2020 Spring New Trends in Dermatology

Hilton West Palm Beach
West Palm Beach, FL
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Reagan Anderson, D.O., FAOCD
Activity Moderator
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Continuing Medical Education Statements
This activity will change your practice and improve patient outcomes!

Content included in AOCD’s Educational conferences will not include individually identifiable health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), as amended.

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

The American Osteopathic College of Dermatology AOCD designates this live activity for a maximum of 26 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians.

The American Osteopathic College of Dermatology designates this program for a maximum of 26 AOA Category 1-A credits and will report CME and specialty credits commensurate with the extent of the physician’s participation in this activity.

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.
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.

Vision, Mission & Values
The vision of the American Osteopathic College of Dermatology is to advocate for our members and patients.
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.
The American Osteopathic College of Dermatology will instill the following values in all of our activities:
1. Inclusivity for all members
2. Consciousness of dermatologic issues
3. Excellent patient care
4. Promotion of life-long learning

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:
Content included in AOCD’s Educational conferences will not include individually identifiable health information, in accordance with the Health Insurance Portability and Accountability Act (HIPAA), as amended.
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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 surgical dermatology, oral dermatology, psoriasis treatment updates, dermoscopy, pediatric dermatology, allergies, practice management and physician burnout.

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 upcoming changes to physicians’ reimbursement models, and gain tips for operating a successful practice.
- Attendees will be able to better treat atopic dermatitis and psoriasis effectively, better recognize the risks and benefits of biologic therapy, better select appropriate therapies for specific patient populations, and better recognize the side effects of various psoriasis therapies.
- Attendees will learn new therapeutics for children with skin diseases, better identify common pediatric skin conditions, and learn what is new and interesting in pediatric dermatology.
- Attendees will review osteopathic tenets, the osteopathic approach in delivering bad news to the patient, and dermatologic medical conditions and treatments with an osteopathic approach.
- Attendees will interactively participate in case studies of complex cutaneous oncology and gain a better perspective of the complexities of interdisciplinary approaches common in oncology.
- Attendees will learn the characteristics and treatment options of Morgellons disease and review research on causes of Morgellons disease.
- Attendees will learn about the utilization of a PA in a dermatology office, learn to better define and implement optimal team practice, and gain tips for hiring/employing a PA.
- Attendees will learn common causes of contact dermatitis in children, new treatments for hemangiomas and pyogenic granulomas, and gain new tools to manage atopic dermatitis in children.
- Attendees will become more aware of subtle findings in common lesions, better recognize and identify certain patterns that can assist in formulating a diagnosis, and improve ability to combine histological and clinical information to render a diagnosis.
- Attendees will better understand the cellular processes that lead to skin aging, better evaluate the various anti-aging techniques, and update their knowledge on the science of skin aging.
Attendees will learn legal principles as they affect the practice of dermatology, improve patient satisfaction by emerging compliance with the ADA and similar regulations and better avoid legal missteps by clarifying ambivalent regulations. Attendees will learn which activities the ADA covers, learn how to make these websites compliant with the ADA, and understand how to determine if an animal is a service animal according to the ADA.

Attendees will review a detailed analysis of the three main causes of facial aging, better understand how to approach those causes, and review appropriate and inappropriate treatments.

Attendees will better understand practical aspects of IVIG therapy, the therapeutic pipeline for atopic dermatitis, and differentiating among biologics for psoriasis.

Attendees will better understand the changes to the CPT book in 2020 and 2021, reimbursement challenges dermatologists will face over the next few years, and the ultimate goal of value based healthcare.

Attendees will be able to better evaluate, diagnose, discuss treatment, and treat patients for common dermatologic issues.

Attendees will better recognize the pathogenesis of warts and their similarities to actinic keratosis in terms of morphology, distribution, and responses to treatment. Attendees will better identify basic mechanisms of action of PDT. Attendees will better recognize basic mechanisms of physiological/pathological sweating including hyperhidrosis. Attendees will be able to better analyze and define the various mechanisms of actions of biologic therapies.

Attendees will better understand medical law and know what to look for in medical contracts.

Attendees will review the newest diagnosis techniques and prognostic treatments/methodologies in melanoma.

Attendees will better understand the rheological properties of fillers, the anatomy of the face and will gain a foundation of philosophy related to injections.

Attendees will learn empowering techniques to use in their practices.

Attendees will gain insight into the future of the osteopathic profession and how to enhance the profession.

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.

**AOCD Anti-Trust Statement**
Members participating in meetings, events or activities conducted or sponsored by the American Osteopathic College of Dermatology or the Foundation for Osteopathic Dermatology, have an obligation to review and follow the AOCD’s Antitrust Compliance Policy. They should particularly refrain from making statements or distributing materials at AOCD, Foundation meetings or events that would violate the policy, such as suggesting minimum fees for particular services, urging AOCD members to boycott third party payers based on reimbursement levels or other terms of contracting with such entities, or recommending that AOCD members avoid competing with each other in certain geographic areas or markets or across specialties.

**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  
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Aclaris - AB, C, I
Almirall - AB, C, I
Biofrontera - AB, C, I
BiopharmX - AB, C, I
Dermira - AB, C, I
Encore - AB, C, I
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Galderma - C, G
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Janssen Research & Development, LLC - R
Kadmon Corp., LLC - R
Leo Pharmaceuticals - C, R
Medimmune - R
Meiji Seika Pharma - C
Menlo - C
Mitsubishi - C
Neuroderm - C
Novartis - R
Ortho Dermatologics - R
Pfizer - C, R
Promius/Dr. Reddy’s Laboratories - C
Sciderm - R
Theravance - C
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Meeting Faculty & Needs Assessments

Reagan Anderson, DO, FAOCD – Activity Moderator

Dr. Reagan Anderson specializes in general dermatology and in Mohs micrographic surgery for the treatment of skin cancer. After graduating from Rampart High School in Colorado Springs, CO, Dr. Anderson moved to Vancouver, British Columbia where he attained his Bachelor of Science in biology from the University of British Columbia and a Master of Christian Studies degree from Regent College. Dr. Anderson was then invited to attend the founding osteopathic medical school, Kirksville College of Osteopathic Medicine. Upon matriculation, Dr. Anderson was commissioned in the United States Navy where he spent the majority of his time serving the United States Marine Corps as the First Reconnaissance Battalion Surgeon.

Dr. Anderson left the military in order to pursue dermatology. During his three-year dermatology residency at the Michigan State University Consortium/Oakwood Southshore Medical Center, he was actively involved in academic pursuits, which included national and international lecturing, as well as publishing several dermatologic articles. From October 2008-October 2009, Dr. Anderson represented all osteopathic dermatology residents as the resident liaison for the American Osteopathic College of Dermatology.

Shino Bay Aguilera, DO, FAOCD

Dr. Shino Bay Aguilera is a world-renowned, multi-award winning cosmetic dermatologist, dermatologic surgeon, cosmetic laser expert and is dual board-certified with a fellowship in dermatology from the American College of Osteopathic Dermatology and the American Academy of Dermatology.

With over 17 years of experience and ongoing advanced training in lasers and aesthetics, he is a clinical researcher, publisher, former Chief Medical Director and current Assistant Professor of the Dermatology Residency Program at NOVA University, Assistant Professor of Dermatology for Lake Erie College of Osteopathic Medicine, Suncoast University and Universidad del Rosario, Bogota, Colombia. Dr. Aguilera is also a volunteer Assistant Professor of Dermatology for the University of Miami and was appointed chief resident physician for both of his three year residency programs.

As a medical aesthetic resource Dr. Aguilera contributes to several media outlets including New Beauty Magazine, the Aesthetic Guide, Medaesthetic Magazine, CBS, NBC, MegaTV and Telemundo television stations and he has been consecutively awarded the prestigious national “Best Non-Surgical Facial Enhancement” from the Aesthetic Academy. Dr. Aguilera is internationally recognized as a multi-award winning practitioner of aesthetic dermatology and an industry leader in physician training; however, his true expertise is in understanding individual patients’ needs and his artistry in creating natural rejuvenation and a more youthful appearance.

It was at a very early age that Dr. Aguilera’s work ethic, integrity, passion for people and determination led him to be awarded the title of “Best Young Citizen of Panama” at the age of 15. As a young adult, he moved to Los Angeles to pursue his dream of becoming a doctor, enrolling at Pasadena City College, he learned English in a matter of months and was accepted into UCLA. Dr. Aguilera’s passion for people has continued in his extensive volunteer work nationally and abroad. He is active in his contributions both financially and as a medical volunteer for Hospice, UNICEF, The Red Cross, DOCare International, Handy and Breast Cancer Awareness.

He is the publisher and author of the Amazon bestselling book Be Youthful, a practical guide for patients to stay youthful in mind, body and spirit. He is also co-author of Ethnique and Gender Considerations when doing Fillers and Dermatologic Surgery, and has contributed to numerous journal publications in the field of aesthetic medicine.

Dr. Aguilera is the creator of multiple signature techniques utilizing various dermal fillers and travels the globe to train his colleagues internationally in aesthetic medicine. In addition to his extensive medical knowledge in aesthetic medicine, Dr. Aguilera is highly regarded as a motivational speaker and spiritual advisor, always returning to his passion for people.

Fillers, Is There a Difference?

Objectives:
1. Understanding of rheological properties of fillers
2. An understanding of the anatomy of the face as it relates to aesthetic injectable
3. A foundation of philosophy as it relates to injecting in the 21st century

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment

References:


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

Jean-Paul Azzi, MD

Jean-Paul Azzi, MD, is a Palm Beach facial plastic and reconstructive surgeon specializing exclusively in cosmetic and reconstructive procedures of the face, nose and neck.

Dr. Azzi completed his residency in head and neck surgery/facial plastic surgery at the world-renowned New York Eye and Ear Infirmary in Manhattan and received his board certification. He then completed a fellowship in exclusively facial plastic & reconstructive surgery with the past president of the American Academy of Facial Plastic & Reconstructive Surgery, where he learned cutting edge techniques in facelifting, endoscopic, minimally invasive facelifting, endoscopic brow lifting, endoscopic midface lifting, blepharoplasty (eyelid lifting), otoplasty (ear pinning), neck lifting, fat grafting, skin resurfacing, facial reconstruction, hair transplantation and facial injectable treatments.

In addition to his cosmetic private practice, Dr. Azzi also performs charitable reconstructive procedures in underdeveloped countries such as Vietnam, Guatemala, Ecuador and Colombia. These procedures include repairing cleft lips and palates and reconstructing children with microtia (missing ears) using their rib cartilage.

Dr. Azzi is a Hobe Sound, FL native who enjoys spending time with his family and friends. His interests include tennis, golf and boating. His patients love his sense of humor and warm, caring demeanor.

Cosmetic Facial Surgery

Objectives:
1. Detailed analysis of the three main causes of facial aging
2. How to approach those causes in each specific area of the face
3. Appropriate and inappropriate treatments in each area of the face with before/after photo examples

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

References:

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

Leslie Baumann, MD

Dr. Baumann authored the first textbook about cosmetic dermatology in 2002, and the second edition of Cosmetic Dermatology: Principles and Practice (McGraw Hill) now ranks as the bestselling dermatology textbook in the world and has been translated into 14 languages. In 2005, Dr. Baumann authored The Skin Type Solution, a New York Times bestseller that has been published in many languages. The latest edition of The Skin Type Solution was published in December 2010 to coincide with the PBS special, “Skin Type Solutions with Dr. Leslie Baumann,” which began airing in late 2010. Dr. Baumann's latest textbook, Cosmeceuticals and Cosmetic Ingredients (McGraw Hill) was released in November 2014. Dr. Baumann also pens a bi-monthly column in The Miami Herald and regularly contributes to magazines, trade publications and medical journals.

The Science of Anti-Aging Cosmeceuticals

Objectives:
1. Understand the cellular processes that lead to skin aging
2. Evaluate the various anti-aging techniques
3. Update your knowledge on the science of skin aging
Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new cosmetic techniques
4. Advances in medical knowledge

References:
1. Andrews Disease of the Skin. 11th Ed.

Core Competencies: 2, 3, 4, 6

**Edwin Bayo, JD**
Ed was born in San Juan, Puerto Rico. After graduating in 1978 with a bachelor’s degree in economics (cum laude) from the University of Puerto Rico, he moved to the United States to pursue his legal education. He received his Juris Doctorate from Stetson Law School in 1981.

Ed worked in various capacities for the Florida Office of the Attorney General, including tax litigation, administrative law, cabinet affairs and inspector general. His primary area of practice while in government involved providing advice and representation to regulatory boards under the umbrella of the Department of Health and the Department of Business and Professional Regulation. As Senior Assistant Attorney General in the Administrative Law Section, Ed served as counsel to various professional regulatory boards, including pharmacy, dentistry, osteopathic medicine, chiropractic medicine, veterinary medicine, professional engineers, landscape architecture, clinical social work and harbor pilots. In addition, he handled temporary duties or litigation for several other boards including medicine, psychology, nursing, architecture and accountancy. In 2002, Ed served as the Attorney General Representative to the Pedigree Paper Task Force, created by the Legislature to review and reform Florida's regulation of the prescription drug wholesale industry.

Ed’s current practice at Grossman, Furlow and Bayo includes the representation of professional licensees, regulated entities and interested parties before regulatory agencies, Florida Courts and the Division of Administrative Hearings. He concentrates his practice in the areas of administrative and regulatory law with emphasis on the laws and regulations affecting pharmacies, drug manufacturers and drug wholesalers. He is a frequent speaker before local, state and national professional organizations on licensure and regulatory issues. He has published several articles on these topics.

**Prescribing Controlled Substances**
This course addresses the mandatory content for Physicians in Florida registered to prescribe controlled substances as allowed by Florida law, effective January 1, 2017.

Objectives:
1. Upon completing this course and reviewing the resources, participants should be able to:
2. Explain why the issue of prescribing issue is so important and illustrate best practices
3. Identify the extent of problems that may be encountered in prescribing controlled substances
4. Identify substance abuse screening tools that you can use in your practice
5. Illuminate where to find substance abuse treatment resources in your area
6. Identify the criteria for substance use disorders
7. Highlight the legal requirements for prescribing controlled substances in your practice
8. Describe different prescribing practices that will help keep you out of trouble while prescribing controlled substances

References:
Warts vs. Actinic Keratosis: New Weapons in the Therapeutic Civil War

Objectives:
1. Recognize the pathogenesis of warts and their similarities to actinic keratosis in terms of morphology, distribution, and responses to treatment
2. Identify misconceptions and analyze patient approaches to warts based on knowledge gaps
3. Compare, contrast, and evaluate the multiple modalities available for treatment of warts

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

References:

Core Competencies: 2, 3, 6

Photodynamic Therapy 2020 Update

Objectives:
1. Identify basic mechanisms of action of photodynamic therapy, including various light sources, optimal incubation times, and strategies to improve patient outcomes such as thermal changes to the skin
2. Analyze and differentiate therapeutic strategies for acne, actinic keratosis, skin cancer, and other conditions where using PDT was not previously considered in practice
3. Recognize and evaluate the adjunctive strategies to optimizing tolerability and patient safety when using PDT in dermatology

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

References:

Core Competencies: 2, 3, 6

How to Meet the Challenges of Hyperhidrosis

Objectives:
1. Recognize the basic mechanisms of physiological and pathological sweating including hyperhidrosis
2. Analyze the quality of life and psychosocial impact of hyperhidrosis
3. Identify the anticholinergic and other adverse events associated with therapies for hyperhidrosis

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

References:
1. Doolittle et al, Arch Dermatol Res, 2016; 308(10); 743-9
2. Glaser et al, “Understanding Patient Experience with Hyperhidrosis…” J Drugs Dermatol, 2018; (17(4);392-396

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

How Do Biologics Fit in an Integrative Treatment Plan?

Objectives:
1. Analyze and define the various mechanisms of actions of biologic therapies used in dermatology
2. Recognize the risks of undertreatment of psoriasis patients
3. Interpret and employ measures to maximize safety and efficacy of biologics

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

References:

Core Competencies: 2, 3, 6

Ronald Burns, DO, FACOFP, AOA President
On July 27, 2019, the AOA inaugurated Ronald Burns, DO, FACOFP, as the 2019-20 President of the AOA. Dr. Burns is an AOA board-certified osteopathic family medicine physician in private practice in Orlando, Florida. He has served on the AOA Board of Trustees since 2007.

Active in organized medicine his entire career, Dr. Burns served as president of the Florida Osteopathic Medical Association (FOMA) from 2004–2005, and provided leadership at the local level as a trustee of FOMA and FOMA District Society 3. He has been honored with the FOMA Physician of the Year award and the Distinguished Service award. In addition, he served for nine years on the National Board of Osteopathic Medical Examiners, which assesses competencies for osteopathic medicine and related health care professions.

Dr. Burns built an impressive career of service in the state of Florida by serving on the Florida Board of Osteopathic Medicine, the Florida Health Information Infrastructure Board, the Florida Medicaid Formulary Study Panel and the Florida Pharmaceutical and Therapeutics Committee.

Dr. Burns graduated from the Ohio University Heritage College of Osteopathic Medicine in Athens, Ohio. He completed an internship at Doctors Hospital of Stark County in Massillon, Ohio, and completed residency at Florida Hospital East Orlando. In 2018, the Ohio Alumni Association Board of Directors presented Dr. Burns with the Medal of Merit for achieving distinction in his field.

Dr. Burns and his wife Janet have five children and reside in Winter Park, Florida. He has a long history of service in healthcare legislation, regulation, education and leadership at the national, state and local levels. He brings forth a strong directive for his year of service as AOA president: “Physician directed, physician led.”

The Future of the Osteopathic Profession

Objectives:
1. Learn what the future of osteopathic profession holds
2. Learn how to enhance the osteopathic profession

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

Dr. Steven Feldman is Professor of Dermatology, Pathology, Social Sciences & Health Policy and Molecular Medicine & Translational Science at the Wake Forest School of Medicine. He leads the Center for Dermatology Research, a health services research center whose mission is to improve the care of patients with skin disease. He has done groundbreaking work on patients’ adherence to their medication treatment regimens, the latter leading to the Wake Forest spin off company Causa Research. Feldman's clinical work led him to an interest in patient satisfaction. Feldman created the www.DrScore.com doctor rating/patient satisfaction website. His research has been published in over 1,000 Medline-reference articles. Feldman also serves as the editor of the Journal of Dermatological Treatment and the Journal of Dermatology and Dermatological Surgery and as chief medical editor of The Dermatologist. Feldman's experiences in medicine have led him to try to see how others perceive things, leading to his book Compartments and to attending the 2018 meeting of the Morgellons Disease Foundation, documented in the movie, Skin Deep: The Battle Over Morgellons.

Morgellons

Objectives:
1. To describe the characteristics of Morgellons disease
2. To describe the research on causes of Morgellons disease
3. To describe treatment options for Morgellons disease

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

References:

Core Competencies: 2, 3, 4, 5

Cal Fussman

For over four decades, Cal Fussman has interviewed hundreds of the world’s most influential individuals: Muhammad Ali, Jack Welch, Mikhail Gorbachev, Serena Williams, Jeff Bezos, Jimmy Carter, Kobe Bryant, Richard Branson, and the list goes on.

Now, as a New York Times bestselling author, keynote speaker, world-renowned interviewer, and host of the Big Questions podcast, Fussman travels the world teaching the world’s largest companies, universities, and associations about leadership, storytelling, innovation, teamwork, and more. When Cal speaks, you’re listening to everyone he’s ever interviewed. Lessons and stories from hundreds of world icons, all coming through one man in a fedora.

Over the past several years, Cal has delivered keynotes for industry leading organizations including General Motors, Facebook, Pixar, Twitter, The Vanguard Group, Apple Music, Snapchat, Samsung, Turner Broadcasting, Vans, Lululemon, YPO, and Entrepreneur’s Organization; universities like UCLA and Georgetown; and at conferences as far as South Africa and Kenya. After Cal spoke at Facebook, Chris Sanders in Global Marketing Solutions said: “We literally have people using the term, ‘Cal Question.’ He has become a part of our culture.”

Born in Brooklyn, Fussman spent ten straight years traveling the world, swimming over 18-foot tiger sharks, rolling around with mountain gorillas in Rwanda, and searching for gold in the Amazon. He boxed against then-undefeated world champion Julio Cesar Chavez, won a James Beard award and served as sommelier atop of the World Trade Center.

He now lives with his wife—whom he met while on his quest to discover the world’s most beautiful beach—and his three children in Los Angeles, where he spends every morning eating breakfast with Larry King.
What's Your Story?

Objectives:
1. Techniques that can help both individuals and companies tell their stories in a way that stands out
2. Empower the audience with tools that can be used in their own work and life
3. Provide powerful take-a-ways about how the specific questions you ask can break down barriers, foster understanding and build deeper relationships with everyone you meet

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

References:
1. Coming Soon
2. Coming Soon
3. Coming Soon

Core Competencies: 4

Steven Grekin, DO, FAOCD
Dr. Steven Grekin has made it his personal and professional mission to help his patients put their best face forward. Years of research at the International Skin Rejuvenation Institute in Paris, France, and Quebec, Canada, have led Dr. Grekin to understand the secrets to younger, smoother, more radiant skin. Respected here and abroad as an expert in cosmetic dermatology, Dr. Grekin comes from a long line of physicians – six are dermatologists. He has participated in international teaching and training courses and is an internationally recognized lecturer in his field. Guided by cutting-edge principles of modern dermatology, natural medicine and the highest quality medical care, Dr. Grekin offers his patients an elegant, intelligent program distinguished by its unique flexibility to restore every skin type to its youthful, natural best. His family has been providing health care in the United States for almost ten years. Dr. Grekin is committed to helping patients from all over the world. He now offers his programs online, so that he may reach out and help as many people as he can put their best face forward.

Private Equity

Objectives:
1. What types of practice deliver dermatology care
2. What kind of insurance do the majority of seniors have and does it determine their care

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:
3. ADD practice and advocacy resources

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

Jeffrey Johnson, PA-C, DSDPA
Jeff Johnson is a board-certified physician assistant. He is a 1995 graduate of the United States Air Force Physician Assistant program. He completed his training as an honor graduate at the Air Force Academy in Colorado Springs, CO. Prior to P.A. school, he was an instructor of laboratory medicine at the School of Health Care Sciences at Sheppard AFB, Texas. While on active duty, he was chosen as Physician Assistant of the Year on two separate occasions and twice the Officer of the Year as well. A gifted speaker, he routinely lectures within his community, across the state of Florida and with the Lecture Series Development Program for the American Academy of Physician Assistants. He has given dermatology lectures across the country. Jeff serves as the President of the Florida Society of Dermatology Physician Assistants.
Employing PAs in Your Practice

Objectives:
1. What is the standard education of a physician assistant
2. What is the scope of practice of a physician assistant
3. What does the standard compensation package include for an experienced PA

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

References:

Core Competencies: 3, 4, 5, 6

Mark Kaufmann, MD
Mark Kaufmann, MD, is an Associate Clinical Professor in the Department of Dermatology at the Icahn School of Medicine at Mount Sinai in New York City, a position he has held since 1995. He was in solo private practice for 23 years until he joined The Dermatology Group in November 2017. He now serves as Chief Medical Officer of The Dermatology Group.

He received his medical degree from New York University School of Medicine, completing residency training in dermatology at the Albert Einstein College of Medicine in the Bronx, New York. He is board certified in dermatology.

Dr. Kaufmann has served on the Board of Directors of the American Academy of Dermatology. He now chairs the AAD Workgroup on Innovations in Payment and Delivery, and is Deputy Chair of its Patient Access and Payer Relations Committee. He also serves as an advisor to the Academy RUC team - a position he has held for over a decade.

With many articles published on the topic of health information technology, Dr. Kaufmann is a frequent national lecturer, including the annual meetings of the American Academy of Dermatology, and other societies, and grand rounds.

Dr. Kaufmann’s contributions to the American Academy of Dermatology have been recognized by his receiving a Presidential Citation in 2013, 2014, 2015, and 2017.

The Future of Dermatology Reimbursement

Objectives:
1. To understand the changes to the CPT book in 2020 and 2021
2. To understand the reimbursement challenges dermatologists will face over the next few years
3. To understand the ultimate goal of value based healthcare

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

References:
1. CPT 2020 Professional Edition. AMA
2. CMS Proposed and Final Rules for 2020. CMS. Federal Register

Core Competencies: 3, 5, 7

Kevin Klauer, DO, EJD, FACEP, AOA CEO
Kevin Klauer, DO, EJD, FACEP, serves as the CEO of the American Osteopathic Association (AOA), representing more than 145,000 osteopathic physicians (DOs) and medical students throughout the U.S. In this position, Dr. Klauer leads strategy, operations, organizational growth and advocacy for the osteopathic profession. He partners with the Board of Trustees, affiliated associations and staff to advance the AOA’s strategic vision and execute its programs.

Dr. Klauer previously served as chief medical officer for hospital-based services, chief risk officer and executive director of the patient safety
organization at TeamHealth, a leading clinician services organization. He also served as a clinical assistant professor at Michigan State University College of Osteopathic Medicine and the University of Tennessee Health Science Center College of Medicine.

Prior to his arrival at TeamHealth in January 2015, Dr. Klauer spent 15 years with Emergency Medicine Physicians, Ltd. (EMP), serving in many capacities. He was also a member of the board of directors for Physicians Specialty Limited Risk Retention Group and the EMP Medical Group board of directors.

Outside of full-time professional work, Dr. Klauer is involved in and has been recognized by numerous health care organizations. He was honored by the American College of Osteopathic Emergency Physicians with the 2018 Outstanding Educator of the Year award.

Dr. Klauer was elected to the American College of Emergency Physicians (ACEP) board of directors in October 2016 and he previously served as ACEP Council Speaker. Dr. Klauer also serves as the medical editor-in-chief for ACEP Now, ACEP’s monthly publication, and was editor-in-chief for Emergency Physicians Monthly.

He has received the Emergency Medicine Residents’ Association (EMRA) Robert Dougherty ACEP/EMF Teaching Fellowship as well as the ACEP National Faculty Teaching Award. In 2014, Dr. Klauer was the recipient of the American College of Emergency Physicians Honorable Mention Outstanding Speaker of the Year Award and was recognized by the Ohio Chapter of ACEP with the Bill Hall Award for service.

Dr. Klauer earned his DO degree from the Des Moines University College of Osteopathic Medicine. He also holds an Executive JD, with honors, from Concord Law School.

The Future of the Osteopathic Profession
Objectives:
1. Learn what the future of osteopathic profession holds
2. Learn how to enhance the osteopathic profession

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

References:
1. Coming Soon
1. Coming Soon
1. Coming Soon

Core Competencies: 1, 5

Mark Lebwohl, MD
Dr. Mark Lebwohl graduated summa cum laude from Columbia College in 1974 and graduated from Harvard Medical School in 1978. He completed residencies in internal medicine and dermatology, both at Mount Sinai. Dr. Lebwohl has been practicing dermatology since 1983. He is professor and chairman of the Kimberly and Eric J. Waldman Department of Dermatology of the Icahn School of Medicine at Mount Sinai. Dr. Lebwohl is the President of the American Academy of Dermatology. He is chairman emeritus of the Medical Board of the National Psoriasis Foundation. He is the founding editor of Psoriasis Forum as well as a medical editor of the bulletin of the National Psoriasis Foundation, Psoriasis Advance. He is editor of the Dermatology Section of Scientific American Medicine. Dr. Lebwohl has chaired numerous symposia and has written, edited or co-edited several books including Psoriasis, Mild-to-Moderate Psoriasis and Moderate-to-Severe Psoriasis. He has authored or co-authored over 500 publications including peer-reviewed articles, invited articles and book chapters. Dr. Lebwohl is actively involved in clinical trials of many new dermatologic treatments.

Which Drugs for Which Patient?
Objectives:
1. Treat atopic dermatitis and psoriasis more effectively
2. Recognize the risks and benefits of biologic therapy of atopic dermatitis
3. Select appropriate therapies for specific patient populations with atopic dermatitis and/or psoriasis
4. To recognize the side effects of various psoriasis therapies

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
References:

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

Clifford Lober, MD, JD
Dr. Clifford Lober is a board-certified dermatologist. He received his medical degree from Duke University School of Medicine in 1974. He then completed his internship at Mayo Clinic in 1977 and his residency at the University of Tennessee in 1982.

Dr. Lober has been in the full-time private practice of dermatology in Kissimmee, FL, for 29 years. He is Adjunct Associate Professor of Medicine in the Department of Dermatology and Cutaneous Surgery at the University of South Florida.

Dr. Lober has received four Presidential Citations from the American Academy of Dermatology and was named “Surgeon of the Year” in 1992 by the Florida Society of Dermatology and Dermatologic Surgeons. In addition to being awarded “Practitioner of the Year,” he was awarded the first ever “Distinguished Service Award” by the Florida Society of Dermatology and Dermatologic Surgery. Dr. Lober has served on the Board of Directors of the AAD and chaired its section on Health Practice, Policy and Research.

Pearls from Legally Speaking
Objectives:
1. Learn legal principles as they affect the practices of dermatology
2. Improve patient satisfaction by emerging compliance with the ADA and similar regulations
3. Avoid legal missteps by clarifying ambivalent regulations

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

References:
1. Legally Speaking 12/14 and 6/15
2. Legally Speaking 8/18

Core Competencies: 3

Americans with Disabilities Act – How It Impacts Your Practice
Objectives:
1. Learn which activities the ADA covers
2. Know how to make these websites compliant with the ADA
3. Understand how to determine if an animal is a service animal according to the ADA

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

References:
1. The Americans with Disability Act (ADA)

Core Competencies: 3, 4
Arnold Mackles, MD
Dr. Mackles practiced hospital based neonatal medicine in Florida for over twenty two years after completing a Pediatric Residency at Lenox Hill Hospital in New York City, and a Fellowship in Neonatology at the Cornell University Medical Center. In addition to receiving an MBA from Nova Southeastern University, Dr. Mackles obtained his license as a Healthcare Risk Manager through studies at the University of South Florida. Dr. Mackles was elected to the Board of Directors of The Florida Society for Healthcare Risk Management and Patient Safety for a two year term from 2006-2008, and again for a one year term from 2014-2015. Dr. Mackles has served as an instructor with the University of Florida Distance Education Risk Management and Patient Safety Program, and also participated as a faculty member of the University of South Florida Risk Management Licensure Program. In addition, Dr. Mackles is the author of multiple on-line continuing education courses on patient safety topics for The Sullivan Group. Dr. Mackles now devotes full time to risk management and patient safety issues.

Prevention of Medical Errors
Objectives:
This course addresses the mandatory content for Physicians in Florida. The purpose of this educational activity is to provide physicians with the most current information regarding the prevention of common performance and diagnostic errors. This monograph is specific to Florida statutes. After completing this activity, learners will be able to:
1. Identify the two most common qualities of care violations
2. Name four of the most prevalent diagnostic and performance errors
3. Cite two necessary elements of a root cause analysis
4. Create two risk management measures designed to prevent medical errors and increase patient safety

References:
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2723204/

Michael Morgan, MD
Dr. Michael Morgan is a pathologist in Panama City, Florida and is affiliated with multiple hospitals in the area, including Birmingham Veterans Affairs Medical Center and Central Alabama Veterans Health Care System- Montgomery. He received his medical degree from the University of South Florida Morsani College Of Medicine. Dr. Morgan is board certified in Dermatopathology, Anatomic Pathology and Clinical Pathology from the American Board of Pathology. Dr. Morgan has been in practice for more than 20 years.

New Diagnosis and Treatments for Melanoma
Objectives:
1. Learn the newest diagnostic techniques in melanoma
2. Learn the newest prognostic treatments/methodologies in melanoma
3. Learn of the molecular advancement and rationale for molecular-basis therapies

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, 6, 7
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 pruritus 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.

Brown Stains

Objectives:
1. Increase clinician's awareness of subtle findings in common lesions
2. Recognize and identify certain patterns that can assist in formulating a diagnosis
3. Improve ability to combine histological and clinical information to render a diagnosis

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

References:

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

Leslie Rojas-Whitworth, JD

Leslie A. Rojas, JD, is an attorney who focuses her practice on healthcare regulatory, transactional and corporate matters. Ms. Rojas devotes a substantial portion of her practice to HIPAA and state privacy and security law matters, healthcare fraud and abuse issues, healthcare joint ventures and business transactions, practitioner employment agreements, and Medicare enrollment, billing and reimbursement issues.

Ms. Rojas represents a variety of healthcare businesses and professionals, including physicians and other practitioners, group practices, laboratories, imaging centers, pharmacies, hospitals, home health agencies, assisted living facilities, and healthcare compliance consultants. Through collaboration with other attorneys and law firms, Ms. Rojas ensures that her healthcare clients receive full-service legal representation, including representation related to real estate law, tax law, intellelction property law, litigation services, etc.
Ms. Rojas currently serves on the Governing Council for the Health Care Law Section of the State Bar of Michigan, and serves on the Health Care Law Section's Medical Legal Subcommittee and Technology Subcommittee. She is also a committee member for the American Health Lawyer Association's Physician Organization Practice Group. Additionally, Ms. Rojas has authored many articles for the American Bar Association's Health Law Section.

In her spare time, Ms. Rojas serves as the President of the Paraguayan-American Association of Physicians, a non-profit charity that raises money for the medical school in Asuncion, Paraguay, as well as for other causes in Latin America. Ms. Rojas also serves as Vice-President of the Mental Illness Research Association, which raises money for mental illness related research grants and mental illness educational presentations in secondary schools throughout Michigan and Ohio.

**Medical Law and Contracts**

**Objectives:**
1. Overview of basic medical laws
2. Overview of medical contracts
3. Review current and new medical laws
4. How to prepare a proper contract

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

**References:**
2. *HIPPA Plain and Simple, After the Final Rule*, published by the AAD in 2014.

**Core Competencies:** 4, 7

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**Paolo Romanelli, MD**

Paolo Romanelli, MD, Professor at the Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, is Board Certified in both Dermatology and Dermatopathology. He is the Director of the ACGME-certified UM Dermatopathology fellowship. He has an extensive background in anatomical pathology and dermatology with special expertise in the histopathology of wound healing, deposition disorders and immunohistochemistry. His work on wound histology has been presented nationally and internationally and appears in numerous peer-reviewed journals. His clinical interests are in psoriasis, mycosis fungoides and collagen vascular diseases.

A native of Italy, Dr. Paolo Romanelli earned his undergraduate degree at Collegio Alla Querce and his M.D. from the University of Pisa School of Medicine. He has won several Best Teacher awards, published in peer-reviewed journals, presented lectures at national and international dermatology meetings including the AAD, EADV, and Masters of Pediatrics and co-authored a *Dermatology Therapeutics* book. Dr. Romanelli also sees general dermatology patients and is Director of the Psoriasis Biologics Clinic at Jackson Memorial Hospital.

**General Dermatology**

**Objectives:**
1. Evaluate your patient for common dermatologic issues
2. Diagnose common dermatologic issues
3. Discuss treatment options for common dermatologic issues with patients
4. Treat common dermatologic issues

**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

**References:**
3. Andrews Diseases of the Skin. 11th Ed.

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

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Shoni Rozenberg, DO
Shoni Rozenberg, DO, is a board-certified dermatologist practicing in Woodmere, NY. Dr. Rozenberg earned her medical degree from New York College of Osteopathic Medicine. She completed an internship and dermatology residency at St. John's Episcopal Hospital in Queens, NY. Her interests include surgical, cosmetic and general dermatology. She enjoys traveling, art history and spending time with family and friends.

Osteopathic Manipulative Treatment
Objectives:
1. Review of osteopathic tenets
2. Review osteopathic approach to the different patients and in delivering bad news to the patient
3. Review dermatologic medical conditions and treatments with an osteopathic approach

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

References:
1. JAOCD
2. JAOA

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

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 1992. 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 Adjunct Professor at TouroCOM and LECOM. She has a full-time dermatology practice as well.

Dr. Sirota 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 served on the AOCD Education Evaluating Committee since 2009. For her years of service to the AOCD, Dr. Sirota 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 NBOME POCKET member. Dr. Sirota 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.

Osteopathic Manipulative Treatment
Objectives:
1. Review of osteopathic tenets
2. Review osteopathic approach to the different patients and in delivering bad news to the patient
3. Review dermatologic medical conditions and treatments with an osteopathic approach

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

References:
1. JAOCD
2. JAOA

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

Lisa Swanson, MD
Dr. Swanson is a board-certified dermatologist and pediatric dermatologist. She was born in New Orleans, Louisiana, and raised in Scottsdale, Arizona. 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, Arizona, and went on to complete her dermatology residency at Mayo Clinic in Rochester, Minnesota. After that, she completed a fellowship in Pediatric Dermatology at Phoenix Children’s Hospital in Arizona.

She is a past Treasurer, Vice President and President of the Colorado Dermatologic Society. She is an active lecturer at conferences discussing pediatric dermatology with audiences across the country. She has been selected as a “Top Doc” by 5280 Magazine in 2012 through 2019. She is on staff at Rocky Mountain Hospital for Children where she sees hospital consults and performs procedures.

