CURRENT CONCEPTS IN DERMATOLOGY

Reagan Anderson, D.O., FAOCD
Activity Chair
Acknowledgement of Commercial Support
American Osteopathic College of Dermatology Corporate Members

Ruby Level
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2016 American Osteopathic College of Dermatology Fall Meeting Exhibitors


Continuing Medical Education Statements

This activity will change your practice and improve patient outcomes!

AOA Statement:
The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians. The American Osteopathic College of Dermatology designates this activity for a maximum of 28 AOA Category 1-A credits and will report CME and specialty credits commensurate with the extent of the physician’s participation in this activity. September 15-18, 2016

AAD Statement:
The American Osteopathic College of Dermatology Current Concepts in Dermatology (Activity #698100) is recognized by the American Academy of Dermatology for 28 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology’s Continuing Medical Education Award. September 15-18, 2016

ACCME Statement:
“The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.” September 15-18, 2016
American Osteopathic College of Dermatology
Mission Statement &
Continuing Medical Education Needs Assessment

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

The objectives of this organization are:
1. To maintain the highest possible standards in the practice of dermatology
2. To stimulate study and to extend knowledge in the field of dermatology
3. To promote a more general understanding of the nature and scope of the services rendered by osteopathic dermatologists to the other divisions of medical practice, hospitals, clinics and the public.
4. To contribute to the best interests of the osteopathic profession by functioning as an affiliated organization of the American Osteopathic Association

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

Accreditation:
The AOCD is accredited by the American Osteopathic Association. This activity anticipates being approved for 28 hours of AOA Category 1-A credit pending approval by the AOA CCME, the American Academy of Dermatology (Program #698100). The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

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

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

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

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

In accordance with the ACCME’s Standards for Commercial Support of Continuing Medical Education, the Policy on Collection of Financial Relationships and Resolution of Conflicts of Interest (COI) exists to provide guidance for staff, instructors, planners, reviewers and managers of CME activities sponsored by The American Osteopathic College of Dermatology, (AOCD). This policy addresses the underlying philosophy of disclosure to learners, mechanisms to collect disclosure information and the parties from whom financial disclosure shall be collected, the mechanisms to resolve COI, and requirements to make disclosure to learners prior to the start of an activity.
**Professional Practice Gap Statement:**
Physicians need to understand, update and manage changes in dermatology in order to provide optimal patient care. Dermatologists in private practice may not have immediate access to new updates in therapies and treatments. This activity will help to close gaps in physician’s areas of state rules, regulations and compliance mechanisms, updates in skin cancers, melanomas, rheumatology-dermatology, dermoscopy updates, urticaria, pediatric dermatology, male and female pattern hair loss, therapeutic updates and the use of radiation in treating skin cancers.

**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.

- Explore and discuss state rules, regulations and compliance mechanisms.
- Review of medico-legal issues in an effort to lessen the risk of malpractice or malpractice allegation by improving care in right situations.
- Provide attendees with an understanding of basic principles of irradiation for skin cancer as related to traditional and new approaches.
- Update attendees on the tremendous progress and new research in melanoma therapy in the last five years that has revolutionized the field.
- Provide attendees with an awareness of updates in dermatology and how to implement this knowledge into daily clinical practice and patient care.
- Evaluate the current state of acne, rosacea, eczema and psoriasis in patients and correlate with a management plan.
- Discuss new therapeutics for children with skin disease.
- Provide attendees with an understanding of emerging therapies and management strategies for dermatologic disease, as well as change pre-, peri- and post-operative practices based on recent updates and reviews.
- Provide attendees with an understanding of male and female pattern hair loss.
- Highlight common diseases seen in veterinary dermatology in comparison and contrast to the human counterpart.
- Highlight common infectious diseases that veterinary patients may share with their human owners (your patients).
- Identify common underlying triggers for urticaria/angioedema and help attendees understand the best therapy for treatment.

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

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

**Needs Assessments:**
The activity was developed based upon the needs of physicians within the association identified through:
- An evaluation/survey provided to meeting participants at both our annual and midyear meeting
- Consensus of faculty members within a department or service area
- New advances in dermatologic treatment identified in major publications or research studies
- New methods of diagnosis or treatment
- Availability of new medication(s) or indication(s)
- Development of new technology
- Acquisition of new facilities or equipment
- Input from experts regarding advances in medical knowledge
- Legislative, regulatory, or organizational changes effecting patient care
- Epidemiological data
- Quality assurance/audit data
- Statistics infection control data
- Surgical procedures statistics
- Journal articles/literature citations
The AOCD Continuing Medical Education Committee works to assure the inclusion of appropriate Osteopathic content in the Continuing Medical Education activities presented by AOCD, and to assure that the Continuing Medical Education Programs of the AOCD will achieve the stated objectives of each meeting in a setting which is evidence-based, culturally sensitive and free of commercial bias.

The Continuing Medical Education Committee of the AOCD will monitor the quality of all activities conducted.

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

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

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

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

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

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

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

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

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

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

Reagan Anderson, DO, FAOCD
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.

Osteopathic Dermatology
Topics addressed will describe osteopathic principles and practice and how that relates to dermatology.

Objectives:
1. Define what an osteopathic dermatologist is
2. Encourage new thought on treatments
3. Start a dialogue of what osteopaths offer the world of dermatology

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

Reference:
• “Defining the DO” Dermatology World, 2015 June.
• “Dermatology Incorporated” Dermatology World, 2012 August.

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

Disclosures: No disclosures provided by speaker

Derrick Adams, DO, FAOCD
Growing up in Oklahoma, he earned his Bachelor of Science in Physiology at Oklahoma State University. After graduation he was commissioned into the U.S. Air Force and completed his internship in internal medicine at Wilford Hall Medical Center in San Antonio, TX. Dr. Adams was stationed at Travis Air Force Base where he served as a Captain and General Medical Officer at David Grant Medical Center. After his tour of duty, Dr. Adams spent three intensive years at Michigan State University, where he completed his residency in dermatology with a special focus in dermatological surgery.

Dr. Adams has a special interest in skin cancer and medical dermatology, authoring a wide range of articles across dermatology, pharmacology and dermatological surgery. He treats all diseases of the skin to include: psoriasis, eczema and autoimmune diseases. As the field of dermatology arose from within internal medicine and Dr. Adams’ approach to the skin takes into account the global health and well-being of the patient.

A particular interest for Dr. Adams is evaluating the cost/benefit ratio and science behind treatments. He prides himself on being the “Consumer Reports” of dermatology and not over-treating patients.

Embryology For the Rest of Us
Topics addressed will be embryology and how it relates to daily practice.
Objectives:
1. Broaden knowledge of embryology among practicing clinicians
2. Provide an appreciation for the busy dermatologist and new viewpoint of what is seen day to day

Needs:
1. Advances in medical knowledge

References:

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

The Culture of Wound Cultures
This lecture will discuss how to investigate a wound from an infectious standpoint and raises awareness about the limitations of standard culture.

Objectives:
1. Recognize basis and limitations of standard culture technique
2. Discuss the Human Microbiome
3. Use this information to review current wound culture techniques

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

References:

Core competencies: 1, 2, 3

Disclosures: No disclosures provided by speaker

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**Eric Adelman, DO, FAOCD & John Ramm**

Dr. Eric Adelman earned his medical degree from New York College of Osteopathic Medicine in Old Westbury, NY, in 1998. He completed his dermatology residency at North Broward Hospital in Fort Lauderdale, FL, where he served as chief resident. He then completed an extensive Mohs surgical oncology fellowship in Cincinnati, OH, under accomplished surgeon Dr. Brett Coldiron, MD. Dr. Adelman is a member of the American Academy of Dermatology, American Society of Dermatological Surgery, American College of Mohs Surgery, American Osteopathic Association and the American Osteopathic College of Dermatology. He is an expert in the prevention, detection and treatment of skin cancer, as well as experienced in other disorders of the skin, hair and nails.

After meeting a very successful osteopathic physician who was practicing orthopedics, Dr. Adelman discovered a passion for holistic medicine. He particularly associated with the concept of preventive medicine and found it very rational, which led him to apply to osteopathic medical school.

Dr. Adelman loves doing surgery and feels fortunate that he discovered this passion. He first performed Mohs surgery for a large group in south Florida where he developed an excellent reputation not only for his surgical skills, but for his unique approach to patient care. Dr. Adelman decided in 2007 that he would like to apply his ideas about medicine and patient care to his own practice.
**Business of Dermatology**

A discussion of the business of dermatology including fundamentals: culture, structure, metrics, value.

**Objectives:**
1. Cultural management
2. Practice management
3. Understanding value

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

**References:**
- “Valuing, Selling and Closing a Dermatology Practice”. Pages 191-204.

**Core competencies:** 6

**Disclosures:** No disclosures provided by either speaker

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**Nathanael Brady, DO**

Dr. Nathanael Brady is a board-certified allergist, immunologist and pediatrician. He earned his medical degree from Michigan State University College of Osteopathic Medicine in 2005. Following medical school, Dr. Brady completed a residency in pediatrics at Nationwide Children's Hospital in Columbus, OH in 2008. In 2010, he completed an allergy and immunology fellowship at University Hospitals in Cleveland, OH.

He is a member of the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Christian Medical and Dental Association; Clinical Immunology Society; Colorado Allergy and Asthma Society; Colorado Springs Osteopathic Foundation; and the El Paso County Medical Society.

Dr. Brady resides in Colorado, where he spends his free time with his wife, daughter and two sons. He enjoys outdoor activities such as hiking, camping and running; watching college and professional sports and actively participating in his church.

**Urticaria/Angioedema from an Allergist’s Perspective**

Urticaria/angioedema are common medical conditions seen by primary care providers as well as specialists. Diagnosis and management can be challenging for the medical provider. Optimal management involves identifying possible underlying triggers as well as ruling out other diseases presenting in a similar fashion.

**Objectives:**
1. Differentiate acute versus chronic urticaria/angioedema
2. Identify common underlying triggers for urticaria/angioedema
3. Understand best therapy for treatment of urticaria/angioedema
4. Recognize common types of physical urticaria/angioedema

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

**References:**

**Core competencies:** 2, 3, 5, 6, 7

**Disclosures:** Speaker for Teva, Shire, Merck, Alcon
Dr. Timothy Brant is a practicing radiation oncologist from Crystal River, Florida. He received his undergraduate and medical degrees from the University of Florida in Gainesville. He was on the radiation oncology faculty for five years before moving to central Florida where he joined the Robert Boissonneault Oncology Institute. RBOI has offices in Ocala, the Villages and Citrus county. Dr. Brant is married and has three sons, one of whom is an osteopathic dermatology resident. He is an avid runner and enjoys hunting and fishing. He has given numerous presentations and publications and has a special interest in radiation for skin cancers. He has successfully treated hundreds of patients with skin cancers from early stage to widely metastatic disease.

Treating Skin Cancer with Radiation: Traditional and New Approaches
This lecture will discuss traditional radiation for skin cancer versus new approaches which entail the use of electronic brachytherapy machines, radiation techniques and outcomes.

Objectives:
1. Provide attendees with an understanding of basic principles of irradiation for skin cancer as related to traditional and new approaches
2. Provide attendees with an understanding of indications for irradiation in terms of traditional and new approaches
3. Provide attendees with an understanding of clinical data as related to traditional and new EBT in terms of outcome and complications

Needs:
1. New advances in dermatologic treatment
2. Development of new technology

References:

Core competencies: 2, 3, 5, 6

Disclosures: Off-label: Electronic Brachytherapy - Approved by FDA. Insurance carriers consider investigational because of lack of level 1 clinical data.

Dr. Jacquelyn Campbell received her Doctor of Veterinary Medicine degree in 2006 from Colorado State University. Following veterinary school, Dr. Campbell completed her internship and a three-year residency with Dermatology for Animals in Arizona, where she cared for a variety of patients across the western U.S. and grew her love and passion for animal dermatology.

Dr. Campbell’s special interests include allergic and immune mediated skin disorders and chronic ear disease. Her extensive study on the fungal flora of the canine ear was published in the international journal, Veterinary Dermatology. Dr. Campbell is a member of the American Academy of Veterinary Dermatology, American Veterinary Medical Association, Colorado Veterinary Medical Association and is licensed in Colorado, New Mexico, Nevada, Utah and Nebraska. She feels fortunate to be able to work with family veterinarians, and as a team, improve the quality of life of pets.

Dr. Campbell fills her free time at home with her chef husband, their two children and her array of furry critters, including two dogs and three cats. They can often be found exploring the great Colorado outdoors.

Parallel and Divergence – Veterinary Dermatology and the Human Counterpart
Highlight pathophysiology clinical presentation treatment and comparative species aspects of the following disease: atopic dermatitis, food allergy, sarcoptes, dermatophytosis, pemphigus complex, dermatomyositis, non-inflammatory alopecias, actinic damage, epitheliotrophic lymphoma and thermal injury.
Objectives:
1. Highlight common diseases seen in veterinary dermatology and compare and contrast to the human counterpart
2. Highlight common infectious diseases that our patients may share with human owners (your patients)

Needs:
1. Advances in medical knowledge

References:

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

Disclosures: Sponsor CE meetings yearly (lecture presentations): Zoetis, Bayer

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

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

Osteopathic Continuous Certification Update
Objectives:
1. Provide attendees with an understanding of the OCC process that ensures osteopathic physicians are current in their specialty
2. Provide attendees with an understanding of the five components of OCC which include, Unrestricted License, Lifelong Learning, Cognitive Assessment, Practice Performance and Continuous AOA Membership

Needs:
1. Ensuring college membership understands new requirements for accreditation and maintenance of our board certification

References:
• http://www.osteopathic.org/inside-aoa/development/aoa-board-certification/Pages/osteopathic-continuous-certification.aspx

Core competencies: 1, 3, 5, 6

Disclosures: No disclosures provided by speaker
James Q. Del Rosso, DO, FAOCD
James Q. Del Rosso, DO has been practicing dermatology since 1986 and in the Las Vegas area since 1997. He is Adjunct Clinical Professor of Dermatology at the Touro University of College of Osteopathic Medicine in Henderson, NV and has the distinction of being the first and only Dermatology Residency Program Director in the history of the state of Nevada. Prior to coming to Las Vegas, Dr. Del Rosso served as Head of the Section of Dermatology at the Ohio University College of Osteopathic Medicine in Athens and Visiting Faculty Member in Dermatology at Ohio State University (OSU) in Columbus where he twice was honored as Educator of the Year by the dermatology residents. He received his D.O. degree from Ohio University College of Osteopathic Medicine, interned at Doctors Hospital in Columbus, completed a dermatology residency at Atlantic Skin Disease and Skin Surgery in Fort Lauderdale, FL and a fellowship in Mohs micrographic surgery and cutaneous oncology at OSU.

Dr. Del Rosso is an internationally-renowned dermatologist. He is Clinical Editor of the Journal of Clinical and Aesthetic Dermatology, has published multiple peer-reviewed articles and textbook chapters and was President of the American Acne & Rosacea Society, American Society of Mohs Surgery and the American Osteopathic College of Dermatology. He is one of the most highly-requested and well-respected educators in dermatology, invited to present regularly at dermatology meetings both nationally and internationally.

Therapeutic Update
Review practical considerations and management approaches with acne, rosacea, eczema, psoriasis and other common dermatosis.

Objectives:
1. Evaluate current state of acne, rosacea, eczema, psoriasis in patients and correlate with management plan
2. Correlate clinical manifestations of disease with rational treatment selection and progress monitoring
3. Provide attendees with an understanding of initial doses and follow up adjustments with several medication used to treat the above disorders along with recognition of side effects

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

References:
• Kim, G, Del Rosso, JQ. “Oral Spironolacton in Post-teenage Female Patients with Acne Vulgaris: Practical Considerations for the Clinician Based on Current Data and Clinical Experience” JCAD. March 2012;5(3):37-50.

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

Disclosures: Speaker, consultant, research for Allergan, Anacor, Aqua, Bayer, BioPharmX, Celgene, Cutanea, Dermira, Ferndale, Foamix, Galderma, Genentech, Johnson & Johnson, Leo Pharma, Lilly, Novan, Novartis, Pharmaderm, Promius, Sebacia, SunPharma, Unilever, Valeant; Spouse is a sales representative for Novartis Respiratory Division – No relationship to this lecture

Marc Epstein, DO, FAOCD
Medical Marijuana and Dermatology
What is medical marijuana? Where medical marijuana is legal and what ailments a physician is allowed to treat. The history of medical marijuana.

Objectives:
1. Medical marijuana when used legally and appropriately is a safe and effective treatment modality
2. Medical marijuana does not meet the criteria to be classified as a Schedule 1 Drug
3. Topically applied medical marijuana (THC) can effectively attenuate the inflammation and pruritus of contact allergic dermatitis by decreasing keratinocyte derived pro-inflammatory mediators
Needs:
1. New advances in dermatologic treatment
2. Availability of new medication(s) and indication(s)
3. Development of new technology
4. Advances in medical knowledge
5. Legislative, regulatory, or organizational changes effecting patient care

References:

Core competencies: 2, 3, 6

After graduating from the Philadelphia College of Osteopathic Medicine in 1981, Dr. Epstein completed residencies in internal medicine at Delaware Valley Medical Center, Langhorne, PA and in dermatology at Temple University, Skin and Cancer Center, Philadelphia, PA. He then served in the USAF for nine years active duty as Chief of Dermatology Services at Davis-Monthan Air Force Base in Tucson, AZ, followed by 16 years of reserve duty, obtaining the rank of colonel. Upon leaving active military duty in 1995, Dr. Epstein opened his private dermatology practice in Tucson AZ, where his dermatology skills have been serving the community’s needs for over 20 years.

Dr. Epstein received his board certification in dermatology from the American Osteopathic Board of Dermatology (AOBD) to become a Fellow of the AOCD and then achieved Distinguished Fellow Status. He served on the board of the AOCD as vice president and then President. His professional credentials include former Clinical Instructor of Dermatology at the University of Arizona, former Principal Dermatology Investigator for Argus, Hilltop and then Radiant Research and former dermatology section chief at Tucson Medical Center. His medical community memberships include the Tucson Dermatology Society, where he served as its president for over 6 years, the American Academy of Dermatology, the Arizona Dermatology Society, the Southwestern Dermatology Society and the American Society for Laser Medicine and Surgery.

Disclosures: Off-label: Medical marijuana is state approved (including CA where lecture is being given and 24 other states) but is not yet federally approved.

Rene Gonzalez, MD
Dr. Rene Gonzalez is a board-certified internist and medical oncologist. After earning his medical degree from the University of Honduras, Dr. Gonzalez completed his internship and residency at Wayne State University in Detroit, MI and post-doctoral fellowship in medical oncology at the University of Colorado. He joined the faculty at the University of Colorado in 1994 and became director of the Melanoma Research Clinics the same year. This comprehensive program developed into one of the largest in the U.S. and includes multi-disciplinary melanoma clinics and tumor board and basic research.

Dr. Gonzalez’s clinical interests are malignant melanoma and other cutaneous malignancies. He is the principal investigator on numerous national and local therapeutic trials. Dr. Gonzalez is a co-chair of COMIRB and a member of several professional societies including the American College of Physicians, the American Society of Clinical Oncology and the Society for Melanoma Research. He is associate editor of Therapeutic Advances in Medical Oncology and on the editorial board of Melanoma Management. He has authored or co-authored several book chapters and more than 100 scientific articles that have been published in peer-reviewed journals.

Melanoma: The Modern Black Plague
There has been tremendous progress in melanoma therapy in the last 5 years that has revolutionized the field. It is difficult for the practitioner to keep abreast of the new research and place it in context because of rapid change.

Objectives:
1. Provide attendees with an update on new information and studies
2. Provide attendees with an update new therapies
3. Provide attendees with new detection techniques
Needs:
1. Development of new technology
2. Advances in medical knowledge

Reference:

Core Competencies: 2, 3, 5, 6

Disclosures: Research grants: Roche/Genentech, Novartis, BMS, Merck, Amgen, Polynoma, Millennium, Takeda, Incyte, Reata, Dynavax, Checkmate, Morphotek, Castle Biosciences; Consultant for: Roche/Genentech, Novartis, Amgen, Castle Biosciences; Off-label: Unapproved uses of various drugs

Whitney High, MD
Dr. Whitney High, a native of Colorado, is the director of the laboratory, and he is board-certified in dermatology and dermatopathology. He also has certification in tropical medicine and hygiene. After practicing as a chemical engineer in industry, Dr. High returned to medical school to receive his medical degree from the Mayo Clinic School of Medicine in 2000. He completed his dermatology residency training at the University of Texas Southwestern Medical Center in 2004, serving as chief resident and his dermatopathology fellowship at the University of Colorado in Denver in 2005. He has also studied tropical medicine in Central and South America.

Dr. High is appointed to the Departments of Dermatology & Pathology at the University of Colorado and the Department of Chemistry at the Colorado School of Mines. He serves as the only dermatologist on faculty at the Denver STD/HIV Training Center, a clinic sponsored by the Centers of Disease Control (CDC). Dr. High also has a degree in law from the University of Denver. Dr. High has authored two textbooks, 12 chapters and more than 40 medical papers. He currently serves as one of the youngest editors of the Journal of the American Academy of Dermatology, and he is an editor/editorial board member of other medical journals.

Dr. High’s current research interests include: pigmented lesions, medico-legal issues, infectious disease/sexually transmitted disease, pharmacological and toxicological dermatology/dermatopathology and advanced biochemical testing applied to dermatology/dermatopathology.

Dysplastic Nevi
This lecture highlights what is known of the relationship between benign nevi, dysplastic nevi and melanoma.

Objectives:
1. Provide attendees with an understanding of the conundrum of dysplastic nevi and their relationship to melanoma
2. Help attendees appreciate the difficulties in distinguishing between benign, malignant and indeterminate melanocytic lesions
3. Help attendees recognize situations were uncertainty regarding pigmented lesions manifests in differences in clinical care

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

References:
**Core competencies:** 2, 3, 6, 7

**Common Dermatology Mistakes from a Dermatopathologist Perspective**

This lecture highlights missed opportunities in care at the interface of dermatology and dermatopathology.

**Objectives:**
1. Help attendees recognize limitations in dermatopathology assessment
2. Provide attendees with an understanding of situations where clinicopathologic correlation is requisite
3. Help attendees improve biopsy technique to improve diagnosis with patient 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

**References:**

**Medicolegal Implications of Being a Dermatologist**

This lecture covers the basics of malpractice law and malpractice situations as they apply to dermatology.

**Objectives:**
1. Provide attendees with an understanding of the risk of malpractice in dermatology
2. Help attendees recognize situations in which the risk of malpractice allegation are higher
3. Help attendees lessen the risk of malpractice or malpractice allegation by improving care in high right situations

**Needs:**
1. New methods of diagnosis or treatment
2. Legislative, regulatory, or organizational changes effecting patient care

**References:**

**Disclosures:** Consultant for Myriad Labs, Castle Biosciences; Off-label: Some immunostains used in the diagnosis or melanoma are based on validation at the University of Colorado.
Will Kirby, DO, FAOCD
Board-certified dermatologist, Dr. Will Kirby, has a degree in biology from Emory University. He received his medical degree from Nova Southeastern University and completed his first year of postgraduate training in internal medicine at Mount Sinai Medical Center. His dermatology residency training took place in association with Western University/Pacific Hospital where he was honored by being selected to serve as chief resident in the Department of Dermatology. Academically, Dr. Kirby proudly serves as a Clinical Assistant Professor of Dermatology at Western University of Health Science and as a Clinical Assistant Professor in the Department of Internal Medicine, Division of Dermatology, for Nova Southeastern University. He is also an expert reviewer for the Osteopathic Medical Board of California in dermatology.

Dr. Kirby lectures at national medical conventions, publishes articles in peer reviewed medical journals, authors and co-authors medical text book chapters and has the prestigious honor of serving on the editorial advisory board of popular dermatological publications including the *Dermatologist* and the *Journal of Aesthetic and Clinical Dermatology*. He has served as the national spokesman for Johnson & Johnson’s Neutrogena Dermatologics and Kimberly Clark’s Triust Skin Care lines.

A licensed osteopathic physician and surgeon in the state of California since 2002, Dr. Kirby is recognized as a Fellow by the American Osteopathic College of Dermatology. He is currently a member of the American Osteopathic College of Dermatology (AOCD) and the American Osteopathic Association (AOA). In the past, Dr. Kirby has held membership in the American Medical Association (AMA), the American Society for Laser Medicine and Surgery (ASLMS), the American Society of Dermatologic Surgery (ASDS) and the American Academy of Dermatology (AAD). Having appeared on more than 35 different television shows, Dr. Kirby was a featured physician on E! Entertainment Television’s “Dr. 90210” and has frequently been seen on “The Doctors,” where he showcases his dermatology practice. Other TV appearances have included “The Young & The Restless,” “LA Ink,” “The Real Housewives of Orange County,” “Regis & Kelly,” “The Talk” and “Chelsea Lately” and has appeared on QVC more than 100 times. Dermatologist, professor, spokesman, researcher and author, Dr. Kirby is well-recognized as one of the country’s leading dermatologists!

**Rules, Regulations, Compliance & Medico-Legal Considerations for Cosmetic Medicine**
Topics addressed will include state and federal rules, regulations and compliance and medico-legal considerations. Extremely practical and hands-on information will be presented to those in attendance to assist with a better understanding of the often neglected parts of a dermatological practice.

**Objectives:**
1. Explore state rules and regulations
2. Discuss compliance mechanisms
3. Review medico-legal issues

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

**References:**
- [http://scholarship.law.edu/cgi/viewcontent.cgi?article=1529&context=jchlp](http://scholarship.law.edu/cgi/viewcontent.cgi?article=1529&context=jchlp)
- [http://www.ombc.ca.gov/](http://www.ombc.ca.gov/)

**Core competencies:** 4, 5

**Disclosures:** No disclosures provided by speaker
Karthik Krishnamurthy, DO, FAOCD

Dr. Krishnamurthy is a board-certified dermatologist and a member of the American Academy of Dermatology and was elected to serve as the National President of the American Osteopathic College of Dermatology in 2016. Dr. Krishnamurthy graduated from the University of Missouri with dual degrees in Biochemistry and Medicinal Chemistry and received his medical degree from Nova Southeastern University. After his internship at Cook County Hospital in Chicago, IL, Dr. Krishnamurthy completed his dermatology training at St. Barnabas Hospital in New York, NY, where he served as chief resident.

Dr. Krishnamurthy then joined the academic faculty as Associate Professor at the Albert Einstein College of Medicine in New York, where he served as Chief of Dermatology for Jacobi Medical Center, the largest public hospital in New York City, and created a cosmetic and laser dermatology program at Montefiore Medical Center, serving as its director. Devoted to education, he trained residents daily, and was awarded “Teacher of the Year” in 2014. Dr. Krishnamurthy’s commitment to leadership and research has been recognized by the Kenneth Burnell Research Scholarship, Intendis Research Award, Allergan Research Grant, New York Academy of Medicine and American Academy of Dermatology. Paralleling his academic pursuits, Dr. Krishnamurthy was the recipient of the 2011 Academic Dermatology Leadership Program and the 2012 Editorial Mentorship program, both granted by the American Academy of Dermatology. In addition, he serves as Editor-in-Chief of the Journal of the American Osteopathic College of Dermatology and Dermatologic Surgery and co-authored the textbook Emergencies in Dermatology.

Given his exposure to the varied culture, ethnicity, skin-types and demographics in New York City, Dr. Krishnamurthy is an expert in complex medical dermatology, especially psoriasis, vitiligo, auto-immune diseases (lupus) and phototherapy/excimer laser, as well as dermatologic surgery, nail surgery, earlobe repair and cosmetic/injectable/laser dermatology. He is often called upon as a media expert, contributing to the New York Times, the L.A. Times, Washington Post, WebMD, CBS News, Yahoo News, Good Housekeeping and Weather.com. He relocated to Greater Jacksonville, FL with his wife, Dr. Aneesa Krishnamurthy (Rheumatologist) and twin sons.

Updates in Dermatology

Objectives:
1. Provide attendees with an awareness of updates in dermatology and how to implement this knowledge into daily clinical practice and patient care
2. Change pre-, peri- and post-operative practices based on recent updates and reviews
3. Help attendees understand emerging therapies and management strategies for dermatologic disease

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

References:

Core competencies: 1, 2, 3, 6, 7

Pearls in Dermatology/Rheumatology

Review of literature, studies and new drugs from the last 24 months pertinent to dermatology.

Objectives:
1. Recognize emerging knowledge on disease state processes and management updates in dermatology, specifically rheumatologic disease
2. Analyze new data
3. Apply new knowledge and integrate changes in patient care

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

References:
• Raaschou P, Simard, JF, Hagelberg, CA, Askling J. “Rheumatoid Arthritis, Anti-Tumor Necrosis Factor Treatment, and Risk of Squamous Cell and Basal Cell Skin Cancer: Cohort Study Based on Nationwide Prospectively Recorded Data from Sweden”, BMJ 2016;352:i262.

Core competencies: 1, 2, 3, 6, 7

Disclosures: Off-label: Off-label uses of drugs and investigations devices

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

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

Image Guided Superficial Radiation
Discussion of multiple image guided technologies for the treatment of basal cell carcinoma and squamous cell carcinoma. Discussion of how patient care and expectations will be impacted by image guided technologies. Discussion of the history of radiation in dermatology and modern day advances.

Objectives:
1. Present a new FDA approved technology for treatment of basal cell carcinoma, squamous cell carcinoma and keloids
2. Discuss use of image guided SRT to improve patient compliance, safety and satisfaction
3. Discuss multiple new image guided dermatologic technologies and how they can benefit the specialty of dermatology

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:
• Panizzon, R. “Radiation Treatment and Radiation Reactions in Dermatology”. 2004, pp 53-64.

**Core competencies:** 1, 2, 3, 4, 5, 6, 7

**Disclosures:** Medical director of Center of Excellence, Sensus Healthcare; Medical director, minority shareholder of SkinCure Oncology

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**Ashfaq A. Marghoob, MD**

Dr. Ashfaq Marghoob is a board-certified dermatologist specializing in the diagnosis and treatment of cancers of the skin. He is the director of Memorial Sloan Kettering’s regional skin cancer clinic in Hauppauge, Long Island. In addition to consulting and treating patients in Hauppauge, he also sees patients at the Center’s outpatient facility in Manhattan.

Although providing the best care possible for his patients remains his primary goal, Dr. Marghoob also remains committed to education and clinical research. His hope is that educating physicians and the public about the importance of early skin cancer detection will help save lives.

Dr. Marghoob is active in clinical research and has published numerous papers on topics related to skin cancer with an emphasis on melanoma, atypical/dysplastic nevi and congenital melanocytic nevi. His research interests are focused on the use of imaging instruments such as photography, dermoscopy and confocal laser microscopy to recognize skin cancer early in its development. He frequently lectures on these topics both nationally and internationally.

**Dermoscopy Update**

The lecture is designed to help create a framework to guide Dermoscopy users in evaluating lesions for the purpose of making the most accurate clinical diagnosis and in selecting the most appropriate management decisions.

**Objectives:**
1. Help attendees learn the dermoscopic features to help differentiate melanocytic from non-melanocytic lesions
2. Help attendees learn the dermoscopic features to help differentiate nevi from melanoma
3. Acknowledge the importance of shiny white structures, negative network and vessels in identifying skin cancer

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

**References:**

**Core competencies:** 2, 3, 6

**Disclosures:** No disclosures provided by speaker
E. Victor Ross, MD

E. Victor Ross, MD, is a board-certified dermatologist specializing in laser surgery of the skin. He uses a broad array of technologies to reduce red and brown skin lesions, wrinkles and unwanted hair, improve spider veins of the legs and improve the appearance of scars, including acne scars. Dr. Ross also provides a variety of injectables and fillers to relax upper face lines and replace lost volume of the lower face.

