acid  
E. Vasoactive intestinal peptide

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- 12. A 45-year-old African American female is evaluated for facial redness. She has no history of photosensitivity, joint pains, or oral ulcers. ANA is performed and is negative. Punch biopsy from the cheek shows perivascular and perifollicular infiltrates. Which additional histopathologic finding would suggest rosacea?
- **A. Demodex infestation  
  B. Follicular plugging  
  C. Mucin in the dermis  
  D. Necrotic epidermal keratinocytes  
  E. Perineural lymphocytic infiltrate**

- **The best answer is A Demodex infestation.**
- In a recent comparative analysis of the histopathology of rosacea and cutaneous lupus, demodex infestation was predictive of rosacea, whereas follicular plugging, perineural lymphocytic infiltrate were predictive of lupus erythematosus.
- Abundant mucin deposition was also more prominent in cases of lupus.
- Necrotic epidermal keratinocytes can be found in both rosacea and lupus, but overall more common in lupus. — Brown et al. JAAD. Volume 7, No. 1, July 2014 pages 100-107

- **13. Which bacterium, cultured from a *Demodex folliculorum* mite, has been implicated in rosacea pathogenesis?**
  a. Bacillus  
  b. Chlamydia  
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  A. Abdominal CT  
  B. Calcitonin level  
  C. IgE level  
  D. Urine 5-hydroxyindoleacetic acid  
  E. Vasoactive intestinal peptide

---

- **The answer is A, Bacillus  
  oloronicus.**
- Several microorganisms have been shown to be increased or immunoreactive in patients with rosacea.
- Microbes that have been associated with rosacea include *Demodex folliculorum*, *B.  
  oloronicus*, *S. epidermidis*, *H. pylori*, and *C. pneumoniae*.
- *B.  
  oloronicus* is a non-commensal organism that was initially cultured from the hindgut of a termite, and later isolated from a Demodex mite in a patient with rosacea and in several patients with blepharitis.
- Proteins from *B.  
  oloronicus* were found to trigger a reaction in a statistically significant amount of rosacea patients compared to controls.

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- Jarruda et al. Correlation between serum reactivity to *Demodex*-associated *Bacillus  
  oloronicus* proteins, and altered serum levels of *Demodex*-populated *erythematoelangiitic rosacea* patients. J Med Microbiol. 2014; 63: 258-62
14.
• The answer is urine 5-hydroxyindoleacetic acid
• You should consider ruling out **mastocytosis, carcinoid, and pheochromocytoma** as a cause.

- Louisiana Dermatological Society Meeting September 13, 2015

15
• The answer is vinyl gloves.
• Both thiurams and carbamates are rubber accelerators.
• Many articles currently used in the healthcare sector contain rubber chemicals (e.g. syringes, tracheal tubing, elastic bands, catheters) that can sensitize workers.
  - Rubber gloves = rubber accelerators.
  - Neoprene, nitrile, and styrene gloves = rubber and rubber accelerators.

- Photo: www.wsiat.on.ca

16
• Which occupation has the largest proportion of individuals reporting water exposure >2 hours per day?
  a. Hairdressers
  b. Lab technicians
  c. Midwives
  d. Plant cultivators
  e. Registered nurses

16
• The answer is hairdressers.
• In a recent survey study of over 34,000 people in Sweden, the occupations with the highest proportion of individuals with >2 hours of water exposure were:
  – kitchen assistants,
  – cleaners,
  – restaurant workers and
  – hairdressers.


17

This 48-year-old female was admitted to the orthopedic service with a new history of wrist pain after a fall 3 weeks prior to admission. A physical examination revealed a tender area on the right wrist and finger tips. The patient’s wrist and fingers were swollen and there was a palpable mass. She was treated with antibiotics and NSAIDs but the mass continued to increase in size. The patient was referred to the orthopedic department for evaluation. The MRI scan showed a large mass occupying the entire wrist area with surrounding edema. Bone biopsy was performed and histopathology revealed a malignant soft tissue tumor. The patient was diagnosed with synovial sarcoma and underwent chemotherapy. She is currently undergoing chemotherapy and radiation therapy.
The most likely diagnosis is:
A. Allergic contact dermatitis
B. Bullous impetigo
C. Bullous pemphigoid
D. Eczema herpeticum
E. Erythema multiforme

A 67 year old female presents to the clinic for a 4 day history of a rash on bilateral forearms. She admits to gardening 5 days prior. What is the most likely plant growing in her garden?
A. Avocado
B. Fig
C. Mango
D. Peach
E. Strawberry

The answer is A. Allergic contact dermatitis - likely to an antiseptic or topical agent such as xeroform gauze that was placed on the hand.
Most surgical related allergens are not tested on the test.
Acrylates are the most commonly used surgical adhesives but not tested for using the TRUE test.
Colophony is the only adhesive tested.
Surgical antiseptics allergies also cannot be tested for the TRUE test.

18. A 67 year old female presents to the clinic for a 4 day history of a rash on bilateral forearms. She admits to gardening 5 days prior. What is the most likely plant growing in her garden?
A. Avocado
B. Fig
C. Mango
D. Peach
E. Strawberry

The correct answer is B Fig.
- This patient has a phytophotodermatitis to Fig.
- The fig (ficus carica) belongs to the Moraceae family
- In the leaf sap and shoot sap there are 2 types of furocoumarins - 8 methoxypsoralens and 5-methoxypsoralens.
- Kiwi and Avocado are latex cross reactors.
- Peach and Strawberry are not a cause of phytophotodermatitis.

Phytophotodermatitis

Fig - leaves, branches and skin of fruit have furocoumarins (flesh of fruit does not)
Not all exposures are accidental – Fig is sometimes used intentionally as a folk remedy for dermatologic condition
A decoction of boiled down fig leaves is used to soak skin for treatment of common skin disorders, including onychomycosis


Phytophotodermatitis

Most common plants are
Aplacia/Umbelliferae (celery, carrot or parsley family) and Rutaceae (citrus) family
More prevalent in summer with increased UVA exposure and plant exposure
Lesions present 24 hours after exposure and peak at 48-72 hours
Lesions often blister and cause hyperpigmentation that persists

Phytophotodermatitis

- Cow parsley (hedgehog, wild celery, "pushkie")
- Alaska, Canada as far south as Georgia
- Produces furcocurmin to protect against fungal attack which absorb photons add release energy to the skin
- More furcocurmin exposure to skin with high humidity, perspiration and wet skin
- Can cause "pusklee burns"
- Can occur after as little as 10 minutes of summer sunshine (UVA)


19. This patient most likely has a contact allergy to:

A. Benzalkonium chloride
B. Diazolidinyl urea
C. Methyl methacrylate
D. Paraben mix
E. Potassium dichromate

19. The correct answer is E, potassium dichromate.
- Potassium dichromate is found in leather footwear, cement, and wood finishes.
- In this case, the patient was allergic to leather present in sandals.
- Benzalkonium chloride is a preservative used in ophthalmic solutions.
- Methyl methacrylate is an adhesive used in artificial nails, dental fillings, and artificial joints.
- Paraben mix is used in cosmetics, topical medications, and antiperspirants.


20. A 36-year-old female presents with a pruritic rash on her anterior thighs that you suspect is a contact dermatitis.
- While you are talking to the patient in clinic, you notice she is holding an iPad with a magnet that looks like this.
- If this iPad case is the cause of her allergic contact dermatitis, what is the most likely allergen?
  a. Benzophenones
  b. Dimethyl fumarate
  c. Methylisothiazolinone
  d. Mixed dialkyl thioureas
  e. Nickel
The answer is mixed dialykl thioureas which are an allergen in neoprene, which is the main component of this type of soft protective case.

Neoprene is a special synthetic rubber used in many products (eg, wet suits, elastic supports, gloves, shoes, and orthopedic devices).


The most likely diagnosis is:
A. Acute hemorrhagic edema of infancy
B. Erythema multiforme
C. Juvenile idiopathic arthritis
D. Muckle-Wells syndrome
E. Urticaria multiforme

- Louisiana Dermatological Society Meeting November 15 2015

Urticaria Multiforme

- Reserve corticosteroids for worst cases
- Differentiate from
  - EM (no targets, blistering, necrosis, mucous mem.)
  - serum-sickness like reactions (fever, LA, arthralgias, urticaria and angioedema
- Preceding history of
  - URI,
  - bacterial infection
  - Abx - amoxicillin, cephalosporin, macrolides
  - Vaccination

This premie, 6 days s/p PDA repair began to have erythematous desquamating eruption with crusted patches over trunk and proximal extremities.
The toxin produced in this condition interferes with function of:
A. BP antigen-1
B. Desmoglein 1
C. Plakoglobin
D. Collagen VII
E. Langerhans cells

Staph Scalded Skin Syndrome

The answer is B – desmoglein 1
The condition shown represent staph scalded skin syndrome
Most often caused by staph aureus phage group II, producing ETA and
Toxins cleave desmoglein 1, destruction of cell-cell adhesion with blister
and denuded skin (stratum granulosum)
Represents 5% of staph aureus isolates
Prodrome of irritability, malaise and fever
Positive Nikolsky’s sign
Erythematous tender patches developing over a hour, may have bullous
Epidermal detachment: face, axilla, groin and neck leaving moist, red
Heals without scarring
More common in children less than 5 years old – possibly because children don’t have protective antibodies or kidneys do not excrete toxin.

Staph Scalded Skin Syndrome Adults

Mortality: 40-63 % in adults
Unlike pediatric patients, adult patients generally
immunocompromised
chronic renal disease
HIV infection
GVHD
chemotherapy patients
VHRA
DM
Presentation similar with fever, generalized erythema, bullae, desquamation
Adult source may be more clear; blood cx’s more likely positive
Must be differentiated from TEN – get biopsy
no necrotic keratinocytes in SSSS
both lack inflammation
more superficial in SSSS – below stratum corneum

Staph Scalded Skin Syndrome

- Has been reported and studied in a similar premature infant
- Concern for transmission in NICU or similar health care location – in this study the NICU had 4 cases with horizontal transmission
- In this study, Anti-ETA antibody levels were lower in 4 cases with SSSS but also lower in preterm infants compared to healthy full-term infants
- Plasma IgG levels correlate with gestational age possibly more concerning for premature infants

This skin eruption is most commonly caused by:
- Beta lactam antibiotics
- Macrolide antibiotics
- Non-steroidal anti-inflammatory drugs
- Protease inhibitors
- TNF- alpha inhibitors
23

- The answer is A, beta-lactam antibiotics, which include penicillins, aminopenicillins, and cephalosporins.
- The diagnosis is Acute general exanthematous pustulosis (AGEP), which is an acute febrile drug eruption of small primarily non-t follicular sterile pustules, arising within a large area of edematous erythema.
- More than 90% are due to beta-lactam antibiotics.
- In this case, the patient was HIV positive and on a new antiviral agent containing emtricitabine and tenofovir.
- Louisiana Dermatologic Society Meeting. September 12, 2015

AGEP

- Typically within 48 hours from exposure to reaction onset
- Antibiotics with a median of 24 hours
- Other medications include: sulfonamide, terbinafine, hydrochlorothiazide and fluconazole
- Typically includes fever and elevated neutrophil count
- Differential diagnosis:
  - Bacterial folliculitis
  - Generalized pustular psoriasis
  - DRESS
  - SJS


24

- A 44-year-old male with history of end stage renal disease developed a small painful ulcer that rapidly increased in size over the past 4 weeks. The best next step is:
  a. Skin biopsy for H&E and cultures
  b. Skin swab for culture
  c. Lower extremity Doppler study
  d. Unna boot dressing
  e. Referral to wound care

- The answer is A, skin biopsy for H&E and cultures.
- In this case the biopsy revealed calciphylaxis.
- The best next step is to perform a skin biopsy prior to initiating any definitive therapy (telescopy biopsy from lesion margin or deep incisional wedge give best yield)
- Calciphylaxis clinically presents with severe painful skin lesions
  - (livedo reticularis, reticulate purpura, violaceous plaques, or indurated nodules)
  - that demonstrate poor healing and are frequently complicated by blisters and ulcerations with superimposed infections.
- Ulcerated lesions commonly demonstrate black eschar.
- Calciphylaxis predominantly affects patients with chronic kidney failure treated by dialysis.

Calciphylaxis

However, calciphylaxis is not limited to patients treated by dialysis and also occurs in patients with normal kidney function and those with earlier stages of chronic kidney disease.

One year mortality 45-80%

Obesity reported as risk factor for proximal calciphylaxis (thigh, buttocks, trunk)

Been reported in patients with autoimmune conditions
  - SLE
  - Anti-phospholipid antibody
  - RA

Hypercoagulability may predispose
Hepatitis (infectious, autoimmune and alcoholic) risk factor


Calciphylaxis

- Other risks:
  - Calcium supplements
  - Calcium-based phosphate binders
  - active Vitamin D
  - warfarin
  - corticosteroids
  - iron therapy
  - trauma also associated


Calciphylaxis

Calciphylaxis

Calciphylaxis

Calciphylaxis

Calciphylaxis

Calciphylaxis

Wound management – get wound care involved
Surgical debridement case by case, accomplished surgeon
Hyperbaric oxygen if available
Antibiotics as guided by systemic features
Pain management (fentanyl over morphine due to potential hypotension
Sodium thiosulfate – IV, end of dialysis, also IL parathyroidectomy in refractory hyperparathyroidism
Management of other risk factors


warfarin-associated calciphylaxis

18 patients – 15 from literature and 3 from UCSF
Autoimmune diseases not prominent in cases (few ANA, few APA)
tends to ulcerate below knee
Presents on average 32 months after initiation (warfarin skin necrosis presents 3-10 days)
No calcium imbalance
Sodium thiosulfate and bisphonates seemed to help these patients
Lower mortality in this study 17% (uremic 50-80%)
26. A 44 year old female complains of painful blisters to the forearms as well as subjective fever, malaise, and sore throat for the past 5 days. Yesterday, she was evaluated by an Urgent Care physician and diagnosed with Streptococcal pharyngitis. Complete blood count is normal. Pregnancy test is negative. Biopsy of the one of the blisters shows diffuse neutrophils. Direct Immunofluorescence is negative. What is the treatment of choice?

A. Clofazimine  
B. Cyclosporine  
C. Interferon  
D. Metronidazole  
E. Prednisone

27. Which of the following laboratory values will likely be abnormal?

A. Aldolase  
B. Alkaline phosphatase  
C. Anti-nuclear antibodies  
D. Calcium  
E. Creatine kinase

- The answer is alkaline phosphatase, which is low in patients with zinc deficiency.
- Zinc is an essential trace element for this enzyme.
- Acquired zinc deficiency: alcoholics, malabsorption, inflammatory bowel disease, gastrointestinal surgery, anorexia nervosa, and AIDS.
- Erythema, scale-crusts and erosions → perioral, acral and perineal areas.
- Other presentations: alopecia, paronychia, onychodystrophy, blepharitis, conjunctivitis, stomatitis and angular cheilitis.

• Bariatric patients have high rate of micronutrient deficiencies, pre and post-operatively (1/2 deficient in zinc before)
• Other micronutrients deficiencies are also seen:
  – Thiamine, Folate, B12, iron and copper
• Post-surgically, less absorptive surface area (most absorption is in duodenum and proximal jejunum – competitive absorption with copper)
• Supplements give 1 mg copper for every 8-15 mg of zinc
• Greatest risk for zinc deficiency is with Roux en Y
• Over 300 proteins and 1000 transcription factors incorporate zinc at active sites and DNA binding sites


• Most symptomatic post bypass zinc deficient patients respond to supplementation within 4 weeks (220 mg of zinc sulfate)
• Post bariatric surgery, more common after Roux-en Y, though other procedures done more commonly now; Roux-en Y is still done for high BMI patients

“EACH MORNING I LOOK IN THE MIRROR AND ASK MYSELF THIS QUESTION: IF TODAY WERE THE LAST DAY OF MY LIFE, WOULD I WANT TO DO WHAT I AM ABOUT TO DO TODAY?

AND WHENEVER THE ANSWER IS NO FOR TOO MANY DAYS IN A ROW, I KNOW I NEED TO CHANGE SOMETHING.”

-STEVE JOBS

WHAT IS BURNOUT?

- Defined: physical or mental collapse caused by overwork or stress
- It is not acute, although sometimes it feels that way
- It is an insidious process that sneaks up on you
- Often once you realize it is happening you are deep into burnout
- Burnout leads to:
  - Physical and emotional exhaustion
  - Cynicism and detachment
  - Feelings of inefficacy and lack of accomplishment

WHAT IS BURNOUT?

- Burnout is not just stress
  - “What distinguishes stress from burnout is that you can’t recover from burnout or recharge for the next day in a short period of time.” (Tom Murphy, Physician Burnout)
- Your empathy bank is empty

FEEL THE BURNOUT

ELIZABETH (LISA) SWANSON, MD
ADVANCED DERMATOLOGY COLORADO
ROCKY MOUNTAIN HOSPITAL FOR CHILDREN

DISCLOSURES

- Speaker
  - Valeant
  - Bayer
  - Aqua
  - Promius
  - Amgen
  - Sanofi Regeneron
- Advisory Board Representative
  - Allergan
WHAT IS BURNOUT?

• If burnout is not addressed, it can lead to:
  – Decreased productivity
  – Decreased quality of care and increased medical errors
  – Depression
  – Anxiety
  – Substance abuse
  – Relationship issues: divorce rates among physicians are 10-20% higher than general population
  – Suicide
  – The medical profession has the highest suicide rate of all professions
  – More than 400 physicians commit suicide every year in the US

YOU MAY BE SUFFERING FROM BURNOUT IF...

• You imagine having a human-sized lazy susan constructed for your patient to stand on to facilitate an easier and more efficient skin exam
• You dream about seeing patients
• You frequently feel like a hamster on a wheel
• As you get ready for work you honestly don’t know how you are going to muster up the energy to get through the day
• As you drive to work in the morning, you already feel exhausted or overwhelmed
• Patient tells you about a personal tragedy and your first thought is “how long am I going to be in here”

PHYSICIAN WELL BEING INDEX

1. Have you felt burnout from work in the last month?
2. Have you worried that work is hardening you emotionally in the last month?
3. Have you often been bothered by feeling down, depressed, or hopeless in the last month?
4. Have you fallen asleep while stopped in traffic or driving in the last month?
5. Have you felt that all the things you have to do are piling up so high that you could not overcome them in the last month?
6. Have you been bothered by emotional problems (such as feeling anxious, depressed or irritable) in the last month?
7. Has your physical health interfered with your ability or your daily work at home and/or away from home in the last month?

BURNOUT IS ON THE RISE

• Mayo Clinic Proceedings 2015
  – Overall physician burnout rates rose from 47% to 54% from 2011 to 2014
  – Burnout rates in dermatologists rose from 32% to 57% in that same time period
  – Women had 1.6 times the rate of burnout as men
  – Highest burnout rates are in women with children under 19 in academic positions
WHAT CAUSES BURNOUT?

CAUSES OF BURNOUT

- Working too much
- Negativity everywhere
- Loss of control over your own job and practice
- Insurance hassles
- Increasing non-clinical requirements: MACRA, MIPS, MOC, FML
- Lack of efficiency in the office
- Respect for physicians in general has decreased
  - People are not always thankful, often challenge our expertise with their google search results

CAUSES OF BURNOUT

- Malpractice concerns
  - The US has 2% of the world's population and more than 50% of the world's lawyers
  - Physicians that have made an error or a "near miss" experience the following symptoms:
    - Anxiety about future errors (61%)
    - Loss of confidence (44%)
    - Sleeping difficulties (42%)
    - Reduced job satisfaction (42%)
  - Self-perceived errors are associated with reduced quality of life, increased burnout, and depression
  - The hardest part of dealing with this is forgiving yourself, accepting it, and moving on

CAUSES OF BURNOUT

- Decision fatigue
  - Decision fatigue is real
  - Working in blocks of 90 minutes is ideal
  - Study amongst judges ruling on appeals:
    - Cases heard at the beginning of the day had a 65% chance of getting parole
    - Cases heard at the end of the day had almost zero chance of getting parole
  - People buy more at the mall at the end of their shopping trip than at the beginning
  - Wear the same thing every day
    - Mark Zuckerberg
    - Barack Obama

CAUSES OF BURNOUT

- Online review sites like Yelp and Google Reviews
  - Patients are not customers, but they can rate us like we are a cronut
- EMR
  - Watch "ZDogg EMR video" on YouTube

CAUSES OF BURNOUT

- Technology is great, but also means that we are ALWAYS working
- Btw: 1970s and 2000s, the average American added almost 200 hours of work each year (basically another month!!)
“IT’S BETTER TO BURN OUT THAN TO FADE AWAY.”

- KURT COBAIN

WHAT CAN BE DONE TO TREAT BURNOUT?

“INSANITY IS DOING THE SAME THINGS OVER AND OVER AND EXPECTING A DIFFERENT RESULT.”

- ALBERT EINSTEIN

HOW TO MANAGE BURNOUT

• Step 1: Fine tune your practice
• Step 2: Adjust your mindset
• Step 3: Realize you are only human
• Step 4: Celebrate your successes
• Step 5: Recharge your batteries
• Step 6: Manage your stress (Learn to be Resilient)

STEP 1: FINE TUNE YOUR PRACTICE

“GOD GRANT ME THE SERENITY TO ACCEPT THE THINGS I CANNOT CHANGE, THE COURAGE TO CHANGE THE THINGS I CAN, AND THE WISDOM TO KNOW THE DIFFERENCE.”

- THE SERENITY PRAYER
**FINE TUNE YOUR PRACTICE**

- Think about what properties would make up your ideal practice
  - Patients in a day
  - Staffing expectations
  - To scribe or not to scribe
  - Location
  - Scope of practice: do you want to subspecialize in something? What makes you happy?
- How does that list match up to your current practice?
- What steps can you take to fix that?

**FINE TUNE YOUR PRACTICE**

- What frustrates you during your day?
  - Poor scribe!
  - No shows! Late patients!
  - Patients phone calls!
  - Biopsy inefficiencies!
  - Not having the right supplies!
  - EMR!
- What can you do to ease those inconveniences?
  - Become a “super user” of your EMR
  - Involve your staff: they want to help! They can help you brainstorm!
  - Find the person/people in the office that help you the most: bring them into your circle, lean on them and show your appreciation:
    - No one is an island

**INITIATE A HUDDLE**

- 5 minute huddle at the beginning of the day saves you 30-60 minutes during the day
- Good time to talk about how everyone is feeling, if anyone has any time commitments on the day
- Allows you to get to know your staff personally: they don’t like to feel like minions

**SHOW APPRECIATION!**

- Staff will give more when they get more
- Ask them about their lives
- Start an Employee of the Month program
- Give a thank you note to one staff member every week
- Thank them verbally

**STEP 2: ADJUST YOUR MINDSET**

**IF YOU AREN’T HAPPY, THINK ABOUT YOUR DEFINITION OF HAPPINESS**
WHAT IS YOUR METRIC FOR SUCCESS?

• Everyone has different values that make them feel successful
• By our metrics, Dave Mustaine is a huge success
• But by his metric—“be more popular and successful than Metallica”—he’s a failure

PETE BEST, FORMER BEATLE

• In 1994: “I’m happier than I would have been with the Beatles”
• Getting kicked out led him to meet his wife, have kids, change his values
• He measured life differently—success was a big and loving family, a stable marriage, a simple life
"IF YOU WANT TO CHANGE HOW YOU SEE YOUR PROBLEMS, YOU HAVE TO CHANGE WHAT YOU VALUE AND/OR HOW YOU MEASURE FAILURE/SUCCESS."
-MARK MANSON

STEP 3: REALIZE YOU ARE ONLY HUMAN

A LITTLE PERSPECTIVE

- DJ LeMahieu (Go Rockies!) had the best batting average in MLB in 2016 - .348
- Justin Tucker (Baltimore Ravens) has the best field goal kicking percentage in history - 89.84%
- Drew Brees (Go Saints!) has the best completion rate of all quarterbacks over a career - 66.6%
- Steve Nash (Go Suns!) had the best free throw percentage over a career in the history of the NBA - 90%
- In our career, we strive for 100% and our patients expect (and sometimes rudely demand) 100% and that's just not realistic

PHYSICIANS ARE PERFECTIONISTS

- “As perfectionist physicians, we have a dangerous propensity to assume everything is our fault. There are many instances of physicians expressing profound personal guilt and sorrow about a bad patient outcome that they have carried sometimes for over thirty years…learning to process these feelings can be a big part of the recovery phase.” (Tom Murphy, Physician Burnout)

“SOMETIMES THE BEST DOCTOR IS THE LAST DOCTOR”
-GREEK PROVERB

STEP 4: CELEBRATE YOUR SUCCESSES
CELEBRATE YOUR SUCCESSES

• Have your moment when things go right
• It’s these moments that remind you why you went into medicine/dermatology
• “Physicians are more satisfied when they perceive that they’re delivering high quality care and that they’re doing a good job.” Derm World Sept 2017
• Take the joy from those moments to ride out the frustration and sadness in other moments.

CELEBRATE YOUR SUCCESSES

• Celebrate with your team- staff, members, other doctors
• High fives, fist bumps, celebration dances
• Think about professional athletes
  – The antics of high fives, butt slaps, and celebratory dances in the end zone build positivity and mentality momentum

STEP 5: RECHARGE YOUR BATTERIES

• Think of yourself as your car or your cell phone
  – If your car runs out of gas, it won’t keep going
  – If your cell phone battery dies, you won’t be able order that thing from amazon prime that you needed

“THERE’S NO SUCH THING AS WORK-LIFE BALANCE.
THERE ARE WORK-LIFE CHOICES, AND YOU MAKE THEM, AND THEY HAVE CONSEQUENCES.”

- JACK WELCH

RECHARGE YOUR BATTERIES

• What recharges us is little different for everyone
• Take care of yourself—enough sleep, eat a healthy diet, exercise
• Take vacations!
• Consider having a “Weekly Bucket List” each week
• Schedule time for what matters in your life (and don’t double book)
  – Practice saying no in the mirror. Come up with phrases you are comfortable with.
RECHARGE YOUR BATTERIES

• The power of music
• Make playlists
• Create your “walk out” song
  – Wrecking Ball by Miley Cyrus
  – Fight Song by Rachel Platten
  – Firework by Katy Perry
  – One Moment in Time by Whitney Houston
  – Chandelier by Sia
  – The Dance by Garth Brooks

RECHARGE YOUR BATTERIES

• Consider a “Boundary Ritual” when you get home
  – Take a shower, change your clothes, walk the dog, exercise
  – Your commute can be a boundary ritual: have a playlist to listen to or a TED talk and take some big deep breaths.
RECHARGE YOUR BATTERIES

- Getting more involved in your practice, your community, your medical society, national societies increases your resiliency.
- Attending CME meetings also really helps.
- Allows you to talk with other doctors and realize you are not alone.
  - The connections doctors make with other doctors is really important for each of us.
  - Only doctors know what other doctors go through.
- Allows you to work with the system to make things better for doctors as a whole.
- Participating in free skin cancer screenings can bring back the joy of what we do.

MANAGE YOUR STRESS

- Exercise
- Sleep
- Eat well
- Smile
- Multitasking
- Breathe
- Mindfulness
- Be grateful
- Your brain functions the best when you do all these things and allows you to be the most productive, most creative, most constructive.
- See a therapist or counselor; go to a support group.
  - Venting helps, even if it's just writing a sentence or two in your journal every night.

EXERCISE (AKA A LITTLE BIT OF RITALIN MIXED WITH PROZAC)

- Even a single session of aerobic exercise improves our cognition and energy.
- Also boosts people's mood, motivation, and ability to deal with stress.

SLEEP

- Your brain does not function as well when you are sleep deprived.
- A week of sleeping 4-5 hrs/night causes impairment equivalent to blood alcohol level of 0.1.
SMILE!

• Studies show that smiling can trick your brain into believing that you are happy
• It is also one of the easiest ways to demonstrate empathy
• Being positive is very helpful with patients and a good smile is the first positive step
  – Studies have shown that being near someone in a good mood can lift people’s spirits
  – Being near a grumpy person does the opposite
• In studies, sad people perceived a hill as being higher and steeper than happy people
• Before you enter every room, take a deep breath and show those pearly whites!
• How are you so happy all the time?

• Embrace the beauty of monotasking
• No one can truly multitask
• When it is studied, multitasking actually takes longer and causes more mistakes
• Those who think they are the best at multitasking are typically the worst at it
• Multitasking makes you feel like you are working swiftly, but you are getting less done in more time and doing it all poorly
• If you are doing one task and think of something else that has to be done/remembered:
  – Write it down
  – Tell someone

MONOTASKING

• “To Do” Lists are good
• Reward neurohormones are released when you cross off items on the To Do list
• Don’t put a huge item on the list (aka “World Peace”). Instead, do small things like “Make a To Do List”

MONOTASKING

• Be an email “batcher” and not an email “grazer”

MONOTASKING

• “To Do” Lists are good
• Reward neurohormones are released when you cross off items on the To Do list
• Don’t put a huge item on the list (aka “World Peace”). Instead, do small things like “Make a To Do List”

BREATHE

• We don’t really breathe, especially when we are busy
• Hang loose breathing technique
• Focus on what it feels like to take a deep breath and release it
• Really think about this before encountering a difficult situation

MINDFULNESS: WHAT IS IT?

• Putting down your juggling balls for a little bit
• Embrace the beauty of monotasking
• Paying attention in a particular way: on purpose, in the present moment, and nonjudgementally
"LIFE MOVES PRETTY FAST. IF YOU DON'T STOP AND LOOK AROUND ONCE IN A WHILE, YOU COULD MISS IT."

- Ferris Bueller

HIGH YIELD MINDFULNESS TIDBITS

- Take a second to notice things
  - Raisin fingers
- Start a "Gratitude" journal
  - Write down 2 or 3 things every night that you are grateful for that day
  - Could also write down "3 good things" about a day or "3 funny things"

MINDFULNESS ACTIVITIES

- Anything that lets you "zone out" for a little bit
- Fly fishing
- Tai Chi
- Yoga
- Adult coloring books

MINDFULNESS ACTIVITIES

- Meditation apps that can teach a "non-hippy" how to meditate
  - Headspace
  - Calm

"YOU HAVE BRAINS IN YOUR HEAD. YOU HAVE FEET IN YOUR SHOES. YOU CAN STEER YOURSELF IN ANY DIRECTION YOU CHOOSE. YOU'RE ON YOUR OWN, AND YOU KNOW WHAT YOU KNOW. AND YOU ARE THE PERSON WHO'LL DECIDE WHERE TO GO."

- Dr. Seuss

"PHYSICIAN, HEAL THYSELF: THEN WILT THOU ALSO HEAL THY PATIENT."