Updates in Pediatric Dermatology
Objectives:
1. Understand the burden of atopic dermatitis and learn about numerous treatment options
2. Understand the burden of pediatric psoriasis and learn about associated comorbidities
3. Learn about emerging treatment options for acne and alopecia areata

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

References:

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

Tips & Tricks in Pediatric Dermatology
Objectives:
1. Increased awareness and comfort level with treating vascular lesions in children
2. Learn about existing and emerging treatment options for warts and molluscum
3. Learn about the various ways hand, foot & mouth disease can present in children

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

References:

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

Karysse Trandem, DO
Dr. Karysse J. Trandem is a highly sought-after board-certified Obstetrician and Gynecologic Surgeon specializing in recognizing and treating victims of human sex trafficking. Dr. Trandem speaks around the world about her international experience treating trafficked patients and specific ways to recognize and treat victims. Dr. Trandem was selected for and completed distinguished research fellowships at both the National Institutes of Health in Washington, D.C., and the World Health Organization in Geneva, Switzerland. As the recipient of numerous prestigious local, national, and international awards for patient care, Dr. Trandem brings excellence and expertise to her audiences. Dr. Trandem is the Physician Expert and Speaker for the National Human Trafficking Intelligence Center, and lectures at numerous hospital institutional Grand Rounds presentations. Dr. Trandem has treated trafficked victims cross-culturally and internationally in community, clinic, and hospital settings, and is the volunteer Medical Director at International Wings of Shelter, a non-profit organization specializing in treatment and life rehabilitation of juvenile victims of sex trafficking.

Human Trafficking
Objectives:
This course addresses the mandatory content for Physicians in Florida. The purpose of this educational activity is to provide physicians and other allied professionals how to become part of what is referred to as a “multidisciplinary response” to human trafficking. Providers should be able to identify both the presence of human trafficking within their practice setting and know about resources within their communities to be able to assist trafficking persons. Upon completion of this activity, learners will be able to:
1. Explain what sex and labor trafficking is
2. Identify potential victims of human trafficking
3. Clarify the behavioral dynamics related to human trafficking
4. Encourage routine screening procedures for the possibility of patient history of domestic violence or trafficking
5. Identify the best options for referral to community resources
6. Encourage the establishment of documentation policies in trafficking cases
7. Increase advocacy within the healthcare community for victims of trafficking

References:
1. ohchr.org/Documents/Publications/FS36_en.pdf

Michael Wein, MD
Michael Wein, MD, is Chief of Allergy at Indian River Medical Center and serves on the faculty at Florida State University College of Medicine. He completed his undergraduate work at Brown University, an internal medicine residency at Vanderbilt University, and his post-doctoral fellowship at Johns Hopkins Hospital in the division of Allergy & Immunology. He is board-certified by the American Board of Allergy and Immunology and also by the American Board of Internal Medicine.

Dr. Wein is Past President of the Florida Allergy, Asthma, and Immunology Society and is a Fellow of the American Academy of Allergy, Asthma and Immunology. He has authored several publication including the chapter on allergic rhinitis in Conn’s Current Therapy, 2006 edition, and has served editorial roles for DynaMed Online and Prescribers Letter and is currently an Advisory Board Member of Boston-based Wellness Workdays. He co-authored a study on Epi-pen which was published in Annals of Allergy in 2015 and subsequent featured on CNN. His previous publications relate mostly to allergic inflammation, eosinophils, and adhesion molecules.

His offices are located in Vero Beach and Port Saint Lucie and he enjoys learning about dermatology from his friends practicing dermatology in his community.

Biologics in Dermatology
Objectives:
1. Practical aspects of IVIG therapy
2. Therapeutic pipeline for atopic dermatitis
3. Differentiating among biologics for psoriasis
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

Jason Winn, JD
Jason D. Winn, Esquire, is a 1996 graduate of the University of Maryland and received his Juris Doctorate from Nova Southeastern University - Shepard Broad Law in Ft. Lauderdale, Florida in 2000. Mr. Winn was admitted to the Florida Bar in 2001.

From 2001 until 2004, Mr. Winn worked for the Assistant Public Defender in the Fifth Judicial Circuit where he conducted over 15 jury trials, numerous non-jury trials, and many hearings including, violations of probation, restitution, and early termination motions for defendants in Juvenile, Misdemeanor and Felony Court. Mr. Winn was also an adjunct professor at Lake Sumter Community College teaching Business Law during this time. In 2003, Mr. Winn was appointed by Governor Bush to serve a one-year term on the Judicial Nominating Commission for Judicial Compensation Judges. From 2004-2006 Mr. Winn worked for the law office of Clyde M. Taylor, Jr. focusing on both state and federal criminal defense and parole violation hearings. Beginning in 2005, he opened his own practice, Winn Law, PA, where he is managing partner and continues to focus on administrative, governmental, civil, and legislative consulting.

Mr. Winn currently serves as general counsel for the Florida Osteopathic Medical Association (FOMA), the Florida Podiatric Medical Association (FPMA), the Florida Society of Hearing Healthcare Professionals (FSHHP) and the Gadsden County Sheriff’s Office (GCSO). Mr. Winn lectures throughout Florida on the Laws and Rules that affect health care practitioners, including Osteopathic, Allopathic, Podiatric, and various other licensed health care providers.

He is a member of the Florida Bar, Tallahassee Bar, Legal Services of North Florida. As a member of the Tallahassee Bar, Mr. Winn volunteers his legal services to the Wakulla County Senior Citizens Center, and Legal Services of North Florida. Mr. Winn is a devoted husband, and father to three boys. During his downtime, he enjoys hunting, fishing, golfing, and the great outdoors.

**Florida Laws and Rules Osteopathic Medicine**

Objectives:
This course addresses the mandatory content for Physicians in Florida. Upon completing this course and reviewing the resources, participants should be able to:
1. Understand the CME requirements for continued Florida licensure
2. Be aware of any necessary office signage that must be posted
3. Understanding of applicable laws & rules for licensed osteopathic physicians
4. Knowledge of the disciplinary process
5. Learning of rights afforded to physicians in licensure disciplinary cases
6. Ability to locate applicable statutes and rules through online resources
7. How to protect their right to practice

References:

**Professional Medical Ethics**

Objectives:
This course addresses the mandatory content for Physicians in Florida. Upon completing this course and reviewing the resources, participants should be able to:
1. Fulfill the requirements of the Florida Mandatory CME course on professional medical ethics
2. Address current ethical issues regarding medical ethics in Florida
3. Describe the meaning and importance of medical professionalism
4. Discuss how conflict of interest may compromise professionalism
5. Identify three significant boundary issues and proper limits in relation to each
6. Describe two important ethical issues with respect to operating a practice

References:

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**Edward 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.

**Case Studies in Complex Cutaneous Oncology - An Interactive Discussion**

**Objectives:**
1. Attendees will interactively participate in case studies of complex cutaneous oncology
2. Attendees will gain a better perspective of the complexities of interdisciplinary approaches common in oncology
3. Through interactive participation, attendees will be able to discuss cases relevant to their practices that may have similarities

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

**References:**
1. Overview of the treatment for Head and Neck cancer – *Up-to-Date* (Topic 3380 – V32.0)
2. Cutaneous Melanoma – Management of local recurrence. (Topic 7607. V 30.0)

**Core Competencies:** 2, 3, 4, 6, 7
Thursday, February 20, 2020

7:00 a.m. - 11:00 a.m.  Exhibitor Set Up
                      Oceana B-D

1:00 p.m. - 1:30 p.m.  New Diagnosis and Treatments for Melanoma
                      Michael Morgan, MD

1:30 p.m. - 2:00 p.m.  Private Equity
                      Steven Grekin, DO, FAOCD

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

3:00 p.m. - 3:30 p.m.  Break with Exhibitors
                      Oceana B-D

3:30 p.m. - 4:30 p.m.  Osteopathic Approach in Dermatology
                      Suzanne Sirota Rozenberg, DO, FAOCD
                      Shoni Rozenberg, DO

4:30 p.m. - 5:30 p.m.  Case Studies in Complex Cutaneous Oncology - An Interactive Discussion
                      Edward Yob, DO, FAOCD
Melanoma CPC: Demystifying the Molecular Maze, A Diagnostic & Prognostic Update

M.B. Morgan, MD, Professor Dermatology & Pathology UF/COM
Managing Director, CarePath Diagnostics

No Relevant Disclosures

Case #1
A Baffling Baldhead Blain
What Is Your Diagnosis?

Desmoplastic Melanoma

Precis

- AKA: Neurotropic, 1st described in 1971
- Rare ~ 4% of melanomas, 2♂ : 1♀, 66 years, Caucasian
- 50% H&N, 30% EXT, 17% trunk, 1/3 no surface abnormality
- 50% in accordance w/ lentigo-magna
- 27% correct DX on 1st biopsy, avg. depth 3.5mm, 1/3 no epidermal component
- Bland Spindled cells w/ desmoplastic, neurotropism & lymphoid aggregates
- Antigen infidelity, F (+) SMA, F (-) mart-1, melanoma, tyrosinase, MITF, HMB-45
- 40% pure, 60% mixed w/ conventional melanoma
- Overall survival 72%, EXT, ↓ age, no neurotropism, pure composition, better prognosis
- Nodal involvement rare, SLNB, WLE 2cm > 1cm prognosis, XRT
Precis

- AKA: Neurotropic, 1st described in 1971
- Rare ~ 4% of melanomas, 2:1♂ : 1♀; 66 years, Caucasian
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- Antigen infidelity, F (+) SMA, F (-) mart-1, melanoma, tyrosinase, MITF, mel A45
- 40% pure, 60% mixed w/ conventional melanoma
- Overall survival 72%; EXT, ↑ age, no neurotropism, pure composition, better prognosis
- Nodal involvement rare, SUNB, WLE 2cm > 1cm prognosis, XRT

Molecular Developments

- ↑ Clusterin expression, loss of melanogenesis genes e.g. tyrosinase
- Multiple genetic (non-driver) alterations, UV signature, NF-1, P53, PD-1
Case #2
BLINDED BY THE LIGHT!

38 year old female s/p excision for invasive melanoma with photosensitivity

Gene Expression Profile Assays
- Multiple genetic loci tested associated with your prognosis
- Stratify patient risk for prognosis and benefit from more aggressive therapy
- Performed on achieved tissue blocks
- Independent prognosticator from traditional demographic or pathologic information
- Decision DX
INDICATIONS FOR MELANOMA GENE EXPRESSION PROFILING

- Histologic features of regression
- Transected invasive melanoma < 0.80mm
- Depth of invasion between 0.50 and 0.80mm

Melanoma Associated Retinopathy

- AKA Cancer associated or paraneoplastic retinopathy
- Cross-reacting melanoma associated antibodies elicited antibodies to retinal proteins
- Rare 1:1,000,000 men = women, mean age 61.8 years, strong association with autoimmunity
- Most common with small cell lung cancer > gynecologic > melanoma
- May antedate or follow established diagnosis
- Usually associated with clinical or microscopic features of regression
- Diagnostic criteria: ERG, anti-retinal antibodies, funduscopic optic disk pallor, retinal pigment mottling, attenuated vasculature
- Treatment delays progression (corticosteroids, IVIG, rituximab)

VEMURAFENIB

- Genetic mutation analysis for targeted therapy
- B-raf analysis (1q34)
- B-raf gene encodes for specific genetic threonine protein kinases
- Regulate MAP/ERK signaling pathway
- MAP/ERK regulates cell division/differentiation
- Mutations associated within lymphoma, colonrectal, thyroid, non-small cell lung, small melanoma
- >60% melanomas harbor B-raf mutation
- >90% substitution of glutamic acid for valine at 600# position (V600E)
VEBURAFENIB
- 1st Genetic mutation analysis for targeted therapy
- B-raf analysis (1q34)
- B-raf oncologic gene encodes for specific genetic threonine protein kinases
- Regulates MAP/ERK signaling pathway
- MAP/ERK regulates cell division/differentiation
- Mutations associated with lymphoma, colorectal, thyroid, non-small cell lung, and melanoma
- >50% melanomas harbor B-raf mutation
- >90% substitution of glutamic acid for valine at 600# position (V600E)

B-RAF TESTING
- Versus DNA sequencing (Sanger versus pyroseq testing)
- PCR more sensitive, faster, cheaper than sequencing
- Sequencing more specific, potentially better at detecting V600K, V600D

FUTURE OF MELANOMA & THE LABORATORY/PATHOLOGISTS

BRAF INHIBITOR CUTANEOUS COMPLICATIONS
Case #3
ACRAL LESION IN AN ALL-AMERICAN

WHAT IS YOUR DIAGNOSIS?
ACRAL LENTIGINOUS MELANOMA
Precis

- Melanoma of glabrous/acral non-hair bearing skin
- #1 skin cancer among African Americans, Asian Americans; 1.8/1M
- 3% of melanoma; 36% of melanoma in African Americans; (♂) older age group
- Palmar (75%) > Plantar 20% > nail matrix 4% > oral 1% > anal 0.5%
- Flat lentiginous like growth (radial) → vertical; 10% amelanotic
- Distinctive dermatoscopic findings
- Pathology tricky, dendritic melanocytes, confluence, acrosyringeal extension; 36% melanoma
- Prognosis worse, 94% 5-7 versus 77%, 71% versus 40% stage IIA at diagnosis
- C-kit amplification, c-kit mutations ~ 50% of lesions (triple negative)
- C-kit (mast/stem cell growth factor receptor, receptor tyrosine kinase proto-oncogene; imatinib [Gleevec])
Case # 4

SPOOKY SPITZ AND THE SWORD OF DAMOCLES

Gene Expression May Precede Visible Morphologic Change.

The PLA Samples Gene Expression Across the Entire Lesion.
WHAT IS YOUR DIAGNOSIS?

SPITZOID MELANOMA

Precis

- Malignant Melanoma w/ Histologic Features of Spitz Nevus
- Rare ~ 1/500 Spitz Nevus, all ages, more common in Caucasians
- 3 categories: conventional Spitz Nevus, atypical spitzoid tumor, spitzoid melanoma
- SN (♀ > ♂), AST (♂ = ♀), SM (♂ > ♀)
- Average size at presentation 1.1 cm, 51% amelanotic, 30% H&N, 30% EXT's
- Overlapping histologic features including epithelioid cells with prominent nucleoli, AST larger lesions typically > 1.0 cm, epidermal consumption, loss of maturation, SM associated with ulceration, telangiectasia, epidermal change
- SN (0% sentinel), AST (38%), SM (64%)
- CGH/FISH SN (20% gain in 11p (HRAS) no losses, no more than one alteration, AST (50% variations) 6p25 RRED, 6q23 (MYB), 11q13 (CCND1), 9p21 (INK 4A) SM (96% alteration) 9p21 (homozygous loss), multiple chromosomes gains/losses
- Pathogenesis SN (HRAS activation or BAP1 loss or BRAF V600E), AST (loss of 9p21 w/ loss of p16), SM (complete loss of 9p21, TERT promoter)

SPITZ MELANOCYTIC PARADIGM

<table>
<thead>
<tr>
<th>CONVENTIONAL SPITZ NEVUS</th>
<th>ATYPICAL SPITZOID TUMOR</th>
<th>SPITZOID MELANOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size: 0.6 CM</td>
<td>1.1 CM</td>
<td>1.8 CM</td>
</tr>
<tr>
<td>Gender: 2:1 (♀:♂)</td>
<td>23:2 (♂:♀)</td>
<td>1:1</td>
</tr>
<tr>
<td>Age: 12.1 YEARS</td>
<td>22.2 YEARS</td>
<td>55.1 YEARS</td>
</tr>
<tr>
<td>Symmetry: YES</td>
<td>YES/NO</td>
<td>TYPICALLY YES</td>
</tr>
<tr>
<td>Ulceration: NO</td>
<td>YES/NO</td>
<td>NO</td>
</tr>
<tr>
<td>Subcutaneous Fat: NO</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Kamino Bodies: YES</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Atypical Mitoses: NO</td>
<td>YES/NO</td>
<td>YES</td>
</tr>
<tr>
<td>Conventional 9p21 loss: NO</td>
<td>YES/NO</td>
<td>YES</td>
</tr>
</tbody>
</table>

FLOWFISH IN SITU HYBRIDIZATION

DNA INFECTION AND REPLICATION

Lack of Essential DNA Solution
MELANOCYTIC SUBTYPE
CHROMOSOMAL/GENE ALTERATION

- Melanocytic Subtype
- Spitz Nevus
- Lentiginous melanoma
- Acral lentiginous melanoma
- Mucosal melanoma
- Malignant Blue Nevus

Oncogene

Chromosomal/Gene Alteration

- 1p Gain (13%)
- 1p Loss (42%), 1q Loss (5%), 1q Gain (30%), 22q Gain (17%)
- 1q 32 Loss, 11q 13 Gain
- 1p Gain, 4p Gain, GNAQ

- Melanoma
  - 9p Loss (82%), 9q Loss (56%)
  - Acral lentiginous melanoma
    - 1q 32 Loss, 11q 13 Gain
  - Mucosal melanoma
    - 1q Gain, 6p Gain
- Malignant Blue Nevus
  - 1p Gain, 4p Gain, GNAQ

THANK YOU!

Questions?
Plain as the nose on your Face

Perceptual Acuity
- This is a specific talent
- Some are born with it
- Others have to work at it
- Practice makes perfect
- How do you practice Perceptual Acuity

Exercising Focus
- Watching and listening for different things in the ordinary course of your day.
- Look for structural uncertainty: Bends in the road. In medicine or in other industries.
- Example: If I were giving this lecture ten years ago would Co-pays or deductibles be an issue?
- What percent of your collectable dollars are Co-pays

Disclosures
- Investor in Harvest Partners Advanced Dermatology and Cosmetic Surgery
- Speaker for Celgene
- Speaker for Almiral
- Clinical researcher for Abbvie, Galderma, Brickel Pharm, Pfizer, Ortho Dermatology
Educational Exercises
- Do you use your social group to sharpen your antennae about changes in your practice?
- How can friends help you see the world through different lenses?
- Can an automotive executive help a medical practice?
- Can a manufacturing company CEO help you run your practice?

Practice Types
- Solo Practice
- Single Specialty Group Practice
- Multi-Specialty Group Practice
- Hospital owned Group Practice
- Hospital based Practice
- Academic Institution based Practice
- Private Equity backed Practice

Other types of Practice
- Walgreens Corner of Happy and Healthy
- Minute Clinic
- Free standing Urgent Care Clinic

Pros and Cons
- Who’s the Boss?
- Time spent on Patient Care
- Compliance
- Legal/Employee issues
- Insurance Plans
- Participation agreements

Good Better Best
- Is there one good answer?

NO

DECISIONS
- Time of your career
- State of mind
- State of Industry
- Personal Career Goals
- Outside Interests
**What is Private Equity?**

By definition: An alternative class of investments that consists of capital that is not listed on a Public exchange.

Private Equity (PE) is composed of funds and investors that directly invest in private companies or buyouts of public companies.

---

**Where do they get the $$$$?**

- High net worth individuals 6-7 figures
- Very high net worth individuals at least $5M
- Ultra high net worth individuals at least $30M
- Institutional Investors: Pension funds, groups of accredited investors etc.

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**Why do people invest?**

- As an alternative other than the stock market, real estate, or traditional investment vehicles
- Long Term Capital Gains tax classification

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**Why Medicine**

- First Model: Veterinary Medicine
- Second Model: Dental
- Third Model: Dermatology
- Currently: Ophthalmology, GI, Urology etc.

---

**Is it right for me?**

Perceptual Acuity: What is around the corner?

---

**PE offerings**

- Better ability to negotiate with Insurers
- Typically have a department of Reimbursement and Strategy
- Legal Department
- Compliance department
- Coding Specialists
- Human Resource Departments
PE Offerings

- Financial Analysts
- National Head Hunters
- Recruiting
- Operations Teams
- Overall ability to run medical clinics like a “Big Business”

Practice Models

- Fee for service
- Will it last
- What is the next Model?
- Which Practice types will have better visibility into the next practice model?
- Can your practice successfully negotiate with payers?

Control of Patient lives

- Who will control the lives?
- Is this an issue?
- What is the largest revenue generating segment of the medical insurance industry?

Medicare Advantage

- 33% of total Medicare spending $250 Billion
- Medicare advantage plans bid less than traditional plans but are paid more than traditional Medicare!
- 2018 MA Plan bonuses $6.3 Billion
David vs. Goliath

- Can your Practice type compete?
- Are you big enough to play in the big leagues

Crystal Ball

- Retail Medicine
- Telemedicine
- Medical Kiosks
- Hand Held Medicine
- Glove over your heart sending ECG to your Doctor

Summary

“LIFE BEGINS AT THE END OF YOUR COMFORT ZONE.”
- Neale Donald Walsch
ATOPIC DERMATITIS

Impact of Atopic Dermatitis
- Eczema causes stress, discomfort, and worry for the entire family
- Treating one patient with eczema is an example of "trickle down" healthcare
- Patients with eczema have increased risk of:
  - ADHD
  - Anxiety and Depression
  - Suicidal Ideation
  - Parental depression
  - Osteoporosis and osteopenia (due to steroids, decreased exercise, and chronic inflammation)

Impact of Atopic Dermatitis
- Sleep disturbances are a really big deal
- Parents of kids with atopic dermatitis lose on average of 1-1.5 hours of sleep a night
- When they sleep, kids with atopic dermatitis don't get good sleep:
  - Don't enter REM as much or as long
  - Growth hormone is secreted in REM (JAAD Feb 2018)

Atopic Dermatitis and Food Allergies (My how the turntables have...turned)
- Growing evidence that food allergies might actually be caused by atopic dermatitis
- Impaired barrier allows food proteins to abnormally enter the body and stimulate allergy
- Avoiding foods can be harmful
  - Proper nutrition is important
  - Avoidance linked to increased risk for allergy and anaphylaxis
- Refer severe eczema patients to Allergist before 4-6 mos of age to talk about food introduction
Pathogenesis of Atopic Dermatitis

- Skin barrier “broken”
- Dysregulated immune system process
- Response to microbiome differences?

- Studies show microbiome in lesional/nonlesional atopic dermatitis on the same patient is different from people without atopic dermatitis (JAMA Derm March 2018)
- Result of a “bored” immune system?

- Sensitive skin care
  - All free and clear detergent, no dryer sheets/hab sacred
  - Dove sensitive skin or cetaphil soap
  - Washcloths/reser/enhanced/Aquaphor or moisturizers
  - J&J aloe/hydatol
  - Bleach baths - 1 cup bleach in lukewarm water

Atopic Dermatitis: Standard Treatment

- Topical steroids: always do ointment in little kids
  - Hydrocortisone 2.5%
  - Triamcinolone 0.1%
  - Fluocinonide 0.05%
  - Clobetasol 0.05%

Atopic Dermatitis- Special Sites

- St Louis study: 170 positive cultures (SPD July/Aug 2019)
  - MRSA
  - MSSA

Atopic Dermatitis and Infection

- MRSA
  - 1/2017: 77.5% with MRSA
  - 2/2018: 72.5% with MRSA
Atopic Dermatitis and Bleach Baths

- Sodium hypochlorite body wash (brand name CLN body wash)
- Atopic dermatitis patients with history of staph infection or colonization
- Used 2 times a week
- Improved all outcome measures and reduced use of topical steroids
- Appeared to have limited activity directly on the staph so likely has an additional mechanism of action to help the atopic dermatitis

SPD July/Aug 2019

Atopic Dermatitis: Steroid Burst

- Topical steroid burst for severe eczema/significant flares
  - Clobetasol bid for 5 days
  - Flunisolide bid for 10 days
  - Triamcinolone bid until clear or follow-up appointment

Aron Regimen

- Originated with dermatologist in UK
- Peter Li, MD doing some studies on it
- Compounded medicine:
  - Betamethasone Valerate 0.1% cream- 30 gms
  - Mupirocin cream- 24 gms
  - Vanicream 400 gms
  - Mix to total 454 gms
- Use it 4-5 times daily to start and with improvement slowly decrease the frequency of application

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

Calcineurin Inhibitors- Safety

- Pimecrolimus study from Pediatrics
  - 2400 patient years
  - No increased risk of malignancy or immune system impairment
  - Conclusion: safe even in the younger age group

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Eucrisa (Crisaborole)

- Boron based topical ointment
- Inhibits phosphodiesterase-4 activity (PDE4) and decreases production of proinflammatory cytokines
- Efficacy
  - Sterile and burning
  - Can be used for maintenance
  - 78% of patients went a whole year without needing topical steroids (Eichenfield, JAAD)
  - Might have some side effects
  - Contains propylene glycol (Contact Allergen of Year in 2018)
**Eucrisa (Crisaborole)**
- JAAD May 2019
- Retrospective review of pain with Eucrisa
- 41 patients
- 13/41 - 31.7% had pain
- 5/10 who used it on the face had pain

**Dupixent (Dupilumab)**
- Blocks IL-4 and IL-13 (decreases the TH2 inflammatory response)
- About 70% of patients achieve EASI 75
- Very tolerable
- Good side effect profile
  - Injection site reactions
  - Conjunctivitis- increased risk in severe AD and patient has h/o eye symptoms such as allergic conjunctivitis
- 300 mg subcutaneously every other week
- Real life results better than study data
- Decreases risk of skin infections (JAAD Jan 2018)
- Approved for 12 and up for atopic dermatitis on March 11, 2019!
- Phase 3 data really tough atopic dermatitis
- Severe > Moderate
- Could not use topical steroids for first 16 wks
- Same side effects as in adults
- Dupixent improved the signs, symptoms and quality of life in adolescents that didn’t achieve IGA 0/1 (SPD July 2019 Poster)

**Dupixent in Kids under 12**
- Studies in 6-11 yr olds have been completed and we expect approval in May 2020!
- My personal experience using it in kids down to 6 yr old has been quite good
- I use 200 mg every 2 wks without loading dose
- Once clear, I often decrease to every 4 wks for maintenance
- I don’t often use the 200 mg dose
  - 200 mg = 1.14 ml

**They Don’t Like the Shots, BUT**
- They like being able to sleep
- They like not having itchy all the time
- They like not waking up with bloody sheets
- They like being able to wear the clothes they like
- They like being able to go to school

- 49
5 days after 1st shot:

"Not sure if it is too soon to expect results and we don't want to jinx ourselves, but it seems she has not been scratching at night! She has woken up the past two mornings with smooth hair vs a rats nest that takes forever to comb and signs of eczema bumps are reduced as well.

I will keep you posted...we are cautiously optimistic!"

“Just a little update...we started dupixent last Thursday when it arrived. We are AMAZED!!! He has felt great, just 1 wet wrap needed all week, just using vanicream. All blisters are gone and new skin is emerging. I just wanted to say thank you! Already an enormous difference.

He has been active this week, even wanting to go out to dinner, go out to play, and even on a shopping outing (which is rare for him). We have seen a huge increase in his happiness and hope. Thank you so much for helping us get here!”
Getting Dupixent Approved

- JAAD Feb 2020 - “Off Label Use of Dupilumab for Pediatric Patients with Atopic Dermatitis: A Multicenter Retrospective Review”
- Mean 9 wk delay to get it approved
- Safe and effective in 111 patients age 6-11 yrs old
- “Most of the rules impacting access to medications are about cost, masquerading as safety.”
  - Elaine Siegfried, MD
  - SPD Meeting Jul 2019

Getting Dupixent Approved

- JAAD Sept 2018

Getting Dupixent Approved

- JAAD Feb 2019
  - Both children and adults with atopic dermatitis have increased risk of other autoimmune diseases
  - Systematic review and meta-analysis showing the relationship between atopic dermatitis and depression/suicidal ideation
  - Atopic dermatitis associated with increased depression, suicidal ideation, and psychiatric comorbidities

Getting Dupixent Approved

- JAAD Oct 2018
  - Burden of ER visits for patients with atopic dermatitis
  - Association of atopic dermatitis with depression, anxiety, and suicidal ideation in kids and adults

Getting Dupixent Approved

- JAAD Nov 2018
  - Atopic Dermatitis and Suicide: Metaanalysis of 15 Studies
  - Patients with atopic dermatitis were more likely to have suicidal ideation and 36% more likely to attempt suicide

Getting Dupixent Approved

- JAMA Derm Feb 2019
  - Atopic Dermatitis and Suicide - Metaanalysis of 15 Studies
  - Patients with atopic dermatitis were 44% more likely to have suicidal ideation and 36% more likely to attempt it

Getting Dupixent Approved

- JAAD Feb 2019
  - Increased risk of depression, suicidal ideation, and psychiatric comorbidities in patients with atopic dermatitis
  - Systematic review and meta-analysis showing the relationship between atopic dermatitis and depression/suicidal ideation
Getting Dupixent Approved

"I tear up a little. And then I tear up a lot."
- Phil Dunphy, Modern Family
(and me, when I think about my pediatric patients on Dupixent)

New Regional Dermatoses with Dupixent

17/124 (13.7%) of patients developed new regional dermatoses
14/17 were on the face
12/17 were eczematous, 4/17 were erythematous
Is this allergic contact? Rosacea? Demodex? Seb derm?

Dupixent Facial Redness

Occurred in about 10% of patients
Sometimes triggered by alcohol
All patients chose to continue the Dupixent
Said it didn’t respond to topical steroids or TCIs
Treated patients with topical ketoconazole; patch testing if no response

Treatments on the Horizon

Topical 1% cream activates the aryl hydrocarbon receptor
Tapinarof 1% cream- activates the aryl hydrocarbon receptor
JAAD Jan 2019- EASI 75 in 50% of patients
Tralokinumab- IL 13- Q 2 wks
Lebrikizumab- IL 13- Q 4 wks
Nemolizumab- IL 31
Fezakinumab- IL 22- IV infusion
JAK inhibitors
- Abrocitinib JAK1- Pfizer, 2 phase 3 trials in 12 and up complete
- Baricitinib JAK 1/2
- Upadacitinib JAK 1- breakthrough status, Abbvie
- Hopefully topical JAKs
Nickel Contact Dermatitis

- www.nickelsolution.com
- Comes with nickel alert to detect it and a special clear lacquer to protect your skin from something with nickel in it

Wet Wipe Contact Dermatitis

- Due to preservative MCI/MI (Kathon CG)
- Also think about it in cases of persistent facial dermatitis
- There are now 3 brands of wipes that don’t contain the allergen
  - Honest brand
  - Earth’s Best hypoallergenic
  - Water wipes

Slimer’s Dermatitis

- Making slime has become quite the trend
- The ingredients in slime are all irritating: borax, glue, soap
- Produces a rash on the palms that looks like dyshidrotic eczema with red scaly patches and sometimes teeny vesicles
- Typically extends into webspaces from squeezing the slime
- *“A Slime of the Times” Ped Derm Jan/Feb 2019*

Isobornyl Acrylate

- Contact Allergen of the Year 2020
- Found in glucose monitors that adhere to the skin
- Dexcom or Eversense are safe glucose monitors

PERIORIFICIAL (PERIORAL) DERMATITIS
Periorificial Dermatitis

- Very commonly misdiagnosed in kids
- Can look like eczema, can look like acne, can look like seb derm
- Occurs in perioral, periocular distribution
- Also quite common in nasal alar creases
- Topical steroids will initially make it look like it is getting better, but they actually make it worse in the long run
- Ask about steroid inhalers, nasal sprays, topical steroids, etc
- Most cases are idiopathic

Perioral Dermatitis

- Sometimes hard to differentiate from Lip Licker’s Dermatitis or drool induced irritant dermatitis
- Perioral dermatitis will SPARE the vermilion border
- Perioral dermatitis often has small pink, acneiform papules present in addition to the dermatitis changes

Periorificial Dermatitis in Kids - Additional Treatment Options

- Make sure there are no steroids on the face
- Clindamycin lotion/wipes
- Azelaine cream
- Sodium sulfacetamide products
- Aczone
- Gentamicin 0.3% ophthalmic ointment
- Oral Ivermectin/Soolantra (JAAD March 2017)
- Small study: 8 pts with rosacea, 7 with POD
- Ivermectin given as single dose 200-250 micrograms/kg, 6/8 cleared
- 3 pts treated with aczone cream cleared
- 1 pt treated with oral Ivermectin cleared
- Longer antibiotics
- Azithromycin
- Using chlorhexidine prescribed in mouth for a month
- Bacteriostatic acne agents for 6-7 days, then 3 days off, then repeat
Perioral Dermatitis- Gluteal Variant

- Monomorphic pink papules and pustules on buttocks
- Ddx includes keratosis pilaris, MRSA (I always swab one of the pustules)
- Treatment options
  - Topical clindamycin works about 90% of the time
  - Oral amoxicillin
  - Azithro if PCN allergic

Perioral Derm- Gluteal Variant

PSORIASIS

Epidemiology of Pediatric Psoriasis

- 1% is likely an underestimation- not all patients see a doctor and many are misdiagnosed
- 1/3 of all patients with psoriasis have skin disease that begins in childhood
- 1/3 of kids with psoriasis have family history in a first degree relative
- Patients with a family history are more likely to have early onset disease

The Incidence is Increasing

- The incidence of children with psoriasis has been increasing for years
- Some of this might be because of better diagnosis and awareness of the condition
- A study published in the 2000s showed that rates of pediatric psoriasis more than doubled between 1970-74 and 1995-99
- An explanation for the increase is not known
- One hypothesis is an increase in “trigger factors” like stress, infection, trauma and obesity
- Some blame our pro-inflammatory diet
- Some just think this is due to increased awareness

Epidemiology

- Median age of onset is between 7-10 yr old
- Slight female predominance in kids (opposite in adults)
- Tends to present earlier in girls
- Girls more likely to have scalp involvement
- Boys more likely to have nail involvement
- According to studies, mild-moderate disease (defined as BSA less than 10%)
Pathogenesis
- Typically chronic inflammatory condition
- Environmental factors likely play a role
  - Physical trauma (koebnerization)
  - Certain medications: withdrawal of steroids, lithium, antimalarials, beta-blockers
  - Genomics also contributes
  - 1/3 of kids with psoriasis have family history in a primary family member
  - Often patients with family history have early onset of disease
- Stress
- Certain medications: withdrawal of steroids, lithium, antimalarials, beta-blockers
- Diet
- Infections: especially group A strep and especially in kids
  - Can be perianal strep or strep pharyngitis
  - Viruses can also serve as a trigger
- Genetics also contributes

Pediatric Psoriasis
- Plaque psoriasis: 73.7% of kids with psoriasis
  - Most common variant
  - Doesn’t always look like it does in adults. Patches and plaques are smaller, thinner and less scaly.
- Guttate psoriasis: more common in kids than adults
  - Typically triggered by strep, sometimes viruses
  - Presence or absence of strep might mean something prognostically
  - Strep positive: may spontaneously clear and not progress
  - Strep negative: might persist and become plaque psoriasis. When it starts as guttate psoriasis, it tends to ultimately be more severe plaque psoriasis
- Inverse Psoriasis: commonly mistaken for yeast
  - Exfoliated Psoriasis Overlap
  - Tnf alpha inhibitor associated Psoriasis
- Infant Psoriasis: typically in diaper area
  - Little to no data on the long-term course of babies with diaper psoriasis

Psoriasis/Eczema Overlap
(aka Psoriasiform Dermatitis)
- Very common in kids
  - Might look like eczema in the antecub fossa but looks like psoriasis on the scalp
  - Check the fingernails, check the tongue, check the belly button
  - Look for Koebner phenomenon
  - Sometimes family history of psoriasis helps
  - Lack of response to mild topical steroids is suggestive of psoriasis
  - Treat and observe the patient over time

Diagnosis Issues
- There are misconceptions, particularly amongst primary care, that psoriasis is rare in kids
  - Plus the skin lesions in kids aren’t often the same thick, red, scaly plaques that people are used to seeing in adults
  - This leads to misdiagnoses of:
    - Atopic dermatitis
    - Nummular eczema
    - Seborrheic dermatitis
    - Pityriasis rosea
    - Fungal infection
- There are misconceptions that psoriasis is rare in kids
- Plus the skin lesions in kids aren’t often the same thick, red, scaly plaques that people are used to seeing in adults
- This leads to misdiagnoses of:
  - Atopic dermatitis
  - Nummular eczema
  - Seborrheic dermatitis
  - Pityriasis rosea
  - Fungal infection

Burden of Illness
- The “heartbreak of psoriasis” affects numerous aspects of a person’s life, especially when it affects a child
- Day-to-day routine of topical management
- Care of doctor’s visits and treatments
- Dealing with social stigma and loss of confidence/self esteem
- Incidence of depression and anxiety
- Obesity
- Numerous medical comorbidities
- Incidence of comorbidities in patients younger than 30 with psoriasis (14.4%) is twice that of kids without psoriasis (7.2%)
**Obesity**

- Obesity is the number one association in the pediatric psoriasis population.
- Most often, the obesity happens first and THEN the onset of skin disease.
- Central obesity specifically is statistically associated with moderate-severe psoriasis.
- The association is proportional to the overweightness.
- Overweight patients tend to have mild-moderate psoriasis.
- Obese patients tend to have moderate-severe psoriasis.

**Cardiometabolic Comorbidities**

- Kids with psoriasis have 2-4 times increased risk of:
  - Hypertension
  - Hyperlipidemia
  - Diabetes
  - Crohn's
- Also have higher prevalence of metabolic syndrome (30%) compared to kids without psoriasis (7-9%).
- We attribute this increased risk to the systemic inflammation present in patients with psoriasis.
- Psoriasis is more than just "skin deep."

**Psoriatic Arthritis**

- In adults, incidence of PsA in patients with psoriasis is about 6-41%.
- In kids, it appears to be about 5-10%.
- When PsA occurs in kids with psoriasis, the average age of onset is 9-12 yrs old.
- Typically the oligoarticular type of PsA.
- Usually mild.
- Often onset of skin disease and arthritis occurs simultaneously in kids (different than in adults).

**Psychiatric Comorbidities**

- Kids/teens with psoriasis show increased risks of:
  - Depression
  - Anxiety
  - Bipolar disorder
  - Substance abuse—smoking, drugs, alcohol.
- In addition, kids with psoriasis have issues with:
  - Self esteem and confidence
  - Decreased activity level/refusal to participate in sports
  - Being victimized by bullying.