In addition to his clinical practice, Dr. Ross conducts research on novel approaches to skin rejuvenation. With access to the latest technologies, he is able to conduct research on fractional lasers for acne scars, use of a novel radio frequency device for stretch mark reduction and the use of novel intense pulsed light for the reduction of red and brown spots on the face, chest and extremities. Presently, Dr. Ross and colleagues are conducting a trial that studies laser tattoo removal with fewer treatment sessions and less pain.

Throughout his career, Dr. Ross has achieved many accomplishments. He was the first Navy-sponsored fellow in photomedicine and lasers at Massachusetts General Hospital, where he conducted research and clinical trials in photodynamic therapy and novel laser applications. He was honored with the prestigious Chairman of the Joint Chiefs of Staff Award for Excellence in Military Medicine. He was elected president of the American Society for Laser Medicine and Surgery (ASLMS), the world's largest professional organization dedicated to promoting excellence in patient care. He was also elected to the board of the American Society of Dermatologic Surgery. He was recognized by the American Society for Laser Medicine and Surgery (ASLMS) with the Caroline and William Mark Memorial Award, as well as the Leon Goldman Award, for his lifetime contributions to research.

Presently, he is the director of the Scripps Clinic Laser and Cosmetic Dermatology Center and a frequent lecturer at national and international meetings on cutaneous laser medicine. He also serves on the editorial board of two major dermatologic journals.

**Laser Fundamentals/New Technology**

**Lasers: Lessons Learned**

Review of foundation of laser tissue interactions followed an itemized list of applications in dermatology.

**Objectives:**
1. Help attendees understand laser tissue interactions
2. Help attendees apply lasers and light sources in a logical fashion for cutaneous disorders
3. Help attendees recognize side effects and potential complications of laser procedures

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

**References:**

**Core competencies:** 2, 3, 5, 6

**Disclosures:** Research support (honoraria) from Cynosure, Cutera, Ellipse, Lutronic

Peter Saitta, DO, FAOCD

Dr. Peter Saitta received his Bachelor of Arts from New York University and his medical degree from the University of Medicine and Dentistry of New Jersey. He completed his dermatology residency as chief resident at Oakwood Hospital. Dr. Saitta assists with the osteopathic dermatology residency program at St. John's Hospital in New York and is also a clinical instructor of dermatology at NYU department of dermatology, where he assists in teaching the residents patch testing.
The Classification and Treatment of Hand Dermatitis
This lecture will help dermatologists understand the clinical aspects and treatment options for hand dermatitis. The lecture will review the prevalence, classification of, differential diagnosis of, and treatment options for hand dermatitis patients.

Objectives:
1. Understand the prevalence of hand dermatitis
2. Understand the classification system of hand dermatitis and differential diagnosis
3. Understand the different treatment options for hand dermatitis

Needs:
1. Availability of new medication(s) or indication(s)
2. Development of new technology
3. Advances in medical knowledge

References:

Core competencies: 2, 3, 6

Disclosures: No disclosures provided by speaker

Robert Signore, DO, FAOCD
Dr. Signore was born in Blue Island, IL and was raised on the southwest side of Chicago. After graduating from Bogan High School, he studied at Loyola University of Chicago, where he graduated in 1982 with a bachelor's degree in biology. Dr. Signore attended medical school in Des Moines, IA at the University of Osteopathic Medicine and Health Sciences (now known as Des Moines University) and graduated in 1986 with his D.O. degree.

He completed a rotating internship at Pontiac Osteopathic Hospital in Pontiac, MI. Dr. Signore then completed a family practice residency at St. Joseph Hospital in Flint, MI. He returned to Pontiac Osteopathic Hospital for his dermatology residency, which he completed in 1992. During residency, he received the P.O.H. Resident of the Year Award. Additionally, he trained with John von Weiss, MD at the von Weiss Skin Center in Salem, MA.

Dr. Signore is board-certified in dermatology by the American Osteopathic Board of Dermatology. Dr. Signore has also studied classical homeopathic medicine through the British Institute of Homeopathy (USA). He received his Diploma of Homeopathy (DiHom) from the British Institute of Homeopathy (USA) in 2009. He has implemented classical homeopathic medicine into his dermatology practice for the treatment of patients with skin conditions.

How Classical Homeopathic Medicine Can Be Helpful For Children With Skin Diseases
Topics addressed will be a brief review of classical homeopathic medicine, a description of the four most common clinical homeopathic constitutional patient types and a simplified approach to patient remedy selection.

Objectives:
1. Provide a historical overview of melanoma
2. Provide an overview of rapid advances in the treatment of melanoma since 2011
3. Help attendees target agents and immunotherapy of melanoma
4. Address unanswered questions and future directions

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

References:

**Core competencies: 2, 3**

**Disclosures:** No financial relationships with proprietary entities in healthcare industries or no conflicts of interest; **Off-label:** The treatment of warts and molluscum with classical homeopathic medicines

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**Lisa Swanson, MD**

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

**General Pediatric Dermatology**
Everything new and important in pediatric dermatology from the last year.

**Objectives:**
1. Discuss new therapeutics for children with skin disease
2. Help attendees identify common pediatric skin conditions
3. Help attendees learn about what is new and interesting in pediatric dermatology

**Needs:**
1. Discuss new therapeutics for children with skin disease
2. Identify common pediatric skin conditions
3. Learn about what is new and interesting in pediatric dermatology

**References:**

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

**Interesting Cases in Pediatrics**

**Objectives:**
1. Discuss new therapeutics for children with skin disease
2. Help attendees identify common pediatric skin conditions
3. Help attendees learn about what is new and interesting in pediatric dermatology

**Needs:**
1. Discuss new therapeutics for children with skin disease
2. Identify common pediatric skin conditions
3. Learn about what is new and interesting in pediatric dermatology

**References:**

21
Core competencies: 2, 3, 4, 5, 6, 7

Disclosures: Speaker for Valeant, Bayer; Advisory board: Allergan; Off-label: JAK inhibitors for various derm conditions, topical beta blockers for vascular lesions, topical Rapamycin for derm conditions, Gleevac for stiff skin syndrome.

Craig Ziering, DO, FAOCD
Dr. Craig Ziering received his Doctorate of Osteopathic Medicine from Nova Southeastern University in Miami, FL and completed his residency at Ohio University's Grandview Medical Center in Dayton, OH. After completing a fellowship in hair restoration with Medical Hair Restoration in Orlando, FL, Dr. Ziering became the Associate Medical Director at MHR for a period of ten years before founding his private practice, Ziering Medical. Dr. Ziering is certified by both the American Board of Hair Restoration Surgery and the American Osteopathic Board of Dermatology.

A Past-President of the American Osteopathic College of Dermatology, Dr. Ziering serves on advisory boards for various companies including Merck, Lexington International, Pfizer and on the scientific advisory board of Histogen (Regenerative Medicine). He is on the surgical faculty for the procedural dermatology fellowship at the University of California at Irvine, the dermatology faculty at Western University/Pacific Hospital, Long Beach, CA and the Michigan State University dermatology faculty. Additionally, Dr. Ziering is the Medical Director for Advanced Hair Growth and Apira Science as well as being the Primary Investigator for the clinical trials involving hair cloning and multiplication. In 2003, Dr. Ziering was recognized by his peers at the International Society for Hair Restoration Surgeons for his Whorl Hair Classification System being awarded the prestigious, “Most Original New Idea” at that year’s scientific assembly.

As a recognized expert in the art and science of hair transplant surgery, Dr. Ziering is a frequent guest on television and radio programs, including the Today Show and was invited to perform the very first hair transplant procedure on ABC’s hit show, Extreme Makeover.

Hair restoration is Dr. Ziering’s passion and he has been and continues to be active in the industry through ongoing education and research in the U.S. and abroad, serving frequently as a guest surgeon and lecturer and as primary investigator in various clinical trials. He is the author of many published articles on surgical and non-surgical treatments of hair loss.

Male and Female Pattern Hair Loss
The causes of male and female hair loss as well as therapies both non-surgical and surgical will be discussed and case descriptions will be presented.

Objectives:
1. Provide attendees with an understanding of male and female pattern hair loss
2. Discuss non-surgical therapy for male and female pattern hair loss
3. Discuss surgical therapy for male and female pattern hair loss

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 technologies
5. Advances in medical knowledge
6. Legislative, regulatory, or organizational changes effecting patient care

References:
• Hair loss & Replacements for dummies. William Rassman, MD.
• Hair Transplantation by Unger – Robin Unger.

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

Disclosures: Research and development for Restoration Robotics
Thursday, September 15, 2016

6:30 a.m. - 7:30 a.m.  Breakfast with Exhibitors

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

8:00 a.m. - 9:00 a.m.  The Classification and Treatment of Hand Eczema  
Peter Saitta, DO, FAOCD

9:00 a.m. - 10:00 a.m.  Creative Ways to Maximize Professional Efforts Most Effectively and Avoid Practice Pitfalls  
Will Kirby, DO, FAOCD

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

10:30 a.m. - 11:30 a.m.  Treating Skin Cancer with Radiation: Traditional and New Approaches  
Timothy Brant, MD

11:30 a.m. - 12:30 p.m.  The Business of Dermatology  
Eric Adelman, DO, FAOCD & John Ramm

12:30 p.m. - 1:00 p.m.  Lunch with Exhibitors

1:00 p.m. - 2:00 p.m.  Melanoma: The Modern Black Plague  
Rene Gonzalez, MD

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

2:30 p.m. - 3:30 p.m.  Updates in Dermatology  
Karthik Krishnamurthy, DO, FAOCD

3:30 p.m. - 4:30 p.m.  Pearls in Rheumatology-Dermatology  
Karthik Krishnamurthy, DO, FAOCD

4:30 p.m. - 5:30 p.m.  Taltz (Ixekizumab): An Expert Review of the Clinical Data  
Michael Heffernan, MD  
Lilly Product Theater (No CME awarded)
The Classification and Treatment of Hand Eczema

Objectives

- Period prevalence
- Risk factors
- Classification systems
- Differential diagnosis
- First-line therapy options

Period Prevalence

- Prevalence
  - Number of new cases per time period
- Period prevalence
  - Number of patients with outbreaks during a time period
  - Varies 2-10%¹-³

Hand Eczema Risks

<table>
<thead>
<tr>
<th>STUDY</th>
<th>NO AD / NO IRRITANT WATER EXPOSURE</th>
<th>AD / NO IRRITANT WATER EXPOSURE</th>
<th>AD / IRRITANT WATER EXPOSURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meding et al. 1990</td>
<td>5-9%</td>
<td>14-23%</td>
<td>34-48%</td>
</tr>
<tr>
<td>Nilsson et al. 1988</td>
<td>16%</td>
<td>38%</td>
<td>62-72%</td>
</tr>
<tr>
<td>Rydelit et al. 1985</td>
<td>5%</td>
<td>37-50%</td>
<td>60-81%</td>
</tr>
</tbody>
</table>

Hand Eczema Risks: Atopic Dermatitis

- Atopic dermatitis
  - Lammintausta et al. 1991
  - Coenraads et al. 1998
  - Meding et al. 2000
  - Meding et al. 2004
  - Toledo et al. 2008
- Allergic rhinitis/asthma increases risk of hand eczema
- But not more than atopic dermatitis

**Hand Eczema Risks: Allergic Rhinitis and Asthma**

- Female gender increased risk
  - Coenraads et al. 1983
  - Kavli et al. 1984
  - Lantinga et al. 1984
  - Bryld et al. 2000
  - Yrveson et al. 2000
  - Meding et al. 2001
  - Mortz et al. 2001
  - Dickel et al. 2002

- Meding et al. 5
  - Wet work in 19-29 year-olds
  - 37.5% of women occupationally exposed
  - 18.2% of men
- Learbek et al. 6
  - Private exposures

**Hand Eczema Risks: Female Gender**

**STUDY** | **TYPE OF STUDY** | **STUDY POPULATION** | **INCIDENCE (PER 100)**
---|---|---|---
Lantinga et al. 1984 | Retrospective | General Population | 7.9
Uter et al. 1994 | Prospective | Handdressers | 13.2
Smid et al. 1994 | Prospective | Handdressers Nurses | 128
Braman et al. 1998 | Retrospective | Bakers | M: 16.7, F: 34.4
Uter et al. 1998 | Prospective | Office workers | 41
Funke et al. 2001 | Prospective | Industrial Factory Workers | 47

**Hand Eczema Risks: Occupation**

**ACD**
- Delay onset of effective treatment
- Atopic Dermatitis
- Greater area of involved skin
- > 1 year of duration

**Hand Eczema Risks: Smoking**

Support Risk
- Edman et al.
- Montnemery et al.
- Linneberg et al.

Negative Risk
- Lerbeack et al.
- Berndt et al.

**Poor Prognosis**
- Etiology
- Morphology
  - No clear link between morphology and etiology\(^\text{11}\)
  - Question the need of morphological classification system

Irritant contact dermatitis
Allergic contact dermatitis
Atopic dermatitis
  - 80%
  - Idiopathic
    - 20%

### Classification System

- Irritant Contact Dermatitis\(^\text{11}\)
  - Most common
    - Wet work
    - Water
    - Mechanic / Machinery oils
    - Detergents
    - Tight-fitting gloves
    - Friction

### Wet Work
- Wet hands or glove wearing > 2 cumulative hours daily\(^\text{11,12}\)
- Greater than 20 hand washes daily\(^\text{12}\)

- Allergic Contact Dermatitis
  - Way more common in occupational exposures vs. private exposures (Hobby)\(^\text{11}\)
  - "Hand eczema that spreads"\(^\text{13}\)
- Protein Contact Dermatitis
  - RARE
  - Latex
  - Food proteins
  - Burning, stinging and itching seconds to minutes after contact\(^\text{14}\)
- Systemic Contact Dermatitis
  - VERY RARE
  - Specific definition\(^\text{11}\)
    - Positive patch test
    - Ingest an oral version
    - Vesicular hand/foot rash

- Atopic dermatitis
- Other genetic
  - Filaggrin null mutations\(^\text{15,16}\)
  - Twin studies show that MZ twin individuals having a co-twin with hand eczema had an increased risk of hand eczema compared with DZ twins\(^\text{6}\)
    - Atopic dermatitis adjusted
- Idiopathic CHE
  - 20%\(^\text{11}\)
Guidelines of the Danish Contact Dermatitis Group

- Chronic dry fissured hand eczema
- Vesicular hand eczema
- Hyperkeratotic (Tylotic) hand eczema
- Interdigital hand eczema
- Pulpitis
- Nummular hand eczema
- Mixed
  - 50.5% demonstrate multiple morphologies17
Palmoplantar Psoriasis

- Frequency based on location\textsuperscript{19}
  - 1. Generalized Plaque – 49.3%
  - 2. Localized Plaque – 16.9%
  - 3. Guttate – 12.8%
  - 4. Arthropathic – 7.7%
  - 5. Palmoplantar – 7.5%
  - 6. Pustular – 3.1%
  - 7. Other – 2.7%

Vesicular Hand Eczema

- Intermittent\textsuperscript{20}
  - Intensely pruritic
  - Palms/soles, nail, and sides of fingers
  - Attacks between 1 and 10 months
  - Two historical descriptions
    - Pompholyx
    - Dyshidrosis

- Frequency of location\textsuperscript{20}
  - 1. Hands alone – 46.8%
  - 2. Feet alone – 24.1%
  - 3. Hands and feet – 15.6%
  - 4. Nail apparatus – 13.5%

Vesicular Hand Eczema

- Anatomic Location\textsuperscript{20} | Fungi Positive
  - Hands | 1.2%
  - Feet | 47.8%
  - Epidermophyton interdigitale 100% of foot cases

Vesicular Hand Eczema

- Lane et al.\textsuperscript{21} 25% of any location positive fungal infection
- Pitche et al.\textsuperscript{22} 10% of any location positive fungal infection
- Guillet et al.\textsuperscript{23} 15.8% of any location with T. rubrum or candida infection

- Always check the feet
  - Foot involvement is rare
  - 47.8% dermatophyte infection
Vesicular Hand Eczema
Dyshidrosiform Pattern

- Presence of erythema
  - Controversial
- Progression of lesions\(^{24}\)
  - Early stage
    - Vesicular
  - Late stage
    - Chronic dry fissured presentation
    - Studded with pinpoint necrotic vesicles
    - Wet glazed look with pinpoint necrotic vesicles
Vesicular Hand Eczema: Late Stage Dyshidrosiform Pattern

- Very rare
- Single episode of palms and soles
- Vesicular and **BULLOUS** eruption

Vesicular Hand Eczema: Pompholyx

- Dyshidrosiform bullous pemphigoid
- Herpes gestationis
- Linear IgA
- Lymphoma

Palmoplantar Pustulosis

- Localized to palms and soles\(^{25}\)
  - 1. Soles only 47.36%
  - 2. Palms only 31.57%
  - 3. Both soles and palms 21%
- Mildly pruritic
Middle-aged men
NEVER VESICLES

- Dominant hand
- Site for the start of irritant hand dermatitis$^{26,27}$
Interdigital Hand Eczema

Erosio Interdigitale Blastomycetica

Scabies
- Very rare
- Must rule out atopic dermatitis
  - No elevated IgE or eosinophilia
- Nummular Atopic Dermatitis
  (Bologna)

- Systems good for academic pursuit
- Pure clinical pictures are less likely
  - 50.5% demonstrate multiple morphologies\(^{17}\)
- Morphology changes frequently clinically and histologically\(^{17}\)
- No clear link between morphology and etiology
  - Johansen et al.\(^{28}\)
  - Cronin et al.\(^{29}\)
  - Diepgen et al.\(^{30}\)

Any combination of above

Problems with Current Classification
- Is it an eczematous process?
- Acute – vesicles/bullae
- Subacute/Chronic – scaling/erythema

IF ACUTE
CHECK THE FEET
CHECK THE FEET
CHECK THE FEET

- Hand Eczema
- Evaluation Irritant
  - Do you touch liquids many times a day including water?
- Evaluation Atopic
  - Did you have childhood eczema, allergies or asthma?
- Allergic
  - What do you do for work?

- Standard Series
  - Toledo et al.
  - Linberg et al.
  - Menne et al.
- Worker’s Compensation
- Irritant contact dermatitis
  - Toledo et al.
  - Linberg et al.
  - Menne et al.
  - 21% with positive patch test
  - 30% relevant
  - Nickel (100%)
  - ACD worse prognosis

#1 Treatment is the same
#2 Blow them up
#3 And then juice em up
#4 Don’t stop treatment if it gets better

#5 Shake their hands
#6 What worked before, may not work again
#7 It gets better with time
  - Period prevalence decreases with aging
  - 78% of subjects claimed improvement of symptoms over 15 years
### Treatment: Hand Care Instructions

- Decrease number of washes daily  
  “Your hands are broken, if your leg was broken would you still walk on it”
- Alcohol based disinfectants are less irritating to the skin than soap and water
- Apply emollient within 2-3 minutes of wash  
  - Greasy as possible
  - Fragrance free
  - Apply as many times during day as you like

### Treatment: Gloves

- Use gloves when wet work or dirty work
  - Latex or vinyl
  - Tight-fitting
  - Cotton liner
  - Change when damp

### Alternatives to Topical Steroids

- Tacrolimus 0.1% vs. mometasone furoate
  - 50% improvement in both groups
- Pimecrolimus vs. mometasone furoate
  - Did not reach statistical significance
- Used in combination with steroids
  - Clear (Cohen)
  - 1st week: ½ Steroid Ointment ½ Tacrolimus
  - 2nd week: ⅔ Steroid ointment ⅓ Tacrolimus
  - 3rd week: ⅔ Steroid ointment ⅓ Tacrolimus
  - 4th week: ALL Tacrolimus
  - 5th-on: ALL Tacrolimus Fri, Sat, Sun

### First-Line: Topical Steroids

- Which one should I use?  
  - Potent 65.5%
  - Moderate 30.53%
  - Superpotent 2.3%
  - Mild 1.67%
- How often and for how long?  
  - Once daily dosing equal efficacy as twice daily
  - Two-week intervals
  - Even switching in the same class can prove to be beneficial (Holland)

- First Blow  
  - Prednisone 40-60mg daily initial dose and taper between 3-4 weeks  
  - Intramuscular Kenalog 40-80mg  
    - Limit 4 shots per year (Wolverton)
- Second Blow  
  - Prednisolone 30mg daily for 3 days at onset of eruptions
  - Prednisone 40-60mg x 1 dose on day 1 of the eruption

### First-Line: Systemic Steroids
A Comparison on the Efficacy, Relapse Rate and Side Effects among Three Modalities of Systemic Corticosteroid Therapy for Alopecia Areata

- Triamcinolone acetonide 40mg monthly x 6
- Then 40mg every 6 weeks x 18 months
- Total treatment duration = 24 months (2 years)
- Total of TEN 40mg injections annually

56 subjects IM Triamcinolone acetonide arm (29 in prednisolone)
- 16 dysmenorrhea (vs 3)
- 3 abdominal pain (vs 1)
- 1 worsening acne (vs 0)
- 5 adrenocortical impairment (vs 2)
- Both groups resolved in 2 months without steroid taper

Twelve-year clinico-therapeutic experience in pemphigus: a retrospective study of 54 cases

- Intramuscular triamcinolone acetonide was given in cases of poor compliance
  - 80mg IM on day 0, 4, 7, 28
  - 40mg IM every for weeks x 6 doses
  - Total duration of treatment = 6 months
  - Total of TEN injections
- 1 subject with weight gain
- 1 subject with cushingoid features
- Resolved within 4 months without steroid taper

Triamcinolone acetonide: a new management of noncompliance in nephrotic children

- 8 monthly doses of IM Triamcinolone acetonide 2mg/kg
- Each month dose decreased by 10-20%
- Total duration of treatment = 8 months
- Total of EIGHT injection
- All subjects had decreased longitudinal growth
- Normalized

S. aureus
- Systemic antibiotics superior to topicals

Botulinum toxin A
- Left versus right study
- Vesicular hand dermatitis only
- 100 units plus topical steroids

Botulinum toxin
- Left versus right study
- Vesicular hand dermatitis only
- 162 units of botox but no steroids

Treatment: If infected

Botulinum toxin A
- Left versus right study
- Vesicular hand dermatitis only
- 100 units plus topical steroids

Botulinum toxin
- Left versus right study
- Vesicular hand dermatitis only
- 162 units of botox but no steroids

Treatment: If Hyperhidrosis
**Classification systems**

- Period prevalence
  - 2-10%

- Risk factors
  - Atopic dermatitis, allergic rhinitis/asthma, occupation, wet irritant exposure

- Classification systems
  - Etiology and morphology
  - Not practical day-to-day clinic

- Differential Diagnosis
  - Check the feet
  - First-line therapy options
  - Blow em up and then juice em up

---

**Efficacy PUVA**

- Systemic = Topical = Bath
- Decreased UVA doses due to uniform absorption
- Phototoxicity risk disappears after 2 hours
- Sunblock and gloves
- High dose UVA-1
  - Max single dose of 130J/cm²
  - Cumulative dose 1720J/cm²
  - As effective as cream PUVA
  - • As effective as cream PUVA
  - • As effective as cream PUVA
  - • As effective as cream PUVA

---

**Panagonist RXR, RAR**

**Approved Europe**

- Indicated for chronic hand eczema refractory to topical and systemic steroids
- Not for vesicular hand dermatitis

**Retinoid Adverse Events**

- Headache, mucocutaneous dryness, elevated liver enzymes, elevated blood lipid levels, teratogenicity

No combination studies

---

**Alitretinoin**

- Median time to clear hands is 12 weeks
- Placebo, Alitretinoin 10mg, 20mg, 40mg daily doses for 12 weeks
  - 70% reduction in 50%
- Alitretinoin 10mg, 30mg daily for 24 weeks
  - 100% reduction in 48%
- More response with 30mg


55. UVA1 Irradiation is effective in treatment of chronic vesicular dyshidrotic hand eczema. Acta Derm Venereol.


Creative Ways to Maximize Professional Efforts Most Effectively and Avoid Practice Pitfalls

Disclosures:
No relevant disclosures.
No irrelevant disclosures.

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- Expert Reviewer, Osteopathic Medical Board of California, Division of Dermatology
- Expert Witness, Legal Cases involving Aesthetic Dermatology

Other thoughts...
- My goal is to analyze the business of dermatology efficiently so as to maximize effort
- At least some (if not all) of the action items I’ll discuss today are applicable to your own practice
- Mantra: Money ≠ Success. Freedom = Success!
- Sincere thanks to the AOCD for having a meeting in Los Angeles!

Relevant References
1 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1237745/pdf/westjmed00264-0092.pdf
2 http://scholarship.law.edu/cgi/viewcontent.cgi?article=1529&context=jchlp
5 http://www.ombc.ca.gov/
6 http://www.mbc.ca.gov/Consumers/Complaints/Complaints_FAQ/Practices_and_Protocols_FAQ.aspx

This lecture is not...
- A risk management lecture
- All inclusive
- An economic/business discussion
- Applicable to all state rules/regs
- A substitute for legal advice
This lecture is...

- Encouragement to use non-traditional ways to improve your (not practice but) life...
- A means by which to open the audience’s minds to alternative methods of navigating the current medicolegal environment
- A teaching mechanism for insider tips from the speaker who has spent a decade working in the most litigious city in the most litigious state with the most challenging patient population in the universe

Most Importantly...

- This lecture is intended to give you ten real, actual, inexpensive, tangible action items to strongly consider incorporating into your own practice
- Not only might they prevent an unwanted interaction with a patient but they may likely increase patient satisfaction, employee retention and you might be pleasantly surprised to find that they are emotionally rewarding
- While you’ll experience many academic lectures over the next few days, it is my contention that this one in particular can offer a positive impact on your practice

And...

- You don’t need to take notes
- The material is dense and will be peppered with captivating personal stores and enchanting anecdotes
- I’ll emphasize anything important
- **There will be one page recap at the end highlighting all ten action items!**
- I’ll leave time for Q and A as well

Offense Vs. Defense

- Practitioners are often focused on the maximization of patient volume, management of patient schedule, reimbursement and collections.
- The leaves less time (or the outright neglect) of compliance with rules/regulations, and medicolegal considerations.
- The point?
- Offense makes money and defense protects the practice. And a good practice has both!

What to do?

- Many ways to improve “offense” (which means just increase revenue): Hire practice manager, marketing, advertising, expanding hours, hiring allied health care professions, see more patients, work faster, work longer hours, accept more insurance plans, etc.
- But how do you best manage the “defense”?
- Better put: “Winterize your beach house”

Winterize Your Beach House
But Why?

- Why does it matter if I am familiar with the state rules and regulations? My competitors aren’t.
- Lawsuits are scary… but the State Medical Boards are like Mike Tyson on Redbull and Roofies!
- “If you aren’t at the table then you are on the table”

State Rules and Regulations

- Quagmire
- Overregulated Industry
- Conflicting rules and regulations
- Lack of compliance by competitors
- Absence of uniformity in rules/regs enforcement
- Dearth of transparency in the review process

Hire Health Care Attorney to Review Your Practice

- Paid by the hour. Thus, one could argue that they are incentivized to work slowly and inefficiently
- Often bill to obtain information that you can easy obtain by yourself
- Emotionally taxing for you: Fear based practices lead unnecessary and excess work
- But some are excellent and can help ensure that your “defense” is strong

What to Do About Rules/Regs?

- Simply go to your state medical board website to begin:
  I. Subscribe to the monthly newsletter. They often make useful announcements
  II. Go to the FAQ section of the website.
  III. Review the posted (monthly or quarterly) newsletters to see why others ran into issues.
  IV. Apply to become an expert reviewer...

Expert Reviewer

- The Medical Board will contact you to review cases you’ll be financially compensated for your time and effort
- You are protected from lawsuits related to the case
- In some states you remain anonymous
- They often provide training as to how to be an expert reviewer
- You get to participate in the review process and enforcement of rules/regs = best way to truly understand how to keep your practice in compliance

Quarterly Medical Board Meetings

- Attend in-person
- Most have teleconferences where you can listen in remotely
- You can monitor and assemble bills or senate bills coming down the pike so you can be prepared
- You’ll build professional relationships with lobbyists and influence rules regs
Discussion of Lawsuits

• Expensive to defend
• Time consuming
• May coincide with complaint (and subsequent investigation) to the medical board
• Your insurance company may force you to settle
• Emotionally taxing
• Listed as a malpractitioner in the National Practitioner Data Bank (NPDB) pursuant to the Healthcare Quality Improvement Act of 1986 (HCQIA).

Medical Malpractice Insurance

- DUH

- You obviously need med-mal insurance
- Your insurance broker is not your friend
- They will try to sell you more insurance than you need or could ever use
- But annual med-mal review is a good idea; you might be performing procedures that your policy doesn’t even cover

Medical Malpractice Claims

<table>
<thead>
<tr>
<th>Cause of Action</th>
<th>No. (%) of 174 Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of informed consent</td>
<td>50 (30.1)</td>
</tr>
<tr>
<td>Fraud</td>
<td>15 (8.6)</td>
</tr>
<tr>
<td>Loss of consortium</td>
<td>13 (7.5)</td>
</tr>
<tr>
<td>Assault/battery</td>
<td>9 (5.2)</td>
</tr>
<tr>
<td>Strict products liability</td>
<td>9 (5.2)</td>
</tr>
<tr>
<td>Breach of contract</td>
<td>8 (4.6)</td>
</tr>
<tr>
<td>Infection of emotional distress</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Negligent misrepresentation</td>
<td>7 (4.0)</td>
</tr>
<tr>
<td>Gross negligence</td>
<td>5 (2.9)</td>
</tr>
<tr>
<td>Recklessness</td>
<td>4 (2.3)</td>
</tr>
<tr>
<td>Deceptive trade practices</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Negligence per se</td>
<td>18 (10.4)</td>
</tr>
<tr>
<td>Other</td>
<td>16 (9.2)</td>
</tr>
</tbody>
</table>

Informed Consent

- Informal:
  - Often an informed consent comes informally in the course of discussion with a patient during a routine office visit or similar situation.
- Formal:
  - Informed consent can also be given formally, by having a patient sign a document that states that the health care provider has fully discussed a treatment or procedure and that the patient fully acknowledges and agrees to the risks.

What Happens if You Perform a Treatment Without an Informed Consent?