- Nietzsche
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• Fitch, Staff. “Remedies for Burnout.” 2014.
• Margosian, Emily. “Feeling the Burn.” Dermatology World Sept 2017, pgs 44-42.
Adherence To Treatment

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Professor of Dermatology, Pathology & Public Health Sciences
Director, Psoriasis Treatment Center
Wake Forest University
School of Medicine
Winston-Salem, North Carolina

Objectives

- To describe ways to manage difficult to treat psoriasis
- To describe how well (poorly) patients use dermatological treatment
- To list ways to improve patients’ use of medications

Low Hanging Fruit

- We have treatments that are remarkably effective
- Patients don’t always get better
- Consider resistant atopic dermatitis
  - 12 year old patient
  - Total body, lichenified atopic dermatitis
  - Failed outpatient treatment with high strength topical steroids, sauna suit, methotrexate, cyclosporine

Resistant Atopic Dermatitis

- Solution
  - Admit the patient to the hospital
  - Treat with topical triamcinolone
  - They clear up in 3 days

Adherence Definitions

- Quality of Execution
- Period of Persistence
- Acceptance
- Discontinuation

Three Big Reasons for Poor Treatment Outcome

1. Poor Compliance
2. Poor Compliance
3. Poor Compliance

In an anonymous survey of psoriasis patients, 40% report noncompliance!!!


Psoriasis Resistant to Topical Treatment

- 35 year old male
- Psoriasis of the elbows and knees
- Prescribed combination of betamethasone and calcipotriol
- Returns in 2 weeks with no improvement
- Is the patient genetically deficient in steroid and vitamin D receptors?

Primary Nonadherence

- Many patients don’t even fill the prescription
- Psoriasis patients are among the worst


Secondary Nonadherence

- 45 year old woman with psoriasis of the legs
- Initial good response to topical betamethasone
- Over time, the medication has gradually become less effective and no longer controls the psoriasis
- Why is the disease now resistant?
  - Has she developed mutant T cell steroid receptors?
  - Were the T cells in the lymph nodes exposed to the steroid?

Topicals Stopped Working
Electronic/Self-Reported Adherence

Mean Daily Adherence

Biologic Failure

- 52 year old woman had extensive psoriasis
  - 20% body surface area affected
- Treated with adalimumab
  - Initial very good response
  - Gradual loss of efficacy

Adherence to Biologics

- 52 year old woman had extensive psoriasis
  - 20% body surface area affected
  - Treated with adalimumab
    - Initial very good response
    - Gradual loss of efficacy


Atopic Dermatitis Adherence is Worse

\[ y = -0.0013x + 0.3783 \]
\[ R^2 = 0.0294 \]

Why Are Patients Non-Adherent

<table>
<thead>
<tr>
<th>Poor motivation</th>
<th>The patient may not be particularly bothered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary gain</td>
<td>Seeking disability or other gain</td>
</tr>
<tr>
<td>Lack of trust in doctor</td>
<td>Physician-patient relationship is the foundation</td>
</tr>
<tr>
<td>Fear of medication</td>
<td>Founded or unfounded fear of treatment</td>
</tr>
<tr>
<td>Don’t know what to do</td>
<td>Patients may not remember oral instructions</td>
</tr>
<tr>
<td>Burden of treatment</td>
<td>Sometimes the tx is worse than the disease</td>
</tr>
<tr>
<td>Perceived burden</td>
<td>Sometimes tx seems worse than the disease</td>
</tr>
<tr>
<td>Passing the responsibility buck.</td>
<td>With multiple caregivers, no one may take responsibility</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>“Pavlov’s dog” problem</td>
</tr>
<tr>
<td>Laziness</td>
<td>No energy to follow treatment</td>
</tr>
<tr>
<td>Resignation</td>
<td>Some patients have just given up</td>
</tr>
</tbody>
</table>

We Can Encourage Better Compliance

- Establish a relationship with patients
- Involve patients in treatment planning
  - Make it easy!
- Don’t scare patients with side effects
- Choose fast acting agents
- See patients back for a return visit
- Give clear, written instructions

Getting Feedback From Patients

Good Medical Practice

- Make the right diagnosis
- Prescribe the right treatment
- Get patients to use the treatment
  - Communicate & follow up
    - Project the appearance of empathy
      - *Appeal* caring

Patients Want Caring Doctors

Interventions to Appear Caring

- Sit down
- Examine patients carefully
  - Palpate the rash
  - Waive a lighted magnifier over lesions
- Asking a few questions about the disease
  - “Your previous treatments have probably been very frustrating…”
- Address psychosocial issues
  - Use support groups

Put a clock on the wall behind the patient

- Looking at a watch can be the kiss of death
  - Put clocks behind where patients sit
- I’m doing it now because I care, not because I am in a hurry
- What matters is how it is perceived

Choose a vehicle that the patient will use

- Less messy products seem to be preferred over:
  - Ointment
  - Cream
  - Emollient
  - Gel

Choose from Cormax cream, Cormax solution, Diprolene gel, Diprolene ointment, Luxiq foam, Psorcon E

Scalp, Palm, Face and Body Psoriasis

- 38 year old male presents with scattered lesions of psoriasis
- Treated with:
  - Scalp: fluocinonide and calcipotriol solutions
  - Face: desonide ointment and topical tacrolimus
  - Palms: Clobetasol ointment and tazarotene gel
  - Body: betamethasone/calcipotriene ointment
- Returns in 8 weeks with minimal improvement

Simplify Treatment

- Daytime & Nighttime Vehicle Preference

Resistant Atopic Dermatitis

- 12 year old patient
- Total body, lichenified atopic dermatitis
- Failed outpatient treatment with high strength topical steroids, sauna suit, methotrexate, cyclosporine
- This time, you don’t want to admit him to the hospital
Add a One Week Return Visit

- Kids with atopic dermatitis
- 0.1% tacrolimus ointment BID
- Return in 4 weeks or 1 week/4 weeks


Betamethasone/Calcipotriene Consistent Results

Why did one study, in green, have worse result at 2 weeks?

Basic Drug Information Received is Deficient

<table>
<thead>
<tr>
<th>Patient knowledge and opinion</th>
<th>n</th>
<th>%</th>
</tr>
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<tbody>
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<td>Diagnosis</td>
<td>7</td>
<td>41</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Daily applications by number</td>
<td>12</td>
<td>71</td>
</tr>
<tr>
<td>Application dose by quantity</td>
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<td>12</td>
</tr>
<tr>
<td>Fully satisfied with consultation</td>
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<td>47</td>
</tr>
<tr>
<td>Worried about adverse effects</td>
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<td>47</td>
</tr>
</tbody>
</table>


Curse of Knowledge

- Better informed people find it difficult to think from the perspective of less well-informed people
- Makes it hard to meet patients’ education needs

Give Instructions in Writing

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Written Instructions

- The Action Plan
Motivating Kids

- Positive reinforcement
- Sticker calendar

Side Effects are a Mixed Bag

- Side effects & fear of them can reduce compliance
- Side effects may also be an opportunity
  - For acne patients on spironolactone
    - “This drug is a diuretic. In addition to its effect on your acne, you may also notice some weight loss.”
  - For scalp psoriasis, tell patients: This may sting…
    - That’s because it is so strong.
    - The stinging is a sign that it is working
    - Most guys don’t have what it takes to use this stuff

Framing

- A set point, even an arbitrary one, affects perceptions
- A risk that is more likely than being killed by lightning doesn’t sound nearly as bad as a risk that is less likely than a coin flip

Rates of Serious Infections per 100 Patient-years

- N = number of serious infections per treatment group

Anchoring

- How willing would you be to take a shot once a month?
- How willing would you be to take a shot once a day? Once a month?
Loss Aversion

- Losses make bigger impact than equivalent gains
- Taking a statin
  - If you take this statin regularly, on average, you would live a year longer
  - If you don’t take your statin regularly, on average, you would die a year sooner
- Sunscreen
  - Will keep you looking young
  - If you don’t use it, you will lose the youthful look of your skin

Ariely D. Predictably Irrational

Address Cost Issues

- Prescribe low cost medicines
- Give patients a range of options
  - Lower cost generics
  - Higher cost drugs that have greater benefit
- Patient assistance programs
  - Company-sponsored copay or other assistance programs
  - Local indigent pharmacy resources
- Change the priority/urgency
  - Real and perceived cost/benefit
- Encourage patient to share cell phone with the pharmacist

Inertia/Default Option/Anecdote

- Powerful force
  - Opt out vs opt in
    - Dramatically increases retirement plan participation
    - Keeps people from switching medications
- Also, too much choice isn’t helpful
  - People choose the middle

Assessing Adherence

- The Honest Truth About Dishonesty
  - “Try to recall the Ten Commandments”
- Also, ask indirect questions
  - “Are you keeping the extra syringes you’ve accumulated refrigerated like you are supposed to?”
  - “What do you do with leftover medication? Is it in a locked cabinet or in the medicine cabinet or do you throw it away?”

Adherence to Biologics

- Adherence to biologics is limited
  - Ask, “Are you keeping the extra syringes you’ve accumulated refrigerated like you are supposed to?”
  - Some practices have better adherence rates than others
- Provide structure
  - Have patients pick the one or two days of the week that they take the medicine and stick to it
- Anchoring
  - “You only need to take the injection once a day. Wait, did I say once a day? It’s only every month.”

Resistant Scalp Psoriasis

- 36 year old woman with resistant but limited scalp psoriasis
- Has seen many dermatologists
- Has tried numerous topicals with no benefit
  - She brings a bag full of them, including clobetasol solution
- Is wondering about using a biologic
Scalp Psoriasis is Tough to Treat

- The first phase is active descaling. In case of mild scaling, regular shampooing is an option. Applications of salicylic acid 5% or 10% of urea up to 40% in a wash-off ointment may enhance descaling. An automatic shampooing machine may help at day-care centers for efficient descaling.
- The second phase is active clearing treatment. The first-line approach is a vitamin D3 lotion or emulsion once a day and a superpotent topical corticosteroid in a vehicle that is well accepted by the patient once a day. If this approach is not effective after eight weeks or not acceptable for reasons of intolerance, a concertina topical corticosteroid may be combined with UVA therapy. To obtain optimized phototherapy of the scalp, a hair blower or a UVB light can be used. Another alternative for the second phase is additional tar-based treatment or a daily sauna. If all these approaches are not effective, cultures for Malassezia should be taken and a systemic antifungal treatment can be started. In case all these treatments are not effective, systemic antipsoriatic treatment should be considered with methotrexate, fumarates, cyclosporine or acitretin.
- The third phase of treatment is stabilization with a vitamin D3 analog once or twice daily and a daily application of a corticosteroid. In case a vitamin D3 analog is not tolerated, one may restrict to intermittent applications of the corticosteroid only.
- The fourth phase is the maintenance phase. For this phase, a vitamin D3 alone is preferred treatment either once or twice daily. A tar shampoo may further support this phase.

Example: Piano Lessons

- "Here is your sheet music; recital in 8-12 weeks"
  - Piano lessons once a week -- great recital
  - No weekly lessons -- not such a good recital

Give sheet music Weekly lessons Recital

Give sheet music 6-12 weeks Recital

No weekly lessons

Scalp Psoriasis is Resistant to Treatment?

- Return visits make people get the medicine and use it
  - Focus on initial adherence also promotes habit
  - A cell phone call can do the same thing
- Giving patients your cell phone number is a powerful statement of how much you care about the patient
  - (whether you answer the phone or not)
- Do Not Preprint Your Cell Phone Number on Your Business Card!

Patient Wants Natural Treatment

- 8 year old with atopic dermatitis
  - Mom would like the child treated with all natural treatment
- 25 year old woman with very severe psoriasis
  - She says she wants all natural treatment

Prescribe only “all natural” treatments

- The words we use with patients are important
  - Never label patients "non-compliant"
- Never, ever use the word “steroid” with a mom
- Use reassuring words
  - “All natural”
  - “Complements natural healing pathways”
  - “Holistic”
- “The sun makes vitamin D in your skin naturally”
Internet Survey & Contest

- Half the subjects received a weekly email link to the survey
- For each completed survey, subjects were entered to win an iPod Nano
- For 5 of 6 completed surveys, subjects received a $5 gift card


An Online Survey Improves Adherence

The Impact of Weekly Internet Surveys on Adherence Over Time

Conclusions

- Difficulty clearing psoriasis is often due to poor adherence
  - Improving adherence is low hanging fruit
  - Adherence is a major issue in the treatment of chronic skin diseases
- We can promote better adherence
  - Timing of follow up
  - Easy to use treatments
- We need to look to new ways to enhance patients’ adherence and treatment outcomes
The Latest on AKs and Skin Cancer Prevention: New Supplements, Magical Lights, and Chemoprevention all in one day

Neal Bhatia, M.D.
Director of Clinical Dermatology Therapeutics Clinical Research San Diego, CA 2017 AOCD Fall Meeting

Dr. Bhatia's Disclosures:
- Affiliations with Abbvie, Actavis, Allergan, Aqua, Bayer, Biofrontera, Biofrontera, Castle, Cipher, Dermila, Eiscoro, Exelix, Ferrable, Foamix, Galderma, Intraderm, ISDIN, LaRoche-Posay, Leo, Novan, Novartis, PharmaDerm, Pfizer, Promius, Regeneron, Sanofi, SunPharma, and Valeant
- Some slides from industry were borrowed for explanation of data and scientific background, not for promotion
- Off-label discussion is likely
- Copies of pdf or questions: bhatiaharbor@gmail.com

Objectives
- Review of Definitions
- Topical Prevention Strategies
- Systemic Approaches
- Photodynamic Therapy for Skin CA prevention
- Conclusions

First some definitions...
- What is the disease?
  - Actinic Keratosis can either regress, persists, or progress to SCC?
  - AK as a symptom of Photodamage, a disease that cannot be cured?
  - SCC in situ that should be treated to avoid recurrence or invasion?

Consider the sources
- “AK is the initial clinical manifestation of a disease continuum that progresses to frank SCC…”
- “Actinic Keratosis is a premalignant condition of thick, scaly, or crusted patches of skin.”
  - Referenced the textbook quotes from Bologna and Fitzpatrick chapters and a Canadian FP article as seen in Wikipedia

Survey says…patients don’t care unless we make them care
- 571 pts surveyed at PSU-Hershey: 3 questions about AKs between June 1-July 31 2016, mean age 42, gender equal
- The question that presented AK as a “precancer” had the highest proportion (92.2%) responding they preferred treatment.
- Two questions presenting the risk of AK as not progressing to cancer yielded the lowest proportion of individuals who chose treatment [57.7%] and [60.9%].
- Conclusions: pts' decisions on whether to receive treatment for AK is significantly affected by physician wording, especially if made aware of risk of CA

How we define this to patients and ourselves will help define expectations...
Are Actinic Keratoses the cutaneous version of "cavities"?

Treatment
- Dermas examine for AKs the same way dentists search for dental caries
- One cavity today → ten cavities later
- Filling cavities is like freezing AKs: it is a bandage not a remedy

Prevention
- When you brushed your teeth, did you brush only one tooth or all of them?
- Do we take that same approach for AKs?
- Is sunscreen the same as toothpaste for the skin?

What is a "Subclinical AK?"

- Evolving AKs are still AKs, whether we see them with our eyes, dermatoscope, confocal microscopy, or fluorescence
- To reduce the risk of skin cancer, we treat what is coming and not just what we see today

What is the destiny of an untreated AK?

- Anywhere between 0.025 and 16% of AKs can progress to invasive SCC
- Extrapolation studies suggesting the risk of progression at approximately 8%
- Risks vary with age, gender, chronic UV exposure, and location of AKs

Can AK treatment be simple yet complete...

- Veterans Affairs Keratinocyte Carcinoma Chemoprevention (VAKCC) trial
  - 12 VA medical centers recruited from 2009 to 2011 and followed up until 2013
  - 932 veterans with 2 or more AKs
  - Mean follow-up duration was 2.6 years
  - "A single course of 5% fluorouracil cream effectively reduces AK counts and the need for spot treatments for longer than 2 years."

Is "Spot Treating" better than "Not Treating?"

- 5% FU cream, (n = 468), or vehicle cream (n = 464) to the face and ears bid for 4 weeks
- At 6 months 5-FU group demonstrated:
  - fewer AKs compared with the control group (3.0 vs 8.1, P < .001)
  - higher complete AK clearance rates
  - 53% vs 17% at 6 months
  - fewer spot treatments at 6-month intervals, at and in between study visits during the trial (P < .01 for all)
Ingenol Disoxate (LEO 43204) 0.018% and 0.037%: Ester of Ingenol for Treatment of AKs

- Currently in trials for full face, scalp, and chest—3 day rx with 12 month FU for recurrence
- More potent activation of protein kinase C
- Significantly more exuberant neutrophil bursts
- Superior antitumor effect in B16 mice with melanoma
- Improved stability at ambient temps

New 4% 5-FU cream in Peanut Oil

- Aqueous vehicle cream w/p peanut oil, apply once daily
- 4 wk comparison study against 5% 5-FU bid, n=841
- Results:
  - All in 4% arm achieved 75% clearance (vs. 95%)
  - 80% were 100% clear (vs. 75% for 5% 5-FU)
  - 30% irritation in 4% cream arm compared to 60% in 5% arm
  - Same comparison of stinging, crusting, and itching
- Peanut Oil added moisturizing effects and was safe to use in pts with peanut sensitivity.

What’s coming for AKs

- IKX2-391 Ointment
  - Inhibit T cell migration and endothelial tube, lymphocyte infiltration, angiogenesis
- VDA-1102 Ointment
  - Placebo vs 5% vs 10% for 28 d
  - anti-neoplastic agent
  - selective modulation of VDAC/HK2, unique to glycolysis and mitochondrial
  - selectively triggers apoptosis in cancer cells
- SR-T100 gel—antiproliferative
  - Solanum lycocarpum alkaloidal extract and their constituents, solamargine and solasonine
  - 16 week treatment study, 8 wk FU for recurrence evaluation
- Acckeral (LAS41056)
  - 0.5% 5-fluorouracil (5-FU) and 10% salicylic acid in film-forming base
  - Comparison trial against placebo and LAS100521 similar compound

Imiquimod 5% vs. 5-FU 5% vs. Cryo

- Combination cream of both superior to 5-FU alone
- Induction of TSLP results in recruitment of anti-tumor T cells
- 131 pts applied combo or 5-FU alone bid for 4 days
- 8 weeks after combo 87% mean AK reduction vs. 26% 5-FU
- Face, scalp, and upper arms also tested
- Higher incidence burning and erythema in combo group
- 39% combo group vs. 13% 5-FU alone
- Concerns: stability of combo, treatment time, AEs

Combining Calcipotriol and 5-FU

- Combination of both superior to 5-FU alone
- Induction of TSLP results in recruitment of anti-tumor T cells
- 131 pts applied combo or 5-FU alone bid for 4 days
- 8 weeks after combo 87% mean AK reduction vs. 26% 5-FU
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- Higher incidence burning and erythema in combo group
- 39% combo group vs. 13% 5-FU alone
- Concerns: stability of combo, treatment time, AEs

Management Strategies

- Start slowly
- Wait at least a week after cryotherapy
- Consider regions instead of full face
- Forehead MWF
- Rest of face TuThSat
- Make sure there is no history of HSV tibialis
- Bacteriostatic healing ointment
- Barrier restoration
- Pramoxine lotion
- Mix equal parts with moisturizer to maximize surface areas
- Spray sunscreens
- Turn the radio up or down but not off
Tips for Success

- Have patients fill prescriptions between Monday to Thursday—less likely to be switched than Fridays or weekends
- Have patients start treatments on Sundays so that reactions occur mid week rather than on weekends
- Take at least 4-7 days off before and after destructions or surgery
- Use every adjunct possible except steroids

Chemoprevention with PDT is not old news but should be routine

Does Blue Light PDT using 20% ALA Reduce Occurrence of AK in high risk patients: 52 wk study.

- Submitted as abstract 5194
- Multi-center evaluator-blinded, placebo-controlled study
- Measures occurrence of AKs and development of NMSC subsequent to cryotherapy then multiple treatments with ALA-PDT
  - N=166, facial AKs, a history of NMSC, and histologic evidence of dysplasia within clinically normal-appearing perilesional skin
  - Clinically evident facial AKs were treated with cryotherapy prior to initial PDT, randomly assigned to ALA-2X: (Baseline, Week 4); ALA-3X (Baseline, Week 4, Week 24) or VEH-PDT
  - Placebo treatments matched 1:1 to the two active groups.

Treatment Day

- Remind patients to bring a wide-brimmed hat to shield the treated lesions from ambient light.
- Bring books, music, or something to pass the time
- Put together a package:
  - Topical anesthetics: lidocaine gel, pramoxine
  - Moisturizers, Sunscreens
  - There is no reason to stop meds that are sensitizing in the UV spectrum since PDT works in 410-417nm
  - Antibiotics, Diuretics, Anti-hypertensives
  - If you are worried, then have them hold the drugs on the day before and the day of treatment

Tips from Dr. Andrea Willey: “spa experience”

- Anticipated ALA PDT Response: erythema and edema
  - Edema generated by mast cell degranulation
  - Erythema response is unaffected by H1 blockade
  - More mast cell related over 72 hours than lymphocytic, so steroids not as potentially helpful

Rationale for Antihistamines

- New trial underway to measure LSRs
  - Randomized, Double-blind, Placebo-controlled, 5-20 AKs
  - 20 pts, given Cetirizine 10 mg or placebo prior to and after treatment
  - Measure LSRs: erythema, edema, crusting, exudation, vesiculation/ulceration and erosion ulceration
Return of Red: 10% ALA in nanoemulsion BF-200 (Ameluz®)

- 7.8% ALA free acid equivalent to 10% ALA
- Spectrum around 630 nm
- No PpIX induction below the basal membrane
- European studies: emitting light between 580–1400 nm
- Nanostructure optimizes the transport of 5-ALA through the Stratum Corneum


Nanotechnology Delivery of BF-200 allows penetration of ALA without permeation into dermis

BF-200 MAL

Return of Red: 10% ALA in nanoemulsion gel

- 779 patients skin type I-III
- 4 to 8 AKs
- BF-200 10% gel vs. MAL 21.3% vs. Placebo
- Narrow emission LED lamps 630 nm


BF-200 10% nano-ALA:

Phase III pivotal trials

- Over 60% of the patients were completely cleared after only one PDT
- Over 90% complete response was reached with a maximum of two PDTs
- No new safety issues became apparent with field treatment


Photolyases

- Naturally occurring enzymes
  - Repair UV-induced thymidine dimers
  - Absent in placental mammals
  - Active in organisms with high cumulative UV exposure.
  - Exogenous forms isolated from a cyanobacterium Anacystis nidulans in marine plants
- Long-term use improves:
  - Expression of MMP-1, Ki67, PCNA
  - Mutations of p53, p21


Photolyases Provide Protection Post-PDT

- Sunscreens contain Photolyases encapsulated in liposomes
  - 36 pts, scalp AKs, treated with PDT; biopsies performed pre-PDT, after one month and one year use.
  - Overall reduction of p53 expression (indicative of apoptosis cell) and Ki67 expression in comparison with a sunscreen with SPF 50+

Preventative effects of photolyases compared to conventional sunscreens

- 9 month long study involving 30 patients after treatment with PDT on the face or scalp
- Sustained remission of previously treated AKs and in patients treated ones with PDT
- All patients in the group treated with photolyases avoided a second PDT treatment vs. 10 of 15 subjects in the sunscreen only group needing a second treatment to stay clear

Polypodium leucotomos Extract for Chemoprevention? So far only data in mice

- PLE in UV-irradiated mice delays tumorigenesis
- Increases epidermal p53 expression and the anti-oxidant status of UV-irradiated hairless mice
- In non-tumoral skin, this increase was significantly higher in PL-treated animals than in non-treated mice
- Can contribute in delaying tumor development, either by repairing the damaged DNA or by increasing apoptosis

Studies coming for chemoprevention in humans?


Green Tea Extract (Polyphenols) Derivatives for Chemoprevention

- DNA repair mediated through IL-12 induction
- Anti-photoagogenic activity when green tea added through drinking water in mice models
- Targets for polyphenols: Ras oncogene activator protein-1 (AP-1)
- Potential additives to sunscreens or other topical agents
  - Epigallocatechin gallate (EGCG)
  - Fisetin alcohol from tannins
  - DFMO ornithine decarboxylase inhibitor
  - Selenium, retinoids and salicylates

Nicotinamide 1000 mg daily ($10/mo)

- Phase 3 ONTRAC skin cancer prevention study
- N=386 pts, aged 30-91 years, hx ≥2 NMSC over past 5 years
- Reduced incidence of new skin CA by 23% vs. placebo after 1 year among high risk patients
- Reduced new AKs by 11% at 3 months, 15% after 12 months
- Prevents UV-induced ATP depletion, glycolytic blockade
- Enhances DNA repair
- Reduces UV-induced immunosuppression
- No vasodilatory side effects: HA, flushing, itching, hypotension
Other Supplements to be aware of

**Vitamin D**
- PubMed database search
- 63 observational studies of vitamin D status in relation to cancer risk
- 37 colon, 13 breast, 20 prostate, and ovarian cancer assessed the association of vitamin D receptor genotype with cancer risk.
- Protective relationship between sufficient vitamin D status and lower risk of cancer. Skin CA not isolated.

**Selenium**
- Deficiency decreases glutathione peroxidase and promotes early UV-induced increase in superoxide dismutase and catalase.
- Causal linkage of low plasma selenium levels to increased risk of NMSC in humans.
- Study of hairless mice examined the dietary selenium level and carcinogenesis.
- UV doses of 90 mJ/cm², 3x/week, 20 weeks, all groups developed skin CA.
- Following UV exposure course: Incidence of tumors decreased for mice on 0.5 mg/kg of dietary Se.

**Pearls on using Retinoids**
- Start slow: 10 mg acitretin daily and increase as tolerated, 25 mg qod then qd.
- Titrate up and down to manage side effects.
- If considering women of childbearing age it might be easier to use isotretinoin due to its shorter half-life.
- Risks will rebound with discontinuation so treat with a routine to balance dryness, labs, and risks of alopecia and neuro effects with dose modification.
- Watch expenses also, there is no endpoint...


Thank you
Holy MACRA!

Mark D. Kaufmann, M.D.
Associate Clinical Professor
Department of Dermatology
Icahn School of Medicine at Mount Sinai

October 27, 2017

DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

Mark D. Kaufmann, MD
What's New in Coding
Holy MACRA

Modernizing Medicine, Inc
Stock Options

NPRM 2018 MPFS

- On July 13, 2017 CMS put the following Notice for Proposed Rule Making into the Federal Register.
- In the Proposed Rule, there are several fee schedule changes for 2018 that are very important.

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>2017 Payment Amount</th>
<th>2018 Payment Amount</th>
<th>Percent Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>10040</td>
<td>$103.72</td>
<td>$110.85</td>
<td>+6.87%</td>
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<tr>
<td>96910</td>
<td>$72.14</td>
<td>$112.29</td>
<td>+55.66%</td>
</tr>
</tbody>
</table>

Treating AKs in 2018

- CMS has proposed several changes in the fee schedule that, if finalized, will take effect on January 1, 2018.
- They have also added two new codes for Photodynamic Therapy (PDT)

CPT Code 96567

- Photodynamic therapy by external application of light to destroy premalignant and/or malignant lesions of the skin and adjacent mucosa (e.g., lip) by activation of photosensitive drug(s), each phototherapy exposure session
- **NOTE:** PDT is billed with J7308 Aminolevulinic acid HCL, 20% single Unit dose.
### NPRM Fee Schedule Changes

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>Description</th>
<th>Current Work RVU</th>
<th>RIC Work RVU</th>
<th>CMB Work RVU</th>
<th>MACRA Fee Related</th>
</tr>
</thead>
<tbody>
<tr>
<td>96567</td>
<td>Delamination therapy by manual application of light to dermal papillary layer of the skin and adjacent areas with aspiration and dermabrasion/rejuvenation of abnormal tissues, per day</td>
<td>0.48</td>
<td>0.48</td>
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<td>No</td>
</tr>
<tr>
<td>96X73</td>
<td>Delamination therapy by manual application of light to dermal papillary layer of the skin and adjacent areas with aspiration and dermabrasion/rejuvenation of abnormal tissues, per day</td>
<td>1.01</td>
<td>1.01</td>
<td>NA</td>
<td>No</td>
</tr>
</tbody>
</table>

### NPRM Fee Schedule Changes

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>2017 Payment Amount</th>
<th>2018 Payment Amount</th>
<th>Percent Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>96567</td>
<td>$137.10</td>
<td>$74.50</td>
<td>-45.66%</td>
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<tr>
<td>96X73</td>
<td>NA</td>
<td>$159.80</td>
<td>NA</td>
</tr>
<tr>
<td>96X74</td>
<td>NA</td>
<td>$217.02</td>
<td>NA</td>
</tr>
</tbody>
</table>

### MACRA

- H.R. 2 Passed by the House on 3/26/15 (392-37)
- Passed by the Senate on 4/14/15 (92-8)
- Signed into law by President Obama 4/16/15
- The Medicare Access and CHIP Reauthorization Act of 2015
- MACRA
- CMS releases 2498 page Final rule for MACRA 11/4/16

- Repealed the SGR (Sustainable Growth Rate) avoiding a -3.1% pay cut
- Mandates The Merit based Incentive Payment System begin in 2019 (MIPS)
- Those in Alternative Payment Models (APMs) will be excluded from the MIPS program

- PREVENTED CMS FROM PULLING THE GLOBAL PERIODS FROM OUR CODES!
17000

- Work RVU = 0.61
- 99212 Bundled visit = 0.48
- Work RVU after Global Period Removed? ??

CPT Codes commonly used that have a 10-day global period

- 17000, 17004 Destruction of AKs
- 17110, 17111 Destruction of Benign Lesions
- 172xx Malignant Destructions
- 114xx, 116xx Excisions - Benign/Malignant
- 1203x, 131xx Intermed/Complex Repairs

SGR – RIP!

- • IN GENERAL – Section 1848(c) of the Social Security Act (42 U.S.C. 1395w–4(c)) is amended by adding at the end the following new paragraph:
  • "(8) GLOBAL SURGICAL PACKAGES.
  • "(A) PROHIBITION OF IMPLEMENTATION OF RULE REGARDING GLOBAL SURGICAL PACKAGES.
  • "(i) IN GENERAL. — The Secretary shall not implement the policy established in the final rule published on November 13, 2014 (79 Fed. Reg. 67548 et seq.), that requires the transition of all 10-day and 90-day global surgery packages to 0-day global periods.

SGR - RIP!