**Psoriasis is a Systemic Disease**

New Guidelines in Kids [JAMA Derm July 2017]

- #1 association in children is obesity.
- Talk to them about weight.
- Screen for diabetes every 3 yrs at age 10.
- Screen for NASH every 3 yrs at age 10.
- Screen for HN annually starting at age 3.
- Screen lfts at age 10 and again at 18.
- Ask about arthritis.
- Ask about depression and anxiety.
- Ask about smoking, stress, substance abuse in older kids.

**Quality of Life**

- Quality of life studies in kids with various skin diseases have been done.
- Patients with psoriasis reported high amount of impairment in QoL.
- Stress levels as high as kids with eczema.
- Stress levels higher than kids with hives or acne.
- Impact on quality of life of pediatric psoriasis is similar to the impact of other chronic pediatric diseases like arthritis, asthma, and diabetes.
Quality of Life - Impact of Treatment Regimens

- Most kids with psoriasis are being managed topically.
- The routine of applying all of these things can make day to day life a real struggle.
- Very time consuming.
- It impacts the ability to go to camp, go to sleepovers, go on vacation.
- The topicals have not very socially acceptable.
- Ointments are goopy, preparations for scalp psoriasis are often not ideal, some topicals can sting and burn.

Quality of Life - Social Domain

- Psoriasis dramatically affects the social lives of kids with the disease.
- Several aspects of the disease contribute to this,
- It often affects the face in kids.
- It is often itchy.
- The scaling can be apparent even if the rash is concealed.
- School can be really hard.
- Teasing.
- Bullying.
- Intimidation.
- 15-30% of kids with psoriasis will limit their extracurricular activities - sports, theater, etc.
- Impact of quality of life is proportional to severity of the disease.
- But severity of disease needs to take into account more than just BSA - location of the rash and different aspects of their disease.
- A good way to assess the impact is to ask kids to rate on a scale of 1 to 10 how satisfied they are with the appearance of their skin.

Impact of Pediatric Psoriasis on Parents

- JAAD Feb 2017.
- 65% said their own emotional wellbeing was affected.
- 50% were sad or frustrated.
- 20% were depressed or anxious.
- They felt burdened by all the topical management.
- Had to make no activity accommodations 2/3 of the time because of child's skin disease.
Burden of Disease
Relationship to the Treatment Paradigm
• The treatment of pediatric psoriasis is probably 10 years behind the treatment of adults, but we’re starting to catch up!
• Significant unchecked inflammation that starts in childhood can contribute to major issues in adults.
• The understanding that psoriasis is a systemic illness consisting of systemic inflammation that causes other systemic issues is making it more appealing to treat systemically.
• The hope is that treating the entire disease will have an impact on comorbidities.
• The “psoriatic march” might be something that we can thwart.

Biologics in Kids
• Enbrel (etanercept) - APPROVED FOR KIDS >4 YRS OLD in 2016!!
• Approved in US for JIA in kids >10 yrs at 1999
• 1 study in 111 children with psoriasis 2008-211 patient age 4-17
• 0.8 mg/kg/wk
• 10% achieved PASI 75
• This study has been continued to date and has great long term safety data (JAAD Feb 2016).

Biologics in Kids
• Humira (adalimumab)
• Approved in US for kids with JIA (>2 yrs old) and Crohn’s (>6 yrs old)
• Several case reports of effectiveness in Crohn’s current
• 1 clinical trial: patients age 12-18, 10 patients
• 1.8 mg/kg/wk (PASI 75 at 12 weeks) (JAAD 2015)
• I have several pediatric patients on it.

Psoriasis is a Systemic Disease
• Stelara is associated with decreased systemic and vascular inflammation in patients with mod-severe psoriasis.
• Looked at levels of inflammation using PET CT in the liver, spleen, aorta, descending aorta, renal aorta.
• Only 10 patients.
• They measured the inflammation at baseline and then when PASI 75 was achieved
• JAAD May 2019.
• Humira for 10 years reduced all cause mortality.
• ACAD is associated with increased systemic and vascular inflammation in patients with psoriasis.
• Overall survival and quality of life at 10 years (JAAD Jul 2020).
• Otezla (oral) - phosphodiesterase 4 inhibitor
  • Phase 2 open label study in kids age 6-17 published in JAAD 2020.
  • Overall PASI 68 for adolescents and PASI 79 for kids.
  • Good safety and tolerability, ongoing phase 3 trials.
  • Stelara started at 12 mg/kg, reducing to dose at age 4.
  • Tremfya at 8 mg/kg, reducing to dose at age 4.
  • Taltz at 5 mg/kg, reducing to dose at age 4.
  • Should happen this year.
  • Difficult in younger kids because of the IBD questions.
  • Should we be ordering fecal calprotectin to assess risk of IBD?

ACNE
Seysara (Sarecycline)
- New oral antibiotic to treat acne
- First new oral antibiotic for acne in over 40 years
- Approved for kids 9 and up
- Once daily weight-based dosing
- Seems to avoid side effects of doxycycline and minocycline
  - No esophageal discomfort, no sun sensitivity
  - No vertigo, dizziness, lupus-like syndrome, blue skin
- Has been studied and found to have minimal effect on gut flora

Other Hormone Tidbits
- Progesterone only methods of birth control tend to increase acne
  - Implanon
  - Mirena IUD
- Spironolactone can be helpful in the teenage population, especially if the patient:
  - Is on a progesterone only method of birth control
  - Has features of or a diagnosis of PCOS
- Mayo study: 86 teenage girls - Spiro worked well, but most had to use 100 mg daily

Changes in Isotretinoin Monitoring
- A number of studies in 2017 showed that we have been “over monitoring” with labs for isotretinoin
- New recommendations:
  - 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

Accutane and Depression
- Most recent study from Northwestern presented at AAD 2019
- Examined medical records of 38,000 patients with acne between 2001 and 2017
- 41/1087 patients on Accutane had depression = 3.77%
- 1775/36929 patients not on Accutane had depression = 4.81%
- From 2015-2019, I have had 4 male patients and 2 female patients become severely depressed on accutane. None of them had a mood issue prior.
  - All 6 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
  - All 6 of them cut themselves unbeknownst to their friends and family
  - All 6 of them expressed suicidal ideation
  - 1 of them was admitted to the hospital for psychosis
  - 1 of them attempted suicide by jumping off a ladder head first
  - 1 of them expressed suicidal ideation
  - All 6 of them stopped the accutane and their mood returned to normal

New Treatments on the Horizon
- Amlexanox: topical minocycline foam
  - FDA approved, prescribable Jan 2020
- Trifarotene: new topical retinoid
  - FDA approved, prescribable Jan 2020
- Clascoterone: new topical anti-androgen
  - Anticipating FDA approval (PDUFA Date August 2020)
Did Gluten do this?

- The Dermatologist May 2019
- 0.31% of patients with alopecia areata had celiac disease
- 1% of the general population has celiac disease
- Screening is not necessary and gluten free diet is not needed

JAK Inhibitors

- 2014: 2 Yale Researchers published a case report in JID
  - Male patient w/ h/o arthritis and alopecia totalis
  - Started on tofacitinib (JAK1/3 inhibitor) for arthritis
  - All his hair grew back

JAK Inhibitors Appear Promising

- JAAD, Derm October 2015
  - Case report of tofacitinib working for vitiligo
- JAAD Feb 2014
  - Case report of tofacitinib working for pt with alopecia areata and vitiligo
- JAAD, Derm April 2015
  - Topical 0.6% ruxolitinib cream bid for AA case report - hair regrew
  - Oral tofacitinib for nail dystrophy associated with alopecia areata
    - 3 patients, nails improved in all. Hair regrew in 2/3
- Derm News, July 2016
  - 12 patients, 5/12 had alopecia totalis/universalis
  - 11/12 had regrowth, 7/12 had >50% regrowth
  - Recurrence is an issue

JAK Inhibitors- JAAD Jan 2017

- Tofacitinib for alopecia areata in 90 adult patients
  - Serum alopecia areata (sAA) test discrepant
    - Clinical response in 77%
    - 85% had quiescent complete response over 4-18 mos
    - Consider adding to topical steroids for nonresponders
    - After 12 yr of complete scalp hair loss, pts were unlikely to respond
    - No serious adverse events over 12 mos
    - When to drop treatment not unclear, probably indefinite

JAK Inhibitors- JAAD Jan 2017

- Tofacitinib for alopecia areata in 13 adolescents
  - Ages 12-17
  - Used 5 mg bid dose
  - 11/13 had regrowth, 2/13 had 50% regrowth
  - Safety questions: tofacitinib being studied for treatment of interferon-mediated autoinflammatory syndromes in kids as young as 18 mos and side effects to be the most common side effects in these kids
Alopecia Areata

- Case series of 3 patients under age 5 with alopecia totalis and universalis treated with Xeljanz 2.5 mg daily
- 1 patient increased to 5 mg daily
- Well tolerated and worked well
- JAAD April 2019

JAK Inhibitors

- 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 several patients currently on it for AA and for vitiligo, doing well
- Topical versions probably still 2-3 yrs away
A MOMENT OF REFLECTION

The End!
Any questions: lisawansonmd@gmail.com
Osteopathic Approach in Dermatology

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Conflict of Interest Disclosure
• No conflict of interest to disclose

Objectives
• Delivering Bad News to Patient
• Cutaneous manifestations of systemic disease and OMM findings
  • Hepatitis C
  • Diabetes Mellitus
  • Hypo or Hyperthyroidism
  • Pruritus
• Multifactorial approach to treatment

Delivering Bad News to Patients—Overview
• Appropriate setting
• Provide your expertise and helpful supportive information
• Explain in banal terms
• The Difficult Patient
• Set expectations for treatments
• Provide hope
• Consider patient’s lifestyle and financial means

Together, these methods enhance the relationship between physician and patient and provide a holistic/osteopathic approach to delivering bad diagnosis

Tenets of Osteopathic Medicine
• The body is a unit; the person is a unit of body, mind and spirit.
• The body is capable of self-regulation, self-healing, and self-maintenance
• Structure and function are reciprocally interrelated
• Rational treatment is based upon an understanding of the basic principles of body unit, self-regulation, and the interrelationship of structure and function.
The Art of Medicine

- Tone of voice
- Empathy
- Body language
- Communication

Tone of Voice

- Serious
- Quiet
- Focused
- Compassion

Empathy

- Showing concerns
- Relating to the patient
- Understanding

Body Language

- Standing vs Seated
- Eye contact
- Arm position
- Touching the patient

Communication

- Succinct
- No medical jargon
- Have patient repeat information back to you
- Helping patient with the next step
- Family members

Appropriate Setting

- Create a trusting environment between physician and patient
- Private setting
- Provide tissues
- Sit down and engage in eye contact
- Put away your cell phone
Provide your expertise and helpful supportive information

- Provide reliable websites, pamphlets, and articles for patient to reference
- Provide information for support group or counseling
- Shows your competency and holistic practice

Explain in banal terms

- Explain the disease in simple terms for the patient to understand
- Avoid using medical jargons or abbreviations

The Difficult Patient

Set expectations for treatments

- Be honest
- Show concern and compassion
- “I know this is difficult for you.”

Provide hope

- Provide all available treatment options
- Have a top plan in place
- Explain to patient each person may respond differently to each treatment
- Help provide motivation for compliance

Consider patient’s life style and financial means

- Affordability for medications and treatments
- Practicality and adherence
Hepatitis C
Cutaneous Manifestations

- Lichen Planus
- Necrolytic Acral Erythema
- Polyarteritis Nodosa
- Acquired porphyria cutanea tarda
- Pruritus

Lichen planus
The “Ps”: Pruritic, Purple, Polygonal, Planar, Papules, Plaques.

Necrolytic Acral Erythema
- Well defined, tender, dusky, erythematous plaques on the dorsa of feet
- Center of plaques thicken with disease progression, acquiring a velvety appearance and surrounded by a rim of erythema.
- Does not respond to steroids
- Scale is darker and more verrucous than psoriasis; skin + itch
- Strong association with Hepatitis C; responds to antiviral therapy and zinc supplementation (although normal zinc plasma levels).
Polyarteritis Nodosa

- Segmental necrotizing vasculitis
- Punched out ulcers, livedo reticularis, subcutaneous nodules, and acral gangrene.

Porphyria Cutanea Tarda

- Due to a defective enzyme in the liver (uroporphyrinogen decarboxylase)
- Patients present with increasingly fragile skin on the back of the hands and forearms
  - Erosions following minor injuries
  - Vesicles and bullae
  - Milia
  - Increased sensitivity to the sun
  - Mottled brown patches around the eyes
  - Alopecia

OMM Associations for the Liver

- Sympathetic nervous system
  - Spinal cord T5-T9 (upper GI tract)
  - Greater Splanchnic nerve
  - Celiac ganglion
- Parasympathetic Nervous System
  - Cranial Nerve X
- Chapman point
  - 6th intercostal space, right side only

OMT

- Rib Raising
- Soft tissue paraspinal inhibition
- Celiac ganglion release
- Cranial manipulation
Diabetes Mellitus
Cutaneous Manifestations

- Acanthosis Nigricans
- Diabetic Bullae
- Eruptive Xanthomas
- Necrobiosis Lipoidica
- Perforating dermatoses

Acanthosis Nigricans

Diabetic Bullae

Spontaneous, non-inflammatory, blistering condition occurring in the setting of DM
Blisters are large and often have asymmetrical shape
Most common on acral sites and lower legs
DDX: friction blister, bullous fixed drug, BP, bullous SLE, EBA

Eruptive Xanthomas

Erupt as crops of small, red-yellow papules
Most common over the buttocks, shoulders, arms, and legs
Rare in face or inside the mouth
Lesions may be tender and usually itchy
May resolve spontaneously
Associated with hypertriglyceridemia and DM

Necrobiosis Lipoidica

Most common in women associated with DM
Average age of onset is 30 yrs
One or more tender yellowish-brown patches on the lower legs, the center becomes shiny, pale, thinned, with prominent blood vessels.
Difficult ulceration in 15% of cases, SCC a rare complication
Acquired Perforating Dermatosis

Large papules with central keratin plugs, some form larger plaques. Most common on the legs but can develop on the arms and in the head and neck region. Associated with hepatic, renal or diabetic disorders. Average time of presentation is 30 yr old. Lesions may self-heal without any treatment but often new lesions develop.

OMM Associations

- Sympathetic Nervous system
  - T5-T9 (Upper GI tract)
  - T10-T11 (Middle GI tract)
- Kidneys
- Greater and lesser splanchnic nerve
- Superior and inferior mesenteric ganglion
- Parasympathetic Nervous system
- Cranial Nerve X

Treatment Options
- Condylar decompression
- Manipulation of the OA, AA or C2 joints will influence on parasympathetic tone via vagus nerve.

Hyperthyroidism

Fine, velvety smooth skin
Warm and moist skin due to increased sweating
Hyperpigmentation
Pruritus
Pretibial myxedema
Urticaria
Increase incidence of alopecia

Pretibial Myxedema

OMM

- Sympathetic nervous system
  - T5-T9
- Lymphatic system
- GI system
- Parasympathetic nervous system CNX

Treatment options
- Cervical spine
  - HVA
  - Soft tissue
- Cervical paraspinal/sympathetic ganglia
- Lymphatic system
  - Lymphatic pump (lower, pedal, face)
Urticaria

Hypothyroidism
- Dry, rough, coarse skin; cold and pale
- Boggy and edematous skin
- Yellow discoloration as a result of carotenemia
- Acquired ichthyosis
- Palmo-plantar keratoderma
- Eruptive or tuberous xanthomas
- Vitiligo

Acquired ichthyosis

Causes:
- Vitamin Deficiency: vit A, B6, nicotinic acid
- Infections: Leprosy, TB, syphilis
- Medications: nicotinic acid, clofazemine
- Systemic Diseases: Sarcoid, hypothyroidism, LE, AIDS
- Malignancy: Lymphoma especially Hodgkin's lymphoma; also in NHL, MF, MM

Tuberous Xanthoma
- Firm, painless, red-yellow nodules that develop around the pressure areas such as the knees, elbows, heels and buttocks
- Lesions can join together to form multilobulated masses
- Associated with hypercholesterolemia and hypothyroidism.
- Seen in type II (apo B100/LDL defect) and III (apo E defect) familial hyperlipidemia syndromes.

Pruritus
- C-fibers, unmyelinated - conduct pain, itch
- Pruritic mediators include histamine, tryptase, cathepsin, interleukin 31, PGE2, substance P, u-opioid receptor agonists, NGF, E2
- Chronic itch components: Peripheral sensitizing, central sensitization and dysfunction of itch inhibitory circuits.
- Associated with many systemic and cutaneous disorders
- Difficult to treat
Clinical presentation

Treatment Options

- Capsaicin
- Doxepin
- Menthol
- Pimozine
- Tacrolimus/Pimecrolimus
- Barrier repair
- Ketamine/amitriptyline/lidocaine

- Antihistamines
- Naloxone
- Mirtazapine
- Gabapentin/pregabalin
- Aprepitant

OMT approach

- Suboccipital decompression to normalize the PNS
- Muscle energy to upper thoracic and cervical regions
- Rib raising to normalize the sympathetic nerves
- Counterstrain

Conclusions

- Rational treatment is based upon an understanding of the basic principles of body unit, self regulation, and the interrelationship of structure and function.
- Skin diseases have an immunologic basis for pathogenesis and many systemic diseases have cutaneous findings
- Examine the patient as a whole
- Consider all treatment options to better treat our patients
- Uphold osteopathic tenets and approaches to patient care

References

5. Dermatology. Journ. et al., Volume One, Mosby, 2000...
6. Author's Editor of The Bone, Tosto Edikon, Sanzana Elsion, 2000...
Friday, February 21, 2020

6:00 a.m. - 7:00 a.m.  Breakfast with Exhibitors
Oceana B-D

7:00 a.m. - 8:00 a.m.  Dysplastic Nevi
Reagan Anderson, DO, FAOCD

8:00 a.m. - 9:00 a.m.  Employing PA's in Your Practice
Jeffrey Johnson, PA-C, DSDPA

9:00 a.m. - 9:30 a.m.  Break with Exhibitors
Oceana B-D

9:30 a.m. - 10:00 a.m.  Pediatric Dermatology: Infectious Review
Suzanne Sirota Rozenberg, DO, FAOCD

10:00 a.m. - 10:30 a.m.  Skin Biopsy Technique
Michael Nowak, MD

10:30 a.m. - 11:30 a.m.  Tips & Tricks in Pediatric Dermatology
Lisa Swanson, MD

11:30 a.m. - 1:00 p.m.  General Business Meeting

1:00 p.m. - 1:30 p.m.  Break with Exhibitors
Oceana B-D

1:30 p.m. - 2:30 p.m.  Brown Stains
Michael Nowak, MD

2:30 p.m. - 3:30 p.m.  The Science of Anti-Aging Cosmeceuticals
Leslie Baumann, MD

3:30 p.m. - 4:00 p.m.  Break with Exhibitors
Oceana B-D

4:00 p.m. - 5:00 p.m.  What's Your Story?
Cal Fussman

5:00 p.m. - 6:00 p.m.  Cosmetic Facial Surgery
Jean-Paul Azzi, MD

6:30 p.m.  Reception
Oceana B-D
AGENDA
- Physician Assistant – who are we?
- Why Has This Concept Worked for So Long
- Should You Consider Hiring a PA?
- Retaining a Physician Assistant
- A Look to the Future

Definition of a Physician Assistant
- Physician Assistants (PAs) are medical providers who are licensed to diagnose, treat and prescribe medications for patients. PAs work in offices, hospitals and clinics under the supervision of a licensed physician.
- At our core, PAs are Dependent Practitioners
- Our function within the Physician-led health-care team is directed solely by delegation from our supervising Physician.

Physician Assistants by Another Name
AKA:
- Physician Extenders
- Non-Physician Practitioner
- Mid-level Provider
- Advanced Practice Providers
- Allied Health Providers
- Limited License Provider
- Physician “Associate”

Who are the Typical Applicants?
Greater than 3,000 hours patient contact experience
- Paramedics
- Medical Assistants
- Athletic Trainers
27 years of age on average (24 y/o med. school)
66% are female
Majority will have Bachelor’s Degree
During the 2017 applicant cycle, Boston University received 2,103 applications. Of these, 90 applicants, or 4.2% were offered interviews. Of the 90 students who interviewed, 30 matriculated into the program. The overall acceptance rate for Boston University: 1.4%.

The Pennsylvania State University received 4,786 applications during the 2018 cycle, interviewed 2.4% of applicants, and admitted just 39. The overall acceptance rate for PSU: 0.08%.

Duke University received 2,861 CASPA applications during the 2018 cycle, interviewing 250 students (8.7%) and matriculating just 90 students. The overall acceptance rate for Duke: 3.1%.

Competitive is an Understatement

Brief History of the PA Profession

During the 2017 applicant cycle, Boston University received 2,103 applications. Of these, 90 applicants, or 4.2% were offered interviews. Of the 90 students who interviewed, 30 matriculated into the program. The overall acceptance rate for Boston University: 1.4%.

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Duke University 1965 – First Class of PAs

Recognized Shortage of Primary Care Physicians

Take advantage of military trained combat medics

Training modeled fast track for Physicians during WWII

PAs were to "Think like a Doctor."

Work closely with physician

Standard Educational Program

27 Continuous Months equates to 3 academic years

75 Hours Pharmacology

175 Hours Behavioral Sciences

400 Hours Basic Science

580 Hours Clinical Medicine

2000 Hours of Supervised Clinical Practice

Master’s Degree by 2020 or Lose Accreditation

Scope of Practice

A PA’s scope of practice is determined by their training and experience, state law, facility policy and agreed upon with their supervising physician.

Where Can PAs Practice Medicine?

- PAs are licensed to practice in all 50 states, the District of Columbia, all US territories, and the uniformed services.

- PAs are authorized to prescribe medications in all jurisdictions where they are licensed, except Puerto Rico

Prescribing Controlled Medications

- Three states - Georgia, West Virginia, and Texas—do not allow PAs to prescribe any Schedule II controlled substances

- Two states - Missouri and Arkansas, limit PAs to prescribing hydrocodone combination products only.
Physician Assistant by Specialty

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Medicine</td>
<td>25.9%</td>
</tr>
<tr>
<td>Emergency Medicine</td>
<td>10.5%</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>15.6%</td>
</tr>
<tr>
<td>Dermatology</td>
<td>3.6%</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>4.3%</td>
</tr>
<tr>
<td>Occupational Med.</td>
<td>2.3%</td>
</tr>
<tr>
<td>Surgery Subspecialty</td>
<td>25.1%</td>
</tr>
<tr>
<td>Other</td>
<td>10.4%</td>
</tr>
</tbody>
</table>

"PA-C"

- Physician Assistant is "Certified"
- Pass National Certifying Exam
- 100 Hours of CME every Two Years
- Pass Recertification Exam every 10 years
- No Dermatology Specialty Exam Exists

Should You Consider Hiring a PA

- Allows the physician to focus on the items you want
  - PAs can play a supervisory role
  - Education of staff
  - Interviewing and Hiring of Staff (Other PAs)
- Patients offered appointment with Physician first!
- Told they are seeing a PA when appt made, at confirmation and when the patient is roomed
- Mohs: More Patients Seen = More Cancers Treated

PAs in the Everyday Clinic

- Patient Waiting Times are Decreased
- Readily Available for Follow-ups/Wound Checks
- Education Programs for Community/Cancer Screening
- Minimize Amount of Time On Call
- Assist in Hiring, Training and Managing the Staff
- Most Importantly: Quality Patient Care

Added Benefits of Employing a PA

- Kaiser Permanente research shows patient satisfaction with PAs approaches 96%.
  - Understanding of the Patient’s Problems
  - Quality of Personal Care
  - Confidence in the Provider

Patients Acceptance of PAs
Comparable Acceptance of Care

• Berkeley Healthcare Forum Report, a systematic review of 16 different studies revealed “no significant differences in patient satisfaction between NPPs versus physicians”

• Kaiser Permanente Center for Health Studies has also shown NPPs score equally with physicians in terms of patient satisfaction

Biomedical Central

Conclusion

“PAs are operational in 15 nations; their acceptance appears successful and satisfaction with their care largely indistinguishable from physicians. Findings from this analysis highlight one theory that when patient’s needs are met, satisfaction is high regardless of the medical provider.”

How Did We Get to This Point?

The number of dermatologists emerging from residency programs each year is believed to be insufficient to meet growing patient demand. Aging Baby-Boomers and increased number of insured patients through the ACA worsens that shortage.

Physician Shortage

In 2015, the Association of American Medical Colleges (AAMC) forecasted the U.S. will have 29,800 fewer primary care physicians than it needs which equates to 135 million ambulatory visits annually.

Shortage to Worsen

1. AAMC projects a shortage of 130,600 physicians by 2025.

2. AAMC also found that 60% of patients would prefer an NPP rather than having to wait even a few days for a physician.
**Why Your Colleagues Employ PAs**

1. PAs allow doctors to adjust their roles to meet the needs of the clinic
2. Flexibility in dealing with walk-ins and emergencies
3. Excessive workloads
4. Offer appointments on nights and weekends
5. Help to train and manage the staff
6. Cost Effective Alternative to a Physician

**Does Hiring a PA = Increased Risk**

Theory: PA School is shorter duration
Shorter duration = more errors of cognition and judgement
However, PAs may carry less litigation risk than physicians
PAs often treat patients with less acute conditions
- More complicated patients are left to the physician
- Two people not likely to make the same mistake

**Steps to Minimize the Risk**

- Strict Guidelines Outlining Scope of Authority
- Writing Prescriptions
- Controlled Substances?
- How Much Autonomy is Right?
- Case Presentations

**How do We Do it at Water’s Edge**

- Employ: 48 Practitioners (29 Physicians/23 NPPs)
  - MD - 18
  - DO - 11
  - PA - 14
  - NP - 9
- Patient Offered Appointment with Physician First
- Patient Informed Clearly the Credentials of Provider
  - At the Time the Appointment is Made
  - At Confirmation of the Appointment
  - Upon Rooming the Patient

**Why Does it Work for Us?**

- Variety of Procedures
- General Dermatology (Most See 35 Patients per Day)
- Surgical Dermatology
- Cosmetics
- Assist with Mohs Closures (Advanced Cutaneous Surgery Course)
- All Connected via EMR
- Physician Only Minutes Away – same day evaluation

**Salary**

AVERAGE: $120,000 Annual Salary
Cost to Employ a PA: 30 cents on the Dollar Collected
Salary Breakdown

- Base Salary: $85,000
- To The House: $250,000
- 10%: $350,000
- 15%: $450,000
- 20%: $550,000
- 25%: Over

$500,000 = $120,000 Annual Salary
Total Cost of Employment ~ $150,000

Typical Benefits Package

- "Competitive" Salary
- 401K
- CME Allowance ($1500 - $2000 annually)
- Professional Fees (State Licensing, NCCPA)
- Insurance (Medical, Dental, Life, Malpractice)
- Professional Organizations
- Maternity Leave / Holidays
- Vacation/Personal Days

Hiring a Crucial Member of Your Team

If you are considering hiring a PA, the success of the hire likely rests on a few simple questions:
- What do you want the person to do?
- What are you willing to let them do?
- What Amount of Support Will They Receive?

The Hiring Process

You need to be clear on how you’ll incorporate that person into the practice and how you want them to perform.

Defining the parameters of the job, especially during the interview, may eliminate future problems.

The main reason physician assistants leave is not because of the money, it’s the relationship with their supervising physician, the practice as a whole or the opportunity to grow.

Consider Training PA Students

AAPA’s Data Services and Statistics Division reports that more than 1/3 of all PAs say they met their first employer through clinical rotations while attending PA school.

The Hiring Process

Background Checks are vital for promising applicants
Include a License Check
Ask applicant if they are under investigation
Are they under a Medicare Audit
Part of any pending liability litigation
Ask About Convictions
**Hired a PA: Now What?**
- Notify your malpractice carrier (Nominal Increase)
- Have Written Protocols – update regularly
- Supervise Appropriately (Be aware of your state laws)
- Be Approachable – encourage questions
- Meet or Talk Regularly
- Foster an Environment of Learning
- Take an Active Role in Development

**How to Avoid Liability Pitfalls**
- Hire Experienced, Well-Trained PAs
- New Grads: Ensure Adequate Training
- Establish Guidelines for Practice
- Be a Collaborator Not Just a Boss
- Open Door Policy

**Set the Parameters of the Job**
- Formalize a Job Description
- Additional Duties Beyond Patient Care?
- Will the PA be on call and if so, how often?
- Will the PA be allowed to see new patients?
- What is the level of supervision that will take place?
- How independent they be?
- Will the PA perform procedures; Assist with Mohs?
- Determine how the PA wants to constructive tips

THE MOST IMPORTANT ISSUE IS DO THEY FIT!

**No Surprises Here!**
- Physicians Who Employ PAs Experience:
  - Increased Patient Satisfaction
  - Greater Access to Care
  - Greater Efficiency
  - Improved Quality of Life

**Times are Changing**
When the PA profession began over 50 years ago, physicians were likely to be solo or joint practice owners. The increase in potential liability was offset by the financial and practice benefits of working with a PA.
Changing Landscape for Everyone

- 76.1% of Physicians were Practice Owners in 1983
- 47.1% of Physicians were Practice Owners in 2016
- 38% Decrease from 1983 to 2016

Is OTP Beneficial for You?

- 1. Today, however, physicians are more likely to be employees rather than practice owners and don’t realize the financial benefits of supervising a PA. They only take on the increased potential liability.
- 2. Also, in larger groups as providers come and go it becomes increasingly more difficult to maintain the strict supervisory mandates.

“Optimal Team Practice”

- A political movement underway in the PA profession.
- Just in its infancy
- Discussions are heating up in various states
- May be asked for your professional input
- Dependent Practitioner is at our Core

OTP: What is it?

- Eliminates a Specific Supervising Physician
- A Member of a team of Healthcare Professionals
- Would recognize limits of their knowledge and skill
- PAs would accept liability for the care they provide
- Establish Autonomous State Board

OTP: What it is Not!

- **Independent Practice**: practice without the benefits of physicians or other qualified medical providers for collaboration, consultation, referral or team-based care.
- **OTP**: practice with access to physicians and other qualified medical professionals for collaboration, consultation and referral, as indicated by the patient’s condition and standard of care in accordance with the PA’s education, training and experience.
Advantages for the PA Profession

- The creation of an autonomous medical board of PAs which oversee the licensing and discipline of the professional.
- Allows the degree of collaboration between PA and physician to be determined at the practice level by the physician in their lead role of the health care team.
- Following the lead of the NP profession’s success yet still maintain close collaboration with physicians.

There’s A Lot to Work Out

- Dependent practitioner is the hallmark of who we are.
- This would require legislative action in all 50 states.
- 54% of respondents to AAPA said they do not have the time or are opposed to lobbying activities.
- What happens if some states pass and others do not; resulting in a patchwork of differing PA practice acts.

There’s No Question the World is Changing

So, What’s the Bottom Line Again?

In addition to helping you deliver quality care to your patients …

Questions? Need More Information?

Email: fairways2@comcast.net
FSDPA: www.fsdpa.org
SOPA: www.dermpa.org
AAPA: www.aapa.org
Pediatric Dermatology: Infectious review

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Disclosure

• I have no conflicts of interest or financial relationships to disclose.
• Some medications discussed may be used off-label.

Objectives

• Review of common viral, bacterial and parasitic infections
• Understand the current treatment for infectious conditions in the pediatric population
• Discuss availability of new medications and treatment options.

Pre- test Question

• 1. Verruca Vulgaris, “common warts”, found most frequently on hands, feet and fingers are benign epidermal tumors caused by human papillomavirus, specifically HPV types:
  • A. 1
  • B. 6 and 11
  • C. 16 and 18
  • D. 2 and 4

VIRAL INFECTIONS

• Warts
• VZV
• Gianotti Crosti
• Rubella
• Measles
• Roseola Infantum
• Erythema Infectiosum
• Hand/foot mouth
• Molluscum Contangiosum
• Zikka virus
• Chikungunya
• Ebola Virus
• Coronavirus
**Warts**

- Verrucous papules; mc fingers, hands and feet
- Benign, caused by HPV
- Incubation period: 1-3 months to years.
- Trauma promotes the virus. Resolve within 3-5 years.
- HPV 1 – plantar, HPV 2 and 4 – common, HPV 3 – plana, HPV 6 and 11- condyloma acuminate
- Tx: Salicylic acid, lactic acid, liquid nitrogen, electrocautery and CO2 laser surgery.
- “Ring phenomenon”: secondary to cantharidin 0.7%, and even liquid nitrogen.