- You could be charged with battery or fraud.
- Battery is defined as an unlawful act of applying force to the person of another without consent.
- You could be accused of negligence in a medical malpractice lawsuit.
### Imperative Parts of a Solid Informed Consent

- Layman’s terms
- Offer alternatives to the treatment
- Alternatives included no treatment at all
- Side effects of treatment
- Chances of developing side effects
- Section for patient to document that they understand the informed consent
- Acknowledgement that they aren’t under the influence or were coerced into signing
- Acknowledgement that all questions were answered.
- Acknowledgement that patient requests treatment

### Arbitration Agreement

- Check with a health attorney in your respective state
- If it is allowed in your state then consider incorporating an arbitration agreement
- An arbitration doesn’t take rights away from patients – it just solves disputes much more inexpensively and quickly
- Your fate isn’t in the hands of a jury
- Arbitration agreements many dissuade frivolous lawsuits

### Obtain Proper Training

- Reps aren’t your friends nor are they qualified to teach you how to use a product or a device
- Your training must be documented and quantified
- Your training needs to meet or exceed the community standards
- Consider seeking out an accredited training facility that offers CME to quantify training

### Purge Problem Patients

- Ten percent of your patients cause 90 percent of your problems. And that takes up a lot of time!
- It is very conceivable to think that those problems patients take a big emotional toll on your employees and you.
- Just like any toxic relationship, you can’t change them.
- Make a list of your problem patients and legally dismiss them.
- Dismissal must meet specific state requirements

### Find More Free Time

### Patient Dismissal Letter

- Must provide letter to patient (USPS letter, certified letter, fax, email)
- Must provide emergency care for 14 days
- Must provide them information as to where they can also receive care
- Provide information on how to obtain medical records
Providing Medical Records

- Patients may have a copy (not original)
- You have 14 days to provide records
- You can (and should!) charge for the records
- You should always mail the records to the patient

Hire an NP or a PA

- Add some diversity to your practice
- Allows you to connects with patients you have little in common with
- It’s the future
- Can be a great income source
- Allows you to concentrate on more important things in life
- Dermatology is the holy grail of medicine because of its relationship with NPs or PAs!

Preventing Burnout

- Financial arguments with patients are stressful.
- Consider giving refunds anytime a patient complains.
- When you do give a refund, require that the patient sign a Refund Release form.
- The Refund Release form requires them to agree to your terms (no disparagement, no complaint to the medical board, no legal action, etc.)
- When the patient cashes the refund check...

Join the Academic Faculty of a Dermatology Residency Program

- The time commitment is extremely flexible
- Patients love having young doctors present
- You keep your skills sharp by teaching
- Education is backbone of our profession
- Dermatology residents have a command of the rules/regs!!!

Refund Release Form

- Financial arguments with patients are stressful.
- Consider giving refunds anytime a patient complains.
- When you do give a refund, require that the patient sign a Refund Release form.
- The Refund Release form requires them to agree to your terms (no disparagement, no complaint to the medical board, no legal action, etc.)
- When the patient cashes the refund check...

Improve Your On-Line Reputation

- Wide net vs. efficient net
- Having an excellent on-line reputation will allow you to capture the best patients
- Perception is Reality
- Social media is the future
- Putting your head in the sand won’t make it go away
- You can easily improve your Yelp, Facebook and Google reviews
Case Study: My Practice

The Next Slide...

...is the only slide you need to pay attention to!

TEN POINT RECAP:
1. Monitor updates from your state medical board!
2. Apply to become an expert reviewer!
3. Review your med-mal insurance policy annually!
4. Improve your Informed Consent (and add an Arbitration Agreement if your state allows it!)
5. Obtain Proper Training!
6. Purge Problem Patients (dismiss properly and possibly provide medical records?)
7. Add a Refund Release form to your practice!
8. Hire an NP or a PA!
9. Join the faculty of a dermatology residency program
10. Improve your on-line professional reputation!

Questions and Answers (Tip: All the answers are “no”)
• May I have a copies of your Informed Consents?
• May I have a copy of your Arbitration Agreement?
• May I have a copy of your Refund Release form?
• May I have a copy of your Patient Dismissal Letter?

Questions and Answers (Tip: All the answers are “maybe”)
• Can you refer me to a med-mal insurance broker?
• Can you refer me, or my NP/PA get proper training?
• Can you refer me to a site to improve my on-line professional reputation?

Real Questions and Answers
• Ask me anything you like...
• I’m an open book...
• I’d rather you ask me now than accost me while I eat a stale muffin in eight minutes...
• I might say “no”.
• But you can always email me at anytime in the future if you think of a question at a later date: DrWillKirby@hotmail.com
Thank you!

- Will Kirby, D.O., FAOCD
Treating Skin Cancer with Radiation Traditional and New Approaches

Timothy A. Brant M.D.
With special thanks for slides and information provided by
William Mendenhall M.D. University of Florida
Michael Kasper M.D. Boca Raton Regional Hospital

Disclosure Statement
I have no financial interest in any of the medical devices in the presentation. I also receive no compensation from any manufacturers of the medical devices presented.

How does radiation cure cancer?
•Causes the formation of free radicals that damage DNA.
•Normal cells can repair damage
•Cancer cells cannot
•Most cancer cells are “sterilized not killed immediately”
•Cancer cells that grow slowly die slowly. Therefore a slow growing basal cell carcinoma may still be present at the completion of treatment and be “sterile” but not dead. Biopsy could even be “positive” and the cancer continue to regress and be cured

Types of Skin Cancer
•Basal cell carcinoma
•Squamous cell Carcinoma
•Melanoma
•Others (lymphoma, Merkel cell etc)

Melanoma
•Melanoma is not radioresistant as previously considered, but does have a tremendous ability to repair damage rendered to the tumor cells with standard daily doses of fractionated radiation.
•The use of larger doses of daily irradiation in some form is needed
•“Hypofractionation” larger single daily doses cause more serious late effects
•“Hyperfractionation”(twice a day or more) lower doses given more often causes less late effects.
2010 AJCC Staging System
New Staging System

Primary Tumor (T)*
TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma in situ
T1 Tumor 2 cm or less in greatest dimension with less than two high-risk features**
T2 Tumor greater than 2cm in greatest dimension or Tumor any size with two or more high-risk features*
T3 Tumor with invasion of maxilla, mandible, orbit, or temporal bone
T4 Tumor with invasion of skeleton (axial or appendicular) or perineural invasion of skull base

*Excludes cSCC of the eyelid (see Chap. 48).
**High-risk features for the primary tumor (T) staging:
- Depth/invasion > 2 mm thickness
- Perineural invasion
- Anatomic location: Primary site ear
- Primary site: non-hair-bearing lip
- Differentiation: Poorly differentiated or undifferentiated

RT for Skin Cancer

- Cure rates after surgery and RT are similar
- Choice depends on age, function, cosmesis, primary site, cost, medical condition, treatment availability, and wishes of the patient

RT Alone for Skin Cancer

- Early cancers on the eyelids, nose, and external ear
- Advanced, incompletely resectable cancers – e.g., perineural invasion with cavernous sinus involvement.

Indications for Irradiation of skin cancers

- Large lesions for which surgery would produce unacceptable functional or cosmetic results and or involving bone or cartilage
- Lesions involving fine facial features (nose, eyelids, commissure of the lips, ears)
- Lesions with multiple recurrences post surgical excisions
- Positive margins. (Usually deep margins in difficult locations next to vessels, nerves, tendons or bone)
- Poor surgical risk
- Multiple lesions
- Lesions with metastases to lymph nodes
- Surgeon preference
- Patient preference

Indications to Consider RT

- Fixation to underlying structures, i.e. cartilage or bone
- Perineural involvement
- Poorly differentiated subtypes
- Recurrent disease
- Infiltrative growth patterns
- Rapid growth
### Post-op for Skin Cancer

**Indications**
- Close or positive margins
- Perineural invasion, particularly if more than unifocal involvement and nerves > 0.1 mm
- Invasion for cartilage or bone
- Positive regional nodes

### Post-op RT for Skin Cancer

- Indicated for patients with high likelihood of residual disease following surgery
- Depends on histology (BCC or SCC), location ("free skin" vs. head and neck), life expectancy, likelihood of successful salvage of local-regional recurrence, and prior RT

### RT for Skin Cancer

**Avoid RT for**
- Younger patients due to deterioration of cosmetic outcome over time and likelihood of additional cancer
- Cancers on hands and feet due to increased risk of complications
- Cancers overlying the tibia and calvarium due to risk of bone exposure/necrosis

### Evolution of technology

- X-ray tubes
- Radium
- Cobalt, Cesium and other high energy radioactive sources
- Low Megavoltage generators
- High Megavoltage Linear accelerators
- Particles- electron beam, protons
- Remote afterloading devices for brachytherapy
- Miniature Xray tubes used for brachytherapy (electronic brachytherapy eBT)

### How Basic principles of Radiotherapy relate to Traditional and New approaches of Radiation for Skin Cancer

- Types of Radiation
- Types of delivery systems
- Treatment Planning
- Physics
- Radiobiology
- Indications (which patients to use traditional or new)
- Clinical data as related to traditional and new results of treatment and complications

### What is traditional and what is new

**Traditional**
- Teletherapy with orthovoltage, electrons, photons
- Interstitial brachytherapy
- Treatment planning with "conventional x-ray and simulation techniques"

**New**
- Treatment with remote loading applicators and molds
- Electronic Brachytherapy
- Treatment planning with PET- CT, MRI and fusion techniques and 3D S
- IMRT/IGRT
**What is traditional and what is new (radiation type)**

- **New**
  - Electronic Brachytherapy:
    - roughly 50Kv x-rays
  - Ir192 HDR source
  - Given utilizing special applicators with limited size and depth of penetration

- **Traditional**
  - Everything else

**Current Radiation Treatment Options for Cutaneous Malignancies**

- Grenz Rays, Superficial Therapy, & Orthovoltage
- Electron beam radiotherapy
- Photon therapy
- Brachytherapy
  - Surface applicators (i.e., Leipzig, Valencia)
  - Surface molds (i.e., Freiberg Flap or custom molds)
  - Interstitial therapy

**Characteristics of various Types of irradiation**

<table>
<thead>
<tr>
<th>Low energy x-rays</th>
<th>High skin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>High bone absorption</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High energy x-rays</th>
<th>Lower skin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less bone absorption</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Electrons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher skin dose</td>
</tr>
</tbody>
</table>

- The higher the energy the more skin dose
- Lower RBE (must give higher dose)

<table>
<thead>
<tr>
<th>Protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>High RBE with steep fall off (very limited use in special circumstances</td>
</tr>
</tbody>
</table>

**Types of delivery systems**

**Teletherapy**
- Orthovoltage (kilovoltage)
- Linear Accelerators (megavoltage)
- Radioactive source (cobalt)

**Brachytherapy**
- Interstitial
- Remote after loading systems utilizing applicators and surface molds radioactive source (Ir192)
- Generated low energy x-rays (miniature x-ray tubes)

**Types of delivery of radiation**

**Traditional**
- Teletherapy
- Orthovoltage x-rays
- Electron beam
- Megavoltage x-rays
- Proton beam
- Interstitial implants

**Modern**
- Surface applicators and molds
- Radioactive isotope (Ir192)
- Generated low energy x-rays with miniature x-ray tubes (eBT)

**Orthovoltage teletherapy machines**

- Produce low energy x-rays
- Small to large field size (varies with machines)
- Variable energies available usually 100kv to 250kv
- Require special shielding
- Filtration (Aluminum, copper, Thoreus) necessary to “harden the beam” when desired
Linear Accelerators

- Produce high energy X-rays (photons) and electrons
- Usually single or dual energy X-rays
- Usually multiple energy electrons e.g. 6, 9, 12, 15, 18 MeV
- Require massive shielding
- Very small to very large field sizes

Cobalt machines

- High energy X-rays produced by radioactive decay of Co60
- Small to large field sizes available
- Rarely used in US but still used in other countries
- Can be used without a particularly reliable electricity source

Remote afterloading-radioactive source type (Ir192) machines

Can treat various malignancies depending on the applicator
Requires source changes every 60 to 90 days (1/2 life Ir192=74 days) to keep treatment times reasonable.
Requires special shielding.
### GammaMedplus iX (Varian)

- Radioactive Ir192 source
- Mean energy 0.38MeV, Max 1.06MeV
- Various skin applicators available (Leipzig, Valencia) sizes usually 20 to 45 mm. Flap type surface molds can also be used.
- Requires special vault or shielding
- Available since 1960's

### Microselectron HDR Elekta-Nucletron

- Radioactive Ir192 source
- Mean energy 0.38MeV, Max 1.06MeV
- Various skin applicators available (Leipzig, Valencia) sizes usually 20 to 45 mm. Flap type surface molds can also be used.
- Requires special vault or shielding
- Available since 1960's

### HDR Surface Molds and Flaps: Advantages

- Conforms easily to curvature of skin
- Optimization algorithms are used to improve dose homogeneity at depth
- Can be useful for sites other than skin, i.e., certain H&N sites and IORT
**Leipzig Applicators (Nucletron)**

- Inner diameters of 1, 2, and 3 cm
- SSD of approx 15 mm
- 1 mm thick plastic cap
- Fixed diameter, tungsten steel surface applicators

**Electronic Brachytherapy**

Electronic Brachytherapy is a method of radiation therapy using an electrically generated source of ionizing radiation made with a miniature x-ray tube to deliver a radiation dose at a distance of up to a few centimeters by intracavitary, intraluminal or interstitial application, or by applications with the source in contact with the body surface or very close to the body surface.

**Electronic Brachytherapy machines**

- Generate low energy x-rays usually around 50 kv with a miniature x-ray tube source
- Can be used to treat various malignancies (gyn, breast, brain) in addition to skin with various applicators
- Minimal shielding is required
- Do require maintenance and x-ray tube changes
- Lead “cut outs” can be used in certain instances to shape the beam

**Xoft Axxent (iCAD, Inc)**

- Electronically generated X-rays
- Max energy up to 50kV
- Applicators 10, 20, 35, 50mm

- Available since 2009
Esteya eBT system (Eleckta AB-Nucletron)
- Electronically generated x-rays
- Maximum energy 50kv
- 10, 20, 30, 40mm applicators
- Available since 2013

Intrabeam PRS500 (Carl Zeiss)
- Electronically generated x-rays
- Maximum energy 50kv
- Applicators 10, 20, 30, 40mm
- Available since 2013

Treatment planning for Skin Cancer ("new planning" for "traditional type" treatment)

**Traditional**
- H&P: Pain, paresthesia’s, dysesthesias, visible skin changes palpable nodules or induration, palpable lymph nodes
- Radiographic finding usually plain radiographs, CT and or MRI, bone scan (in advanced cases)

**"New planning"**
- H&P (same as traditional hopefully)
- PET scan or PET bone
- CT planning for depth dose Rx
- Ultrasound for extent and depth
- Fused PET-planning CT IMRT/IGRT (advanced cases)
Treatment Margins

- 4mm – low risk lesions
- 6mm – high risk lesions

- Minimum margin necessary to achieve >95% tumor clearance by Mohs surgery
- Zitelli and Brodland

Risk Stratification

- Zitelli and Brodland criteria for high risk
  - Tumor diam > 2 cm
  - Mod or poorly diff histology
  - >2mm subcutaneous tissue invasion
  - High risk locations: scalp, nose, ears, lips, and eyelids

Radiobiology

- RBE - Radiobiological effectiveness
- X-rays low and high energy are greater than electrons in general
- (Electron doses should therefore be higher to achieve the same effect)
- Early effects = acute reactions during and immediately following treatment
- Late effects = anything after the acute reaction is over

RT for Skin Cancer

- Orthovoltage RT (if available) unless exit dose is undesirable – e.g. scalp
- Electrons for scalp cancers (free flap reconstruction if post-op)
- Photons for advanced cancers – e.g. invasion of 7th nerve; SCC metastatic to parotid nodes
- Protons to minimize risk of late complications – e.g. PNI of V2 to cavernous sinus

Treatment Planning

Orthovoltage or Electrons

- Draw field on skin surface
- Make stone impression of target area
- Make lead mask to collimate on skin (1 cm larger for electrons)
- Make custom lead block to secondarily collimate electrons with light field 1 cm larger than opening in lead mask
- Increase dose 10% for electrons due to Radiobiological Effectiveness (RBE)

Ortho vs. electrons secondary collimation on skin
Orthovoltage vs Electrons

Advantages:
• Maximum dose is at surface
• Less beam constriction, particularly at depth
• Easier to shield the eyes

Disadvantages:
• Increase exit dose
• Increased differential absorption in bone and cartilage

*Reduce with Thorax filter to harden the beam; disadvantage is increased treatment time compared with half Copper filter.

Prescribed dose is based on:
• Size of lesion (volume of skin)
• Extent of local invasion
• Contiguous normal tissues (site)
• Histology
  • BCC and SCC are very radiosensitive
  • Melanoma is less radiosensitive; requires higher dose per fraction.

Dose as related to complications

• Late effects or complications are related to total dose and fractionation. Higher total dose and higher dose/fx are more likely to cause late complications.
Typical doses for applicators (HDR or eBT)

- 4000cGy /8fx given 2fx/wk*
- 4000cGy/10fx given 5fx/wk
- 4850cGy/10 fx given 2-5fx/wk
- 4200cGy/7fx given 1fx/wk

* Usually specified at 3mm depth

**fractionation used in Bhatnagar, A, BRACHY : 2013.

Dose comparison BED

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose/fx (Gy)</th>
<th># Fractions</th>
<th>Total Dose</th>
<th>BED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>2.5</td>
<td>20</td>
<td>50</td>
<td>74</td>
</tr>
<tr>
<td>Electron</td>
<td>2.5</td>
<td>23</td>
<td>57.5</td>
<td>71.9</td>
</tr>
<tr>
<td>HDR (LEIPZIG)</td>
<td>7.0</td>
<td>6</td>
<td>42</td>
<td>71.4</td>
</tr>
<tr>
<td>HDR (LEIPZIG)</td>
<td>4.85</td>
<td>10</td>
<td>48.50</td>
<td>72.0</td>
</tr>
<tr>
<td>HDR (LEIPZIG)</td>
<td>6.0</td>
<td>7</td>
<td>42</td>
<td>67.2</td>
</tr>
<tr>
<td>HDR (LEIPZIG)</td>
<td>3.5</td>
<td>15</td>
<td>52.5</td>
<td>79.9</td>
</tr>
</tbody>
</table>

Severe acute skin xer.
Pt undergoing chest wall RT for CA Breast post mastectomy. The skin is a target organ and intentionally receives high doses of irradiation.

<table>
<thead>
<tr>
<th>Size</th>
<th>Primary BCC</th>
<th>Primary SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 cm</td>
<td>64/66 (97%)</td>
<td>11/11 (100%)</td>
</tr>
<tr>
<td>1.5-3 cm</td>
<td>71/75 (99%)</td>
<td>19/21 (90%)</td>
</tr>
<tr>
<td>3.1-5 cm</td>
<td>11/13 (85%)</td>
<td>7/8 (88%)</td>
</tr>
<tr>
<td>&gt;5 cm</td>
<td>12/13 (92%)</td>
<td>3/5 (60%)</td>
</tr>
<tr>
<td>Not Specified</td>
<td>4/4 (100%)</td>
<td>0/1 (0%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>162/171 (95%)</td>
<td>40/48 (87%)</td>
</tr>
</tbody>
</table>

Control By Size And Histology
• 520 pts. since 1987
• Sites: skin of face, oral cavity, perianal and external genitalia
• Mostly BCC and SCC of the skin but also others
• Dose: 30 to 40 Gy in 5 to 10 Gy fxs, once or twice/wk
• 92% local control rate; no severe late reactions

Traditional treatment results

Traditional Tx results Large Lesions

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>Basal Cell Carcinoma</th>
<th>Squamous Cell Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10 cm</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>10-15 cm</td>
<td>85%</td>
<td>80%</td>
</tr>
<tr>
<td>&gt; 15 cm</td>
<td>71%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Electronic Brachy Tx Results

Bhatnagar, A. BRACHY:2013

• 122 patients with 171 NMSC lesions were treated with EBT (Isoflex)
• 40 Gy / 8 fractions 2fx per wk specified at 3mm unless otherwise dictated by CT scan
• Mean age 73yrs
• Included 3 lesions which were T cell lymphoma, 2 Merkel cell 4"not available"
• No recurrences after a mean f.u. of 10 months (range 1-28 months)
• 46 lesions (42 patients) had a f.u. of more than 1 year
• Cosmesis was excellent in 93% and good in 7%
Gauden, S. et al. BRACHY Vol 7, April 2008

- 85 pts / 92 lesions tx’d with the Leipzig Applicator
- Histology – 43 BCC, 41 SCC, 1 Merkel Cell
- Sites – 78 H&N, 10 Extremity and 4 trunk
- Dose – 36 Gy / 12 fx
- Median F/U – 37 mo
- Local Control – 90/92 (97%)
- Cosmesis – good to excellent 81/92 (88%)
- Late hypopigmentation in 10 pts (11%)

”Ultrasound guided electronic brachytherapy”

- Pilot study 19 pts, 23 lesions (20 BCC, 3 SCC) treated with Xoft eBT.
- 5 lesions excluded from total of 28 as they could not be visualized by U/S.
- U/S measured depth was the Rx depth. Limited to depth of ≤5mm
- 7 mm radial margin was added to U/S determination of lateral margins

• Dose was 4000cGy/10 Fxs given every other day.
• Two lesions one nose tip another upper lip received 500cGy/20fxs due to “anatomical locations and greater depths.”
• One pt stopped after 32 Gy “due to grade 3 erythema”
• Mean depth 2.1 mm
• No failures (6-22 month follow up)
• No “prolonged skin toxicities have occurred.
• Goyal, Uma et al. J Contemp Brachytherapy. 2015 Oct7(5) 374-380

”Ultrasound guided electronic brachytherapy”

• Post-op patients
• Advanced or large lesions
• T4 lesions
• Lesions involving or close to ears, eyes, nose and lip.
• Scalp, unless very small
• Positive lymph nodes
• Perineural invasion

Recommendations “in general when radiation has been decided to be appropriate”

Traditional
- New
- Small lesions on free skin- not on face or normally exposed skin in younger patients
- Elderly patients who are not candidates for surgery and do not require “traditional” treatment

Fig. 1 A. Women with wall skin cancer in chest treated with 3D conformal external beam radiotherapy. (a) Wound healing at 8 weeks, (b) Appearance at 8 weeks, (c) Appearance at 12 weeks, (d) Appearance at 18 weeks, (e) Appearance at 20 weeks.
Mohs and post op RT with incidental PNI

<table>
<thead>
<tr>
<th></th>
<th>CI</th>
<th>CI5</th>
<th>CI95</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mohs</td>
<td>84</td>
<td>84</td>
<td>83</td>
</tr>
<tr>
<td>Other</td>
<td>76</td>
<td>68</td>
<td>66</td>
</tr>
</tbody>
</table>

P-value: 0.0006, 0.0009, 0.809

University of Florida
Practical recommendations for Dermatologists from a Radiation Oncologist

• In general don’t give radiation treatments to patients who have had prior radiation from a Radiation Oncologist for other malignancies. With modern IMRT techniques the location and amount of skin irradiation may be impossible for you to determine.
• Don’t try to treat larger skin lesions than are appropriate with surface applicators and never match or overlap applicator fields to try to cover larger lesions.

Post Radiation treatment biopsies

• Interpret with caution because:
  • False positives occur due to delayed tumor regression
  • False negatives can occur due to sampling error
  • Uncertain or indeterminate results are common showing radiation changes and questionable viable tumor
  • Can cause necrosis, infection, and worsen cosmetic result
  • In general don’t biopsy unless there is clear evidence of progression

Practical recommendations

• Be cautious in treating facial lesions with applicators as there can be significant acute and late skin effects. The dose/fix for applicators is high (and needs to be to cure some lesions). Radiation Oncologists can prescribe a lower dose/fix giving more treatments, a higher total dose and achieve a cure without as much late complications.

Cost from skin cancer connection blog-web

<table>
<thead>
<tr>
<th>External beam orthovoltage</th>
<th>Electronic Brachytherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Up to $2200 per lesion</td>
<td>• Up to $16,500</td>
</tr>
<tr>
<td>• 4wk course</td>
<td>• 4wk 20fxs</td>
</tr>
<tr>
<td>• 4-6 wk course of electron beam given 5 days/wk is roughly</td>
<td>• 4wk @ 2fxs per wk would be roughly 1/2 because some planning and physics charges are the same for both</td>
</tr>
<tr>
<td>• $5000 (actual reimbursement not charges)</td>
<td></td>
</tr>
</tbody>
</table>

Insurance carriers

• BCBS North Carolina Corporate policy 4/16 next review 4/17
  • “Electronic Brachytherapy for nonmelanoma skin cancer is considered investigational for all applications, BCBSNC does not provide coverage for investigational services or procedures,
  • GroupHealth (same)
  • Medicare??? (depends on location and oversight authority)
Multi-Fraction Payer Coverage – Jan 2016

<table>
<thead>
<tr>
<th>Payer</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>WPS</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>NGS</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Noridian</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Palmetto</td>
<td>Silent</td>
<td>Negative</td>
</tr>
<tr>
<td>First Coast</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>CGS*</td>
<td>Positive</td>
<td>Silent</td>
</tr>
<tr>
<td>Novitas</td>
<td>Silent</td>
<td>TBD</td>
</tr>
<tr>
<td>Cahaba</td>
<td>Silent</td>
<td>Silent</td>
</tr>
</tbody>
</table>

*Underlined represents a change from 2015*

REFERENCES

Physicians in private practice have to accept that they are businessmen as well as healing professionals, and that both the clinical and business sides of the practice come with important responsibilities.

“There is the notion of the more time you spend practicing, the more money you make, sure,” he says. “But as a business owner, you have certain responsibilities. In that sense, running and owning a medical practice if you are in private practice is really no different than owning the UPS store.”


Fundamentals

- Culture
  What is the character of my practice?

- Structure
  Is the way I run my practice defined?

- Metrics
  How do I know what works and what does not?

- Value
  What is my business worth?

Culture

- Development of staff
- Development of awareness
- Internal and external customers
- Management system
- Unique patient experience
- Team building
- Employee satisfaction measurements
Processes, Protocols and Work Instructions

- The Business Bible
- Accountability
- Consistency
- Understanding
- Communication

Goal: To remove the subjective Nature of the environment.

“Nothing is personal”.

Roles & Responsibilities

- Who, What & Where

Accountability & Transparency

Goal: Create a fair and consistent environment for all members in the organization.

Training & Development

- Everything works together such that WI, Protocols, Roles and Responsibilities becomes the foundation of the training platform.

- Poor Training is the "number one cause" of:
  - Poor communication
  - Inconsistent performance
  - Error rates

FRUSTRATION FOR PROVIDERS!
Operational Metrics
- Referrals
- Scarcity/Opportunities
- Marketing/Referrals
- Internal/Opportunities
- Closures/Opportunities
- Referral Source

Strategic & Financial Metrics
Trends (weekly, monthly, annually)

Growth Metrics
- Visits per office
- New vs. established visits
- Type of visits (procedural vs. non-procedural)
- Procedural hit rates (Labs, Mohs Cures, others)
- % Market Capture for Area

Performance Metrics
- CPT Analysis, by Location & Provider
- Average Revenue per visit
- Average Revenue per main service lines
- Average Revenue billed, Total Revenue
- Average Adjustment Ratio
- Average billed & Unbilled by Location & Provider

Financial Metrics
- Average Adjustment Ratio (billed vs. collected)
- Revenue by Location & Provider
- Gross Margin
- Net Margin
- Top Ten Expense Categories
- Margin before and after Provider Remuneration

Billing Metrics
- Days in AR: 30, 60, 90
- Payment Plans
- Collection rates
- Bad Debt by category
- Adjustments by category
- Denial Ratio
- Clean Claims
- Non-Contractual errors (Front Office & Back Office)

Metrics
Philosophy of Metrics is the methodology of understanding the world through logical patterns and esoteric processes. From the ancient philosophy of primitive man, to the stock market of today, there is a pattern in everything and a process which can explain everything. We simply need to observe and create the comprehensive view and macro dimensions which point towards a deeper understanding of the world of business and natural improvement.

Operational
1) Operational
2) Strategic and Financial

Example 1 – 10 TBD
Melanoma the Modern Black Plague
A Brief History
Rene Gonzalez M.D.

Disclosures
- Merck
- Roche/Genentech*
- Novartis*
- BMS
- Amgen*
- Polynoma
- Millennium/Takeda
- Incyte
- Reata
- Dynavax
- Checkmate
- Morphotek
- Castle Biosciences*

Metastatic melanoma:
Survival in the era before targeted therapy & checkpoint inhibitors
Korn et al. JCO 2008

2011 Year of Melanoma
- Ipilimumab
- Vemurafenib
The Targets

PET Scans at Baseline and Day 15 After Vemurafenib

Comparison of Maximum Response With Vemurafenib and Dabrafenib

Responses BRIM 2

Vemurafenib

February 2010

May 2010

Photosensitivity
**Examples of Brain Metastases Responses to Dabrafenib**

**Baseline Week 8**

**Baseline Week 32**


**MEK INHIBITION**

**Trametinib**

**Most Common AEs**

- Rash (2 mg QD; n=68)
  - Mostly acniform
  - 46% G1
  - 28% G2
  - 4% G3

- Diarrhea (2 mg QD; n=68)
  - Intermittent (median reported duration = 2.5 days)
  - Controlled with supportive care
  - 41% G1
  - 12% G2
  - 2% G3

**Ocular Toxicity**

- Central serous retinopathy (CSR)
  - Blurry vision
  - Fluid accumulation in the macular region between retinal pigment epithelium and outer segment
  - 3 cases in 199 patients
  - 2 diagnosed cycle 1 (4 mg QD and 10/10/3 mg)
  - 1 diagnosed cycle 2 (6/6/2 mg)
  - All reversible upon withholding GSK1120212

- Retinal vein occlusion
  - Dosed at 2mg QD; diagnosed in cycle 7
  - Significant vision improved with intracocular anti-VEGF therapy

**Flaherty et al NEJM 2012**

Flaherty et al NEJM 2012
Frequency of Acquired Resistant Mechanisms to BRAF Inhibitors

Frequency of Acquired Resistant Mechanisms to BRAF Inhibitors

Mechanism of Resistance to BRAF Inhibition

BRAF + MEK INHIBITION
Dabrafenib + Trametinib
Vemurafenib + Cobimetinib
LGX 818 + MEK 162

Combined BRAF & MEK inhibition:
Preclinical data & PET scan response

Vemurafenib
February 2010  May 2010

Histologic Evidence of BRAF Resistance

Histologic Evidence of BRAF Resistance

Cell Proliferation

Cell Proliferation
coBRIM: OS

- Early evidence of improved OS with vemurafenib + cobimetinib over vemurafenib alone (not yet statistically significant)\(^1\)
- Final OS analysis expected in late 2015\(^2\)


- Median duration of follow-up was 20.0 months
- 221 (36%) patients remained progression-free and alive at analysis

**BRAF + MEK INHIBITION**

Vemurafenib + Cobimetinib
Dabrafenib + Trametinib

**BRAF/MEK inhibition: Overall survival at 3 years**

**Part C: Overall Survival by Study Arm**

<table>
<thead>
<tr>
<th>Study Randomized</th>
<th>PFS Events, n</th>
<th>OS Events, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMBI-v</td>
<td>352</td>
<td>155</td>
</tr>
<tr>
<td>COMBI-d</td>
<td>211</td>
<td>139</td>
</tr>
<tr>
<td>Phase 1/2</td>
<td>54</td>
<td>42</td>
</tr>
<tr>
<td>TOTAL</td>
<td>617</td>
<td>396</td>
</tr>
</tbody>
</table>

- Treatment-naive patients randomized to dabrafenib 150mg BID + trametinib 2mg QD:
  - **COMBI** vs **vemurafenib**
  - **COMBI-d** vs **dabrafenib**

**Combined BRAF & MEK inhibition:**

- Phase 1/2: dabrafenib + trametinib\(^1\)
- COMBI-d: dabrafenib + trametinib vs dabrafenib\(^2\)
- COMBI-v: dabrafenib + trametinib vs vemurafenib\(^3\)

**Combined BRAF & MEK inhibition**

**Pooled Overall Survival: Dabrafenib + Trametinib**

(N = 617)

- Median (95% CI), mos
  - 3-yr: 25.6 (23.1-34.3)
  - 5-yr: 34.8 (32.6-37.5)
  - 7-yr: 37.6 (35.3-39.9)
Immunotherapy of Melanoma

Anti-CTLA-4 Antibodies

MDX010-20: OS

Unique Kinetics of Response in Patients Treated With Ipilimumab

Objective Response to Ipilimumab After Significant Progression With Tumor Volume Increase

Pooled Analysis of Long-term Survival Data From Phase II and Phase III Trials of Ipilimumab in Metastatic or Locally Advanced, Unresectable Melanoma


1 University Hospital Essen, Essen, Germany; 2 Dana-Farber Cancer Institute, Boston, MA, USA; 3 Institute Gustave Roussy, Villejuif, France; 4 Moffitt Cancer Center, Tampa, FL, USA; 5 University of Washington, Seattle, WA, USA; 6 The Angeles Clinic and Research Institute, Los Angeles, CA, USA; 7 Bristol-Myers Squibb, Wallingford, CT, USA; 8 Bristol-Myers Squibb, Lawrenceville, NJ, USA; 9 Memorial Sloan-Kettering Cancer Center, New York, NY, USA.