• • IN GENERAL. — Subject to clause (i), the Secretary shall through rulemaking adopt a policy to establish a set of uniform procedures under which payments are made for and services furnished in connection with the performance of medical services included in global surgical packages provided that:
• • (B) COLLECTION OF DATA ON SERVICES INCLUDED IN GLOBAL SURGICAL PACKAGES. —
• • (i) IN GENERAL. — Subject to clause (ii), the Secretary shall through rulemaking develop and implement a process to gather, from a representative sample of physicians, beginning not later than January 1, 2017, information needed to value surgical services. Such information shall include the number and level of medical visits furnished during the global period and other items and services related to the surgery and furnished during the global period, as appropriate. Such information shall be reported on claims at the end of the global period or in another manner specified by the Secretary.

99024

- Postoperative follow-up visit, normally included in the surgical package, to indicate that an evaluation and management service was performed during a postoperative period for a reason(s) related to the original procedure.

99024

• IF I won’t be paid……why bother?
• IF you live in the following states it started to matter in July 2017.
• Any group of 10 or more physicians/qhp needs to start reporting code 99024 on ALL visits that take place in the global period.
99024 States

- Florida
- Kentucky
- Louisiana
- Nevada
- New Jersey
- North Dakota
- Ohio
- Oregon

Performance Period and Payment Year

Performance Year 1

Payment Year 1

Two Tracks: MIPS and Advanced APMs

MIPS Options

- Test the program – report on a subset set of data to avoid penalty only
- Partial participation – report more data for at least 90 days to receive a small incentive
- Full participation – report all elements for 90 days or more to receive full incentive

Advanced APM Option

- Join an Advanced APM
- Must receive 25% of Medicare Part B payments or see 20% of Medicare Part B patients through an advanced APM in 2017
- Potential to earn a 5% incentive payment in 2019

Track One:

MIPS (Merit-based Incentive Payment System)

In 2017, the MIPS score will factor performance in 3 weighted categories:

- Quality
- Improvement Activities
- Advancing Care Information

Comparison of current policies to proposed policies:

<table>
<thead>
<tr>
<th>Policy Topic</th>
<th>Current Transition Year (Final Rule CY 2017)</th>
<th>Year 2 Proposed (Rule CY 2018)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Volume Threshold</td>
<td>Exclude individual MIPS eligible clinicians or groups with $30,000 in Part B allowed charges OR $100,000 in Part B allowed charges during a low-volume threshold determination period that occurs during the performance period or a prior period.</td>
<td>Increase the threshold to exclude individual MIPS eligible clinicians or groups with $90,000 in Part B allowed charges during a low-volume threshold determination period that occurs during the performance period or a prior period. Starting with 2019 MIPS performance period, test clinicians opt in to terms if available.</td>
</tr>
</tbody>
</table>

*Not reporting in 2017 will result in a 4% payment penalty in 2019*
2017 MIPS Performance

Test Pace: Avoid Penalties
- Report ONE of the following:
  - Six quality measures in the quality performance category at least 60 days
  - One activity in the improvement activity category
  - Five required measures making up the base score of the advancing care information (ACI) category

Partial Participation: Small Incentive
- Report ONE of the following for at least 90 days:
  - More than one quality measure in the quality performance category
  - More than one improvement activity
  - More than five required measures in the ACI category

Full Participation: Larger Incentive
- Report ALL of the following for at least 90 days:
  - Six quality measures in the quality performance category
  - One high-weighted improvement activity or two medium-weighted improvement activities
  - Five required measures making up the base score of the ACI category

*The AAD strongly recommends reporting more than one measure or reporting at least one measure over a 90-day period as an insurance policy in the event of submission issues or inaccuracies. Failure to correctly report one measure or activity in 2017 will result in a 4% penalty in 2019.

2017 is a Transition Year — Pick Your Pace

MIPS: Dermatology Quality Measure Set

<table>
<thead>
<tr>
<th>Measure ID</th>
<th>Measure Title</th>
<th>Outcome/High Priority Diagnosis/Area of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>130</td>
<td>Medications: Current Medications Documented in Medical Record</td>
<td>High Priority Medications</td>
</tr>
<tr>
<td>137</td>
<td>Melanoma: Coordination of Care - Recurrence System &amp; Follow-Up</td>
<td>High Priority Melanoma</td>
</tr>
<tr>
<td>138</td>
<td>Melanoma: Coordination of Care - Recurrence System &amp; Follow-Up</td>
<td>High Priority Melanoma</td>
</tr>
<tr>
<td>224</td>
<td>Melanoma: Overutilization of Imaging Studies</td>
<td>High Priority Melanoma</td>
</tr>
<tr>
<td>226</td>
<td>Tobacco Use: Screening and Cessation Intervention</td>
<td>Tobacco Use</td>
</tr>
<tr>
<td>265</td>
<td>Biopsy Follow-Up</td>
<td>High Priority Biopsy</td>
</tr>
<tr>
<td>317</td>
<td>High Blood Pressure: Screening and Follow-Up</td>
<td>High Priority High Blood Pressure</td>
</tr>
<tr>
<td>337</td>
<td>Psoriasis: Tuberculosis Prevention for People with Psoriasis or Psoriatic Arthritis on a Biologic Immune Response Modifier</td>
<td>Psoriasis</td>
</tr>
<tr>
<td>374</td>
<td>Closing the Referral Loop: Receipt of Specialist Report</td>
<td>High Priority Referrals</td>
</tr>
<tr>
<td>402</td>
<td>Tobacco Use and Help with Quitting Among Adolescents</td>
<td>Tobacco Use</td>
</tr>
<tr>
<td>410</td>
<td>Psoriasis: Clinical Response to Oral Systemic or Biologic Medications</td>
<td>High Priority Psoriasis</td>
</tr>
</tbody>
</table>

- https://qpp.cms.gov/mips/quality-measures
Skate to where the puck is going, not to where it is."

—Wayne Gretzky

Disruptive Innovation

- an innovation transforms an existing market or sector by introducing simplicity, convenience, accessibility, and affordability where complication and high cost are the status quo.

- Initially, a disruptive innovation is formed in a niche market that may appear unattractive or inconsequential to industry incumbents, but eventually the new product or idea completely redefines the industry.

Disruptive Innovation

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- Initially, a disruptive innovation is formed in a niche market that may appear unattractive or inconsequential to industry incumbents, but eventually the new product or idea completely redefines the industry.
"We must shift away from a fee-for-service system that reimburses only on volume and move toward a system that holds providers accountable for outcomes and allows them to innovate. Providers need the freedom to design and offer new approaches to delivering care. Our goal is to increase flexibility by providing more waivers from current requirements."

-- Seema Verma, WSJ 9/20/17

**Volume to Value**

- No longer paid for how much you do, but rather on your results
- Financial incentive is reversed as you try to see the patient less often, do fewer procedures, AND try to shift to less expensive interventions (procedures and/or pharmacologic)
- Consolidation into larger group practices
- Increase use of extenders
- Increase use of Telemedicine
- Increase treatment of "forgotten" disease states (e.g. wound healing, genital dermatoses)
APMs

- Alternative Payment Models
- Can include: Medical homes, Accountable Care organizations (ACOs), Bundled Payments
Data is the new Currency of Healthcare
"Don’t find fault - find a remedy."

–Henry Ford

mark.kaufmann@mountsinai.org
Bureaucracy, Regulations, and Burnout
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Icahn School of Medicine at Mount Sinai
New York, NY
October 27, 2017

DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY
Mark D. Kaufmann, MD
Bureaucracy, Regulations, and Burnout
none

MACRA
MIPS
PQRS
VM
VBM
ICD-10
EHR
ACI
SGR

Second Opinion

Autonomy

GOVERNMENT
A Van From the Problems We Create Are Real. 
Just Wait Until You See Our Solutions.
“There is building resentment against the shackles of the present EHR; every additional click inflicts a nick on physicians’ morale.”

“At present, the spectacular effects of computers in science and in the secular world are not reflected in the EHR, which for physicians remains burdensome, all-consuming, and far from intuitive; this is not surprising, when the dominant EHRs are designed for billing and not primarily for ease of use by those who provide care.”
“Don’t find fault - find a remedy.”

–Henry Ford

“Existing EHRs also have yet to seize one of the greatest opportunities of comprehensive record systems—learning from what happened to similar patients and summarizing that experience for the treating physician and the patient.”

“Current records miss opportunities to harness available data and predictive analytics to individualize treatment. Meanwhile, sophisticated advances in technology are going untapped. Better medical record systems are needed that are dissociated from billing, [are] intuitive and helpful and allow physicians to be fully present with their patients.”

mark.kaufmann@mountsinai.org
Saturday, October 28, 2017

6:00 a.m. - 7:00 a.m.  Breakfast with Exhibitors

7:00 a.m. - 8:00 a.m.  *Amelanotic and Desmoplastic Melanomas: Pathogenesis, Diagnosis and Treatment*
Ali Banki, DO, FAOCD  
*Desmoplastic Melanoma: Surgical Management and Adjuvant Therapy*
Dale Han, MD

8:00 a.m. - 8:50 a.m.  *Dermoscopy Simplified: The TADA Algorithm*
Ashfaq A. Marghoob, MD

8:50 a.m. - 9:40 a.m.  *Updated Medical Treatment for Melanoma*
Sanjiv Agarwala, MD

9:40 a.m. - 10:15 a.m.  *Surgical Approach to Melanoma*
Merrick I. Ross, MD

10:15 a.m. - 10:30 a.m.  Break with Exhibitors

10:30 a.m. - 11:30 a.m.  *Case Studies in Melanoma: An Interactive Panel*
Sanjiv Agarwala, MD; Ashfaq A. Marghoob, MD; Merrick I. Ross, MD & Edward H. Yob, DO, FAOCD - Moderator  
*Select Dermatopathology Topics for the Practicing Dermatologist*
Sean Stephenson, DO, FAOCD

12:30 p.m. - 1:30 p.m.  *Learn about an Innovation in the Treatment of Persistent Facial Erythema*
Katherine Holcomb, MD, FAAD  
Allergan Product Theater (No CME Awarded)

1:30 p.m. - 2:00 p.m.  Break with Exhibitors

2:00 p.m. - 3:00 p.m.  *Updates in Pediatric Dermatology*
Lisa Swanson, MD

3:00 p.m. - 4:00 p.m.  *Psoriasis*
Bradley Glick, DO, MPH, FAOCD

4:00 p.m. - 5:00 p.m.  *BAP-oma & Beyond*
Michael Nowak, MD
Desmoplastic and Amelanotic Melanomas

Ali Banki, D.O, FAOCOD, FAAD
Assistant Clinical Professor, Univ. of New England College of Osteopathic Medicine
Clinical Associates, University of Connecticut, Department of Dermatology

- I have no conflicts of interest to report

Desmoplastic Melanoma (DM)

- Accounts for less than 4% of primary cutaneous melanomas
- Elderly individuals
- Found on chronically sun-damaged skin
- The male to female ratio is approximately 2:1

Desmoplastic Melanoma

- DM most often affects the head and neck region (51%)
- Extremities (30%)
- Trunk (17%)

Clinical presentation

- It can arise de novo:
  - tan, erythematous, firm papule, nodule, or plaque, usually
  - lacking any epidermal component or as an ill-defined scar like lesion

- It can be associated with other melanoma subtypes, mainly lentigo maligna type:
  - It is recommended to palpate the skin overlying a lentigo maligna to detect for any dermal tumors
DermNetNZ.org

Differential Diagnosis

- **Benign:**
  - Dermatofibroma
  - Scar
  - Cyst
  - Neurofibroma

- **Malignant:**
  - Sarcoma
  - Basal cell carcinoma
  - Squamous cell carcinoma
  - Amelanotic melanoma

Histopathological Subtypes

- Two subtypes, based on the degree of desmoplasia:
  
- 1. Pure DM: More than 90% of the tumor shows desmoplastic features

- 2. Mixed DM: Desmoplastic features in less than 90% but more than 10% of the lesion


Histopathological Subtypes

- Pure DM is less likely to affect the lymph nodes and has a less aggressive course compared to the mixed DM

- Fig 4. Desmoplastic melanoma, mixed type. A, One part of invasive melanoma displays fibrosing spindle cell component. B, Another part of melanoma is composed of densely cellular aggregates of epithelioid tumor cells. (Hematoxylin-cosin stain.)
- Fig 5. Desmoplastic melanoma, pure type. A, Amelanotic spindle cell melanoma is associated with collagenous stroma and lymphocytic aggregates. B, Individual hyperchromatic fusiform melanocytes are dispersed in fibrous matrix. (Hematoxylin-cosin stain.)

Perineural invasion

- DM frequently show perineural invasion and such tumors are termed desmoplastic neurotropic melanoma.
- Aggressive, higher tendency for local recurrence.

---

### Dermoscopy review (vasculature)

---

**Table II. Key features of pure and mixed desmoplastic melanoma**

<table>
<thead>
<tr>
<th>Features</th>
<th>Pure DM</th>
<th>Mixed DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>Frequency, dermal nodules or plaque</td>
<td>Higher and associated with LKM1 or ISM</td>
</tr>
<tr>
<td></td>
<td>Less often contains clinical pigmentation</td>
<td>Higher cellular density</td>
</tr>
<tr>
<td>Histology</td>
<td>Psammocellular</td>
<td>Prominent desmosmas, more melaotic index, increased CD117</td>
</tr>
<tr>
<td>Upper regional lymph node</td>
<td>4.1%–26%</td>
<td>12.4%–39%</td>
</tr>
<tr>
<td>Distant metastasis</td>
<td>11.3%</td>
<td>12.4%</td>
</tr>
</tbody>
</table>

---

**Mixed desmoplastic melanoma**

0.95 mm SSM with focal invasive DM

---

**6.1 mm, Pure desmoplastic melanoma**

---

**Figure 2.** (a-f) Vascular morphologies (a-f) of various morphological categories of vascular patterns: (a) comma-shaped, (b) stellate (stellar), (c) linear, (d) branching, (e) star-shaped (opaque), (f) circular (opaque). (g-i) Diabetic dermopathy. (j) Nodular melanoma. (k) Linear. (l) Spitz naevus. (m) Malignant melanoma. (n) Sclerosing liposarcoma. (o) Metastatic renal cell carcinoma. (p) Lymphangioma. (q) Capillary hemangioma (angiomiylomatous). (r) Amelanotic melanoma. (s) Teleangiectatic melanoma. (t) Fibrous histiocytoma (angiomatous). (u) Angioma. (v) Angioma of the skin. (w) Angioma of the cutis. (x) Angioma of the dermis. (y) Angioma of the subcutis. (z) Angioma of the subcutaneous tissue.
Sebaceous hyperplasia

Bowen's disease

Melanoma

Hypomelanotic nodular melanoma

Hypomelanotic melanoma

Melanoma Specific Structures
Dermoscopic Features

- The most common dermoscopic features in DM include atypical vascular structures, peppering, and occasionally other melanoma-specific structures.

- The most common melanoma-specific structures after atypical vascular structures were as followed:
  - regression structures (peppering and scarlike areas),
  - blue-white veil
  - atypical globules
  - atypical network


- **Peppering** was more frequent in pure DM than mixed DM

- Crystalline structures, polymorphous vessels, and milky red area were more commonly seen in mixed DM than in pure DM

- It can be hypothesized that since mixed DM has more of a melanoma specific structures (crystalline structures, polymorphous vessels, milky red area) therefore it can be more easily be diagnosed than pure DM

- At least one of the 14 melanoma-specific features evaluated on dermoscopy was found in 100% of DM

- Dermoscopy may be a useful tool for identification of DM
Both this study and Jaimes et. al found a high prevalence of atypical vascular structures in DM.

Both studies found melanoma-specific structures in 100% of cases.

**Key points**

- DM head and neck, elderly individuals
- Non-pigmented, tan or erythematous, nodule or plaque
- Associated with lentigo maligna, palpate the underlying skin
- Two forms histologically: Pure and Mixed
- Mixed DM more aggressive form, more likely to invade the regional lymph nodes

**Dermoscopy**

- Atypical vascular structures (high prevalence)
- Dotted blood vessels, linear irregular blood vessels, Polymorphous blood vessels, Milky-red areas
- Melanoma specific structures (100% of cases)
- Peppering more frequent in pure DM
- Crystalline structures, polymorphous vessels, and milky read area more common in mixed DM

**Amelanotic Melanoma**

- Accounts for 2-8% of all melanomas
- Sun exposed skin, elderly individuals
- Nodular or superficial spreading
- Males: found on the trunk
- Females: found on the limbs
Clinical Presentation

- Can be classified into three groups according to the extent or absence of pigment:
  - 1. Amelanotic - complete lack of melanin even under dermoscopy
  - 2. Partially pigmented - pigmentation is found in less than 25% of the lesion
  - 3. Lightly colored melanoma - faint brown pigmentation that covers more than 25% of the lesion but without dark brown, blue or black pigmentation

Clinical Presentation

- Truly amelanotic melanoma:
  - Superficial: asymmetrical or symmetrical erythematous macules or patches with or without scale
  - Nodular: flesh colored, pink, red. EFG (Elevated, firm, growing), lacking ABCDs of melanoma

- Hypomelanotic melanoma:
  - Look for signs of pigmentation (especially pigmentation pattern with dermoscopy)
Differential Diagnosis

- Benign:
  - Eczema
  - Contact dermatitis
  - Pyogenic granuloma
  - Nevus
  - Hypergranulation tissue
  - Hemangioma

- Malignant:
  - Basal cell carcinoma
  - Bowen's disease

- Superficial spreading type:
  - Scaly, erythematous macules and patches, with a relatively circular to oval symmetric shape, and regular border

---


Dermoscopic criteria of melanomas lacking pigment, depends on the analysis of its vascular structures:

- Most common vascular structures:
  - Dotted vessels
  - Milky-red areas
  - Linear irregular vessels (serpentine)
  - Polymorphous vessels
- AM should be strongly considered if one of the following three vascular structures is present:
  - more than one shade of pink, dotted and linear irregular (serpentine vessels) and predominant central vessels

This study showed that 90% of the lesions has at least one of the vascular criteria:
- More than one shade of pink most common (80%)
- Dotted and linear irregular (serpentine vessels) (60%)
- Predominant central vessels (20%)

Main outcome measures:
- sensitivity, specificity, and odds ratio for individual features and models for the diagnosis of melanoma and malignancy
The most common predictor of melanoma lacking significant pigment:

- blue-white veil
- scarlike depigmentation
- multiple blue-gray dots (peppering)
- irregularly shaped depigmentation
- irregular brown dots/globules
- 5 to 6 colors
- predominant central vessels


The most significant negative predictors of melanoma:

- multiple >3 milia like cysts
- comma vessels with a regular distribution
- comma vessels as the predominant vessel
- symmetrical pigmentation pattern
- multiple blue-gray globules


---

Table 7. Simple Dermoscopic Model for the Diagnosis of Melanoma Lacking Significant Pigment*

<table>
<thead>
<tr>
<th>Negative features (if present, nonmelanoma)</th>
</tr>
</thead>
<tbody>
<tr>
<td>multiple &gt;3 milia like cysts</td>
</tr>
<tr>
<td>comma vessels with a regular distribution</td>
</tr>
<tr>
<td>comma vessels as the predominant vessel</td>
</tr>
<tr>
<td>symmetrical pigmentation pattern</td>
</tr>
<tr>
<td>multiple blue-gray globules</td>
</tr>
</tbody>
</table>

*In the training set, sensitivity was 78% and specificity was 66% for the diagnosis of melanoma (area under the receiver operating characteristic curve, 0.74; SE, 0.03). In the independent test set, sensitivity was 79% and specificity was 54% (area under the receiver operating characteristic curve, 0.69; SE, 0.07).


---

Thickness of Amelanotic Melanoma

Filipovic, J.et. al. Dermatoscopy of amelanotic and hypomelanotic melanoma. JDDG. 2014; p. 467-472

Filipovic, J.et. al. Dermatoscopy of amelanotic and hypomelanotic melanoma. JDDG. 2014; p. 467-472

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Key Points

- Sun exposed skin, elderly individuals
- Accounts for 2-8% of all melanomas
- Can be classified into three groups according to the extent or absence of pigment: Amelanotic, partially pigmented, lightly colored melanoma
- Spotting amelanotic melanoma can be challenging, due to a broad differential diagnosis and lack of significant pigment

Key Points

- Nodular Amelanotic melanoma:
  - **EFG (Elevated, Firm, Growing)**, despite lacking ABCDs of melanoma
  - Biopsy these lesions
Thank You.
### Table 3. Dermoscopic Characteristics of DMMs

<table>
<thead>
<tr>
<th>Dermoscopic Feature</th>
<th>(n = 9)</th>
<th>(n = 20)</th>
<th>(n = 21)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanomatosus structures present</td>
<td>4 (44)</td>
<td>2 (10)</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Structures (irregular)</td>
<td>9 (97)</td>
<td>3 (15)</td>
<td>7 (41)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Pigment network (irregular in shape)</td>
<td>3 (30)</td>
<td>1 (5)</td>
<td>1 (5)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Depigmentation (irregular)</td>
<td>0</td>
<td>3 (15)</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Translucency (irregular)</td>
<td>0 (0)</td>
<td>3 (15)</td>
<td>4 (20)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Melanomatosus structures present</td>
<td>33 (34)</td>
<td>31 (164)</td>
<td>31 (16)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Melanomatosus structures</td>
<td>3.4 (4.8)</td>
<td>2.6 (1.6)</td>
<td>21 (2)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Translucency</td>
<td>1.1 (1.1)</td>
<td>14 (1)</td>
<td>0 (0)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Atypical melanocytes</td>
<td>1.4 (1.4)</td>
<td>1.1 (1.2)</td>
<td>1.2 (1)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Atypical keratinocytes</td>
<td>1.1 (1.2)</td>
<td>1.1 (1.2)</td>
<td>1.1 (1.2)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Blue-white veil</td>
<td>2 (22)</td>
<td>3 (15)</td>
<td>1 (5)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels</td>
<td>1 (11)</td>
<td>3 (15)</td>
<td>4 (20)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels</td>
<td>1 (11)</td>
<td>3 (15)</td>
<td>4 (20)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels</td>
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<td>3 (15)</td>
<td>4 (20)</td>
<td>&gt; .05</td>
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<td>3 (15)</td>
<td>4 (20)</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels</td>
<td>1 (11)</td>
<td>3 (15)</td>
<td>4 (20)</td>
<td>&gt; .05</td>
</tr>
</tbody>
</table>

### Table 4. Ultraviolet Analysis of Melanomas on All Dimensions

<table>
<thead>
<tr>
<th>Feature</th>
<th>Sample Size</th>
<th>Sample Size</th>
<th>Sample Size</th>
<th>Sample Size</th>
<th>Sample Size</th>
<th>Sample Size</th>
<th>Sample Size</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma characteristics</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Pigment network (irregular)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels (irregular)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels (irregular)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels (irregular)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels (irregular)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
<tr>
<td>Reticular vessels (irregular)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&gt; .05</td>
</tr>
</tbody>
</table>

Note: *P Values are calculated using the chi-square test with Yates’ correction for continuity.
Desmoplastic Melanoma: Surgical Management and Adjuvant Therapy

Dale Han, MD
Assistant Professor
Department of Surgery
Section of Surgical Oncology
Yale University School of Medicine

Background
- Desmoplastic melanoma (DM) represents <4% of melanomas
- Older patients (median age: ~65 years)
- More common in males and on head and neck
- Often thicker tumor compared with non-DM
  - Median thickness for DM: 2.5 – 3.7 mm
  - In contrast, for all newly diagnosed melanomas
    - 70% are thin melanomas (≤1 mm)
    - Median tumor thickness approximately 1 mm
- Distinct biology with clinical behavior that is unique compared with non-DM

Background
- Histologically divided into pure and mixed subtypes based on the extent of desmoplasia
- MSKCC classification system
  - Pure DM: spindle cell melanoma with ≥90% desmoplasia
  - Mixed DM: desmoplasia involving <90% but >10% of the spindle cell melanoma

Background
- DM histologic subtype correlated with outcome
- In 2004, Busam et al. classified DM as pure or mixed/combined
  - Histologic subtype significant predictor of disease-free survival (DFS) on multivariable analysis
  - Mixed DM: 3.5 times greater risk for death or metastases (95% CI 1.3 – 9.6) compared with pure DM

Background
- Hawkins et al. compared DM histologic subtypes
  - Classified as pure or mixed DM
  - 5-year melanoma-specific mortality (MSM) varied by histologic subtype
    - 31% for mixed DM
    - 11% for pure DM (P<0.01)
- Melanoma variant with unique biology

No disclosures
Treatment of Primary Melanoma

- **Wide local excision (WLE)**
  - Margins:
    - 0.5 - 1 cm for in situ
    - 1 cm for ≤1 mm
    - 1 or 2 cm for >1-2 mm
    - 2 cm for >2 mm
  - Resect to fascia
  - Closure of defect
  - Local control + remove microscopic satellites


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School of Medicine

Wide Local Excision Margin for Desmoplastic Melanoma

5-year overall survival: 79.6% for pure vs. 61.3% for mixed DM (P=0.001)

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Nodal Status for Melanoma

- Nodal status predicts survival for melanoma
  - Majority with no clinical evidence of nodal spread
  - Microscopic nodal spread
  - Morton et al. reported on sentinel lymph node biopsy (SLNB) for melanoma as a less invasive technique to evaluate nodal status


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School of Medicine

Sentinel Lymph Node Biopsy for Melanoma: MSLT-I

Within SLNB group, melanoma-specific survival (MSS) differs significantly based on SLN status in intermediate thickness (1.2-3.5 mm) and thick groups (>3.5 mm)


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School of Medicine
Is Nodal Status Also Prognostic for Desmoplastic Melanoma?

- Nodal status predicts survival for melanoma but is this also true for DM variant?
- Feng et al. studied DM patients in the SEER database (1992 – 2007)
- Nodal metastasis correlated with higher risk for DM-specific death
- Not consistently seen in other SEER-based studies on DM

Is Nodal Status Prognostic for Desmoplastic Melanoma?

- Most studies on DM unable to assess prognostic significance of nodal status due to low numbers
- Recent large study evaluated predictors of survival in DM patients
  - 316 patients presented with local disease
  - Median follow-up: 5.3 years
  - Positive nodal status included:
    - Positive SLN patients
    - Negative SLN patient who developed nodal recurrence
    - No SLNB and developed nodal recurrence

Nodal Metastasis Rate for Desmoplastic Melanoma

- Initial and early reports showed relatively high nodal disease rates
  - Conley et al.: 3 of 7 (42.9%) patients
  - Devaraj et al.: 4 of 13 (30.8%) patients
- Larger and more recent studies on DM (2001 onward) show much lower overall nodal metastasis rates
  - SEER-based studies: 2.8 – 4.3%
  - Single institution studies: 9 – 18%

Nodal Metastasis Rate for Desmoplastic Melanoma

- Lower nodal disease rate for DM compared with non-DM
  - Nodal metastasis rates for non-DM of comparable thickness (>3 mm) is >25%
  - Livestro et al.:
    - Case-matched DM and non-DM patients by age, gender, tumor thickness
    - SLN metastasis rates lower for DM (8%) compared with non-DM (33.8%, P=0.013)
  - Melanoma variant with unique biology
Sentinel Node Biopsy for Desmoplastic Melanoma

- Given the lower nodal metastasis rate for DM, use of SLNB for DM is debated
- SLN disease rates for DM
  - Contemporary series: 0 to 18.2%
  - Several studies report a zero rate of SLN metastases for DM
    - Small series assessing <25 patients who underwent SLNB
    - Of these, one study specific for head and neck but was also the only one to assess histologic subtype

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Studies Evaluating SLNB in DM

<table>
<thead>
<tr>
<th>Year</th>
<th># SLNB performed</th>
<th>+SLN (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Han et al. 2013</td>
<td>205</td>
<td>13.7%</td>
</tr>
<tr>
<td>Maurici et al. 2010</td>
<td>100</td>
<td>9%</td>
</tr>
<tr>
<td>Maurici et al. 2010</td>
<td>252</td>
<td>6.7%</td>
</tr>
<tr>
<td>Pawlik et al. 2006</td>
<td>65</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

+SLN rate:
- If exclude zero rate of +SLN: 6.2-18.2%
- If exclude studies with <50 patients: 6.2-13.7%

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Sentinel Node Metastasis Rates for Desmoplastic Melanoma

- Although lower rate of nodal disease for DM compared with non-DM, nodal status appears to predict survival in DM patients
- SLN disease rate in the range of 6 – 14%
- If a 5% risk threshold for nodal disease is utilized to justify a procedure, SLNB would in general be indicated for DM

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Additional study demonstrated that a positive SLN status was significantly correlated with a higher MSM

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Prognostic Value of SLN Status in Desmoplastic Melanoma

- Most studies on DM are unable to assess prognostic significance of SLN status due to low numbers
- Two studies showed that SLN status significantly predicted DFS

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Which DM Patients are at Higher Risk for a Positive SLN?

- Rates vary with histologic subtype
- Significantly higher positive SLN rate in mixed versus pure DM
  - SLN disease rate for mixed DM: 8.5 – 24.6%
    - Potentially mirrors what is seen for non-DM
    - Pawlik et al, compared non-DM with mixed DM and pure DM
      - Non-DM positive SLN rate 17.5%
      - Mixed DM positive SLN rate 18.6%
    - SLN disease rate for pure DM: 2.2 – 9%

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Which Patients with DM Should Be Offered SLNB?