**Stubborn warts...**

- Contact sensitizers: Squaric acid, rhus extract, diphenylcyclopropenone, topical retinoids
- Squaric acid (GADRE): apply 2% in office q3wks and 0.2% TIW at home (JAAD May 2000)
- Intraligamental Candida antigen: Injected into 1-2 of the warts every 3 wks; typically 3-5 treatments
- Shornycin.
- topical Imiquimod (MWF qhs x 8wks)
- Podophyllotoxin
- Cantharidin compound product: cantharidin 1%, salicylic acid 30%, and Podophyllotoxin 5%
- Cimetidine 25-40mg/kg/day
- PDL: attack the vessels

**VZV aka Chicken pox**

- Caused by HHV3
- Transmitted via airborne droplets or direct contact with fluid
- Viral replication in LN, liver and spleen → enters the epidermis and travels to mucocutaneous lesions → goes to dorsal root ganglion remains latent
- Infectious 1-2 days prior to skin lesions develop and until all are crusted over

**Clinical:**
- Malaise, myalgia, fever
- Erythematous, pruritic macules and papules starts on face → spread to trunk
- Develop into vesicles with clear halo “dew drops on a rose petal” → form crusting
- Will see all stages of development

**Complications**
- Encephalitis rare
- Pneumonia- 10-30% mortality if untreated
- Tx
  - Acyclovir or valacyclovir within 3 days of lesion onset → decreased severity and duration
VZV

Gianotti- Crosti

- #1 cause in US EBV
- #1 cause worldwide Hep B
- Exanthem arising in setting of viral trigger or vaccine
- Clinical: symmetric monomorphic skin colored to erythematous papules on face (cheeks), extremities and buttocks
- TX: Spontaneous resolution 1-2 months

Gianotti- Crosti

Rubella

- Caused by rubella virus (RNA virus, togaviridae family)
- Transmitted via respiratory droplets
- Infection in nasopharynx → spread to LN
- Clinical:
  - Prodrome: fever, headache and URI
  - Exanthem: morbilliform eruption start on head/neck → spread cephalocaudal
  - Enanthem: Forchheimer's syndromes (palatal petechiae)
  - Painful suboccipital / postauricular / cervical lymphadenopathy

Rubella

- Complications
  - Arthritis, arthralgias. Thrombocytopenia, myocarditis
- DX
  - Rubella specific IgM or 4-fold increase in IgG
  - PCR
- TX
  - Supportive
  - Immunoglobulin in pregnant of exposed pregnant women

Rubella
Measles

• Occurs in areas where immunization rates are low
• Caused by measles virus (RNA virus, paramyxovirus family)
• Transmitted via respiratory droplets → spread to LN → blood
• Clinical:
  3 C’s - cough, coryza, conjunctivitis
  Exanthem: Koplik spots on buccal mucosa
  Exanthem: morbilliform eruption starts on hairline and postauricular areas → spread cephalocaudal

Measles

• Complications
  Encephalitis
  Myocarditis
  Subacute sclerosing panencephalitis - years after infection
• DX
  IgM, 4-fold increase in IgG
  PCR
• TX
  Vitamin A supplementation recommended for 6 mo-2 years
  MMR(live) vaccine at 12-23 months and second dose 4-6 yrs

Roseola infantum

• Cause by HHV-6 (DNA virus)
• Transmitted by oral secretions
• Clinical
  Very high fever > 40° C for 5 days
  Causes febrile seizures
  Fever resolves → exanthem
  Generalized subtle maculopapular eruption resolves 2-3 days
  Nagayama’s spots (red macules on soft palate and uvula)

Roseola infantum

• TX:
  Supportive
  Resolves without complications
• Remains within CD4 T cells
  Implicated pathogenic factor in DRESS
**Erythema Infectiosum**

- Parvovirus B19 (ssDNA)
- Transmitted via respiratory droplets, blood and placenta to fetus
- Replicates in erythroid precursor cells → transient decrease in hemoglobin
- Clinical
  - Fever, myalgias and headaches
  - Slapped cheeks and “lacey reticulated eruption” on extremities
  - Arthritis of small joints
- No longer contagious once eruption develops

**Hand/Foot Mouth Disease**

- Caused by Coxsackie A16 virus
- Coxsackie A6 shown to be more widespread and severe vesiculobullous eruptions and is a/w atypical HFMD
- Transmitted fecal-oral and respiratory route → infection of pharyngeal and GI tract → lymphoid involvement → skin

**Erythema Infectiosum**

- Complications:
  - Aplastic crisis and pancytopenia in patients with sickle cell
  - Fetal infection
    - Greatest risk <20 weeks gestation
    - Fetal loss rate highest in 2nd trimester
    - Can develop hydrops fetalis, intrauterine fetal demise, high output cardiac failure
- TX: supportive

**Hand/Foot Mouth Disease**

- Clinical
  - Fever and malaise
  - Vesicular eruption palms/soles and buttocks
  - Erythematous macules and oval, deep seated erythematous vesicles and bullae with gray center
  - Can have onychomadesis
**Molluscum Contagiosum**

- Poxvirus
- Affects 15-20% children
- Spreads via direct contact
- Several months - 4 years, mean duration 12 months
- Incr incidence AD
- MC Dermatitis 39%
- Inflamed MC lesion 22% / Furuncle-like
- Gianotti-Crosti-like Id Reaction

**Treatment:**
- Cantharidin
  - No pain, wash off in 4 hours, intraepithelial blister
- Light Cryotherapy
  - Spray for about 6 seconds, some pain, possible residual pigmentary alteration
- Curettage
  - Minimally painful, rapid clearance, have band aids available!
  - Can pretreat with EMLA or liposomal lidocaine

**MC**

- **EMLA**: Eutectic mixture of local anesthetics: 2.5% lidocaine/2.5% prilocaine
  - Apply under occlusion 60-120 minutes prior to procedure shorter for mucosal, genital skin, diseased skin
  - Maximum recommended dose 10g with 1-2g/cm²
  - Obtain maximum depth of 5mm of analgesia
  - Can cause some local irritation
  - Patch formulation
  - Caution: Methemoglobinemia (prilocaine)

**Zika Virus**

- Caused by ssRNA virus within Flaviviridae
- Transmitted by the *Aedes* mosquito
- Location: Africa, Asia, central and south America, Puerto Rico and Caribbean
- Transmitted via blood transfusions, vertical transmission, sexual contact (live in sperm for 62 days)

**Clinical features:**
- Fever, arthralgias, myalgia and headaches
  - Rash: maculopapular or papular begins 3-12 days after infection starts on face → cephalocaudal spread
  - Petechiae and bleeding gums
  - Symptoms resolve within 1 week
  - Risk to fetus: 1% risk of developing microcephaly if contracted during 1st trimester

**DX:**
- RT-PCR / ELISA in first 7 days
- Zika specific IgM

**TX:**
- Prevention with DEET
- Men can transmit to pregnant women if approximately 6 months
Zika Virus
- ss-RNA virus belonging to togaviridae
- Transmitted via Aedes Aegypti mosquito
- Location: Africa, India, Southeast Asia, Latin America and Caribbean
- Clinical
  - High fevers, marked arthralgias, arthritis and conjunctivitis
  - Morbilliform eruption, mucosal ulcers, PIH of face, facial edema and ecchymosis

Chikungunya
- dx:
  - PCR if <7 days
  - RT-PCR
- Tx:
  - Supportive
- Can develop post chikungunya rheumatic symptoms
  - NSAIDS, Systemic steroids, MTX, biologics and antimalarials

Ebola Virus
- Caused by ssRNA ebolavirus
  - 5 different ebolavirus, Zaire ebolavirus most virulent
- Location: Central Africa
- Transmission: direct contact with infected body fluid
- Clinical:
  - Fever and flu like symptoms
  - Maculopapular eruption 4-5 days after fever
  - Pinpoint papules around hair roots on extremities and spreads centrally → erythroderma
  - Bleeding, petechiae, purpura, ecchymosis and hematomas

Ebola virus
- dx:
  - RT-PCR
- Management
  - Supportive measures
  - Isolation
  - Aseptic burials
- Often deadly within 14-21 days
**Ebola Virus**

- Caused by SARS-CoV-2, COVID-19
- Location: Wuhan, China, now in the US
- 13 confirmed cases in the US
- As of Feb 20th, approximately 70,748 confirmed cases in China and worldwide and 2,129 deaths confirmed. 2 deaths of US citizens as of this morning from the cruise ship.
- Transmission: animal to person, person to person
- Clinical manifestations: occurring within 2-14 days of exposure
  - Fever
  - Cough
  - Shortness of breath
  - Medium time to develop ARDS 8 days

**Corona Virus**

- **DX**
  - RT-PCR
- **Treatment:**
  - Prevention is key
  - As a provider: look for patients with flu-like symptoms who have traveled to China
  - Face mask should be worn by people with signs and symptoms are the illness

**Corona Virus**

- **What we are doing?**
  - The US department of Homeland Security’s custom and border protection began screening at US airports
  - US is currently 14-day quarantine of anyone traveling from Hubei Province, China, and are considered high risk
  - As a provider, criteria for testing is based on clinical discretion
  - If you suspect someone with this contact the CDC immediately

**Bacterial Infections**

- Impetigo
- Ecthyma
- Scarlet fever
- Blistering distal dactylitis
- Perianal strep
- Lyme disease

**Impetigo**

- Non-bullous – caused by *Staph. Aureus* (*mc*) or *strep. pyogenes*
- 35% of population are carriers (anterior nares)
- Clinical
  - Honey colored crust
  - Traumatized, abraded or exacerbatous
- Tx
  - Self resolves in 2 weeks
  - Topical Bactroban
  - Decolonization-topical Bactroban BID to nares for 7-10 days +/- chlorohexidine wash
- *Strep. pyogenes* impetigo has risk of post-streptococcal glomeralonephritis not altered with abx
**IMPETIGO**

- Bullous impetigo
- Caused by *staphylococcus aureus* phage group II (type 55 and 71) → produces exfoliatin A and B → cleaves desmosome I → subcorneal/ intergranular acantholysis
- Clinical
  - Flaccid bullae + erosions with collarette of scale, minimal erythema
- Tx:
  - Oral β-lactamase resistant PCN, clinda or first generation cephalexin
  - Complicated: IV ceftriaxone

**Bullous Impetigo**

**ECTHYMA**

- Caused by *Strep. Pyogenes*
- Deep variant of impetigo
- Clinical
  - Punched out ulcer with purulent base and hemorrhagic crust
  - Lower legs
  - Resolves with scarring
- TX
  - Dicloxacillin
  - Cephalexin

**ECTHYMA**

**SCARLET FEVER**

- Caused by Group A beta hemolytic strep
- Produces streptococcal pyrogenic toxin A,B,C
- Young children (1-10), setting of strep pharyngitis/tonsillitis
- Clinical
  - Sore throat, fever
  - "Sandpaper" like rash on trunk, Pastia’s lines, circumoral pallor, palmoplantar desquamation
  - Strawberry tongue
- TX
  - PCN
  - Erythromycin
- Complication
  - Post-strep glomerulonephritis
  - Rheumatic fever
### SCARLET FEVER

![Image of SCARLET FEVER](image)

### BLISTERING DISTAL DACTYLITIS

- **Caused by** *S. Pyogenes*
- **Result of** Picking nose/trauma
- **Clinical**
  - Darkening of skin of **distal finger** → progress to purulent vesicle/ bullae
- **Treatment**
  - I&D
  - Beta-lactam abx 10 days

### BLISTERING DISTAL DACTYLITIS

![Image of BLISTERING DISTAL DACTYLITIS](image)

### PERIANAL STREP

- **Boys > 4 years old**
- **Clinical**
  - Sharply demarcated red plaque spreading up to 3cm from anus
  - Pain with defecation
  - Blood in stool
  - A/W guttate psoriasis
- **DX**
  - Skin culture confirmatory
- **TX**
  - Oral ceftriaxone (tsc)
  - PCN

### PERIANAL STREP

![Image of PERIANAL STREP](image)

### Lyme disease

- **Agent:** *Borrelia Burgdorferi* (# 1 in US), *R. garinii* and *R. afzelii* (#1 Europe)
- **Reservoir:** white tailed deer and white footed mouse
- **Vector:** *Ixodes*
  - *Ixodes scapularis* (US)
  - *Ixodes pacificus* (western US)
  - *Ixodes Ricinus* (Europe)
- **Tick must be attached for > than 24 hrs to transmit disease**
Lyme Disease

- Three clinical stages
  - Early localized: Erythema migrans 7-14 days post-tick attachment (*bulls eye reaches 5cm*)
    - Favor trunk
    - Self resolves in 4 week
  - Early disseminated- hematogenous spread
    - Arthritis – knee (m/c)
    - Borreial lymphocytoma *(B.Afzelii and B.Garinii)*- firm plum colored tender nodule on ear lobes(kids) areola (adults)
    - Bells palsy
    - AV block

- Chronic
  - Acrodermatitis chronic atrophicans *(B.Afzelii and B.Garinii)*
    - Erythematous plaques with doughy skin on distal extremity -> progess to atrophic "cigarette-paper" with telangiectasis
  - Encephalopathy
  - Neuropathy
  - Chronic arthritis

- DX
  Diagnosing erythema migrans (most sensitive)
  IgM often negative for 2 weeks (only 41% positive and 88%) after 2 weeks

- Treatment
  - Amoxicillin and cefuroxime
  - Doxycycline
  - In 2018 American academy of peds endorsed short term (<21 days) use of doxy for Lyme disease in children less than 8
  - Mainly for single prophylaxis dose in high risk tick bite or Lyme meningitis

Lyme disease

Post test question

- A 7 year old boy presents with fevers, chills and a sore throat. Parents report he seems to be developing a rash on that started on the trunk and now is becoming more widespread. Which test would you order to confirm the dx and what is this patient at risk for?
- A. CBC, thrombocytopenia
- B. Anti-DNAse B, post-streptococcal glomerulonephritis
- C. CMP, post-streptococcal glomerulonephritis
- D. IgM, IgG and IgG levels, rheumatic fever
Post-test question

• A 7 year old boy presents with fevers, chills and a sore throat. Parents report he seems to be developing a rash on that started on the trunk and now is becoming more widespread. Which test would you order to confirm the dx and what is this patient at risk for?
  • A. CBC, thrombocytopenia
  • B. Anti-DNAse B, post-streptococcal glomerulonephritis
  • C. CMP, post-streptococcal glomerulonephritis
  • D. IgM, IgG and IgG levels, rheumatic fever

Takeaways

• Multiple different infectious conditions present in young children
• Understanding the underlying infectious etiology allows for rapid diagnosis and treatments for patients and parents

References

• Visual DX images
• CDC Corona Virus information
SKIN BIOPSY TECHNIQUE

MICHAEL A NOWAK, MD

CONFLICTS

- No conflicts with the content of this lecture

SKIN BIOPSY

- Helps in cases of dilemma
- Opportunity to find something extraordinary
- Document diagnosis and justify treatment

CHOOSING THE LESION

- Classical, well-formed lesion
- Exceptions (early lesions in vasculitis and BP)
- Avoid lesions that are modified

CHOOSING THE SKIN BIOPSY TECHNIQUE

- Size of Lesion
- Anatomic location
- Disease category or clinical diagnosis
- Proficiency or preference of clinician

SKIN BIOPSY TECHNIQUES

- Punch biopsy
- Shave biopsy
- Saucerization biopsy
- Wedge biopsy
- Incisional biopsy
- Excisional biopsy
SPECIAL CIRCUMSTANCES

- Urticaria pigmentosa
- Scalp biopsy trichoglyphics
- Immunofluorescence
- Lupus erythematosus

LOCAL ANESTHESIA

- Lidocaine: Infiltration, ring, or field block
- Topical: EMLA with 2 hours occlusion = 5 mm
- Lidocaine with epinephrine:
  - Use with caution in digital block
  - Use with caution in pregnancy

COMPLICATIONS

- Hypersensitivity to local anesthetic
- Discomfort associated with local anesthetic
- Bleeding
- Scarring
- Infection

PRACTICAL CONSIDERATIONS

- Optimal strength (10%) and volume of formalin solution (10X)
- Minimal handling of tissue to avoid crush artifact from forceps
- Place tissue in bottle (not in the cap)
- Infiltrate with optimal local anesthetic to avoid “artificial edema”
- Avoid electrocautery or cryotherapy artifact
- Avoid secondary or treated lesions

PRACTICAL CONSIDERATIONS

- Non-specific findings or misdiagnosis can result from improper:
  - Biopsy site selection
  - Lesion selection
  - Technique (superficial specimen)
  - Choice of transport media
- Examples include:
  - False-negative DIF and sampling error in NMSC or large pigmented lesions
  - Multiple biopsies in polymorphic lesions and large pigmented lesions

SKIN BIOPSY IN SPECIFIC DISEASES

- Bullous diseases
- Lupus erythematosus
- Vasculitis
- Paniculitis
- Hair disorders
- Epithelial neoplasms
- Malignant melanoma
- Dermatofibrosarcoma Protuberans
- T and B cell lymphomas
SKIN BIOPSY IN SPECIFIC DISEASES

Bullous Diseases

- Early non bullous lesional or perilesional skin within 1 cm of a bulla from the trunk is preferred for pemphigoid (DIF)
- Brief immersion in formalin produces false negative DIF results in only pemphigus
- Punch biopsy (small vesicle) or scooped shave biopsy
- Light microscopy (H&E) specimen in formalin
- DIF specimen in Michel or Zeus media (or normal saline)

SKIN BIOPSY IN SPECIFIC DISEASES

Bullous Diseases (DIF)

- Normal saline is superior to Michel or Zeus for DIF specimens delivered to the lab within 48 hours
- Mucosal surfaces: Perilesional within 5 mm from erosion
- Epidermolysis bullosa (EB): Fresh blister (< 12 hours)
- Inducing a blister: Firm downward pressure with traction for 1-2 minutes and biopsy at least 5 minutes after inducing erythema

SKIN BIOPSY IN SPECIFIC DISEASES

Bullous Diseases

- BP: Lesional and/or perilesional
- PV/PF: Lesional and/or perilesional
- DH: Non lesional
- Bullous Lupus Erythematosus: Lesional and non lesional

SKIN BIOPSY IN SPECIFIC DISEASES

Bullous Diseases (DIF)

- BP: Lesional and/or perilesional
- PV/PF: Lesional and/or perilesional
- DH: Non lesional
- Bullous Lupus Erythematosus: Lesional and non lesional

SKIN BIOPSY IN SPECIFIC DISEASES

Lupus Erythematosus

- 4 mm punch biopsy minimum
- Lesional skin only for cutaneous LE and tumid LE
- Chronic cutaneous LE and tumid LE: established lesion (> 6 months) highest yield for H&E and DIF

SKIN BIOPSY IN SPECIFIC DISEASES

Lupus Erythematosus (DIF)

- Chronic and subacute cutaneous LE: Lesional
- SLE: Lesional and non lesional
- Drug-induced LE: Lesional and/or non lesional
- Dermatomyositis: Established lesion for H&E and DIF

SKIN BIOPSY IN SPECIFIC DISEASES

Vasculitis

- Deep punch: Post capillary venule and deep plexus
- Highest yield H&E: Established lesions (>72 hours)
- Highest yield DIF: Acute lesion (< 24 hours)
- IgA vasculitis retains positive DIF in established lesions
SKIN BIOPSY IN SPECIFIC DISEASES

Panniculitis

- Deep incisional biopsy (not shave biopsy)
- Double punch technique or electric rotary power punch
- 6 mm punch minimum size divided for culture and H&E

Hair Disorders

- More than 1 biopsy is helpful
- Established lesion
- 4 mm punch is ideal:
  - Remember trichoglyphics
  - Remember to obtain adequate depth (4-5 mm)
- Normal scalp biopsy is not essential
- Transverse sections, vertical sections, or both

- Tyler Technique - 3 pieces, vertical and transverse
- HoVert Technique - 4 pieces, vertical and transverse
SKIN BIOPSY IN SPECIFIC DISEASES
Epithelial Neoplasms

- Shave biopsy: Epidermal lesions
- Punch or wedge biopsy: Dermal lesions
- Curettage: Potential interpretation limitations
- Special considerations: Microcystic adnexal carcinoma

SKIN BIOPSY IN SPECIFIC DISEASES
Malignant Melanoma

- Complete excision
- Saucerization: Macular lesions
- Orientation: Score or suture
- Partial biopsy specimens are associated lower yield
- Lentigo Maligna: Broad shave or shaves (not punch)
- Multicolor lesions: Multiple shaves
SKIN BIOPSY IN SPECIFIC DISEASES

Dermatofibrosarcoma Protuberans
- DFSP requires a deep biopsy to show the characteristic honeycomb pattern involving the subcutis
- Deep incisional biopsy is recommended
- Superficial biopsies result in a dilemma:
  - Cellular dermatofibroma vs. DFSP
  - Immunostains can be helpful in superficial specimens

Cutaneous T-cell Lymphoma
- T = T-cell and Top Heavy
- Broad shave biopsies include a wide area of the dermoepidermal junction to help demonstrate epidermotropic lymphoid cells
- Broad shave biopsies are also ideal for immunostains and gene rearrangement studies
- Multiple shave biopsies from different anatomic sites may be needed to establish the diagnosis
SKIN BIOPSY IN SPECIFIC DISEASES
Primary Cutaneous B-cell Lymphoma

- B = B-cell and Bottom Heavy
- B-cell lymphoma requires a deep biopsy showing the infiltrate’s architecture and zonal immunostaining patterns
  - B-cell lymphoid hyperplasia vs. B-cell lymphoma
- Superficial biopsies can result in misinterpretation due to insufficient sampling of the deep dermal infiltrate
- Deep incisional biopsy is recommended

Summary

- Choosing the biopsy site and lesion:
  - Lesional vs. perilesional
  - Early vs. established
  - H&E vs. DIF
- Choosing the skin biopsy technique:
  - Superficial vs. deep
- Practical considerations: Avoid artifacts
- Skin biopsy techniques for specific diseases
- Multiple biopsies especially in polymorphic lesions

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SHELDON: AND EMILY, I’M SORRY FOR SAYING DERMATOLOGISTS AREN’T REAL DOCTORS…
AND I’M SURE YOU ARE TIRED OF HEARING THAT.
EMILY: DO YOU HONESTLY THINK I HEAR THAT A LOT?
SHELDON: WELL, WHEN YOUR JOB IS POPPING ZITS AND SQUIRTING BOTOX IN OLD LADY FACES…
- BIG BANG THEORY
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 (Sep-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
- Erythematous nose, lips, mastoid/auricular, genital area
- Dome shaped hemangiomas
- Even when they involute, there is usually residual parenchymal tissue
INFANTILE HEMANGIOMAS

- 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)
- More recent study shows the same at age 7, specifically no cognitive impairment (SPD Sept/Oct 2017)
- Topical timolol 0.5% gel forming solution can work for superficial hemangiomas - applied BD

PYOGENIC GRANULOMAS

- "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 BD

PYOGENIC GRANULOMAS

- Initial study in March/April 2014 SPD journal using timolol 0.5% gel forming solution BD
- Great results with clearance after 2-3 mos
- Bleeding stopped relatively instantly
- Likely working by vasoconstriction
- Important to follow up these patients to ensure improvement (Spitz nevi, even melanoma in DDX)
WARTS

- COUNTLESS TREATMENT OPTIONS
- LIQUID NITROGEN
- CANTHARIDIN
- OTCS
- CANDIDA
- LASER
- BLEOMYCIN
- BEST THING EVER - WARTPEEL!
  - NICASA PHARMACY - IOWA
  - SALT ACID + 5FU
  - MAGIC IN A BOTTLE
  - APPLIED AT BEDTIME UNDER “STICKY TAPE”
  - $89 AND WORTH EVERY PENNY!

WARTPEEL- WOW!

WARTPEEL- AMAZING!

RING PHENOMENON

- TYPICALLY ASSOCIATED WITH CANTHARIDIN
- CAN HAPPEN WITH LIQUID NITROGEN
- THE TREATED WART MAY OR MAY NOT GO AWAY AND THEN A RING OF WARTS DEVELOPS AROUND THE INITIAL WART
- IF YOU CONTINUE THAT TREATMENT, THE RING GETS BIGGER
- I FEEL IT IS HAPPENING MORE AND MORE COMMONLY WITH CANTHARIDIN THESE DAYS
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.

INTRALESIONAL VS INTRAMUSCULAR HPV VACCINE FOR WARTS (JAAD JAN 2020)

• 46 adult patients
• 22 were treated with 0.5 mL HPV vaccine (Cervarix) at months 0, 1, and 6
• 22 were treated with 0.1-0.3 mL of HPV vaccine into largest wart at 2 wk intervals until clearance of max of 6 sessions

• Results
  - IM vaccine: 63.3% showed complete clearance, 6 pts had partial responses
  - IL treatment: 81.8% showed complete clearance, 3 pts partial response, faster

MOLLUSCUM CONTAGIOSUM

• Caused by a poxivirus
• 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 3 yrs to resolve on their own
• 2015 study of 170 kids, half treated, half not treated
  - Molluscum resolved in the same amount of time

MOLLUSCUM TREATMENT OPTIONS

• Imiquimod
  - Apply at bedtime
  - A 2-week interval, good for use of irritation and bad
• Zymaderm
  - All natural OTC product, botanical based
  - Applied once
• Candida antigen injections
  - Prednisone 1 mg/kg for molluscum 3 x weeks
  - Tretinoin 0.05%, 5 x treatments
  - Methylprednisolone 41mg
• Cantharidin
  - Used fro the face
  - Molluscum can be red
  - Protocol with each treatment is success
  - Hard to get these days
• Wartreme
  - Pretty easy, may at bedtime
  - Last times 3 x
  - Use sticky tape
• Curetage
• Liquid nitrogen
• Topical retinoic acid
• KOH 10% daily

MOLLUSCUM TREATMENT OPTIONS ON THE HORIZON

• Verrica - 0.7% cantharidin
  - Due for approval shortly
• SB206 - Nitric oxide product applied daily
  - Complete clearance at week 12 for most patients in Phase 2
  - Phase 3 trials in 2019
• Picato
  - JAAD JAN 2020
  - 19 patients; 12 week study
  - 10 treated with Picato 0.015 QD X 3 days a week - 90% clearance
  - 9 treated with imiquimod 5 days a week - 33% clearance

• Verrica - 0.7% cantharidin
• Due for approval shortly
• SB206 - Nitric Oxide Product Applied Daily
• Complete Clearance at Week 12 for Most Patients in Phase 2
• Phase 3 Trials in 2019
• Picato
  - JAAD JAN 2020
  - 19 patients; 12 week study
  - 10 treated with Picato 0.015 QD X 3 days a week - 90% clearance
  - 9 treated with imiquimod 5 days a week - 33% clearance
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
USING TOPICAL STEROIDS WILL NOT SPREAD THE MOLLUSCUM

MOLLUSCUM DERMATITIS

MOLLUSCUM DERMATITIS

MOLLUSCUM DERMATITIS

MOLLUSCUM DERMATITIS

MOLLUSCUM DERMATITIS

MOLLUSCUM DERMATITIS

PSEUDOFURUNCULOID MOLLUSCUM

LOOK LIKE PIMPLES/BOILS
DUE TO BODY'S IMMUNE SYSTEM RESPONSE
NOT INFECTED, JUST INFLAMED
NOTE SIGN: BEGINNING OF THE END

PSEUDOFURUNCULOID MOLLUSCUM

PSEUDOFURUNCULOID MOLLUSCUM

PSEUDOFURUNCULOID MOLLUSCUM

PSEUDOFURUNCULOID MOLLUSCUM

PSEUDOFURUNCULOID MOLLUSCUM

PSEUDOFURUNCULOID 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”

PF MOLLUSCUM AND ID REACTION

PF MOLLUSCUM AND ID REACTION

PF MOLLUSCUM AND ID REACTION

PF MOLLUSCUM AND ID REACTION

PF MOLLUSCUM AND ID REACTION

PF MOLLUSCUM AND ID REACTION

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 AROUND IN SOCIETY ALLOWS IMMUNITY TO WANE AND SHINGLES GETS A CHANCE TO BLOSSOM
HERPES ZOSTER

- 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)

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 4-5 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 (jul/aug 2016)

HFMD AND ONYCHOMADESIS

- When a child with history of eczema gets HFMD, it can cause a widespread worse rash called eczema coxsackium
- Similar to eczema herpeticum
- The eczema allows the virus to spread more easily, the virus flares the eczema and you get a bad rash
- Favors face, hands, arms, feet, legs, diaper area
- Very impressive
- Sudden onset
- Treatment: treat the eczema. The HFMD will pass
ECLIPSE NEVI

- Very common on the scalp of children
- Frequently biopsied because of somewhat atypical coloring, large size, history of changing
- Often read out as atypical on pathology, but these are known to be completely benign
- Probably a “special site” that isn’t currently recognized as a special site

BIRTHMARK TIPS AND TRICKS

THE FUTURE OF BIRTHMARK TREATMENT

- Port wine stains are due to mutations in GNAQ > GNA11 and PIK3CA (JAMA Derm April 2019)
- Giant congenital nevus responds to trametinib (MEK inhibitor) (Derm News May 2019)
- Epidermal nevus with acanthosis nigricans features responds to topical sirolimus (SPD July/Aug 2019)
- Lymphangiomma circumscriptum responds to topical sirolimus
- Deep neurofibroma in NF1 patient treated with topical sirolimus had complete resolution after 18 months and it did not recur. They used 0.5 mg of sirolimus compounded into 30 g lipo philic gel and applied BID (SPD May/June 2019)

TOPICAL SIROLIMUS

- Systemic sirolimus levels are not detectable when used topically for vascular malformations (SPD July 2019 poster)
- Chemistify in Philadelphia: $139 for 30 grams if insurance doesn’t cover

RASH TIPS AND TRICKS

LICHEN NITIDUS

- Mean age of onset: 9 yrs old
- Mean duration: 13 months (1-48 months in study)
- Mostly boys
- 41% generalized
- Pruritus is rare
- No treatment is needed, but if generalized, light therapy and topical steroids are often effective
- Ped’s Derm March/April 2019
**LICHEN NITIDUS**

**HYPERKERATOTIC PAPULES OF THE KNEES AND ELBOWS**
- Likely a variant of Keratosis Pilaris
- Common in boys/girls, typically age 4-12
- Causes flat-topped papules on elbows and knees
- Often mistaken for molluscum and warts but definitely not
- No treatment needed, children will outgrow it

**MISCELLANEOUS SPOTS TIPS AND TRICKS**

**PINE TAR CALLUS**
- A mimicker of melanocytic nevi and/or warts on the hands
- Baseball players
- Pine tar is used in baseball
- SFD May/June 2019

**RETENTION HYPERKERATOSIS (TERRA FIRME-FORME DERMATOSIS)**
- Isopropyl alcohol works, but can be irritating
- An alternative: 5% salicylic acid compounded in petrolatum and applied daily for 2 weeks
- SFD July/Aug 2019
MANIC

• “MEDINE ANTERIOR NECK INCLUSION CYST”
• GIANT MILIA IN THE SUPRASTERNAL NOTCH AT BIRTH
• BENIGN
• CAN BE REMOVED OR CAN RESOLVE ON OWN
• SHAVE CAN BE USED TO REMOVE

PRINCESS PACKAGE AT DISNEYLAND
SPD MAY/JUNE 2018

• 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

MAM AIR PACIFIER

THE END!

• FEEL FREE TO CONTACT ME WITH ANY QUESTIONS
• LISASWANSONMD@GMAIL.COM
BROWN STAINS

MICHAEL A NOWAK, MD

CONFLICTS

• No conflicts with the content of this lecture

IMMUNOHISTOCHEMICAL STAINS

• Antigen-Antibody reaction
• Different techniques
• Different chromogens
• Adjunct to H&E to confirm differentiation
• Diagnostic
• Prognostic

IMMUNOHISTOCHEMICAL STAINS

• Panels or combinations of stains to determine differentiation
• References exist for positive and negative stain percentages for specific lesions
• References exist for percentages of lesions that are positive or negative for specific stains
• Histologic patterns initiate a stain panel
• Some EMRs are equipped with a reflex stain panels

IMMUNOHISTOCHEMICAL STAINS

Specific Patterns

• Pagetoid pattern
• Spitzoid melanocytic pattern
• Epidermal hypermelanosis pattern

DIFFERENTIAL DIAGNOSIS

Erythematous plaque of groin
CLINICAL DIFFERENTIAL DIAGNOSIS

- Eczematous dermatitis
- Psoriasis
- Tinea
- Candidiasis
- Granular parakeratosis
- Malignancy (high index of suspicion)

IMMUNOHISTOCHEMICAL STAINS

Pagetoid Pattern

- Atypical intraepidermal epithelioid cells involving upper and lower layers in small clusters of solitary cells.
- Differential diagnosis: Paget’s disease, extramammary Paget’s disease, melanoma in-situ, pagetoid SCCIS, sebaceous carcinoma, pagetoid reticulosis, merkel cell carcinoma

IMMUNOHISTOCHEMICAL STAINS

Pagetoid Pattern

- Pankeratin
- CK34
- CEA
- CK7
- S100
- Melan A (Mart-1)
- EMA

Pagetoid Pattern

- Paget’s and extramammary Paget’s disease: CEA and CK7
- Melanoma in-situ: S100, Mart-1 (Melan A), MITF, SOX10
- Pagetoid SCCIS: Pankeratin
- Sebaceous carcinoma: CEA, EMA
- Pagetoid reticulosis: CD3
- Merkel cell carcinoma: CK20 dot-like
**CYTOKERATIN 7 (CK7) STAIN: POSITIVE**

**EXTRAMAMMARY PAGET’S DISEASE**

**PAGET’S DISEASE**
- Mammary
- Extramammary
- Bone
- Microscopic pattern

**MAMMARY PAGET’S DISEASE**
- 1874 Sir James Paget
- Mammary skin involvement especially the nipple
- Associated with an underlying breast cancer in virtually 100% of cases.
- Poor prognosis.

**EXTRAMAMMARY PAGET’S DISEASE**
- 1889 Radcliffe Crocker
- Occurs in anatomic sites rich in apocrine glands
- Frequently confined to the skin without an underlying internal cancer.
- Good prognosis.

**EXTRAMAMMARY PAGET’S DISEASE**
- Sharply demarcated erythematous patch or plaque
- Pruritus and burning pain are common
- Vulva (most common), male genital area, perianal area, and axilla
PERIANAL PAGET'S DISEASE

- Subset of extramammary Paget's disease frequently not limited to the perianal skin
- Similar to mammary Paget's in behavior since it is frequently associated with underlying visceral malignancy
- Referrals and bad prognosis

EXTRAMAMMARY PAGET'S DISEASE

Microscopic Findings

- Paget's cells: Large mucin containing cells
- Single cells or small clusters at all levels of the epidermis
- Basal layer is frequently spared and compressed forming "eyeliner sign"
- Occasional signet ring (vacuolated) cells

Perianal Paget's disease: distinguishing primary and secondary lesions using immunohistochemical studies including gross cystic disease fluid protein-15 and cytokeratin 20 expression.

Nowak MA, Guerriere-Kovach P, Pathen A, Campbell TE, Deppisch LM
Western Reserve Care System

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 of greater than 4 mm.
• Associated with a poor prognosis.

EXTRAMAMMARY PAGET’S DISEASE

Treatment

• Topical chemotherapy
• Wide local excision (Stage 1 and 2A)
• AP resection (Stage 2B and Stage 3)
• Medical oncology (Stage 4)
• Radiation (Stage 4)
• Referrals
• Long term monitoring

EXTRAMAMMARY PAGET’S DISEASE

Summary

• Mammary vs. Extramammary
• Clinical Differential Diagnosis
• Microscopic Differential Diagnosis
• Primary vs. Secondary (GCDFP-15, CK20, MUC2)
• Treatment and referrals
• Long term monitoring
CLINICAL DIFFERENTIAL DIAGNOSIS

- Melanocytic nevus
- Basal cell carcinoma
- Pyogenic granuloma
- Juvenile xanthogranuloma
- Nodular melanoma

DIFFERENTIAL DIAGNOSIS
Pink papule on scalp

IMUNOHISTOCHEMICAL STAINS
Dermal Spitzoid Melanocytic Pattern

- Dermal epithelioid cells with large nuclei and abundant cytoplasm
- Dermal Spitz nevus, nodular or metastatic melanoma, poorly differentiated squamous cell carcinoma, metastatic carcinoma, anaplastic large cell lymphoma
IMMUNOHISTOCHEMICAL STAINS
Dermal Spitzoid Melanocytic Pattern

- S100
- Melan A (Mart-1)
- SOX10
- HMB-45
- Pankeratin
- LCA

• Dermal Spitz nevus: S100, Melan A, MITF, SOX10, HMB-45
• Melanoma: S100, Melan A, MITF, SOX10, HMB-45
• Squamous cell carcinoma: Pankeratin
• Metastatic carcinoma: Pankeratin
• Anaplastic large cell lymphoma: LCA

IMMUNOHISTOCHEMICAL STAINS
Dermal Spitzoid Melanocytic Pattern

• Dermal Spitz nevus vs. melanoma
• Additional immunohistochemical stains
• Consultation to an expert for a second opinion

Human Pathol. 1996 June;27(6):528-31
Disconrder in the histopathologic diagnosis of melanoma and melanocytic nevi between expert pathologists.

Farmer ER, Gonin R, Hanna MP
Department of Dermatology, Indiana University School of Medicine
IMMUNOHISTOCHEMICAL STAINS
Dermal Spitzoid Melanocytic Pattern

- The combined kappa statistic for the 8 observers and 3 possible outcomes (benign, malignant, or indeterminate) was 0.50.
- 62% had unanimous agreement or only one discordant designation.
- 38% had two or more discordant interpretations.
- The results suggest the criteria for the diagnosis of melanomas and nevi need to be refined and more consistently applied.
- Better stains?

IMMUNOHISTOCHEMICAL STAINS
Dermal Spitzoid Melanocytic Pattern

- BRAF (acquired nevi and superficial spreading melanoma)
- KIT (acral and mucosal melanoma and lentigo maligna)
- HRAS (subset of Spitz nevi)
- GNAQ and GNA11 (blue nevi and uveal melanoma)

IMMUNOHISTOCHEMICAL STAINS
Dermal Spitzoid Melanocytic Pattern

- BRAF: V600E mutation (VE1 stain) - BRAF gene 7q34
- p16: MTS1 protein - CDKN2A gene 9p21.3
- BAP-1: BRCA-1 associated protein - BAP1 gene 3p21.1
IMMUNOHISTOCHEMICAL STAINS
Stain Results

- BRAF-positive
- P16-positive
- BAP1-negative
- This combination of results = BAPoma

A distinct subset of atypical Spitz tumors is characterized by BRAF mutation and loss of BAP1 expression.
Wiesner T, Murali R, Fried I, Cerroni L, Busam KJ, Kutzner H, Bastian BC
Sloan Kettering, New York, NY

BAPoma

- Wiesner's nevus
- Clinically indolent similar to Spitz nevus
- Solitary or multiple
- Can be a marker for a germline mutation 3p21.1

BAPoma Clinical Findings

- Circumscribed pink to tan papule(s) occasionally polypoid
- Average size of 5 millimeters
- Second to third decade of life in any anatomic location
- Solitary or multiple
- Dermoscopy: pink to tan structureless areas and peripheral irregular dots, globules, or network pattern

BAPoma Histologic Findings

- Dome-shaped dermal epithelioid melanocytic proliferation
- Generally lacks epidermal component
- Frequently biphasic: Large and small melanocytes
- Mild inflammation, minimal pigmentation, and rare mitoses
- Differs from Spitz nevus
BAPoma vs. Spitz Nevus Histologic Findings

- In contrast to Spitz nevus, BAPoma:
  - Lacks epidermal involvement and hyperplasia
  - Lacks clusters of spindle cells
  - Lacks Kamino bodies
  - BRAF V600E mutation present (positive)
  - BAP-1 loss (negative)
  - Like Spitz nevus p16 expression is preserved (positive)

BAPoma What would I see on a report?

- Atypical Spitzoid tumor with BAP-1 loss
- BAP-1 inactivated Spitzoid nevus (‘BAPoma’)
- BRAF V600E positive
- BAP1 negative
- P16 cyclin-dependent kinase inhibitor 2 (CDKN2A gene) positive

BAPoma

- Continuum 1
  - BAPoma (p16+) → Intermediate → Melanoma with BAP1 loss (p16-)
- Continuum 2
  - Spitz nevus (p16+) → Intermediate → Spitzoid melanoma (p16-)
**BAPoma**

**What do I do next?**

- Complete excision for solitary lesions
- Look for additional lesions
- Inquire about eye tumors and mesothelioma
- Long term surveillance similar to a melanoma patient
- Referrals for multiple lesions (germline mutation)
- Multiple lesions followed for change in clinical appearance, radiologic studies, and genetic counseling

**BAPoma**

**Germline Mutation**

- Associated with multiple BAPoma lesions
- Frequently microscopically homogeneous
- Familial mesothelioma (non-asbestos related)
- Uveal melanoma
- Cutaneous melanoma
- Other malignancies especially renal cell carcinoma

**BAPoma**

**Summary**

- Wiesner's nevus
- Different from Spitz nevus
- BAP-1 inactivated Spitzoid nevus ('BAPoma')
- Solitary (excise) or multiple (follow and referrals)
- Germline mutation is associated with multiple nevi, uveal melanoma, cutaneous melanoma, familial mesothelioma, and other cancers
DIFFERENTIAL DIAGNOSIS
Tan-brown patch on sun exposed skin

CLINICAL DIFFERENTIAL DIAGNOSIS
- Solar lentigo
- Seborrheic keratosis
- Pigmented actinic keratosis
- Lichenoid keratosis
- Lentigo maligna

IMMUNOHISTOCHEMICAL STAINS
Epidermal Hypermelanosis Pattern
- Epidermal hypermelanosis with a gradient of low to high density of melanocytes and minimal cytological atypia
- Solar lentigo, pigmented actinic keratosis, lichenoid keratosis, lentigo maligna

IMMUNOHISTOCHEMICAL STAINS
- Pankeratin
- S100
- Melan A (Mart-1)
- HMB-45
- MITF
- SOX-10

Solar lentigo: Pankeratin positive
Pigmented actinic keratosis: Pankeratin positive
Lichenoid keratosis: Pankeratin positive
Lentigo maligna:
- Pankeratin negative (silhouette of unstained melanocytes)
- S100, Melan A, HMB-45, MITF, SOX10 positive
IMMUNOHISTOCHEMICAL STAINS
Lentigo Maligna

- Sufficient sampling is key: Multiple shaves (not punch)
- High density: Confluence of melanocytes in basal layer
- Follicular involvement
- Dermal-epidermal and intercellular separation
- Moderate involvement of spinous layer
- Multinucleate melanocytes and minimal atypia
PRAME Expression in Melanocytic Tumors.
Lezcano C, Jungbluth AA, Nehal KS, Hollman TJ, Busam KJ
Sloan-Kettering, New York, NY

- PRAME is preferentially expressed antigen in melanoma (PREFERentially expressed Antigen in MElanoma).