Abstract Number 24LBA
**Pooled OS Analysis Including EAP Data: 4846 Patients**

- Median OS (95% CI): 9.5 (9.0–10.0)
- 3-year OS Rate (95% CI): 21% (20–22%)

**OS Relative to Historical Data**

- Historical controls
  - Phase II: 1278 patients in 42 cooperative group trials from 1975 to 2005
  - Phase III: 3739 patients in 10 trials from 1999 to 2011

---

**Patient 015-105**

- Baseline: April 13, 2012
- April 9, 2013

---

**MK 3475 Clinical Activity, Patient 015-105**

- 72-year-old male with symptomatic progression after bio-chemotherapy, HD IL-2, and ipilimumab

---

**Pembrolizumab (MK 3475)**

- ORR: 38%
- Highest dose ORR: 52%
  (by RECIST 1.1 with confirmation assessed by ICR)

**Nivolumab + Ipilimumab**

- ORR: 40%
- Highest dose ORR: 53%
  (by investigator-assessed irRC with confirmation)
Updated Results From a Phase III Trial of Nivolumab Combined With Ipilimumab in Treatment-naïve Patients With Advanced Melanoma (Checkmate 067)

Joel S. Hobrick,1 C. Lance Cowey,6 Christopher D. Lao,7 Dirk Schadendorf,8 Pier Francesco Ferrucci,9 Michael Smylie,10 Reinhard Dummer,11 Andrew Hill,12 John Haanen,13 Michele Maio,14 Grant McArthur,15 Dana Walker,16 Joel Jiang,16 Christine Horak,16 James Larkin,17* F. Stephen Hodi18*

Updated Results From a Phase III Trial of Nivolumab Combined

43 patients 34% RECIST Response by IRC

• 190 no prior Ipi 40%

• 221 prior PD Ipi 28%

• 88% ongoing at Oct 2013 (6-76+ weeks)

• 1 yr Survival 69%

• Median OS not reached

CA209-067: Study Design

Randomized, double-blinded, phase III study to compare NIVO+IPI vs NIVO alone to IPI alone

Response To Treatment
**Common Treatment**

*Pre-treatment tumor specimens were centrally assessed by PD-L1 immunohistochemistry (using a validated BMS/Dako assay). Database lock Nov 2015*

| Immune-modulating medicines used to manage adverse events and led to resolution rates of immune mediated AEs, % |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Renal            | Skin            | Pulmonary        | Gastrointestinal | Hepatic         | Colitis         | Pruritus         | Hypothyroid      |
| 6.4 (1.9-1.0)    | 1.9             | 1.0             | 0.3             | 2.6             | 0.3             | 32.3 (5.8-15.7)  | 11.6 (4.7-21.7)  |
| 47.6 (15.3-21.7) | 2.9             | 37.3 (11.6-47.6) | 11.6 (3.9-23.8) | 37.3 (11.6-47.6) | 11.6 (3.9-23.8) | 37.3 (11.6-47.6) | 11.6 (3.9-23.8) |

<table>
<thead>
<tr>
<th>Elevated creatinine, %</th>
<th>Diarrhea, %</th>
<th>Elevated AST, %</th>
<th>Elevated ALT, %</th>
<th>Hypothyroidism, %</th>
<th>Colitis, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2 (0.3-0.6)</td>
<td>45.4 (9.6-20.8)</td>
<td>15.7 (6.1-4.2)</td>
<td>17.9 (8.6-3.8)</td>
<td>16.0 (0.3-9.3)</td>
<td>11.5 (8.0-2.2)</td>
</tr>
</tbody>
</table>

**Response to Treatment by Tumor PD-L1 Expression***

<table>
<thead>
<tr>
<th>PD-L1 (ES)</th>
<th>ORR, % (95% CI)</th>
<th>Median Duration of Response (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5%</td>
<td>54.8 (48.4-61.6)</td>
<td>16.1 (6.7-24.9)</td>
</tr>
<tr>
<td>&lt;5%</td>
<td>34.6 (23.8-48.4)</td>
<td>15.5 (8.0-NR)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PD-L1 (ES)</th>
<th>ORR, % (95% CI)</th>
<th>Median Duration of Response (months)</th>
</tr>
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<td>≥5%</td>
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</tr>
<tr>
<td>&lt;5%</td>
<td>34.6 (23.8-48.4)</td>
<td>15.5 (8.0-NR)</td>
</tr>
</tbody>
</table>

**Safety Summary**

- Updated safety information with 9 additional months of follow-up consistent with the initial report

<table>
<thead>
<tr>
<th>Treatment-related AEs</th>
<th>NIVO+IPI (N=306)</th>
<th>NIVO (N=208)</th>
<th>IPI (N=202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients reporting event, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-related death</td>
<td>0.3 (0.3-0.3)</td>
<td>0.3 (0.3-0.3)</td>
<td>0.3 (0.3-0.3)</td>
</tr>
<tr>
<td>Treatment-related adverse event</td>
<td>95.8 (56.5-84.0)</td>
<td>84.0 (19.8-85.9)</td>
<td>73.0 (27.0-85.9)</td>
</tr>
<tr>
<td>Discontinuation</td>
<td>38.7 (30.7-10.5)</td>
<td>30.7 (7.3-15.4)</td>
<td>10.5 (13.5-5.4)</td>
</tr>
<tr>
<td>Treatment-related AE leading to discontinuation</td>
<td>25.5 (15.4-35.5)</td>
<td>15.4 (7.3-23.5)</td>
<td>5.4 (13.5-23.5)</td>
</tr>
</tbody>
</table>

**Conclusions**

- Targeted agents and Immune Therapies have been significant advance in melanoma
- Combinations better than single agents
- Optimal combinations and sequencing not determined
- Adjuvant treatment under investigation
Thank You!
Updates in Dermatology
Karthik Krishnamurthy, DO, FAOCD
Associate Professor
Residency Program Director

Overview
Navigating the old biologics, new biologics, and biosimilars
Other new drugs on the market
Outpatient propranolol usage
Interesting reports
Longevity of Biologics

Obesity (BMI > 30)
- 23 months vs 37.3 months drug survival

Biosimilars

What is a biosimilar?
- Concept sanctioned by the PPA/ACA of 2010
- An almost-identical copy of an existing biologic product
  - May need to be reverse-engineered

Biosimilars

How are they approved?
- Alternate FDA approval pathway to show similar efficacy
  - Cannot show increased efficacy
- Extrapolation: Can be approved for all “reference product” indications but not required to be studied in each condition
- Can gain “interchangeable” status by FDA
  - Must meet 3 demonstrative criteria

Biosimilars

Biosimilars in the derm world
- Infliximab vs Infliximab-dyyb (Inflectra®) [NI]
- Etanercept vs Etanercept-szzs (Erelzi®) [NI]
- In the pipelines
  - Adalimumab vs ABP 501 (Amgen) vs GP2017 (Sandoz) vs CHS-1420 (Coherus) vs xxx (AbbVie?)

Biosimilars

Brodalumab

An IgG2 mAb against IL-17A RECEPTOR (C,F) and IL-25

Brodalumab

Development history
- 3700 pts......6 suicides during clinical trials
- Those with psychiatric history were not excluded
  - 17% psychiatric disorders, 23% mod-severe depression/anxiety
  - 18X risk of suicide in this group
- 4/6 had a hx, however 2/6 had no history and passed the Columbia Suicide Severity Rating scale
- Amgen dumps drug: Astra-Zeneca + Valeant

AMAGINE-1 Trial

At Week 12

PASI 100 at Week 52

AMAGINE-2 & AMAGINE-3 Trials
Brodalumab

AMAGINE-2 & AMAGINE 3 Trials

Brodalumab

210 mg dose for the whole 52 weeks

CLEAR Trial

Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis CLEAR, a randomized controlled trial

CLEAR Trial

Primary endpoint
PHOENIX 1 & 2 Trial

Efficacy and safety of ustekinumab, a human interleukin-12/23 monoclonal antibody, in patients with psoriasis: 52-week results from a randomised, double-blind, placebo-controlled trial (PHOENIX 2)

UNCOVER Trials

Phase 3 Trials of Ustekinumab in Moderate-to-Severe Plaque Psoriasis

UNCOVER-1 (vs placebo)

12 week data

UNCOVER-2 & 3 (vs placebo/etanercept)

Comparison of ustekinumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials

60 week data
UNCOVER Trials

11 Cases of Inflammatory Bowel Disease onset or exacerbation in the treated group in addition to 3 more in the placebo withdrawal arm (who received drug weeks 0-12).

2 suicide attempts in treated group (one did not disclose truthful history), none completed

Recap?

- Neutralising Ab’s found in <5% of these new drugs, but did not have clinical relevance
- Secukinumab demonstrated superiority to Ustekinumab
- Brodalumab demonstrated superiority to Ustekinumab
  - Suicide risk is concerning
- Ixekizumab & Secukinumab also IL-17A inhibitors
  - Target the molecule, not the receptor (Brodalumab)
  - Clinical significance?
  - Inflammatory bowel disease is a concern for all IL-17 drugs
Tofacitinib versus etanercept or placebo in moderate to severe chronic plaque psoriasis: a phase 3 randomised non-inferiority trial


Other AEs:
- Neutropenia
- URI’s / nasopharyngitis

WARNING: SERIOUS EFFECTS AND MALIGANO
See full prescribing information for complete Brand Product

- Nocere drug-related death, eating or serious adverse events, including infections and respiratory symptoms, e.g., pneumonia, viral pneumonia, or bacterial pneumonia
- Maladie: JL-11
- JL-11 or JL-12
- Jal-JL-11 or JL-12
- Jal-JL-11
- Jal-JL-12

- Jal-JL-11
- Jal-JL-12
- Jal-JL-11
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- Jal-JL-12
- Jal-JL-11
- Jal-JL-12
- Jal-JL-11
- Jal-JL-12

FDA declines to expand approval of Pfizer arthritis drug

Tofacitinib Citrate for the Treatment of Vitiligo
A Pathogenesis-Directed Therapy

British J. Drugs 08: 89-94.
Tofacitinib

Treatment of recalcitrant atopic dermatitis with the oral Janus kinase inhibitor tofacitinib -strac

Guselkumab (CNTO 1959 – Phase II)

An IgG1 mAb against IL-23 only
200 mg interval doses like Ustekinumab

**PIONEER-1 & 2**

**PRIMARY ENDPOINT:**

*HiSCR (Hidradenitis Suppurativa Clinical Response Measure)*

- 50% reduction in inflammatory lesion count (abscesses + inflammatory nodules)

- No increase in abscesses or draining fistulas when compared with baseline.

**Sartorius Hidradenitis Suppurativa Score**

- Anatomic region involved (axilla, groin, genital, gluteal, or other inflammatory region left and/or right): 3 points per region involved

- Number and scores of lesions (abscesses, nodules, fistulas, scars): 2 points for each nodule, 4 points for each fistula, 1 point for each scar, 1 point each for "other"

- Longest distance between 2 relevant lesions (i.e., nodules and fistulas, in each region, or size if only 1 lesion): Less than 5 cm, 2 points; less than 10 cm, 4 points; more than 10 cm, 8 points

- Lesions clearly separated by normal skin in each region: If yes, 0 points; if no, 6 points

**Other tools**

- **Sartorius Hidradenitis Suppurativa Score**

- Anatomic region involved (axilla, groin, genital, gluteal, or other inflammatory region left and/or right): 3 points per region involved

- Number and scores of lesions (abscesses, nodules, fistulas, scars): 2 points for each nodule, 4 points for each fistula, 1 point for each scar, 1 point each for "other"

- Longest distance between 2 relevant lesions (i.e., nodules and fistulas, in each region, or size if only 1 lesion): Less than 5 cm, 2 points; less than 10 cm, 4 points; more than 10 cm, 8 points

- Lesions clearly separated by normal skin in each region: If yes, 0 points; if no, 6 points
Doppler Ultrasound

Color Doppler ultrasound assessment of morphology and types of fistulous tracts in hidradenitis suppurativa (HS)

Ximena Vortman, MD; Joel Cerrato, MD; and Andre Ungerer, MD

Orange Park Medical Center

New “measure” for staging, tailoring treatment, and assessing response objectively

Hate treating SKs????

A Randomized, Double-blind, Vehicle-Controlled, Parallel Group Study of the Dose-Response Profile of A-101 (H₂O₂) Solution in Subjects with Seborrheic Keratosis of the Face

Pre-Treatment with A-101

Post-treatment with A-101

New Drugs

The 12-month analysis from Basal Cell Carcinoma Outcomes with IDE225 Treatment (OBODY): A phase II, randomized, double-blind study of obinutuzumab in patients with advanced basal cell carcinomas

New Drugs
New Drugs

- Oritavancin non-inferior to Vancomycin in the treatment of ABSSSI
  - Trial 1: Orbactiv: 82.3% vs. Vancomycin: 78.9% responders
  - Trial 2: Orbactiv: 80.1% vs Vancomycin: 82.9% responders
  - Oritavancin is a Single Dose IV
  - Also showed a 19% decrease in AE's compared to Vancomycin/Cephalexin

- Dalbavancin non-inferior to Vancomycin in the treatment of ABSSSI
  - Trial 1: Dalvance: 83.3% vs Vancomycin/Linezolid: 81.8%
  - Trial 2: Dalvance: 76.8% vs Vancomycin/Linezolid: 78.3%
  - The vancomycin group allowed to switch over to linezolid day 3
  - Dalbavancin dosing: day 1 and day 8 (weekly) IV

- Both showed good MRSA activity
- Similar side effect profile (nephro- and ototoxicity not established)

TMP/SMX and Abscesses

- Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

Propranolol & IH

- Initiation and Use of Propranolol for Infantile Hemangioma: Report of a Consensus Conference
Inpatient hospitalization for initiation is suggested for the following: infants <8 weeks of gestational age or any age infant with inadequate social support or any age infant with comorbid conditions affecting the cardiovascular system, the respiratory system including symptomatic airway hemangiomas or blood glucose maintenance.

---

Outpatient Use of Oral Propranolol and Topical Timolol for Infantile Hemangiomas: Survey Results and Comparison with Propranolol Consensus Statement Guidelines

Monique G. Kumar, M.D., Carrie Conflaglia, M.D., and Susan J. Raya, N.D.
Division of Dermatology, Department of Internal Medicine and Pediatrics, School of Medicine, Washington University and St. Louis Children’s Hospital, St. Louis, Missouri

Pediatrics Dermatology Vol. 31 No. 3 171-178, 2013

The most often cited reasons for why practitioners did not follow these monitoring guidelines were that regular monitoring of vital signs was not necessary and that adequate staffing was not available to perform suggested monitoring.

---

OTC Retinoid

FDA approves Differin Gel 0.1% for over-the-counter use to treat acne

Proactiv America’s #1 Acne System

---
Management of Complications Caused by Permanent Fillers in the Face: A Treatment Algorithm

Daniel Canavesi, M.D.
Marco Pigani, M.D.
Laura V. Pescatori, M.D.
Giulia Benincasa, M.D.
Antonio Nengo, M.D.
Giorgio De Sarlo, M.D.
Milano and Milan, Italy

Plastic and Reconstructive Surgery
Issue: Volume 138(2), August 2016, p 215e–227e
<table>
<thead>
<tr>
<th>Reference</th>
</tr>
</thead>
</table>
Introduction

Rheumatologic diseases
- Aka connective tissue diseases, collagen vascular diseases
- Polygenetic & heterogeneous group of autoimmune disorders with classic cutaneous and extracutaneous findings
- Autoantibody associations

Overview

- Lupus Erythematosus
- Dermatomyositis
- Systemic Sclerosis
- Mixed Connective Tissue Disease
- Sjögren's Syndrome
- Dermatoses associated with arthritis

Autoantibodies

Circulating immunoglobulins detected in autoimmune diseases

Profile contributes to disease phenotype

Etiology / inciting event not completely understood

<table>
<thead>
<tr>
<th>Autoantibodies</th>
<th>Autoantibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA</td>
<td>Histone</td>
</tr>
<tr>
<td>SSA (Ro)</td>
<td>RF</td>
</tr>
<tr>
<td>SSB (La)</td>
<td>Ku</td>
</tr>
<tr>
<td>dsDNA</td>
<td>Mi-2</td>
</tr>
<tr>
<td>ssDNA</td>
<td>Jo-1</td>
</tr>
<tr>
<td>Sm</td>
<td>Scl</td>
</tr>
<tr>
<td>U1RNP</td>
<td>PCNA</td>
</tr>
<tr>
<td>U2RNP</td>
<td>A-RO/RF</td>
</tr>
<tr>
<td>Th/To RNP</td>
<td>PL-7</td>
</tr>
<tr>
<td>Cardiolipin</td>
<td>PL-12</td>
</tr>
<tr>
<td>R2-glycoprotein 1</td>
<td>pS20</td>
</tr>
<tr>
<td>PM-Scl</td>
<td>Centromere</td>
</tr>
<tr>
<td>Scl-70</td>
<td>Calpainin</td>
</tr>
<tr>
<td>HMG</td>
<td>Fer</td>
</tr>
<tr>
<td>Mas</td>
<td>Ku</td>
</tr>
<tr>
<td>SRP</td>
<td>C1q</td>
</tr>
<tr>
<td>U2RNP (thorlatin)</td>
<td></td>
</tr>
</tbody>
</table>
Antinuclear Antibody (ANA)

Screening tool
- Good sensitivity (assay-dependent)
- Low disease specificity
- False positives

Assays used to identify ANA
- Immunofluorescence
  - Directed against nuclear antigens on Hep-2 cells (human SCC tumor line)
  - ↑ # of antigens, ↑ sensitivity, ↓$
- ELISA
  - Solid phase immunoassay
  - ↓ # antigens, ↓ sensitivity, ↓$

Immunofluorescence staining pattern
A: Homogeneous
B: Peripheral
C: Speckled
D: Nuclear
E: Centromeric

Bolognia et al. Dermatology. 2007

False Positives

Mutasim, et al. JAAD Feb 2000

"Normal" ANA cut-off < 1:160

Table IX. ANA patterns and their antigen and disease associations

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Disease</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>nDNA</td>
<td>SLE</td>
<td>10.14,18</td>
</tr>
<tr>
<td>nDNA</td>
<td>SLE</td>
<td>14.161</td>
</tr>
<tr>
<td>nDNA</td>
<td>SLE</td>
<td>14.161</td>
</tr>
<tr>
<td>nDNA</td>
<td>SSC</td>
<td>14158.16</td>
</tr>
<tr>
<td>nDNA</td>
<td>SSC</td>
<td>14161</td>
</tr>
<tr>
<td>nDNA</td>
<td>SSC</td>
<td>14161</td>
</tr>
<tr>
<td>nDNA</td>
<td>SLE, SSc</td>
<td>80, 80</td>
</tr>
<tr>
<td>nDNA</td>
<td>SLE, SSC</td>
<td>14161</td>
</tr>
<tr>
<td>nDNA</td>
<td>Synthetic</td>
<td>Syndrome</td>
</tr>
</tbody>
</table>

Mutasim, et al. JAAD Feb 2000

Table VIII. Positive fluorescent ANA test in healthy persons (on Hep-2 cells)

<table>
<thead>
<tr>
<th>ANA</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:40</td>
<td>32%</td>
</tr>
<tr>
<td>1:80</td>
<td>13%</td>
</tr>
<tr>
<td>1:160</td>
<td>5%</td>
</tr>
<tr>
<td>1:320</td>
<td>3%</td>
</tr>
</tbody>
</table>
Antinuclear Antibody (ANA)

- Centromere
- dsDNA
- SSA (Ro)

CREST
Nephritis
Photosensitivity
Vasculitis

90% of La (+) are also Ro (+)
50% of Ro (+) are also La (+)

Overview

Lupus Erythematosus
Dermatomyositis
Systemic Sclerosis
Mixed Connective Tissue Disease
Sjogren’s Syndrome
Dermatoses associated with arthritis

Lupus Erythematosus (LE)

Chronic Cutaneous LE
Subacute Cutaneous LE
Acute (systemic) LE

Epidemiology

- SLE
  - F:M 6:1 (? Hormonal)
  - African Americans 4X more likely than whites
- CCLE
  - F:M 3:1
  - CCLE → SLE ~ 5-20%

Pathogenesis

- Genetic?
- Foreign antigen/molecular mimickry?
- Autoantibodies not organ specific

Lupus Erythematosus (LE)
Chronic Cutaneous LE

CCLE
- Classic Discoid LE
- Tumid LE
- Lupus Panniculitis
- Chilblain LE

Discoid LE
- Face, scalp, ears, with associated alopecia
- Less frequently on trunk and ext’s
- Mucosa: lips, oral, nasal, genital
- No clear association with UV exposure
- May have arthralgias

Discoid LE (CCLE)
- Erythematous papules evolve into scaly plaques
- Follicular plugging
  - Carpet tack / cat-tongue scale
  - Disfigurement is the worst sequela
- Scarring alopecia
- Atrophic, hypopigmented plaques
- Rarely, SCC may develop in older lesions
Chronic Cutaneous LE

- Superficial, deep, interface and perifollicular lymphocytic infiltrates
- Epidermal atrophy with/without hyperkeratosis
- Follicular plugging
- Colloid bodies
- Melanin incontinence
- May see mucin
Chronic Cutaneous LE

Tumid LE
- Erythematous dermal plaques
- Lacks scale or follicular plugging
- No residual scar or atrophy
- Can leave residual dyspigmentation
- Head/neck, upper trunk, proximal UE's
- Reproducible with UV exposure
- Same / similar to entity Jessner's Lymphocytic Infiltrate

Chronic Cutaneous LE

Lupus Panniculitis
- Deep, tender, inflammatory nodules occurring at the lever of subcutaneous fat
- Heal with scarring and depression of overlying skin (lipoatrophy)
- Favors face, UE's, upper trunk, breast, buttock, thighs
- Chronic, remitting and relapsing course
- Only 10-15% meet criteria for SLE
- If DLE overlies panniculitis, referred to as Lupus Profundus

Chilblain LE
- Red-purple papules and plaques on acral skin
- Fingers, toes, nose, elbows, knees, LE's
- Exacerbated by cold
- Chronic
- May be differentiated from ordinary chilblains by evolution in discoid lesions both clinically and histologically
Subacute Cutaneous LE

SCLE
- Classic
- Papulosquamous and Annular variants
- Neonatal LE
- Complement deficiency syndromes
  - C2 and/or C4 deficiency
  - Resembles classic SCLE

Subacute Cutaneous LE

Classic type
- Papulosquamous and/or Annular eruption
- Predilection for UV-exposed areas
- No follicular plugging or scarring
  - Can leave dyspigmentation
- Ro (SSA) antibodies (90% via ELISA)
- Many “meet criteria” for SLE
- Many cases are drug induced (more later)
  - Diltiazem (CCB), HCTZ, Terbenafine, NSAIDS, Griseofulvin

Subacute Cutaneous LE

Neonatal LE
- Newborns of (+) Ro, La, or RNP mothers
- Erythematous thin scaly plaques
  - UV sensitive: face/ext’s > trunk
  - May be present at birth (intrauterine)
  - May leave residual dyspigmentation or telangiectasia
- Usually resolves by 6 months (maternal Ab’s degraded)

Subacute Cutaneous LE

Neonatal LE
- Congenital heart block (3rd degree)
  - Permanent, 20% mortality
  - Up to 2/3 require a pacemaker
- Hepatobiliary disease
- Thrombocytopenia
- EKG, CBC, LFT’s, aggressive sun protection
- 25% risk with subsequent pregnancies
**Neonatal LE (SCLE)**

**Acute Cutaneous LE**

**ACLE**
- Malar Rash
- Discoid Lesions
- Diffuse non-scarring alopecia
- Raynaud’s phenomenon
- Nailfold telangiectasias and erythema
- Vasculitis
- Cutaneous signs of antiphospholipid syndrome: livedo reticularis, acrocyanosis, atrophie blanche
- Palmar erythema, dorsal erythema sparing IP joints.
- Papular and nodular mucinosis

**SLE Criteria**
- Discoid Lesions
- Oral ulcers
- Photosensitivity
- (+) ANA
- Malar Rash (butterfly rash)
- Immunologic markers (dsDNA, Sm)
- Neuropsychiatric disturbances
- Renal (nephritis)
- Arthritis
- Serositis
- Hematologic (hemolysis, anemia, thrombocytopenia)

**Malar Rash (ACLE/SLE)**

**Palmer Erythema / Vascular(ACLE/SLE)**
Special Considerations

Bullous SLE
- Ab’s to Collagen VII
- SLE may occur with other blistering disease

Overlap syndromes
- Lichen Planus / LE overlap

Associations
- Erythema Multiforme + SLE = Rowell’s Syndrome
- Pemphigus Foliaceus + SLE = Senear-Usher Syndrome

Drug-Induced SLE

SLE
- <30% have skin manifestations
- Musculoskeletal and serosal complaints
- Procainamide, Hydralazine, Isoniazid, Chlorpromazine, Phenytoin, Methyldopa, Minocycline
- Induces anti-Histone Ab’s
- Etanercept & d-Penicillamine induce dsDNA ab’s
- Methimazole and PTU induce ANCAs

Table: 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Immunologic Criteria</th>
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<tbody>
<tr>
<td>1. Acute Cutaneous Lupus</td>
<td>1. ANA</td>
</tr>
<tr>
<td>2. Chronic Cutaneous Lupus</td>
<td>2. Anti-dsDNA</td>
</tr>
<tr>
<td>3. Oral or nasal ulcers</td>
<td>3. Anti-PM</td>
</tr>
<tr>
<td>4. Non-scarring alopecia</td>
<td>4. Antiphospholipid Ab</td>
</tr>
<tr>
<td>5. Arthritis*</td>
<td>5. Low complement (C3, C4, CH50)</td>
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<tr>
<td>7. Renal*</td>
<td></td>
</tr>
<tr>
<td>8. Neurological*</td>
<td></td>
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<tr>
<td>9. Hemolytic anemia</td>
<td></td>
</tr>
<tr>
<td>10. Leukopenia*</td>
<td></td>
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<tr>
<td>11. Positive antinuclear antibody*</td>
<td></td>
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<tr>
<td>12. Positive anti-double stranded DNA antibody* (by a standard method)</td>
<td></td>
</tr>
<tr>
<td>13. Presence of anti-Sm, anti-nRNP, anti-Scl-70, or anti-SSA/SSB antibodies</td>
<td></td>
</tr>
<tr>
<td>14. Presence of anti-SSA/SSB antibodies</td>
<td></td>
</tr>
<tr>
<td>15. Triosomies of chromosomes 1, 19, or X</td>
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</tr>
</tbody>
</table>

Footnote: Systemic Lupus International Collaborating Clinics
* For notes, see clinical criteria.
(1) Acute Cutaneous Lupus OR Subacute Cutaneous Lupus

• Acute cutaneous lupus: lupus malar rash (do not count if malar discoid), bullous lupus, toxic epidermal necrolysis variant of SLE, mucocutaneous lupus rash, phototoxic lupus rash (in the absence of dermatomyositis).

• Subacute cutaneous lupus: nonindurated psoriaform and/or annular polycyclic lesions that resolve without scarring, although occasionally with postinflammatory hypopigmentation or telangiectasia.

(2) Chronic Cutaneous Lupus

• Classic discoid rash localized (above the neck) or generalized (above and below the neck); hypertrophic ( verrucous) lupus, lupus panniculitis (profundus), mucosal lupus, lupus erythematosus tumidus, chilblains lupus, discoid lupus/subcutaneous overlap.

(3) Oral Ulcers OR Nasal Ulcers

• Oral: palate, buccal, tongue

• Nasal ulcers

Do the absence of other causes, such as vasculitis, Behçet’s disease, infection (herpesvirus), inflammatory bowel disease, reactive arthritis, and acidic foods.

(4) Nonscarring alopecia

• Diffuse thinning or hair fragility with visible broken hairs, in the absence of other causes such as alopecia areata, drugs, men deficiency, and androgenic alopecia.

Dermatomyositis

Dermatomyositis

DM

• Proximal, extensor, symmetric, inflammatory myositis

• Photodistributed and classic skin findings

• May overlap with other rheumatologic diseases

• Adult forms associated with internal malignancy

• Amyopathic form exists

Skin Findings

• Photodistributed poikiloderma (neck, shawl)

• Heliotrope rash (periorbital erythema)

• Scalp dermatitis

• Nailfold telangiectasias

• Gottron’s papules: violaceous papules over IP’s

• Gottron’s sign: over knees and elbows

• Calcinosis cutis (more in juvenile variant)

• Mechanic Hands: ragged cuticles, hyperkeratosis, scaling, and fissuring of distal fingers

Dermatomyositis

Epidemiology

• Adult F:M 6:1

• Juvenile F:M 2:1

Pathogenesis

• Genetic, humoral immunity, cellular immunity, drug precipitants, infectious etiology

• Paraneoplastic phenomenon

Extracutaneous

• Proximal muscle weakness

• Pulmonary disease

  – Interstitial lung disease

  – Anti-RNA synthetase Ab’s (Jo-1)

• Other

  – If GI, Renal, arthritis, or Raynaud’s, consider overlap

  – Anti-SRP Ab’s associated with cardiac disease

  – Anti-Ku Ab’s associated with DM and SSc overlap

  – Anti-Mi-2 Ab’s associated with shawl sign and good prognosis
**Dermatomyositis**

**Malignancy Risk**
- Up to 50% in Adult form
- #1: Ovarian Cancer
- Less commonly breast, lung, gastric

**Juvenile Variants**
- Brunsting Type (more common)
  - Myositis + calcinosis
  - Indolent, progressive, steroid responsive
- Banker Type
  - Vasculitis of muscles and GI tract
  - Rapid, difficult to treat, high mortality

**Work-up**
- Muscle enzymes: CK, aldolase, AST
- EMG or MRI helpful for myositis
- Pulmonary function tests
- Malignancy screening

**Poikiloderma (DM)**

**Poikiloderma D/Dx:**
- Dermatomyositis
- Actinic damage
- CTCL
- GVHD
- TMEP (not true poikiloderma)
- Radiation recall
- Chronic photodrug reaction
- Porphyrias
Gottron’s Papules (DM)

Benign papulosquamous dermatosis
Over MCP’s and IP’s
Repetitive trauma (sports, occupational, etc)

Gottron’s Sign (DM)

Ragged Cuticles (DM)

Improved compliance with measurements
Recommends 6.5 mg/kg/day (max 400 mg/day)

Hydroxychloroquine Blood Levels in Systemic Lupus Erythematosus: Clarifying Dosing Controversies and Improving Adherence
Laura Duncan, William A. Clark, Laurence S. Mandel, and Michelle Petri

Results: The proportion of patients with HCQ levels in the therapeutic range differed significantly by age, sex, and Vitamin D level. There was a trend toward lower levels with renal failure. Blood levels were similar regardless of height and ideal body weight. Comparing those with undetectable subtherapeutic, and therapeutic levels, disease activity decreased (SLE Disease Activity Index 2.02 ± 1.2 vs. 2.84 ± 0.06 for renal). At first 56% were therapeutic, and by the third measurement the increased to 80% (p < 0.0001).