- Older population: consider age and comorbidities
- Based on a 5% risk threshold for nodal disease, SLNB should be offered for mixed DM
- Controversy over use of SLNB for pure DM
  - Often thicker but lower positive SLN rate
  - If follow lower range for a positive SLN (2-4%): SLNB probably should not be done
  - If follow upper range for a positive SLN (5-9%): SLNB probably should be offered
- Remains debated and further studies are needed

### Studies Evaluating SLNB in DM

<table>
<thead>
<tr>
<th>Year</th>
<th>SLNB performed</th>
<th>Overall SLN (%)</th>
<th>+SLN mixed (%)</th>
<th>+SLN pure (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Han et al. 2013</td>
<td>205</td>
<td>13.7%</td>
<td>24.6%</td>
<td>9%</td>
</tr>
<tr>
<td>Berner et al. 2013</td>
<td>22</td>
<td>18.2%</td>
<td>25%</td>
<td>14%</td>
</tr>
<tr>
<td>Egger et al. 2013</td>
<td>47</td>
<td>17%</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Murotchi et al. 2010</td>
<td>100</td>
<td>0%</td>
<td>13.7%</td>
<td>4%</td>
</tr>
<tr>
<td>Murali et al. 2010</td>
<td>252</td>
<td>8.1%</td>
<td>8.5%</td>
<td>4.9%</td>
</tr>
<tr>
<td>George et al.* 2008*</td>
<td>40*</td>
<td>12.9%*</td>
<td>22.4%*</td>
<td>0</td>
</tr>
<tr>
<td>Maurichi et al. 2010</td>
<td>100</td>
<td>0%</td>
<td>15.8%*</td>
<td>2.2%</td>
</tr>
<tr>
<td>Posner et al. 2006</td>
<td>11</td>
<td>0%</td>
<td>0</td>
<td>0</td>
</tr>
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<td>Lokevsky et al. 2005</td>
<td>23</td>
<td>0%</td>
<td>0</td>
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</tr>
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<td>Sun et al. 2003</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>O'Connell et al. 2003</td>
<td>24</td>
<td>0%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Theimo et al. 2001</td>
<td>16</td>
<td>0%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Jaroszewski et al. 2001</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Includes both SLN and elective lymph node dissection cases

---

### Completion Lymph Node Dissection for Melanoma

- Completion lymph node dissection (CLND) recommended for positive SLN
  - SSO/ASCO and NCCN guidelines
  - Based on data showing unknown survival benefit
  - Recommended for regional disease control
- Rate of additional nodal disease in CLND after positive SLNB:
  - Range: 15-32%
  - MSLT-I: 16%, Sunbelt Melanoma Trial: 16%
  - Meta-analysis: 20.1%

### Completion Lymph Node Dissection for Desmoplastic Melanoma

- For DM, what is the rate of finding additional nodes with metastatic disease after a positive SLNB?
  - Limited data due to low numbers of positive SLN patients
  - 2 larger studies (>200 patients) reported on positive CLND rates
    - Moffitt Cancer Center: 4 of 24 (16.7%) positive SLN patients with additional positive CLND nodes
    - Melanoma Institute Australia: 4 of 17 (23.5%) positive SLN patients with additional positive CLND nodes
  - Positive CLND rate for DM also appears consistent with reported literature

### Does Performing CLND Improve Survival?

- DeCOG-SLT Trial
- MSLT-II Trial

---

### Adjuvant Radiation Therapy for DM

Adjuvant Radiation Therapy for DM

Summary

- DM is histologically categorized into pure and mixed subtypes
- WLE margins for DM are similar to what is used for non-DM, but thinner cases of pure DM may need 2 cm margins
- As for non-DM, nodal status is also prognostic for this melanoma variant
- Nodal metastasis rate in DM is lower than for non-DM but varies by histologic subtype

Adjuvant Systemic Therapy Options for Nodal Disease

- Interferon
- High dose ipilimumab (10 mg/kg)
- Clinical trials
  - Neoadjuvant (for macroscopic nodal disease) vs. adjuvant
  - Targeted therapy
  - Various immunotherapy regimens

Summary

- SLNB for DM provides key prognostic data
  - Significantly higher positive SLN rate for mixed DM compared with pure DM (similar to non-DM)
  - For medically fit cases, SLNB should be offered for patients with mixed DM
  - Controversial if SLNB should be used for pure DM cases and further studies needed
- Adjuvant radiation may be used to improve local control, particularly in cases with positive margins or other high risk features
Melanoma specific structures

1. Angulated lines-Altypical network (ICC = 0.05-0.21)
2. Irregular streaks (pseudopods &/or radial streaming) (ICC = 0.21-0.23)
3. Negative pigment network (ICC = 0.15)
4. Shiny white lines or Crystalline structures (only with PD) (ICC = 0.16)
5. Atypical dots & globules (ICC = 0.06-0.14)
6. Irregular blotch (ICC = 0.10)
7. Blue-white veil over raised areas (ICC = 0.34)
8. Regression structures (BWV over flat, peppering, scar) (ICC = 0.11-0.2)
9. Atypical vascular structures (ICC = 0.15)
10. Peripheral tan/brown structureless areas (ICC = 0.06)

While the intraclass correlation for any given melanoma specific structure was poor, each of these structures were in fact associated with melanoma!
Insights from UDA study by IDS

While many structures have the power to discriminate nevi from melanoma, most have extremely poor inter-observer agreement.

- The most powerful discriminator was "architectural disorder" (disorganized/dermoscopic asymmetry) with an OR of 6.6.
- The feature with highest inter-observer agreement was also "architectural disorder" (the subjective view had higher agreement than the objective view!)

Entropy - Chaos

This does not require knowing or being able to identify the presence or absence of specific colors or structures within a lesion (objective). It simply requires (blink) determining whether the colors and structures (whatever they may be) are distributed in an organized or disorganized manner (subjective).
Next slide

Organized or disorganized?

Similarly, you do not need to be able to identify specific structures to know if lesion is organized or disorganized.

You do not need to be able to identify the objects on the table to know if the desktop is organized or disorganized.

Degree of entropy:
Goal
Find skin cancer!

Are there simpler dermoscopic methods for melanoma (skin cancer) detection?

Triage algorithm
- Simplify dermoscopy (bare-bones)
- Identify concerning lesions
- High sensitivity with reasonable specificity
- Easy to teach, learn, & implement

What has been published
- 3-point checklist
- AC rule
- BB rule
- Chaos & clues
- Prediction without pigment algorithm
What are their deficiencies?

- **3-point checklist (2004)**
  - Only for pigmented lesions (not amelanotic)
  - Designed to detect MM & pBCC (not pSCC)
  - Miss non-SSMM such as nodular

- **AC rule (2011)**
  - Cannot be used for amelanotic lesions
  - Miss detection of symmetric cancers such as nodular MM

- **BB rule (2011)**
  - Idea of symmetry w/ blue-black color

- **Chaos & Clues (2012)** — recognition importance of SWS
  - Only for pigmented lesions (not amelanotic)
  - Miss symmetric cancers such as nodular MM
  - More convoluted — requires looking for 8 structures (poor kappa)

- **Prediction without pigment**
  - Only for non-pigmented lesions. Complex

Insights gained from teaching experience

- **SK, hemangioma & DF are usually easy to identify (for dermoscopists) and should be excluded from entering algorithm**

- **Clear cut benign or malignant lesions should be excluded from entering algorithm**

- **Only lesions for which the diagnosis is unknown enter the algorithm**

Newer structures that have been shown to have discriminatory power

- Intraclass correlation for any given melanoma specific structure was poor ranging from 0.05 to 0.34!

Aim: amalgamate these triage algorithms & new insights into something better

- Select features from each with the most discriminatory power to identify malignancy
- Address deficiencies found in each
- Add newly described features with high sensitivity for skin cancer (SWS) — This requires use of polarized dermoscopy!
- Harness features with high kappa (harness brains normal power — UDA)
This algorithm does not apply to lesions on glabrous skin (i.e., palms, soles, mucosal surfaces), and nails.

May require toggling between PD & NPD since SK and DF are easier to recognize with NPD.

Patients should continue self-monitoring, and changes in morphology or symptoms should raise concern.

Colors & structures distributed in an asymmetric/chaotic fashion.

Monitoring can include short-term, long-term, or self-monitoring for change.

Seborrheic Keratoses (SK)
- Sharply demarcated borders
- Milia-like cyst
- Comedo-like opening
- Fissures & ridges (gyri & sulci)
- Fingerprint-like
- Hairpin vessels
- Moth-eaten borders

Dermatofibroma (clinical info is critical)
- Delicate network (exception)
- Central scar-like/crystalline
- Ring-like globules
- Vessels/flush in center

Angioma/hemangioma
- Lacunae separated by BWV septae
  - Red
  - Maroon
  - Blush
  - Clear

*This algorithm does not apply to lesions on glabrous skin (i.e., palms, soles, mucosal surfaces), and nails.*
Definition of:
Symmetry (organized) / Asymmetry (disorganized)
- Symmetry of SHAPE (but disorganized pattern)
- Organized PATTERN (but asymmetry of shape)

According to dermoscopy this lesion is considered asymmetric (disorganized)
According to dermoscopy this lesion is considered symmetric (organized)

Examples
- Symmetry in pattern
  - No symmetry of shape (asymmetric shape)
  - According to dermoscopy this is symmetric & organized
- No symmetry in pattern (asymmetric pattern)
  - Symmetry of shape
  - According to dermoscopy this is asymmetric & disorganized

Examples
- Pizza Margherita
  SYMMETRY (organized)
- Pizza Quattro Stagioni
  ASYMMETRY (disorganized)

Disorganized: BCC, SCC, MM
Cancers on occasion manifest an organized pattern

- Nodular MM / MM on sun damaged skin
  - blue, black, gray

- Spitzoid MM
  - negative network or starburst pattern

- Amelanotic cancers (BCC, KA, MM)
  - SWS, vessels, ulceration

Difficult due to morphology

- Up to 2/3 of melanomas fail to manifest clinical morphologic features to aid in their detection (lack ABCD)

- Dermoscopy has been the beacon in helping to define the morphologic features of subsets of melanoma that were routinely being missed on clinical examination
Dermoscopic features of Nodular Melanoma

They lack features of BCC, banal nevi & SK

<table>
<thead>
<tr>
<th>Pigmented</th>
<th>Amelanotic</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Network - Arborizing vessels</td>
<td></td>
</tr>
<tr>
<td>- Streaks - Comma vessels</td>
<td></td>
</tr>
<tr>
<td>+ Symmetry + Symmetry</td>
<td></td>
</tr>
<tr>
<td>+ BWV + Atypical vessels</td>
<td></td>
</tr>
<tr>
<td>+ Blue/Black color + Crystalline structures</td>
<td></td>
</tr>
<tr>
<td>+ Multi-colored + Atypical vessels</td>
<td></td>
</tr>
</tbody>
</table>

Pigmented Amelanotic
- Network
- Streaks
- Regression
+ Symmetry
+ BWV
+ Blue/Black color
+ Multi-colored
+ Atypical vessels

They lack features of BCC, banal nevi & SK

Pigmented Amelanotic
- Network
- Streaks
- Regression
+ Symmetry
+ BWV
+ Blue/Black color
+ Multi-colored
+ Atypical vessels

Difficult to diagnose melanomas

Amelanotic
- Arborizing vessels
- Comma vessels
+ Symmetry
+ Atypical vessels
+ Crystalline structures

Difficult to diagnose melanomas

Nodular

Desmoplastic

Nevus

Amelanotic

Epidermotropic metastatic

Verrucous

Face

Non-facial skin

MM on chronic sun damaged skin

Spitzoid

Other

Difficult to diagnose melanomas

Verrucous MM

Collision: MM with SK

Epidermotropic metastatic

Difficult to diagnose melanomas

Other

Nodular

Desmoplastic

Nevus

Amelanotic

Epidermotropic metastatic

Verrucous

Face

Non-facial skin

MM on chronic sun damaged skin

Spitzoid

Other

Difficult to diagnose melanomas
Milky red globules

Dermoscopic features of Nodular Amelanotic Melanoma

- Arborizing vessels
- Comma vessels
- Symmetry
- Atypical vessels
- Crystalline structures

Already Discussed
The Blink sign
CONCLUSIONS AND RELEVANCE. Seborrheic keratosis-like melanomas can be dermoscopically challenging, but the presence of the blue-black sign, pigment network, pseudopods or streaks, and/or blue-white veil, despite the presence of other SK features, allows the correct diagnosis of most of the difficult melanoma case.

- Blue-black color
- Network
- Streaks
- Blue-white veil
Rhomboidal structure
Wavy angulated lines (incomplete rhomboidal structures)

Pigmented
Amelanotic
Nodular
Pure (clinically)
Associated with LM
Desmoplastic
Nevoid with conventional SSMM features
Nevoid with nevus like features
Non-nodular
Amelanotic
Epidermotropic metastatic
Verrucous MM
Collision: MM with SK
Verrucous
Facial skin
Non-facial skin
MM on chronic sun damaged skin
Spitzoid
MM in children
Other
Difficult to diagnose melanomas

Polygonal structures
Difficult to diagnose melanomas tend to be symmetric & have one of the following dermoscopic features:

- Starburst pattern
- Blue-black or gray color
- White structures
- Negative network
- Vessels/Ulceration

- Shiny white structures (PD)
- White circles (PD or NPD)
The majority of these “other” lesions are:

Nevi in general should be monitored (self/clinician/app)
Overall Sensitivity | Overall Specificity | Malignancies
---|---|---
Three-Point | 91.0 | 71.9 | Melanoma, pBCC
Chaos and Clue | 90.6 | 82.7 | Melanoma, pSCC
Blue-Ring Rule | 78.2 | 80.5 | Melanoma
AC Rule | 94.0 | 62.0 | Melanoma
TADA | 94.8 | 72.3 | Melanoma, pBCC, pSCC

How did TADA perform

TADA results by lesion type and dermoscopic training

Thank you
Medical Treatment for Melanoma

Sanjiv S. Agarwala, MD
Professor of Medicine
Temple University School of Medicine
Chief, Oncology & Hematology
St. Luke’s Cancer Center, Bethlehem, PA

Disclosures
None

Overview
• Current Therapy for Metastatic Disease
  – Immunotherapy
  – Targeted Therapy
• Current Status of Adjuvant Therapy

Current Therapeutic Options for Patients with Metastatic Melanoma
• For BRAF-WT Patients
  – Immunotherapy
    • Monotherapy or combination?
• For BRAF+ Patients
  – Immunotherapy or targeted therapy
    • What is the correct sequence?

Transforming the Landscape
Hit a Target
Immunotherapy
Target host
Target tumor
Targeted Therapy

Current Therapeutic Options for Patients with Metastatic Melanoma
• For BRAF-WT Patients
  – Immunotherapy
    • Monotherapy or combination?
• For BRAF+ Patients
  – Immunotherapy or targeted therapy
    • What is the correct sequence?
Targeted Immunotherapy = Checkpoint Inhibitors

What is a “Check-Point”?

T-Cell Activity Is Regulated By Immune Checkpoints to Limit Autoimmunity

What is a “Check-Point” Inhibitor?

Check-Point Inhibitors Approved for Melanoma

- Anti CTLA4 (ipilimumab)
- Anti PD-1 (pembrolizumab, nivolumab)
- Combination anti CTLA-4 and anti-PD1 (ipilimumab and nivolumab)
**Clinical Results with Ipilimumab (2nd and 1st line)**

Ipilimumab vs vaccine and Ipi + DTIC vs DTIC

<table>
<thead>
<tr>
<th>HR: 0.66 and 0.68</th>
<th>Pre-treated pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab 3 mg/kg +/- gp100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HR: 0.72</th>
<th>First line</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab 10 mg/kg + DTIC</td>
<td></td>
</tr>
</tbody>
</table>

Pre-treated pts


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**Immune Checkpoint Inhibitors Provide Durable Long-term Survival for Patients with Advanced Melanoma**

**Keynote-006 Front-line Pembrolizumab vs Ipilimumab**

- **Patients**
  - Unresectable, stage III or IV melanoma
  - 33 prior therapy, excluding anti-CTLA-4, PD-1, or PD-L1 agents
  - Known BRAF status
  - ECOG PS 0-1
  - No active brain metastases
  - No serious autoimmune disease

- **Patients enrolled from 83 sites in 16 countries.**

- **Prior anti-BRAF targeted therapy was not required for patients with normal LDH levels and no clinically significant tumor-related symptoms or evidence of rapidly progressing disease.**

- **Defined as membranous PD-L1 expression in ≥1% of tumor cells as assessed by IHC using the 22C3 antibody.**

- **Patients**
  - Pembrolizumab 10 mg/kg IV Q2W
  - Pembrolizumab 10 mg/kg IV Q3W
  - Ipilimumab 3 mg/kg IV Q3W x 4 doses

- **Primary end points: PFS and OS**
- **Secondary end points: ORR, duration of response, safety**

**Tumor Response (irRC, investigator)**

<table>
<thead>
<tr>
<th>Pembrolizumab</th>
<th>Ipilimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 856</td>
<td>N = 278</td>
</tr>
<tr>
<td>ORR (% 95% C)</td>
<td>42 (38-46)</td>
</tr>
<tr>
<td>Best overall response, % (95% C)</td>
<td>16 (12-21)</td>
</tr>
<tr>
<td>CR</td>
<td>13 (11-16)</td>
</tr>
<tr>
<td>PR</td>
<td>29 (25-33)</td>
</tr>
<tr>
<td>SD</td>
<td>21 (18-25)</td>
</tr>
<tr>
<td>PD</td>
<td>29 (26-33)</td>
</tr>
<tr>
<td></td>
<td>36 (33-45)</td>
</tr>
</tbody>
</table>

**Kaplan-Meier Estimates of Survival (Median Follow-Up, 33.9 mo)**

<table>
<thead>
<tr>
<th>OS (%)</th>
<th>Pembrolizumab</th>
<th>N = 856</th>
<th>Ipilimumab</th>
<th>N = 278</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mo</td>
<td>62%</td>
<td>60%</td>
<td>63%</td>
<td>63%</td>
</tr>
<tr>
<td>24 mo</td>
<td>50%</td>
<td>44%</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>36 mo</td>
<td>43%</td>
<td>39%</td>
<td>43%</td>
<td>43%</td>
</tr>
<tr>
<td>48 mo</td>
<td>39%</td>
<td>35%</td>
<td>39%</td>
<td>39%</td>
</tr>
</tbody>
</table>

**PFS per irRC by Investigator**

<table>
<thead>
<tr>
<th>PFS (%)</th>
<th>Pembrolizumab</th>
<th>N = 856</th>
<th>Ipilimumab</th>
<th>N = 278</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mo</td>
<td>32%</td>
<td>30%</td>
<td>32%</td>
<td>32%</td>
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<tr>
<td>24 mo</td>
<td>26%</td>
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<tr>
<td>36 mo</td>
<td>23%</td>
<td>21%</td>
<td>23%</td>
<td>23%</td>
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<tr>
<td>48 mo</td>
<td>20%</td>
<td>18%</td>
<td>20%</td>
<td>20%</td>
</tr>
</tbody>
</table>

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**Ipilimumab became the standard of care in 2011**

But can we do better?
Anti PD-1 is better than ipilimumab frontline and responses are durable even after stopping treatment

But what about combining CTLA-4 and PD-1?

**Updated Response To Treatment**

<table>
<thead>
<tr>
<th></th>
<th>NIVO+IPI (N=314)</th>
<th>NIVO (N=316)</th>
<th>IPI (N=315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR, % (95% CI)*</td>
<td>58.9 (53.3–64.4)</td>
<td>44.6 (39.1–50.3)</td>
<td>19.0 (14.9–23.8)</td>
</tr>
<tr>
<td>Best overall response — %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>17.2</td>
<td>14.9</td>
<td>4.4</td>
</tr>
<tr>
<td>Partial response</td>
<td>41.7</td>
<td>29.7</td>
<td>14.6</td>
</tr>
<tr>
<td>Stable disease</td>
<td>11.5</td>
<td>9.8</td>
<td>21.3</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>23.6</td>
<td>38.6</td>
<td>51.1</td>
</tr>
<tr>
<td>Unknown</td>
<td>8.1</td>
<td>7.0</td>
<td>8.6</td>
</tr>
<tr>
<td>Median duration of response—months (95% CI)</td>
<td>NR (NR-NR)</td>
<td>31.1 (31.1-NR)</td>
<td>18.2 (8.3-NR)</td>
</tr>
</tbody>
</table>

*By RECIST v1.1; NR = not reached.

- At the 18-month DML, the CR rate for NIVO+IPI, NIVO and IPI was 12.1%, 9.8% and 2.2%, respectively.
**Updated Progression-Free Survival**

- NIVO + IPI (N=314)
- NIVO (N=316)
- IPI (N=315)

<table>
<thead>
<tr>
<th>Months</th>
<th>NIVO + IPI</th>
<th>NIVO</th>
<th>IPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>11.7 (8.9–21.9)</td>
<td>6.9 (4.3–9.5)</td>
<td>2.9 (2.8–3.2)</td>
</tr>
</tbody>
</table>

**Percentage of PFS**

<table>
<thead>
<tr>
<th>Months</th>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
<th>60%</th>
<th>70%</th>
<th>80%</th>
<th>90%</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td>IPI</td>
<td>NIVO + IPI</td>
<td>NIVO</td>
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</tbody>
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**Checkmate 067: Safety Summary**

- With an additional 19 months of follow-up, safety was consistent with the initial report.
- Most select AEs were managed and resolved within 3-4 weeks (85–100% across organ categories).
- ORR was 70.7% for pts who discontinued NIVO + IPI due to AEs, with median OS not reached.

### Patients reporting event, %

<table>
<thead>
<tr>
<th>Treatment-related adverse event (AE)</th>
<th>Any Grade</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment-related AE leading to discontinuation</td>
<td>15.0</td>
<td>10.5</td>
</tr>
<tr>
<td>Treatment-related death, n (%)</td>
<td>2 (0.6)</td>
<td>1 (0.3)</td>
</tr>
</tbody>
</table>

- Cardiomyopathy (NIVO + IPI, n=1); Liver necrosis (NIVO + IPI, n=1). Both deaths occurred >100 days after the last treatment.
- Neutropenia (NIVO, n=1); colon perforation (IPI, n=1).

- Skin (n=18)
- Gastrointestinal (n=46)
- Endocrine (n=15)
- Hepatic (n=60)
- Pulmonary (n=3)
- Renal (n=6)

**Checkmate 067: Safety Data in CheckMate-067 Trial of IPI vs. NIVO vs. IPI/NIVO**

- Median OS, months (95% CI) NR (29.1–NR)
- HR (99.5% CI) vs. IPI 0.55 (0.42 – 0.72)*
- HR (99.5% CI) vs. NIVO 0.88 (0.69 – 1.12) – –

**Updated Survival**

- Decision Point: Immunotherapy
- PD-1 alone
- PD-1/CTLA-4 Combination

*Cardiomyopathy (NIVO + IPI, n=1); Liver necrosis (NIVO + IPI, n=1). Both deaths occurred >100 days after the last treatment.

# Larkin J et al. NEJM 2015;373:23–34.

**Checkmate 067: Safety**

- Onset Grade 3–4 Treatment-Related Select AEs
- Circles represent medians; bars signify ranges.

# Larkin J et al. ECC 2015.
Can a biomarker help us decide?

Keynote 001 Pembrolizumab
PD-L1 Expression and Response

**APS, Allred proportion score.**

- **PD-L1 Positive**
  - 1-10% Staining
    - APS = 2
  - 10-33% Staining
    - APS = 3
  - 66-100% Staining
    - APS = 5

- **PD-L1 Negative**
  - 0% Staining
    - APS = 0

**ORR, % (95% CI)**

<table>
<thead>
<tr>
<th>PD-L1 Level</th>
<th>ORR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1% PD-L1</td>
<td>NR (26.5 – NR)</td>
</tr>
<tr>
<td>≥1% PD-L1</td>
<td>23.5 (13.0 – NR)</td>
</tr>
</tbody>
</table>

**HR (95% CI)**

<table>
<thead>
<tr>
<th>PD-L1 Level</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1% PD-L1</td>
<td>0.74 (0.52 – 1.06)</td>
</tr>
<tr>
<td>≥1% PD-L1</td>
<td>1.03 (0.72 – 1.48)</td>
</tr>
</tbody>
</table>

**Median OS, mo**

<table>
<thead>
<tr>
<th>PD-L1 Level</th>
<th>Median OS (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1% PD-L1</td>
<td>NR (17.1 – 29.7)</td>
</tr>
<tr>
<td>≥1% PD-L1</td>
<td>22.1 (17.1 – 29.7)</td>
</tr>
</tbody>
</table>

**Current Therapeutic Options for Patients with Metastatic Melanoma**

- For BRAF-WT Patients
  - Immunotherapy
  - Monotherapy or combination?
- For BRAF+ Patients
  - Immunotherapy or targeted therapy
  - What is the correct sequence?

**Melanoma is not one disease**

**MAPK Pathway**

- Growth Factors → RAS → BRAF → MEK → ERK → Cell proliferation and survival

**BRAF Mutation**

- Growth Factors → BRAF → MEK → ERK → Cell proliferation and survival

**MAPK Pathway Targeted Therapy**

- **BRAFi (dabrafenib)**
  - PFS HR, 0.37 vs DTIC
  - Hyperproliferative skin AEs

- **BRAFi (vemurafenib)**
  - PFS HR, 0.38 vs DTIC
  - Hyperproliferative skin AEs

- **MEKi (trametinib)**
  - PFS HR, 0.45 vs chemotherapy

**Decision Point**

- **BRAF mutation test**
- **BRAF** mutation negative
- **BRAFi** mutation positive
- Immunotherapy

**Antitumoral response: Targeted therapies vs. Immunotherapies (CTLA-4 antibodies)**

- Targeted Therapies vs. Immunotherapy vs. Immunotherapies (CTLA-4 antibodies)

**Dabrafenib + Trametinib: Long Term FU**

- Part C: Study Design (phase 2)
OS (Intent-to-Treat)

Pembro Keynote 001: 4 Year OS

Analysis cut-off date: September 3, 2014.
Pembrolizumab Q2W vs ipilimumab
Pembrolizumab Q3W vs ipilimumab

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>Overall</th>
<th>Male</th>
<th>Female</th>
<th>Age &lt;65 y</th>
<th>Age ≥65 y</th>
<th>White race</th>
<th>US</th>
<th>Rest of world</th>
<th>ECOG PS 0</th>
<th>ECOG PS 1</th>
<th>White race</th>
<th>US</th>
<th>Rest of world</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>1</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

First-line therapy
Second-line therapy
PD-L1 positive
PD-L1 negative
BRAF wild type
BRAF mutant, prior anti-BRAF
BRAF mutant, no prior anti-BRAF
No prior immunotherapy

Phase III KEYNOTE-006:
PFS in Prespecified Subgroups

KEYNOTE-001: Phase I
RECIST Response (v1.1)

<table>
<thead>
<tr>
<th>Treatment naïve n=152</th>
<th>ORR 45%</th>
<th>CR 14%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population n=581</td>
<td>ORR 33%</td>
<td>CR 8%</td>
</tr>
</tbody>
</table>

BRAF Inhibitors

Vemurafenib
Dabrafenib

Phase 1 2 3 1 2 3
RR 56% 57% 57% 56% 59% 59%
PFS 6.7 6.9 5.5 6.3 6.9
OS 13.8 15.9 13.6 13.1 18.2

D+T: Long Term FU
LDH < ULN and < 3 metastatic sites (ITT)
Contemplating the Options

Anti-PD1 therapy
BRAF-targeted therapy

EA6134

Will sequence not matter in the future??

- BRAF inhibitor alone or BRAF + MEK inhibitors → rapid and clinically significant responses
- Immunotherapy → less frequent objective responses, but clinically significant durability
- Combining targeted therapy with immunotherapy
  - Can harness and perpetuate the enhanced anti-tumor response following targeted inhibition
  - May lead to durable response and prolonged survival

Combining Targeted Therapy With Immunotherapy

Figure modified from Ribas A et al. Clin Cancer Res 2012 and Hamid O et al. SMR 2015.

Melanoma survival curves depending on the type of therapy

Targeted-immuno triplets: BRAF + MEK + PD1/L1

- Dabrafenib + Trametinib + Pembrolizumab
- Dabrafenib + Trametinib + PDR-001
- Vemurafenib + Cobimetinib + Atezolizumab

Targeted-immuno triplets: BRAF + MEK + PD1/L1

Multiple Triplet Combinations Launching Into Phase III:
- Dabrafenib + Trametinib + Pembrolizumab
- Dabrafenib + Trametinib + PDR-001
- Vemurafenib + Cobimetinib + Atezolizumab

Overview

- Current Therapy for Metastatic Disease
  - Immunotherapy
  - Targeted Therapy
- Current Status of Adjuvant Therapy

Distribution of Melanoma Burden by Stage

The burden of high risk disease dwarfs that of advanced melanoma and is an important clinical problem

- Systemic Therapy
- Adjuvant Therapy
- Prevention
Adjuvant Therapy

• The Old
  – Interferon
• The New
  – Ipilimumab
• The Future

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Dose</td>
<td>3 MIU</td>
<td>3 x weekly</td>
<td>18 – 24 months</td>
</tr>
<tr>
<td>Intermediate Dose</td>
<td>10 MIU</td>
<td>5 x weekly</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Maintenance</td>
<td>10 MIU</td>
<td>3 x weekly</td>
<td>12 – 24 months</td>
</tr>
<tr>
<td></td>
<td>5 MIU</td>
<td>3 x weekly</td>
<td>24 months</td>
</tr>
<tr>
<td>High Dose</td>
<td>20 MIU/m²</td>
<td>5 x weekly</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Maintenance</td>
<td>10 MIU/m²</td>
<td>3 x weekly</td>
<td>11 months</td>
</tr>
<tr>
<td>Short Course</td>
<td>X 1 20 MIU/m²</td>
<td>5 x weekly</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Intermittent</td>
<td>X 3 20 MIU/m²</td>
<td>20 MIU/m²</td>
<td>Q 4 months</td>
</tr>
</tbody>
</table>

Log-rank test: \( P_2 = 0.02; P_1 = 0.01 \)

E1684: Updated Efficacy
(ITT at 12.6 yr Median Follow-up)

Tweaking Interferon

• Shorten the duration of HDI – high dose IV only
• Use pegylated IFN – once weekly dosing, lower dose with comparable AUC

Study design: ECOG 1697

Patients with intermediate- and high-risk melanoma

E1697 Induction Only HD IFN vs Observation
EORTC 18991 (PEG-IFN): Design

Stratified by:
- Microscopic (N1) vs. palpable (N2)
- 1 vs. 2-4 vs. 5+ nodes
- Breslow
- Ulceration
- Gender
- Site

Observation Peg-IFN alfa-2b
- Induction (8 weeks) 6 µg/kg/week
- Maintenance (5 years or distant metastasis) 3 µg/kg/week
- Dose reduction to 3, 2, 1 to maintain performance status

Primary Endpoints:
- Relapse-free survival (RFS)
- Distant metastasis-free survival (DMFS)

Patients (n=1,256):
Resected TxN1-2M0 melanoma, within 7 weeks of lymphadenectomy

Randomization

No. Patients At Risk
368 629 397 311 220 76 5
328 627 428 346 243 85 14

P = .01 HR = 0.82 (95% CI 0.71, 0.96)


Adjuvant Therapy

- The Old
  - Interferon
- The New
  - Ipilimumab
- The Future

Ipilimumab in Melanoma

- Standard Dose
  - 3mg/kg
  - Approved in metastatic melanoma
- High Dose
  - 10mg/kg
  - Approved in adjuvant therapy of melanoma

Ipilimumab (HD) vs Placebo
EORTC 18071/CA184-029: Study Design

Primary Endpoint: Recurrence-free Survival (IRC)

N=475
N=476

Week 1 Week 12 Week 24

Stratification factors:
- Stage (IIIA vs IIIB vs IIIC ≥4 positive lymph nodes vs IIIC ≥4 positive lymph nodes)
- Regions (North America, European countries and Australia)

Patients alive (\%)

*Stratified by stage at randomization

Deaths/patients

<table>
<thead>
<tr>
<th></th>
<th>Ipilimumab (n = 471)</th>
<th>Placebo (n = 474)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 3/4</td>
</tr>
<tr>
<td>Any AE, %</td>
<td>98.7</td>
<td>54.1</td>
</tr>
<tr>
<td>Treatment-related AE, %</td>
<td>49.4</td>
<td>45.4</td>
</tr>
<tr>
<td>Treatment-related AE discontinuation, %</td>
<td>66.6</td>
<td>22.2</td>
</tr>
<tr>
<td>Any immune-related AE, %</td>
<td>94.1</td>
<td>45.4</td>
</tr>
</tbody>
</table>

No new deaths due to drug-related AEs compared with the primary analysis
- 5 patients (1.1\%) in the ipilimumab group
  - 3 patients with colitis (2 with gastrointestinal perforations)
  - 1 patient with myocarditis
  - 1 patient had multiorgan failure with Guillain-Barré syndrome
- No deaths related to study drug in the placebo group

EORTC 18071: Overall Survival

65\% 54\%
5-year difference 11\%
CI = confidence interval; NR = not reached.