- Among 400 melanocytic tumors including 155 primary and 100 metastatic melanomas and 145 melanocytic nevi.

- PRAME is diffusely expressed in 87% of metastatic and 83.2% of primary melanomas.

- PRAME was diffusely expressed in 94.4% of acral melanomas, 92.5% of superficial spreading melanomas, 90% of nodular melanomas, 88.6% of lentigo maligna melanomas, and 35% of desmoplastic melanomas.

- PRAME expression was seen in both in situ and non-desmoplastic invasive melanoma components.

PRAME

- 86.4% of the 140 cutaneous melanocytic nevi were completely negative.

- Occasional melanocytes were positive in 13.6% of cutaneous nevi.

- Rare junctional melanocytes were also positive in solar lentigines and benign non-lesional skin.

- Useful to support a diagnosis of melanoma.

- Margin assessment of a known PRAME-positive melanoma.

- Expression in nevi, solar lentigines, and benign non-lesional skin can represent a pitfall.

Unstable Solar Lentigo

- A lentigo with areas of melanocytic hyperplasia not extending past the margin of the lesion.

- Macular pigmented lesion arising on sun-damaged skin.

- Clinically differ from usual solar lentigines, often being solitary or larger and darker than adjacent solar lentigines.

- They can arise in close proximity to lentigo maligna.

Australas J Dermatol 2016 Aug;57(3):229-34
Unstable solar lentigo: A defined separate lesion.
Byron I, Barksdale S, Wadton D, Mair J
Queensland, Australia
IMMUNOHISTOCHEMICAL STAINS

Unstable Solar Lentigo

- Single lesions can demonstrate changes of solar lentigo, unstable solar lentigo, and lentigo maligna.
- Unstable lentigo is likely a precursor to lentigo maligna.
- Lentigo maligna can arise within a solar lentigo through an intermediate lesion (unstable solar lentigo).
- Difficulties in the diagnosis of single cell predominant melanocytic proliferations
- Unstable lentigo is now recognized as a separate entity.

EPIDERMAL HYPERMELANOSIS PATTERN

Summary

- Sufficient sampling is key
- Density, confluence, and follicular involvement
- Nuclear stains are superior (MITF and SOX10)
- PRAME
- Lentigo maligna: Complete excision
- Unstable lentigo: Follow and additional sampling

IMMUNOHISTOCHEMICAL STAINS

Notable Stains

- CK7
- BAP-1
- p16
- PRAME
- SOX10

- CK7: Positive in Extramammary Paget’s disease
- BAP-1: Negative in BAPOMA
- p16: Positive in nevi and negative in melanoma
- PRAME: Positive in melanoma and negative in nevi
- SOX10: Nuclear melanocytic marker like MITF that does not overemphasize melanocyte density
Summary

- Why do we do immunohistochemical stains?
  - Identify or confirm differentiation
  - Panels are used because of overlapping stain results
  - Histologic patterns initiate brown stains
  - Concepts change after new stains are available

Michael A. Nowak, MD
man2004@comcast.net
Saturday, February 22, 2020

6:00 a.m. - 7:00 a.m.  Breakfast with Exhibitors
Oceana B-D

7:00 a.m. - 8:00 a.m.  Biologics In Dermatology
Michael Wein, MD

8:00 a.m. - 9:00 a.m.  The Future of Dermatology Reimbursement
Mark Kaufmann, MD

9:00 a.m. - 10:00 a.m.  Cutaneous Mucinoses and Systemic Diseases
Paolo Romanelli, MD

10:00 a.m. - 10:15 a.m.  Warts vs. Actinic Keratosis: New Weapons in the Therapeutic Civil War
10:15 a.m. - 10:30 a.m.  Photodynamic Therapy 2020 Update
10:30 a.m. - 10:45 a.m.  How to Meet the Challenges of Hyperhidrosis
10:45 a.m. - 11:00 a.m.  How Do Biologics Fit in an Integrative Treatment Plan
Neal Bhatia, MD

11:00 a.m. - 11:30 a.m.  Break with Exhibitors
Oceana B-D

11:30 a.m. - 12:30 p.m.  Product Theater Regeneron
Diagnosing and Assessing Uncontrolled Atopic Dermatitis
Bradley Glick, DO, FAOCD
Coral A-B
(No CME Awarded)

12:30 p.m. - 1:00 p.m.  Break with Exhibitors
Oceana B-D

1:00 p.m. - 2:30 p.m.  The Future of the Osteopathic Profession
Ronald Burns, DO, FACOFP, AOA President
Kevin Klauer, DO, EJD, FACEP, AOA CEO

2:30 p.m. - 3:00 p.m.  Pearls from Legally Speaking
Clifford J. Lober, MD, JD

3:00 p.m. - 3:30 p.m.  Break with Exhibitors
Oceana B-D
3:30 p.m. - 4:30 p.m.  
Psoriasis: Which Drug for Which Patient?  
Mark Lebwohl, MD

4:30 p.m. - 5:00 p.m.  
Americans With Disabilities Act: How It Impacts Your Practice  
Clifford J. Lober, MD, JD

5:00 p.m. - 5:30 p.m.  
Fillers, Is There a Difference?  
Shino Bay Aguilera, DO, FAOCD
**Cutaneous Mucinoses and Systemic Diseases**

**Paolo Romanelli, M.D.**

Professor
Director UM ACGME Dermatopathology Fellowship
Director Psoriasis Biologics Clinic JMH
Dr. Philip Frost Dermatology and Cutaneous Surgery
L. Miller School of Medicine
University of Miami

No Conflict of Interest

---

**Mucin**

(glycosaminoglycans)

- Jelly-like substance which is a normal component of skin connective tissue produced in small amount by fibroblasts

In disease conditions, mucin is increased and since it holds water (hygroscopic), the dermal connective tissue is swollen

Cutaneous mucinosis in Shar-pei

---

Collagen bundles widely spaced with basophilic finely granular material and fibroblasts (H&E stain)

---

From Bolognia J. Dermatology, Mosby, 2012

Table 47.1: Staining characteristics of acid glycosaminoglycans (mucopolysaccharides)
New techniques to detect glycosaminoglycans

- Monoclonal antibodies to heparan sulfate proteoglycans
- Family of hyaluronan synthases (HS1, HS2, HS3) and hyaluronidases (HYAL1, HYAL2)
- Hereditary cutaneous mucinosis in Shar pei dogs is associated with increased HYAL2 mRNA transcription by cultured dermal fibroblasts

The cutaneous mucinoses

- **Primary Mucinoses**
  - Mucin deposit is the main histologic finding resulting in clinically distinctive lesions

- **Secondary Mucinoses**
  - Mucin deposit is only an additional histologic finding

Secondary mucinoses

- Granuloma annulare
- Dermatomyositis
- Scleroderma
- Lupus erythematosus
- Degos’ disease

Granuloma annulare

- Mucin deposition is an additional histologic finding associated with necrobiotic granuloma

Primary Mucinoses

**Dermal**
- Lichen Myxedematosus
- Reticular erythematous mucinosis (REM)
- Sclerodema
- Pretibial myxedema
- Cutaneous focal mucinosis
- Myxoid cyst
Lichen Myxedematosus (Papular mucinosis)

- Generalized and sclerodermoid type (Scleromyxedema) with monoclonal gammopathy and systemic manifestations
- Localized type with only cutaneous involvement

Scleromyxedema

- Generalized sclerodermoid eruption with stiff infiltration and redundant folds

Scleromyxedema

- Closely spaced papules on sclerodermoid skin
- Papules in a linear fashion

Scleromyxedema

- Doughnut sign

Scleromyxedema

- Deep longitudinal furrows on the glabella
Histopathology: microscopic triad of scleromyxedema

1. Mucin
2. Fibroblast proliferation
3. Fibrosis

Scleromyxedema is associated with a monoclonal gammopathy IgGλ (rarely progressing to myeloma)

Scleromyxedema is associated with systemic, even lethal, manifestations

- Muscular (dysphagia, myositis) 30%
- Pulmonary 17%
- Rheumatologic (carpal tunnel) 15%
- Neurologic (neuropathy, psychosis, coma) 10%

Scleromyxedema and coma (Dermato-neural syndrome)

- Worsening skin lesions with flu-like prodromes, fever, seizures, and coma
- Recovery over 20 days with supportive therapy or death
- Encephalopathy of obscure pathogenesis
- Brain autopsy non-contributory

Cardiomiopathy in Scleromyxedema

Inflammatory fibrosing hypertrophic cardiomiopathy with interstitial mucin leading to patient’s death

Rongioletti et al, Br J Dermatol, 2001

Mucin in striated muscle

Pitfalls in scleromyxedema

A 65 year-old-man with sclerodermoid features and chronic renal disease...

Histopathology suggestive of scleromyxedema...

Nephrogenic systemic fibrosis

- Clues for NSF:
  - Renal disease and exposure to Gadolinium-containing Contrast Agents
  - More deep fibrosis with CD34+ cells

- Clues for Scleromyxedema:
  - Involvement of face and monoclonal gammopathy
  - Precollagen I

Lichen Myxedematous (Papular mucinosis)

- SCLEROMYEDEMA
  - Generalized papular and sclerodermoid
  - Mucin with fibrosis
  - Monoclonal gammopathy (systemic involvement)
  - Chronic disabling course
  - Unpredictable prognosis

- LOCALIZED LICHEN MYXEDEMATOSUS
  - Papular eruption (nodules, plaques)
  - Mucin without fibrosis
  - No monoclonal gammopathy or systemic involvement
  - Good prognosis
Localized lichen myxedematosus

- Discrete type
- Acral persistent papular mucinosis
- Cutaneous mucinosis of infancy

 localized lichen myxedematosus (discrete type)

Chronic eruption of papules from just a few to hundreds on trunk and limbs

Mucin with variable fibroblast proliferation and no fibrosis

Acral persistent papular mucinosis

Rongioletti et al, 1986

Cutaneous mucinosis of infancy

(paediatric variant of localized lichen myxedematosus)

Lichen Myxedematosus (Papular mucinosis)

Rongioletti & Rebora, JAAD, 2001

- A distinction between scleromyxedema and localized lichen myxedematosus is important for prognosis and therapy
- Localized lichen myxedematosus needs no therapy (“wait and see” approach)
- Scleromyxedema is a disease with substantial morbidity/mortality that needs to be treated

Treatment of scleromyxedema

- Corticosteroids
- Psoralen-UVA
- Systemic Retinoids
- Electron-beam radiation
- Extracorporeal photochemotherapy
- Plasmapheresis
- Granulocyte colony-stimulating factor
- Cyclosporine
- Interferon alfa

- Chemotherapy
  - Melphalan
  - Cyclophosphamide
  - Methotrexate
  - Chloroambucil
  - Cladribine
Scleromyxedema

26 patients
17 treated with melphalan
9/17 (53%) death related to melphalan complications (infections or hematologic malignancies)

New therapies for scleromyxedema

- High dose intravenous immunoglobulins (IVIg)
- Thalidomide
- Autologous stem cell transplantation (+ high dose melphalan)

Scleromyxedema and IVIg:

- Multicenter study on 30 patients
- 13 patients on IVIg (2 mg/Kg/die/5 days/month)
  - 4 complete remission
  - 9 partial remission
- Mean treatment duration of 2 years
- Relapse after stopping treatment
- Maintenance infusions spaced out to every 2 months are required

Scleromyxedema before IVIg
- (2g/Kg/month)

Before IVIg After 1 month After 3 months

Scleromyxedema

Before IVIg After IVIg (5 months)
Primary Mucinoses

Dermal
Lichen Myxedematosus
Reticular erythematous mucinosis (REM)
Scleredema
Pretibial myxedema
Cutaneous focal mucinosis
Myxoid cyst

Reticular erythematous mucinosis
(Plaque-like cutaneous mucinosis)

Primary Mucinoses

Dermal
Lichen Myxedematosus
Reticular erythematous mucinosis (REM)
Scleredema
Pretibial myxedema
Cutaneous focal mucinosis
Myxoid cyst

Scleredema

- Symmetrical diffuse non-pitting induration of the upper part of the body
- Hands and feet spared
- 3 types:
  1. Upper respiratory tract infection (streptococcal)
  2. Monoclonal gammopathy IgGk
  3. Diabetes

Scleredema

- Interstitial mucin in a thickened dermis with fenestration of collagen

Scleredema

- No specific treatment available
- Scleredema with infection clears in 6 months
- Scleredema with monoclonal gammopathy or diabetes persists for years or never heals
Therapy of sclerodema

- UVA-1 phototherapy
- IVIg
- Need large randomized, controlled trials

Primary Mucinoses

Dermal
- Lichen Myxedematous
- Reticular erythematous mucinosis (REM)
- Scleredema
- Pretibial myxedema
- Cutaneous focal mucinosis
- Mxoid cyst

Localized (pretibial) myxedema

- Indurated waxy plaques on the shins with peau d'orange appearance
- Associated with hyperthyroidism (mostly Graves’ disease) often following treatment of thyroid
- Frequent association with exophthalmos and thyroid acropachy

Localized (pretibial) myxedema

1. diffuse, non-pitting edema (43%)
2. plaque (27%)
3. nodular (18%)
4. elephantiasis (5%)

"Monster" elephantiasis-like (pretibial) myxedema

Thyroid dermopathy

Courtesy B.Cribier, Strasbourg

Courtesy of Shyam Verma
Clinical case

An obese woman with swollen pitting oedema of the legs and bilateral semitranslucent papules and nodules on the shin. No thyroid disease.

Obesity-associated lymphedematous mucinosis


- Pretibial mucinosis is associated with morbid obesity (IBM>40) and lymphoedematous features of the legs
- A low-calorie diet coincided with a clinical improvement and partial resolution of the papules and nodules of pretibial mucinosis.

Biopsy specimen from a nodule on the shin of a woman

Pretibial Myxedema?

Mucin (oedema) in the superficial dermis
Epidermal atrophy with effacement of the rete ridge
Angioplasia with vertical running of vessels
Stellate or linear fibroblasts
Haemosiderin deposition

Obesity-associated lymphedematous mucinosis


Before diet

After diet

New cutaneous mucinoses
AESOP

- Aesop (620-564 BCE) was a Greek writer credited with a number of popular fables.

AESOP robot system for video-assisted surgery

- Automated Endoscopic System for Optimal Positioning (AESOP) for holding and maneuvering the endoscope.

AESOP syndrome

- Adenopathy
- Extensive
- Skin patch
- Overlying
- Plasmocytoma

AESOP

- Enlarging reddish plaque on the chest with superficial vessels and regional lymphadenopathy
- Increased dermal mucin and vascular proliferation (mucinous angiomatosis)
- No inflammation

The red plaque with histological features of mucinous angiomatosis is the skin sign of an underlying plasmocytoma of the ribs or sternum.
At this stage the plasmacytoma and the associated POEMS syndrome are still curable. When these patients were treated with a combination of surgery, chemotherapy and radiotherapy, prognosis was favorable.

Contiguous Skin inflammation
- Some angiogenic (VEGF) and growth-factor cytokines (TGF-β, TNF-α) mediated by plasmacytoma reach the skin through the blood and lymphatic stream and promote the vascular hyperplasia and mucin deposition.

Cardio-cutaneous mucinosis
Patients with mitral valve prolapse who developed heart complications seem to have an increased amount of mucin in normal skin in comparison to patients with a benign prognosis.
- A high content of mucin in the skin could be a sign of a severe myxomatous alteration of the mitral valve.
- Expression of a more generalized connective tissue disorder.
Table I

<table>
<thead>
<tr>
<th>Classification of Mitral Valve Prolapse</th>
<th>Mitral Valve Prolapse Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral Valve Prolapse (Anatomic)</td>
<td>Patients with mitral valve prolapse</td>
</tr>
<tr>
<td>Common mitral valve abnormality with</td>
<td>Symptom complex: chest pain,</td>
</tr>
<tr>
<td>a spectrum of structural and</td>
<td>palpitation, arrhythmia, fatigue,</td>
</tr>
<tr>
<td>functional changes, mild to severe</td>
<td>exercise intolerance, postural</td>
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<tr>
<td>The basis for:</td>
<td>phenomena, dyspnea, neurogenic</td>
</tr>
<tr>
<td>Systolic click, mid-late systolic</td>
<td>neuropathic symptoms</td>
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<tr>
<td>murmur</td>
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<tr>
<td>Mild or progressive mitral valve</td>
<td>Neuropathic or autonomic</td>
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<tr>
<td>dysfunction</td>
<td>dysfunction (increased adrenergic</td>
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<td>Progressive mitral regurgitation,</td>
<td>activity, hyper-response to</td>
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<tr>
<td>atrial fibrillation, congestive heart</td>
<td>adrenergic stimulation, abnormal</td>
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<td>failure</td>
<td>vagal tone, baroreceptor</td>
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<tr>
<td>Infectious endocarditis</td>
<td>abnormality, hypovolemia) may</td>
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<td>Embolic phenomena</td>
<td>provide explanation for symptoms.</td>
</tr>
<tr>
<td>Characterized by long natural history</td>
<td></td>
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<tr>
<td>May be heritable, or associated with</td>
<td>Mitral valve prolapse—a possible</td>
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<tr>
<td>heritable disorders of connective</td>
<td>marker for autonomic dysfunction.</td>
</tr>
<tr>
<td>tissue</td>
<td></td>
</tr>
<tr>
<td>Conduction system involvement, possibly leading to arrhythmias and conduction defects</td>
<td></td>
</tr>
</tbody>
</table>
Echocardiographically Documented Mitral Valve Prolapse: Long term follow up of 237 Patients
R.A. Nishimura, MD, M.D.
McGregor, MD, C. Slish, MD,
F.A.J. Miller, MD, D.M.
Bstrup, MD, A.J. Tajik, MD

Screening for Hypertrophic Cardiomyopathy in Young Athletes
D. Corrado, MD, C. Basso,
MD, M. Schilders, MD, G.
Thiene, MD

Marfan Syndrome
R. Graham et al
Br J Rheum. 1994;33:126-31

Ehler-Danlos Syndrome
Leer et al
Ann Int Med. 1980;92:711-78

Pseudoxanthoma Elasticum
M.G. Leduc et al

Cutch Laxa
L.J. Swine et al

MVP
• Accumulation of mucinous material in:
  - valve leaflets
  - membranous and atrial septum
  - mitral and tricuspid valve rings
  - attachment regions of chordae tendineae
  - supportive tissue of
    • sino-atrial node
    • atrio-ventricular node
    - HIS-Purkinje conduction tracts

Myxoid Heart Disease
An Assessment of Extravascular Cardiac Pathology in Severe Mitral Valve Prolapse
Human Pathology Vol. 23, No. 2, Feb 1992
A.R. Morales, MD, R. Romanelli, MD,
R.J. Bouck, MD, L.G. Tate, MD,
T.T. Alvarez, MD and J.T. Davis, MD
Temporomandibular Joint Dysfunction: connective tissue variation in skin biopsy and mitral valve function
L. Westling, DDS S. Holm, PhD,
J. Wallentin, MD, PhD.

Study Design
- Eight patients with severe MVP and 4 controls with no cardiac symptoms were selected for this study.
- Criteria for selection of the patients:
  - Age < 55 yr
  - Echocardiography proven severe Mitral valve prolapse
- Two 4 mm punch biopsies of left forearm were performed. One for histologic evaluation and the other for biochemical analysis.

Study Demographics
- **Patients**
  - 52 yr man, MVP, A.Fib.
  - 39 yr man, MVP, Palp.
  - 33 yr man, MVP, Mild chest discomfort
  - 43 yr old man, MVP, Chest pain, TMJ dysfunction
  - 42 yr old man, MVP, Palp.
  - 53 yr woman, MVP, Palp.
  - 48 yr woman, MVP, Arrhythmia
  - 53 yr man, MVP, Arrhythmia.
- **Controls**
  - 41 yr man
  - 31 yr man
  - 40 yr man
  - 38 yr man

Proteoglycan Biochemical Analysis (mg/gr. wet weight)

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
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Mitrval valve prolapse syndrome (MVP) is a relatively common disorder of the mitral valve and most cases take a benign clinical course. Only a small subset of patients develop severe clinical symptoms such as arrhythmia, insufficiency of the mitral valve or infective endocarditis. As a consequence, sudden death might occur in these patients, though to be caused by an arrhythmogenic event. By presenting six cases of sudden unexpected death in young female students, we point out clinical and pathological data from the literature, which are not based in the viewpoint of legal medicine. The incidence of MVP in autopsy series has been reported to be about 4-4.5% in female and 1.5% in male patients. The presented cases suggest that even clinically benign cases of MVP in young adults might result in sudden unexpected death. Such cases are not included in hospital based studies on the topic. This might lead to an underestimation of the fatal risk associated with the disease, even if sudden death might be a rare event in MVP.
Mitrail valve prolapse syndrome as cause of sudden death in young adults.

Andresen S., Ehm S., Behnke F., Pauschel K.,

Institute of Legal Medicine, University of Hamburg, Burefeld 34, 20259 Hamburg, Germany.

Mitrail valve prolapse syndrome (MVP) is a relatively common disorder of the mitral valve and most cases take a benign clinical course. Only a subset of patients develop severe clinical symptoms such as arrhythmia, insufficiency of the mitral valve or infective endocarditis. As a consequence, sudden death might occur in these patients, thought to be caused by an arrhythmogenic event. In presenting six cases of sudden unexpected death in young female adults, we point at clinical and pathological data from the literature, which are of interest from the viewpoint of legal medicine. The incidence of MVP in autopsy series has been reported to be about 4–5%, while clinical data hint at an incidence of about 2.5%. The presented cases suggest that even clinically benign cases of MVP in young adults might result in sudden unexpected death. Such cases are not included in hospital based studies on the topic. This might lead to an underestimation of the total risk associated with the disease, even if sudden death might be a rare event in MVP.
Heart problems can elude detection

Saturday, April 28, 2006

By Joe D'Amico, Pittsburgh Post-Gazette

Maggie Dixon's enlarged heart put her at greater risk for developing a potentially fatal arrhythmia, or abnormal heart rhythm, a heart specialist said yesterday.

Ms. Dixon, 28, the Army women's basketball coach, died at Westchester Medical Center in Valhalla, N.Y. last Thursday, a day after she was admitted with what her brother, Pitt men's coach Jamie Dixon, called an arrhythmic heart episode.

After an autopsy yesterday, the Westchester County medical examiner's office said the cause of death, pending further study and investigation, was cardiomyopathy -- or an enlarged heart -- with prolapse of the mitral valve, located between the left upper and lower chambers of the heart.

It also noted that she arrived one day in a coma and had swelling of the brain.

Mitrval valve prolapse involves a bulging back of the mitral valve toward the upper chamber of the heart, said Dr. John H. Ward, chief of cardiology at Mercy Hospital's Heart Institute. It is common in men, but women generally are not associated with serious health problems, he said.

Mr. Dixon likely had an arrhythmia in a lower chamber of the heart that kept it from pumping effectively and led to decreased blood flow to her brain, Dr. Ward said.

What might cause her enlarged heart is unclear, he said, though it could have resulted from a number of factors, including a virus.

Mitrval Valve Prolapse

Complications

Although uncommon with mitral valve prolapse, complications can be serious. These include:

- Mitral valve regurgitation. The most common problem in mitral valve prolapse is regurgitation of blood backflowing from the left atrium to the left ventricle (regurgitation occurs in 50% to 90% of patients).
- Atrial fibrillation. Mitral valve prolapse can cause atrial fibrillation. If fibrillation occurs, a cardioversion to normal heart rhythm may be necessary.
- Thrombosis (formation of blood clots). A thrombus may form in the left atrium, which can lead to a pulmonary embolus if it migrates to the lungs. This is a potential complication of mitral valve prolapse.
- Surgery. If the heart is enlarged or becomes enlarged, surgery may be required. Surgery may be performed to control blood pressure, improve left ventricular function, or prevent further mitral regurgitation.

ClinicalTrials.gov

Linking patients to medical research

Home | Search | Library | Inquiries | Help | What's New | About
2. Investigator(s):
Strengths
• Dr. Romanelli has a very unique background, being formally trained in pathology, family medicine and dermatology. He also has had exposure to the pathology of patients with sudden death, some of whom had mitral valve prolapse.
• His publications appeared to have increased significantly in the past few years.
Weaknesses
• Dr. Romanelli’s history of funded research is limited.

3. Innovation:
Strengths
• This is a very novel approach to identifying risk factors for adverse outcomes with MVP.
Weaknesses
• None noted.

1 R21 HL106194-01 4 CICS
ROMANELLI, P

Weaknesses
• Although the histopathology is innovative and described in detail, the echocardiography is relatively routine. More expertise in echocardiography would likely be welcomed.
• The preliminary data is presented with many and varying numbers of digits. A bit more care from the precision of the measurement to the significant digits displayed would be more reassuring.

5. Environment:
Strengths
• The environment is adequate for the proposed studies.
Weaknesses
• Minimal.

Thank you
promanelli@med.miami.edu

Conclusion
Skin biopsy may be a useful adjunct to echocardiography in the detection of clinically significant MVP. Knowing the extent of the skin involvement in such patients would provide new insights into the pathogenesis of possible cardiac complications.
Cardio Cutaneous Mucinosis of Romanelli P. Rongioletti F. Romanelli R.

What ever language you speak, live in Italian… …in Miami!
Warts vs. Actinic Keratosis: New Weapons in the Therapeutic Civil War

Neal Bhatia, M.D.
Director of Clinical Dermatology
Therapeutics Clinical Research
San Diego, California
2020 AOCD Spring Meeting

Dr. Bhatia’s Disclosures:
- Affiliations with AbbVie, Almirall, Biofrontera, BiopharmX, Dermira, Dr. Reddy’s, Encore, EPI Health, Ferndale, Foamix, Galderma, Intraderm, ISDIN, LaRoche-Posay, Leo, Mayne, Menlo, Novartis, Ortho, Pfizer, Pierre-Fabre, Regeneron, Sanofi, SkinFix, Soligentix, SunPharma, Vidal, and Vyome
- 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
- Acknowledgments: Adam Friedman, MD; Ted Rosen, MD

Is there a civil war between AKs and Warts? Or is it sibling rivalry?
- They look alike, can linger for a long time untreated, share a similar trigger (HPV), and resist host apoptosis and defenses
- Patients often overlook them until they either grow, bleed, change in size, or meet their deductibles
- Dermatologists usually take the same approach with each disease: freeze and go
- There are few prevention strategies that are either adhered to, are approved, or actually work
- The topical management strategies for these are usually painful, expensive, or impossible to get covered by insurance

HPV: The Double Agent
- HPV 21, 23, 38 linked to AKs and SCC
- Induced anti-apoptotic effects in UV-damaged cells
- Multiple phenotypes of warts linked to HPV
- E6 and E7 proteins essential for accumulation of further mutation
- E6 of the cutaneous HPV types 5, 8, 20, 22, 38, 76, 92, and 96 (betaPV types) degrade BAK
- Binds and inactivates p53 and BAK—slows DNA repair
- Anti-apoptotic effect of the E6 protein in HPV proposed as a tumor inducing factor

Transmission and Life Cycle of HPV

Subclinical or precursor warts more often over genitals or cervical disease

Innocent lateral skin often without clinical change despite histological presence of HPV-infected keratinocytes

Koilocytosis delayed after initial infection

If there are “Subclinical AKs,” what about “Subclinical Warts?”
- Evolving AKs are still AKs, whether we see them with our eyes, dermatoscope, confocal microscopy, or fluorescence
- Atypical keratinocytes not often correlated clinically except as photodamaged skin
- Subclinical or precursor warts more often over genitals or cervical disease
- Innocent lateral skin often without clinical change despite histological presence of HPV-infected keratinocytes
- Koilocytosis delayed after initial infection
Similar Weapons in the War

- Same destructive and immune-based therapies approved for AKs have been studied off-label for warts
  - Topical 5-FU, Tazarotene, Imiquimod, Ingenol Mebutate, Sinecatechins, ALA-PDT all for AK, also in combo with cryo
  - Imiquimod, IM gel, and Sinecatechins studied for genital warts
- Impact on the “field” effects of warts still poorly understood
- Costs, tolerability, and compliance are all limiting factors
- Summaries of combination studies with cryo for warts are incomplete unless studied against topical therapies alone

Cryo-necrosis induces destruction

5 Seconds
10 seconds

Courtesy Adam Friedman, MD

What does Dr. Google prescribe?

- Banana Peels
- Duct Tape
- Vicks Vaporub/Robitussin
- Teatree oil—One study against HSV not HPV
- Apple Cider Vinegar
- Salicylic Acid—40% or bust
  - Mediplast, Occlusal HP
  - Solution of salicylic acid 17%
  - DuoFilm, Compound W, Occlusal HP
  - Apply after wart has been wet (eg, in shower)
  - Apply every other night
  - Pare or file (at home) twice monthly (after soaking)

Zinc for Warts

- Multiple trials (Korea and Brazil): 62.5-87.7% success
- MOA: increases APC activity
- Zinc sulfate 10mg/kg/day (max 600mg): Rx up to 3 mo
  - Failures: insufficient dose, too short treatment regimen
  - Gastritis/Gastric perforation
  - Use divided doses after meals, not to exceed 120-140mg elemental zinc per day

Cimetidine vs Zinc Sulphate

- Randomized, DB prospective study 18 pts 7-20 yo with multiple (11-120) warts (VV, flat, plantar)
  - 9/9 completed 35 mg/kg/d cimetidine x 3 m
    - 0/9 Complete
    - 4/9 Partial
    - 5/9 No response
  - 8/9 completed 10 mg/kg/d zinc sulphate x 3 m
    - 5/8 Complete
    - 2/8 Partial
    - 1/8 No response

Old and New

- 5-FU: Study comparing 5% 5-FU cream plantar warts under tape occlusion vs. tape occlusion alone, n=40
  - 19/20 patients (95%) in active group 5% 5-FU with tape occlusion had complete eradication within 12 weeks
  - Average time to healing 9 weeks, 3 recurrences by 6 months

- New Keratolytic: 28.5% salicylic acid extended release antiviral film-forming solution is the only extended release salicylic acid available for wart removal
- Thermal pad 2 hours exposure, raises local temperature to 42-43°C for with recalcitrant warts
  - Proof of concept study, n=3, all clear by 4-5 wks

Courtesy Adam Friedman, MD
Females

- 0.05% gel for two days
- Mebutate

Males

- 2
- 0.7% preparation applied topically in office.

J Cosmet Laser Ther.

- From desmosomes

Bhatia, 45% Topical Solution

- Ingenol

- LSRs and tolerability assessments at Days 8, 29, and 57
- 2
- Off

Ages 8 and up

Excluded plantar and periungual

for

group vs reduction

0.87 points in A

Day 56 on the target warts was

Mean

but not thickness or intact callus

PWA score measured diameter
twice weekly application in office

N=159, 1

- 5 common warts on palms or palmar surface of digits

- Removed then replaced after second dose applied

Largest wart occluded with adherent dressing for 24 hours,

Warts pared down on day 1, treated for two days

Occlusion of warts on the digits gave the best results

Smucker & Jatsov 2000

- 20% ALA, 3h incubation, local anesthetic, LED (635nm) light, up to 5 tx, controlled, n=24

- ALA+PDT: 48 of 64 (75%) warts completely healed

- ALA+PDT: 13 of 57 (22.8%) warts completely healed

PDT: 48 of 64 (75%) warts completely healed

VEH-PDT: 13 of 57 (22.8%) warts completely healed

- ALA, PDL, 5% ALA, 3h incubation, 10% FA or LED (595 nm), 1-3 tx, vehicle control, n=47

- PDL: 81% cure rate, mean of 3.94 tx

- ALA+PDT: 100% cure rate, mean of 1.95 tx

- ALA+LED: 96% cure rate, mean of 1.52 tx

Hall: Jeffrey A. Hall, MD; Pamela J. Keller, RN; Gregory S. Keller, MD.

Rationale: Furosemide and Digoxin

- Risk of significant pain associated with swelling

- Risk of significant pain associated with swelling

- Induces anti viral immune response

- Painless during (good for kids)

- Cantharidin

- 0.7% preparation applied topically in office

- MOA: Activates neutral serine proteases that cause

degeneration of the desmosomal plaque, leading to
detachment of tonofilaments from desmosomes

- ? Induces anti-viral immune response

- Repeat in-office applications within 14-21 days may be necessary.

- Painless during (good for kids)

- No FDA approved (for now)

Bhatia, N, "An open-label exploratory study evaluating the efficacy and safety of ingenol mebutate gel 0.05% for the treatment of genital warts," J Am Acad Dermatol, Vol 78, Issue 3, 595-604

Bhatia, N, "An open-label exploratory study evaluating the efficacy and safety of ingenol mebutate gel 0.05% for the treatment of genital warts," J Am Acad Dermatol, Vol 78, Issue 3, 595-604

Other Medical Treatments for Warts

- Actavis Therapeutics A-101
- 45% Topical Solution Ph 2

- N=159, 1+6 warts, 56 days of twice weekly application in office

- PWA score measured diameter but not thickness or intact callus

- Mean reduction in PWA score at Day 66 on the target warts was

- 48.7 points in A-101

- 45% treated

- group vs reduction of 0.17 points for placebo group (p<0.001)

- Excluded plantar and perilungal

- ages 8 and up

- Cutanea CLS006 Furosemide

- Topical Gel, 0.125%

- N=480, 1+6 warts, 3-10 mm

- Daily application of gel at home

- Ages 2 and up

- Includes Periungal but not Plantar

- Rationale: Furosemide and Digoxin

- impair viral DNA synthesis by

- inhibition of cell membrane transport

- of Na+ and K+

- Creates intradermal K+ depletion and slows HPV proliferation


- Cantharidin

**Battle Molluscum**

- **CAMP-1**: 46% of patients had achieved completion lesion clearance at day 84 vs. 18% of placebo.

- **CAMP-2**: Pts on VP-102 54% clearance vs. 13% placebo.

  - No issues in terms of safety, no serious adverse events (SAE)

---

**Hyperthermic effects on HPV**

- Higher body temperatures can lead to high clearance rates of the HPV lesions (53% vs 11%).

- The PI3K Pathway (responsible for suppressing Langerhans activity) is downregulated during Hyperthermia: Allows Langerhans cells to detect the HPV infected cells.

---

**VP-102**

Percent of subjects with complete clearance of all treatable warts (baseline and new) at Day 84.

- Study drug (VP-102) is administered topically to each treatable wart to a maximum of 4 applications. Cohort 1 is treated until clear. Cohort 2 receives one additional treatment at the first visit clearance was observed up to a maximum of 4 total applications.

- Q14 days: no paring

- Q21 days until clear: paring beforehand

---

**CONCLUSIONS**

- VP-102 demonstrated efficacy in the reduction of the percentage of common warts from baseline to D84 as well as the rates of complete clearance of warts.

- VP-102 showed a favorable tolerability and safety profile. The most common treatment-emergent AEs were mild to moderate and included application site blistering, pain, pruritus, erythema, and scabbing. These were considered related to the pharmacodynamic action of cantharidin.

- Due to the higher complete clearance rate observed in Cohort 2 (51% complete clearance at D84), the treatment regimen of Cohort 2 will be utilized in future Phase 3 studies.
Non-ablative Immune Modulation

**FDA approval 2018**

- **MOA:** rapidly-elevating tissue temperature into the Hyperthermic Range: 43-46 C
- **Microwaves produce dielectric heating and cause rapid temperature elevation in tissue**
  - 50 J over a 7 mm diameter application area (130 J/cm²) over 5 seconds

**Conclusion:** Keratinocyte-skin dendritic cell cross-talk is integral to host defence against HPV infections, and this pilot study supports the concept of microwave induction of anti-HPV immunity which offers a promising approach for treatment of HPV-induced viral warts and potentially HPV-related cancers.

---

**Microwave energy rapidly elevates tissue temperature and creates precise, localized cell destruction**

**Figure 1.** Inoculated tissue can exist several micrometers below the surface and can therefore be difficult to treat using traditional methods, resulting in either untreated tissue or significant damage.

**Figure 2.** Microwaves travel into the tissue, water molecules begin colliding at the interface tissue causing localized heat energy – quickly destroying all infected tissue within a predetermined depth.

**Figure 3.** Swift delivery of highly controlled energy dose.

---

**Intralesional Versus Intramuscular Bivalent Human Papillomavirus Vaccine In the Treatment of Recalcitrant Common Warts**

- **N= 44 adults with recalcitrant warts**
- **Intralesional bivalent human papillomavirus (HPV) 16, 18 vaccine**
  - 2-week intervals up to 6 vs intramuscular bivalent HPV vaccine at 0, 1, and 6 months
- **Intralesional group (n=22), 81.8% complete clearance of warts compared vs 63.3% of those IM group (P=.287).**
- **Clearance rate of warts was significantly faster in the intralesional group (3.22 months vs 4.75 months; P=.005).**
- **AE: pain at the injection site and localized itching**

Courtesy Adam Friedman, MD

HPV vaccines for Warts

- Indicated for prevention of HPV-related cervical, vulvar, vaginal and anal cancer: 16, 18, 31, 33, 45, 52, and 58.
  - Cervical intraepithelial neoplasia (CIN) grade 2/3 & cervical adenocarcinoma in situ
  - Cervical intraepithelial neoplasia (CIN) grade 1
  - Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3
  - Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3
  - Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3
  - Genital warts (condyloma acuminata) caused by HPV types 6 and 11
- Gardasil quadrivalent vaccine now approved for ages 9-45 but no evidence for treatment

So what are the pearls?