The Journal of Rheumatology 2013; 40:11
Systemic Sclerosis

PSSc, Scc, Scleroderma

- Autoimmune fibrosis of skin and organs
- Localized and Systemic presentations
  - Systemic form is progressive and morbid
- Epidemiology
  - F:M 15:1
  - Dx occurs 30-50 yo
  - No racial predilection

Systemic Sclerosis

Pathogenesis

- Endothelial cell damage, inflammation, and collagen deposition
- Unknown inciting factors
  - Spanish toxic oil, L-tryptophan, vinyl chloride, bleomycin
- TGF-β overproduction
- Different antibodies affect clinical expression

Systemic Sclerosis

Variants

- Localized
  - Localized and Generalized Morphea
  - Atrophoderma of Pasini and Pierini
  - Linear Morphea
- Generalized
  - CREST Syndrome
  - Progressive Systemic Sclerosis

Systemic Sclerosis

Variants

- Localized
  - Localized and Generalized Morphea
  - Atrophoderma of Pasini and Pierini
  - Linear Morphea
- Generalized
  - CREST Syndrome
  - Progressive Systemic Sclerosis

Systemic Sclerosis

Variants

- Localized
  - Localized and Generalized Morphea
  - Atrophoderma of Pasini and Pierini
  - Linear Morphea
- Generalized
  - CREST Syndrome
  - Progressive Systemic Sclerosis
Systemic Sclerosis

Skin Findings
- Fibrosis
  - Generalized skin sclerosis
  - Inability to open mouth
  - "Bird Facies"
  - Sclerodactyly
- Dystrophic calcinosis
  - Digital ulcers, pitting
- Salt & Pepper sign (confetti depigmentation)
- Nailfold Telangiectasias

Raynaud’s Phenomena
- Vasomotor disease precipitated by cold
- 2° phenomena associated with autoimmune disease
- Distinguishable from 1° disease
  - Ischemic injury occurs
  - > 5 attacks per day
  - Lack of autoantibodies

Treatment
- Overall disease
  - Azathioprine, methotrexate, cyclophosphamide
  - CsA may worsen renal disease
  - d-Penicillamine may induce other AI disease
- Renal disease: ACE inh
- Vasospasm: CCB’s, peripherally acting
- Calcinosis: CCB’s
- Skin sclerosis: High dose UVA1 (340-400nm)
- Reflux: PPI’s
- Physical therapy
- Smoking cessation

Differential Diagnosis
- Only PSS displays Raynaud’s + autoAb’s
- Mimickers
  - Eosinophilic Fasciitis
  - Scleromyxedema
  - Scleredema
  - Nephrogenic Systemic Fibrosis
  - Toxin-Induced
  - GVHD
Systemic Sclerosis

**DDx: Eosinophilic Fasciitis**
- Precipitated by strenuous activity
- Fibrosis at the level of fascia, not dermis
- Spontaneously remits
- Peripheral eosinophilia

**DDx: Scleromyxedema**
- Mucin depositional disorder
- Varied clinical presentation (localized to systemic)
- Monoclonal IgG $\lambda$-light chain gammopathy

**DDx: Scleredema**
- Mucin depositional disorder
- Three subtypes
  - Post-streptococcal
  - Gammopathy associated
  - Diabetes associated
- Localized skin induration with internal involvement

**DDx: Nephrogenic Systemic Fibrosis**
- AKA Nephrogenic Fibrosing Dermopathy
- Progressive, diffuse fibrosis of skin and internal organs
- Associated with Gadolinium exposure (MRI contrast) in patients with ESRD (Cr>5)
- Mortality ~ 50%

**DDx: Toxin Induced**
- Spanish Toxic Oil
- L-tryptophan (Eosinophilia-Myalgia syndrome)
- Bleomycin, plenomycin
- Taxanes
- Cisplatin, Carboplatin
- Gemcitabine
- Etopi Alkaloids
- Cocaine
- Vinyl Chloride (in autoclaves)
- Trichlorethene/ethane
- Epoxy resins
- Silica

*Oral Metformin Ameliorates Bleomycin-Induced Skin Fibrosis*
Mixed Connective Tissue Disease

MCTD
- Raynaud's, dactylitis, fever, arthritis
- Heterogeneous expression of other features from SLE, DM, PSS
- Heavily associated with U1RNP Ab's
  - If also Sm (+), then dx of SLE is made

Sjögren’s Syndrome

SS
- Autoimmune disorder affecting secretory glands
  - Classic Triad: Keratoconjunctivitis sicca, Xerostomia, Arthritis
- F:M 9:1
- Antibody:
  - Anti-fodrin 70%
  - SSA (Ro) 60%
  - SSB (La) 20%

Dermatoses associated with arthritis

Juvenile Idiopathic Arthritis

Adult-onset Still’s Disease
AOSD
- Fever spikes in afternoon or early evening
- Evanescent salmon-colored erythematous eruption
- Koebner Phenomenon
- Extremely high ferritin levels (>3000)
- Arthritis: carpal ankylosis

JIA / Adult Still’s Disease
D/Dx
- Infectious: Parvovirus, EBV, Malaria
- Childhood Leukemia
- Familial Mediterranean Fever (FMF)
- Hyper-IgD syndrome with periodic fever (HIDS)
- TNF-receptor associated fever syndrome (TRAPS)
- Cryopyrin-associated periodic fever syndromes (CAPS)
  - Muckle Wells Syndrome
  - Familial Cold Autoinflammatory Syndrome
  - Neonatal onset multisystem inflammatory syndrome

Parvovirus
Caused by ssDNA virus
AKA: B19, 5th disease
Viral prodrome
3 phases
- Slapped cheek (spares NLF), lasts 2-4 days
- Then morbilliform rash → lacy rash (2-8 days)
- Adults present atypically, with more systemic manifestations. Check Parvovirus IgM if suspicious.

Parvovirus & RA
Adult cases mimic RA
Slapped-cheek uncommon
Lacy, transient rash common
B/L, symmetric arthropathy of the hands, wrists and feet
Transient RF (+) in 20%
Check B19 IgM

Parvovirus & AOSD
Mimics Adult-onset Still’s Dz
Salmon-colored patches are evanescent
Appears for a few hours with the “noon fever spike”
RF, ANA, CCP (-)
Check B19 IgM

Extremely high serum ferritin levels as diagnostic tool in adult-onset Still’s disease
E.C. White, A. Cuhna, A.J.M. Coon, E. van den Burg

Kevin has described in a few other cases. Other conditions in which ferritin levels may be elevated are infections, malignancies (hepatoma, lymphoma), liver diseases and haemochromatosis. However, in these conditions serum ferritin concentrations greatly exceed values of 5000 μg/L. Besides in adult Still’s disease, serum ferritin levels of >5000 μg/L have only been described in severe liver disease, after multiple blood transfusions or in the haemochromatotic syndrome. So the ferritin level may be an...
Erythema Marginatum
Mimics Adult-onset Still’s Dz
Seen in 5% of acute Rheumatic Fever patients
Extremely evanescent
Both entities have arthralgias
70% of ARF pts recall antecedent pharyngitis
(+ cardiac findings

Rheumatoid Arthritis
Skin findings
• Rheumatoid Nodules
  – High RF titers, periarthritis on extensor surfaces
  – Rheumatoid nodulosis: seen after initiation of MTX
• Rheumatoid Vasculitis
  – High RF titers, late stage RA, may affect any size vessel
  – Bywater’s lesions: LCV on distal digits
• Felty’s Syndrome
  – RA, granulocytopenia, splenomegaly, leg ulcers
• Neutrophilic dermatoses
  – Pyoderma Gangrenosum, Sweet’s syndrome

Rheumatoid arthritis, anti-tumour necrosis factor treatment, and risk of squamous cell and basal cell skin cancer: cohort study based on nationwide prospectively recorded data from Sweden

PARTICIPANTS
CoHort of patients with rheumatoid arthritis naive to biologics (n=64 049), cohort of patients with rheumatoid arthritis starting TNF inhibitor treatment as first biologic in 1998-2012 (n=12 558), and matched general population comparator cohort, identified through national quality of care and health registers.

BMJ 2016;352:i262

RA Vs Psoriasis and NMSC

ORIGINAL ARTICLE
An increased risk of non-melanoma skin cancer during TNF-inhibitor treatment in psoriasis patients compared to rheumatoid arthritis patients probably relates to disease-related factors

Results: The incidence of melanoma was significantly higher in the psoriasis group compared to the rheumatoid arthritis group, suggesting a higher risk of melanoma in patients treated with TNF inhibitors.

JAD 2015; 26: 702-79

BMJ 2016;352:i262

American Academy of Dermatology
Psoriasis: TNF inhibitors general recommendations

The potential risk of melanoma, cutaneous T-cell lymphoma, and nonmelanoma skin cancer in patients treated with the TNF inhibitors has been raised by several case reports. A large observational study of patients with rheumatoid arthritis demonstrated an increased risk for the development of nonmelanoma skin cancer (odds ratio 2.5, 95% confidence interval 1.2-5.1) and a trend toward increased risk of melanoma (odds ratio 2.3, 95% confidence interval 0.9-5.3) in patients treated with biologic agents targeted to the TNF inhibitors. Importantly, this large study also demonstrated an increased risk of any other type of solid cancer. These findings contrasted with the results of a meta-analysis of rheumatoid arthritis studies examining patients treated with adalimumab and etanercept, which revealed an increased risk of solid cancers.
Psoriasis patients already have a 22% increase baseline risk of liver fibrosis

Ultrasonography and Liver biopsy no longer recommended
Recommend PIIINP testing

Manchester Guidelines

Where do you send it?

QUEST and LABCorp do not perform the test......

References


Isenberg DA, Lesavre P. Lupus nephritis: assessing the evidence, considering the future. Lupus 2007; 16:210-211.


References


Multimedia

Use of all clinical pictures granted with permission by:

Karthik Krishnamurthy, DO

Molecular cartoons adapted from Bolognia, et al. Dermatology (2007)

Friday, September 16, 2016

6:30 a.m. - 7:30 a.m.  Breakfast with Exhibitors

7:00 a.m. - 8:00 a.m.  Medical Marijuana: The Medical Uses of Cannabis  
Marc Epstein, DO, FAOCD

8:00 a.m. - 9:00 a.m.  Embryology For the Rest of Us  
Derrick Adams, DO, FAOCD

9:00 a.m. - 10:00 a.m.  How Classical Homeopathic Medicine Can Be Helpful for Children with Skin Diseases  
Robert Signore, DO, FAOCD

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

10:30 a.m. - 11:30 a.m.  Parallels and Divergence: Veterinary Dermatology and the Human Counterpart  
Jacquelyn Campbell, DVM

11:30 a.m. - 12:30 p.m.  Dysplastic Nevi and Pigmented Lesions  
Whitney High, MD

12:30 p.m. - 1:30 p.m.  Urticaria/Angioedema from an Allergist's Perspective  
Nathanael Brady, DO

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

2:00 p.m. - 5:00 p.m.  Dermoscopy Primer Updated: 2-Step Dermoscopy Algorithm  
Ashfaq A. Marghoob, MD

5:30 p.m.  Welcome Reception
Medical Marijuana – The Medical Uses of Cannabis
Harnessing the wisdom that mother nature has been giving us

Introduction: History of Marijuana / Cannabis Use

Introduction: Medical Marijuana / Cannabis

Objectives
• What is marijuana?
• What is medical marijuana?
• Detoxify your views on medical marijuana.
• Demystify your views on medical marijuana.
• How and why medical marijuana is going to become another highly effective drug class, like steroids and biologics, in your toolbox.

Genesis 1:29
Then God said, “Behold, I have given you every plant yielding seed that is on the surface of all the earth, and every tree which has fruit yielding seed; it shall be food for you.”
Introduction: Medical Marijuana / Cannabis

- The Flowering Plant: Cannabis - one of the most ancient cultivated non-food and food crops
- Indigenous to Central and South Asia - over 6000+ years ago
- 2 Main Cannabis Species - C. Sativa and C. Indica plus hybrids made with a 3rd species, C. Ruderalis.
- Hemp or Industrial Hemp is a variety of the C. Sativa plant grown specifically for uses in industry
- One of the fast growing plants that is self sustaining - does not usually require fertilizer.

Introduction: History of Marijuana / Cannabis Use

- (Industrial) Hemp from C. Sativa plant
- One of the first plants spun into useable fiber 6,000+ years ago
- Hemp fiber refined for millennia into commercial products: paper, clothing, rope, bowstrings, cordage, construction materials, insulation, mulch, animal bedding and litter.

Introduction: History of Marijuana / Cannabis Use

- (Industrial) Hemp fibers from C. Sativa plant
- Hemp fibers can used alone (the feel of linen) or with other organic fibers such as flax, cotton or silk to make textiles such as woven fabrics.
- Has been often used to make sail canvas for ships
- The word CANvas derives from CANnabis

History of Marijuana / Cannabis Use

- President George Washington grew hemp at Mount Vernon.
- "Mr. Pearce, on my farming plantation(s), I want you to make the most of Hemp and plant it everywhere on my farmlands that haven’t been previously reserved for other things."
History of Marijuana / Cannabis Use

- The first denim (De Nimes, France) jeans were manufactured with hemp.
- Calvin Klein “I believe hemp is going to be the fiber of choice for the millennium.”

“HEMP ROCKS”

History of Marijuana / Cannabis Use

- Which famous books and documents were printed on hemp ‘paper’, which is why they have been able to survive so well and for so long.

HEMP ROCKS

History of Marijuana / Cannabis Use

- Which famous items were printed on hemp paper?
  - The Gutenberg’s Bible
  - The American Constitution
  - The Declaration of Independence

History of Marijuana / Cannabis Use

- Hemp was right on the money – A hemp harvest printed on a 1914 series $10 bill made from 100% hemp.
- Hemp was legal tender in most of the Americas from 1631 until early 1800’s to encourage farmers to grow more of it.
- One could pay their taxes with hemp throughout America for over 200 years. If one did not grow hemp during periods of shortages, they could be jailed.

Introduction: History of Marijuana / Cannabis Use

- (Industrial) Hemp fibers from C. Sativa plant
- Composite automobile panels use hemp in their mix.

Introduction: History of Marijuana / Cannabis Use

- (Industrial) Hemp fibers from C. Sativa plant
- New cars contain up to 20 Kg of hemp in the form of plastic interiors of car doors, plastic glove boxes & plastic columns.
Introduction: History of Marijuana / Cannabis Use

- (Industrial) Hemp fibers from C. Sativa plant
- What's new is old: Ford's Prototype 1941 Plastic Biofuel Car

Introduction: History of Marijuana / Cannabis Use

- The woody core of hemp (hurds, sometimes called shives) of hemp makes remarkably good animal bedding
- The Hurd makes an excellent litter for pets as they can absorb up to five times their weight in moisture (50% higher than wood shavings)

Introduction: History of Marijuana / Cannabis Use

- Hemp seeds from the Flowering Cannabis Plant as a non-food crop:
  - Dried (oxidized) seed oil becomes a solid and used in the manufacture of
  - oil based paints
  - MOISTURIZING AGENTS in Creams
  - in biodegradable plastics.

Introduction: History of Marijuana / Cannabis Use

- Flowers and Leaves from the Flowering Cannabis Plant as a non-food crop:
  - Flowers and upper leaves undergo steam distillation to produce fragranced Cannabis Flower Essential Oil or Hemp Essential Oil.
  - The oil is used as a scent in perfumes, cosmetics, soaps and candles

Introduction: History of Marijuana / Cannabis Use

- Flowers, Leaves and Seeds from the Cannabis Plant as a food crop:
  - In its fresh, raw state Cannabis is virtually NON-psychoactive.
  - It ONLY becomes a psychoactive drug when Cannabis is DRIED or HEATED.

Introduction: History of Marijuana / Cannabis Use

- Flowers and Leaves from the Cannabis Plant as a food crop:
  - Flavoring agent in foods: primarily candy and beverages.
  - In salads

Introduction: History of Marijuana / Cannabis Use

- The flowers and leaves from the Cannabis Plant as a food crop:
  - Flavoring agent in foods: primarily candy and beverages.
  - In salads

Introduction: History of Marijuana / Cannabis Use

- The flowers and leaves from the Cannabis Plant as a food crop:
  - Flavoring agent in foods: primarily candy and beverages.
  - In salads
Introduction: History of Marijuana / Cannabis Use

- Hemp Seeds from the Flowering Cannabis Plant as a food crop:
  - Edible seeds - eaten raw, ground into a meal, sprouted, made into a can be used in cooking, bird and animal feed.
  - Cold Pressed Hemp Seed Oil is high in unsaturated fatty acids.
  - Seeds and oils used in foods such as Granola
  - Hemp Seed Milk from ground soaked seeds yields a beany-nutty-cream-flavored substance

Introduction: History of Marijuana / Cannabis Use

- Hemp seeds from the Flowering Cannabis Plant as a food crop:
  - Female plant yields nearly half it's weight in a highly nutritious edible seeds containing a perfect balance of the key essential nutrients
  - Seeds contain Omega 3 (alpha-linolenic) and Omega 6 (linoleic acid) essential fatty acids in the ratio 1:3; An ideal ratio for humans
  - Seeds contain a high percentage of the very rare Gamma Linoleic Acid, a powerful hormonal balancer and anti-inflammatory
  - Around 73% of the energy of hemp seeds is in the form of Free Fatty Acids

Introduction: History of Marijuana / Cannabis Use

- Hemp seeds from the Flowering Cannabis Plant as a food crop:
  - Seeds contain a complete protein source with all eight essential amino acids plus its high in globular edestin, the most edible and digestible form of protein
  - Hemp seed amino acid profile as a source of protein is comparable to meat, milk, eggs and soy
  - 100 grams of hulled hemp seeds supply 586 calories providing 64% of the Daily Value of Protein per 100 gram serving

Introduction: History of Marijuana / Cannabis Use

- The Flowering Plant: Cannabis - one of the most ancient cultivated crops
  - Medicine from the female plant and its resin
  - Recreation
  - Non-medical ingestion
  - Use in making sporting equipment & clothing
  - Religious ceremonies
  - Used as a spiritual and religious sacrament in rituals and ceremonies from ancient to modern times

Introduction: What is Marijuana / Cannabis

- Cannabis buds refers to the dried flower tops of the Female plant of Cannabis.
- This herbal product is also commonly known as marijuana or marihuana.
- Street names of Marijuana: MJ, Bud, Grass, Green, Hash, Herb, Mary Jane, Pot, Reefer, Smoke, Tea & Weed
Introduction: What is Marijuana / Cannabis

- Cannabis Trichomes - glistening translucent resin outgrowths or 'hairs' protruding from the buds, leaves, and just about everywhere else on the plant
- Trichrome's sticky coating is home to the active cannabis compounds; processed to make Hashish
- Postulated they evolved as a defense mechanism – an evolutionary shield to protect the plant and its seeds from the dangers of its environment and allowing it to reproduce
- Provides a protective layer against offensive insects
- Helps insulate the plant from high wind and low humidity
- Acts as a natural 'sunscreen' to protect against UV-B
- 3 Types: Capitate-Stalked (red), Capitate-sessile (blue) & Bullous (yellow).

History of Medical Marijuana / Cannabis Use

- *C. sativa* medicinal preparations of flowers & resin
- China (2,700 BCE) – Emperor Shen Nung, Father of Chinese Medicine & Pharmacology, used hemp for menstrual disorders, gout, rheumatism, malaria, constipation & absent-mindedness
- Egyptian physicians – suppositories for relieving hemorrhoidal pain.
- Medieval Times / Islamic physicians (8th thru 18th centuries) – nausea & vomiting, epilepsy, inflammation, pain & fever.
- Western Medicine
  - Common analgesic in 1800s before aspirin. Dentists used it in the mouth and on the tongue as a topical anesthetic.
  - Doctors in the 1800s literally understood the benefits of cannabis better than contemporary physicians, publishing more than 100 papers on the topic.
History of Medical Marijuana / Cannabis Use for Ailments

- In 1839, WB O'Shaughnessy, MD, Professor of Chemistry & Natural Philosophy, Medical College, Calcutta, introduced therapeutic use of cannabis to Western Medicine in his 40 page monograph, “On the Preparation of Indian Hemp, or Gunjah,” presented to the College.

- Sir O'Shaughnessy, 7 years earlier, at the end of his medical training in Edinburgh, Scotland, invented IV fluid & electrolyte replacement therapy during a cholera epidemic.

History of Medical Marijuana / Cannabis Use for Ailments

- Western Medicine
  - In 1890, British physician J.R. Reynolds, President of the Royal College of Physicians, published his 30 years of experience with cannabis, the most influential reports of the 19th century.
  - Like many contemporary doctors 125 years later, he recommended it for multiple conditions.
  - He believed cannabis was useful for treating migraine headaches, epilepsy, asthma, depression and painful cramps. As ‘Physician in Ordinary’ to NM Queen Victoria, he infamously prescribed a cannabis tea for her menstrual cramps.

- Dr J.Russell Reynolds in 1890 stated for insomnia, “I have found nothing comparable in utility to a moderate dose of Indian hemp [cannabis].”

- His medical stature at that time, along with his 30 years of clinical cannabis experience, served to give credence to his emphatic statement that “Indian Hemp, when pure and administered carefully, is one of the most valuable medicines we possess.”

History of Medical Marijuana / Cannabis Use for Ailments

- The 100 years between 1837 and 1937 has been referred to as the Golden Age of Medical Cannabis.

- During that time, it was a common medical ingredient in a wide variety of commercially available pharmaceutical treatments.

- Sir William Osler, in his 1916 textbook, Principles & Practice of Medicine on p. 1089, states that Cannabis indica is probably the most satisfactory remedy for migraine headache.

  "He who studies medicine without books walks on uncharted sea, but he who studies medicine without patients does not go to sea at all.”
Many of the pharmaceutical companies (e.g., Eli Lilly, Parke Davis, Merck) sold various cannabis tinctures, tablets, or topical preparations.

One museum identified over 600 medical products listing cannabis as a chief ingredient prior to its prohibition in 1937.

C sativa medicinal preparations of flowers & resins
In 1st half of the last century
- glaucoma
- pain (analgesic)
- nausea & vomiting (antiemetic) including from chemotherapy
- insomnia (sleep aide)
- Anxiety
- epilepsy (anticonvulsant)

In 2nd half of the last century
- All those from the 1st half of the century
- appetite stimulation including anorexia-cachexia from HIV or cancer chemotherapy
- muscle spasms including from MS
- HIV sensory neuropathy
- Tourette’s syndrome
- bronchospasm including asthma (bronchodilator), Crohn’s disease
- intractable hiccups

Medical Cannabis use began to decline around 1890
- Cannabis potency, like plant derived digitalis, was unpredictable, likely due to the relatively poor plant genetics and cultivating techniques of the day.
- Introduction of the hypodermic syringe in the 1850s allowed a variety of drugs and opiates to be directly injected, delivering quick pain relief. Unfortunately cannabis, which is not water soluble, cannot be administered by injection.

Medical Cannabis use began to decline around 1890
- With the use of opioids for pain relief, opioid addiction became problematic.
- Ironically, Cannabis was found to be effective in treating opioid addiction for decades prior to its Schedule I banishment
- Unlike Cannabis, Deaths from opioid overdose has reached epidemic proportions.
- More profitable and predictable synthetic drugs, such as aspirin and barbiturates, became available.
History of Medical Marijuana / Cannabis Use for Ailments
- Medical Cannabis use began to decline around 1890
- Unfortunately, unlike Cannabis, these newer drugs carry the risk of dependency and/or death.
- More than a thousand people die each year in the United States alone from bleeding produced by aspirin.
- Medical cannabis, although more difficult to administer in a standardized fashion due to varying potency, has produced no documented deaths.

History of Medical Marijuana / Cannabis Use
- By the 1930s, Alcohol Prohibition had ended and the first commissioner of the Federal Bureau of Narcotics and Dangerous Drugs under the Treasury Department, Harry Anslinger, spearheaded a campaign to demonize cannabis.
- At that time cannabis was being used recreationally by jazz musicians in the South, who called it “reefer,” and by Mexican soldiers and Mexican migrant farm workers, who called it “marijuana.”

History of Medical Marijuana / Cannabis Use
- Anslinger spread propaganda about “a new drug menace called marijuana” causing users to commit violent crimes or to go insane (Bonnie and Whitebread, 1974; Abel, 1980).
- His efforts led to the passage of the Marijuana Tax Act of 1937, which resulted in a prohibitive tax on the medication, and that ultimately led to its removal from the U.S. Pharmacopoeia by 1941.

History of Medical Marijuana / Cannabis Use
- Unfortunately, since then cannabis has no longer been included as a medication in US pharmacology texts, and US healthcare professionals are taught only that marijuana is a dangerous drug of abuse.
History of Medical Marijuana / Cannabis Use

- In 1969, Timothy Leary PhD convinced the supreme court that part of the Marijuana Tax Act was unconstitutional as it was in violation of the 5th amendment - obtaining a stamp would be self incriminating.
- In 1970, the 1937 Marijuana Tax Act was repealed by Congress at the very same time they passed the Controlled Substance Act (CSA) as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.

History of Medical Marijuana / Cannabis Use

- The Controlled Substances Act (CSA, 1970) created a system to regulate psychoactive drugs and an organization to enforce the system, the Bureau of Narcotics Department (BNDD) - the DEA’s predecessor.
- In 1973 the Drug Enforcement Agency (DEA) was created as a single federal agency to consolidate and coordinate the government’s drug control activities.

History of Medical Marijuana / Cannabis Use

- Five levels (Schedules I to V) were established by the Controlled Substances Act (CSA) to categorize drugs according to their medical utility, abuse potential, and safety of use under medical supervision.
- Schedule V is the least restrictive category and Schedule I is the forbidden drug category.

History of Medical Marijuana / Cannabis Use

- To belong in Schedule I, a drug must meet three criteria:
  - It has NO currently accepted medical use in treatment (in the United States).
  - It has a high potential for abuse (highly addictive).
  - It has a lack of accepted safety for use under medical supervision (not safe for medical use).
- Disregarding the known medical benefits of Marijuana, it was wrongfully and purposely listed as a Schedule I drug along with Heroin, LSD, Mescaline, MDMA (Ecstasy), Psilocybin & Methaqualone.

History of Medical Marijuana / Cannabis Use

- Schedule II drugs [coca, opioids (morphine, dilaudid, codeine) and dexedrine] are highly addictive, but have been shown to have medicinal value.
- Prescriptions for these medications are limited in the amount that can be prescribed and the prescription cannot be “called in or ePrescribed”
History of Medical Marijuana / Cannabis Use

- Responding to questions about the wrongful placement of marijuana in Schedule I, President Richard Nixon appointed experts to review the science and report back.
- They found that cannabis did NOT meet criteria for Schedule I (National Commission on Marijuana and Drug Abuse, 1972).
- Unfortunately, Nixon ignored the commission’s findings, and cannabis remained forbidden.

- Numerous challenges to the cannabis prohibition arose over the years.
- Years later, the Alliance for Cannabis Therapeutics (ACT) joined the petition, and finally in 1988 the DEA’s administrative law judge, Francis Young, ruled on the petition that marijuana should be moved to Schedule II (Young, 1988).

- Van M Sim, former research psychiatrist for the NIMH (National Institute of Mental Health), reported to Medical World News in the July 16, 1971 issue that clandestine research in 1967 revealed ‘Marijuana...is probably the most potent anti-epileptic known to medicine today.’

Current Uses of Medical Marijuana / Cannabis

- Charlotte Figi has become “the girl who is changing medical marijuana laws across America,” after her ordeal and medical marijuana rescue from certain permanent brain damage and death was featured in the 2013 CNN documentary “WEED” by Sanjay Gupta, MD, chief CNN medical correspondent.
- Media coverage increased demand for Charlotte’s Web (developed by the Stanley Brothers grower’s in CO) and other High CBD, Low THA varietals to treat childhood epilepsy.
- Her case provoked Dr. Gupta to publically change his position on medical marijuana calling for a “full-scale federal legalization of medical marijuana in no uncertain terms.”
Current Uses of Medical Marijuana / Cannabis

- In 2011, 5 y.o. Charlotte Figi’s unresponsive Dravet Syndrome or SMEI (Severe Myotonic Epilepsy of Infancy) came under control with Charlotte’s Web medical cannabis high in CBD, low in THC (< 0.3%)

Canna Care (CCD) is a network of facilities that qualifies patients into medical marijuana programs in Rhode Island, Massachusetts, Maine, Connecticut, Delaware and the District of Columbia.

Dr. Gary Witman of CCD, stated “We have a statewide epidemic of opioid deaths. As soon as we can get people off opioids to a nonaddicting substance — and medicinal marijuana is nonaddicting — I think it would dramatically impact the amount of opioid deaths.”

Dr. Witman, working in the Massachusetts Canna Care clinic
- Treated about 80 patients (early 2015) with cannabis who were addicted to opioids, anti-anxiety medication or muscle relaxers through a one-month tapering program.
- More than three-quarters of patients successfully stopped taking the harder drugs.

Effects of MJ Smoking on long term health
- MJ Smoke contains several known carcinogens and 50% more carcinogens in its tar than cigarettes. MJ smoke deposits 4 times as much tar.
- Scientists surprised - a study of over 2,000 MJ smokers showed no increased risk of lung cancer.
- Scientist found that MJ smokers in LA County who smoked more than 20,000 joints in their lifetime had no increase risk of lung cancer


Acute psychoactive effects of cannabinoids:
- feeling of increased wellbeing (pleasurable and relaxing) that can give way to dysphoria, and anxiety or panic.
- impairment of memory, reductions in psychomotor and cognitive performance, disordered perception of the passage of time and euphoria.
- sensory perception is often heightened

Acute psychoactive effects of cannabinoids:
- May induce schizophrenic psychosis in vulnerable individual
- doubles the risk of schizophrenia in adolescents
- Psychosis is therefore regarded as a contraindication to treatment with cannabinoid medications, although two case series have shown a positive effect of THC in the treatment of refractory schizophrenia.
Medical Marijuana / Cannabis Safety / Side Effects

- Only extremely high consumption at levels hardly ever used for therapeutic medical purposes may lead to irreversible cognitive impairments.
- The risk is much higher in children and adolescents (particularly before puberty). Therefore, the advisability of (long-term) treatment of patients in this age group with cannabinoids must be weighed up very carefully.

Physical side effects of cannabinoids:
- Tiredness
- Dizziness
- Tachycardia, Orthostatic Hypotension that may increase risk of MI in predisposed individuals
- Dry mouth
- Decreased Lacrimation
- Muscle Relaxation
- Increased Appetite

Tolerance develops to many of the undesired effects of cannabinoids—particularly tiredness, dizziness, and cardiovascular and psychoactive effects—over a period of days or weeks.

Withdrawal symptoms only in heavy users after abrupt cessation. Similar in character and intensity to those experienced after sudden cessation of cigarette smoking and include uneasiness, irritability, sleeplessness, increased perspiration, and loss of appetite.