Years
0 1 2 3 4 5 6 7 8
0 10 20 30 40 50 60 70 80 90 100

Eggermont AMM et al. NEJM 2016

Ipilimumab
Placebo

E1609 Phase III Ipilimumab

Patients with resectable stage IIIB or IIIC or IV (M1a or M1b)
N=1500 +

High dose interferon

Ipilimumab 10mg/kg
Ipilimumab 3mg/kg

Primary Endpoint: RFS, OS
Secondary Endpoints: Safety, Quality of life, Immunologic correlates of RFS, OS
Completed accrual: 8/2014 - Results anticipated: 2018

Study Chair: A Tarhini

RFS: Ipi10 vs. Ipi3
(Concurrently randomized patients)

Safety Summary

<table>
<thead>
<tr>
<th></th>
<th>Ipilimumab (n = 516)</th>
<th>Placebo (n = 553)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade</td>
<td>Grade 3/4</td>
</tr>
<tr>
<td>Any AE, %</td>
<td>98.4</td>
<td>63.2</td>
</tr>
<tr>
<td>Treatment-related AE, %</td>
<td>56.0</td>
<td>36.0</td>
</tr>
<tr>
<td>Treatment-related AE, leading to discontinuation, %</td>
<td>34.9</td>
<td>26.2</td>
</tr>
<tr>
<td>Any immune-related AE, %</td>
<td>77.8</td>
<td>18.8</td>
</tr>
</tbody>
</table>

Treatment Related Deaths

Ipilimumab (Ipil) vs. Placebo (Pbc):
- Ipil3 (2 patients/516; 0.4\%)
- Ipil10 (8 patients/553; 1.6\%)

Clinicaltrials.gov

Study Chair: A Tarhini

ASCO ANNUAL MEETING'17 - BASCOT

ASCO ANNUAL MEETING'17 - BASCOT
Adjuvant Therapy

- The Old
  - Interferon
- The New
  - Ipilimumab
- The Future

The Future

- Anti PD-1 antibodies are better than anti CTLA-4 in metastatic melanoma
- Makes sense to test them in adjuvant therapy
- What about BRAF+ patients?

CA209-238: Study Design

- Patients with high-risk, completely resected stage IIIB/IIIC or stage IV melanoma
- Enrollment period: March 30, 2015 to November 30, 2015
- Follow-up: Maximum treatment duration of 1 year
- NIVO 3 mg/kg IV Q2W and IPI placebo IV Q3W for 4 doses then Q12W from week 24
- IPI 10 mg/kg IV Q3W for 4 doses then Q12W from week 24 and NIVO placebo IV Q2W
- Stratified by:
  1) Disease stage: IIIB/C vs IV M1a-M1b vs IV M1c
  2) PD-L1 status at a 5% cutoff in tumor cells

Primary Endpoint: RFS

Safety Summary

- There were no treatment-related deaths in the NIVO group
- There were 2 (0.4%) treatment-related deaths in the IPI group (marrow aplasia and colitis), both >100 days after the last dose

EORTC 1325/ KEYNOTE 054
Adjuvant Targeted Therapy

COMBI-AD: STUDY DESIGN

Key eligibility criteria:
- Completely resected, high-risk stage IIIA (lymph node metastasis > 1 mm), IIIB, or IIIC cutaneous melanoma
- BRAF V600E/K mutation
- Surgically free of disease ≤ 12 weeks before randomization
- ECOG performance status 0 or 1
- No prior radiotherapy or systemic therapy

Stratification:
- BRAF mutation status (V600E, V600K)
- Disease stage (IIIA, IIIB, IIIC)

Treatment: 12 months

- Dabrafenib 150 mg BID + trametinib 2 mg QD (n = 438)
- 2 matched placebos (n = 432)

Follow-up until end of study

Primary endpoint: RFS

Secondary endpoints: OS, DMFS, FFR, safety

Group

Events, n (%)

Median (95% CI), mo

HR (95% CI)

Dabrafenib

166 (38)

NR (44.5-NR)

0.47 (0.39-0.58); P < .001

Placebo

248 (57)

16.6 (12.7-22.1)

P = .0000000000000153

Conclusions: Metastatic

- Monotherapy or combination immunotherapy are both appropriate options for all patients
- Anti-PD1 is better than anti-CTLA4
  - Improved RR, PFS and OS
  - Less toxicity
  - Combination anti-CTLA4 and anti-PD1 has higher RR and PFS compared to anti-PD1 but not improved OS and higher toxicity

Conclusions: Adjuvant Therapy

- IFN is in retirement phase
- Ipilimumab high-dose is FDA-approved but should not be used
- PD-1 beats ipilimumab
- BRAF/MEK combo for BRAF+ patients
Surgical Treatment of Melanoma Across the Disease Spectrum: Standards of Care and Evolving Paradigms

Merrick Ross, M.D.
Professor of Surgical Oncology
M.D. Anderson Cancer Center

AOCD Annual Fall Meeting
October 28th, 2017
New Orleans, Louisiana

The New Melanoma Landscape
• Recently approved systemic therapies for Stage IV
  - B-Raf mutant: Vemurafenib, dabrafenib, trametinib, dabrafenib / trametinib
  - Ipilimumab, anti-PD-1, (combination of anti-CTLA4 / anti-PD-1)
• Survival rates of resected Stage IV disease
• Novel intralesional agents (oncolytic immunotherapy)
• Integration of Sentinel Lymph Node (SLN) biopsy
  - the new Stage I / II disease
  - the new Stage III disease

Stage I and II Primary Melanoma
Components of Treatment
1. Wide excision
   - margins appropriate for thickness
   - reconstruction
2. Sentinel Node Biopsy
   - indications
   - technique

Lymph Node Involvement and Melanoma
• Regional nodes, most common site of first recurrence after wide excision of primary melanoma
  - 15%-50% chance for in-basin failure
  - > 50% chance for distant relapse

Surgical Treatment of Melanoma Across the Disease Spectrum
Topics
• Stage I and II
  - SLN biopsy
• Stage III
  - completion dissection?
  - neo-adjuvant strategies for advanced nodal disease
• Stage IV
  - metastasectomy in the new melanoma landscape
Sentinel Node Biopsy

Goals

- Minimally invasive approach to nodal staging
- Improve the disease outcome for the node positive patients
  - survival
  - regional control

Prevent the development of clinical nodal involvement

Regional Control?

Risk Factors for Regional Recurrence After Surgery Alone

<table>
<thead>
<tr>
<th>Reference</th>
<th>Regional Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fuhrmann, 2001</td>
<td>26%</td>
</tr>
<tr>
<td>Kretschmer, 2001</td>
<td>34%</td>
</tr>
<tr>
<td>Lee, 2000</td>
<td>30%</td>
</tr>
<tr>
<td>Shen, 2000</td>
<td>14%</td>
</tr>
<tr>
<td>Hughes, 2000</td>
<td>25%</td>
</tr>
<tr>
<td>Monsour, 1993</td>
<td>52%</td>
</tr>
<tr>
<td>Miller, 1992</td>
<td>12%</td>
</tr>
<tr>
<td>O’Brien, 1991</td>
<td>24%</td>
</tr>
<tr>
<td>Calabro, 1989</td>
<td>17%</td>
</tr>
<tr>
<td>Bowsher, 1986</td>
<td>15%</td>
</tr>
<tr>
<td>Byers, 1986</td>
<td>16%</td>
</tr>
</tbody>
</table>

Weighted average:

692 failures / 3350 patients = 21%

Risk Factors for Regional Recurrence After Surgery Alone

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Regional Failure Rate</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracapsular extension</td>
<td>31% - 63%</td>
<td>Lee, Calabro, Shen, Monsour</td>
</tr>
<tr>
<td>≥4 involved lymph nodes</td>
<td>22% - 63%</td>
<td>Lee, Calabro, Miller, Kretschmer</td>
</tr>
<tr>
<td>Lymph node ≥3 cm</td>
<td>42% - 80%</td>
<td>Lee</td>
</tr>
<tr>
<td>Cervical lymph node location</td>
<td>33% - 50%</td>
<td>Lee, Bowsher, Monsour</td>
</tr>
</tbody>
</table>

30%–50% if high-risk features present

In-Basin Failure

Selective Lymphadenectomy vs ELND (Node Positive Only)

<table>
<thead>
<tr>
<th>% Nodal Failure</th>
<th>ELND</th>
<th>SLN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopic</td>
<td>Slingluff, 1997</td>
<td>MDACC Study, 2003</td>
</tr>
<tr>
<td>Macroscopic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Does early treatment of lymph node disease improve survival?
MSLT I: Trial Design

- **Melanoma >1 mm or > Clark IV**

Wide excision alone 40% 60%
Wide excision + SLN

Randomization
DFS: Secondary Endpoint
DSS: Primary Endpoint

Occult Stage III
CLND for Recurrence Immediate CLND

No recurrence: observation

Melanoma Specific Survival – Node+
Final Dataset (intent to treat)

![Graph showing survival data](image)

DSS: Primary Endpoint
DFS: Secondary Endpoint

Occult Stage III

40% 60%

Morton A 50 Year Odyssey 111509 14

Melanoma Specific Survival
– Node+

Final Dataset (intent to treat)

Time (years)
Survival (%)

HR: 0.56
95% C.I. (0.37 - 0.84)
Log Rank P=0.006

Unraveling Heterogeneity of Stage I/II Melanoma 5-Year Survival Rate by T-Classification System

The new stage I / II

<table>
<thead>
<tr>
<th>T-category 6th Edition</th>
<th>SLN Subset*</th>
</tr>
</thead>
<tbody>
<tr>
<td>95 ± 0.4</td>
<td>97 ± 1.1</td>
</tr>
<tr>
<td>91 ± 1.0</td>
<td>95 ± 1.5</td>
</tr>
<tr>
<td>89 ± 0.7</td>
<td>95 ± 0.6</td>
</tr>
<tr>
<td>77 ± 1.7</td>
<td>86 ± 2.0</td>
</tr>
<tr>
<td>79 ± 1.2</td>
<td>85 ± 1.5</td>
</tr>
<tr>
<td>63 ± 1.5</td>
<td>76 ± 2.5</td>
</tr>
<tr>
<td>67 ± 2.4</td>
<td>76 ± 3.6</td>
</tr>
</tbody>
</table>

AJCC 7th Edition

45 ± 1.9

*Stage-appropriate use of SLN biopsy

SLN Biopsy
Multi-Disciplinary Components

- Pre-operative lymphoscintigraphy
  - accurate technique
  - accurate reading
  - surgeon to look at images
- Surgical approach
  - injection of radio-colloid and blue dye
  - removal of all SLN’s
  - images in the room
- Pathological evaluation
  - serial sections and immuno-stains

Constellation of Node Positive Disease

New Stage IIII

AJCC Stage III 5-Year Survival by Tumor Burden, # of Nodes, and Primary Tumor Ulceration

<table>
<thead>
<tr>
<th>Ulceration</th>
<th>No. of Nodal Micrometastases (± SE)</th>
<th>No. of Nodal Macrometastases (± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>1 2-3 4+ 1 2-3 4+</td>
<td>1 2-3 4+ 1 2-3 4+</td>
</tr>
<tr>
<td>81.5±1</td>
<td>73.2±3.7</td>
<td>51.6±7.2</td>
</tr>
<tr>
<td>(777)</td>
<td>(246)</td>
<td>(75)</td>
</tr>
<tr>
<td>Present</td>
<td>56.6±2.9</td>
<td>49.4±6.2</td>
</tr>
<tr>
<td>34.0±8.3</td>
<td></td>
<td>37.7±6.2</td>
</tr>
<tr>
<td>(531)</td>
<td>(223)</td>
<td>(88)</td>
</tr>
</tbody>
</table>

Balch, Gershenwald, Soong et al., J Clin Onc, May 2010
**Rationale for CLND**

- Probability of + NSLN (Staging)
- Improved regional control
- Improved survival
- Less morbidity

**Only patients with non-sentinel lymph node involvement can derive benefit from CLND**

**10%-20% have additional nodes involved by routine histology**

* A selective approach to completion dissection is rational!
* Assessment of risk for non-sentinel node metastases
CLND for melanoma
Completion LND - positive NSLN

- The strong independent prognostic significance of a positive NSLN has been confirmed by four separate studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th># + NSLN</th>
<th>HR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghafouri</td>
<td>2009</td>
<td>71</td>
<td>1.92</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Weiner</td>
<td>2010</td>
<td>60</td>
<td>1.76</td>
<td>0.03</td>
</tr>
<tr>
<td>Brown</td>
<td>2010</td>
<td>51</td>
<td>2.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pasquali</td>
<td>2014</td>
<td>353</td>
<td>1.34</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- CLND is a great (though very expensive and morbid) staging tool.

CLND for melanoma
Clinical equipoise: Prevailing practice

- A review of the NCDB identified 2942 melanoma patients with a positive sentinel node treated 2004-2005.
- Only half of these patients went on to completion lymph node dissection.
- Predictors of CLND included treatment at an NCI designated cancer center, non lower extremity primary tumors, and age < 75.

What is the fractional benefit of the CLND above what is achieved by just removing the involved SLN(s)?

Patients with MM ≥ 1mm (n=4650)

SLNB

SLNB positive (n=3460)

SLNB negative (n=1190)

Exclusion criteria
Patients refusal

Randomization (n=5588)

Follow-up

Arm A: Observation*(n=279)

Radical lymphadenectomy and follow-up*(n=279)

Arm B: Radical Lymphadenectomy and Follow-up*(n=279)

German Trial Design (DeCOG-SLT)

Melanoma - specific survival

Arm A: 84.3% (78.8%; 89.8%)

Arm B: 82.7% (76.6%; 88.8%)

HR (Arm B vs. Arm A) 1.01 (0.64; 1.59)
p=0.98
**Tumor load**

<table>
<thead>
<tr>
<th>SN per patient</th>
<th>Arm A (Observation) N = 233</th>
<th>Arm B (Radical LAD) N = 240</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>158</td>
<td>67</td>
<td>0.124</td>
</tr>
<tr>
<td>2 - 3</td>
<td>67</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>&gt; 3</td>
<td>7</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>n.a.</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**Histological criteria**

- H&E positive
- Immunohisto. pos. (S100, HMB45, Melan A)
- not specified

<table>
<thead>
<tr>
<th>Tumor load</th>
<th>Arm A (Observation) N = 233</th>
<th>Arm B (Radical LAD) N = 240</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>64-68% of Pts with &lt; 1mm of SLN tumor burden</td>
<td>144</td>
<td>61.8%</td>
<td>73</td>
</tr>
</tbody>
</table>

**Size of metastases in the SLN**

<table>
<thead>
<tr>
<th>Size of metastases in the SLN</th>
<th>Arm A (Observation) N = 233</th>
<th>Arm B (Radical LAD) N = 240</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>single cells / &lt;0.5 mm</td>
<td>76</td>
<td>32.6%</td>
<td>68</td>
</tr>
<tr>
<td>0.5 - 1.00 mm</td>
<td>42</td>
<td>18.3%</td>
<td>45</td>
</tr>
<tr>
<td>1.01 - 2.00 mm</td>
<td>43</td>
<td>18.5%</td>
<td>49</td>
</tr>
<tr>
<td>2.01 - 5.00 mm</td>
<td>12</td>
<td>5.2%</td>
<td>11</td>
</tr>
<tr>
<td>5.01 - ... mm</td>
<td>4</td>
<td>1.7%</td>
<td>5</td>
</tr>
<tr>
<td>others</td>
<td>16</td>
<td>6.9%</td>
<td>25</td>
</tr>
</tbody>
</table>

**CLND for melanoma**

Clinical equipoise: MSLT-II trial

- Positive SLN N=1755
- Stratify by extent of nodal involvement
- Completion LND
- Observation (with nodal basin US)
- Observation
- Therapeutic LND
- Observation

**Nodal Basin Control According to Randomized Treatment Arm**

**Overall Melanoma-Specific Survival According to Treatment Arm**

**Surgical Morbidity of Lymphadenectomy Microscopic vs Palpable disease (MSLT-1)**

- Compared morbidity of formal dissection in node positive patients
  - SLN positive vs delayed for palpable nodal disease
- Hospital stay
  - shorter for SLN positive patients
- Symptomatic lymphedema
  - less in SLN positive group, 12% vs 20%, p=0.04


**Reasons for CLND after Positive SLNBx**

- complete staging
  - need 2 positive nodes for high priority adjuvant trial of Anti-PD-1 vs IFN
  - number of + nodes and presence of non-SLN involvement prognostic
- Improved regional disease control and less post-dissection morbidity for patients with non-sentinel node involvement
Completion Node Dissection

Conclusions
• No direct evidence that CLND provides a survival benefit
• SLN biopsy may be therapeutic for the patients with only SLN disease (80% of the SLN+ patients)
• Prognosis in patients with non-SLN involvement is particularly unfavorable
• A selective approach based on predicted risk of non-SLN involvement is rational
• Improved regional disease control and accurate staging may be the only benefits of CLND

Working Model
Predicting Risk for Additional Positive Nodes

<table>
<thead>
<tr>
<th>Score</th>
<th>No. of pts in group</th>
<th>No. additional pos LN</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>128</td>
<td>5</td>
</tr>
<tr>
<td>3-4</td>
<td>126</td>
<td>28</td>
</tr>
<tr>
<td>5+</td>
<td>30</td>
<td>14</td>
</tr>
</tbody>
</table>

*Score = sum of:
- Breslow thickness (0 or 1 for ≤ 2 mm or > 2 mm, respectively)
- SLN focus (0, 1, 2, or 3 for ≤ 0.5, >0.5 and ≤ 2, >2 and ≤ 10, or > 10 mm, respectively)
- Number of SLNs harvested (0, 1, or 2 for >3, 2, or 1 respectively)

Gershenwald et al, JCO 2008

NCCN Guidelines Version 2.2016 Melanoma

CLINICAL/PATHOLOGIC STAGE WORKUP PRIMARY TREATMENT

Stage III (Sentinel nodes positive)
- Consider baseline imaging for staging (category 2B) and to evaluate specific signs or symptoms (CT scan, PET/CT, MRI)
- Discuss and offer complete lymph node dissection

Spectrum of Advanced Disease
• Nodal disease (Stage IIIb/c)
  - with or without known primary
  - resectable vs "unresectable"
• Limited local/satellite/intransit metastases
  - stage IIIb: intransit only
  - stage IIIc: with nodes
• Resectable (oligometastatic) stage IV disease

Resectable Stage III and Selected Oligometastatic Stage IV Melanoma

Standard of care
• Upfront Surgery
• Selective use of adjuvant nodal basin irradiation (stages III b/c)
• Systemic adjuvant therapy
  - resected stage III: interferon, ipilimumab, or clinical trial
  - resected stage IV: clinical trial or observation

Advanced Stage III Melanoma

Management Goals
• Durable Local/Regional Control
  - long term survival
  - palliation (expectant palliation)
  - minimize morbidity and functional deficits
• Reduce the risk for distant failure
Stage III patients have a high risk of recurrence after upfront surgery—70%. Adjuvant therapy options are not optimal: controversy with high dose interferon, peg-intron, and high dose ipilimumab. Nodal basin irradiation has significant risk of lymphedema. Delay in the treatment of the micrometastatic disease.

**Surgery → Adjuvant Therapy**

Disadvantages:
- Tumor shrinkage → Decreased surgical morbidity
- Better regional disease control
- Avoid the morbidity of adjuvant XRT
- Destruction of micrometastases → Prevent distant disease spread
- Objective measure of patient’s response to therapy → Personalization of adjuvant therapy
- Potential pathway for new drug evaluation/registration

**Neoadjuvant → Surgery → Adjuvant Therapy**

Potential Advantages:
- Tumor shrinkage → Decreased surgical morbidity
- Better regional disease control
- Avoid the morbidity of adjuvant XRT
- Destruction of micrometastases → Prevent distant disease spread
- Objective measure of patient’s response to therapy → Personalization of adjuvant therapy
- Potential pathway for new drug evaluation/registration

**Treatments for Melanoma: A New Era**

- Pre-1998: Approvals (o/o +) randomized trials
- 1998-2011: Approvals for metastatic disease, 2 adjuvant
- 2011-2015: Approvals: 10 for metastatic disease, 2 adjuvant

**Activity of Dabrafenib + Trametinib in Stage IV**

- 617 patients, median PFS 11.1 months, median OS 25.6 months
- Overall response rate 67%, Disease control rate 91%:
  - Very favorable outcomes in patients that achieved a CR (16%)
  - Best predictors of CR: ↓ Sum of diameters & < 3 metastatic sites

**Poor Outcomes for Clinical Stage III Melanoma**

8th Edition AJCC Draft

**Case Example (1)**

- 47 yo female with prior hx of R arm melanoma presented with bulky adenopathy in R axilla (? resectable). Biopsy: melanoma (BRAF mut)
- Treated with neoadjuvant BRAF/MEKi x 8 weeks with excellent radiologic response: Path = fibrosis, no viable tumor cells (pCR)
**Pathological Response**

Before: Lymph node with extensive fibrosis and melanin deposition in the extracapsular tissue.

After: (Image of pathological response)

**Neoadjuvant BRAF and MEK Inhibition**

Neoadjuvant and Adjuvant Dabrafenib and Trametinib Compared to Upfront Surgery in Patients With Clinical Stage III or Oligometastatic Stage IV Melanoma (Combi-Neo)

Phase 2 Randomized Trial vs Standard of Care of Surgery + Adjuvant

**Combi-Neo**

Patients with stage IIIB/IIIC or oligometastatic stage IV (<3 lesions), + BRAF mutation

- Blood draw and tumor biopsy
- Pre-treatment
- Neoadjuvant BRAF/MEK x 8 weeks
- Blood draw and tumor biopsy at surgery
- Restaging CT scans every 3 months with blood draws
- Blood draw and tumor biopsy at relapse

**Arm A**

- Upfront surgery

**Arm B**

- Neoadjuvant BRAFi/MEKI

**Surgical resection**

**Restaging via CTs followed by surgical resection**

**Scheduled within 0-4 weeks**

**On treatment biopsy / blood draw (arm B only)**

**Adjuvant BRAF/MEK x 44 weeks**

**Standard of care adjuvant therapy (interferon vs. observation)**

**Pathologic assessment of tumor + research biopsy**

**Clinical and radiographic follow up**

**Assess relapse-free survival, overall survival, toxicity**

**n=28**

**n=56**

**Excellent Responder: 79% decrease by RECIST and Pathologic CR**

**Poor Responder: 23% decrease by RECIST and viable tumor at surgery**

**Neoadjuvant and Adjuvant D+T Significantly Improved RFS over SOC**

HR 60.2

95% CI (6.7-7965)

P<0.0001

**Patients with pCR had Improved RFS compared to those without pCR**
Neoadjuvant Strategy
Checkpoint Blockade

Neoadjuvant and Adjuvant Checkpoint Blockade in Patients With Clinical Stage III or Oligometastatic Stage IV Melanoma (NCT02519322)
Nivolumab vs Ipi / Nivo
Phase 2 randomized trial

Tumor Burden Change From Baseline from CheckMate-067

NIVO + IPI
Median change: -51.9%
NIVO
Median change: -34.5%
IPI
Median change: +5.9%

Confirmed responder
30% reduction in tumor burden by RECIST v1.1

Baseline reduction from baseline in target lesions (%)

\( \geq 25\% > -50\% \) to \(< 25\% \)
\(-100\% \) to \(\leq -50\% \)

Intralesional Therapy (Oncolytic Immunotherapy): Goals

- Locally ablative therapy for local disease control
  - High, local concentration
  - Palliation/symptom control
- Induction of systemic host immune antitumor activity
  - Augment the local injected response
  - Response in distant and uninjected regional metastases
  - Systemic adjuvant response (treat micrometastases)
  - Limited systemic toxicity
  - Durable response

Drug Agencies in US and Europe Approve T-VEC

October 27, 2015
- T-VEC: US approval for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery

December 16, 2015
- T-VEC: EU approval for Stages IIIB, IVM1a metastatic melanoma

Lesion-level and patient-level responses to T-VEC

Lesion type: injected

\( \geq 50\% \) decrease 64% OR 33%
100% decrease 47% OR 15%

Lesion type: uninjected non-visceral

\( \geq 50\% \) decrease 15% OR 14%
100% decrease 9% OR 3%

Lesion type: uninjected visceral

\( \geq 50\% \) decrease 34% OR 18%
100% decrease 22% OR 6%
The first International Neoadjuvant Consortium was held in November at the SMR.

A growing international interest has emerged in designing and completing neoadjuvant trials.

Ideal model for discovering and validating biomarkers of response and resistance.

Improved regional disease control and survival outcomes will lead to new treatment paradigms.

Novel combinations to "raise the tail of the curve" in the stage IV setting will be tested in the neoadjuvant setting.

The first International Neoadjuvant Consortium was held in November at the SMR.

Risk set, n

Kaplan–Meier percent

GM-CSF 21.5 (17.4, 29.6)

T-VEC 18.9 (15.3, 25.2)

Unadjusted log-rank P = 0.71 (descriptive)

HR = 1.07 (95% CI: 0.75, 1.52)

GM-CSF 15.9 (10.2, 19.7)

100 Log rank: P = 0.001 (descriptive)

Exploratory OS subgroup analysis by disease stage

Stage IIIb/C, IV M1a

Week 13

Log-rank: P = 0.031 (prespecified)

Stage IV M1b/c

Week 13

Log-rank: P = 0.071 (prespecified)

Primary overall survival

Resectable stage III b/c and M1a, N=150

Randomized phase 2 trial of standard of care upfront surgery + adjuvant vs pre-op T-VEC 12 weeks followed by surgery.

Combination Trials of Oncolytic Immunotherapy and Anti-CTLA-4 or Anti-PD-1 are ongoing.

Neo-Adjuvant T-VEC

Resectable stage IIIb/c and M1a, N=150

Randomized phase 2 trial of standard of care upfront surgery + adjuvant vs pre-op T-VEC 12 weeks followed by surgery.

Combination Trials of Oncolytic Immunotherapy and Anti-CTLA-4 or Anti-PD-1 are ongoing.

Neo adjuvant Therapy for Advanced Resectable Melanoma

Where are we Now and Where are we Going?

A growing international interest has emerged in designing and completing neoadjuvant trials.

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Surgery for Stage IV Disease

Why?

Ten new approvals in last 5 years

Robust response with BRAF inhibition, but not durable.

Low response rate with ipilimumab.

High response rate with combination checkpoint blockade but significant toxicity.

Surgery well tolerated, 100% response rate.

199
Surgery for Stage IV melanoma: Patient selection

- Curative intent
  - can a complete resection be performed?
  - symptoms?
  - morbidity of planned surgery?
  - associated co-morbidity?

- Favorable biology?
  - target the right patient population

- Palliation
  - improve quality of life
  - candidates for effective systemic therapy

SWOG S9430: Phase II Trial – Complete Resection for Stage IV Melanoma

- Prospective registry - surgical resection, stage IV
- 1996-2005, 18 centers
- 77 patients enrolled
  - 8 pts: not completely resected to NED
  - 3 pts: no tumor in specimen
  - 2 pts: locoregional disease only
- 64 patients included in primary analysis
  - median age 54y, M:F ≈2:1
  - sites: any visceral, 31%; non-visceral only, 69%
  - >1 site resected, 22%
  - 11 received some type of systemic adjuvant (8 IFN)
- Median RFS, 5mos; median OS, 21mos

Canvaxin Stage IV Placebo-Controlled Randomized Trial

- Two sites, 5 nodules, complete resection, no brain mets within 6 months of surgery
- NED based on repeat staging within 45 days of randomization
- Trial stopped by DSMB short of planned accrual April 2005 after 2nd interim analysis
- 38 months median and 40% 5-year survival!
Select Dermatopathology Topics for the Practicing Dermatologist

Sean Stephenson, D.O.
Laboratory Director: DLCS Michigan
Assistant Clinical Professor: MSU-COM
sstephenson@dermpathlab.com

Overview of Lecture

• Cutaneous Squamous Cell Carcinoma staging update
• Changes to melanoma staging from AJCC7 to AJCC8
• Sentinel lymph node biopsy and complete dissection evidence
• Melanoma prognosis predictors
• Genetics of melanocytic neoplasms including Spitz tumors and melanoma
• Prognostic factors of Spitz tumors
• Problems with interpreting melanocytic neoplasms
• Molecular tests for melanocytic neoplasms
• Re-excision of dysplastic Nevi

Cutaneous Squamous Cell Carcinoma staging update

AJCC 7th Edition
Cutaneous SCC and Other Cutaneous Carcinomas
AJCC 8th Edition
Cutaneous SCC of the Head and Neck

AJCC 7 vs AJCC8

Differences:
- T category changes with T1-2 based purely on size, and T3 based on size and high risk features.
- High risk feature: depth of invasion changed to beyond the SC fat or >6mm.
- Differentiation, and anatomic location no longer are high risk features.