- Wait at least a week after cryotherapy to start any topicals
- Topical anesthetics as needed
- Encourage callus reduction between destructions
- But what about Freeze and go? Costs costs costs...
Photodynamic Therapy 2020 Update

Neal Bhatia, M.D.
Director of Clinical Dermatology
Therapeutics Clinical Research, San Diego, CA
2020 AOCD Spring Meeting

Objectives for PDT day

Lecture
- Review MOA
- Acne and PDT 101
- New AK updates
- Extremities

Workshop
- Office Logistics
- Coding
- Skin Cancer updates
- Daylight vs. Office
- Video demo
- Discussion

MOA of PDT - 3 Essential Ingredients

Photosensitizer
concentrated in target tissue
10% or 20% ALA
Light Source
Variable wavelength and energy
Oxygen Molecules

PDT - MOA: ALA to PpIX Conversion

Hydrophilic solution
penetrates stratum corneum
ALA enters epidermal cells
ALA enters endogenous heme synthesis pathway
ALA converts to photosensitizer Protoporphyrin IX (PpIX)

PDT - MOA: Intracellular Events

Mitochondria
Nucleus
Mitochondria
ROS
O2
NADH
Mitochondria
Mitochondria
Cell death
Apoptosis
Necrosis
Autophagy

Dr. Bhatia’s Disclosures:

- Affiliations with Abbvie, Aclaris, Almirall, Bayer, Biofrontera, BiopharmX, Dermira, Encor, EPI Health, Ferndale, Foamix, Galderma, Intraderm, ISDIN, LaRoche-Posay, Led, Mayne, Menlo, Novartis, Ortho, Pfizer, Pierio-Fabre, Promius, Regeneron, Sanofi, Skinfix, Soligenix, SunPharma, and Vida
- 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


MacCormack D. 2007, Photodynamic Therapy, Advances in Dermatology, v. 22, p.220

Incubation and Light Strategies

- The label says incubate for 14 hours, meaning treat the day before and stay indoors to avoid activating the light.
- Reality says incubate for 2 hours if possible and 1 hour realistically.

Fluorokinetics of a Single AK Lesion

Temperature impacts Apoptosis

- Human skin fibroblasts treated with ALA as specific concentrations and temperatures.
- Cell death, apoptosis and superoxide ROS levels were quantified.
- Thermal PDT with 0.5 mmol L(-1) ALA resulted in significant temperature-dependent increases in total apoptosis and superoxide ROS generation between 33 °C and 42 °C.

Microneedle Photodynamic Therapy II (MNPDT-II) study

- Randomized, single-blinded, split-face controlled, n=32
  - ALA-BLU PDT, 20 min or 10 min incubation, after treatment with microneedle (200 um)
    - sham roller blind to laterality
    - measure AK resolution, and assess pain associated with microneedle pretreatment
  - 20-minute incubation: AK clearance was 76% vs 58% on the sham side (P < .01)
  - Pain assessment was not significantly different between the microneedle and sham sides (0.5, 0.6, P = .26, respectively)
  - 10-minute incubation: AK clearance was 43% vs. 38% on the sham side (P = .66)
  - Pain during the blue light exposure was not significantly different between the microneedle and sham sides, 4.5 mm and 3.4 mm (P = .21, respectively)

Conclusions: PDT with microneedle pretreatment at a 20-minute ALA incubation time significantly improved AK clearance and procedure was virtually painless, but 10-minute ALA incubation time did not result in significantly different AK clearance.

Why PDT for acne?

- P. acnes accumulates porphyrins
  - Mainly coproporphyrin and PpIX
  - High uptake of ALA and PpIX in sebaceous lobules
- Blue light activates porphyrin-induced cell death in the bacteria
- Anti-inflammatory effect on PMNs and lymphs
- Clinically:
  - When antibiotics either fail or patients refuse

PDT for Acne instead of Antibiotics

- ALA-PDT vs. Doxycycline + Adapalene
  - N=46 moderate inflammatory acne patients (18-30 years old)
  - ALA-PDT: 20% ALA solution (90 min w/ occlusion); red light illumination (37J/cm²) with 0.1% adapalene gel 1X daily for 6 wks
  - Antibiotics: 100mg/day doxycycline with 0.1% adapalene gel 1X daily for 6 wks

Timecourse:

- PDT #1: 3 weeks
- PDT #2: 6 weeks
- Antibiotic: 6 weeks
- Follow-ups: 6 weeks FU
ALA-PDT vs. Doxycycline + Adapalene

**Median Reduction in Number of Lesions**

**With PDT/adapalene:**
- pain during treatment (3/10)
- desquamation
- edema
- mild sterile purulent eruption
- transient acne flare

**With doxycycline/adapalene:**
- abdominal pain
- nausea/vomiting
- photosensitivity
- scaling
- erythema
- stinging/burning

**Adverse Events**

**Photodynamic Therapy Group**
-**With PDT/adapalene:**
  - pain during treatment (3/10)
  - erythema
  - desquamation
  - mild sterile purulent eruption
  - transient acne flare

**Antibiotics Group**
-**With doxycycline/adapalene:**
  - abdominal pain
  - nausea/vomiting
  - photosensitivity
  - scaling
  - erythema
  - stinging/burning

What about the acne meds?

In most of the studies on PDT and acne, the patients had a 7 day washout before tx.

Therefore:

- Cleanse and moisturize as normal
- Stop antibiotics the day before in case there are concerns, and there always are
- Avoid everything else the night before and day of treatment to reduce potential photosensitization
- Stop retinoids at least 3-5 days before to reduce post-PDT erythema, but maintain in regimen

Reference: Me, plus probably Jim and Hilary too

Poikiloderma of Civatte treated with PDT

**Objective:** evaluate PDT for the treatment of Poikiloderma of Civatte (PC)

**Case report:** n=1 (45 years) with PC

**ALA-PDT Protocol**
- Roughen skin with monofilamentous fiber pad
- 10% ALA gel
- 3-hour incubation w/ occlusion
- 635 nm/10 min = 37 J/cm²
- 2 sessions
- 14 days between both sessions

**Improvement in PC signs, mainly changes in pigmentation and better tolerance to sun exposure**

Navarro-F et al. Dermatologic Therapy 2018.e 12648

Efficacy of ALA-PDT in the Treatment of Actinic Keratoses on the Upper Extremities

**Post Hoc Analysis of Phase 3, Randomized Trial**
- 132/135 (97.8%) pts randomized to ALA-PDT; 130/134 (97.0%) VEH-PDT treatment completed the study

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<th>ALA-PDT (N=135)</th>
<th>VEH-PDT (N=134)</th>
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<td>Age, years, mean (SD)</td>
<td>67.6 (8.6)</td>
<td>67.6 (9.4)</td>
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<td>92 (68.1)</td>
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<td>Grade 1</td>
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<td>574 (49.9)</td>
<td>569 (49.5)</td>
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<td>Lesions per patient, mean (SD)</td>
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<td>8.6 (3.4)</td>
</tr>
<tr>
<td>Mean cumulative disease area, mm²</td>
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**Results**

Percent cumulative disease area cleared

Week 8 | Week 12
--- | ---
ALA-PDT | 37.2% | 56.8%
VEH-PDT | 31.4% | 41.0%

**More than half of patients treated with ALA-PDT experienced complete clearance of larger, lesions ≥ 25 mm² (92.0%) patients exhibited complete clearance of lesions 25 to 36 mm² and 25/42 (93.2%) patients exhibited complete clearance of lesions ≥ 36 mm².**
Simultaneous PDT

- Bilaterally controlled, intrapatient study, n=23 pts
- 20% ALA was applied to the entire face and/or scalp
- One side: blue light started immediately and continued for either 30, 45, or 60 min ("simultaneous PDT")
- Contralateral side, blue light began 1 h after ALA application and lasted 1000 sec ("conventional PDT")
- Pain was evaluated on a 0-10 scale. AK counts were determined by clinical exam and photography.

Conclusion: Simultaneous PDT regimen is essentially painless with efficacy similar to conventional PDT

The study was relatively small

Additional studies are recommended


Daylight PDT with 10% ALA vs. 16% MAL

- Randomized, observer-blind, intra-individual study
- N = 52 patients with 3-9 AKs on each side of face and scalp

Recurrence at 12 months

BF-200 ALA

MAL BF-200 ALA

Clinically visible lesions 79.8% 76.5% 19.9% 31.6%

Face only 85.2% 84.2% 20.1% 25.0%

Scalp only 74.2% 67.5% 23.4% 43.7%

Unfavorable Weather Conditions

Cloudy 80.1% 70.4% 15.9% 20.8%

Sunny 84.5% 73.5% 18.7% 39.9%

Temperature >20°C (>68°F) 79.5% 74.6% 18.6% 36.1%

PDT-associated Pain

(Mean VAS 0-10; BF-200 ALA arm)

1st PDT 5.5 1.2
2nd PDT 5.8 NA
Daylight PDT for Actinic Cheilitis

N=11 (3 females, 8 males) mean age 59; 2-3 treatments
• Biopsy to prove diagnosis and exclude SCC, repeated at end of study
• Sunscreen + Curettage of lip lesion + thick layer MAL uncovered
• 2-3 hrs of sun between 8-11 am then remained indoors

Adjuncts for pain control
- Refrigerated HOCl spray—apply daily for 7 days during treatment, 6 inches away from face and cover eyes
- Premedicate? Even after treatment? tolerated?
- Pramoxine 1% lotion every 4-6 hours, mix with emollients
- Stay indoors as long as possible for two days

Results
• Treated every 2-4 weeks until remission or intolerant
• Followed between 6-8 months
• Mild erythema and pain during exposure hours rarely lasted more than 2 days
• Small study but design allows for clinical relevance

A Split Face Evaluation of a Novel Topical Oxygen Emulsion on the Healing Process Following PDT

N=10; 9 male & 1 female; ages 52-76, Type [II], skin: baseline photos and AK count

Treatment protocol:
1. Alcohol gel followed by acetone prep; topical ALA entire face, 120 minutes
2. Photodynamic activation with BLU665 light source for 16 minutes; Zimmer chiller
3. Post-treatment written instructions; 48 hour UV avoidance
4. TOE applied to left face; Aquaphor to right face (R), bid, written leg
5. Patients returned for photo documentation frequently
6. Post-treatment questionnaire:
   a. Evaluate product’s effects on side effects: edema, erythema, stinging, pain
   b. Did one side heal faster?
   c. Would they request this additional PDT treatments?
7. Pre and post treatment photos compared for clinical post treatment side effects: erythema, edema, etc.
8. Efficacy of treatment based on lesion counts at 30 & 60 days
9. Follow up for 12 month evaluation

Results
• No AE’s (e.g. contact dermatitis, irritation) due to TOE
• Post treatment photos demonstrated a sharp contrast on the TOE side (L) compared to the control-Aquaphor side (R) at 24 hours with reduced edema and erythema, and subsequent days of 1st week
• Speed of healing was more rapid on the left face in all patients
• All patients reported an immediate cessation of burning and stinging post initial application (within 10 minutes) on the treated side
• Follow between 6-8 months
• Small study but design allows for clinical relevance
• Treatment side (L) did not demonstrate any reduced efficacy of AK clearance based on comparison of lesion counts
So now what?
- Antihistamines? Yes
  - 2 days before, twice day of, and two days after
- Occlusion and 3 hours for extremities? Yes
- Microneedling and PDT? Yes Get paid for it? Good luck
- Daylight PDT—Great idea? Yes Get paid for it? Good luck
- Does it work better with warmer skin? 2 hours incubation? Yes
- Does a PDT regimen reduce skin cancer risk? Yes
- Which product is better—10% gel or 20% stick? Really?

Treatment Day
- 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

TABLE 2. Photodynamic Therapy General Treatment Protocol
| Patient washes the area to be treated with soap and water. Acetone- or alcohol-soaked 4 x 4 gauze is used to remove any remaining debris and oil. The photosensitizer is usually applied to the entire area to be treated. A second coat of the photosensitizer can be applied, after the first coat has dried. Allow the photosensitizer to incubate for 0.5-4 hours (see below for more comprehensive recommendations). Activate the photosensitizer with the appropriate light source. Patient to wash the treated area with soap and water to remove any residual photosensitizer. The patient must stay out of the sun or direct sunlight for 48 h. | 
--- | --- |
| Incorporate Methods to Improve Outcomes with PDT | All PDT codes should be billed with the appropriate J code! |
| CHEMICAL | 
5-Fluorouracil Pretreatment
Retinoid Pretreatment
ALA Formulation (Carrier/Vehicle)
Debridement (microdermabrasion, Curettage)
Enhanced ALA Penetration, Cellular Uptake and PpIX Accumulation |
| PHYSICAL | 
Microneedling
Thermal
Fractional CO2
Cryosurgery Pretreatment

| 20% ALA | 10% ALA |
| J7308 | J7345 |

CPT Codes
- 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
  - This code should now ONLY be used only when a physician does not directly participate in the PDT treatment delivery.
- 96573 and 96574
  - The physician or other practicing clinician MUST apply the photosensitizer AND initiate the light illumination
  - 96574 is with curettage or debridement
  - The code means applying the ALA and turning on the light
  - Talckesesthesia and hand-holding are not included but make the experience better

Courtesy Mark Kaufmann, MD
5 Things to Remember

- Don’t shortchange incubation, make the patients do the time especially for extremities.
- Label indication for 20% ALA/Blue light is a modified version of daylight PDT, but turn it on (again)
- Every adjunct for pain control except steroids will help, even a little alprazolam keeps the doctor away
- PDT is probably our best chemoprevention strategy
- Acne and CTCL are the present not just the future

More to come in the PDT Workshop… stay tuned!
How to Meet the Challenges of Hyperhidrosis

Neal Bhatia, M.D.
Director of Clinical Dermatology Therapeutics Clinical Research San Diego, California 2020 AOCD Spring Meeting

Learning Objectives
- After participating in this activity, learners will be better able to:
  - Review the impact of HH on patient’s QOL
  - Use appropriate tools and scales to assess severity of HH
  - Understand the most commonly used and latest treatment approaches
  - Discuss strategies to personalize treatment approaches
  - Recognize the urgency of prompt treatment of HH

Why do we need to sweat?
- Perspiration allows for thermal regulation
- 2 to 4 million sweat glands
- Temperature rises → Sweating maintains cooling
- Physiological Triggers of Sweat:
  - Emotions: anger, fear, anxiety
  - Stimulants: exercise, alcohol, drugs, sex, caffeine, spicy food
  - Stressors: Pain, Fever, Illness, Cardiac, Neurogenic
- Hyperhidrosis vs. Excessive Sweating
  - Some physiologically sweat more often with triggers and stop
  - Hyperhidrosis is a faucet that does not turn off

Primary Focal Hyperhidrosis
- Visible and excessive sweating, >6 months duration
- No clear trigger or cause
- >70% sweat from more than one area: axillary, axilla, etc.
- At least 2 of these criteria:
  - Bilateral and relatively symmetric
  - Impairs daily activities
  - Age of onset less than 25 years
  - Positive family history
  - Cessation of sweating during sleep

Generalized Hyperhidrosis
- Generalized Secondary Hyperhidrosis involves sweating on larger surfaces or diffusely over the body
- Sweating often while sleeping
- Age of onset
  - Generalized hyperhidrosis often starts in adulthood
  - Primary hyperhidrosis usually starts in childhood or adolescence

Dr. Bhatia’s Disclosures:
- Affiliations with Brickell Biotech, Dermira
- Some slides from industry and www.sweathelp.org 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
- Several slides borrowed from Seemal Desai, MD

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  - Primary hyperhidrosis usually starts in childhood or adolescence
Quality of Life

- Published surveys: multifocal hyperhidrosis is more common than singular focal hyperhidrosis
- 81% of patients reported 3 or more focal hyperhidrotic sites
- Symptom severity does not improve with age
- Stays the same or gets worse without seasonal variation


Hyperhidrosis Clinical Trials Endpoints

- Subjective measuring scales:
  - Hyperhidrosis Disease Severity Score (HDSS): severity rating
  - Hyperhidrosis Disease Severity Measure Axillary (HDSM-Ax): subjective outcome, symptom overview, and disease impact
- Primary endpoints:
  - dose-related 2-grade improvement in HDSS statistically significant
  - 2-grade improvement in the HDSM-Ax
- Adverse Events of Special Interest (AESI):
  - Urinary Retention, Mydriasis, Arrhythmias, Xerostomia, CNS Stimulation

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- Primary endpoints:
  - dose-related 2-grade improvement in HDSS statistically significant
  - 2-grade improvement in the HDSM-Ax
- Safety and Tolerability at all concentrations
- Adverse Events of Special Interest (AESI):
  - Urinary Retention, Mydriasis, Arrhythmias, Xerostomia, CNS Stimulation

Current and Future Treatments

Medical

- Topical
  - Antiperspirants
  - Glycopyrrolate cloths
  - Sofipronium gel
- Systemic
  - Glycopyrrolate
  - Oxybutynin
  - Beta blockers
- Iontophoresis
- Minimally invasive
- Neuromodulator injections
- Microwave Thermolysis
- Destruction of axillary glands
- Surgical
  - Excision of axillary glands
  - Thoracic Sympathectomy

Antiperspirants 101

- Aluminum Chloride MOA: aluminum salt blockage of the distal acrosyringium
- Leads to functional and structural degeneration of the eccrine acini
- Aluminum Zirconium Trichlorohydrex
- Less irritating than aluminum chloride
- Antiperspirant soft-solid formula
- Apply bid and qHS with gentle massaging into dry skin
- Increased irritation if skin is wet
- No benefit to occlusion

Glycopyrillum Tosylate: Mechanism of Action

- Inhibits sweat gland activation by blocking acetylcholine receptor
- Glycopyrillum tosylate (GT) acts as a cholinergic receptor antagionist
- GT inhibits interaction between acetylcholine and cholinergic receptors responsible for sweat gland activation and sweat production

Study Design

ATMOS-1 and ATMOS-2

ATMOS-1 and ATMOS-2 were Phase 3, randomized, double-blind, vehicle-controlled trials. ATMOS-1 and ATMOS-2 were Phase 3, randomized, double-blind, vehicle-controlled trials. ATMOS-1 and ATMOS-2 were Phase 3, randomized, double-blind, vehicle-controlled trials. ATMOS-1 and ATMOS-2 were Phase 3, randomized, double-blind, vehicle-controlled trials. ATMOS-1 and ATMOS-2 were Phase 3, randomized, double-blind, vehicle-controlled trials.

Antiperpersant 101

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- Antiperspirant soft-solid formula
- Apply bid and qHS with gentle massaging into dry skin
- Increased irritation if skin is wet
- No benefit to occlusion
Sofpironium Bromide

Brickell Biotech, Inc: BBI-4000

**Common TEAEs Reported in ≥25% of Patients**

<table>
<thead>
<tr>
<th>TEAEs</th>
<th>AI MOS-1</th>
<th>AI MOS-2</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common TEAEs, n (%)</td>
<td>n=114</td>
<td>n=113</td>
<td>n=227</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>4 (3.5)</td>
<td>3 (4.0)</td>
<td>10 (4.4)</td>
</tr>
<tr>
<td>Paresthesia, ear pain</td>
<td>11 (9.6)</td>
<td>1 (0.9)</td>
<td>13 (5.7)</td>
</tr>
<tr>
<td>Mydriasis</td>
<td>5 (4.5)</td>
<td>5 (4.5)</td>
<td>10 (4.4)</td>
</tr>
<tr>
<td>Orthognathal pain</td>
<td>1 (0.9)</td>
<td>1 (0.9)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (0.9)</td>
<td>3 (2.7)</td>
<td>4 (1.8)</td>
</tr>
</tbody>
</table>

- Commonly reported TEAEs in the GT group included some events associated with anticholinergic activity (dry mouth, mydriasis)

**Proposed Mechanism of Action**

- **Soft drugs**
  - *active* antihyperthermic analogues of a lead compound
  - deacivated after achieving their therapeutic peak
  - designed to be rapidly metabolized into inactive species

- **Sofpironium Bromide**
  - *soft glycopyrrolate* analog (anti-cholinergic) active only at the local site of administration, hydrolyzed upon reaching the systemic circulation
  - Inhibits binding of neurotransmitter acetylcholine to cholinergic receptor
  - Proposed to suppress eccrine sweat stimulation

**Phase II studies**

- 23 sites, n=227, randomized 1:1:1:1 sofipironium bromide gel, 5%, 10%, 15% or vehicle qd to the axillae for 42 days
- Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax) scores of 3 or 4 (scale, 0-4)
- Combined axillary gravimetric sweat production (GSP) of 150 mg/5 minutes

**The 15% dose was more efficacious than the other doses, while the 5% dose was better tolerated**
Sofpironium bromide application resulted in statistically significant higher response rates as measured by the HDSM-Ax at end of therapy.

Sofpironium bromide application resulted in significantly higher response rates as measured by the HDSM-Ax as early as Day 8 and sustained over time.
Coding algorithms for Hyperhidrosis

- ICD-10: L74.510
- CPT Codes for Neuromodulators
  - Face/Head Primary Hyperhidrosis: 64653
  - Plantar and/or Palmar Primary Hyperhidrosis: 64999
  - Axillary Primary Hyperhidrosis: 64650
  - Botulinum toxin: J0585
- CPT Codes for Treatment of Hyperhidrosis with Iontophoresis: for each 15-minute session 97033

Courtesy Seemal Desai MD
How Do Biologics Fit in an Integrative Treatment Plan?
Neal Bhatia, M.D.
Director of Clinical Dermatology Therapeutics Clinical Research, San Diego, CA
2020 AOCD Spring Meeting

Dr. Bhatia’s Disclosures:
- Affiliations with Aclaris, Almirall, Biofrontera, BiopharmX, Dermira, Encore, EPI Health, Ferndale, ISDIN, LaRoche Posay, Leo, Mayne, Menlo, Novartis, Ortho-Derm, Pierre-Fabre, Pfizer, Regeneron/Sanofi, and Sun Pharma
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- Copies of pdf or questions: bhatiaharbor@gmail.com
- Acknowledgements: Mark Lebwohl, M.D
  Bruce Strober, M.D., PhD
  Leon Kircik, M.D.

Objectives
- Who’s afraid of Big Bad Biologics?
- How do these treatments “naturally” work?
- Who, When, and Why? And more importantly, Why Not?
- Talking points for getting patients and physicians off the ledge of phobia and misconception
- Prescribing considerations: gender, weight, age
  - Comorbidities
  - Logical Candidates

How can we justify treating severe patients with topical therapy alone?

Risks of Undertreating Psoriasis
- Pts with psoriasis (n=18,353) ages ≥20-35 hospitalized
- Comparative analysis comparing associations between sex, age, extent of metabolic and vascular disease (atherosclerosis and/or venous thromboembolic disease.
  - Also compared with those matched patients without psoriasis
- Overall psoriasis pts were more often:
  - Obese (16% vs. 6%); and/or smokers (31% vs. 17%); dx diabetes mellitus (10% vs. 6%), hypertension (16% vs. 8%), and hyperlipidemia (6% vs. 2%)
  - ASCVD (2.2% vs. 1.6%), and deep vein thrombosis (6% vs. 4%)

Risks of Undertreating Psoriasis

- When stratified by sex:
  - Women with psoriasis were more likely to have multiple cardiovascular risk factors and ASCVD odds 2.6 vs. 1.2 men

Conclusion: Psoriasis was associated with cardiovascular disease and risk factors in young hospitalized patients, with stronger associations among women than among men.


Costs aside... Why are only ~20% of dermatologists prescribing biologics?

- Black Box Warnings?
  - MTX and CSA have more than any biologic agent

- Safety?
  - GI, Rheum, and Oncology don’t hesitate to treat aggressively

- Efficacy?
  - Topical therapies and Systemic Immunomodulators do not mechanically address the big picture of psoriasis

- Addressing all Metabolic issues and Comorbidities should be a Dermatologist’s priority.

5 WARNINGS AND PRECAUTIONS

5.1 Depression

Treatment of OTEZLA was associated with an increase in adverse reactions of depression. During the 0 to 16 week placebo-controlled portion of the 3 controlled clinical trials, 1.0% (15/1,500) of patients treated with OTEZLA reported depression or decreased mood compared to 0.4% (4/945) treated with placebo. During the clinical trials, 0.7% (11/1,441) of patients treated with OTEZLA discontinued treatment due to depression or decreased mood compared to none in placebo-treated patients (0/945). Depression was reported as serious in 0.3% (5/1,441) of patients exposed to OTEZLA, compared to none in placebo-treated patients (0/945). Incidences of suicidal ideation and behavior were not increased in OTEZLA-treated patients with depression.

Before starting OTEZLA in patients with a history of depression and/or suicidal thoughts or behavior, prescribers should carefully weigh the risks and benefits of treatment with OTEZLA in such patients. Patients, their caregivers, and families should be advised of the need to be alert for the emergence or worsening of depressive, suicidal thoughts or other mood changes, and if such changes occur to contact their healthcare provider. Prescribers should carefully evaluate the risks and benefits of continuing treatment with OTEZLA in such events occur.

Courtesy Leon Kircik, M.D.

Biologic Agents

- TNF Inhibitors
  - Adalimumab
  - Etanercept
  - Infliximab
  - Certolizumab

- IL-17 Inhibitors
  - Secukinumab
  - Ixekizumab
  - Brodalumab (receptor)

- IL-12/23 Inhibitors
  - Ustekinumab
  - Guselkumab
  - Tildrakizumab
  - Risankizumab

- What’s coming?
  - Minkizumab (IL-23)
  - Bimabkizumab (IL-17)

Studies have shown the patients with psoriasis are 33% more likely to attempt suicide and 20% more likely to commit suicide than those without psoriasis.

Those who are younger and have more severe psoriasis are at the greatest risk of committing suicide.

The level of IL-17 is significantly higher in activated T cells among those with anxiety or depression compared with controls.

T cell functional dysregulation may contribute, at least in part, to the higher risk of mental disorder in patients with psoriasis.

SILIQ [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC.Courtesy Leon Kircik, M.D.
If not biologics, then what?

- Topical Therapy
  - Steroids
  - Calcipitriol
  - Tazarotene
  - Calcineurin Inhibitors
  - Combo products
  - Coal Tar
  - OTC

- Phototherapy
  - UVB/nb-UVB/PUVA

- What’s coming?
  - JAK Inhibitors
  - JAK 1, 2
  - JAK/TYK combo

- Small Molecules
  - Methotrexate
  - Cyclosporine
  - Acitretin
  - Apremilast

- Combo products

- Topical Therapy
  - Steroids
  - Calcipitriol
  - Tazarotene

- Immunosuppressive?

Mechanism of Methotrexate

- Innate immunity
  - Keratinocyte
  - Th1 cell
  - TNF-
  - INF-
  - Th22 cell
  - IL-17A
  - IL-17F
  - Th17 cell
  - IL-17F

- Adaptive immunity
  - Natural killer T cell
  - IL-23
  - TNF-
  - INF-
  - Th17 cell
  - IL-20

- Macrophage
  - IL-6
  - TNF-

Mechanism of Cyclosporine

- Innate immunity
  - Keratinocyte
  - Th1 cell
  - TNF-
  - INF-
  - Th22 cell
  - IL-17A
  - IL-17F

- Adaptive immunity
  - Natural killer T cell
  - IL-23
  - TNF-
  - INF-
  - Th17 cell
  - IL-20

- Macrophage
  - IL-6
  - TNF-

Mechanism of TNF blockers

- Innate immunity
  - Keratinocyte
  - Th1 cell
  - TNF-
  - INF-
  - Th22 cell
  - IL-17A
  - IL-17F

- Adaptive immunity
  - Natural killer T cell
  - IL-23
  - TNF-
  - INF-
  - Th17 cell
  - IL-20

- Macrophage
  - IL-6
  - TNF-

Mechanism of Ustekinumab

- Innate immunity
  - Keratinocyte
  - Th1 cell
  - TNF-
  - INF-
  - Th22 cell
  - IL-17A
  - IL-17F

- Adaptive immunity
  - Natural killer T cell
  - IL-23
  - TNF-
  - INF-
  - Th17 cell
  - IL-20

- Macrophage
  - IL-6
  - TNF-

Mechanism of Secukinumab, Ixekizumab & Brodalumab

- Innate immunity
  - Keratinocyte
  - Th1 cell
  - TNF-
  - INF-
  - Th22 cell
  - IL-17A
  - IL-17F

- Adaptive immunity
  - Natural killer T cell
  - IL-23
  - TNF-
  - INF-
  - Th17 cell
  - IL-20

- Macrophage
  - IL-6
  - TNF-

Adaptive immunity

Keratinocyte

Natural killer T cell (NK)

Adaptive immunity

Myeloid dendritic cell

Macrophage

IL-17A

IL-17F

IL-17R

IL-12

Antimicrobial peptides

IL-6

TNF-α

S100

CXCL8

CXCL9

CXCL10

CXCL11

CCL20

Activation

Natural killer T cell

Keratinocyte

Myeloid dendritic cell

Plasmacytoid dendritic cell

Macrophage

IL-1

IL-6

TNF-α

INF-γ

Th1 cell

Th2 cell

Th17 cell

Expression

Keratinocyte

Activated via TNF


How do these things work?

Janus Kinase Inhibitors

1. Cytokine binding to its cell surface receptor leads to receptor polymerization.
2. Tofacitinib inhibits the phosphorylation and activation of JAKs.


Janus Kinase...Signal Transducer and Activator of Transcription (JAK-STAT)

• Pathway utilized to transmit extracellular signals to the nucleus.
• Dysregulation of this pathway is responsible for immune deficiency syndromes and myeloproliferative neoplasms.
• Phosphorylation after ligand binding leads to translocation and gene expression regulation.
• JAK/STAT pathway suppresses:
  - dendritic cell activation, T-cell mediated inflammation

4 JAK (1,2,3, TYK 2) and 6 STAT (1-6) interact to send cytokine signals to nucleus

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Starting Lineup:

- JAK 1
- STAT 1
- JAK 2
- STAT 2
- JAK 3
- STAT 3
- JAK 4
- STAT 4
- STAT 5a
- STAT 5b
- STAT 6

Phosphorylation after ligand binding leads to translocation and gene expression regulation.

JAK/STAT pathway suppresses:

- dendritic cell activation, T-cell mediated inflammation

Copyright Steven Hays, Pharm D, Pfizer Medical Information

How do these things work?

Janus Kinase Inhibitors

1. Cytokine binding to its cell surface receptor leads to receptor polymerization.
2. Tofacitinib inhibits the phosphorylation and activation of JAKs.
3. JAKs cannot phosphorylate the cytokine receptors.
4. Therefore, the receptors can no longer signal to the nucleus.
5. Since the STATs cannot dock, they are not phosphorylated or activated.
6. Gene transcription and cytokine production is thereby inhibited.

Copyright Steven Hays, Pharm D, Pfizer Medical Information
**Are these safe?**

- Perform all immunizations before starting
- Rare elevations of lipids (total, HDL, LDL)
- no reported strokes or worse
- Pancytopenia worse
- JAK2 signaling mediated by erythropoietin, thrombopoietin, and GCSF
- Low CA risk across specialties
- Monitoring — TB test to start and annually
- Lipids and LFTs 4–8 wks after start
- CBC/diff at start and 4–8 wks then q 3 mo

**Lipid Levels in Patients with PsA reported elevations with Tofacitinib**

- n=783 pts, pooled data from two phase 3 studies and an ongoing long-term extension study
- Assessed fasting lipid levels, blood pressure, and MACE
- Percentage increases of LDL and HDL ranged from 9% to 14% for 5 mg and 10 mg doses of tofacitinib at 3 and 6 mo
- No meaningful changes in LDL/HDL or total cholesterol/HDL ratios.

**Risks more concerning in Transplant Patients?**

- Concern with JAK inhibitors is a theoretical increased risk for malignancy—dampen antitumor surveillance?
  - Initial studies of tofacitinib in renal transplantation:
    - 1% of patients treated with tofacitinib developed post-transplant lymphoproliferative disorder
    - Myelofibrosis and polycythemia vera treated with ruxolitinib
  - No increased risk for developing a second malignancy has been shown
- Topical JAK inhibitors
  - Monotherapy in less severe disease (Vitiligo, AD, patchy AA)
  - Potential maintenance therapy after oral treatment
- Safer options for children (Vitiligo, AD, AA) would prefer to topical if viable and avoid systemic side effects.

**Higher S. aureus frequency associated with higher severity in Atopic Dermatitis**

- Lower S. aureus frequency at baseline predicts (p<0.03) higher probability for a sustained EASI response 14 days after end-of-treatment, and in consequence significantly (p<0.001) predicts lower EASI at day 43
- A significant (p=0.005) dose-dependent decline in S. aureus frequency in LS was exhibited at day 29 in 86% of patients, in comparison to placebo (33%), and correlated with EASI decline (R=0.7, p=0.003)

**Conclusions:**

- JAK/SYK inhibition with ASN002 not only improves clinical scores and Th2/Th22 inflammation markers but also reducing S. aureus frequency in lesion
- Conversely, lower baseline S. aureus frequency in lesion correlated with ASN002 sustained efficacy post-treatment.
**Which complementary therapies are effective in treating psoriasis?**

- Up to 51% of patients with psoriasis use complementary and alternative medicine (CAM) in their treatment regimen
- 57 trials and 3 meta-analyses
- Most robust evidence of efficacy:
  - Indigo Naturalis
  - Curcumin
  - Dietary modification
  - Fish Oil
  - Meditation and Acupuncture

**What dietary interventions help patients with psoriasis?**

- 55 studies and 4534 patients with psoriasis
- Hypocaloric diet in overweight and obese patients with psoriasis
- Gluten-free diet and supplementation with vitamin D varies by subpopulations of adults with psoriatic diseases
- Evidence is low for the utility of specific foods, nutrients, and dietary patterns in improving psoriasis.

**Impact of body weight on efficacy of tildrakizumab at 12 weeks in moderate to severe chronic plaque psoriasis**

- Pooled analysis from 3 RCTs: reSURFACE 1 and 2 and P05495
- 1st endpoint: reSURFACE 1/2, PASI 75 and PGA 0/1 at Week 16
- Study P05495, PASI 75 at Week 16
- Randomized patients stratified by body weight (<90 kg, >90 mg: ≤100 kg, >100 mg)
- Authors concluded that PASI and PGA responses were numerically greater in patients with lower vs higher body weight

**Weight and Efficacy of Biologics**

- Obesity is an under-reported predictor of inferior response to anti-TNF agents
- 54 cohorts including 19,372 patients (23% obese)
- Patients with obesity had 60% higher odds of failing therapy
- Dose-response relationship was observed (obese vs. normal BMI: overweight vs. normal BMI: 1kg/m2 increase in BMI was associated with 6.5% higher odds of failure)
- Obesity as an effect modifier in clinical trials is warranted, and intentional weight loss may serve as adjunctive treatment in patients with obesity failing anti-TNF therapy.

**Which of these will help Biologics?**

**Antioxidants**

- EPA: Eicosapentaenoic acid
- Omega-3 fatty acid derived from fish oil
- Regulates inflammation in the body
- Support's skin resistance against UV-induced sunburn
- Zeaxanthin
- Powerful antioxidant derived from paprika
- Protects the skin from free radical damage
- Filters high energy light
- Lutein
- Powerful antioxidant derived from marigold flowers
- Like zeaxanthin, protects skin from free radical damage and filters high energy light
- Vitamin D
- Same form as produced in the skin when exposed to sunlight
- Helps reduce skin inflammation

**PASI 90 responses with guselkumab and adalimumab stratified by patient weight**

- PASI 90 at Week 16
- Patient weight: ≤76 kg, >76 kg
- Placebo, Adalimumab, Guselkumab
- Weight quartile
- PASI 90 at Week 24

*From VOYAGE 1 & 2*
Who are logical candidates for Biologics?

- Women of Childbearing potential: washout, avoid post-flare
- Patient with medical benefit (e.g. medicare) but incomplete (or no) pharmacy benefit
- Patient with medicare part D who can’t afford the donut hole
- Frequent traveler: Military, Travel for work, College age
- Institutionalized patients: prison, psychiatric, etc.
- Elderly who cannot self-inject or take own pills
Psoriasis: Which Drug for Which Patient?

Mark Lebwohl, MD

Waldman Professor
And Chairman
Kimberly and Eric J. Waldman Department of Dermatology
Icahn School of Medicine at Mount Sinai

Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial.

Mease PJ, et al.

Etanercept ACR Response at 3 Months

Sharp score or van der Heijde score measures joint damage on x-ray: narrowing and erosions

Biannual radiographic assessments of hands and feet in a three-year prospective follow-up of patients with early rheumatoid arthritis.
Etanercept Inhibited Bone Erosion

Mean Change in Erosion Score at 12 Months

<table>
<thead>
<tr>
<th>Group</th>
<th>Change from Baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=104)</td>
<td>0.66</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Etanercept (n=101)</td>
<td>-0.09</td>
<td></td>
</tr>
</tbody>
</table>

*stratified rank test


Etanercept Inhibited Joint Space Narrowing

Mean Change in JSN Score at 12 Months

<table>
<thead>
<tr>
<th>Group</th>
<th>Change from Baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=104)</td>
<td>0.34</td>
<td>0.044*</td>
</tr>
<tr>
<td>Etanercept (n=101)</td>
<td>0.05</td>
<td></td>
</tr>
</tbody>
</table>

*stratified rank test


Etanercept Inhibited Structural Damage

Mean Change in Total Sharp Score at 12 Months

Primary Radiographic Endpoint

<table>
<thead>
<tr>
<th>Group</th>
<th>Change from Baseline</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=104)</td>
<td>1.00</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Etanercept (n=101)</td>
<td>-0.03</td>
<td></td>
</tr>
</tbody>
</table>

*stratified rank test


Adalimumab Effectiveness in Psoriatic Arthritis Trial Study Group. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial.