Withdrawal symptoms seldom a problem in the controlled medical administration of marijuana

Ability to drive and operate machinery safely may be impaired - greatest risk when initiating treatment, during the dose-finding phase, and if the dose is changed.

Patients on marijuana at a constant dosage over an extensive period of time often develop tolerance to the impairment of psychomotor performance, so that they can drive vehicles safely.

Successful alleviation of symptoms with medical marijuana may actually distinctly improve the patient’s ability to drive motor vehicles (compared with no treatment).

THC is metabolized mainly in the liver by cytochrome P-450 isoenzymes (principally CYP2C), it may interact with other medications metabolized in the same way. Cannabis smoking can reduce the plasma concentration of individual antipsychotics (clozapine, olanzapine).

In AIDS patients & in cancer patients the plasma level of various antiretroviral drugs or cytostatics were not altered by simultaneous treatment with cannabinoids.
Recreational marijuana itself is not a true gateway drug.

Recreational marijuana is illegal and as such it is often sold by dealers (pushers) who sell other harder illegal drugs, such as cocaine and heroin which are extremely addicting.

These harder illegal drugs are the true gateway drugs offered up to or pushed onto recreational marijuana users.

By continuing to be illegal, marijuana will continue to be utilized by dealers (pushers) to entice its users to try these harder drugs.

States & DC that have legalized Medical Marijuana / Cannabis

- 1996 – California
- 1998 – Alaska, Oregon, Washington
- 1999 – Maine
- 2000 – Colorado, Hawaii, Nevada
- 2004 – Montana, Vermont
- 2006 – Rhode Island
- 2007 – New Mexico
- 2008 – Michigan
- 2010 – Arizona, District of Columbia, New Jersey
- 2011 – Delaware
- 2012 – Connecticut, Massachusetts
- 2013 – Illinois, New Hampshire
- 2014 – Minnesota, Maryland, New York
- 2016 – Ohio, Pennsylvania
States & DC that have legalized Medical Marijuana / Cannabis

<table>
<thead>
<tr>
<th>State</th>
<th>Year</th>
<th>How Passed</th>
<th>Possession Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maryland</td>
<td>2014</td>
<td>House Bill 60 (23-9-442 S)</td>
<td>30-day supply to be examined</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>2012</td>
<td>Ballot Question 3 (33%)</td>
<td>60-day supply or personal medical use [10 oz]</td>
</tr>
<tr>
<td>Michigan</td>
<td>2008</td>
<td>Proposal 1 (6%)</td>
<td>2 oz usable, 12 plants</td>
</tr>
<tr>
<td>Minnesota</td>
<td>2014</td>
<td>Senate Bill 235 (65-18-104)</td>
<td>30-day supply of non-medicinal marijuana</td>
</tr>
<tr>
<td>Montana</td>
<td>2004</td>
<td>Initiative 148 (92%)</td>
<td>1 oz usable, 4 plants (mature), 12 seedings</td>
</tr>
<tr>
<td>Nevada</td>
<td>2000</td>
<td>Ballot Question 1 (43%)</td>
<td>2 oz usable, 12 plants</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>2013</td>
<td>House Bill 76 (24A-6-416)</td>
<td>Two courses of usable cannabis during a 10-day period</td>
</tr>
<tr>
<td>New Jersey</td>
<td>2013</td>
<td>Senate Bill 19 (66A-16-356, 113)</td>
<td>2 oz usable</td>
</tr>
<tr>
<td>New Mexico</td>
<td>2017</td>
<td>Senate Bill 125 (56-9-5215)</td>
<td>6 oz usable, 15 plants (mature), 42 immature</td>
</tr>
</tbody>
</table>

Covered Medical Marijuana / Cannabis Ailments by State

History of Medical Marijuana / Cannabis Use

Medical Marijuana legalization

Upcoming State Ballots – 11/16

- Arkansas – poll 58% support
- Florida – Amendment 2 – poll 69% support
- Massachusetts – Question 4 – poll 41% support
- Michigan – poll 53% support
- Missouri – poll 72% support
- North Dakota – poll 47%
- Oklahoma – poll 71%
On November 02, 2010, Arizona Proposition 203, the “Arizona Medical Marijuana Act” was approved by 50.13% of voters.

The Act effectively removed all state-level penalties on the use, possession and cultivation of marijuana, by patients who have been issued with a "written or oral recommendation" by their primary care physician, stating that he or she "would benefit from medical marijuana."

As of October 2011, a total of 14852 marijuana patients have received their Arizona medical marijuana cards.

12,367 people, or 83% of total applicants, also requested a permit to grow their own medical marijuana.
Arizona Medical Marijuana / Cannabis Program

- Qualifying Conditions for granting a medical marijuana identification card:
  - Cancer
  - Glaucoma
  - Human Immunodeficiency Virus
  - Acquired Immune Deficiency Syndrome
  - Hepatitis C
  - Amyotrophic Lateral Sclerosis
  - Crohn’s disease

- Agitation of Alzheimer’s disease
- Cachexia or wasting syndrome
- Severe and chronic pain
- Severe nausea
- Seizures, including those characteristic of epilepsy
- Severe/persistent muscle spasms, including MS
- Post Traumatic Stress Disorder (PTSD) recently added

Arizona Medical Marijuana / Cannabis Program

- AZ Medical Marijuana Facts (one year after passing)
  - 3 out of 4 medical marijuana patients were male (74.50%)
  - Only 12 patients were minors under the age of 18; 38 patients were over the age of 81.
  - The vast majority of marijuana patients, over 75% were over the age of 30; most in the 51-60 age group, or about 24% of the total.
  - 86% of Arizona patients report chronic pain as their qualifying condition. Muscle spasms came in second with 15% & nausea was third with almost 13%.
  - The least common qualifying condition was sclerosis: only 15 patients or 0.1% reported it.

Medical Marijuana: Routes of drug administration

- Most common delivery form - Inhalation (fastest effects) via smoking, water filtered aerosolization or heat vaporization (safer, no pyroletics) of plant components - leaves, buds, flowers or extracts (Hash, Kief, Tincture or Hash oil)
- Ingestion (slowest but stronger & longer lasting effects) via plant components or extractions (concentrates or tinctures - plant free) in oil based capsules, beverages, butter, oils or baked goods
- Topical – extracts in oils, lotions, creams & ointments
- Transdermal delivery patches
Medical Marijuana: Routes of drug administration

Plant Components

Extracts

• Most common delivery form – Inhalation (fastest effects) via smoking, water filtered aerosolization or heat vaporization (safest, no pyroletics) of plant components - leaves, buds, flowers or extracts (Hash, Kief, Tincture or Hash oil)

Medical Marijuana: Routes of drug administration

• Ingestion (slowest but stronger & longer lasting effects) via plant components or extractions (concentrates or tinctures - plant free) in oil based capsules, beverages, butter, oils or baked goods

Medical Marijuana: Routes of drug administration

• Topical – extracts in oils, lotions, creams, ointments & bath salts

Medical Marijuana: Routes of drug administration

• Transdermal delivery patches

Timeline – Cannabinoid & Endocannabinoid Research
Nearly all early research was devoted to clarification of cannabinoid chemistry and pharmacology and was mainly done using synthetic compounds.

Following the isolation and structure elucidation of the plant cannabinoids, particularly of cannabidiol (CBD) and of Δ⁹-tetrahydrocannabinol (Δ⁹-THC), pharmacological and physiological work was initiated.

The identification of cannabinoid receptors of endogenous cannabinoids and of receptor antagonists made possible extensive pharmacological and neurobiological research. This research lead to cloning of the anandamide-degrading enzyme fatty acid amide hydrolase (FAAH), the discovery of retrograde signaling by 2-arachidonoyl glycerol (2-AG), the discovery of allosteric sites on cannabinoid receptor 1 (CB1), the discovery that endocannabinoids bind to receptors other than CB1 and CB2.

Medical Cannabis can provide benefits for a wide variety of ailments and conditions:
- Agitation of Alzheimer’s Disease
- Acquired Immune Deficiency Syndrome / Human Immunodeficiency Virus
- Amyotrophic Lateral Sclerosis
- Anorexia Nervosa
- Anxiety Disorder
- Arthritis
- Asperger’s syndrome
- Asthma
- Autism
- Cachexia or Wasting Syndrome
- Cancer
- Crohn’s Disease
- Diabetes Adult Onset
- Diabetic Renal Disease
- Epilepsy
- Fibromyalgia
- Glaucoma
- Graves Disease
- Hepatitis C
### Ailments Treated with Medical Marijuana / Cannabis

- Medical Cannabis can provide benefits for a wide variety of ailments and conditions:
  - Insomnia
  - Intractable Hiccups
  - Lyme Disease
  - Lymphoma
  - Malignant Melanoma
  - Migraine Headaches
  - Other Skin Cancers

| Medical Cannabis can provide benefits for a wide variety of ailments and conditions: |
|---------------------------------|------------------|
| * Multiple Sclerosis            |
| * Nail Patella                  |
| * Nausea                        |
| * Opiate Dependence             |
| * Premenstrual Tension          |
| * Prostate Cancer               |

| Medical Cannabis can provide benefits for a wide variety of ailments and conditions: |
|---------------------------------|------------------|
| * Reiter’s Syndrome            |
| * Severe and chronic pain      |
| * Seizures (including those characteristic of epilepsy) |
| * Severe and persistent muscle spasms |
| * Schizophrenia                |
| * Shingles                     |

### Ailments Treated with Medical Marijuana / Cannabis

| Medical Cannabis can provide benefits for a wide variety of ailments and conditions: |
|---------------------------------|------------------|
| * Testicular Cancer             |
| * Thyroiditis                   |
| * Tourette’s Syndrome           |
| * Uterine cancer                |

- Endocannabinoid System (ECS) involves virtually every cell and tissue type and organ systems. Components:
  - Endocannabinoids (EC)
  - Enzymes involved in EC biosynthesis or metabolism
  - Two G-protein-coupled EC receptors, CB1 & CB2 that bind to and mediate the effects of cannabinoids.

  **Endocannabinoids - Bioactive lipid mediators produced in virtually all tissues and organs**
- Often exert their biologic effects through the EC receptors
- 2 extensively studied: AEA (N-arachidonylethanolamine) 
  & 2-AG (2-arachidonoylglycerol)
Clinical Pharmacology of Medical Marijuana / Cannabis

- Cannabinoids – Group of substances structurally related to Δ⁹-TetraHydroCannabionol (THC)
- They bind to cannabinoid receptors (CB1 or CB2) or by other mechanisms to modulate the endocannabinoid system.
- Classes of cannabinoids
  - PHYTOcannabinoids produced by cannabis plants
  - ENDOcannabinoids produced by our bodies
  - SYNTHETIC cannabinoids synthesized in the lab to target cannabinoid receptors &/or enzymes involved in the production or metabolism of endocannabinoids

Two Major Neuroactive Cannabinoids of Cannabis

- Psychoactive Δ⁹-TetraHydroCannabionoid: Δ⁹-THC responsible for the “High”
- NON-Psychoactive Cannabidiol: CBD which does have some anti-anxiety properties.
- Other minor non psychoactive cannabinoids exist

Minor non-psychoactive Cannabinoids

- cannabigerol (CBG)
- cannabichromene (CBC),
- Δ⁹-tetrahydrocannabivarin (Δ⁹-THCV) &
- cannabidivarin (CBDV)

Cannabis sativa usually has higher Δ⁹-THC:CBD ratios than Cannabis indica so C. sativa is typically more psychotropic and stimulating while C. indica more sedating

Drying or heating converts native THCA to its active psychotropic THA form
Clinical Pharmacology of Medical Marijuana: Δ⁹-THC

- Δ⁹-THC activates and exerts its effects on the body’s endocannabinoid system.
- Δ⁹-THC binds to 2 endocannabinoid G-protein-coupled cell membrane receptors: Cannabinoid Type 1 (CB₁) and Type 2 (CB₂).
- In the Central Nervous System (CNS), the endocannabinoid system influences synaptic communication and modulates eating, anxiety, learning & memory, and growth & development.

Clinical Pharmacology of Medical Marijuana: CBD

- CBD - Unlike Δ⁹-THC - Does NOT activate the endocannabinoid system’s CB₁ & CB₂ Receptors and is likely why it lacks psychotropic activities.
- CBD - is a multitargeting drug - interacting with many non-endocannabinoid signaling systems.

Clinical Pharmacology of Medical Marijuana: CBD

- Consroe (1998) presented an excellent review of CBD in neurological disorders. In some studies, it ameliorates symptoms of Huntington’s disease, such as dystonia and dyskinesia.
- CBD mitigates other dystonic conditions, such as torticollis, in rat studies and uncontrolled human studies.
- CBD functions as an anticonvulsant in rats, on a par with phenytoin (Dilantin™, a standard anti-epileptic drug).

Clinical Pharmacology of Medical Marijuana: Terpenoids

- The unique smell of cannabis does not arise from cannabinoids, but from over 100 terpenoid compounds (Turner et al. 1980).
- These compounds are easily extracted from plant material by steam distillation or vaporization. This distillate is called the essential oil or volatile oil of the plant.
- Terpenoids are lipophilic and permeate lipid membranes. Many cross the blood-brain barrier (BBB) after inhalation (Buchbauer et al. 1993, Nasel et al. 1994).
- Meschler and Howlett (1999) discussed several mechanisms by which terpenoids modulate THC activity. For instance, terpenoids may bind to cannabinoid receptors.
Terpenoids might modulate the affinity of THC for its own receptor, by sequestering THC, by perturbing annular lipids surrounding the receptor, or by increasing the fluidity of neuronal membranes. Further downstream, terpenoids may alter the signal cascade by remodeling G-proteins. Terpenoids may alter the pharmacokinetics of THC by changing the BBB; cannabis extracts are known to cause a significant increase in BBB permeability (Agrawal et al. 1989).

Terpenoids may also act on other receptors and neurotransmitters. Some terpenoids act as serotonin uptake inhibitors (as does Prozac), enhance norepinephrine activity (as do tricyclic antidepressants), increase dopamine activity (as do monoamine oxidase inhibitors and bupropion), and augment GABA (as do baclofen and the benzodiazepines).

The essential oil of cannabis is traditionally employed as an anti-inflammatory in the respiratory and digestive tracts without known contraindications at physiological dosages (Franchomme and Penoe 1990).

The essential oil of black pepper, Piper nigrum, has a composition of terpenes that is qualitatively quite similar to that of cannabis (Lawless 1995). A recent study has shown that inhalation of black pepper essential oil vapor significantly reduced withdrawal symptoms and anxiety in tobacco smokers (Rose and Behm 1994).
Cannabinoids Exhibit Anti-Tumor Activity In Many Animal Models of Cancer

Id-1, an inhibitor of basic helix-loop-helix transcription factors, has recently been shown to be a key regulator of the metastatic potential of breast and additional cancers.

Metastatic breast cancer cells became significantly less invasive in vitro and less metastatic in vivo when Id-1 was down-regulated by stable transduction with antisense Id-1.
**Medical Marijuana Research and Breast Cancer**

- It is not possible at this point to use antisense technology to reduce Id-1 expression in patients with metastatic breast cancer.
- Cannabidiol (CBD), is the first NON-toxic exogenous agent shown to significantly decrease Id-1 expression in aggressive human metastatic breast cancer cells leading to the down-regulation of tumor aggressiveness.

**Antitumoral Action of Cannabinoids**

- Cannabidiol (CBD), is the first NON-toxic exogenous agent shown to significantly decrease Id-1 expression in aggressive human metastatic breast cancer cells leading to the down-regulation of tumor aggressiveness.

**THC Activates The Autophagy-Mediated Cell Death Pathway in Human Glioblastoma Samples**

- THC activates the autophagy-mediated cell death pathway in human glioblastoma samples.

**Medical Marijuana / Cannabis & The Cardiovascular System**

- Cardiovascular System
  - ECS is dysregulated (CB1 > CB2) in CV Disease:
    - CB1 has proinflammatory effects - atherogenesis, endothelial and cardiac dysfunction and fibrosis
    - CB2 has cardioprotective effects - against atherosclerosis, improved endothelial and cardiac function

**Endocannabinoid signaling at the periphery: 50 years after THC**

- Cardiac System

**Endocannabinoid signaling at the periphery: 50 years after THC**

- GastroIntestinal System
  - Nearly all gut functions are regulated by eCBs - motility, barrier fx, immune fx & control of food intake & energy balance
  - The ECS of the gut is critical for CNS control of the metabolic and homeostatic functions of the body
  - CB1 – enteroendocrine cells
  - CB1 & CB2 – enteric nerves, immune cells & enterocytes
Medical Marijuana / Cannabis & The Gastrointestinal System

**GastroIntestinal System**
- Liver - Pathophysiological conditions up regulate the expression of CB receptors
- CB1 activation - promotes ascites, fat accumulation, insulin resistance & fibrosis
- CB2 activation - decreases reperfusion injury, reduces fat accumulation & is antifibrotic

Medical Marijuana / Cannabis & The Immune System

**Immune System**
- eCBs involved with the Adaptive (Humoral & Cellular) immune system
- Immune cells primarily express CB2 receptors acting through 2-AG inhibit the migratory activities of immune cell types
- CB2 receptors acting through AEA inhibit immune fx - inhibit proinflammatory cytokines: IL-2, TNFα, IFNφ, IL-6, IL-8

Medical Marijuana / Cannabis & The Musculoskeletal System

**Musculoskeletal System**
- Muscle cells produce eCBs & express CB1, CB2 & eCB enzymes
- eCBs involved in control of skeletal muscle energy metabolism and in formation of new skeletal muscle fibers via CB1 through AEA and 2-AG.

Medical Marijuana / Cannabis & The Reproductive System

**Reproductive System**
- Female - eCB signaling, both silenced and amplified, operates in all critical stages of pregnancy.
- ECS based drugs for treatment of infertility
- PEA (PalmitoylEthanolAmide, an endocannabinoid lipid) containing creams to treat painful dysfunctions: vestibulodynia, vulvodynia and vaginismus
Medical Marijuana / Cannabis & The Reproductive System

Endocannabinoid signaling at the periphery: 50 years after THC

- Reproductive system
  - eCB signaling involved in the preservation of normal sperm function and male fertility
  - eCB levels of AEA, PEA and OEA (OleoylEthanolAmine an endocannabinoid lipid) are significantly lower in infertile males
  - Manipulation of the ECS might improve male fertility and sperm dysfunction

Medical Marijuana / Cannabis and The Cutaneous System

The endocannabinoid system of the skin in health and disease: novel perspectives and therapeutic opportunities

- Cutaneous System
  - ECS is a key player in the regulation of the skin’s biological processes - proliferation, growth, differentiation, apoptosis and cytokine, mediator or hormone production of various cell types of the skin and its appendages (e.g. hair follicles, sebaceous glands)

Medical Marijuana / Cannabis and The Cutaneous System

Main physiological function of the cutaneous ECS – Constitutive control of the proper & well-balanced proliferation, differentiation, & survival, as well as immune competence &/or tolerance of skin cells.

Medical Marijuana / Cannabis and The Cutaneous System

Disruption of this delicate ECS balance appears to lead to the development of pathological conditions and diseases (e.g. itch & pain, hair growth disorders, acne, seborrheic dermatitis, allergic dermatitis, psoriasis, sclerosis & cancer)

Medical Marijuana / Cannabis and The Cutaneous System

MRSA causes over 72,000 severe infections and over 10,000 deaths each year (CDC) and is the direct evolution of overusing antibiotics

Sources: hospitals, gyms, asymptomatic pet carriage, sharing hygiene products, beach sand (reproduce) and seawater (live for days)

Medical Marijuana / Cannabis and The Cutaneous System

MRSA can present as Impetigo, Folliculitis, Cellulitis, an Abscess and Ulceration
Medical Marijuana / Cannabis and The Cutaneous System

Italy's University del Piemarte and Britain's University of London revealed 5 major cannabinoids (D9-THC, CBN, CBD, CBC and CBG) showed potent activity against MRSA strains of current clinical relevance, including Epidemic EMRSA.

No substantial difference in potency was observed, with a minimum inhibitory concentration in the range 0.5–2 mg/mL.

The cannabinoids use a unique but unknown mechanism of action which prevents the MRSA strains from allowing their adaptations to develop resistance.

The cannabinoids (CBD and CBG (non-psychoactive)) are the most promising to development:

- Topical antiseptics (salves, ointments, lotions, creams)
- Whole cannabis lozenges
- Systemic antibacterial agents (whole cannabis extract, tinctures)
- Topical application of cannabinoids agents to treat ulcers and wounds in a hospital would decrease the burden of using systemic antibiotics.

Six new non-cannabinoid compounds were isolated from a high potency Cannabis sativa variety. Some had strong antimicrobial, antileishmanial, antimalarial and anti-oxidant activities.

Figure 6: Functions of the cutaneous ECS. Prototypic endocannabinoids such as anandamide (N-arachidonoylethanolamine, AEA) and 2-arachidonoylglycerol (2-AG) are produced locally in various cellular compartments of the skin (i.e. epidermis, sebaceous gland, hair follicle) (green arrows). These endocannabinoids, via binding to cannabinoid receptor subtypes 1 and/or 2 (CB1/CB2), constitutively control the proper and well-balanced cutaneous functions (e.g. sensation, growth, survival, immune competence and/or tolerance) (red arrows). For example, activation of CB1 and CB2 on epidermal keratinocytes by locally produced endocannabinoids results in the suppression of cellular proliferation, differentiation and the release of inflammatory mediators as well as the induction of apoptosis. Likewise, endocannabinoids, via CB1/CB2, inhibit inflammatory processes of resident and infiltrating immune cells. Furthermore, activation of CB1 in the hair follicle by AEA attenuates hair shaft elongation and interfollicular proliferation, whereas it stimulates apoptosis and the development of catagen regression. On another member of the pilosebaceous unit (i.e. the sebaceous gland derived sebocytes), locally released endocannabinoids markedly enhance lipid production and apoptosis via CB1. Finally, skin-derived endocannabinoids inhibit various sensory phenomena (e.g. pain and itch) via CB1 expressed on sensory afferent nerves.
Modulations of the fine-tuned tone of the cutaneous endocannabinoid system (ECS) could have therapeutic values in the management of a large variety of human skin diseases. For example, suppression of the skin ECS tone (using e.g. CB antagonists and/or agents that attenuate the local production of endocannabinoids) could be used in the therapy of certain hair growth (e.g. forms of alopecia, effluvium) and sebaceous gland disorders (e.g. acne, seborrhea).

Modulations of the fine-tuned tone of the cutaneous endocannabinoid system (ECS) may have therapeutic values in the management of skin diseases. Augmentation of the tone of the cutaneous ECS (using e.g. CB agonists and/or agents that stimulate the local production of endocannabinoids) could be beneficial in the treatment of various benign and malignant skin tumors, hyperproliferative skin diseases (e.g. psoriasis), excessive hair growth (e.g. hirsutism), different forms of dermatitis, dry skin conditions and sensory phenomena (e.g. pain, itch).

The endocannabinoid system (ECS) regulates multiple physiological processes, including cutaneous cell growth and differentiation.

The major nonpsychotropic phytocannabinoid of Cannabis sativa, cannabidiol (CBD) behaves as a highly effective sebostatic agent on human sebaceous glands.

Cannabidiol exerts sebostatic and antiinflammatory effects on human sebocytes

Administration of CBD to cultured human sebocytes and human skin organ culture inhibited the lipogenic actions of various compounds, including arachidonic acid and a combination of linoleic acid and testosterone, and suppressed sebocyte proliferation via the activation of transient receptor potential vanilloid-4 (TRPV4) ion channels.
Medical Marijuana / Cannabis and Acne

Cannabidiol exerts sebostatic and anti-inflammatory effects on human sebocytes

• CBD also exerted complex anti-inflammatory actions that were coupled to A2a adenosine receptor-dependent upregulation of tribbles homolog 3 (TRIB3).
• Findings suggest the combined lipostatic, antiproliferative, and anti-inflammatory effects, CBD has potential as a promising therapeutic agent for the treatment of acne vulgaris.

Medical Marijuana / Cannabis and Scleroderma

Adenosine A2A receptor activation stimulates collagen production in scleroderma dermal fibroblasts either directly and through a cross-talk with the cannabinoid system

• In Systemic Sclerosis (SSc) (limited & diffuse forms) Adenosine A2A receptors (A2Ar) are overexpressed by SSc dermal fibroblasts and directly promote dermal fibrosis by increasing abnormal collagen production
• A2Ar can also promote the same dermal fibrosis indirectly by activating CB1 receptors in SSc fibroblasts.
• Raising CB2 receptor activity over CB1 receptor activity has clear anti-fibrotic effects

Medical Marijuana / Cannabis and Melanoma

Exploiting cannabinoid-induced cytotoxic autophagy to drive melanoma cell death.

• Global incidence of cutaneous melanoma is increasing but survival rates for metastatic melanoma remain < 10%.
• Targeting autophagy is a means to promote cancer cell death in chemotherapy-resistant tumors.
• Treatment with THC activated autophagy, loss of cell viability and activation of apoptosis.
Administration of Sativex-like (equal amounts THC and CBD) to mice bearing BRAF wild type melanoma xenographs inhibited melanoma viability, proliferation and tumor growth paralleled by an increase in autophagy and apoptosis compared with standard single-agent temozolomide.

Recent studies - atopic dermatitis (AD) - mast cells synthesize, store and release Nerve Growth Factor (NGF) - both appear to be involved in tissue inflammation and neuroimmune interactions, with NGF acting as a general “alert” molecule capable of recruiting and priming both local tissue and systemic defense processes following stressful events. Increased number of mast cells correlates with raised plasma levels of nerve growth factor (NGF) - a possible key role of their interaction in the pathogenesis of AD.

Increase in NGF leads to mast cell hyperactivity, enhanced degranulation and proinflammatory mediator release resulting erythema, edema and pruritus.
Specific endocannabinoids belonging to the class of alicanides known as “autacoid local inflammation antagonism” (ALIA), cause local modulation of mast cell function – down regulating mastocyte reactivity in part through CB1 and CB2 receptors.

Pilot study to assess efficacy and safety of a topical emulsion containing adelmidrol 2%, a novel alicamide, in the treatment of mild AD in pediatric subjects.

Twenty patients with mild AD (11 male and 9 female), mean age 8 years (range 3-16).

Decrease of erythema and pruritus in 12 (60%) patients by 10-15 days of treatment.

Clinical resolution in 16 (80%) patients after 4 weeks of treatment (Figs. 1 and 2); no relapses at 4-week follow up; no treatment side effects were observed.

Medical Marijuana / Cannabis and Atopic Dermatitis

Pruritus, Skin Inflammation, Stress and Anxiety

- Eczemas – atopic, neuro, nummular, irritant and contact
- Psoriasis
- Intractible itching
- Xerosis
Medical Marijuana / Cannabis and Itching

Medical Marijuana / Cannabis and Xerosis

Medical Marijuana / Cannabis and Dysesthesia
- Neuropathy - Pain, Burning, Tingling and numbness
- MS induced (along with muscle spasms and cramps)
- Chemotherapy induced
- Diabetes induced
- Post Herpetic Neuralgia induced

Medical Marijuana / Cannabis and Dysesthesia
- Non neuropathic Pain
- Nail-Patella Syndrome
- HSV
- Eosinophilia-Myalgia Syndrome
- Inflammatory Myalgia Syndrome
- Bechet’s
- Burns
- Advanced cancer

Medical Marijuana / Cannabis Nail Patella Syndrome
- also known as hereditary osteoonychodyplasia
- genetic disease: a mutation in the gene encoding transcription factor LMX1B, mapped on the long arm of chromosome 9 (9q34).
- Manifestations: fingernail dysplasia, absent or hypoplastic patellae, the presence of posterior iliac horns, & abnormalities of the radial heads.
- Patients are also at risk for kidney disease and glaucoma.

Medical Marijuana / Cannabis Herpes Simplex
Medical Marijuana

The endocannabinoid system (ECS) has been found in nearly all cells in each of our organ systems.

The ECS has been shown to be central in maintaining each organ system’s homeostatic balance.

When one or more organ systems’ homeostatic ECS become(s) impaired out of balance and cannot correct itself; it appears that re-adjusting these ECS by using the appropriate agonist or antagonist, including the use of disease-tailored medical marijuana (MMJ) could correct and re-establish those organ systems’ homeostasis.

Isn’t MMJ helping to fulfill the goal of our Holistic Osteopathic Philosophy in treating the individual from their cellular level to their organ system level to their body as a whole?

Conclusion: Medical Marijuana / Cannabis

- Objectives Accomplished
  - What marijuana is.
  - What medical marijuana is.
  - Detoxified your views on medical marijuana.
  - Demystified your views on medical marijuana.
  - Answered how and why medical marijuana is going to become another highly effective drug class, like steroids and biologics, in your toolbox.
Embryology For the Rest of Us
Derrick Adams, DO, FAOCD
Private Practice
Red Bluff, CA

Conflicts of Interests
- No conflicts
- My Id is in conflict with my Ego

I DON'T NORMALLY LIKE TO TALK ABOUT EMBRYOLOGY
BUT WHEN DR. ADAMS TEACHES IT, I CANNOT GET ENOUGH!

Ectoderm
- Follicular Units
- Keratinocytes
- Merkel Cells
- Melanocytes
- Eccrine glands
- Apocrine glands
- Sebaceous glands
- Nerves
- Teeth
- Facial Cartilage
- CNS – brain/spinal chord
- Eye
- Eye lid glands
- Parotid gland
- Lacrimal gland
- Lens
- Cornea
- Ear bones
Are you looking…?

Anterior 2/3 of Tongue?
Parotid Duct & Gland?
Teeth?
Distal Urethra of Penis?
Lower 1/3 of Anal Canal?
Hard Palate?
Buccal Mucosa?
Mammary Gland & Ducts?

Basic Germ Layers

- Ectoderm
- Mesoderm
- Endoderm
- Gastrulation
- Selective Affinity

Dr. Heinz Christian Pander
“Founder of Embryology”

Trilaminar Embryo

- Ectoderm
- Mesoderm
- Endoderm

Neurulation

- Refers to the folding process in vertebrate embryos, which includes the transformation of the neural plate into the neural tube.

Neural Plate

- Surface Ectoderm
  (Periderm & Epidermis)
- Neural Tube
  (Neural Crest & CNS)
Question?

- What happens to the notochord at the termination of embryological development?

Let's Build an Epidermis!

PERIDERM

Plato movie?
Periderm

- Prevents Adhesions
- Transport
- Antimicrobial
- Antioxidant
- Electrically neutral?
- Form Vernix after sloughed
Absent Periderm?