Comparison of BWH alternative staging system vs AJCC8

New stratification system with management recommendations

New stratification system with management recommendations

Risk Stratification

Follow up recommendations

Changes to melanoma staging from AJCC7 to AJCC8

AJCC 7th Edition
Melanoma of the Skin

AJCC 7th Edition
Melanoma of the Skin

Important Changes in Melanoma Staging
AJCC8 vs AJCC7

- Measurement to the nearest 0.1mm (from .01mm).
- Mitoses are no longer part of the T1 category for thin Melanoma <1mm.
- T1 category uses 0.8 mm as a threshold with T1b category defined as 0.8 – 1 mm with or without ulceration.
- "Microscopic" and "macroscopic" detection of tumor in lymph nodes is now referred to as "clinically occult" and "clinically detected."
- New N3c, N2c, and N3c categories that take into consideration the presence of microsatellites, satellite metastases, and in-transit metastases.
- New M1d for distant metastasis to CNS.
AJCC8

T Category

- pT1: Melanoma 1.0 mm or less in thickness
- pT1a: Melanoma <0.8 mm in thickness, no ulceration
- pT1b: Melanoma 0.8 to 1.0 mm in thickness, ulceration
- pT2: Melanoma >1.0 to 2.0 mm in thickness, ulceration
- pT2a: Melanoma >1.0 to 2.0 mm in thickness, no ulceration
- pT2b: Melanoma >1.0 to 2.0 mm in thickness, ulceration
- pT3: Melanoma >2.0 to 4.0 mm in thickness, ulceration
- pT3a: Melanoma >2.0 to 4.0 mm in thickness, no ulceration
- pT3b: Melanoma >2.0 to 4.0 mm in thickness, ulceration
- pT4: Melanoma >4.0 mm in thickness, ulceration
- pT4a: Melanoma >4.0 mm in thickness, no ulceration
- pT4b: Melanoma >4.0 mm in thickness, ulceration

AJCC8

Changes to pT1 category

- pT1: Melanoma 1.0 mm or less in thickness
- pT1a: Melanoma <0.8 mm in thickness, no ulceration
- pT1b: Melanoma 0.8 to 1.0 mm in thickness
- pT1c: Mitoses no longer used for subcategory b. Subcategory b changed to Breslow depth of 0.8mm (0.75-0.84). Ulceration remains unchanged.

How could this affect your practice?

- Based on AJCC7 criteria any invasive melanoma <1mm with a single mitosis merited consideration of discussing a SLNB with a patient.
- This is no longer the case.
- The National Comprehensive Cancer Network (NCCN) advises the following concerning a thin melanoma and SLNB.

For melanoma ≤0.75 mm thick, unlike significant uncertainty about the adequacy of microstaging.

For melanoma >0.75 to 1.0 mm thick, SLNB may be considered in the appropriate clinical context. In patients with thin melanomas (>0.75 mm), apart from primary tumor thickness, there is little consensus to what should be considered "high-risk features" for a positive SLN. Conventional risk factors for a positive SLN, such as ulceration, high mitotic rate, and lymphovascular invasion (LVI), are very uncommon in melanomas <0.75 mm thick. When present, SLNB may be considered on an individual basis.

AJCC8

N Category

- pN0: No regional lymph node metastasis detected
- pN1: One tumor-involved node or in-transit, satellite, and/or microsatellite metastases with one tumor-involved node
- pN1a: One clinically occult tumor-involved node (ie, detected by sentinel node biopsy) with no in-transit, satellite and/or microsatellite metastases
- pN1b: One clinically detected tumor-involved node with no in-transit, satellite and/or microsatellite metastases
- pN1c: Presence of in-transit, satellite and/or microsatellite metastases with no regional lymph node disease
- pN2: Metastasis in two to three regional nodes or in-transit, satellite, and/or microsatellite with one tumor-involved node
- pN2a: Two to three clinically occult tumor-involved nodes (ie, detected by sentinel node biopsy) with no in-transit, satellite and/or microsatellite metastases
- pN2b: Two to three tumor-involved nodes, at least one of which was clinically detected with no in-transit, satellite and/or microsatellite metastases
- pN2c: One or more clinically occult tumor-involved nodes (ie, detected by sentinel node biopsy) with no in-transit, satellite and/or microsatellite metastases
- pN3: Metastasis in four or more regional nodes, or in-transit, satellite, and/or microsatellite metastases with two or more tumor-involved nodes or any number of matted nodes with in-transit, satellite and/or microsatellite metastases

AJCC8

M Category

- pM1: Distant metastasis
- pM1a: Distant metastasis in skin, subcutaneous tissues, soft tissues including muscle and/or nonregional lymph nodes
- pM1b: Distant metastasis to lung with or without M1a sites of disease
- pM1c: Distant metastasis to non-CNS visceral sites with or without M1a or M1b sites of disease
- pM1d: Distant metastasis to CNS with or without M1a, M1b or M1c sites of disease

AJCC8

Sentinel Lymph Node Biopsy

- What is the evidence?
Thought process/theory of performing SLNB and if positive complete lymph node dissection

1. When melanoma normally progresses/metastasizes it first drains to the regional lymph nodes.
2. Pt’s with clinically palpable lymph nodes have a worse prognosis.
3. Micrometastasis and SLNB is a strong predictor of the surrounding regional nodes.
4. Therefore, by performing a SLNB and if positive complete lymph node dissection tumor burden is reduced which will lead to a better outcome (ie. melanoma specific survival).

But is point number 4 true?

So what is the evidence in the literature?

Multicenter Selective Lymphadenectomy Trial-1 (MSLT-1)
- Randomized controlled study with 2,001 patients were studied with intermediate depth melanoma (1.2mm to 3.5mm) and deep melanoma (>3.5mm).
- The primary end point to determine the melanoma specific survival in patients that underwent SLNB (and if positive complete dissection) versus patients that did not undergo SNB with observation of lymph nodes.
- There was a 10 year follow up period. 1,667 were included in the final results.
- Conclusion: No improvement in melanoma specific survival (MSS).
- secondary end points including relapse-free survival (RFS) and melanoma-specific survival for the subset of node-positive patients showed improvement (these conclusions are controversial).

"The importance lies in the identification of patients with distant micrometastatic disease that would be candidates for adjuvant therapies."

What about thin Melanoma (<1mm)?
Where did the NCCN recommendation for SLNB come from?
- Small retrospective study of thin melanoma, 6.4% showed a positive SLNB.
- All nodal metastases were found in the group with a Breslow thickness of 0.76-1.0 mm, resulting in 12.8% of positive SNBs in this subgroup ($X^2$ p = 0.02).
- In AJCC stage 1a, 4.3% had a positive SLNB, in AJCC stage 1b the SLNB positive proportion was 9.4% ($X^2$ p = 0.38).
- Disease free survival in the node-positive group was 100%.
- Breslow thickness only appears to be a practical tool in predicting lymph node involvement.
- Recommendation: SLNB can be omitted in melanoma patients with a Breslow thickness <=0.75 mm.

SLNB for thin Melanoma Considerations
- SLNB for melanoma 0.75-0.99mm should be considered in patients age ≥45, Breslow depth ≥0.85 mm, mitotic rate >1mm2, and/or with ulceration.
- Thin melanoma <0.85mm without high-risk features may be treated with WLE alone.
SLNB for thin Melanoma Considerations

Is age a factor?

It appears so, but maybe not what you would have guessed

- Patients younger than 40 years with category T1b tumors 0.50 to 0.75 mm, who would generally not be recommended for SLNB, had an LN positivity rate of 5.6% (95%CI, 3.3%-8.6%).
- Patients 65 years or older with T1b tumors 0.76mm or larger, who would generally be recommended for SLNB, had an LN positivity rate of only 3.9% (95%CI, 2.7%-5.3%).


If the SLNB is positive does complete dissection improve survival?

No

- Immediate completion lymph-node dissection increased the rate of regional disease control and provided prognostic information.
- Did not increase melanoma-specific survival among patients with melanoma and sentinel-node metastases.


Prognostic factors beyond TNM staging and positive SLNB

- Gene Expression Profile

Melanoma Prognosis Predictors

- Criteria based on
  - Primary or metastatic
  - Age of patient
  - Location
  - Breslow depth
  - Ulcerated vs non-ulcerated
- Estimates 1, 2, 5, and 10 year survival dates

Melanomaprognosis.org

What about Gene Expression Profile(GEP)?

- Original poster presentation at 2013 Summer AAD
- A 31-gene expression profile signature was created to help accurately predict metastatic risk in Stage I and II cutaneous melanoma primary tumors that are negative for SLNB.
- Showed improved prognostic accuracy compared to SLNB for overall survival.
- Small study: N=268.
- Test divides melanoma into two categories
  - Class 1 (Low risk)
  - Class 2 (High risk)
Gene Expression Profile

Gene Expression Profile

• In all, 43 (21%) cases had discordant GEP and AJCC classification (using 79% cutoff).
• Eleven of 13 (85%) deaths in that group were predicted as high risk by GEP but low risk by AJCC.

Additional GEP studies

• GEP outcome was a more significant and better predictor of each end point in univariate and multivariate regression analysis, compared with SLNB.
• In combination with SLNB, GEP improved prognostication. For patients with a GEP high-risk outcome and a negative SLNB result, Kaplan-Meier 5-year disease-free, distant metastasis free, and overall survivals were 33%, 49%, and 54%, respectively.

Additional GEP studies

• LDH positivity with metastatic melanoma has a worse prognosis.
• Elevated S100-Beta Protein correlates to tumor burden, disease progression and poor outcomes (Stage III and IV). Some have suggested it should replace LDH in AJCC staging criteria.
• Melanoma Inhibitory Activity (MIA).
• Elevated C-Reactive Protein correlates to tumor burden (Stage III and IV).
• Elevated plasma IL-12p40 (common subunit of inflammation- and tumor growth-controlling cytokines IL-12 and IL-23) was associated with melanoma recurrence, a poorer melanoma specific survival and overall survival (Stage I and II only).
Genetics of Melanocytic Neoplasms

Acquired melanocytic nevi: vast majority (>80%) show activating hotspot mutations leading to an amino acid exchange at codon 600 of BRAF (BRAFV600E/K).

Congenital melanocytic nevi: often activating NRAS hotspot mutations (~75%), most commonly affecting codon 61.

Blue nevi: most show activating mutations of GNAQ or GNA11, commonly affecting codon 209.

Genetics of Spitzoid Melanocytic Neoplasms

BAP1 inactivation occurs in ~5% of Spitz tumors and is predominantly intradermal with enlarged epithelioid nuclei. Spitz tumors with BAP1 loss are associated with a hereditary tumor predisposition syndrome.

HRAS mutations occur in ~15% of spitzoid lesions, are often associated with desmoplasia, and are commonly designated as desmoplastic Spitz nevi.

Genomic rearrangements (translocations, kinase fusions) ~50 of various receptor tyrosine kinases, including ALK, ROS1, RET, and MET, or the serine-threonine kinase BRAF. The most characteristic features of ALK+ spitz tumors are plexiform, intersecting fascicles of predominantly fusiform melanocytes in the dermis.

Genetics of Melanoma

~50% characterised by BRAF V600E mutations (BRAF subtype) (intermittently sun-exposed skin).

Activating mutations in RAS genes account for approximately 25% of melanoma (RAI subtype), and subsume cases with NRAS mutations (~24%), as well as HRAS and KRAS hot-spot mutations (~1%).

~10% have NF1 aberrations affecting genes that mildly activate the MAPK/ERK pathway. Occur more frequently in desmoplastic melanoma and in melanoma of chronically sun-exposed skin.

Melanomas lacking BRAF, N/H/KRAS, or NF1 mutations comprise the heterogeneous group of ‘triple wild-type subtype’, which includes KIT mutations (more frequently found in acral and mucosal melanoma), GNAQ/GNA11 mutations (uveal melanoma), or genomic rearrangements involving BRAF or RAF1.

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Activating mutations in RAS genes account for approximately 25% of melanoma (RAI subtype), and subsume cases with NRAS mutations (~24%), as well as HRAS and KRAS hot-spot mutations (~1%).

~10% have NF1 aberrations affecting genes that mildly activate the MAPK/ERK pathway. Occur more frequently in desmoplastic melanoma and in melanoma of chronically sun-exposed skin.

Melanomas lacking BRAF, N/H/KRAS, or NF1 mutations comprise the heterogeneous group of ‘triple wild-type subtype’, which includes KIT mutations (more frequently found in acral and mucosal melanoma), GNAQ/GNA11 mutations (uveal melanoma), or genomic rearrangements involving BRAF or RAF1.

Genetics of Melanocytic Neoplasms

The spectrum of melanocytic neoplasms with enlarged epithelial and or spindle cells

Spitz Nevus (benign)

Atypical Spitz Tumor (indeterminate behavior and capable of regional lymph node metastasis, but rare systemic spread and normally displays indolent behavior)

Spitzoid Melanoma (malignant)
The problem: lack of consensus based on histopathology

- 17 of 30 Spitzoid lesions yielded no clear consensus as to diagnosis; in only one case did six or more pathologists agree on a single category, regardless of clinical outcome.
- These results illustrate (1) substantial diagnostic difficulties posed by many Spitz tumors, especially those with atypical features, even among experts, and (2) the lack of objective criteria for their distinction from melanoma and for gauging their malignant potential.


Poor histopathologic prognostic factors for AST

- Factors most correlated with adverse behavior:
  - frequent mitotic activity
  - deep mitoses
  - lack of symmetry
  - high-grade cytologic atypia
  - ulceration

What about IHC?

p16
- Not helpful
- P16 aberrations more likely in AST and Spitzoid melanoma

Spitz Tumor
Molecular abnormalities

- Molecular abnormalities identified:
  - Gain of 11p (and rarely 7q)
  - Deletion of 6p23 and 3p21
  - Gain of 6p25 and 11q13 (poorer prognosis)
  - Hemizygous deletions of 6p21 (poorer prognosis)
  - **BRAF** mutation and loss of BAP1 expression
  - HRAS mutation
  - Gene fusions involving receptor tyrosine kinases ALK, ROS1, NTRK1, and RET or the serine threonine kinase **BRAF** (seen in lesions without HRAS mutation or loss of BAP1)

Poor prognostic indicators

FISH
- Gains in 6p25 or 11q13 associated with aggressive clinical behavior.
- Homozygous 9p21 deletion was highly associated with clinically aggressive behavior (extension beyond the SLN) and death due to disease.

Is SLN bx a helpful prognostic factor?
No

“Our results suggest that having a positive sentinel lymph node biopsy does not seem to be predictive of a poorer outcome for patients. We therefore suggest that no prognostic benefit can be gained from doing a sentinel lymph node biopsy in patients with atypical Spitz tumours.”

“Our results show that 99% of patients with atypical Spitz tumours and positive sentinel lymph node biopsy did not have disease progression beyond the regional draining lymph nodes over 5 years.”

Subjectivity
The good news is most dermatopathologist using standard criteria for melanocytic proliferations tend to agree on the same “subjective” diagnosis

What happens when dermatopathologists using similar criteria come to differing conclusions about whether a melanocytic proliferation is benign or malignant?

Problems with interpreting melanocytic neoplasms

“In brief, morphological diagnosis, whether of birds, fish, plants, or pathological processes in human beings, is 100% subjective.”

A. Bernard Ackerman

Poor prognostic indicators
TERT Promoter mutations

• TERT p mutations identified all 4 (of 56) patients that developed hematogenous metastasis.
• Negative in tumors from patients who had favorable outcomes.

Poor prognostic indicators
Imaging Mass Spectrometry

• Uses a proteomic signature
• Predicted clinical outcome better than histopathology
• Diagnosis of Spitzoid melanoma by was strongly associated with aggressive clinical behavior.
Discordance Studies in Melanocytic Proliferations

- "Changes in diagnosis occurred in 168 of 478 cases (35%), more frequently when the original diagnostician was a general pathologist."

- "Patient treatment is affected in more than 10% of cases."

- "The discordance rate of melanomas and nevi between the referring centers and UCSF was 14.3%."

- "Thirty-eight percent had two or more discordant interpretations."

- "However, a high level of disagreement was found in 25% of the cases."

- "Evaluation of 17 Spitzoid lesions yielded no clear consensus as to diagnosis; in only one case did six or more pathologists agree on a single category, regardless of clinical outcome."

**Best Subjectivity Study to Date**

- Intraobserver reproducibility: class I 76.7%, class V 82.6%. Class II 35.2%, class III 59.5%, and class IV 63.2%.

- Interobserver concordance rates of experienced pathologists: Class I 92%, Class II 25%, Class III 40%, Class IV 43%, Class V 72%.

- It is estimated that at a population level, 82.8% of melanocytic skin biopsy diagnoses would have their diagnosis verified if reviewed by a consensus reference panel of experienced pathologists.

- Overinterpreting by the initial pathologist and 9.2% underinterpreted.


Discordance Studies in Melanocytic Proliferations

What do the studies tell us?

- Even among expert dermatopathologists there is a disagreement on the interpretation of a subset of melanocytic lesions as to whether they are benign or malignant.

Tools to aid in a more definitive diagnosis (less subjective, more interobserver agreement)

- Immunohistochemistry
  - Ki-67/Mart1 dual stain
  - pHH3/Mart1 dual stain
  - HMB-45
  - p16

- Molecular studies
  - FISH
  - CGH
  - GEP
  - NGS
  - TERT
  - Immunomass spectrometry

**The Molecular Study (of melanocytic lesions)**

- Comparative genomic hybridization (CGH)
  - Hybridize gene chips containing human genome
  - Signal from genomic variants

- Comparative genomic hybridization (CGH) was performed on 186 melanocytic tumors (132 melanomas and 54 benign nevi) to determine DNA copy number changes in using.

- Significant differences found between melanomas and nevi.

- 127 (96.2%) of the melanomas had some form of chromosomal aberrations; only 7 (13.0%) of the benign nevi cases had aberrations.

- Melanomas
  - gains in chromosomes 6p, 1q, 7p, 7q, 8q, 11q, 11p, and 18q
  - losses in 9p, 9q, 10q, 10p, and 6q.

- All seven cases with aberrations were Spitz nevi, in six of which the aberration was an isolated gain involving the entire short arm of chromosome 11.

- Increases in chromosome 11 was not observed in any of the 132 melanomas.

- Original sensitivity of 86.7% and specificity of 95.4%.

- Additional probes that are helpful
  - 9p21
  - 8q24

- FISH
  - Original sensitivity of 86.7% and specificity of 95.4%.

- Additional probes that are helpful
  - 9p21
  - 8q24
  - Up to 96% sensitive and 99% specific.

**Florescent In situ hybridization (FISH)**

- Disease-related mutations are detected as abnormal numbers of copies of genes

- Uses chromogen or fluorescent-labeled DNA probes that are visualized microscopically

- Semi-quantitative measure of the abnormal gene copies in a tissue section

- Standard 4-probe FISH assay targets
  - 6p25 (RREB1)
  - 6q23 (MYB)
  - Cep6 (centromere 6)
  - 11q13 (CCND1)

- Original sensitivity of 86.7% and specificity of 95.4%.
FISH compared to CGH

• The overall concordance in aberrations detected using the two methods was 90%.
• Most discrepancies were due to a minor abnormal clone identified via FISH that was below analytical sensitivity of the aCGH test.

Gene Expression Profile (GEP)

• Unique, clinically validated molecular test that uses qRT-PCR methodology to measure 23 genes.
• Detects expression of genes involved in cell differentiation of tumor cells (PRAME), cell signaling (S100A9 group), as well as the immune response within the tumor microenvironment (multiple genes).
• 91.5% sensitivity and a specificity of 92.5%.

Next Generation Sequencing Panel

• Analyzes millions of DNA segments in parallel, thus allowing to sequence multiple cancer-driving genes in a single assay, with improved sensitivity in mutation detection.
• Provide similar information to aCGH with additional sequence information (e.g., TERT promoter mutation).
• Well accepted for detecting single molecular alterations to predict drug sensitivity (e.g., BRAF mutation or ALK fusion).
• More studies are needed to determine how the results of this complex testing correspond with clinical outcomes and response to therapy.

Re-excision of Dysplastic Nevi

• Controversial with newer literature suggesting re-excision for only moderate to high grade (moderate to severe atypia) and high grade lesions (severe atypia) and observation for low grade and moderate grade lesions (mild and moderate atypia).
• Standard of care not rigorously defined in literature or by AAD.

What is the evidence?

• Retrospective study
• Excision of biopsy diagnosed mildly or moderately dysplastic nevi is unlikely to result in a clinically incorrect diagnosis, and risk of transformation to melanoma appears very low.
• Moderately-to-severely and severely dysplastic nevi are more often associated with melanoma, and excision may be beneficial for melanoma detection or prevention.

What is the evidence?

• Retrospective study
• Rates of clinical recurrence after biopsy of DN (3.6%) and benign nevi (3.3%) were extremely low.
• Re-excision of nevi, including mildly to moderately DN with a positive margin, may not be necessary.
What is the evidence?

• Retrospective study

• 3.3% recurrence rate in observation group

• 2.0% of observed group developed melanoma

• In cases of mild and moderate DN with microscopically positive, non-concerning clinical residual lesion, observation, rather than resection, was a reasonable management option.


What is the evidence?

• Retrospective study

• 765 of 1809 (42.3%) of mildly and moderately DN were reexcised, 495 (64.7%) had positive surgical margins. Melanocytic residuum was present in 18.2% of re-excisional specimens.

• Re-excision resulted in a clinically significant alteration of the diagnosis in only 1 case (0.2%).

• Re-excising mildly and moderately DN results in a low histopathological yield and rarely results in a clinically significant change in diagnosis. As such, clinical monitoring of margin-positive lesions may be warranted.


What is the evidence?

• Retrospective study

• During long-term follow no patient developed melanoma at the site of an incompletely or narrowly removed DN

• Routine re-excision of mildly or moderately dysplastic nevi may not be necessary.


What is the evidence?

• Retrospective study

• 134 excisions 34% of DN were excised because of the presence of moderate or severe atypia, personal history of melanoma, or both.

• None of the excised lesions showed evidence of melanoma

• 14% of excised lesions were found to have residual lesions

• 4.4% showed recurrent nevi


What is the evidence?

• Retrospective study

• In 451 patients with SDN, re-excision was performed on 36.6%. 2 melanomas were diagnosed in the re-excision specimens.

• Re-excision of all SDN may not be necessary.


Pigmented Lesion Subcommittee Consensus Statement

• Mildly and moderately DN with clear margins do not need to be reexcised.

• Mildly DN biopsied with positive histologic margins without clinical residual pigmentation may be safely observed rather than reexcised.

• Observation may be a reasonable option for management of moderately DN with positive histologic margins without clinically apparent residual pigmentation; however, more data is needed to make definitive recommendations in this clinical scenario.

Pigmented Lesion Subcommittee Consensus Statement

• "If a partial or incisional biopsy is performed revealing a DN with positive margins and the remaining clinical pigmentation is not reexcised, the clinician and patient should be aware that the level of histopathologic dysplasia in the remaining lesion may not be identical to that in the biopsy specimen. The biopsy site needs to be monitored for clinical warning signs of melanoma and reexcised if there are unusual clinical changes."

• "The decision to reexcise DN should be based on both the degree of clinical concern and the histologic findings. If the prebiopsy level of concern for a pigmented lesion is high, one should consider reexcision if the biopsy reveals positive margins, even if the level of histopathologic dysplasia is low. Similarly, if the pathology report reveals severe dysplasia with positive margins, reexcision to achieve a 2- to 5-mm clinical margin is generally recommended."

• "There may be clinical scenarios in which complete excision or reexcision of a mildly, mildly to moderately, or moderately DN may be warranted, including strong patient preference."


Re-excision of Dysplastic Nevi

• My opinion (based on my training, experience, and literature) is that some flexibility is necessary due to the inherent subjectivity of melanocytic neoplasms, and the problem that most melanocytic neoplasms are removed by the shave technique and not excisional biopsy (margin of safety)."

• "The gray zone of lesions with higher grade that extend to or closely approach a specimen margin is problematic, as one dermatopathologist’s moderately atypical nevus may be another’s melanoma."


Re-excision of Dysplastic Nevi

• Low grade lesions (mild cytologic atypia)
  • Low risk for recurrence and misdiagnosis of melanoma.
  • No re-excision necessary even with a positive margin.

• Moderate grade lesions (moderate cytologic atypia)
  • Low risk for recurrence but an increased risk of misdiagnosis of melanoma.
  • If cut in the planes of section examined (shave or punch), and clinically completely removed, likely ok to observe for recurrence.
  • If it extends to the margin and clinically completely removed observation for recurrence is likely ok.
  • If it extends to the margin and clinically is visible, I would suggest completely removing (shave, punch, ellipse).
  • Will this lead to dermatopathologists upgrading nevi that in the past would be called moderate to now be called moderate to severe to ensure being completely excised?

• High grade lesions (severe cytologic atypia)
  • Higher risk for misdiagnosis of Melanoma.
  • Full thickness elliptical excision recommended (with up to 5mm margin of normal skin).
  • If diagnosis is confirmed by FISH, CGH, or GEP I would still do a full thickness elliptical excision.

• I am a big proponent of re-excisioning any recurrent or changing melanocytic neoplasm regardless of the previous diagnosis.

• You never know when melanoma will arise in a precursor benign or dysplastic nevus (up to 36% of melanomas are a/w a precursor nevus).

One other caveat
What’s New In Atopic Dermatitis?

Eczema causes stress, sleeplessness, discomfort and worry for the entire family.
- Loss of sleep can decrease growth hormone secretion
- The parent of a child with eczema gets 1-1.5 hours less sleep a night on average
- Treating one patient with eczema is an example of “trickle down” healthcare
- Patients with eczema have increased risk of anxiety, ADHD (JAAD Oct 2016), injuries (likely due to distraction), and infections (Cutis June 2016)

Pathogenesis of Atopic Dermatitis

- Skin barrier is “broken”
- Overactive immune system process
  - Filaggrin defect allows staph to get in, attach, colonize which triggers the immune system reaction
  - 57% MSSA, 19% MRSA, 23% culture negative (DermNews May 2016)
  - Result of a “bored” immune system?

Atopic Dermatitis: Standard Treatment

- Sensitive skin care
  - ALL free and clear detergent, no dryer sheets/fab soft
  - Dove sensitive skin or cetaphil soap
  - Vanicream/Vaseline/Aquaphor as moisturizers
  - Robathol bath oil
  - Bleach baths- ¼ cup bleach in full tub water
Atopic Dermatitis- Standard Treatment

- **Topical steroids** - always do OINTMENTS in little kids
  - HC 2.5
  - Triam 0.1
  - Fluocinonide 0.05
  - Clobetasol 0.05
- No need to "soak and smear". Skin can be wet or dry (JAAD Aug 2016)

Atopic Dermatitis: Steroid Burst

- **Topical steroid burst for severe eczema/significant flares**
  - Clobetasol bid for 4 days
  - Fluocinonide bid for 10 days
  - Triamcinolone bid until clear or followup appt

Calcineurin Inhibitors

- **Elidel (pimecrolimus) 1% ointment**
- **Protopic (tacrolimus) 0.1% ointment**
- Great for areas like face and folds
- Can be used as part of a maintenance routine
- **Black Box Warning**
  - Pimecrolimus study from Pediatrics
    - 2418 patients age 3-12 mos old
    - Pts followed for 5-10 yrs
    - Found no evidence of lymphoma, malignancy or immune system impairment
    - Concluded it was safe even in the younger age group

NEW Treatments- Crisaborole

- Boron based topical ointment
- Inhibits phosphodiesterase-4 activity (PDE4) and decreases production of proinflammatory cytokines
- Several studies showing its efficacy down to age 2
- 65% of patients in preliminary studies were clear/almost clear
- Early and sustained improvement in pruritus
- Well tolerated; 4.4% of patients had stinging/burning
- Safety studies so far look great
- FDA approved in Dec 2016; NOW AVAILABLE!

NEW Treatments- Dupilumab!

- Blocks IL-4 and IL-13 (decreases the TH2 inflammatory response)
- 1 phase 2 study, 3 phase 3 studies show improvement in IGA and EASI scores
- Quality of life improves; itching decreases
- 300 mg subcut every other week (after 600 mg initial injection)
- **Good side effect profile**
  - Injection site reaction
  - Conjunctivitis
  - ?HSV
## Dupilumab in Kids
- Studies are happening right now
- Small study presented at AAD 2017
  - 78 kids and adolescents; 38 age 6-11, 40 age 12-17
  - Used doses of either 2 mg/kg or 4 mg/kg every other week
  - Improved EASI and itch
  - Adverse effects: “mild, transient, and unrelated”

## Treatments on the Horizon
- **Nemolizumab** - IL 31 blocker
  - Phase 2 12 wk study- 260 pts- 60% improvement in pruritus
  - Qwk dosing
- **Lebrikizumab** - IL 13 blocker- also see increased HSV and conjunctivitis
- **Tralokinumab** - IL 13 blocker
- **Ustekinumab** - probably helpful for a subgroup of patients with AD
  - Small study in JAAAD Jan 2017- all pts showed gradual improvement with 50% reduction in EASI score by week 16
  - 45 mg at wk 0, wk 4, wk 12 and then every 8 wks

## Atopic Dermatitis: Natural Therapy
- **Coconut oil**
  - Has good antibacterial properties, but doesn’t seem to help the eczema itself
- **Sunflower seed oil**
  - Does appear to help with eczema- difficult to find a good preparation
  - Aroma Workshop in Chicago
  - hello@aromaworkshop.com
  - Patients can call 773-871-1985
  - 8 oz spray bottle for $22 plus $5.50 shipping

## Atopic Dermatitis: Prevention
- **Smoking**
  - Active and passive exposure to smoke associated with increased atopic dermatitis prevalence (JAAD Dec 2016)
- **Probiotics**
  - Taken by a child with eczema appear to have no impact
  - But if a pregnant woman takes probiotics 2 weeks prior to having a baby and for 3 mos after having the baby, it reduces the risk of eczema in that baby by 20-30%
- **Transepidermal Water Loss (TEWL)**
  - TEWL in first weeks of life associated with increased risk of eczema
  - Families with h/o eczema should be managing their new baby with the same sensitive skin care strategies to try to prevent the eczema
  - 50% reduction in eczema by simply using sensitive skin care in first weeks of life (JAMA Peds Online Dec 2016)
Genetic Variants of AD
- To include or not?
- JAMA Derm March 2017
- See pink book for details
- 842 kids from PEER registry
- All patients underwent genotyping for 4 most common FLG LOF mutations and TSLP SNP

Will My Child Outgrow This?
- JAAD Oct 2016 Systematic review and metaanalysis of persistence of AD
  - Most childhood AD remits by adulthood
  - Kids with persistent disease, later onset, and more severe disease had increased persistence of AD
  - 1/5 kids had disease persistence beyond 8 yrs

Eczema and Peanut Allergy
- Early peanut exposure in severe eczema patients actually DECREASES the rate of peanut allergy (New Eng J Med)
- Consensus statement in SPD Jan/Feb 2016 showed an 11-25% reduction in risk of peanut allergy in high risk infants when peanuts were introduced between 4 and 11 mos of age

Pityriasis Alba
- Study compared topical steroids with topical calcineurin inhibitors for Pityriasis Alba
- Concluded that protopic/elidel work better than topical steroids (SPD Nov/Dec 2015)
- Could also consider treatment with calcipotriene or excimer laser

What’s New in Pediatric Allergic Contact Dermatitis?