Mease PJ, et al.

The Infliximab Multinational Psoriatic Arthritis Controlled Trial (IMPACT): results of radiographic analyses after 1 year.

Kavanaugh A, et al.


Effect of certolizumab pegol on signs and symptoms in patients with psoriatic arthritis: 24-week results of a Phase 3 double-blind randomised placebo-controlled study (RAPID-PsA)


Ustekinumab, an anti-IL-12/23 p40 monoclonal antibody, inhibits radiographic progression in patients with active psoriatic arthritis: results of an integrated analysis of radiographic data from the phase 3, multicentre, randomised, double-blind, placebo-controlled PSUMMIT-1 and PSUMMIT-2 trials.


ACR20/50/70 Responders at Week 24


*\(p<0.001\)

**Primary Endpoint**

PSUMMIT 1

Ustekinumab

<table>
<thead>
<tr>
<th></th>
<th>0.0</th>
<th>0.2</th>
<th>0.4</th>
<th>0.6</th>
<th>0.8</th>
<th>1.0</th>
<th>1.2</th>
<th>1.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 52</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Placebo (n=310)

UST 45 mg (n=308)

UST 90 mg (n=309)

**FUTURE 2**

ACR20 Response Through Week 52

Secukinumab

TNFi-Naive

- Secukinumab 75 mg SC (n=65)
- Secukinumab 150 mg SC (n=63)
- Placebo (n=63)
- Secukinumab 300 mg SC (n=67)
- Secukinumab 75 mg SC (n=34)
- Secukinumab 150 mg SC (n=37)
- Placebo (n=35)
- Secukinumab 300 mg SC (n=33)

**FUTURE 2**

ACR50 and ACR70 Response Through Week 52

Secukinumab

TNFi-Naive

- ACR50
- ACR70

*Patients who did not receive UST are excluded

Missing values were imputed as nonresponse (nonresponder imputation) through Week 52.


ACR20=American College of Rheumatology 20% improvement; SC=subcutaneous; TNFi=tumor necrosis factor inhibitor.

*\(P<0.0001\); \(P<0.001\); §\(P<0.01\); \(P<0.05\) vs placebo.

Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1.


FUTURE 1: Radiographic progression in PsA patients stratified by MTX use

Baseline to Week 24 (full analysis set)

Week 24 to Week 52 (X-ray completers)

<table>
<thead>
<tr>
<th></th>
<th>MTX: Yes</th>
<th>MTX: No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pooled SHB doses</td>
<td>ePRO</td>
<td>Pooled SHB doses</td>
</tr>
<tr>
<td>Mean change in mTSS</td>
<td>Overall population</td>
<td>MTX: Yes</td>
</tr>
<tr>
<td>0.21</td>
<td>0.29</td>
<td>0.25</td>
</tr>
<tr>
<td>0.21</td>
<td>0.29</td>
<td>0.25</td>
</tr>
</tbody>
</table>

*\(P<0.05\) vs PBO

Change in mTSS >0.5 considered progression of radiographic disease

Gottlieb AB, et al. EADV 2015, P0348 Sponsored by Novartis Pharma AG

Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebo-controlled and active (adalimumab)-controlled period of the phase III trial SPIRIT-P1.


Brodalumab Phase 2 PsA study: Clinical response and improvement in psoriasis in subjects with PsA

Mease P, et al. AAD 2014, P7605

ACR20 response rate at Week 24

<table>
<thead>
<tr>
<th></th>
<th>PBO (n=50)</th>
<th>BRO 140 mg q2w (n=57)</th>
<th>BRO 280 mg q2w (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (% SE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
<tr>
<td>4</td>
<td>0.52</td>
<td>0.29</td>
<td>0.10</td>
</tr>
<tr>
<td>8</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
<tr>
<td>12</td>
<td>0.52</td>
<td>0.29</td>
<td>0.10</td>
</tr>
<tr>
<td>24</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
</tbody>
</table>

* Indicates time point at which all subjects began receiving BRO 280 mg q2w

Therapeutic response of PsA to TNFi and brodalumab

- No head-to-head trials
- BRO trial is Phase 2, not placebo controlled
- Others are Phase 3 and placebo controlled

DISCOVER-2

ACR 20/50/70 Responses at Week 24

GUSELKUMAB

<table>
<thead>
<tr>
<th></th>
<th>PBO (n=246)</th>
<th>GUS 100 mg q8w (n=248)</th>
<th>GUS 100 mg q4w (n=245)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Responders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACR20</td>
<td>32.9</td>
<td>14.2</td>
<td>4.1</td>
</tr>
<tr>
<td>ACR50</td>
<td>63.7</td>
<td>33.1</td>
<td>18.5</td>
</tr>
<tr>
<td>ACR70</td>
<td>64.1</td>
<td>31.5</td>
<td>13.1</td>
</tr>
</tbody>
</table>

DISCOVER-2

ACR 20 Responses Through Week 24 (Secondary Endpoint)

<table>
<thead>
<tr>
<th></th>
<th>PBO (n=246)</th>
<th>GUS 100 mg q8w (n=248)</th>
<th>GUS 100 mg q4w (n=245)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Responders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
<tr>
<td>4</td>
<td>0.52</td>
<td>0.29</td>
<td>0.10</td>
</tr>
<tr>
<td>8</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
<tr>
<td>12</td>
<td>0.52</td>
<td>0.29</td>
<td>0.10</td>
</tr>
<tr>
<td>24</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
</tbody>
</table>

DISCOVER-2

LS Mean Change From Baseline in PsA-modified vdH-S Score at Week 24 (Controlled Major Secondary Endpoint)

<table>
<thead>
<tr>
<th></th>
<th>PBO (n=246)</th>
<th>GUS 100 mg q8w (n=248)</th>
<th>GUS 100 mg q4w (n=245)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS Mean Change From Baseline</td>
<td>0.95</td>
<td>0.52</td>
<td>0.29</td>
</tr>
</tbody>
</table>

*Adjusted p-value vs. placebo.
**Efficacy: ACR20, Primary Endpoint**

![Graph showing ACR20 response rates across different treatment groups.](image)

**Efficacy: ACR50/70**

![Graph showing ACR50/70 response rates across different treatment groups.](image)

**Efficacy: Enthesitis**

<table>
<thead>
<tr>
<th>Total LEI Score</th>
<th>Baseline, mean ± SD</th>
<th>6 weeks</th>
<th>12 weeks</th>
<th>26 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>BKZ 200 mg Q4W</td>
<td>3.1 ± 1.7</td>
<td>2.8 ± 1.7</td>
<td>2.8 ± 1.7</td>
<td></td>
</tr>
<tr>
<td>BKZ 200 mg Q12W</td>
<td>3.2 ± 1.8</td>
<td>3.1 ± 1.7</td>
<td>2.8 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>BKZ 100 mg Q12W</td>
<td>3.2 ± 1.8</td>
<td>3.1 ± 1.7</td>
<td>2.8 ± 1.8</td>
<td></td>
</tr>
<tr>
<td>BKZ 20 mg Q12W</td>
<td>3.1 ± 1.7</td>
<td>3.2 ± 1.8</td>
<td>3.1 ± 1.7</td>
<td></td>
</tr>
<tr>
<td>PBO</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05 compared with PBO. Data represents % change from baseline ± SD.

---

**ACR50 response rates at Week 12 (NRI)**

![Graph showing ACR50 response rates at Week 12.](image)

**ACR20 and ACR70 response rates at Weeks 12 and 48 (NRI)**

![Graph showing ACR20 and ACR70 response rates at Weeks 12 and 48.](image)
**Bimekizumab BE ACTIVE study**

**PASI90 response rates increased up to Week 24 and were maintained through the study (NRI)**

![Graph showing PASI90 response rates](image)

- **Week 12**
  - Placebo: 20.7%
  - BKZ 160 mg: 53.8%
  - BKZ 320 mg: 68.2%
  - BKZ 160 mg (320 mg LD): 70.0%

**Week 48**
- Placebo: 28.6%
- BKZ 160 mg: 56.5%
- BKZ 320 mg: 69.6%
- BKZ 160 mg (320 mg LD): 70.4%

**Percentage of patients with resolution of enthesitis at Weeks 12 and 48 (NRI)**

![Graph showing percentage of resolution of enthesitis](image)  

- Placebo: 7.1%
- BKZ 160 mg: 20.7%
- BKZ 320 mg: 46.4%

**Adverse events for special monitoring up to Week 48**

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Placebo (n=42)</th>
<th>BKZ 16 mg (n=41)</th>
<th>BKZ 320 mg (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>0</td>
<td>1 (2.4)</td>
<td>2 (4.9)</td>
</tr>
<tr>
<td>Malignancies</td>
<td>0</td>
<td>0</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oral candidiasis</td>
<td>0</td>
<td>1 (2.4)</td>
<td>1 (2.4)</td>
</tr>
<tr>
<td>Candida infections</td>
<td>0</td>
<td>6 (12.2)</td>
<td>4 (10.2)</td>
</tr>
<tr>
<td>Fungal oesophagitis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total adverse events</td>
<td>0</td>
<td>6 (12.2)</td>
<td>10 (25.6)</td>
</tr>
</tbody>
</table>

- There were no cases of inflammatory bowel disease, major cardiovascular events or hypersensitivity and anaphylactic reactions during the study.
- All candida infections were of mild or moderate intensity and did not lead to treatment discontinuation.

**Longterm methotrexate therapy in psoriatic arthritis: clinical and radiological outcome.**

- Abu-Shakra M, et al.
- Mtx does not prevent joint damage on x-ray.

**CHAMPION: Effect of BMI on the efficacy of adalimumab**

- Weight response analysis
- Body weight correlated to lower levels of response in CHAMPION, including in placebo group

**CHAMPION: Effect of BMI on the efficacy of adalimumab**

- Weight response analysis of CHAMPION: Effect of BMI on the efficacy of adalimumab.
- Compared to normal weight, overweight, or obese at baseline

**CHAMPION: Effect of BMI on the efficacy of adalimumab**

- Effect of BMI on the efficacy of adalimumab
- Weeks 12 and 50 response in patients, stratified by normal weight, overweight, or obese at baseline

**Apremilast, an oral phosphodiesterase 4 inhibitor, in patients with psoriatic arthritis and current skin involvement: a phase III, randomised, controlled trial (PALACE 3).**

PASI 75 Response by Treatment Week According to Baseline Body Weight Group, NRI
Induction Period, ITT Population (UNCOVER-2)

Across all baseline body weight categories, IXE-treated patients achieved significantly greater PASI 75 response rates vs. PBO at Week 12

PASI 90 Response by Treatment Week According to Baseline Body Weight Group, NRI
Induction Period, ITT Population (UNCOVER-2)

Across all baseline body weight categories, IXE-treated patients achieved significantly greater PASI 90 response rates vs. PBO at Week 12

PASI 100 Response by Treatment Week According to Baseline Body Weight Group, NRI
Induction Period, ITT Population (UNCOVER-2)

Across all baseline body weight categories, IXE-treated patients achieved significantly greater PASI 100 response rates vs. PBO at Week 12
Skin Clearance Response Rates improve over time on treatment with Brodalumab 210 mg Q2W in Non-obese and Obese Patients

- Rates of achieving sPGA 0/1, PASI 75, PASI 90, and PASI 100 were higher among nonobese patients than obese patients at weeks 12 and 52.
- The percentage of patients achieving PASI 100 increased from week 12 to week 52 in both nonobese and obese patients.

The safety associated with brodalumab 210 mg Q2W was comparable between nonobese and obese patients (data not shown).

Impact of body weight on efficacy of tildrakizumab at 12 weeks in moderate to severe chronic plaque psoriasis

- Pooled analysis from 3 RCTs: reSURFACE 1 and 2 and P05495 reSURFACE 1/2, PASI 75 and PGA 0/1 at Week 16.
- Randomized patients stratified by body weight (≥90 kg, >100 kg, ≤100 kg, >100 mg).

Authors concluded that PASI and PGA responses were numerically greater in patients with lower vs higher body weight.

Scott E, et al. EADV 2017, P1722 Sponsored by Merck & Co., Inc.

ESTEEM 1 & 2/PALACE 1–3: Long-term pooled safety of apremilast (≥156 weeks): Body weight assessments

<table>
<thead>
<tr>
<th>Assessment</th>
<th>0 to 52 wks n=1844</th>
<th>52 to 104 wks n=1161</th>
<th>&gt;104 to 216 wks n=831</th>
<th>Cumulative event* 0 to 216 wks n=4844</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline weight, mean, kg</td>
<td>89.54 (21.54)</td>
<td>89.50 (21.61)</td>
<td>89.54 (21.54)</td>
<td>89.54 (21.54)</td>
</tr>
<tr>
<td>Mean (SD) change from baseline in weight, kg</td>
<td>-0.42 (4.85)</td>
<td>-0.54 (5.22)</td>
<td>-0.70 (5.52)</td>
<td>-0.70 (5.22)</td>
</tr>
<tr>
<td>Mean (SD) % change from baseline in weight</td>
<td>-4.18 (5.38)</td>
<td>-5.38 (6.17)</td>
<td>-6.13 (6.52)</td>
<td>-5.18 (5.64)</td>
</tr>
<tr>
<td>Patients with &gt;5% weight loss, n/nt (%)</td>
<td>312/1843 (16.9)</td>
<td>284/1160 (24.5)</td>
<td>212/831 (25.5)</td>
<td>388/1843 (21.1)</td>
</tr>
</tbody>
</table>

APR-exposure periods include all patients who received APR regardless of when APR exposure started.
*Cumulative APR-exposure is based on APR-exposed patients at any time point.

169 liver bx’s in 71 psoriasis pts on MTX

- Hepatic fibrosis: 71%
- In pts with risk fks: 96%
  - obesity 14/15
  - diabetes 7/7
  - ETOH 9/9
- LFT’s not associated with fibrosis

**The effect of weight reduction on treatment outcomes in obese patients with psoriasis on biologic therapy: a randomized controlled prospective trial.**

Al-Mutairi N, Nour T.

- TNF blocker x 24w; diet vs control
- PASI 75 was achieved by 85.9% in the diet group, and 59.3% in the control group (p < 0.001)
- w 24: mean ↓ wt = 12.9 ± 1.2 kg w diet
  -1.5 ± 0.5 kg control

---

**Early increase of abdominal adiposity in patients with spondyloarthiritis receiving anti-tumor necrosis factor-α treatment.**

Hmamouchi I, Roux C, Paternotte S, Kolta S, Dougados M, Briot K.

---

**CONCLUSIONS**

- In obese patients higher doses or stronger medications are more effective
- Weight loss helps

---

**Risk of myocardial infarction in patients with psoriasis.**

Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB.
JAMA 2006;296:1735-41

age 30, severe psoriasis
HR: 3.10

---

**Association Between Tumor Necrosis Factor Inhibitor Therapy and Myocardial Infarction Risk in Patients With Psoriasis.**

Wu JJ, Poon KY, Channual JC, Shen AY.

- MI incidence TNF inhibitor/ oral or photoRx /topical: 3.05, 3.85, and 6.73 per 1000 patient-years
- adjusted HR 0.50 vs topical Rx 95% CI, 0.32-0.7
Association of Ustekinumab vs TNF Inhibitor Therapy With Risk of Atrial Fibrillation and Cardiovascular Events in Patients With Psoriasis or Psoriatic Arthritis.

Psoriasis Patients Treated With Biologics and Methotrexate Have a Reduced Rate of Myocardial Infarction: A Collaborative Analysis Using International Cohorts.

Coronary artery plaque characteristics and treatment with biologic therapy in severe psoriasis: results from a prospective observational study.

Table 4 Change in non-calcified coronary plaque burden over one year between treatment groups

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Change over one-year (mm²) (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-TNF therapy (n = 40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vs. Anti-T22/23</td>
<td>0.36 (-1.7)</td>
<td>0.10</td>
</tr>
<tr>
<td>vs. Anti-T17</td>
<td>-0.62 (-5.2)</td>
<td>0.27</td>
</tr>
<tr>
<td>vs. NBT</td>
<td>-0.25 (-1.7)</td>
<td>0.06</td>
</tr>
<tr>
<td>Anti-T22/23 therapy (n = 19)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vs. Anti-T17</td>
<td>-0.82 (-4.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>vs. NBT</td>
<td>-0.46 (1.3)</td>
<td>0.09</td>
</tr>
<tr>
<td>Anti-T17 therapy (n = 23)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vs. NBT</td>
<td>-0.15 (-4.3)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Values are reported as Mean (% change) for continuous data. Two-tailed P-values less than 0.05 significant (bold values).
IL, interleukin; NBT, non-biologic treated.

In patients on biologics, for which malignancies is there evidence of an increase?
- NMSC
- MM
- Lung ca in COPD
- Lymphoma
- NOT in most solid tumors
What do package inserts say? TNF blockers

Lymphoma, new primary malignancy
Lymphoma and other new primary malignancy have been reported in adults and pediatric patients; fatal cases have been reported in children and adolescents. Use of etanercept by patients with a history of malignancy or current malignancy may be unadvisable. The effect of TNF inhibition on the development and course of malignancies is not fully understood.

Results: Age and Gender Adjusted Cumulative Rates of Malignancies (excluding NMSC) per 100 Patient-Years (PY) Based on Any Exposure to Therapy (Figure 1)

Figure 1. Cumulative Rates of Malignancies

IL-17 Mediated Inflammation Promotes Tumor Growth and Progression in the Skin

D. He, et al

IL-23 → IL-17 → ↑tumor growth

Could blocking IL-17 be protective against cancer?

Secukinumab
PUBMED search
1/1/19
NO report of ↑ MALIGNANCES

Ixekizumab
PUBMED search
1/1/19
NO report of ↑ MALIGNANCES

Brodalumab
PUBMED search
1/2/19 NO report of ↑ MALIGNANCES
Exposure-Adjusted Malignancy Event Rates Through 52 Weeks Were Lower in the All-Brodalumab Group Than Those in the Ustekinumab Group

**Figure.** Malignancy events in psoriasis studies (52-week results).

- **Adjudicated malignancies**
- **SEER-adjudicated malignancies**
- **Basal cell carcinoma**
- **Squamous cell carcinoma**
- **Bowen’s disease**

NMSC

**Exposure-Adjusted AEs, rate per 100 PY**

- **Ustekinumab (N=613; 495 PY)**
- **Constant brodalumab 210 mg Q2W (N=1335; 1042 PY)**
- **All brodalumab (N=4019; 3446 PY)**

Exposure-adjusted AEs, rate per 100 PY.

- **IL-23** is increased in colon adenocarcinoma

Secukinumab, Ixekizumab & Brodalumab Package Inserts

No mention of Malignancy as Contraindication

Guselkumab

1/2/19 NO report of ↑ MALIGNANCIES

<table>
<thead>
<tr>
<th>SearchTerm</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guselkumab</td>
<td>1/2/19 NO report of ↑ MALIGNANCIES</td>
</tr>
</tbody>
</table>

Secukinumab, Ixekizumab & Brodalumab Package Inserts

No mention of Malignancy as Contraindication

Tildrakizumab

1/2/19 NO report of ↑ MALIGNANCIES

Tildrakizumab

1/2/19 NO report of ↑ MALIGNANCIES

IL-23 is increased in colon adenocarcinoma
Recurrence of Melanoma after Starting Apremilast for Psoriasis.

Salopek TG.

h/o 2 melanomas:
2009 - 1.53mm Clark IV
2012 - 0.9mm Clark IV
2015 started apremilast
>4mos. later→recurrence near first MM

Apremilast Package Insert

No mention of malignancy

Incidence of melanoma and other malignancies among rheumatoid arthritis patients treated with methotrexate.
Buchbinder R et al.

• RA pts started on MTX pre 1986
• State cancer registry (not NMSC)
• 4,145 person-years (avg. 9.3 yrs)

MTX associated with:
• 50% ↑ risk of malignancy
• 3-fold ↑ in melanoma
• 5-fold ↑ in nonHodgkins lymphoma
• 3-fold ↑ in lung ca.

- 18.8%, <5 years
- 24.8%, 5-10 years
- 33.3%, 10-20 years
- 47.1%, >20 years


- 1252 patients for up to 5 years (average 1.9)
- 6-fold ↑ skin cancer
- No ↑ nonskin cancer

Metastatic melanoma after solid organ transplantation: An interdisciplinary, institution-based review of management with systemic and targeted therapies.


Invasive Melanomas ↑2 fold
M:F ratio 14:1


- Acitretin 30 mg/d
- 2/19 → 2 SCCs vs 9/19 → 18 SCCs

Chemoprevention of skin cancer in xeroderma pigmentosum.

- 121 BCCs or SCCs in 5 patients 2 years prior to Rx
- Isotretinoin 2 mg/kg/d → 25 tumors over 2 years of Rx
The role of antinuclear autoantibodies in patients with psoriasis treated with anti-tumor necrosis factor-alpha agents: a retrospective long-term study.


Autoimmunity

Treatment with ENBREL® may result in the formation of autoantibodies (see ADVERSE REACTIONS: Autoantibodies) and, rarely, in the development of a lupus-like syndrome (see ADVERSE REACTIONS: Adverse Reaction Information from Spontaneous Reports) which may resolve following withdrawal of ENBREL®. If a patient develops symptoms and findings suggestive of a lupus-like syndrome following treatment with ENBREL®, treatment should be discontinued and the patient should be carefully evaluated.

Antinuclear antibodies associate with loss of response to antitumour necrosis factor-α therapy in psoriasis: A retrospective, observational study.


- 60 on 1st agent ➔ ANA 16.7%
- 22 stopped 1st agent ➔ ANA 54.5%
- 9 stopped 2 agents ➔ ANA 77.8%
- 6 stopped 3 agents ➔ ANA 83.3%

Drug-Induced SLE Associated with Etanercept Therapy†

- 4 patients.
- Manifestations including fever, arthritis, discoid skin changes, rash, pleuritic pain, ANA, anti-dsDNA, anti-histone, hypocomplementemia, anti-Sm, anti-RNP.
- No baseline serologies.
- All resolved with discontinuation of etanercept and/or addition of corticosteroids.


Regression of subacute cutaneous lupus erythematosus in a patient with rheumatoid arthritis treated with a biologic tumor necrosis factor alpha-blocking agent: comment on the article by Pisetsky and the letter from Aringer et al.


- ↓proteinuria, arthritis, C4
- ↑autoantibodies
**TNF- Inhibitor Induced Lupus**

<table>
<thead>
<tr>
<th></th>
<th>Classic DILE</th>
<th>TNF- inhibitor DILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA</td>
<td>&gt;95%</td>
<td>100%</td>
</tr>
<tr>
<td>Anti-DNA</td>
<td>&lt;1%</td>
<td>91%</td>
</tr>
<tr>
<td>Anti-histone</td>
<td>&gt;95%</td>
<td>57%</td>
</tr>
<tr>
<td>Increased C6</td>
<td>&lt;1%</td>
<td>59%</td>
</tr>
<tr>
<td>Rash</td>
<td>27%</td>
<td>72%</td>
</tr>
</tbody>
</table>

1. Benucci et al Clin Rheumatol 27;91-95

---

Treatment of coexistent psoriasis and lupus erythematosus.
Varada S, Gottlieb AB, Merola JF, Saraiya AR, Tintel SJ.

“Anti-TNF-α agents, ustekinumab, and abatacept may be valid treatment options for patients with concomitant LE and psoriasis. Clinical lupus flares in LE patients treated with TNF-α inhibitors were infrequent.”

---

Anti-nuclear antibody positivity and the use of certolizumab in inflammatory bowel disease patients who have had arthralgias or lupus-like reactions from infliximab or adalimumab.
Verma HD, Scherl EJ, Jacob VE, Bosworth BP.

- 5/6 patients → arthralgias or lupus-like symptoms resolved after being switched to certolizumab (P < 0.001)
- 2/4 ANA positive patients → ANA negative

---

Efficacy and safety of ustekinumab, an IL-12 and IL-23 inhibitor, in patients with active systemic lupus erythematosus: results of a multicentre, double-blind, phase 2, randomised, controlled study.

- 62% of ustekinumab treated patients reported response vs 33% in the placebo group (P=0.006) at week 24

---

Apremilast for discoid lupus erythematosus: results of a phase 2, open-label, single-arm, pilot study.
De Souza A, Strober BE, Merola JF, Oliver S, Franks AG Jr.

---

A 2 year, open ended trial of methotrexate in systemic lupus erythematosus.
Wilson K, Abeles M.

Discoid lupus erythematosus: successful treatment with oral methotrexate.
Goldstein E, Carey W.
Hypertrophic lupus erythematosus treated successfully with acitretin as monotherapy.

Efficiency of acitretin in the treatment of cutaneous lupus erythematosus.

Low dose cyclosporine A in the treatment of resistant proliferative lupus nephritis.

Therapeutic drug monitoring of cyclosporine microemulsion in patients with corticosteroid-resistant systemic lupus erythematosus.

TNF neutralization in MS: results of a randomized, placebo-controlled multicenter study.

- MS exacerbations ↑ with lenerecept.

Demyelination occurring during anti-tumor necrosis factor alpha therapy for inflammatory arthritides.

- 17 – etanercept, 2 – infliximab
- partial or complete resolution on d/c
- 1 positive rechallenge


- UST → no effect on MS

Activity of secukinumab, an anti-IL-17A antibody, on brain lesions in RRMS: results from a randomized, proof-of-concept study.
Secukinumab, a human anti-IL-17A monoclonal antibody, for moderate to severe Crohn's disease: unexpected results of a randomised, double-blind placebo-controlled trial.


Secukinumab not effective

Secondary area under the curve analysis (weeks 4-10) showed a significant difference (mean ΔCDAI=49; 95% CI (2 to 96), p=0.043) in favour of placebo.

Post hoc subgroup analysis showed that unfavourable responses on SEK and/or faecal CDAI=62; 95% CI (-1 to 125), p=0.054 in favour of placebo.

Entire treatment period exposure - adjusted (52 weeks)

Phase III incidence rate as expected with psoriasis

No dose relationship between secukinumab doses

<table>
<thead>
<tr>
<th>Drug</th>
<th>AIN457 300 mg (n=1410)</th>
<th>AIN457 150 mg (n=1395)</th>
<th>Placebo (n=793)</th>
<th>Etanercept (n=323)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory bowel disease</td>
<td>3 (0.26) [0.05, 0.75]</td>
<td>4 (0.35) [0.10, 0.90]</td>
<td>0 (0.00) [0.0, 1.83]</td>
<td>1 (0.34) [0.01, 1.90]</td>
</tr>
<tr>
<td>Colitis ulcerative</td>
<td>2 (0.17) [0.02, 0.61]</td>
<td>2 (0.18) [0.02, 0.63]</td>
<td>0 (0.00) [0.0, 1.83]</td>
<td>1 (0.34) [0.01, 1.90]</td>
</tr>
<tr>
<td>Anal fistula**</td>
<td>1 (0.08) [0.0, 0.47]</td>
<td>0 (0.00) [0.0, 0.32]</td>
<td>0 (0.00) [0.0, 1.83]</td>
<td>0 (0.00) [0.0, 1.26]</td>
</tr>
</tbody>
</table>

** Not associated with inflammatory bowel disease

Inflammatory bowel disease among patients with psoriasis treated with ixekizumab: A presentation of adjudicated data from an integrated database of 7 randomized controlled and uncontrolled trials.


EXPLORATORY END POINT: PROPORTION OF SUBJECTS ACHIEVING MUCOSAL HEALING (MES 51 AND GEROBS <2) AT WEEK 12 (ITT, NR)

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>Apremilast 30 mg BID</th>
<th>Apremilast 40 mg BID</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/N</td>
<td>9/58</td>
<td>19/57</td>
<td>12/56</td>
</tr>
<tr>
<td>P=0.0326</td>
<td>P=0.4815</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucosal Healing (%)</td>
<td>15.5%</td>
<td>33.3%</td>
<td>21.8%</td>
</tr>
</tbody>
</table>

MEDIAN PERCENT CHANGE FROM BASELINE (LOCF) IN HSCRP

Does exposure to isotretinoin increase the risk for the development of inflammatory bowel disease?

A meta-analysis.


NO

Isotretinoin and inflammatory bowel disease: trial lawyer misuse of science and FDA warnings.


Injectable fillers: what to choose?

Wrinkles around Eyes
Small particle hyaluronic acid such as Juvederm Volbella or Restylane silk is the choice. Do not use large particle HAs such as Perlane, Calcim hydroxyapatite, or Poly-L-lactic acid.

Wrinkles like Nasolabial Fold, Frown Line & Marionette Line
If you prefer completely degradable, easily removable filler, large particle hyaluronic acid (Perlane) is the choice even if its effect lasts only for 6 to 9 months. If you prefer completely degradable filler, Calcium hydroxyapatite (Radiesse) is the choice even if it is not easy to remove until it is degraded spontaneously. If you prefer longest acting filler, bio collagen stimulators like Sculptra is the choice although it takes longer to see results.

Forehead Wrinkles
My filler of choice for these types of lines is Juvederm ultra, but Restylane Silk and Belotero also do a fine job in this anatomical area.

Augmentation of Lips
If you prefer completely degradable filler in spite of short action, large particle HA Restylane is the choice. If you...
Hyaluronic Acid (HA) Must Be Cross-linked Before Use as a Dermal Filler

HA is a naturally occurring linear polysaccharide that is a natural component of the skin. Unmodified HA has a short half-life (~24 hours).

**Therefore:**
HA must be cross-linked to prevent rapid post-injection clearance.

BDDE is a common cross-linking agent utilized by JUVÉDERM®, Restylane®, and BELOTERO BALANCE®.

HA is a naturally occurring linear polysaccharide that is a natural component of the skin. Unmodified HA has a short half-life (~24 hours).

Different ways of HA manufacturing


- **Homogenized gel** (Sieved gel)
  - Different-sized particles create a uniform blend
  - Sieving creates many small particles
  - Resulting in a smooth-consistency gel
  - Resulting in a granular-consistency gel

Currently Marketed HA Fillers

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>HA Conc., mg/mL</th>
<th>Type</th>
<th>Lidocaine</th>
<th>Needle Size, G</th>
<th>US FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belotero Balance</td>
<td>22.5</td>
<td>Cohesive Poly-densified Matrix HA</td>
<td>No</td>
<td>27 or 30</td>
<td>2011</td>
</tr>
<tr>
<td>Juvéderm Ultra</td>
<td>24</td>
<td>Hylacross HA</td>
<td>Yes</td>
<td>30</td>
<td>2006</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus</td>
<td>24</td>
<td>Hylacross HA</td>
<td>Yes</td>
<td>30</td>
<td>2011, 2015 (lip)</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus XC</td>
<td>24</td>
<td>Hylacross HA</td>
<td>Yes</td>
<td>30</td>
<td>2016</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus</td>
<td>22</td>
<td>Vycross HA</td>
<td>Yes</td>
<td>27</td>
<td>2013</td>
</tr>
<tr>
<td>Juvéderm Voluma</td>
<td>20</td>
<td>Vycross HA</td>
<td>Yes</td>
<td>25 or 27</td>
<td>2013</td>
</tr>
<tr>
<td>Juvéderm Volure XC</td>
<td>17.5</td>
<td>Vycross HA</td>
<td>Yes</td>
<td>30</td>
<td>March 2017 (moderate-severe facial wrinkles/folds)</td>
</tr>
<tr>
<td>Juvéderm Volbella</td>
<td>15</td>
<td>Vycross HA</td>
<td>Yes</td>
<td>30</td>
<td>June 2016 (lips)</td>
</tr>
<tr>
<td>Restylane</td>
<td>20</td>
<td>NASHA</td>
<td>No</td>
<td>30</td>
<td>2003, 2011 (lips)</td>
</tr>
<tr>
<td>Restylane-L</td>
<td>20</td>
<td>NASHA</td>
<td>No</td>
<td>30</td>
<td>2007, 2015 (cheek, midface)</td>
</tr>
<tr>
<td>Restylane Silk</td>
<td>20</td>
<td>NASHA</td>
<td>Yes</td>
<td>30</td>
<td>2014 (lips, perioral rhytids)</td>
</tr>
<tr>
<td>Restylane Lyft</td>
<td>20</td>
<td>NASHA</td>
<td>Yes</td>
<td>30</td>
<td>2016 (moderate-severe, deep facial wrinkles + folds)</td>
</tr>
<tr>
<td>Restylane Defyne</td>
<td>20</td>
<td>NASHA</td>
<td>Yes</td>
<td>30</td>
<td>2016 (moderate-severe, deep facial wrinkles + folds)</td>
</tr>
</tbody>
</table>

Measuring Cohesivity was Made Possible With the Gavard-Sundaram Cohesivity Scale

5-point Visual Reference Scale Developed to Represent Patterns of Cohesivity

- **Fully dispersed**
- **Mostly dispersed**
- **Partially dispersed; partially cohesive**
- **Mostly cohesive**
- **Fully cohesive**

In vitro data does not imply clinical significance.
### Elasticity & Viscosity Values

<table>
<thead>
<tr>
<th>Product</th>
<th>Elasticity</th>
<th>Viscosity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiesse (+) integral lidocaine</td>
<td>1,165</td>
<td>310,305</td>
</tr>
<tr>
<td>Restylane-L</td>
<td>565</td>
<td>131,310</td>
</tr>
<tr>
<td>Restylane-Lyft</td>
<td>549</td>
<td>127,090</td>
</tr>
<tr>
<td>Restylane</td>
<td>514</td>
<td>119,180</td>
</tr>
<tr>
<td>Juvéderm Voluma</td>
<td>274</td>
<td>92,902</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus XC</td>
<td>136</td>
<td>32,152</td>
</tr>
<tr>
<td>Juvéderm Ultra XC</td>
<td>111</td>
<td>27,034</td>
</tr>
<tr>
<td>Juvéderm Ultra Plus</td>
<td>75</td>
<td>17,699</td>
</tr>
<tr>
<td>BELOTERO BALANCE</td>
<td>30</td>
<td>9,217</td>
</tr>
<tr>
<td>Juvéderm Ultra</td>
<td>28</td>
<td>7,307</td>
</tr>
</tbody>
</table>

*All measured at 0.7 Hz (physiologically relevant for stresses common to skin).


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### Rheology ReDefyned: xStrain

- More spread
- Less lift, firmer
- More lift, firmer
- Less spread

FLEXIBILITY IS MEASURED BY xStrain
Rheological Properties as a Scientific Rationale When Selecting the Appropriate Filler For Specific Facial Applications

**Elasticity (G')**
- **Gelatin:** stiffer, resists deformation
- **Pudding:** softer, more susceptible to deformation

**Viscosity (n*)**
- **Peanut butter:** thicker, more resistant to spreading
- **Room-temperature butter:** easily spreadable

**Cohesivity**
- **Honey:** intrinsically sticky, resists dispersion
- **Brown Sugar:** not sticky, more easily dispersed

*This chart is a simplification where the actual ratios of a gel's response to deformation/viscosity are not directly compared. It serves as a visual representation of the general concept of gel properties and their impact on filler selection.*
Fat

A youthful look depends on having the right amount of facial fat in the right places. Redistribution, accumulation, and atrophy of fat lead to facial volume loss.1-5

- Some areas lose fat. Examples are the forehead and cheeks.
- Other areas gain fat. Examples are the mouth and jaw.
- Modification of the fat pads leads to contour deficiencies.2-5

In addition, the areas of fat tend to become farther apart. Instead of a smooth, almost continuous layer, the fat pads appear as separate structures.4

Bone

There is a significant loss of facial bone with age.6 Aging of the craniofacial skeleton may be due to changes in the relative dynamics of bone expansion and bone resorption. Bone resorption leads to biometric volume loss.2,4

Without the structural support of bone, there are noticeable changes in the other layers of overlying soft tissue and skin.3,4

retaining ligaments of the face

1. JUVÉDERM VOLUMA™ XC Directions for Use, 2013;
2. Data on file, Allergan, Inc.
Non-HA Fillers

- Calcium hydroxylapatite – CaHA
  - Radiesse and Radiesse plus
  - Indicated for subdermal implantation for the correction of moderate to severe facial wrinkles and folds such as nasolabial folds.
  - Recently approved with addition of lidocaine

- Poly-L-lactic acid (PLLA)
  - Sculptra
  - Indicated for correction of hollows to deep nasolabial fold contour deficiencies and other facial wrinkles in which deep dermal grid pattern (cross-hatch) is appropriate

- Polymethylmethacrylate (PMMA)
  - Bellafill (formerly Artefill)
  - Indicated for the correction of nasolabial folds and moderate to severe, atrophic, distensible facial acne scars on the cheek in patients over the age of 21 years

---


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CaHa Mode of Action

**Before RADIESSE®**

- Destruction of collagen scaffolding in a woman results in thin skin, wrinkles, and hollows.