- Peridermopathies
- Popliteal Pytergium Syndrome
- Cocoon Syndrome
- Intraoral epithelial fusions in murine models

- Keeps developing intermediate keratinocytes from fusing
- “Teflon Coat” no stick surface

Pytergium syndromes

Vernix Caseosa

The Power of Vernix - Why baby isn't getting a bath straight away
Vernix

- Lanugo hair, periderm, and sebum
- Can be absent preterm
- Protection?
- Moisturization?
- Antibacterial?
- Lubrication? Birth Canal
- Potentially swallowed

Collodion Membrane

col-o'di-onə
syrupy solution of nitrocellulose in a mixture of alcohol and ether, used for coating things, chiefly in surgery and in a former photographic process.
Word usage peaked in 1850
Spinous Kertinocytes (stratified)

P63, P73-LIKE
- Allows epi to stratify and proliferate
- Adult (acro-dermatoungual-lacrimal-tooth)
- Ectrodactyly ectodermal dysplasia-cleft lip/palate
- Ankyloblepharon-ectodermal dysplasia clefing syndrome (AEC, “Hay-Wells”)

Corneocytes (s. corneum)
- Interconnected by histidine rich protein called filaggrin which is derived from components of the keratohyalin.
- Through friction or degradation of desmosomes and filagrin they eventually shed (1300 cells/cm2/hour on forearm)
- Desmoglein 1 alpha
- Desmocollin
- Dust in your house

- Progression of keratinization# of keratohyalin and lamellar body granules increases
- Increase in # of organelle-depleted cornified cells
- Neonate’s skin barrier not completely mature until a few weeks after birth
- Full barrier function 3 wks of age
Development of epidermis

<table>
<thead>
<tr>
<th>EGA</th>
<th>EVENTS</th>
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</thead>
<tbody>
<tr>
<td>3 Weeks</td>
<td>Single Layer Of Flattened Epithelial Cells</td>
</tr>
<tr>
<td>4 Weeks</td>
<td>Basal Germinative Layer &amp; Periderm</td>
</tr>
<tr>
<td>3 Months</td>
<td>Intermediate Cells</td>
</tr>
<tr>
<td>5 Months</td>
<td>Keratohyaline Granules, signs Of Cornification Starts</td>
</tr>
<tr>
<td>6 Months</td>
<td>Cornification Completed</td>
</tr>
<tr>
<td>Term</td>
<td>Increase In Thickness Of Cornified Layers</td>
</tr>
</tbody>
</table>

- Defects of Epidermal Maturation
- X-linked ichthyosis
- Steroid sulfatase
- Lamellar ichthyosis
- TGase 1

Ectodermal Dysplasia

- Ectodermal dysplasia (almost 180 and counting)
- Hypohidrotic Ectodermal hypoplasia (peg teeth, sparse hair, poor sweating, xerosis)
- Pachyonychia Congenita and its variants (dystrophic nails, natal teeth, keratoderma)
- EEC: Ectrodactyly Ectodermal Dysplasia Cleft palate syndrome (lobster claw, hair, deafness, dry skin, nails dystrophy, cleft palate)
- All these are Ectodermal with some mesodermal related structures.

Let’s Build Our Dermis!

Mesor Derm
What is the difference between a carcinoma and a sarcoma embryologically?

Team Mesoderm
- Langerhans cells
- Adipocytes
- Fibrocytes
- Macrophages
- Blood and lymph vessels
- Muscles

Somites
- Building blocks of the vertebrate body plan
- Template for nervous system
- Bone & musculature development
- Segmentation

Somities “Induce” Into...
- sclerotome (cartilage)
- syndotome (tendons)
- myotome (skeletal muscle)
- dermatome (dermis)
- endothelial cells

Somitogenesis
- Clock & Wave
  - NOTCH Signaling
Somities “Induce” Into...

- sclerotome (cartilage)
- syndotome (tendons)
- myotome (skeletal muscle),
- dermatome (dermis)
- endothelial cells

Dermatomes

We now have our epidermis and dermis

EXITING MESODERM

We now have our epidermis and dermis
Induction

**Neural Plate**
- Surface Ectoderm (Periderm & Epidermis)
- Neural Tube (Neural Crest & CNS)

**Dermis controls epidermis**

**NEURAL CREST**
**Neural Crest**

- What comes from neural crest?
- Common origin of diseases/syndromes
- Doctor why do you look at my teeth and eyes? I’m here for a skin problem!

**Neurocristopathies**

- Cleft lip/palate
- neurofibromatosis
- phakomatosis pigmentovascularis
- Dermal melanocytosis
- Waardenburg syndrome
- Piebaldism
- Many, many more!
Waardenburg Syndrome

- Pax3 -- migration from neural crest & activation of melanocyte proliferation
- Which types of Waardenburg Syndrome involve Pax3 mutations?

Piebaldism

- Belongs to a family of proteins called receptor tyrosine kinases
- Growth, proliferation, and migration of melanoblasts depend upon Steel Factor binding
- Nonfunctional KIT results in Piebaldism

Melanocytes

- Skin
- Hair
- Iris
- Inner ear
- Nervous system
- Heart
- Blood vessels
- Leptomeninges

What do Melanocytes Do?

- Make about 1 gram of it
- Evolutionary function of feathers
- Basal keratinocytes for basal keratinocytes
- Upregulate IL-6 and IL-8
- Role in control of adipocytes
- Calcium pump of keratinocytes (confetti hypopigmentation of Darier's disease)
- Antibiotic (mycosis in darker skin)
- Anti-inflammatory (preventing feather breakdown)
- Sympathetic fight or flight (changing skin colors in reptiles)
- Detoxification of free radicals
- Provide dopamine to aid in synapse formation in early nerve development

- Arianayagam S, Ryan TJ. Human pigmentation: A side effect adapted from a primitive organism’s natural, symbiotic cell rearrangement with an affinity for the keratinocyte and melanocyte. Part I. Indian Dermatol Online J 2014;5:201-9
Arianayagam S, Ryan TJ. Human pigmentation: A side effect adapted from a primitive organism’s survival, acting through cell attachment with an affinity for the keratinocyte and the collagen. Part I. Indian Dermatol Online J 2014;5:201

“...The melanocyte is part of a caring community of cells surviving in a threatening environment; a nurse maid that uses the electromagnetic spectrum and mechanical forces and evolves over 500 million years to a point at which its original behavior is forgotten and skin color and its social influence dominates the literature read by dermatologists. “

Melanocyte Timeline
- Present in epidermis in 1st trimester
- Fully functional in 2nd
- Melanin production begins at 3-4 months
- Transfer to keratinocytes at 5th month

**Melanoblasts travel with peripheral nerves**

Melanocytes
- Melanoblasts arise from neural crest along dorsal neural tube (more to follow...)
- Migration & Differentiation into melanocytes
- Middle of 1st Trimester in epidermis
- Melanin genesis and transfer

How do melanocytes populate the skin?
- *Dorso-lateral migration (remember piebaldism example)
- * Ventral neural crest (Schwann Cells)

Melanocyte Puberty
- Melanoblasts multiply as they travel
- MITF crucial
- Tyrosinase appears
- (c-kit) tyrosinase kinase receptor
- SOX10, Pax 3, TYRP-2
- Wnt/FRIZZLED protein
- B-catenin signaling pathway
- Notch and MAPK
Melanoblasts Reservoirs in adult skin?

- Bulge area
- Dermis
- Cutaneous nerve stem cells
- Schwann Cells
Melanocytes accumulate around elastin
Electron microscopy shows dermal melanocytes encircling elastin fibers
“Elastin guide wire”
Tangential arrangement in upper dermis
Horizontal in lower dermis

(My obligatory Osteopathic slide)

Intruders

Dermal Melanosis & Dermal Melanocytomas

What is the difference between a blue nevus, nevus of Ito/Ota and a Mongolian spot?
By Week 20 all dermal melanocytes should be absent (by conventional thinking)*
Fibrous extracellular sheath on EM
Dermal Melanosis

- Mongolian Spots
- Nevi of Ito
- Nevi of Ota

Ota

- Segmental pattern in cranial nerves V & VII
- Hint at relationship with Schwann cells
- So what pathway would these have migrated through?

Why do Mongolian Spots resolve and Ito/Ota do not?

- Unique phenomenon
- Extracellular protective fibrous sheath starts to degrade in womb
- Early childhood sees most intense destruction

Mongolian Spots

- Inborn errors of metabolism
- Hurler’s disease & GM1 gangliosidosis are most common
- When to suspect?
- Part of the Phakomatosis spectrum
- Other genodermatosis

Merkel Cell

- Not Neural Crest origin in mammals (including here for traditional reasons)\(^7\)
- Epidermal origin
- Probably Merkel cells and “Merkel-like” cells

Mammalian Merkel cells are descended from the epidermal lineage. *Dev Biol.* 2009 Dec 1, 336(1):76-83
Langer Lines
- Not really an embryology issue
- Cadaver lines
- Never meant to guide surgery
- Borges’s and Kraissl’s lines are better guides for elective incisions

Blaschko Lines

Mosaicism
- denotes the presence of two or more populations of cells with different genotypes in one individual who has developed from a single fertilized egg.

Blaschko’s Lines

Blaschko’s
- Incontinentia pigmenti
- Focal dermal hypoplasia
- CHILD syndrome
- Epidermal nevus
- Sebaceous Nevi
- Segmental vitiligo
- Hypomelanosis of Ito
- ILVEN
- X-linked dominant skin disorders
- Lichen striatus
-Linear perforantria
- Conradi Hunermann Syndrome
- (Many are X-linked dominant)
Causes of Mosaicism

- Postzygotic Mutation
- Half Chromatid mutation
- Chromosomal non-disjunction
- X-Linked Inactivation (Lyonization)*
- Chimerism*

What is a Chimera?

When they did another ultrasound a few weeks later, they discovered, that I had resorbed the other fetus.

Craniofacial Structures
Embryologic Fusion Lines

Epithelial to Mesenchymal Transition

Mammalian Facial Development
NC cells contribute:
- Skeletal elements (face, hyoid, etc.)
- Cartilage elements (e.g., in trachea)
- Inner ear bones
- Cranial nerves (V, VII, IX, X)

Maxillomandibular prominence
Upper and lower jaws
Stomodenum

Neural Crest Cells in Head and Face

Arch 1
Arch 2
Arch 3
Meckel's cartilage
Rheehert's cartilage
Incus
Malleus
Stapes
Hyoid
Accessory Tragus

- 1st Arch
- Goldenhar syndrome
- Hearing
- Vertebral defects
- Renal US?

Branchial Cleft Cysts

Embryologic Fusion lines?


Role of Embryologic Fusion Planes in Basal Cell Carcinoma: A Classic Mix-up of Causation and Correlation. PRSGlobalOpen. 2015. 10


The Neanderthal in the Mirror

Neanderthal range in Eurasia

POU2F3 -- 66% of East Asians
BNC2 -- 70% of Europeans
Significance?

NOT EVERYONE AGREES

References


HOW CAN HOMEOPATHIC MEDICINE BE HELPFUL TO TODAY'S DERMATOLOGIST?

(LECTURE HANDOUT)

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WHAT IS HOMEOPATHIC MEDICINE?

• WHAT IS IT?

• IS THERE ANY RESEARCH?

• WHAT CAN YOU DO WITH IT?

WHAT IS HOMEOPATHIC MEDICINE?

• GREEK: Homoios – ‘similar’ or ‘like’

Pathos – ‘suffering’

• HOMEOPATHIC MEDICINE - IS A LOW-COST, NON-TOXIC SYSTEM OF MEDICINE USED BY 500 MILLION PEOPLE WORLD-WIDE WHICH USES MICRODOSES OF SUBSTANCES DERIVED FROM PLANTS, MINERALS, OR ANIMALS FOR THE PURPOSE OF STIMULATING THE NATURAL HEALING RESPONSE.

SAMUEL HAHNEMANN, MD (1755-1843)

• He ingests cinchona (Peruvian bark) & experiences malaria-like symptoms

• He hypothesizes cinchona helps malaria patients because it causes similar symptoms in a healthy person

The LAW OF SIMILARS


SAMUEL HAHNEMANN, MD

• While translating a scientific book, Hahnemann wondered at the author’s claim that cinchona (Peruvian bark) was effective against malaria because it was bitter.

• Hahnemann knew of other bitter medicines which didn’t cure malaria

3 PRINCIPLES OF HOMEOPATHIC MEDICINE

1. LAW OF SIMILARS - CURE IS ACHIEVED BY GIVING SUBSTANCES WHICH ARE CAPABLE OF INDUCING SIMILAR DISEASE-LIKE SYMPTOMS IN THE HEALTHY PERSON

2. EMPLOY INFINITESIMALLY SMALL, PROPERLY POTENTIZED DOSES

3. ADDRESS THE WHOLE PERSON

Common Homeopathic Potencies

<table>
<thead>
<tr>
<th>Common Potencies</th>
<th>Dilution Factor</th>
<th>Number of Dilutions</th>
<th>Exponent Designation</th>
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<td>MM</td>
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How does Homeopathic Medicine Work?

- MODE OF ACTION IS NOT KNOWN
- DILUTIONS NEED TO BE ACCOMPANIED BY VIGOROUS SHAKING
- HOMEOPATHIC MEDICINES DO NOT WORK AFTER BEING HEATED TO 70°C (158°F), FREEZE-THAWED, OR ULTRASONIFIED

Common Homeopathic Potencies

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Homeopathic treatment of minor aphthous ulcer: a randomized, placebo-controlled clinical trial

Fukersh T, Nasser M, Hashem H, Salib N, Al-Saleh M, Al-Masri M. Department of Oral Medicine, Faculty of Dentistry, University of Alexandria, Alexandria, Egypt

Objective: The objectives of this study were to clinically determine the efficacy of homeopathic granules in the treatment of minor aphthous ulcers (MALI). Design intervention: A randomized, single-blind, placebo-controlled clinical trial of homeopathic granules. Subjects and methods: One hundred patients with minor aphthous ulcers were treated with homeopathic granules and compared with placebo. Patients were given either 15 drops of neutralized homeopathic granules in 50 ml of distilled water every 4-6 h at bedtime and in the morning. Patients were evaluated for healing at baseline and at 1, 2, and 3 weeks. Results: All patients tolerated the medication. Treatment group differences were not significantly different at baseline or any of the other visits. Conclusions: The results suggest that homeopathic treatment is an effective and safe method in the treatment of MALU. Keywords: Homeopathy, aphthous ulcer, randomized, placebo controlled.
**APHTHOUS ULCERS - SIZE**

![Graph showing change in size of lesions over time](image)

**APHTHOUS ULCERS - PAIN**

![Graph showing mean change in pain VAS (100 mm)](image)

**CONCLUSIONS**

- Individualized homeopathy can reduce pain intensity & size of aphthous ulcer
- First published study of homeopathy & tx of aphthae
- No adverse effects seen
- *Borax* & *Natrum Muriaticum* most common remedies (women)
- *Borax* & *Mercurius Solubilis* most common remedies (men)
- Study limitation: single-blind (PT)

**RESULTS**

- *Calendula* ointment was superior to *Trolamine* in all categories (except ease of application)
- *Conclusion:* *Calendula* is highly effective in preventing acute radiation dermatitis in patients undergoing post-op radiation tx for breast cancer.

**HOMEOPATHIC PREVENTION OF ACUTE RADIATION DERMATITIS**

<table>
<thead>
<tr>
<th></th>
<th>Calendula</th>
<th>Trolamine</th>
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<tbody>
<tr>
<td># Women</td>
<td>126</td>
<td>128</td>
</tr>
<tr>
<td>Allergic Reactions</td>
<td>None</td>
<td>4 (Pruritus Urticaria)</td>
</tr>
</tbody>
</table>

**Homeopathic prevention of acute radiation dermatitis**

- Single-blinded phase III randomized comparison

- *Calendula* ointment was statistically significantly more effective than *Trolamine* in preventing acute radiation dermatitis (grade 2 or higher)
- *Calendula* ointment had significantly better self-assessed pt satisfaction regarding pain and dermatitis
**ORIGINAL PAPER**

*Ignatia in the treatment of oral lichen planus*

Mousavi F, et al.

Department of Oral Medicine, Tehran University of Medical Sciences, Iran

Objective: To evaluate the effectiveness of Ignatia homeopathic HC in management of oral lichen planus (OLP).

Methods and materials: In this single-blind randomized controlled clinical trial, 30 consecutive patients with oral lichen planus (non-tender and tender) were randomly divided into two groups: the treatment group received Ignatia homeopathic HC while the control group received placebo. Both groups were treated for 5 months. The lesions size and pain intensity were recorded at baseline and after treatment.

Results: Mean decrease in the lesions size and pain intensity was statistically significant between the treatment and control groups (p < 0.05).

Conclusions: Our results suggest that Ignatia has a beneficial effect in treatment of OLP in selected patients. Homeopathy 2008; 98: 40-44.

---

**IGNATIA – TX ORAL LICHEN PLANUS**

- SINGLE-BLIND RANDOMIZED CONTROLLED CLINICAL TRIAL
- 30 CONSECUTIVE PTS WITH ORAL LICHEN PLANUS
- 15 – TX WITH IGNATIA
- 15 – TX WITH PLACEBO
- TX DURATION: 4 MONTHS


---

**LESION SIZE**


---

**PAIN**


---

**IGNATIA – TX ORAL LICHEN PLANUS**

**CONCLUSIONS**

- IGNATIA HAS BENEFICIAL EFFECT IN TX OF ORAL LICHEN PLANUS
- DECREASED PAIN & DISCOMFORT OF LESIONS
- REDUCED SIZE OF LESIONS
- STATISTICALLY SIGNIFICANT OVER PLACEBO (p < 0.05)

**HOMEOPATHIC VS. CONVENTIONAL TX OF CHILDREN WITH ECZEMA: A COMPARATIVE COHORT STUDY**

- INSTITUTE FOR SOCIAL MEDICINE, EPIDEMIOLOGY & HEALTH ECONOMICS, CHARITE UNIVERSITY MED CENTER, BERLIN, GERMANY
- FIRST LONG-TERM, PROSPECTIVE, MULTI-CENTER COHORT STUDY TO COMPARE HOMEOPATHIC VS. CONVENTIONAL TX OF ECZEMA IN CHILDREN
- SIGNS / SYMPTOMS & QUALITY OF LIFE

(N = 118 CHILDREN)
(54 HOMEOPATHIC & 64 TRAD TX)
FOLLOW-UP PERIOD: 12 MONTHS
IMPROVEMENT OF ECZEMA (OBSERVED BY DRS.) WAS SIGNIFICANTLY GREATER IN HOMEOPATHIC GROUP (p < 0.001)
ECZEMA SYMPTOMS IMPROVED IN BOTH GROUPS (NO STATISTICAL DIFF)
DISEASE-RELATED QUALITY OF LIFE IMPROVED EQUALLY IN BOTH GROUPS

**CLINICAL CASE HISTORIES**

**Homeopathic treatment of Japanese patients with intractable atopic dermatitis**

R. Hosoya and R. Itamura

The objective of the study was to evaluate the efficacy of homeopathic treatment of intractable atopic dermatitis (AAD). Treatment of AAD patients was based on individualized homeopathic treatment in addition to conventional therapeutic therapy for 6 months to 2 years and 3 months. Although all of the patients had previously been treated with conventional medicine and various psychological approaches, they had persistent condition of disease. The effects of the homeopathic treatment were observed in 17 Japanese patients suffering from intractable atopic dermatitis. The patients' subjective assessments were used in a self-assessment method. The results showed that the homeopathic treatment was effective in all patients, in addition to 15 of 17 patients, who showed improvement of AAD. In 9 patients, the improvement was observed by 50% of the patients and in 6 patients by 80% of the patients. The results of the study showed that homeopathic treatment was effective in intractable AAD patients. However, the results of the study were reported by 15 out of 17. Two intractable case histories are included. Homeopathy 2003; 92:108-114.

Keywords: intractable atopic dermatitis, individualized homeopathic treatment, efficacy of homeopathic treatment, patient's self-assessment.

**SEVERITY (RAJKA & LANGELAND CRITERIA)**

- 13 SEVERE ECZEMA PATIENTS
- 4 MODERATE ECZEMA PATIENTS

**INTERVENTION**

- INDIVIDUALIZED HOMEOPATHIC TX IN ADDITION TO CONVENTIONAL TX

**OUTCOME MEASUREMENT**

- 9 POINT OUTCOME SCALE
- ASKED 7 PATIENT QUESTIONS
- PRE-TX AND Q 3 MONTHS

**DURATION TX & FOLLOW-UP**

- 6 – 31 MONTHS

**RESULTS**

- 1 - COMPLETE CLEARING
- 7 - PARTIAL (80% BETTER)
- 9 - PARTIAL (50% BETTER)

HOMEOPATHIC TREATMENT OF JAPANESE PATIENTS WITH INTRACTABLE ATOPIC DERMATITIS


Dept. of Dermatology, Obitsu Sankei Hospital.

CLASSICAL HOMEOPATHIC MEDICINE CAN BE HELPFUL AS A "STEROID - SPARING" AGENT & AS AN "ANTIBIOTIC - SPARING AGENT"

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HOMEOPATHIC TX – ATOPIC ECZEMA

• OBSERVATIONAL STUDY
• N = 3981 CONSECUTIVE PATIENTS
• N = 225 CHILDREN WITH ATOPIC ECZEMA
• ALLOWED TO USE CONVENTIONAL TX
• FOLLOW-UP: 24 MONTHS

Witt CM, et.al. Homeopathic Tx of Children with Atopic Eczema. A Prospective Observational Study with Two Years Follow-up. ADV. 2009: 89(2); 182-183.

HOMEOPATHIC TX – ATOPIC ECZEMA

RESULTS
• SEVERITY OF ECZEMA IMPROVED
• CHANGE IN SEVERITY ASSESSMENT WERE OF LARGE EFFECT SIZE: MONTHS 0-24 (COHEN'S d = 1.76)
• REDUCTIONS IN USE OF DERMATOLOGY DRUGS WERE OBSERVED

Witt CM, et.al. Homeopathic Tx of Children with Atopic Eczema. A Prospective Observational Study with Two Years Follow-up. ADV. 2009: 89(2); 182-183.

Effect size, often measured as Cohen's d, is defined as the difference between two means divided by a standard deviation for the data. An effect size of 0.8 is considered large. http://www.leeds.ac.uk/educol/documents/00002182.htm

CASE SERIES (N = 6)
• IRRITANT CONTACT DERMATITIS (3)
• ATOPIC ECZEMA (3)
• ICD APPEARS TO RESPOND FASTER & MORE READILY THAN ATOPIC ECZEMA
• 4 / 6 PTS: NON-DERM ISSUES IMPROVED

Witt CM, et.al. Homeopathic Tx of Children with Atopic Eczema. A Prospective Observational Study with Two Years Follow-up. ADV. 2009: 89(2); 182-183.
**TREATMENT OF PRURITUS IN HEMODIALYSIS PATIENTS**

- RANDOMIZED, DOUBLE-BLIND
- PLACEBO-CONTROLLED TRIAL
- PROSPECTIVE, MULTI-CENTER
- (N = 28)
- EACH PATIENT RECEIVED “INDIVIDUALIZED” TX WITH 1 OR MORE HOMEOPATHIC MEDICINES
- FOLLOW-UP: UP TO 60 DAYS

**DOLICHOS PRURIENS (6C)**

**SOURCE:** PLANT (COW HAGE, COW-ITCH)

**KEYNOTES:**
- GENERALIZED PRURITUS WITHOUT ERUPTION
- JAUNDICE
- CONSTIPATION
- ABDOMINAL BLOATING
- PAIN IN THROAT, WORSE WITH SWALLOWING (“FEELS LIKE SPLINTER”)
- AT NIGHT, SCRATCHING, WARMTH, & RIGHT SIDE

Borenski W. Borenski OE. *Homeopathic Materia Medica*. 1927

Clarke JH. *A Dictionary of Practical Materia Medica*. 1921

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**“THERAPEUTIC & PATHOGENETIC ANIMAL MODELS FOR DOLICHOS PRURIENS”**

**RESULTS**

- **DEMONSTRATED THERAPEUTIC EFFECTS OF HOMEOPATHIC DOLICHOS PRURIENS IN RATS WITH HEAT-INDUCED PRURITUS:**
  - INHIBITION OF ITCHING
  - INHIBITION OF SKIN LESIONS
  - INHIBITION OF FUR THINNING
  - (Kruskal-Wallis/Dunn, P=0.001)
  - NO ADVERSE EFFECTS

*ORIGINAL ARTICLE*

Homeopathic treatment of patients with psoriasis – a prospective observational study with 2 years follow-up

CM Witt, R Ladam/SM Witt/

Institute for SocialResearch, Cosmetology and Health Economics, Korea University Medical Center Seoo, Republic

Correspondence: Githi. E-mail: RelatedItems@.

**Abstract**

Objective: Prospective multicenter observational study.

Methods: Between March 2004 and December 2006, 3981 consecutive homeopathy patients were enrolled. The diagnostic and exclusion criteria of homeopathic treatment were: a disease that is not treatable by conventional medicine. The patients were randomized into 3 groups: 1) homeopathic treatment with ascending potencies of DOLICHOS PRURIENS 6C, then 9C, 12C, 30C (10 days each); 2) placebo (ETOH 30% in water); 3) Standard temperature & no treatment.

Results: The severity of psoriasis improved significantly in the homeopathic group compared to the placebo group (Kruskal-Wallis/Dunn test, P=0.001). The quality of life improved significantly in the homeopathic group compared to the placebo group (Kruskal-Wallis/Dunn test, P=0.001). The use of conventional treatment and health services was significantly reduced in the homeopathic group compared to the placebo group (Kruskal-Wallis/Dunn test, P=0.001).

**REFERENCES**


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**HOMEOPATHIC TX - PSORIASIS**

- **PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY**
- **n = 3981 CONSECUTIVE HOMEOPATHY PTS**
- **n = 82 ADULTS PSORIASIS PTS**
- **FOLLOW – UP: 24 MONTHS**
- **STANDARDIZED QUESTIONNAIRES**
- **ALLOWED TO USE CONVENTIONAL TX**

**IN VIVO STUDY OF ANTI-INFLAMMATORY EFFECT OF HOMEOPATHIC RHUS TOX**

- **IN VIVO STUDY IN RATS**
- **CARRAGEENAN-INDUCED PAW EDEMA**
- **HOMEOPATHIC RHUS TOX TREATED RATS SHOWED STATISTICALLY SIGNIFICANT INHIBITION OF PAW EDEMA (P<0.05)**
- **6C POTENCY SHOWED STRONGEST EFFECT**
- **EFFECT SIMILAR TO INDOMETHACIN (THE POSITIVE CONTROL)**


---

**HOMEOPATHIC TX & HYPERHIDROSIS**

**RESEARCH QUESTION:**

WHAT % OF HYPERHIDROSIS PATIENTS GET *MEANINGFUL IMPROVEMENT IN SWEATING?*

"("Noticeable & clinically important improvement in sweating by the patient & by the physician")

**PROSPECTIVE CASE SERIES (N=9)**

(JULY, 2012 – AUGUST, 2013)


---

**HYPERHIDROSIS CASE SERIES (n=9)**

<table>
<thead>
<tr>
<th>AGE</th>
<th>S</th>
<th>FHx</th>
<th>LOCATION</th>
<th>DUR (Y)</th>
<th>REMEDY</th>
<th>IMPROVE</th>
</tr>
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<tbody>
<tr>
<td>1. 20 M NO A, P, S 14 SULFUR YES</td>
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<tr>
<td>2. 19 M YES A, P, S 9 IGNATIA YES</td>
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<td>3. 20 M YES P, S 11 SULFUR YES</td>
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<tr>
<td>4. 71 F NO H, A, T, G MANY YRS SULFUR YES</td>
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<tr>
<td>5. 17 M YES A, P 4 SULFUR YES</td>
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<tr>
<td>6. 19 M NO P, S 9 SULF, SIL NO</td>
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<tr>
<td>7. 30 F YES P, S 23 SIL, SULF NO</td>
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<tr>
<td>8. 14 F NO A 3 SEPIA NO</td>
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<tr>
<td>9. 17 F NO A 1 NaCl YES</td>
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**HYPERHIDROSIS & HOMEOPATHIC TX**

- **6 OF 9 (67%) RESPONDED**
  - ALL 6 NOTICED IMPROVEMENT IN OTHER MEDICAL ISSUES:
    - ANXIETY, OBSESSIVE THOUGHTS, PREMENSTRUAL CRAMPS, FATIGUE, ECZEMA, & DIETARY INTOLERANCE
- **3 OF 9 (33%) NONRESPONDERS**
  - ALL THREE HAD IMPROVEMENT OF OTHER MEDICAL ISSUES:
    - BROMHIDROSIS, CONSTIPATION, & MENSTRUAL CRAMPS

---

**TWO HELPFUL HOMEOPATHIC CLINICAL PEARLS FOR DERMATOLOGISTS**

1. **BACH FLOWER ESSENCES RESCUE REMEDY®**

2. **HOMEOPATHIC RHUS TOXICODERON 30C PELLETS**


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TIP #1 – Rescue Remedy®

• OVER-THE-COUNTER
• “HOMEOPATHIC-LIKE”
• NATURAL PRODUCT
• FOR STRESS RELIEF
• CONTAINS ESSENCES OF FIVE FLOWERS:
  - Star of Bethlehem (Orithogalum umbellatum)
  - Rock Rose (Helianthemum)
  - Cherry Plum (Prunus cerasifera)
  - Impatiens (Impatiens glandulifera)
  - Clematis (Clematis vitalba)

DOSE:
4 DROPS p.o.
QID & pm stress
(less than $15.00)

DILUTED TO 1x10⁻⁵

Rescue Remedy® & Anxiety Study

• RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL
• RESCUE REMEDY VS. PLACEBO
• NURSING STUDENTS (n=111)
  - 18 – 49 YEARS OLD
• TREATMENT GROUP (N=53)
• PLACEBO GROUP (N=58)
• SPIELBERGER STATE-TRAIT ANXIETY INVENTORY (STAI)
• HIGH-STATE ANXIETY SUBGROUP:
  - SIGNIFICANT DIFFERENCE BETWEEN PRETEST & POSTTEST SCORES (p<.03)

Conclusion: Rescue Remedy may be effective in reducing high levels of situational anxiety.


Skin Diseases Which Flare with Stress:

• Acne Vulgaris
• Acne Rosacea
• Perioral Dermatitis
• Atopic Eczema
• Nummular Dermatitis
• Psoriasis
• Herpes Simplex

May consider adjunct treatment of these dermatology diseases with RESCUE REMEDY®

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TIP #2 – PREVENTION OF POISON IVY CONTACT DERMATITIS WITH OTC HOMEOPATHIC Rhus Tox 30c PELLETS

PROTOCOL

HOMEOPATHIC RHUS TOX 30C
ONE PELLET P.O. EACH MONTH
(MARCH – NOVEMBER)
(MUST BEGIN ONE MONTH PRIOR TO EXPOSURE)

ACKNOWLEDGEMENT: HELEN TORDJ, MD – 2004 AAD Meeting

Available: Over-The-Counter - $10.00 (= 8 year supply!)

Signore RJ. Accepted for publication. January, 2017

Gross ER. Industrial Medicine & Surgery. 1958; 27 (March) 142-144.
HOMEOPATHIC “CONSTITUTIONAL TYPE”:
encompasses an individual patient’s mental / emotional, & physical characteristics, as well as his / her likes, dislikes, and unique ways of reacting to stresses of daily living.

1. HOMEOPATHIC SODIUM CHLORIDE
   - RESERVED, HIDE THEIR EMOTIONS
   - FASTIDIOUS, METICULOUS
   - FEEL RESPONSIBLE FOR EVERYONE ELSE
   - SADNESS
   - GUILT
   - WORSE WITH CONSOLATION
   - HIGHLY ETHICAL, HONEST
   - DESIRE REVENGE (IF BETRAYED)
   - OILY SKIN (esp. FACE)
   - ECZEMA
   - HERPES SIMPLEX
   - INTOLEANCE TO SUNLIGHT!
     (PHOTOPHOBIA, HEADACHES)
   - CRAVE SALTY FOODS

* THE FOUR MOST COMMON CLASSICAL HOMEOPATHIC CLINICAL TYPES

- SODIUM CHLORIDE
- PULSATILLA
- SULPHUR
- CALCIUM CARBONATE

(Which type are you?)

* There are over 3000 homeopathic remedies!