Contact Dermatitis in Kids
- Either on the rise or being recognized more commonly
- 1 exposure to the triggering agent causes a rash for 3 weeks (patients cannot intermittently use their allergen)
Patch Testing Considerations in Kids

- TRUE test is helpful in kids
  - The causative agent was identified in 71% of kids with the TRUE test (SPD Meeting Summer 2016)
  - Use IQ chambers in kids less than 10 yrs old (Finn chambers have aluminum and vaccines do too so kids can be sensitized)
- Even though it can be helpful, it is not often pursued in children due to the inconvenience of it, cost of it, etc
- Most of the time, we try to identify the culprit based on the pattern of the rash

Wet Wipe Contact Dermatitis

- Due to preservative MCI/MI (Kathon CG)
- Also think about it in cases of persistent facial dermatitis
- There are now 2 brands of wipes that don’t contain the allergen
  - Honest Brand
  - Earth’s Best Hypoallergenic

Nickel Contact Dermatitis

- Most common allergen
- Present in almost anything metal
  - Jewelry
  - Snaps on jeans
  - Belt buckles
- Strict avoidance is the only option
- www.nonickel.com
- Dimethylglyoxime test
- Can trigger an id reaction

Id Reaction
**Id Reaction**

- An Id reaction is a sympathy rash to the primary problem
- Most commonly triggered by allergic contact dermatitis, but can be triggered by molluscum or tinea

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**Gianotti Crosti**

- Also causes monomorphic skin colored to pink papules all over arms, legs and cheeks
- Check the ears
- More common in patients with h/o atopy
- Typically caused by EBV but several viruses can do it
- Can take up to 8 wks to resolve
- Topical steroids help if itchy

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**Shin Guard Dermatitis**

- Can be irritant or allergic
- First step is to try the following steps:
  - Drysol (or OTC Certain Dri) applied to shins
  - Shin guard liners
  - Shin guards
  - Some suggest putting duct tape on shin guards as barrier
- Fluocinonide or clobetasol to treat
- Patch testing if initial plan doesn’t work
Toilet Seat Dermatitis

- Either a reaction to a cleanser being used on the seat or to the components of the seat itself
- Characteristic distribution on the lateral buttocks and post thighs
- "Soft and Comfy" toilet seat covers- Amazon $5.99
- Treat with hydrocortisone or desonide

Pediatric Psoriasis

- Plaque psoriasis
- Guttate psoriasis- triggered by strep
  - Some pts have HLA-Cw6 homozygosity which is associated with strep assoc psoriasis and tonsillectomy is "curative" (JAAD Nov 2016)
- Inverse psoriasis- nearly always mistaken for yeast/tinea cruris in kids/teens
- Anti TNF induced psoriasis- most common on scalp
  - 1st- Infliximab, 2nd- Humira (SPD Meeting Summer 2016)
- Check the nails, check the tongue, check the belly button
  - 32% of kids have nail involvement and that is closely associated with psoriatic arthritis (SPD Jan/Feb 2017)

Psoriasis is a Systemic Disease

- #1 association in children is obesity
  - Talk to them about weight
- Ask kids about smoking and stress
- Consider checking blood pressure
- Still unclear if we should be screening for hypercholesterolemia or diabetes in kids with psoriasis, but they are associated
- Psoriasis is associated with avascular necrosis, esp in young adults, males and pts with PsA- consider it when localized pain in weight bearing joint (JAAD May 2017)
- Both PsO and PsA are associated with osteopenia, osteoporosis, osteomalacia, ankylosing spondylitis, and multiple types of fractures (JAAD June 2017)

Psoriasis Affects the Whole Family

- JAAD Feb 2017
- Dramatic impact of pediatric psoriasis on the parents

What’s New in Pediatric Psoriasis?

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**Pediatric Psoriasis- Topical Treatment**

- Clobetasol cream/ointment- body
- Clobetasol foam (Olux/Olux E Foam)- scalp
- Taclonex suspension or Enstilar foam
- Elidel or Protopic- face and folds
- I personally don’t think calcipotriene alone or tazorac is that helpful
- Light therapy

**Psoriasis**

- Topical steroids continue to be the mainstay for pediatric psoriasis
- Systemic therapy options have been largely limited to cyclosporine, acitretin, methotrexate
- Biologic therapy is difficult because of lack of FDA approval, lack of data
- Systemic effects of psoriasis are making it more advantageous to consider systemic therapy, even in children

**Biologics in Kids**

- **Enbrel (etanercept)**- NOW APPROVED FOR KIDS >6 YRS OLD!!
  - Approved in Europe for psoriasis in kids >6 yrs old
  - Approved in US for JIA in kids >2 yrs old
  - 1 study in US in children- 2008- 211 patients age 4-17
    - 0.8 mg/kg/wk
    - 57% achieved PASI 75
    - This study has been continued to date and has great long term safety data (JAAD Feb 2016)

- **Humira (adalimumab)**- CURRENTLY PURSUING PED PSOR INDICATION
  - Approved in US for kids with JIA (>2 yrs old) and Crohn’s (>6 yrs old)
- **Stelara (ustekinumab)**
  - Several case reports of effectiveness and safety
  - 1 clinical trial- patients age 12-18, 110 patients
    - 80% reached PASI 75 at 12 wks (JAAD Oct 2015)
  - Large study outside US is in progress
  - I have several pediatric patients on it

**Biologics in Kids- Vaccines**

- **Live vaccines**
  - Common ones
    - MMR (given at 12-15 mos and then again at 4-6 yrs)
    - Varicella (given at 12-18 mos and then again at 4-6 yrs)
    - Herpes Zoster
    - Intra nasal Flu
  - Uncommon ones
    - Oral typhoid, yellow fever, oral polio, vaccinia/smallpox, BCG, rotavirus
- Double check that children are up to date on their vaccinations

**Psoriasis- Alternative Treatments**

- **Balneotherapy (Bath therapy)**
  - Dead Sea
  - Blue Lagoon in Iceland
  - 1 cup baking soda in bath Q week
- **Fish Oil**
  - Probably works as antiinflammatory
  - Small 28 pt study showed improvement
What’s New with Pediatric Rashes?

### Perioral Dermatitis

- Always ask about steroid use- topicals, inhalers, nasal sprays, etc
- **Standard treatment**
  - Elidel bid
  - Amoxicillin 30 mg/kg/day divided bid for a month

### Perioral Dermatitis in Kids- Additional Treatment Options

- Tacrolimus 0.1% ointment
- Clindamycin lotion/wipes
- Metronidazole cream
- Sodium sulfacetamide products
- Azzone
- Gentamicin 0.3% ophthalmic ointment
- Oral Ivermectin/Soolantra (JAAD March 2017)
  - Small study: 8 pts with rosacea, 7 with POD received either single dose ivermectin 200-250 micrograms/kg or soolantra daily for 3 mos
  - 8/9 cleared with oral iver and 6/6 cleared with topical soolantra
- Longer antibiotics
- Azithromycin
  - I have classically prescribed it MWF for a month
  - Some providers are using it for 5-7 days, then 2 weeks off, then repeat
- Make sure there are no steroids on the face

### Diaper Rashes

- Most common causes are irritant contact dermat and yeast
- Symmetrical, moist appearing pinkness with satellite pustules suggests yeast
- Dermatitic like symmetrical rash that involves contact with soiled areas, frictional creases suggests irritant contact
- Regardless, I suggest zinc oxide barrier cream (Desitin) with each diaper change
- Pick one (go with your gut) and treat
  - Hydrocortisone 2.5% ointment bid
  - Econazole 1% cream bid
Diaper Rashes- Irritant Contact!

- Diaper rashes are less common in breastfed babies
- Buying “superabsorbent” diapers reduces the risk for diaper rashes
- Cloth diapers can cause diaper rashes that are more vesicular with bullae and erosions
- Interestingly, candida is more common in babies that are being treated with wet wipes

Diaper Rashes- Yeast!

- SPD May/June 2016

Diaper Rashes- Yeast again!

- Hand, Foot and Mouth Disease

- Causes somewhat annular red-purple-gray patches on hands, feet, and around the mouth sometimes with intraoral lesions
- Previously coxsackie A16 and enterovirus 71 were the most common causes
- Coxsackie A6 has emerged over the past 2-3 yrs as the primary causative agent
- Produces more severe rash with prominent diaper area involvement
- Adults have been getting it
- Commonly produces onychomadesis 1-2 mos later (SPD July/Aug 2016)
HFMD and Onychomadesis

Tinea Capitis

- Systemic antifungal treatment for tinea capitis in kids: an abridged Cochrane review (JAAD Feb 2017)
- Griseofulvin and Terbinafine are considered 1st line
- Griseo better for microsporum, Terb better for trichophyton
- Terbinafine daily x 4 wks, Griseo bid x 6-8 wks
- Griseofulvin: 20-25 mg/kg/day divided bid always with fatty food
- All side effects were mild and equivalent thru all meds (no specific comment on LFTs)
- Itraconazole and Fluconazole are alternatives (never use oral ketoconazole)

Pediatric Onychomycosis

- It happens!
  - (SFD Jan/Feb 2017: San Diego experience)
  - Often there is family history
  - Evaluate for tinea pedis
  - Treat with terbinafine for 3 mos
    - <20 kg: 62.5 mg daily (1/4 pill)
    - 20-40 kg: 125 mg daily (1/2 pill)
    - >40 kg: 250 mg daily
  - Itraconazole can be used in a pinch (comes in syrup)
  - Liver function tests- to test or not to test
  - Griseofulvin doesn’t work

Pediatric Onychomycosis

Lichen Sclerosus

- Probably doesn’t go away for most prepubertal girls
- Maintenance treatment is better than as needed treatment (SFD July/Aug 2015)
- My regimen:
  - Clobetasol ointment bid for 2 wks, then once daily for 2 wks, then followup
  - Repeat that course if needed until clear
  - Then clobetasol MWF once daily or elidel once daily for maintenance
  - I see the girls every month until they are clear and then at minimum every 6 mos on maintenance

Herpes Zoster

- Since the chicken pox vaccine has been more regularly administered to children, cases of herpes zoster in children have been on the rise (Cutis Aug 2016)
- We don’t know why immunity seems different with the vaccine vs having the chicken pox
  - One theory: less varicella round in society allows immunity to wane and shingles gets a chance to blossom
- Patient is contagious to people who have not had the chicken pox (can’t catch shingles from shingles)
- Need to avoid unimmunized kids and pregnant women
- Treatment with Acyclovir 30-50 mg/kg/day divided TID (valtrex if old enough to take pills)
Pediatric Rashes- Herpes Zoster

- Small brownish papules typically on dorsal and anterolateral surface of the tongue
- Kids and young adults in dark skin phenotypes
- Appear rare, but probably because of lack of reporting
- Completely benign and harmless
- SPD Meeting Summer 2016 and JAAD Feb 2017

HSP (Henoch Schoenlein Purpura)

- Predictors of renal involvement:
  - Scrotal involvement
  - GI symptoms
  - High D Dimer
  - Age > 4 yrs

Crohn’s Disease

- Penile and scrotal swelling is underrecognized presentation of crohn’s, esp in prepubertal and teenage kids
- Also can cause odd, persistent rashes on labia majora
- SPD Sept/Oct 2016 presented case report of anogenital swelling in a teenage girl as presenting sign of Crohn’s
- Biopsy shows granulomatous inflammation

Urticaria Pigmentosa

- Lots of solitary mastocytomas
- Not scary, but looks scary and parents are often freaked out
- Most kids outgrow it
- No reason to check serum tryptase
- No risk of mast cell leukemia
- Manage with topical steroids prn
- Antihistamines +/-
**Urticaria Pigmentosa**
- Great article in SPD March/April 2017 summarizing UP in kids
- 26 kids
- Mean duration: 9-10 yrs
- Complete resolution in up to 56% of patients
- Majority probably don’t resolve before adolescence
- Resolution at less than 12 yrs old: male, younger at onset, fewer lesions
- Tryptase >20 can signal systemic involvement (1/26 had elevated tryptase and workup was normal)
- Epipens are unnecessary
  - 17/26 had general anesthesia and only 1 reported mild reaction
  - No reaction to Ibuprofen
  - 3 had bee stings- mild adverse reactions

**Dangerous Mast Cell Issues**
- Bullous Mastocytosis- presents as blistering in a newborn; ddx includes EB
- Diffuse Cutaneous Mastocytosis- the skin is diffusely infiltrated by mast cells so it becomes yellowish and rubbery diffusely
- Only these 2 mast cell issues in children carry risk of mast cell leukemia and require systemic workup and hem/onc involvement

**Be Careful with your Mirvaso!**
- JAMA Derm April 2017
- 4 yr old accidentally used mirvaso as toothpaste
- Rinsed and spit it out
- Ok at first
- 45 mins later developed bradycardia and somnolence requiring ambulance ride to ICU
- Symptoms lasted 12 hours

**What’s New with Nevi?**
- Giant Congenital Nevi
  - >20 satellite nevi increases chance for neurocutaneous melanosis (SPD Meeting Summer 2016)
  - Number of satellites also increases risk of melanoma
  - Risk of melanoma greatest in area overlying spinal cord
  - New classification- 6 patterns (SPD March/April 2017)
    - Bolero- upper back including neck
    - Back- back but not buttocks or shoulders
    - Bathing trunk- some say this has highest risk
    - Breast/Belly
    - Body Extremities
    - Body- bolero + bathing trunk

**What’s New with Acne?**
Acne
- Happening younger and younger
- Used to be abnormal before age 9, now abnormal before age 7
- Most acne medicines are technically approved for age 12 and up (epiduo approved age 9 and older)
- Helpful to work through the mail order pharmacies in these situations
  - GenRx- Prugen products
  - YourRx- Allergan products

Mid Childhood Acne
- Acne in kids age 3-7
- Ask about inhaled steroid use- can be the cause
- Good idea to order labs and/or refer to peds endocrinology
  - Total/free testosterone
  - DHEA-S
  - LH/FSH
  - Bone age- plain film of left hand and left wrist

Food and Acne
- Skim milk appears to be associated with increased acne, but not other milk or dairy
- Diet with a high glycemic index (high carb, high sugar) appears to worsen acne

Changes in Isotretinoin Monitoring
- A number of studies have shown that we have been “over monitoring” with labs for isotretinoin
- New recommendations are to check lipids and LFTs at baseline and then at 2 mos into therapy. If normal, that is all that is necessary.
- No need to check CBC

Isotretinoin and Depression
- JAAD June 2017- Isotretinoin and depression- a systematic review and metaanalysis done in Taiwan
- Reviewed 31 studies
- DID NOT show an association
- Most kids had an improvement in their mood

Accutane and Depression
- During 2015 and 2016, I had 3 male patients and 1 female patient become severely depressed on accutane. None of them had h/o mood issues prior.
- Appears to happen acutely
- All 4 admitted that they felt the symptoms early on, but had lied to me about it because they saw the improvement the accutane was having with their skin
- 2 of them were cutting themselves unbeknownst to their friends and family
- All 4 of them expressed suicidal ideation
- 1 of them was admitted to the hospital on a psych hold
- 1 of them attempted to commit suicide by jumping off a ladder head first
- All 4 of them stopped the accutane and their mood returned to normal
Topical Acne Meds on the Horizon

- DRM01- topical sebum inhibitor- more on next slide
- FMX101- topical minocycline foam
  - 4%, applied once daily, studies in Israel
- SB204- topical nitric oxide releasing gel that works in antimicrobial and antiinflammatory ways (JCAD Aug 2016)
  - 1% and 4% strength being studied
  - BID dosing, appears effective and tolerable
- SEB002- topical to work with blue light. Delivers light absorbing gold-coated silica microparticles that are absorbed into the pilosebaceous unit and then enhance the PDT (Practical Derm Oct 2015)

Olumacostat Glasaretil (aka DRM01)
JAAD Jan 2017

- Topical sebum inhibitor
- Phase 2A study
- Also seems to reduce sebaceous gland size in animals
- Significant improvement in both inflammatory and noninflammatory lesions
- Well tolerated

Oral Contraceptive Pills

- Given desire to decrease oral antibiotic use, the use of OCPs has become more appealing
- My counseling routine
  - How to start the pill
  - Weight gain, nausea, mood issues
  - Blood clots, heart attack, stroke
  - Health benefits
  - Timeliness is important

OCPs

- Retrospective review of 2147 patients on OCPs for acne (JDD June 2016)
  - All OCPs help with acne
  - Triphasics probably help a little more than monophasics
  - Non estrogen component matters for efficacy:
    - Best- Drospirenone (Yaz, Yasmin)
    - 2nd Best- Norgestimate/desogestrel (ortho tri cyclen, ortho cyclen/mirette, desogen)
    - 3rd Best- Norethindrone/levonorgestrel (loestrin, ortho novum/seasonale)

- Typically want to try to avoid OCPs in girls less than 14 yrs old or girls that have had their period for less than 2 yrs
- Rifampin and Griseofulvin are the only antiinfectives that definitely decrease the efficacy of OCPs when preventing pregnancy
- Risk of clots is greatest when a patient is first starting the pill

Contraindications to OCPs (W.H.O.)

- Pregnancy
- Current breast cancer
- Breastfeeding <6 wks postpartum
- Age >35 yrs and a heavy smoker
- HTN
- Diabetes with end organ damage
- Diabetes > 20 yrs duration
- History of or current DVT/PE
- Major surgery with prolonged immobilization
- Ischemic heart disease or Valvular heart disease with complications
- History of CVA
- Headaches (migrane with focal neuro symptoms at any age or without aura if >35 yrs old)
- Active viral hepatitis
- Severe decompensated cirrhosis
- Liver tumor (benign or malignant)
Other Hormone Tidbits

- Progesterone only methods of birth control tend to increase acne
  - Implanon
  - Mirena IUD
  - Progesterone mini pills
- Spironolactone can be helpful in the teenage population, especially if the patient has features of or a diagnosis of PCOS

What’s New with Hemangiomas?

Infantile Hemangiomas

- Propranolol is still great!
  - Suspension is 20 mg/5 ml
  - 2 mg/kg/day divided TID
    - If you are doing the math correctly, the dose ends up being around 1 ml TID for most babies
  - Always give with food
    - To prevent hypoglycemia
  - Don’t be afraid: if the hemangioma needs it, use it!
  - Typically used during growth period (1st 8-12 mos of life), but can work even beyond the proliferative phase (SPD May/June 2015)

Which Hemangiomas Need Propranolol?

- Large hemangiomas
- Ulcerating hemangiomas
- Hemangiomas in functional locations that will interfere with crawling, walking, etc
  - Knees, hands, elbows
- Special site hemangiomas
  - Eyelids, lips, parotid glands, genital area
  - Nasal hemangiomas have high rate of complication and early treatment is best (SPD Nov/Dec 2016)
- Dome shaped hemangiomas
  - Even when they involute, there is usually residual fibrofatty tissue
Infantile Hemangiomas

- Post Propranolol recurrences occur <25% of the time
  - Females
  - Deeper component of hemangioma
  - D/ced propranolol prior to 9 mos old (JAAD Oct 2016)
- Long term studies show no risk of developmental adverse effects or growth impairment at age 4 in pts treated with at least 6 mos of propranolol (JAAD July 2016)
- Topical timolol 0.5% gel forming solution can work for superficial hemangiomas- applied BID

Pyogenic Granuloma

- “Little ball of capillaries”
- Common in kids and pregnant women
- Some people remember trauma to the area prior to its growth
- 2 Treatment Options
  - Shave removal
  - Topical timolol bid

Pyogenic Granulomas

- Initial study in March/April 2014 SPD journal using timolol 0.5% gel forming solution BID
- Great results with clearance after 2-3 mos
- Bleeding stopped relatively instantly
- Likely working by vasoconstriction
- Important to followup these patients to ensure improvement (spitz nevi, even melanoma in ddx)
- How much to use?
  - Typically 1 drop is more than enough
  - Max 6-8 drops per day

What’s New in Genodermatoses?
Genodermatoses Potpourri

- NEMO gene (Incontinentia Pigmenti) is now called IKBKG
- PIK3CA- responsible for lymphatic malforms, vascular malformation with overgrowth syndromes (like klippel trenaunay and CLOVES)
- Icthyoses can be associated with vitamin D deficiency and can improve with supplementation
  - Consider checking vitamin D levels (SPD Meeting Summer 2016)
- Zorblisa is a new topical on the horizon for EB
  - 0% allantoin
  - Really helps with the wounds- 82% get wound closure by 2 mos (Derm News May 2016)

CALSs and Predicting NF-1 (JAAD June 2017)

What’s New with Hyperhidrosis?

Hyperhidrosis Treatment Options

- Drysol or OTC Certain Dri at bedtime
- Oral robinul- 1 mg daily, then 1 mg bid
- Iontophoresis- good for hands/feet
  - Fischer MD1A is the best unit- $6-800
- Botox
- Miradry- just for armpits
- Carpe Lotion- OTC- applied once daily
  - 25% reduction in sweating
  - Have to use at least 4 wks, no adverse events

Hyperhidrosis- Other Options

- “Secure” Robinul (glycopyrrolate) 1% wipes
  - Available via an online Canadian pharmacy
  - DRM04- topical anticholinergic wipes being made by Dermira for daily use- on the horizon
- Oral oxybutynin
  - Start with 2.5 mg daily and increase by 2.5 mg daily at 2 wk intervals. Max 12.5 mg daily
- Topical botox- on the horizon
- Topical oxybutynin- on the horizon

More About Oxybutynin (Ditropan)

- SPD Sept/Oct 2015- oxybutynin for palmoplantar hyperhidrosis
  - 2.5 mg daily x 1 wk, then 2.5 mg bid x 2 wks, then 5 mg bid
  - Dry mouth
  - Available as 5 mg pills or 5 mg/ml solution
- SPD May/June 2016- Spain- kids/teens
  - Oral robinul not available in Spain
  - 2.5 mg daily and increase by 2.5 mg daily at 2 wk intervals until results are seen
  - Contraindications: bladder/intestinal obstruction, severe ulcerative colitis, glaucoma, myasthenia
  - No monitoring needed
  - Oropharyngeal xerosis is most common side effect

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  - No monitoring needed
  - Oropharyngeal xerosis is most common side effect
### What’s New with Cooties?

**Scabies**
- In infants, it tends to present as a widespread “dirty” appearing rash with various morphologies—pink papules, urticarial papules, pustules, eczematosus patches
  - Check palms and soles for pustules—very typical
- In older kids, presents more typically with increased involvement in webspaces and groin area
- If itch is out of proportion to the rash, consider scabies

**Scabies Treatment**
- **Permethrin 5% cream**
  - Apply neck down tonight, wash off in am. Repeat in 1 wk
  - Safe down to any age and safe in pregnant women
- **Ivermectin 0.2 mg/kg**
  - Take one dose today and another dose in 1 wk
  - I will use it if rash is extensive, affects face/scalp, or has failed permethrin
- **Precipitated Sulfur-10% in white petrolatum at compounding pharm**
  - Apply bid for 3 days
  - Very stinky, but no resistance has been seen (Winter Clinical Jan 2016)

**Scabies Treatment**
- Wash all towels, clothes, sheets in hot water
- Vacuum carpet and upholstery
- Anything that can’t be washed should be placed in a closed plastic garbage bag and tied closed for 72 hrs

### Post Scabetic Dermatitis
- Post scabetic dermatitis is very common
- Itchy, eczematous rash that waxes and wanes for up to 2-3 mos after the scabies has been treated
- Important to warn patients it will probably happen
- Schedule a followup visit
- Some of it can be a little bit psychological; important to examine and reassure
- Treat with topical steroids
Warts

- Countless treatment options
  - Liquid nitrogen
  - Cantharidin
  - OTCs
  - Candida
  - Squaric Acid (contact sensitizers)
  - Laser
  - Bleomycin

- Best Thing Ever - WartPeel!
  - Nucara Pharmacy - Iowa
  - Sal acid + 5FU
  - Magic in a bottle
  - Applied at bedtime under “sticky tape”
  - $89 and worth every penny!

WartPeel

Warts and HPV Vaccination

- Mounting number of case reports showing that when pre-teens and teens are given HPV vaccine, their warts go away
- It will be interesting to see if we notice a decrease in incidence of warts over time as more and more people get immunized
Molluscum Contagiosum

- Caused by a poxvirus
- Very common in kids- pretty much all kids get them
- Spread by direct contact and spread like crazy in water (including swimming pools)
- Treatment is not mandatory as they will go away with time
  - Can take up to 2 yrs to resolve on their own
  - Recent study of 170 kids- half treated, half not treated
    - Molluscum resolved in the same amount of time

Molluscum Treatment Options

- Imiquimod/Zyclara
  - Apply MWF at bedtime x 8 wks
  - A little irritation- good; a lot of irritation- bad
- Zymaderm
  - All natural OTC product, botanical based
  - Applied BID
- Candida antigen injections
  - Injected into 1-2 of the molluscum every 3 wks
  - Tolerable; typically 3-5 treatments
  - Side effect profile
  - Case report of halo nevi after 1 candida treatment (SPD March/April 2017)
- Cantharidin
  - Never use it in the axilla
  - Blisters can be bad
  - 50% resolution with each treatment is success
  - Hard to get these days
- Curettage
  - SPD Nov/Dec 2016- curettage for molluscum- applied EMLA prior- 93% success after 1 treatment
- Liquid Nitrogen
- Topical retinoids

Molluscum Dermatitis

- Some kids will get an eczema like rash around the molluscum
- Important to treat it as it itches so kids scratch and then spread the molluscum

Pseudofurunculoid Molluscum

- Look like pimples/boils
- Due to body’s immune system response
- Not infected, just inflamed
- BOTE sign- Beginning Of The End

Pseudofurunculoid Molluscum and Id Reaction

- Some kids will get an eczema like rash around the molluscum
- Important to treat it as it itches so kids scratch and then spread the molluscum
PF Molluscum and Id Reaction

- Treat the Id Reaction with topical steroids
- Treat the PF molluscum with oral antibiotics or bleach baths
- F/u 2-3 wks
- Usually everything is "all better"

What's New with JAK Inhibitors?

JAK Inhibitors

- 2014- 2 Yale Researchers published a case report in JID
  - Male patient with h/o arthritis and alopecia totalis
  - Started on Tofacitinib (Xeljanz- JAK1/3 inhibitor) for arthritis
  - All his hair regrew

JAK Inhibitors Appear Promising

- JAMA Derm October 2015
  - Case report of Tofacitinib working for vitiligo
- JAAD Feb 2016
  - Case report of ruxolitinib working for pt with alopecia areata and vitiligo
- JAMA Derm April 2016
  - Topical ruxolitinib 0.6% cream bid for AA case report- hair seen at 12 wks
  - Oral ruxolitinib for nail dystrophy associated with alopecia areata (JAMA)
    - 3 patients. Nails improved in all. Hair regrew in 2/3
- Derm News July 2016
  - 12 patients. 9/12 had alopecia totalis/universalis
  - 11/12 had regrowth, 7/12 had >50% regrowth
  - Recurrence is an issue
- September 2016- Oclacitinib approved to treat doggy eczema

JAK Inhibitors- JAAD Jan 2017

- Tofacitinib for alopecia areata in 90 adult patients
  - Severe alopecia areata, alo tot, alo univ
  - Clinical response in 77%
  - 58% had intermediate-complete response over 4-18 mos
  - Consider adding in pulse pred for nonresponders
  - After 10 yrs of complete scalp hair loss, pts are less likely to respond
  - No serious adverse events over 12 mos
  - When to stop treatment still unclear; probably indefinite

JAK Inhibitors- JAAD Jan 2017

- Tofacitinib for alopecia areata in 13 adolescents
  - Ages 12-17
  - Used 5 mg bid dose
  - Hair regrowth in 70% of patients
  - Safety questions- baricitinib being studied for treatment of interferon-mediated autoinflammatory syndromes in kids as young as 18 mos and URI appears to be the most common side effect in those kids
Good summary article of where things stand with JAKs and skin disease

- **8 Adolescents with alopecia universalis treated with Xeljanz**
  - 12-19 yrs old, all with 100% hair loss
  - 5 mg bid x 5-18 mos
  - No lab abnormalities
  - All had >50% regrowth in scalp hair by 5 mos
  - All slow for the first 5 mos and then rapid
  - All patients satisfied and continuing the medicine

Xeljanz (Tofacitinib) 5 mg bid

- Appears well tolerated- side effects include headache, GI upset
- **Baseline labs**
  - CBC with diff, CMP, lipid panel
  - TB test, Hep B, Hep C, HIV
- Repeat CBC with diff, CMP and lipid panel every month for 3 mos, then every 3 mos
- I have 2 patients currently on it for AA and 2 patients on it for vitiligo, doing well
- Topical versions probably still 2-3 yrs away
Birkenstocks!

Miscellaneous Tips and Tricks for Kids

MAM Air Pacifier
- For kids that have persistent dermatitis around the mouth, drool and irritation from pacifiers are a common cause
- Recommend the MAM Air Pacifier which is more open than most

Buzzy
- www.buzzyhelps.com
- Vibrates and you can attach a reusable ice pack to add cold
- Distracts the nerve fibers so the child feels buzzy and minimizes the pain they feel
- Place it on the skin “between the brain and the pain”
- Comes in plain black, a bee, and a ladybug
- Costs $70
- Easy to wipe down with an alcohol swab
Prize Box

- If you see a lot of kids, it really helps to have a small prize box or sticker box
- Cheap to buy things to fill it (most of the items cost less than a $1)
- Can help serve as a distraction
- Can help make kids feel comfortable
- Can "make a negative a positive" after painful procedures

The End!

- Feel free to contact me with any questions
  lisawansonmd@gmail.com
BAP-oma & BEYOND

MICHAEL A NOWAK, MD

CONFLICTS

• No conflicts with the content of this lecture

BAP-oma

• Wiesner 2011: Families with multiple tan dome-shaped papules of head, neck, trunk, and extremities.
• Lesions with BAP-1 loss are termed BAP-oma or Wiesner’s nevus.
• Most Wiesner’s nevi are solitary (sporadic somatic mutation) and behave in an indolent fashion.
• Multiple Wiesner’s nevi: consider BAP-1 germline mutation especially with a family history of mesothelioma or uveal melanoma.