**Immediate 1:1 correction**

- Gel matrix with CaHA microspheres immediately fills lost volume

**Collagen neogenesis**

- CaHA microspheres form a scaffold that stimulates fibroblasts to produce collagen

**Collagen network strengthens dermis**

- A firm collagen fiber network is formed in the dermis
- The aqueous gel carrier is naturally absorbed
- CaHA microspheres are naturally metabolized by macrophages

---

**High density of collagen**

- Patient’s own natural collagen is left behind, providing structural support for the dermis and facilitating the long-lasting effects of RADIESSE®

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**Case Report**


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**Calcium hydroxylapatite (+) Case Report**

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**PLLA**
FRONTOPLASTY

Lower Eye lid rejuvenation
Sunday, February 23, 2020

6:30 a.m. - 8:00 a.m.  Breakfast

7:00 a.m. - 8:00 a.m.  Professional Medical Ethics/Florida Laws and Rules
                       Jason Winn, JD

8:00 a.m. - 10:00 a.m.  Prescribing Controlled Substances
                        Edwin Bayo, JD

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

10:30 a.m. - 12:30 p.m.  Prevention of Medical Errors
                        Arnold Mackles, MD

12:30 p.m. - 1:30 p.m.  Human Trafficking
                        Karysse Trandem, DO
Resident Poster Presentations

Recalcitrant Generalized Granuloma Annulare Treated with Methotrexate
Ryan Brothers, DO

Case Report: Atypical Ulceronecrotic Lymphomatoid Papulosis Treated Successfully with Brentuximab Vedotin
Jessica Collins, DO

Intraoperative Tissue Expansion to Allow Primary Linear Closure of Two Large Adjacent Surgical Defects
Kelsey Ferrell, DO

Pilomatrical Carcinoma in a 70-Year-Old Hispanic Female
Jeffrey Harbold, Jr., DO

Severe Drug Induced Thrombotic Vasculopathy in a Female Patient After a Single Dose of Taxotere
Brandon Mackey, DO

Lichen Planus Pemphigoides in a Patient After Combination Ipilimumab and Nivolumab Therapy
Marc Mitton, DO

SAPHO Syndrome
Diana Rivers, DO

Wound Closure Forces on Sutures When Applying the Rule of Halves
Lacey Roybal, DO

A Novel Injection Method to Improve Perioral Cosmesis with Hyaluronic Acid Filler
Anny Xiao, DO

Confluent and Reticulated Papillomatosis vs. Acanthosis Nigricans
Sonya Zarkhin, DO
Treated with Methotrexate

INTRODUCTION

Generalized granuloma annulare is a variant of granuloma annulare (GA) which affects middle aged and elderly patients and is less likely to resolve spontaneously. Many therapies have been used in the treatment of this resistant type of GA. We present a case of an elderly gentleman that failed treatment with adalimumab, cyclosporin, and hydroxychloroquine who responded well to monotherapy with methotrexate.

CASE REPORT

A 74 year-old white male with a history of localized GA presented with new and enlarging erythematous annular plaques and papules that had spread to his torso and legs (Fig. 2; A & B). These lesions had previously been confined to his hands and forearms for the past 8 years. Punch biopsies (Fig. 1) revealed interstitial and palisading GA that was clinically consistent with generalized GA. In the past, the patient was treated with several systemic therapies. A course of cyclosporin was mild-moderately successful, but lesions recurred shortly after discontinuation. Hydroxychloroquine and adalimumab were also used but were ineffective. The patient was trialed on a course of topical and oral steroids. This led to minimal improvement with new and enlarging erythematous annular plaques and papules that had spread to his torso and legs (Fig. 2; A & B). These lesions were indicated as first choice systemic therapies. Despite this new approach to the treatment GGA, there is limited evidence supporting any particular regimen when a patient has recalcitrant disease. This issue is further compounded by factors such as cost, patient co-morbidities and compliance. Our patient was resistant to cyclosporin, hydroxychloroquine, and adalimumab, and reluctant to do light therapy. Given our patient’s response to intramuscular methotrexate alone, we recommend this medication as an option for clinicians treating patients with recalcitrant disease and/or limitations as described above. It is effective, cheap, easy to monitor and, in a majority of patients, well-tolerated with GI upset being the biggest complaint.

DISCUSSION

There is a myriad of therapies reported in the literature for the treatment of generalized granuloma annulare (GGA). They include: Topical, intralessional and systemic steroids, retinoids, PUVA, PDT, UVA1 phototherapy, fumaric acid esters, topical tacrolimus and pimecrolimus, dapson, hydroxychloroquine, methotrexate, TNF-α inhibitors, niacinamide, allopurinol, hydroxyurea, tetracyclines, clofazimine and rifampin, zidovudine, pentoxifylline, interferon-α therapy, vitamin E, pulse dye laser, excimer laser and surgery.1

REPRESENTATIONS (cont.)

All have been used with variable success. In a retrospective case series of 11 patients receiving methotrexate for GGA, 64% had improvement of skin lesions, of which 43% achieved complete clearance and 57% partial on 12.5 to 15mg weekly.2 An established guideline for treatment is still lacking. In one systemic comparison of available treatments, the authors proposed a step-wise approach starting with topical steroids and calcineurin inhibitors. When physical modalities like PDT, PUVA or UVA-1 were unavailable, the use of hydroxychloroquine, retinoids, dapson or IL-2 inhibitors were indicated as first choice systemic therapies.3 Despite this new approach to the treatment GGA, there is limited evidence supporting any particular regimen when a patient has recalcitrant disease.4 This issue is further compounded by factors such as cost, patient co-morbidities and compliance. Our patient was resistant to cyclosporin, hydroxychloroquine, and adalimumab, and reluctant to do light therapy. Given our patient’s response to intramuscular methotrexate alone, we recommend this medication as an option for clinicians treating patients with recalcitrant disease and/or limitations as described above. It is effective, cheap, easy to monitor and, in a majority of patients, well-tolerated with GI upset being the biggest complaint.5

REFERENCES

Case Report: Atypical Ulceronecrotic Lymphomatoid Papulosis Treated Successfully with Brentuximab Vedotin

Jessica G. Collins, DO (PGY-3); Catherine G. Chung, MD; Basem William, MD

A 68-year-old Caucasian woman presented with a six-month history of a vasculitis and ulcerative eruption on the bilateral hands associated with significant pain and disability. She also had a worsening ulcerative and eroded lesion on the chest and back with similar symptoms. Due to concern for eczema herpeticum, tissue PCR for HSV and VZV were performed and were negative. Skin biopsies performed from multiple sites demonstrated an atypical lymphocytic infiltrate with increased CD4:CD8 of 4:1 and large cells with CD30-positivity. She was started on methotrexate 20mg weekly and an oral prednisone taper with only modest response. Brentuximab vedotin at 1.2mg/kg every three weeks was initiated, with complete resolution of all lesions. Treatment was continued for a total of six cycles and the patient achieved a sustained remission of nearly one year.

Case Presentation:

The patient is a 68-year-old Caucasian female who presented with a 10-year history of a waxing and waning polymorphic eruption. Lesions were red, scaly, and pruritic plaques located on trunk and extremities. Also present were vesicles and ulcerative papules most prominent on the hands and wrists, but also scattered throughout the trunk and arms. Patient had recurrent skin infections secondary to skin breakdown. Severe pain from ulcerations on the hands resulted in disability. Many non-diagnostic biopsies were performed. However, repeat biopsy of a lesion on the left breast demonstrated ulcerated and necrotic skin with an atypical cellular infiltrate. The infiltrate stained positively with CD3, CD45, CD4, CD5, CD7, and CD8 with a CD4:CD8 ratio of 4:1. A scant number of CD20 positive B-cells were observed. CD30 marked many of the enlarged mononuclear cells forming loose aggregates within the dermis. CD15 marked some of these cells as well. CD1A highlighted mild hyperplasia of Langerhans cells in the epidermis and dermis. No significant reaction for CD68, EMA, pancytokeratin, CD31, and S100 was observed. Direct immunofluorescence demonstrated no patterned deposition for albumin, IgG, IgA, IgM, C3, and C5b-9. Nonspecific C5b-9 was demonstrated in endothelia. CBC and CMP were non-contributory. Given the clinical history and biopsy demonstrating CD30+ lymphoproliferative disorder the patient was diagnosed with Ulceronecrotic CD30+ Lymphoproliferative disorder.

Clinical Response to Treatment:

Figure 1. Palmoplantar ulcerative and necrotic papules on bilateral hands [n=4] and red scaly pruritic plaques with inflammatory crusts on trunk and extremities (f)

Clinical Response to Treatment:

Figure 2. Resolution of all lesions on bilateral hands with residual post-inflammatory hyperpigmentation.

Clinical Response to Treatment:

Discussion and Conclusion:

• LyP proves a diagnostic challenge with one study demonstrating an average of 45 months from onset of symptoms to diagnosis.
• Histologically, LyP is divided into five subtypes that most commonly demonstrate an infiltrate of CD30-positive T-cells. However, CD30-negative variants, CD8-positive cytotoxic T-cell variants, and angioinvasive variants are described. There is much overlap in the histological presentation of these subtypes.
• LyP has an excellent prognosis with a 5-year disease specific survival of 100%. However, there is debate in the literature regarding the individual patient’s risk of developing a secondary cutaneous lymphoma or systemic lymphoma. Depending on the study, 10-60% will develop another lymphoma such as systemic ALCL, Hodgkin’s, or mycosis fungoides.
• Commonly prescribed treatments include: MTX, PUVA, topical steroids. Effective treatment for severe forms of LyP has been lacking.
• Our patient completed 6 cycles of Brentuximab vedotin at reduced dose of 1.2mg/kg with complete resolution of the lesions on the hands. Methotrexate was continued at 20mg per week with folate supplementation.
• We demonstrate that reduced-dose of 1.2mg/kg was as effective as the full dose of 1.8mg/kg.
• In conclusion, severe LyP cases have difficult to treat with historical treatment routines. This case demonstrates an atypical presentation of LyP and its successful treatment with BV with excellent results.

References:


Opti-West/Arrowhead Regional Medical Center/Aspen Dermatology Residency Program; The Ohio State University
Introduction

It is becoming increasingly common for patients to have multiple skin cancers treated with Mohs micrographic surgery on the same day, and sometimes these lesions can be near one another. The final size of the adjacent defects along with the amount of tissue remaining between them will determine how to best repair both defects.

We present a case of two large, adjacent postsurgical defects where intraoperative tissue relaxation allowed for primary linear closure of both defects.

Case Report

A 70-year-old male presented for treatment of two invasive squamous cell carcinomas located on left temple and left frontal scalp. Mohs micrographic surgery was performed on both lesions, and the final defect sizes measured 2.0 x 1.4 cm and 3.0 x 1.6 cm respectively.

Different repair options were discussed with the patient including allowing one or both lesions to heal via secondary intention or utilizing a skin flap or graft. We also discussed using an intraoperative skin relaxation device in order to stretch the skin around both defects in order to perform linear closures, which is what the patient ultimately decided on.

A suture retention device was secured centrally over both defects at a 90-degree angle to one another for 60 minutes to provide intraoperative tissue relaxation (Figure 1).

The temple defect had adequate relaxation to allow primary linear closure. The scalp defect, while not completely approximated, was over 60% smaller and able to be closed at both wound edges. A central area approximately 4 mm wide was left to heal by secondary intention (Figure 2).

The patient tolerated the procedure well. Sutures were removed on day 14 without complication. The patient was seen one month post-operatively with excellent cosmetic results (Figure 3).

Discussion

The methods of repairing two adjacent post-surgical defects are numerous and vary depending on the size of the individual defects, the location of the defects, and the amount of normal skin remaining between them. Various methods of closure for the adjacent defects include healing by secondary intention, primary linear closure, skin grafts, skin flaps, creating one larger wound to be repaired, or a combination of these approaches.

In our patient, closing the high-tension wound of the scalp would have prevented both wounds from being closed in linear fashion without first stretching the tissue. Many wounds will heal well by secondary intention despite a large size, but many patients prefer the cosmetic appearance and shorter healing time of wounds that have been closed with sutures. In our case, we closed the majority of the wound and left a small, central portion to heal on its own. The overall outcome was excellent and healed much quicker than leaving the entire scalp defect to heal on its own.

Intraoperative tissue relaxation can be used to allow primary closure of adjacent wounds. Even in cases where the defects cannot be completely approximated, closing the wound edges to create a smaller central defect can decrease healing time and lead to an excellent cosmetic outcome without the need for a flap or graft.

References


Disclosures

There were no funding sources for this poster. Dr. Lear is co-founder and shareholder in SUTUREGARD® Medical. The remaining authors have no conflicts of interest to disclose.
Pilomatrical Carcinoma in a 70-year old Hispanic Female
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Bay Area Corpus Christi Medical Center - South Texas Dermatology Residency Program, McAllen, TX

BACKGROUND
Pilomatrical carcinoma is a rare cutaneous malignancy of follicular matrix origin that was first described in the English literature by Lopransri and Mihm in 1980.[1] Since that first description over 130 cases have been reported.[2] Pilomatrical carcinoma is associated with mutations in the CTNNB1 gene responsible for encoding β-catenin, a protein implicated in cell differentiation and proliferation.[3] It demonstrates locally aggressive behavior with high recurrence rates.[2] Histological features include predominant hyperchromatic basaloid cells with high mitotic rate and nuclear pleomorphism. Anucleate matrical corneocytes or “ghost cells”, central necrosis and occasional dystrophic calcification can also be present. Lesions are most prevalent on the head and neck and predominate in a geriatric population and among male patients.[4] Treatment of the lesion is wide excision with negative margins. Radiation treatment can also be considered in the case of recurrence.[5]

CASE PRESENTATION
Our patient is a 70-year-old Hispanic Female former-smoker with an exophytic tumor on the right nasal ala. No other significant dermatologic history was reported. The patient reports a 3-year history of the lesion with rapid growth in the past 7 months. She denies pain and pruritus of the area. She admits to manipulating the lesions with her fingers, as she reports “trying to pop” the lesion. On physical exam, a 1.1 cm pedunculated friable tumor with crust is noted on the right nasal ala (Figure 1). On initial visit, a shave biopsy was obtained and histology demonstrated zones of basaloid cell that predominate over areas of necroses (Figure 2). Nuclear pleomorphism is noted on higher power (Figure 3). Immunostaining was positive for CEA, CK7, CK-AE1/AE3, chromogranin, CK20 and synaptophysin. After discussion of treatment options, the patient elected to have the lesion treated with wide excision.

DISCUSSION
The most described treatment for Pilomatrical Carcinoma is wide excision. Wide excision of the malignancy has demonstrated lower rates of recurrence. In the Herrmann et al. review, tumors removed with simple excision recurred at a rate of 83% while recurrence in wide excision was only 23%.2] The data is less clear on whether wide excision is effective in preventing metastasis. A review by Melancon et al. showed reduced rates of metastasis in pilomatrical carcinomas treated with wide excision (10.3%) versus simple excision (20.5%), however, these differences (with p<.11) did not meet the criteria for statistical significance.[6] Wide excision of the tumor is effective in preventing recurrence, however rates of metastasis may not be improved.

Other treatment modalities for pilomatrical carcinoma mentioned in the literature are Mohs surgery, radiation therapy, both alone and as an adjuvant, and chemotherapy. Radiation has shown mixed results, while chemotherapy has not been proven effective.[6] Mohs surgery shows promise as a treatment modality due to the ease of identifying pilomatrical carcinoma with hematoxylin-eosin stain.[7] However, due to the limited reports in literature of treatment with Mohs surgery, further research is needed.

REFERENCES
Severe Drug induced thrombotic vasculopathy in a female patient after a single dose of Taxotere

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Abstract:
Drug induced thrombotic vasculopathy can be a rare side effect of several chemotherapy agents with a wide range in severity and presentation. In this case report, we discuss a patient who had a severe form of that rare outcome in association to medication that has only been reported a small handful of times. A 73 year old female was given a single dose of Taxotere, then developed severe vaso-occlusive vasculopathy which resulted in necrosis in a large portion of her body surface area of her arms and legs. After hospitalization and high dose steroids, the patient slowly recovered.

Introduction
With increasing age and increase size of the world population, the incidence of cancer is rising. In 2022 there were 14.1 million new cancer cases. That number expected to rise to 23.6 million new cases by 2030(6). Many of these new cancer cases will be treated using classical and new anti-cancer agents. Anti-cancer agents have been associated with many side effects from alopecia to xerosis(3). One of the potentially more serious side effects of these medications is vasculopathy.

Drug induced thrombotic vasculopathy can be a rare side effect of several chemotherapy agents with a wide range in severity and presentation. In this case report, we discuss a patient who had a severe form of that rare outcome in association to medication that has only been reported a small handful of times. A 73 year old female was given a single dose of Taxotere, then developed severe vaso-occlusive vasculopathy which resulted in necrosis in a large portion of her body surface area of her arms and legs. After hospitalization and high dose steroids, the patient slowly recovered.

Management and clinical Course:
The patient was immediately referred for inpatient care. Biopsy at that time showed vaso-occlusive disease with possible fibrin thrombi in dermal capillaries and eccrine necrosis consistent with recent chemotherapy. During hospital admission the patient was given high dose IV steroids and it was recommended that she transfer to the burn unit. The patient then refused transfer, and her condition was closely managed by a multispecialty team including oncology, internal medicine, hematology, pharmacy, and infectious disease until discharge. The patient underwent extensive laboratory evaluation to rule out disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, paroxysmal nocturnal hemoglobinuria, antiphospholipid syndrome and purpura fulminans which were all effectively ruled out. The patient was closely monitored with strict I/O’s, hydration and electrolyte monitoring, infection precautions, and antibiotic management. After the patient’s condition stabilized and improved, the patient was switched to oral steroids and discharged to outpatient management. Since discharge, the patient has continued recovery with close monitoring by the managing physicians feeling this case was more likely mediated by cytotoxic epithelial damage rather than antibody formation, which was mildly supported by histopathologic examination. The differential diagnosis included several other conditions including paraneoplastic eruptions, hematologic disease, and infectious disease. These conditions where all effectively ruled out through laboratory workup while admitted. Because of the extensive area of necrosis, special care was given to prevent secondary infection.

This likely represents a very rare side effect of Taxotere which is sparsely published elsewhere. Given the potentially serious nature of the adverse event, greater awareness of adverse events like these can aid physicians in the future for their patients and avoid a more serious outcome.

Conclusion:
This case report and the very limited number of similar cases suggest that Taxotere may cause drug induced thrombotic vasculopathy. With continued research, a better understanding of this medication and its side effects can be better understood and increase awareness of its more serious side effects.

References:
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Disclosures:
The authors and institutions involved in this case have no conflict of interests to disclose
Lichen Planus Pemphigoides in a Patient After Combination Ipilimumab and Nivolumab Therapy

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HISTORY OF PRESENT ILLNESS: 61 year-old Hispanic male presents with a one-month history of a diffuse rash with associated altered mental status, pain and pruritus. At the onset of the rash patient was undergoing treatment with ipilimumab and nivolumab for cT4N0M1a (stage IV) adenocarcinoma of the lung with metastasis to the ipsilateral lung and mediastinum. The patient completed four cycles before stopping therapy due to an inpatient psychiatric hospitalization. Thirty-to-sixty days after his last immunotherapy cycle, he developed a diffuse rash which continued to worsen, prompting dermatology evaluation.

MEDICAL/SURGICAL HISTORY: Stage IV adenocarcinoma of the lung, stage 3 CKD, bipolar disorder with suicidal ideations, CAD, Type II DM, HTN, cirrhosis, diastolic CHF, previous alcohol abuse

MEDICATIONS: Amlodipine, aspirin, atorvastatin, cholecalciferol, folic acid, furosemide, gabapentin, insulin, isosorbide mononitrate, melatonin, mupirocin, oxcarbazepine, prednisone, prochlorperazine, propranolol, quetiapine, thiamine

PREVIOUS TREATMENTS: Methylprednisolone 1mg/kg BID, eight-week prednisone taper beginning at 60mg BID

PHYSICAL EXAMINATION: Diffuse hemorrhagic crusted plaques on upper and lower lips. Multiple necrotic, black, crusted papules and plaques on chest, back, upper extremities, and thighs, worse on extensor and weight-bearing areas. Occasional non-blanching, pink papules noted on central back and right thigh. Multiple, bleeding ulcerations with violaceous borders on sacral region and buttocks.

LABORATORY DATA: Glucose 316mg/dL (65-99), Cr 2.0mg/dL (0.53-1.30), Na 127mmol/L (135-145), Albumin 2.8g/dL (3.5-4.8), AST 62U/L (<41), GFR 35mL/min/1.73m2 (>60), PT 16.6 sec (12-14.6), NT-proBNP 839pg/mL (<125), CBC, remaining CMP all WNL.

STUDIES: CT chest, abdomen and pelvis on 11/2018 showed multiple small pulmonary nodules are stable to slightly decreased in size since previous exam.

BIOPSY: Health Network Laboratories (S18-50470, 11/10/18) Central back and right thigh: “Interface dermatitis with eosinophils; superficial impetiginization.” Mayo Medical Laboratories (S18-50470, 11/10/18) Central back DIF: “continuous strong linear deposition of IgG and C3 along the BMZ. Scattered and clumped cytopsids of IgM and IgA in the papillary dermis. Continuous strong shaggy deposition of fibrinogen along the BMZ.”

Lichen planus pemphigoides is an autoimmune disease that is thought to be a combination of lichen planus and bullous pemphigoid. It is initiated by lichen planus causing damage to the epidermis and dermoepidermal junction which releases hidden antigens. These antigens lead to circulating IgG antibodies against portions of the basement membrane. The most common antibody is against the MOW-4 epitope of the NC16A4 domain of BPAg2, but several others have been reported.

There are several associations reported with lichen planus pemphigoides. Many cases are idiopathic, but medications such as ACE inhibitors, simvastatin, PD-1 inhibitors, and antituberculous drugs as well as PUVA, sun exposure, pregnancy, and, rarely, malignancy have also been reported as causes.

Therapy with immune checkpoint inhibitors, such as PD-1, PD-L1, and CTLA-4 inhibitors, is a rare cause of lichen planus pemphigoides, but commonly causes cutaneous toxicity. The most common manifestations are pruritus and a morbilliform eruption. However, lichenoid reactions, psoriasis, acneform eruptions, vitiligo, sarcoidosis, bullous pemphigoid, dermatomyositis, and alopecia areata have also been reported. While each medication has the propensity for this toxicity by itself, combination CTLA-4 and PD-1 inhibitors have been implicated in the development of earlier, more frequent and more severe reactions.

REFERENCES

Figure 1: Erosions and crusted lesions of LPP
Figure 2: Lichen planus lesions with hemorrhage
Figure 3: Mucosal involvement of LPP
Figure 4: H&E highlighting lichen planus changes with dermo-epidermal clumping and eosinophils

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**SAPHO Syndrome**

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**HISTORY OF PRESENT ILLNESS:** 53 year-old Caucasian male presents with non-healing, painful ulcers with purulent drainage for several months. Additionally, he had a history of chronic discharge from the right medial thigh following his right hip arthroplasty which improved with clobetasol. He followed with orthopedics post-operatively and received multiple courses of antibiotics, despite several negative tissue cultures. The right lower leg ulcer improved with intralesional triamcinolone, topical corticosteroids and collagenase. However, new ulcers continued to appear involving the left cheek and left dorsal hand. These new lesions responded well to intralesional corticosteroids and topical clobetasol.

**MEDICAL HISTORY/SURGICAL HISTORY:** Acne, pyoderma gangrenosum, rheumatoid arthritis, osteoarthritis, atrial fibrillation, hypercholesterolemia, adrenal insufficiency, diverticulitis, right hip arthroplasty

**PREVIOUS TREATMENTS:** Clobetasol propionate, silver sulfadiazine, collagenase

**PHYSICAL EXAMINATION:** Right lower leg, 4x3 cm ulcer with cribriform surface at the periphery, fibrin coat, and mild surrounding erythema. Hands with swelling and joint deformity. Left neck with a 1 cm erythematous nodule with purulent discharge. Right medial leg with a large, 8x7 cm pink, boggy area of skin with three small draining fistulas. Single, 2x2 cm ulcer with yellow, fibrinous material.


**BIOLOGY:** Health Network Laboratories (518-8148, 2/27/18) Right lower leg: “ulceration with dense, neutrophilic inflammation. A few blood vessels show patchy fibrinoid change, slight fibroplasia and mural thickening and focal neutrophilic inflammation. PAS, GMS, Fite stains negative.”

**REFERENCES**


**DISCUSSION:** Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare entity that was first defined in 1987 by Chamot, et al. Incidence is less than 1:10,000 and mean age of initial symptom onset is 29 years old. This syndrome is manifested by a combination of inflammatory cutaneous disorders and musculoskeletal findings. The pathogenesis of this inflammatory condition is poorly understood.

Diagnosis of SAPHO syndrome is based on clinical and radiographic findings. Although multiple diagnostic criteria have been proposed, none have been validated. Cutaneous and osteoarticular manifestations have an insidious onset and may occur years apart which leads to delayed diagnosis and management. The most common cutaneous manifestations include palmoplantar pustulosis, acne conglobata, acne fulminans, hidradenitis suppurativa, pustular psoriasis, pyoderma gangrenosum, psoriasis vulgaris, and Sweet syndrome. Osteoarticular manifestations (ostitis, hyperostosis) cause bone pain, swelling, and restricted mobility. The sternum, clavicles, and sternoclavicular joints are affected in 90% cases. Spondyloarthritides, osteoarthritis, and paravertebral ossifications of the spine occur in 30% of cases. Additionally, 33% of patients have metadiaphyses of the femur, tibia, and/or fibula. The average number of bone lesions per patient in a review of 120 cases was 1.92. Sapho affects the sacroiliac, sternoclavicular joints, hips, or knees in up to 20% of patients.

During acute flares, C-reactive protein and erythrocyte sedimentation rate may be elevated. Occasionally, the alkaline phosphatase level may also be increased. Radiographically, osteolytic, sclerosis, and hyperostosis are seen. Technetium-99 scans may detect early or sub-clinical osteoarticular lesions. Histopathologically, bone biopsies show sterile osteomyelitis which is indistinguishable from infective osteomyelitis. Skin biopsies show neutrophilic pseudo-abscesses in the acute stage, mononuclear cells with occasional non-caseating granulomas in the intermediate stage, or mononuclear cells, fibrosis and new bone formation in the chronic stage.

Due to the rarity of this condition, treatment algorithms are not established. Retrospective studies and case series support non-steroidal anti-inflammatory drugs (NSAIDs) as first line. Bisphosphonates, corticosteroids, and methotrexate are considered second line agents. In studies and case series support non-steroidal anti-inflammatory drugs (NSAIDs) as first line. Bisphosphonates, corticosteroids, and methotrexate are considered second line agents. In patients who fail these therapies, biologic agents have been used with success. In a recent review of 66 cases treated with biologics, TNF blockers had the best response rate in osteoarticular and skin disease. Other biologics reported to be efficacious include IL-1 inhibitors, IL-17 inhibitors, and IL-23 inhibitors.
INTRODUCTION

- Elliptical or fusiform excisions are the most common form of excision performed for skin lesion removal. These advantages include simplicity, minimization of tissue removal, minimization of scar lines and acceptable cosmetic outcomes. Traditionally, an elliptical excision is designed with a 3:1 length-to-width ratio to minimize “dog ear” formation. This involves initial closure of the middle portion of the wound, followed by closure of the lateral halves.

- Our aim was to analyze the wound closure forces across the center and two bisected halves of elliptical skin lesions closed according to the rule of halves. Understanding the magnitude of these forces will provide guidance for planning and anticipating complications in elliptical excisional surgery.

STUDY DESIGN

- A prospective, single-center, IRB-approved (SHS IRB18-083) trial was performed with 18 patients (N = 11 male aged 56 – 86, N = 7 female aged 49 – 91) who presented for removal of skin cancers.

- All excisions were marked with a 3:1 ratio of length-to-width. After local anesthesia with 0.5% lidocaine with 1:1,000,000 epinephrine, full thickness excision was performed in each case followed by electrosurgery for hemostasis.

- The middle portion of the wound was initially closed using a large bite percutaneous 2-0 nylon suture.

- A force clamp was secured to the end of the suture to measure the force required to bring the wound edges into contact (Figure b).

- After measuring that tension, the nylon suture was removed and replaced with a 3-0 Polysorb buried suture. The two bisected halves of the wound were closed in the same manner, with the identical force measurement procedure. Wound dimensions and closure forces are shown in Table 1.

RESULTS

- Force data was not normally distributed (Shapiro-Wilk test); accordingly, the Kruskal-Wallis test was applied, p < 0.05 considered statistically significant. There was no significant effect of gender, so all data were grouped together.

- The average force to close the center of the wounds was six times larger than that of the bisected halves, and this difference was statistically significant (p < 0.001).

- There was no statistically significant difference between the force required to close the bisected halves.

- While it is not surprising that the force is lower for the bisected halves, the magnitude of the difference is of practical interest. The forces to close the bisected halves were consistently small and essentially negligible (<0.5 N) for ~50% of the cases.

- This study highlight the two phases of wound closure: initial approximation of the wound followed by subsequent addition of supports (e.g. sutures, staples, or adhesives) to maintain closure. The results suggest that when using the rule of halves, such novel techniques can likely be limited to the center suture since the bisecting sutures experience very small forces.

- In deeper wound under higher tension a bi-layered closure is standard with the placement of buried dermal sutures (BDS) and superficial non-absorbable sutures. Deep absorbable sutures have been found to decrease tension, approximate wound edges and minimize dead space during healing.

- Commonly the deep sutures are placed across the center of the wound to support the middle portion with the highest tension. Surgeons often place the initial suture near one end of the wound and progressively lower the tension as they progress toward the central portion of the wound in order to ease the wound closure. Although BDS are useful for decreasing tension during wound healing in full thickness wound closures, studies have demonstrated that they do not necessarily provide increased wound strength.

REFERENCES


Injectable fillers for facial rejuvenation have become one of the most frequently performed nonsurgical cosmetic procedures in the U.S.1 Perioral aesthetics play an integral role in maintaining a youthful appearance. Aging of the perioral area may result from repetitive contraction of the perioral muscles, sun exposure, thinning of the skin, atrophy of subcutaneous fat, ptosis of the malar fat pads and loss of structural bone support.2 Volume loss from the nasolabial and labiomandibular folds leads to deeper creases and shadows. The lips become thinner with decreased definition in the vermilion border and loss of subcutaneous fat in surrounding skin accentuates the perioral fine wrinkles from repetitive orbicularis oris contraction.3 Injections of hyaluronic acid (HA) filler can address many of these concerns in the perioral region to provide optimal facial harmony and rejuvenation.

PERIORAL ANATOMY

CONVENTIONAL TECHNIQUES FOR PERIORAL HA FILLER

Percutaneous injection techniques and indications:4-5

• Retrograde linear threading: Needle is withdrawn as filler is injected like a thread
  • Labiomandibular folds, labiomental crease, nasolabial folds, perioral vertical rhytids, oral commissures
  • Anterograde linear threading: Filler is injected like a thread ahead of the advancing needle
  • Oral commissures, perioral vertical rhytids
  • Fanning: Retrograde linear threading as the needle is withdrawn but changing direction prior to being removed, producing a wheel spoke pattern
  • Labiomandibular folds, nasolabial folds, deeply etched lines
  • Cross-hatching: Retrograde or anterograde linear threads are injected in perpendicularly
  • Nasolabial folds, Perioral vertical rhytids, deeply etched lines
  • Depot: Needle remains static while an aliquot of filler is injected
  • Oral commissures

Advantages

• Decreased soft tissue trauma compared to percutaneous injection techniques, resulting in less swelling and bruising.

Limitations

• Theoretical higher risk of bacterial infection due to direct puncture of oral cavity, although anecdotally not observed

DETERMINATION OF THE BEST INJECTION TECHNIQUE

Intraoral injection technique for perioral rejuvenation

This technique was developed by Dr. Will Kirby and inspired by multiple patients who reported an improvement in their perioral aesthetics while wearing dental retainers. As such, this technique is designed to place HA filler intraorally in the same area that would be volublized by dental retainers. While previous intraoral injection techniques have been described for correction of volume deficiencies in the midface, with placement of filler in the deep subcutaneous and supraperiosteal planes to restore volume in the malar cheeks,6,7 this injection technique is a new application of the intraoral injection approach specifically designed for perioral aesthetic rejuvenation.

1. Review informed consent with patient, including potential side effects of any HA filler injections, including swelling, tenderness, bruising, erythema, nodules, and vascular compromise.

2. Provide the patient with a mirror and review their perioral anatomy to discuss goals and realistic expectations. Assess the extent of perioral lines, folds, and shadows to customize treatment to each patient.

3. Determine which HA filler with low elasticity and low viscosity will be used for injection.

4. Cleanse the oral cavity with a chlorhexidine-based mouthwash and cleanse the perioral skin with chlorhexidine solution.

5. Utilize non-dominant hand to manually evert the patient’s upper lip with to expose the internal mucosal side of the lip. Figure 3

6. Inject approximately 0.1 cc aliquots of filler in four evenly spaced depot injections in the lower mucosal lip, approximately halfway down the vertical length of inferior mucosal lip, with each aliquot directly opposing one of the four mandibular incisors. The size of the aliquots, total amount injected, and placement of each aliquot may be adjusted according to the patient’s specific deficits. Figure 4-5

7. Repeat the same technique on upper lip. Use non-dominant hand to manually evert patient’s upper lip to expose the internal mucosal side of the lip. Figure 6

8. Inject approximately 0.1 cc aliquots of filler in four evenly spaced depot injections in the upper mucosal lip, approximately halfway up the vertical length of the superior mucosal lip, with each aliquot directly opposing one of the four maxillary incisors. Figure 7-8

9. Avoid injecting too close to the vermilion-mucosa junction in the superior labial mucosa to minimize the risk of injury to the anastomotic arch of the superior labial arteries. Tansanti et al described the typical position of the superior labial artery 4.5mm deep along the upper lip between the oral mucosa and the orbicularis oris muscle just above the vermilion-mucosa junction.5 As with all filler injections, intravascular injection risk can be minimized by precise needle placement and injecting very slowly.5

10. Manually massage the injected areas by pinching the upper and lower lips with the index fingers intraorally and thumbs on the external cutaneous lips. Apply gentle to moderate pressure to smooth out superficial lumps and contour irregularities.

11. Cool compresses/ice packs can be utilized to minimize post-procedural swelling.

REFERENCES


Confluent and Reticulated Papillomatosis vs Acanthosis Nigricans

Sonya Zarkhin, DO PGY 3
Cindy Hoffman, DO Program Director

Abstract
Confluent and reticulated papillomatosis (CARP) and acanthosis nigricans (AN) are two benign conditions commonly seen in medical dermatology. While they may present differently, clinically they may have similar morphological presentations as well as nearly identical histopathology and in some cases etiology. We present a case of an overweight 20 year old Hispanic male who presented to dermatology with a thick, hyperpigmented, papular and reticulated rash involving the axillae, neck and antecubital fossae. This patient was initially treated for AN by primary care and was directed to dermatology when a significant portion of his rash did not clear with keratolytic agents. A 3 mm punch biopsy was performed in the dermatology clinic and was determined to be papillated epidermal hyperplasia based on histology. The patient was treated for CARP and put on a course of Doxycycline 50 mg twice daily which subsequently cleared his rash. We believe this case highlights the important clinical and histopathological overlap of these entities.

Confluent and Reticulated Papillomatosis
- Can be keratotic
- Red-brown papules
- Starts intermammary and spreads out in a reticulated pattern
- Begins around puberty
- F > M

Acanthosis Nigricans
- Hyperpigmented, velvety plaques
- Localized skin disorder
- Favors flexural and intertriginous areas
- Associated with stimulation of insulin-like growth factors on keratinocytes and fibroblasts
- 25X more common in African Americans

Our Patient – Clinical

Figure 1: CARP (Bolognia et al.,)

Figure 2: AN (Bolognia et al.,)

Our Patient - Histopathology

Figure 3: Hypopigmented macules neck, hyperpigmented reticulated plaques axilla and AC fossae

Figure 4: 3 mm punch biopsy right axillae demonstrating papillated epidermal hyperplasia

Comparative Histopathology

Figure 5: CARP – papillomatosis of epidermis with deep depressions (Soeprono et al.,)

Figure 6: AN – papillomatosis of the epidermis with thin rete ridges (Soeprono et al.,)

Differential Diagnosis

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<thead>
<tr>
<th>Pityriasis Versicolor</th>
<th>Prurigo Pigmentosa</th>
<th>Sarcoid</th>
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<tr>
<td>Terra Firma</td>
<td>Granular Parakeratosis</td>
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<td>Lichen Planus</td>
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CARP & AN: Similarities
- Both associated with endocrinopathies
  - Diabetes mellitus
  - Insulin resistance
  - Obesity
  - Polycystic ovary syndrome
- Pathogenic link may be due to insulin resistance and consequent hyperinsulinemia
  - High levels of insulin activate tyrosine kinase receptors > mitogenic and antiapoptotic effects
  - May explain epidermal proliferation and papillomatosis seen in both

- On staining: increased expression of Ki-67
- On staining: increased expression of keratin 16

Source: Park et al.,

CARP & AN: Differences
- Location:
  - CARP seems to favor trunk
  - AN seems to favor flexural areas
- Histopathology:
  - AN biopsies seem to have more melanocytes
- Culture:
  - CARP seems to grow more bacteria

Source: Park et al.,

Take Home Points
- CARP and AN may often look similar clinically
- CARP and AN often look similarly on histopathology
- CARP should be in the differential diagnosis of patients evaluated for AN and vice versa
- More studies are needed to understand the pathogenic mechanism of CARP and AN as well as their common association with high levels of insulin

Source: Kang et al.,

Citations
Upcoming Meetings:

2020 AOCD Fall Meeting
Hyatt Centric Chicago Magnificent Mile
Chicago, IL
October 8 - October 11

2021 AOCD Spring Meeting
Hilton West Palm Beach
West Palm Beach, FL
February 22 - February 27

2021 AOCD Fall Meeting
Westin Denver Downtown
Denver, CO
October 7 - October 10

2022 AOCD Spring Meeting
JW Marriott Orlando Grande Lakes
Orlando, FL
March 10 - March 13