BAP-oma

• BAP-1 gene - chromosome 3p21
• Cell cycle regulation, differentiation, cell death, DNA damage response
• Many different types of mutations
• Immunohistochemistry is procedure of choice for detection BAP-1 mutations

BAP-oma

• Cancer syndrome involving predisposition to mesothelioma, multiple melanocytic nevi, uveal melanoma, and cutaneous melanoma.
• Concomitant BRAF mutation is frequent
• 85% of metastatic uveal melanomas have BAP-1 mutation
• Histone deacetylase inhibitors used for uveal melanoma with BAP-1 mutation
• Lack of BAP-1 expression associated with worse survival in cutaneous melanoma

BAP-oma

• Solitary or multiple
• Well circumscribed pink papule or nodule
• Often polypoid
• Frequently present since childhood
BAP-oma

- Lesions are often Spitzoid or Epithelioid
- Spitzoid cytology without epidermal hyperplasia, Kamino bodies, and clefts
- Various populations with different degrees of atypia (HETEROGENEITY)
- Contain highly cellular areas with pleomorphic melanocytes that are BAP-1 negative

What would I see on a report?

- Atypical Spitzoid tumor with BAP-1 loss
- Wiesner’s nevus is associated with BRAF EXPRESSION and typically lacks epidermal hyperplasia and Kamino bodies
- P16 - cyclin-dependant kinase inhibitor 2 (CDKN2A gene) tumor suppressor is EXPRESSED.
- Therefore, “melanocytic tumor of uncertain biological potential” is the best description
What do I do next?

- Complete excision with generous clear margins (margin of error) and look for additional lesions
- Inquire about eye tumors and mesothelioma
- Long term surveillance similar to a melanoma patient
- Referrals for multiple lesions with suspected germline mutation
- Multiple lesions followed for change in clinical appearance, radiologic studies, and genetic counseling

Summary

- Solitary or multiple
- Risk of melanoma is surprisingly low
- Melanocytic tumor of uncertain biological potential (different from Spitz nevus)
- Wiesner's nevus
- Nevus, uveal melanoma, cutaneous melanoma, Familial mesothelioma (non-asbestos related)
EXTRAMAMMARY PAGET’S DISEASE

- Overview
- Presentation
- Differential Diagnosis
- Treatment
- Review

PAGET’S DISEASE

- Mammary
- Extramammary
- Bone
- Prototype (microscopic pattern)

- Sir James Paget 1874
PAGET’S DISEASE

- 1874 Sir James Paget
- Mammary skin involvement (nipple) associated with an underlying breast cancer in virtually 100% of cases.
- Poor prognostic sign

EXTRAMAMMARY PAGET’S DISEASE

- 1889 Radcliffe Crocker
- Occurs in anatomic sites rich in apocrine glands
- Frequently NOT associated with an underlying glandular carcinoma (confined to the skin).

EXTRAMAMMARY PAGET’S DISEASE

INTRAEPIDERMAL APOCRINE CARCINOMA
CYTOKERATIN 7 POSITIVE

EXTRAMAMMARY PAGET’S DISEASE

- Vulva most common
- Male genital area
- Perianal area
- Axilla

PERIANAL PAGET’S DISEASE

- Similar to mammary Paget’s since it is frequently associated with underlying visceral malignancy
- Frequently NOT limited to the perianal skin
- More referrals and worse prognosis

EXTRAMAMMARY PAGET’S DISEASE

- Perianal
- Sharply demarcated erythematous patch
- Pruritus and burning pain are common
- Primary vs. secondary
MICROSCOPIC FINDINGS

- Paget’s cells: Large mucin containing cells
- Single cells or small clusters at all levels of the epidermis - primarily lower layers
- Basal layer is frequently spared and compressed forming “eyeliner sign”
- Occasional signet ring cells and tubular structures

MICROSCOPIC FINDINGS

- Limited to epidermis
- Invasive - Depth of Invasion (4mm)
- Cell of origin - likely adnexal stem cell origin (primary)

PERIANAL PAGET’S DISEASE

- Primary lesions (limited to skin): CK20 negative/GCDFP-15 positive, good prognosis, high 5 year survival, intraepidermal apocrine carcinoma.
- Secondary lesions (skin and rectal involvement): CK20 positive/GCDFP-15 negative, poor prognosis, low 5 year survival, rectal carcinoma involving skin vs. invasive Paget’s involving rectum.
Signet ring cell perianal paget disease: loss of MUC2 expression and loss of signet ring cell morphology associated with invasive disease.

Grelck KW, Nowak MA, Doval M

PERIANAL PAGET’S DISEASE

- Morphology (loss of signet ring cell features)
- Immunohistochemical (loss of Muc2 expression)
- Depth of invasion (> 4 mm): Depth of invasion associated with a worse prognosis (shift in phenotype and differentiation)

DIFFERENTIAL DIAGNOSIS

- Erythematous plaque of groin
- Eczematous dermatitis including irritant and allergic contact dermatitis
- Tinea Cruris
- Candidiasis
- Intertrigo
- Psoriasis/Sеборей
- Zoon’s
- Granular Parakeratosis
- Malignancy (high index of suspicion)
MICROSCOPIC DIFFERENTIAL DIAGNOSIS

- Paget's/Extramammary Paget's disease
- Melanoma/Melanoma in-situ
- Squamous cell carcinoma in-situ
- Sebaceous carcinoma (and other adnexal)
- Pagetoid reticulosis
- Merkel cell carcinoma (Golgi CK20 +) - Polyomavirus?

MORPHOLOGIC CLUES

- Eyeliner sign (thin vs. thick)
- Pigmentation
- Parakeratosis
- Sebaceous cells
- String of pearls
- Nuclear molding
- Dermal involvement (differentiation)
SPECIAL STAINS

- EMPD vs. SCCIS vs. MIS
- Primary vs. Secondary
- Invasion (CKNBD-56 expressed, MUC-2 lost)
- Lymphatic involvement (D2-40)
SPECIAL STAINS

- PAS +
- Mucicarmine +
- Alcian Blue +
- CK7 +
- GCDFP-15 +/- (primary/secondary EMFP)
- CK20 +/- (primary/secondary EMFP)

SPECIAL STAINS

- S100 = MIS
- CK5/6 (LMW) = SCC
- EMA/Oil-red-O = sebaceous carcinoma
- CK7 = EMPD
- GCDFP-15 = primary
- CK20 diffuse = secondary
- CK20 perinuclear = Merkel

WORK UP

- Clinical trial with topical therapy
- Medium potency steroid and antifungal
- NR in compliant patient at 3-4 weeks
- Biopsy (4 mm punch in formalin)
- History and Physical (pelvic, rectal, breast, lymph nodes)
- Referrals and Staging (Internist, GYN, GE, surgical and medical oncology)
- Procedures (culposcopy, sigmoidoscopy, cystoscopy)

TREATMENT

- Topical chemotherapy
- Wide local excision (Stage 1 and 2A)
- AP resection (Stage 2B and Stage 3)
- Medical oncology (Stage 4)
- Radiation (Stage 4)
- Other referrals
- Long term monitoring
EXTRAMAMMARY PAGET’S DISEASE
TREATMENT RESPONSE

Summary

- Mammary vs. Extramammary
- Primary vs. Secondary
- Clinical Differential Diagnosis
- Microscopic Differential Diagnosis
- Referrals and treatment
- Long term monitoring
Resident Poster Presentations

**Congenital Psoriasis: A Rare Entity**
Isaac Bryan, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

**Management of Radiation Dermatitis**
Soham Chaudhari, D.O.
Texas OPTI/Bay Area Corpus Christi Medical Center

**Cutaneous Myiasis**
Mojgan Hosseinipour, D.O.
NYCOMEC/St. Barnabas Hospital

**Perforating Folliculitis Associated with Poison Ivy Dermatitis Successfully Treated with Topical Adapalene 0.1% Gel: A Case Report**
Monica Huynh, D.O.
NYCOMEC/St. Barnabas Hospital

**Atypical Staining Histiocytosis CD1a Positive, S100 Negative: A Potentially Reactive Process?**
Christopher Mancuso, D.O.
NYCOMEC/St. Barnabas Hospital

**Lichen Planus Pigmentosus: Atypical Presentation and Progression of Rare Disorder**
Shoni Rozenberg, D.O.
LECOMT/St. John’s Episcopal Hospital, South Shore

**Beware of Tube Wells: A Case of Arsenical Keratosis**
Adrian Tinajero, D.O.
LECOMT/St. John’s Episcopal Hospital, South Shore
**INTRODUCTION**

The diagnosis of congenital psoriasis is rare, nationally the prevalence of adults with psoriasis can be as high as 3% while estimations for the pediatric population is 1%. Psoriasis is an immune mediated inflammatory process that produces activation of T helper cells that lead to abnormal keratinization. Certain genetic factors have been described, the most strongly associated human leukocyte antigen type is Cw6. We present a case of a biopsy proven psoriasis since birth. We review the comorbidities associated with psoriasis for consideration in pediatric patients with this chronic disease.

**CASE REPORT**

A three-week old female presented with pink patches and plaques with a fine scale to the axilla, neck, inguinal folds and scalp. She was born full term via spontaneous vaginal delivery without complications during pregnancy or delivery.

On exam there were pink patches and plaques with a fine scale to the axilla, neck, inguinal folds and scalp.

She had previously been treated with mometasone 0.1% cream daily for one week with little improvement. Family history was negative. A punch biopsy was obtained more fully ascertain if there was an underlying systemic process due to the presentation and poor response to a potent topical steroid.

One week following the biopsy the patient presented with an acute flare of erythematous plaques and plaques to the body. The patient was admitted to the hospital for observation, treated with topical corticosteroids and wet wraps.

Family history was negative.

On exam there were pink patches and plaques with a fine scale to the axilla, neck, inguinal folds and scalp. She was born full term via spontaneous vaginal delivery without complications during pregnancy or delivery.

**HISTOLOGY**

Figure 4 and 5 Mounds of parakeratosis with pustular aggregates of neutrophils within and below the cornfield layer. There is epidermal hyperplasia and dilated tortuous blood vessels present at the tips of the dermal papillae.

**COMORBDITIES**

**DISCUSSION**

**Congenital Psoriasis**

Rare presentation of an autoimmune, chronic skin disorder

**Clinical Presentation**

Erythematous plaques and patches with adherent scale over a wide distribution. Typically involves that face and scalp and spares the diaper area.

**Histology**

Parakeratosis overlying a thickened epidermis and absent granular layer. Elongated rete ridges with dilated capillary loops and collections of neutrophils in the epidermis.

**Pathogenesis**

Inflammatory cascade of T cells (Th2 and Th17) and the production numerous inflammatory cytokines leading to systemic inflammation, rapid keratinocyte turnover and other systemic involvement. Triggers of psoriasis can be infectious, traumatic, stress or idiopathic. Genes implicated in psoriasis reside on chromosome 6 more commonly PSOR1. HLA types Cw6, B13, B17.

**CONCLUSION**

Congenital psoriasis is a less commonly encountered disease. That requires a skin biopsy to give a definitive diagnosis and better direction therapy. Treatment can be fraught with complications and patient education. In these pediatric patients have rheumatology or pediatric dermatologists involved will help to maximize patient outcome. A great deal of education for parents of these children is required to understand expectations as well as the prognosis and future comorbidities.

**REFERENCES**

Management of Radiation Dermatitis
Chaudhari S1, Lin R2, Gorcey L3, Chennupati S4, Kalnicki S3, McLellan B3
1: Bay Area Corpus Christi Medical Center, Corpus Christi TX ; 2: Dermatology Clinic of McAllen, McAllen TX; 3: Albert Einstein College of Medicine, Bronx NY; 4: Diablo Valley Oncology & Hematology Group, Pleasant Hill CA

Introduction
In 2015, there will be an estimated 1,658,370 new cancer cases diagnosed in the United States, two thirds of which are expected to undergo radiotherapy as part of their treatment. 1 Approximately 90% of patients receiving radiotherapy will experience an adverse skin reaction. 2 Acute radiation dermatitis (RD) occurs in a dose-dependent fashion and typically manifests within a few days to weeks after commencing external beam radiation therapy. Its presentation varies in severity and can include erythema, dry or moist desquamation, and ulceration when severe. 3 Chronic changes can occur within several months to years and include dyspigmentation, hair loss, atrophy, fibrosis, telangiectasias, ulceration and necrosis of underlying structures. 4 RD can significantly impair quality of life and patient compliance, possibly leading to treatment interruption. Therefore, prevention and treatment of RD is crucial. 5

Objective
Due to the inconclusive evidence for available treatment options, management of RD varies among practitioners. Prior surveys in other countries such as Australia have demonstrated variation in skin care practices and that a considerable number of these practices were based only on anecdotal evidence. 5 Furthermore it is unknown what the practice patterns for RD are currently in the United States. Therefore, this study defines and reviews the current treatments for RD in the United States, providing guidance for practicing physicians as well as directions for future research.

Methods
We conducted a patterns of care survey of the current management of RD from August 2014 to January 2015 across the United States. The study was approved by the Albert Einstein College of Medicine institutional review board, and the survey was developed with an online directory, which included radiation oncologists, residents, fellows, physician assistants, nurse practitioners, registered nurses and other care providers. Data was analyzed using simple summary and descriptive statistics.

Table 1

<table>
<thead>
<tr>
<th>Title</th>
<th>% Recomended by the MACSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attending physician</td>
<td>96%</td>
</tr>
<tr>
<td>Fellow</td>
<td>67%</td>
</tr>
<tr>
<td>Resident</td>
<td>54%</td>
</tr>
<tr>
<td>Time in practice</td>
<td></td>
</tr>
<tr>
<td>1-5 years</td>
<td>19.2%</td>
</tr>
<tr>
<td>6-10 years</td>
<td>18.3%</td>
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<tr>
<td>11-15 years</td>
<td>10.8%</td>
</tr>
<tr>
<td>16-20 years</td>
<td>12.5%</td>
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<td>&gt;20 years</td>
<td>11.5%</td>
</tr>
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<td>Practice Setting</td>
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<tr>
<td>Private practice</td>
<td>34.1%</td>
</tr>
<tr>
<td>Academic setting</td>
<td>22.5%</td>
</tr>
<tr>
<td>Oncology center</td>
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<tr>
<td>Multidisciplinary center</td>
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</tr>
<tr>
<td>Community hospital</td>
<td>24.8%</td>
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<tr>
<td>Leucemia institute</td>
<td>1.1%</td>
</tr>
<tr>
<td>Veterans Affairs hospital</td>
<td>1.9%</td>
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<tr>
<td>Other</td>
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<td>No</td>
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<tr>
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<tr>
<td>Observational evidence</td>
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</tr>
<tr>
<td>Evidence-based research</td>
<td>81.4%</td>
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<tr>
<td>Comfort level in managing RD</td>
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</tr>
<tr>
<td>Very comfortable</td>
<td>68.6%</td>
</tr>
<tr>
<td>Moderately comfortable</td>
<td>29.4%</td>
</tr>
<tr>
<td>Uncomfortable</td>
<td>1.1%</td>
</tr>
<tr>
<td>Moderately uncomfortable</td>
<td>0.1%</td>
</tr>
<tr>
<td>Very uncomfortable</td>
<td>0.1%</td>
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<tr>
<td>Benefit of patient significance of RD</td>
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<tr>
<td>Large impact</td>
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<tr>
<td>Moderate impact</td>
<td>84.4%</td>
</tr>
<tr>
<td>Small impact</td>
<td>15.1%</td>
</tr>
<tr>
<td>No benefit</td>
<td>15.9%</td>
</tr>
<tr>
<td>Had to shortend radiation because of RD</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>52.6%</td>
</tr>
<tr>
<td>No</td>
<td>47.4%</td>
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</table>

Table 2

<table>
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<tr>
<th>Topical Agent</th>
<th>% Recommended by the MACSC</th>
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<tbody>
<tr>
<td>Aloe vera</td>
<td>77.6%</td>
</tr>
<tr>
<td>Continuous prophylaxis</td>
<td>66.9%</td>
</tr>
<tr>
<td>Topical corticosteroids</td>
<td>70.3%</td>
</tr>
<tr>
<td>Baseline</td>
<td>21.6%</td>
</tr>
<tr>
<td>Calendula</td>
<td>15.0%</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>11.9%</td>
</tr>
<tr>
<td>Silver sulfadiazine cream</td>
<td>5.6%</td>
</tr>
<tr>
<td>Barrier</td>
<td>3.7%</td>
</tr>
<tr>
<td>topical antibiotics</td>
<td>1.2%</td>
</tr>
<tr>
<td>Hyaluronic acid</td>
<td>2.7%</td>
</tr>
<tr>
<td>No treatment</td>
<td>1.9%</td>
</tr>
<tr>
<td>Topical anesthetic</td>
<td>1.9%</td>
</tr>
<tr>
<td>DRESS (hydrophilic/hydrocolloid)</td>
<td>1.5%</td>
</tr>
<tr>
<td>Honey impregnated ointment</td>
<td>1.0%</td>
</tr>
<tr>
<td>Sulfates</td>
<td>1.1%</td>
</tr>
<tr>
<td>Urea</td>
<td>1.1%</td>
</tr>
<tr>
<td>Medicated</td>
<td>1.0%</td>
</tr>
<tr>
<td>Lidoceaine</td>
<td>0.6%</td>
</tr>
<tr>
<td>Saccharate</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

Table 3: Grade 1 RD Therapies used by physicians

<table>
<thead>
<tr>
<th>Topical Agent</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand ()</td>
<td></td>
</tr>
<tr>
<td>Aloe vera</td>
<td>77.6%</td>
</tr>
<tr>
<td>Continuous prophylaxis</td>
<td>66.9%</td>
</tr>
<tr>
<td>Topical corticosteroids</td>
<td>70.3%</td>
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<tr>
<td>Baseline</td>
<td>21.6%</td>
</tr>
<tr>
<td>Calendula</td>
<td>15.0%</td>
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<tr>
<td>Vitamin E</td>
<td>11.9%</td>
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<tr>
<td>Silver sulfadiazine cream</td>
<td>5.6%</td>
</tr>
<tr>
<td>Barrier</td>
<td>3.7%</td>
</tr>
<tr>
<td>Topical antibiotics</td>
<td>1.2%</td>
</tr>
<tr>
<td>Hyaluronic acid</td>
<td>2.7%</td>
</tr>
<tr>
<td>No treatment</td>
<td>1.9%</td>
</tr>
<tr>
<td>Topical anesthetic</td>
<td>1.9%</td>
</tr>
<tr>
<td>DRESS (hydrophilic/hydrocolloid)</td>
<td>1.5%</td>
</tr>
<tr>
<td>Honey impregnated ointment</td>
<td>1.0%</td>
</tr>
<tr>
<td>Sulfates</td>
<td>1.1%</td>
</tr>
<tr>
<td>Urea</td>
<td>1.1%</td>
</tr>
<tr>
<td>Medicated</td>
<td>1.0%</td>
</tr>
<tr>
<td>Lidoceaine</td>
<td>0.6%</td>
</tr>
<tr>
<td>Saccharate</td>
<td>0.1%</td>
</tr>
</tbody>
</table>

Results

A) Response Rate
i. Out of the 5,626 email addresses for the 2013 ASTRO members, 121 emails were bounced back, leaving 5,505 emails delivered.
ii. 781 providers responded to our survey, which resulted in an overall response rate of 14.19%.
iii. 709 physician respondents were left for our analysis, resulting in a corrected response rate of 12.9%.
B) Physician Responder Background

i. Physician respondents were well represented in various geographic locations, demographics, and practice settings.
ii. Although 84.7% of physicians felt that RD had a moderate or large impact on patients’ quality of life during cancer treatment, only 30.1% received special training or specific instructional courses in treating RD during their medical training.

C) Prophylaxis of RD
i. There was a wide variety of recommendations given by the providers (Table 2).
ii. Although 89% of surveyed physicians rely on observational and/or anecdotal findings to guide treatment decisions, and only 51.4% reported using evidence-based treatments.

D) Treatment of Acute RD

i. Out of the 709 physician respondents, 83% of respondents treat RD during their medical training.
ii. 781 provider respondents.
iii. 89% of surveyed physicians rely on observational and/or anecdotal findings to guide treatment decisions.
iv. Only practicing physicians were included, therefore leaving 5,505 emails delivered.
resulting in an overall response rate of 14.19%.

E) Comparison to MASCC

Conclusions

This study is unique in that it highlights the practice patterns for the prophylaxis and treatment of RD by many radiation oncologists across the United States.

Given the relative lack of evidence to support specific management strategies, the results of this study highlight the need for utilization of evidence-based guidelines for the prevention of RD and for the need of more high-quality studies looking at the treatment for acute RD. Given the cost, morbidity and mortality associated with managing RD and the problems associated with having to shorten radiation therapy should severe RD develop, better adherence to evidence-based guidelines may improve patient compliance, quality of life and cancer outcomes.

Bibliography

Myiasis, a zoonotic disease, is defined as an infestation of human tissue by eggs or larvae from flies of the order Diptera. Myiases have become increasingly prevalent, particularly when human activity is carried out in environments with poor hygiene. Human myiases generally are present in cavities or wounds but also can affect tissue such as the skin, eyes, oral cavity, intestines, or urogenital area. Cutaneous presentations are most common and include furuncular, migratory, and wound myiasis, depending on the type of infesting larvae.

A 60-year-old male with past medical history significant for AIDS with CD4 count of 20 on presentation, Hepatitis C with liver cirrhosis, illicit drug abuse and chronic venous stasis presented to the emergency department with worsening left leg pain of 2-month duration with increasing serous/serosanguineous discharge. Physical examination revealed bilateral lower extremities with circumferential, indurated, and hyperpigmented verrucous plaques. The left lower extremity had extensive dome-shaped nodules with adherent scale, fissuring and distal red-yellow discoloration. Numerous live insects were evident between nodules on the left leg.

Clinically our patient had elephantiasis nostras verruciformis secondary to long term lymphedema. With his immunocompromised states and vascular compromise, he developed an external infestation secondary to fly larva. He was treated with an occlusion suffocation approach. Petroleum jelly was applied to the left lower extremity every 3 hours to coax emergence and removal of all visible larva. Wound care recommendations included daily anti-septic cleansing and dressing changes. He responded well to treatment, thus debridement and use of larvicides was not necessary.

Myiasis is a clinical diagnosis, with definitive diagnosis achieved by extraction and identification of the fly larvae. Removal of the larvae is curative in all types of myiasis, and all treatment regimens attempt to accomplish this goal. Wound myiasis can be treated by irrigation with saline or a dilute antimicrobial such as hydrogen peroxide. The treatment of wounds with living fly larvae, known as maggot therapy, includes occlusion, manual extraction of the larva, and use of larvicides. Occlusion deprives the larva of oxygen and either kills the larva or induces it to move upward in search of air. Ivermectin is a synthetic of a broad-spectrum antiparasitic that has been used successfully as a larvicide in human myiasis. If not directly larvicidal, ivermectin will at least induce larval migration out of the skin.

We present this case of cutaneous myiasis for clinical interest. Although we obtained a live fly for microbiological review, identification of dipterous larvae is highly specialized and requires the skill of an experienced pathologist, entomologist, or parasitologist. Therefore, we were unable to receive definitive identification of the species of our patient’s wound infestation.

Figures 1-3. Lower extremity wound myiasis with visible nodules and serosanguinous drainage.

Selected References


Perforating folliculitis associated with poison ivy dermatitis successfully treated with topical adapalene 0.1% gel: a case report.

Monica Huynh DO, Nikki Vyas MD, Cindy Hoffman DO

Background

Perforating dermatoses are a group of papulonodular skin disorders characterized by a central keratotic plug or crust in which there are extrusions of dermal connective tissue (collagen or elastic fibers). The disease is classified into two main groups: primary or secondary. The four prototypical diseases in the primary group include reactive perforating collagenosis, elastosis perforans serpiginosa, perforating folliculitis, and Kyrle’s disease. The secondary form is known as acquired perforating dermatosis. This disease usually develops in adulthood and is associated with systemic diseases such as diabetes mellitus and renal failure, including hemodialysis.

Case

A 70-year-old female presented to our clinic with a 1 month history of skin eruptions to her bilateral arms. The patient was initially assessed by a physician assistant. At the time of the visit, the patient reported that she was exposed to poison ivy while gardening which resulted in extremely pruritic skin eruptions to bilateral arms. The patient admitted to scrubbing and excoriating both arms frequently. The patient was treated as allergic contact dermatitis with fluocinonide 0.05% ointment daily to affected areas. The patient returned one month later to report she had worsening of her skin lesions despite being compliant with topical medication. On examination, she had multiple 1 cm erythematous rough scaly papules with central keratotic crusts. She denied any other symptoms. She had no past medical history, took no medications, and had no known allergies. A punch biopsy was obtained from the right forearm which revealed perforating folliculitis. The patient was then recommended to start applying adapalene 0.1% gel to skin lesions nightly. She returned three months post-treatment and had resolution to most lesions. The patient admitted she was still excoriating the residual lesions but was happy about her progress.

Clinical Photographs

Figure A,B. Bilateral forearms with multiple erythematous rough scaly papules with central keratotic crust. Figure B. One month post-treatment with adapalene 0.1% gel

Dermatopathology

Punch biopsy of right forearm. Figure C,D Punch specimen showing focal ulceration with fibrinopurulent exudate, irregular acanthosis, focal hyperkeratosis and fibrosis of the reticular dermis. Figure E,F EVG highlights elimination of elastin fibers. Collagen transepidermal elimination is also identified.

Discussion

The pathogenesis for perforating dermatoses is still unknown. “Perforating” may be a misnomer as many have noted it is unlikely that dermal connective tissue actively perforate into the epithelium. Some authors have argued “transepidermal elimination” is a more accurate term. Some of the proposed mechanisms include abnormally premature keratinization, primary alteration of connective tissue, or deposition of foreign material within the superficial dermis with subsequent engulfment and elimination by proliferative follicular epithelium. The role of fibronectin has been raised as levels are shown to be increased in the serum of patients with diabetes and uremia, and also found to be increased within the skin at sites of transepidermal elimination.

Currently there are no well-designed, well-controlled studies to evaluate therapeutic options. Small case series and individual reports of therapeutic outcomes include the use of topical emollients, topical/intralesional/oral steroids, topical/oral retinoids, cryotherapy, ablative laser, and phototherapy. We report a case of a female with recalcitrant perforating folliculitis, refractory to topical corticosteroids, that was responsive to topical adapalene 0.1% gel nightly. She tolerated the medication without any side effects. She had remarkable improvement in one month of treatment. We propose this medication to be considered given its potential efficacy, cost, and accessibility.

References

Abstract

It has been estimated that the contamination of water with arsenic in Bangladesh is one of the biggest poisonings of a population in history. The pathogenesis of the toxicity of arsenic to humans is thought to be through the interference with cellular respiration and uncoupling of oxidative phosphorylation among others. Exposure to arsenic has shown to have an increased risk of development of skin cancers including basal cell carcinoma and squamous cell carcinoma. By the 1990s there were up to 95% of the population in Bangladesh drinking from tube wells. The World Health Organization provides guidelines regarding the max amount of arsenic allowed in water as 0.01 mg/L. However, testing in Bangladesh has shown that up to 30% of tube wells had levels exceeding 0.05 mg/L which represented approximately 26 million people at risk of drinking water with unsafe levels of arsenic. This case report highlights the importance of being aware of this rare presentation, since early treatment and close monitoring is key to prevent cutaneous malignancies.

Case

A 44-year-old male presented to clinic for evaluation and treatment of scaly plaques on his palms and soles. On physical exam, there were diffuse punctate hyperkeratotic yellow/brown plaques on both palms and soles. Skin biopsy showed arsenical keratosis.

This patient was native of Bangladesh where he lived until 2009 when he moved to the United States. During most of his life he drank water from tube wells which were the only available sources of water in his town. He started developing the lesions approximately 15 years ago, which started as a small scaly plaque.

Atomic number thirty-three also known as arsenic was the discovered by Albertus Magnus close to the year 1250. Arsenic is a compound that occurs in the environment and can be combined with other elements to create inorganic arsenic compounds. Arsenic changes its form in the environment by reacting with oxygen and other molecules in the air, water or soil. This element has the capacity to attach itself to large or small capacity molecules which can settle in soil. The pathogenesis of the toxicity of arsenic to humans is thought to be through the interference with cellular respiration and uncoupling of oxidative phosphorylation among others. Arsenic can also cause direct effects to DNA including processes such as transcription, repair and amplification. In recent articles, investigating the role of arsenic in inducing oxidative stress has gained some traction. There is a broad spectrum of cutaneous findings as a result of arsenic exposure which ranged from hyperpigmentation, hyperkeratosis of palms and soles, Bowen’s disease, squamous cell carcinoma, and basal cell carcinoma. One of the earliest finding of arsenical exposure is changes in pigment, especially in palms as these areas are more likely to have higher metastatic risk than those arising from normal skin. The most important pillar in the management of arsenical keratosis is recognition as lesions may develop into cutaneous malignancies and chronic exposure can lead to visceral malignancies. In acute arsenic toxicity, chelation therapy in the mainstay therapy with a 3mg/kg intramuscular injection of dimercaprol or BAL (British antilewisite) every four hours for two days and every six hours subsequently for one day followed by every twelve hours for ten days. For cutaneous lesions, therapy modalities have included cryotherapy, topical chemotherapy, photodynamic therapy and retinoids.

Images

Multiple brown-yellow hyperkeratotic plaques on palms and soles

Distribution of documented problems with arsenic in groundwater (>15ug/L)

Discussion

Our patient was native of Bangladesh where he lived until 2009 when he moved to the United States. During most of his life he drank water from tube wells which were the only available sources of water in his town. He started developing the lesions approximately 15 years ago, which started as a small scaly plaque.


Conclusion

Although rare, it is not far fetched that a case of arsenical keratosis may present in a primary care office in communities where there is a high immigrant population or close to US regions where arsenic is still found in the groundwater (see map). The key to clinical management as with numerous cutaneous lesions, is an expansive differential in hyperkeratotic lesions. The goal is early identification and treatment as delay or misdiagnosis can result in neoplastic processes. In the dermatology community there has been consensus regarding the various modalities in treating skin lesions. Arsenic is a naturally occurring mineral and it is unlikely that cases of arsenical keratoses or arsenic toxicity will decline significantly. It is imperative that public health officials continue the work in identifying contaminated water systems. Regarding investigative opportunities in dermatology, there is still room for investigation regarding photodynamic therapy as well as the possible synergistic efficacy of various topical chemotherapeutic and keratolytic agents.

References


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Upcoming Meetings:

2018 AOCD Spring Meeting
Hilton West Palm Beach
West Palm Beach, FL
March 21 - March 24, 2018

2018 AOCD Fall Meeting
Westin San Diego - Gaslamp Quarter
San Diego, CA
October 9 - October 13, 2018

2019 AOCD Spring Meeting
JW Marriott Orlando
Orlando, FL
April 7 - April 13, 2019

2019 AOCD Fall Meeting
Omni Nashville Hotel
Nashville, TN
September 24 - September 28, 2019