2. HOMEOPATHIC PULSATILLA
   - gentle, mild personality type
   - initially shy (later becomes more talkative)
   - warm-blooded (worse in warm room)
   - better in open air (outdoors, open window)
   - better with consolation!
   - desire creamy food, butter
   - worse with heavy foods (nausea)
   - Tend to weep / become tearful (when painful surgical procedures are discussed)
3. HOMEOPATHIC SULPHUR

- WARM-BLOODED
- WORSE IN WARM ROOM
- HYPERHIDROSIS (SWEAT IS WARM)
- DESIRE SWEETS, CHEESE, SPICY FOODS
- DISLIKE EGGS
- EXTROVERTED
- GET ANGRY (BUT, NOT FOR LONG)
- SLOPPY, UNTIDY
- LOOSE STOOLS (DIARRHEA IN A.M.)
- ORIFICES ARE VERY RED (LIPS, ANUS)

4. HOMEOPATHIC CALCIUM CARBONATE

- 40% BABIES & INFANTS NEED CALC CARB
- CHUBBY
- CRAVE EGGS, MILK, CHEESE
- CONSTIPATED
- SWEATY HEAD & NECK (DURING NAPS & NIGHT)
- COLD SWEATY FEET
- "SOUR SMELL"
- STUBBORN
- CHILLY
- WORSE WITH COLD
- BETTER WITH WARMTH

HOMEOPATHIC MEDICINE

- WHAT IS IT?
  A NON-TOXIC, LOW COST NATURAL SYSTEM OF HEALING USED BY 500 MILLION PEOPLE WORLD-WIDE
- IS THERE ANY RESEARCH?
  YES, THERE ARE SOME DATA
- WHAT CAN YOU DO WITH IT?
  IT CAN BE VERY HELPFUL IN TX OF COMMON DERMATOSES & MAY ALLOW REDUCED DEPENDENCE ON ANTIBIOTICS & TOPICAL STEROIDS

CONCLUSIONS

CLASSICAL HOMEOPATHIC MEDICINE CAN BE HELPFUL TO TODAY'S CLINICAL DERMATOLOGIST:
- IF ENOUGH TIME & EFFORT IS PUT INTO STUDY (To get reproducible clinical results, you must do a 3 to 5 year course in classical homeopathic medicine):
  http://www.bihint.com/courses.php
  http://www.homeopathy.ca/livecourses.shtml
- IF COMPLETE CASE HISTORY & REPERTORIZATION ARE PERFORMED

CONCLUSIONS

- EVEN WITHOUT EXTENSIVE STUDY, HOMEOPATHIC MEDICINE COULD BE QUITE HELPFUL TO TODAY'S DERMATOLOGIST...

CONCLUSIONS -- PEARLS

- USE 30C POTENCIES (SAFEST)
- HOMEOPATHIC Rhus Toxicodendron 30C - TAKE 1 PELLET (sublingually) EACH MONTH during poison ivy season TO HELP PREVENT OR DECREASE SEVERITY OF ACUTE ALLERGIC CONTACT DERMATITIS FROM POISON IVY (begin taking one month prior to exposure to poison ivy!)

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CONCLUSIONS -- PEARLS

- KNOW 3 HELPFUL HOMEOPATHIC REMEDIES FOR TX OF PAIN IN ACUTE HERPES ZOSTER PATIENTS:
  1) RHUS TOXICODENDRON 30C
     (If pain is worse with initial movement, but better with continued movement and better with warmth!)
  2) MEZEREUM 30C
     (If pain is worse at night!)
  3) RANUNCULUS BULBOSUS 30C
     (Esp. in Left thoracic location of zoster!)
     (Works esp. well in alcoholic patients or patients who get adverse effects from drinking alcohol)

Homeopathic TX of: POST-HERPETIC NEURALGIA:
  1) Kalmia latifolia (Mountain laurel)
     (If RIGHT-SIDED orbital / eye pain)
     - Pain shoots downward, with numbness
  2) Magnesia phosphorica
     (If RIGHT-SIDED face / eye pain)
     - Pain BETTER with Heat!
  3) Spigelia (Pinkroot)
     (If LEFT-SIDED face / eye pain)
     - Worse with touch, motion, noise
  4) Prunus spinosa (Black-thorn)
     (If FACE OR EYE pain)
     (Esp. when “bursting pain” of eye)

CONCLUSIONS -- PEARLS

- KNOW 3 MOST COMMONLY HELPFUL HOMEOPATHIC REMEDIES FOR TX OF RECURRENT HERPES SIMPLEX OF LIPS (“HERPES LABIALIS”):
  1) SEPIA
  2) RHUS TOXICODENDRON
  3) SODIUM CHLORIDE

CONCLUSIONS -- PEARLS

- KNOW 3 MOST COMMONLY HELPFUL HOMEOPATHIC REMEDIES FOR TX OF ACUTE URTICARIA:
  1) URTICA URENS
  2) APIS MELLIFICA
  3) SODIUM CHLORIDE

HOW CAN HOMEOPATHIC MEDICINE BE HELPFUL TO TODAY’S DERMATOLOGIST? (LECTURE HANDOUT)

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“PARALLELS AND DIVERGENCE”: VETERINARY DERMATOLOGY AND THE HUMAN COUNTERPART

Jackie Campbell, DVM, Diplomate ACVD

Disclosure

- I have no actual or potential conflict of interest in relation to this program/presentation.

Dermatology for Animals?

- Common diseases we treat and parallels
  - Atopic Dermatitis and Cutaneous Adverse Food Reactions
  - Immune mediated diseases: Pemphigus Complex, Uveodermatologic Syndrome, Vasculitis
  - Neoplasia: Squamous cell carcinoma, Cutaneous T cell Lymphoma
  - Miscellaneous “fun” stuff

Zoonotic Aspect

- What can our patients give your patients?
  - Methicillin resistant staphylococcus
  - Dermatophyte
  - Sarcoptes
  - Allergen dander contribution

Canine Atopic Dermatitis

- The most common dermatologic disease we treat in all species
- Canine atopic dermatitis increasingly common disease
  - Pruritus
  - Secondary pyoderma
  - Secondary Malassezia
  - Otitis
  - Pododermatitis

Clinical Signs
Canine Atopic Dermatitis

- Comparable counterpart to human AD
- Pruritus, erythema
  - Conjunctivitis, rhinitis not typical
- Pruritus frustrating for pet owners
- Secondary skin infections
  - Secondary pyoderma
    - Resistant Staph Pseudintermedius increasingly common
  - Malassezia dermatitis
- Typically progressively worsens with age

Hypothesis of Canine AD

- Genetic mutations associated with impaired epidermal barrier
  - Filaggrin, ceramides
  - Alterations in microbiome
  - Breed predisposition
- Development of allergen specific IgE
- Th2 mediated response in acute phase
  - IL4, IL6, IL13, IL31
- Th1 shift in more chronic stages
Atopic Dermatitis - Pathophysiology

- Gene mutations
  - Downregulation cornified envelope
    - Filaggrin mutations
      - Decreased filaggrin expression
      - Decreased ceramides
      - Loss of function mutation
      - Increased transepidermal water loss

- Barrier Function Alterations
  - Disorganized lipid lamellae
  - Widened intercellular spaces
  - Release of lamellar bodies
  - Altered microbiome

- Histamine
  - Levels similar or lower in dogs with AD compared to normal counterpart
    - Antihistamines have minimal therapeutic benefit in canine patients
- Leukotrienes
  - No differences noted in AD dogs versus normal dogs

Immunologic Abberations

- Total IgE's not significantly different between normal and atopic dogs as seen in human medicine
- Acute lesions
  - CD4+, TH2 lymphocytes, eosinophils, and release of IL4 and IL13
  - Increased survival and maturation of eosinophils
- Chronic lesions
  - Macrophages, TH1 cytokines IL2, IL12, IFN gamma

Canine AD – Secondary Infections

- Contribute to pruritus
- Staphylococcus pseudintermedius
  - High prevalence in AD canine patients
    - Altered barrier function and cornified envelope
    - Altered microbiome
    - Lower microbial diversity in AD
- Malassezia pachydermatis
  - Greater IgE response in AD canines versus normal

Human AD

- Extensive human literature on staph and role of superantigens in the pathophysiology
- Immunologic mechanisms by which staph precipitate AD
  - Epithelial presentation to TH2 cells
  - TH2 response and IgE production
  - Treg subversion
  - Expansion and migration of skin homing T cells
  - Modulation of chemokines
  - IgE super-antigen production
### Secondary Staphylococcal pyoderma
- Normal dogs do not develop skin infections
- Primary disease must be sought
- Hypersensitivity disorders most common cause
- Systemic disease
  - Cushing’s
  - Hypothyroid
- Which came first lesions or pruritus?
- Itch that rashes or rash that itches?

### Canine Staphylococcus
- Staph pseudintermedius predominant canine strain
- S. aureus strains diagnosed in companion animals typically the same strains that cause disease in humans.
- “Humanosis” of MRSA
- Pet owners and veterinary personnel may carry S. pseudintermedius (considerations in epidemiology)
- Other important Staphylococci
  - S. schleiferi (coag + species and coag – species)
  - S. lugdunensis

### MRSA and MRSP
- Owners share their MRSA
- Dogs share their MRSP
- Disease causing ability depends on immune status of whom they are sharing with
- Decontamination procedures of households
- Pet bedding a source
- Antibiotic resistance can cut both ways

### Diagnosis of Canine AD
- History, clinical signs, and exclusion of other pruritic diseases
  - Food allergy
  - Parasite hypersensitivity
  - Dermatophytosis
- Criteria
  - Hanifin and Rajka – adapted Willens Criteria, modified over the years
    - Onset
    - Glucocorticoid responsiveness
    - Pinnae, paws, and cheilitis

### Treatment Options for K9 AD
- Supportive
  - Avoidance, bathing, antihistamines, fish oil
  - Glucocorticoid therapy
  - Cyclosporine therapy
  - Calcinurin inhibitor thus decrease TH2 cytokines
- Allergen immunotherapy
  - Induction of IgG
  - Induction of T regulatory cells, IL10
- Oclacitinib (Apoquel®)
  - Janus Kinase Inhibitor
  - Canine Atopic Dermatitis Immunotherapeutic
  - Anti-IL31 monoclonal antibody therapy

### Allergen Immunotherapy for K9 AD
- Intradermal allergen testing gold standard
- Percutaneous testing in pilot study (felines)
- 75% of patients symptoms improve by 50% or more
- Allergen immunotherapy initiated
  - Subcutaneous q1-2 weeks
  - Non-aqueous sublingual daily
- Multiple allergens included in extracts
  - Potency of allergen 2,000PNU to 20,000PNU
  - Allergen monotherapy not generally utilized
Allergen Immunotherapy for K9 AD
- Pollens
  - Trees, weeds, grasses
- Dusts and mites
  - Dust mites - D. farinae, D. pteronyssus
  - Storage mites - Tyrophagus
- House dust
- Danders
  - Human, cat, cattle, sheep, mouse epithelia
- Molds
- Insect hypersensitivity

Intradermal allergy testing

Oclacitinib (Apoquel®)
- Janus Kinase Inhibitor
  - Developed by Zoetis for Canine AD
  - Janus Kinases activate intracellular signal transducers and activators of transcription (STAT)
    - Activates biologic response and cytokine production

Ligand - Receptor - JAK - Function

Apoquel® Oclacitinib
- Primarily Janus Kinase 1 (JAK1) inhibitor
  - Decrease IL2, IL6, IL13
  - Decrease in "Itch cytokine" IL31
- Mild JAK3 activity
- Minimal JAK2 activity
- Hematopoiesis
- Effective in 85% of patients with AD
- Excellent safety profile at prescribed dosage protocol and at this stage of usage

Human Counterpart?
Canine Atopic Dermatitis
Immunotherapeutic

- Based on the model of IL31 = Itch in atopic dogs
- IL31 levels significantly higher in AD dogs compared to normal counterpart
- Caninized monoclonal antibody to bind IL31
- Injection available on conditional licensing
- Provided control of pruritus for up to 4 weeks
- Safety profile unparalleled

Food Allergy

- Type I Immunologic mechanism best studied in humans
- Type I, III, IV implicated in veterinary patients
- Incidence reported 1% to 10% of all allergic skin diseases occurring in veterinary patients
- GI disease
- Dermatologic disease
  - 20% can have concurrent GI symptoms

Food Allergy

- Can mimic atopic dermatitis
- Clinical variability
  - Any age
  - Non-seasonal
- Pruritus most common complaint
  - Some pets only recurrent otitis
  - Ears, rears
  - Poor response to glucocorticoids

Food Allergens

- Allergen immunogenicity depends on stimulation of IgE production and histamine release of mast cells after bridging of the allergen between two IgE molecules on the surface of the mast cell membrane.
- In humans food allergens almost exclusively 10-70kDa molecular weight
  - No such data available in canine patients
  - Hydrolyzed diets variable size hydrolysate
    - 1kDa to 1000kDa

Food Allergens

- Most common allergens
  - Beef, chicken, dairy, soy, wheat
- Diagnosis based on response to strict elimination dietary trial
  - Challenge diet to confirm
- Blood allergy testing not a sensitive tool for diagnosis
  - High false positive and negative
  - IgE measurement – Type I reaction only

Sarcoptes

- Geographic variations in incidence
  - High prevalence Colorado/Utah
  - Variability in other areas of the country
- Initially mimics atopic dermatitis
  - Initial response to steroids
  - Chronic disease becomes refractory to steroid therapy and fails to respond to cyclosporine
  - Intense pruritus
    - Ear margins, elbows, hocks, ventrum
Sarcoptes

- Transmission via fox, coyotes, dogs
  - Does not require direct contact
  - Survives off host for 4 to 21 days at ideal temps (50-59°F)
  - Humans and other animals can be transient carriers
- Mites can be difficult to recover in skin scrapings

Sarcoptes Household

- All in contact animals treated
- Humans/Owners often affected in chronic cases
  - Factors that increase human transient carrier state
    - Dog sleeps with owners
    - Duration of infestation of the dog
    - Immune status of the human owner
    - Immune status of the pet
  - Papular pruritic rash torso, inner aspect of arms
    - Typically do not require treatment
    - Immunocompromised individual may require treatment

Other Parasites

- Cheyletiella
- Demodex
- Lice
- Fleas
- Ticks
- Bird mites

Dermatophytosis

- Highly variable clinical presentation
  - Pruritus and mild seborrhea sicca
  - Marked alopecia and pruritus
  - Acantholysis
  - Nodular to kerion
- Diagnosis via
  - DTM remains most sensitive tool
    - Poor confidence in referral practitioners' interpretation of DTM
    - Failure to treat appropriately common
Dermatophytosis

Environmental Concerns

- Arthropores from infected pets can remain in the environment for 12-24 months
- Environmental cleaning
- Isolation of pet

Immune Mediated Diseases

- Less common than hypersensitivity disorders
- Focus for today
  - Pemphigus Folateceus
  - Dermatomyositis
- Fun topics for another day
  - Vasculitis
  - Primary versus secondary
  - “Lupoid” diseases
    - Discoid lupus, Lupoid onychodystrophy, mucocutaneous, systemic
  - Sterile panniculitis
  - Erythema multiforme, Sweet’s syndrome, TEN
**Pemphigus Complex**

- Pemphigus Foliaceus
  - Most common disease we treat after hypersensitivity disorders
- Pemphigus vulgaris
  - Much less common in animals than in man

**Pemphigus Targets**

- Pemphigus foliaceus
  - Similar clinically to human counterpart
  - Human autoantibody target desmoglein-1
  - Veterinary autoantibody target desmocollin-1
- Pemphigus vulgaris
  - Autoantibody to desmoglein-3 paralleled
  - Clinical presentation similar

**Dermatomyositis**

- Cause humans and canines is unknown
  - Familial history variable in humans
  - Common in collies and Shetland sheepdogs
  - Breeding studies in collies support autosomal dominant with variable expressivity
- Clinical similarities
  - Face/periocular, areas of mechanical trauma
  - Myositis typically months after skin lesions and correlates with skin lesion severity

**Non-inflammatory alopecia**

- Endocrine disease
  - Cushing
    - Atypical Cushing
  - Hypothyroid
  - Alopecia X
  - Seasonal Flank Alopecias
- Owner topical hormone replacement
  - Can affect pet even with barrier precautions
### Owner utilizing topical estrogen prescribed as birth control

![Image of a dog with estrogen application](image1.png)

### Infectious Disease

- **Atypical bacterial infections**
  - Actinomycetes, Nocardia
  - Post-grooming Pseudomonas furunculosis
- **Atypical systemic fungal infections**
  - Sporotrichosis
  - Coccidiomycosis, Cryptococcosis, Blastomycosis, Histoplasmosis
- **Viral disease**
  - Herpes, papilloma

### Post Grooming Furunculosis

- **Veterinary**
  - Pseudomonas contaminated shampoo
  - Malaise, febrile, painful
  - Systemic fluoroquinolone treatment
- **Human Parallel**
  - "Hot tub folliculitis"
  - Lesions develop days after exposure
  - Malaise, low grade fever
  - +/- systemic treatment

### Pseudomonas Folliculitis

- **Veterinary**
- **Human**
  ![Image of Pseudomonas folliculitis](image2.png)

### Sporotrichosis

- **Veterinary**
- **Human**

### Otic Disease

- **Veterinary**
- **Human**
  ![Image of otitis externa](image3.png)

- **Chronic otitis externa**
- **Otitis media**
- **Otic foreign bodies**
- **Otic masses**
Neoplasia

- Melanoma
  - Human tyrosinase DNA vaccine utilized for treatment of canine melanoma
  - Each dose contains plasmid DNA that expresses the gene coding for human tyrosinase
  - Upon injection, the DNA is taken up by muscle cells which then express the human tyrosinase protein
  - Stimulates an immune response effective against canine melanoma cells which express tyrosinase

- Epitheliotrophic lymphoma

- Solar induced
  - Actinic keratoses
  - Hemangioma/hemangiosarcoma

Actinic keratoses

Squamous cell carcinoma

Hemangiomas

Epitheliotrophic lymphoma

Miscellaneous

- Thermal burns
- Dorsal thermal necrosis
- Topical steroid overuse
- Delusional parasitosis of pet owner
Thermal Burn

Pathophysiology Thermal Burns
- Not well understood
- Multifactorial
  - Hydration and health status
  - Neurosensory input
  - Duration of exposure and direct sunlight
  - Color of the dog
- Human parallel
  - Women post breast reconstruction

Topical steroid overuse
- Atrophy
- Telangectasia
- Milia
- Comedones
- Spay scar atrophy and slight gapping

Delusional Parasitosis
- Clients bring jars, bags, samples of hair, clippings
  - "Matchbox" sign
  - Report seeing bugs, fibers
- Perform complete parasite treatment trial for the household
- Treat all in contact animals
- Exclude true possibility of parasite

References
Development of a model of IL-31 induced pruritus in beagle dogs

- W. HUMPHREY, T. FLECK, M. ALEO, E. COSCARELLI, B. GALVAN, M. MULINS, B. HUMMEL, J. MESSAMORE, S. MAHABIR, A. GONZALES and R. MCCALL Veterinary Dermatology, 23 (Suppl. 1), 35
- Skin biopsies from pruritic and non-pruritic lesions in cases of human and mouse atopic dermatitis (AD)
- Up-regulation in interleukin-31 mRNA levels implicating a contributory role of this cytokine in the development of pruritus.
- Using recombinant canine IL-31 (cIL-31 or IL-31), we have developed an anti-pruritic screening model in dogs using exogenous IL-31 to induce episodes of pruritus in the presence/absence of test article treatments.
- IL-31 produced significant pruritus compared to mock protein or saline injections.
- The model was validated by demonstrating that administered prednisolone significantly decreased IL-31 induced pruritus. Additionally, the Janus kinase inhibitor, oclacitinib, reduced IL-31 induced pruritus in the dog. This data indicate that IL-31 produces pruritus in the dog and this can be used as a basis for a model to identify antipruritic compounds.
NEVUS
(when melanocytes nest together nicely)

MELANOMA
(when good melanocytes go bad)
So, how do we suspect melanoma, clinically and who do we diagnose melanoma histologically?

Interesting tidbits about acquired nevi…

- Eruptive nevi can develop on injured skin after blistering illness (burns, TEN)
- Strong evidence suggests acquired nevi are related to sun-exposure in childhood
  - may explain nevi > in whites than others
  - may explain distribution of nevi upon skin
  - may corroborate observation that use of sunscreen lessens development of nevi

Colorado Study

- N=743 white children (5-6 y/o), 3 years f/u
- Nevus density = boys (36/m²) > girls (31/m²)
- Greatest density upon face, neck, forearms
- Higher # in chronically exposed vs. intermittently exposed skin (P < 0.0001)
- In 2 years, most (69%) had received at least one sunburn, and number of nevi was associated with the number of burns
- Similar findings in Australian study

Clinical Examination

(this is where we suspect the diagnosis… at least enough to perform a biopsy)

- A – asymmetry
- B – border irregularity
- C – color variegation
- D – diameter > 6 mm
- E – evolution

Where do nevi come from?

No one really knows, for sure.
Clinical Features of Atypical/Dysplastic Nevi

<table>
<thead>
<tr>
<th>Common Nevus</th>
<th>Dysplastic Nevus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Distinct</td>
<td>Indistinct (fuzzy)</td>
</tr>
<tr>
<td>Uniform brown</td>
<td>Variegated (blacks, greys, whites)</td>
</tr>
<tr>
<td>&gt;6 mm</td>
<td>&lt;6 mm</td>
</tr>
<tr>
<td>Usually asymptomatic</td>
<td>Sometimes with symptoms/changing behavior</td>
</tr>
</tbody>
</table>

The “Ugly Duckling”
One mole that looks nothing like the other “signature” nevi!

Grim Reaper and Atypical Nevi?

So why do we want to find atypical nevi?
There are two good reasons depending upon what you believe.

Marker of an “At Risk” Person

- Strong evidence suggests:

<table>
<thead>
<tr>
<th>Number of Dysplastic Nevi</th>
<th>Risk Above General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 4</td>
<td>2-3x</td>
</tr>
<tr>
<td>&gt;10</td>
<td>12x</td>
</tr>
<tr>
<td>&gt;50 (w/o family h/o)</td>
<td>184x</td>
</tr>
<tr>
<td>&gt;50 (w family h/o)</td>
<td>500x</td>
</tr>
</tbody>
</table>

One of the strongest risk factors for melanoma is the presence of multiple

Table I. Risk factors for Malignant Melanoma

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
</tr>
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Grim Reaper and Atypical Nevi?

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</table>
Regional Approaches to Atypical Nevi

- Grading
  - usually “mild,” “moderate,” “severe”
  - based on cytology or architecture or both
- No Grading (“allegedly”)
  - nevus, Clark’s nevus, Clark’s nevus – excise

“Everybody’s a critic…”

Dysplastic/atypical nevi may also be precursor lesion for melanoma…

- 20-80% of melanoma arises in a nevus
- ? premalignant condition (controversial)
- Alternative explanation:
  - we are simply bad at distinguishing atypical nevi from melanoma
Atypical Nevus - Architectural

Bizarre nest size and arrangement

Fibrosis

Atypical Nevus - Cytology

Clear cytologic atypia - large cells - pleomorphic nuclei

Lymphocytes

Atypical Nevus - Cytology

Hyperchromasia

Thick nuclear membrane

Pleomorphism

Large nucleolus

Atypical Nevus - Cytology

Poor Vertical Maturation
How good is grading?

- Duncan et al. (1993)
  - 10 cases of nevus, dysplastic nevus (mild, mod, sev) and melanoma
  - concordance 68-80% for nevus vs dysplastic nevus vs melanoma
  - only 35-58% concordance for grading of dysplasia

- Piepker, et al. (1994)
  - 146 atypical nevi graded by 6 expert dermatopathologists
  - re-interpreted 6 mos later by same dermatopathologist
  - correlation coefficients 0.5-0.70 ("moderate" to "substantial")

- Farmer, et al. (1996)
  - 37 "classic" pigmented lesions among 8 "expert" dermatopathologists
  - only 13 cases (35%) with complete agreement (6 benign & 5 MM)

The honest truth of the matter…

> 6000 Mutations in Melanoma

Makes for Messy Model

“True” Developmental State of Pigmented Lesion Analysis
So what can be done to assist us in recognizing melanoma?

Will immunostains help?

Immunostains in Pigmented Lesions - Bottom Line

There is NO single “Melanoma Stain.”

S-100

- In melanocytic neoplasms
  - expressed by 98% of melanomas
  - expressed in 95% of desmoplastic MM
    (often negative for all other markers)

Missed Desmoplastic MM

Melan-A/MART-1

- Melanocytic-associated Antigen (A103)
- Melanoma Antigen Recognized by T cells-1 (M2C107)
- Highly specific, just not as sensitive
  (particularly for desmoplastic MM)
HMB-45

- Benign melanocytic lesions:
  - junctional/superficial component stain
  - normal zonation in the deeper dermis
- Confusing in situations of dusty cells:
  - deeply pigmented nevi
  - deep penetrating nevi
  - clonal nevi

P16


- Studied P16, E-cadherin, cyclin D1 (Spitz and Melanoma)
- Dermal P16 staining was best discriminator:
  - loss of nuclear staining (<25% of cells)
    - 3 fold more likely to be melanoma
  - loss of nuclear and cytoplasmic staining
    - 8 fold more likely to be melanoma

Combination stains...
Other Tests that Might be Employed to Diagnose Melanoma

Comparative Genomic Hybridization (aCGH)

Fluorescent In Situ Hybridization (FISH)

Gene Expression Profiling (GEP)

Comparative Genomic Hybridization

- Assesses entire genome
- Detects only gains or losses in copy number
- >95% of melanoma has gains and losses
- Most benign lesions lack such gains or losses
- Some Spitz nevi may have gain 11p

FISH for Deletions

- 4 probes with highest diagnostic discrimination:
  - chromosome 6p25, 6 centromere, 6q23, and 11q13
- Correctly classified melanoma with:
  - 86.7% sensitivity
  - 95.4% specificity
- Correctly identified melanoma in 6 of 6 cases with ambiguous pathology but later mets

Only 60% sensitivity and only 60% specificity in ambiguous lesions.
• Acknowledged for difficult Spitzoid lesions “old” probe set only about 70% sensitive
• Proposed new probe set - 6p25, 9p21, 11q13, and 8q24
• Particularly interesting is addition of loss of 9p21 (p16)
• Overall improvement in sensitivity reported to be 94%

New commercial assay for melanoma based upon “genetic signature”
Measures mRNA via qRT-PCR

23 Gene Expression Profiling
• qRT-PCR on FFPE that is microdissected
• Developed and validated on N=400+ nevi/MM
  Validation using N=437 (few Spitz and no desmo MM)
  Reported Sensitivity = 94%, Specificity = 90%
  9% of lesions classified as “Indeterminate”

How might this uncertainty be reflected in the management of atypical/dysplastic nevi?

Management of Atypical Nevi
• 1992 NIH Consensus Panel
  – only attempt at consensus (not achieved)
  – recommend removal of atypical nevi
• Recent papers advocated
  – mildly AN need not be excised
  – Moderately AN may not need to be excised

HOWEVER, THERE IS NO CLEAR CONSENSUS REGARDING THE TOPIC
Points to Consider

• No argument that AN mark a person at increased risk for melanoma
• No argument that melanoma arises in association with AN (although 20-80%)
• Tsao et al. reported a 1:10,000 lifetime risk of AN transforming into MM
• Assuming Tsao et al. is correct a “properly powered” study would be very very LARGE

Hocker et al. paper

• Looked back into Mayo Clinic tissue banks before term “AN” came into play
• Found only 10% BN would be reclassified as AN (N=115)
• Principle finding: none of the AN that “involved or approached (<0.2mm) a margin” went on to be melanoma

Problems with Hocker et al.

• Transformation is only “negative” outcome
• Severely underpowered study (Tsao et al.)
• Why just 10% of all “nevi” in files atypical?
• No information on how many had actual vs. “close” surgical margins.
• How does one know that the grading at MC can be replicated anywhere else?

Hocker Criticism

• Drs. Elston, McNiff and Maize wrote an editorial critical of the Hocker et al. paper
• Would the result matter to even one person who died of their “atypical nevus”?
• For example, varicella zoster vaccine has:
  – NNT=175 prevent one case of zoster ($35,000)
  – NNT = 1087 prevent one case PHN ($217,400)
• Probably won’t save you from a deposition!
More critical review of what is said...

- 2936 nevi, of which 871 were atypical
- Precise degree of atypia and margin status unknown
- 85% of re-excisions had no melanocytic process anyway
- Median follow up was just 12 months

Interview with Author

- Author prefers to “saucerize” nevi “…to obtain clear margins…”
- “Isn’t prepared to make blanket recommendations…”
- “[D]on’t think you can make a hard and fast rule… if there are multiple atypical nevi… be a little more cautious and do the excision…”

Revisiting a question…

“Are we simply bad at distinguishing atypical nevi from melanoma?”

Illustrative Example…

Re-examination of Original

Called compound “moderately” atypical nevus by a well-known Colorado dermatopathologist.

No stains or levels were performed.
Do some lesions even have an answer?
Do we know enough to say?
Tale of the “Spitz tumor”…

- 17 year-old girl seen in 2007
- Eruptive lesion on leg
  - only noticed for a “few weeks”
- No personal or FH of melanoma
- Otherwise healthy
No win situation.

- Overcall and a 17 year-old receives:
  - huge disfiguring scar
  - ruined insurance status
  - chronic leg edema
  - no real hope

- Undercall and there are:
  - medicolegal issues
  - is the patient harmed?

My Report

- “Atypical Spitz Tumor”
  - “lesion of uncertain biologic potential…”
  - “…seen cases like this with nodal involvement…”
  - “…even when SLN deposits are present, the disease often behaves in a manner less aggressive than conventional melanoma.”

Her Sentinel Lymph Node

CU pt survival 100% at 35 months.
Similar Experiences are Later Published

2012

Real case…
Patient presented in 2016 with right sided cervical LAD and was told initially was “mononucleosis.” Ultimately, she had melanoma in a cervical lymph node, and tumoral nodules in the right lung.

Pithy Quotes from Major Papers (“state of the art” in 2014-2016)

- “Retrospective review... demonstrated that 13% of melanocytic lesions defied diagnosis.”
- “No diagnostic ‘gold-standard’ for Spitz-like lesions has been established.”
- “Accurate classification… of some melanocytic neoplasms remains a challenge, even for experts.”
- “Perhaps [FISH is] not appropriate for the differential diagnosis of spitzoid tumors in children.”

Demarchis et al. 2014; Masi et al. 2015; Dika et al., 2015
Urticaria/Angioedema from the Allergist’s Perspective

Nathanael Brady, D.O.
Pikes Peak Allergy & Asthma
Colorado Springs, Colorado
Assistant Professor, Adjunct Clinical Faculty
Rocky Vista University, Parker, Colorado

Objectives
• Differentiate acute versus chronic urticaria/angioedema
• Identify common underlying triggers for urticaria/angioedema
• Understand best therapy for treatment of urticaria/angioedema
• Recognize common types of physical urticaria/angioedema

Disclosures
• Speakers Bureau
  • AstraZeneca
  • Merck
  • Novartis
  • PuraCap
  • Shire
  • Teva
• Clinical Study
  • Baxalta
• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation

Background
• Acute versus Chronic
  • Based on duration of disease with daily or almost daily symptoms
    • Acute <6 weeks duration
    • Chronic >6 weeks duration
• Distribution
  • Urticaria with angioedema 65%
  • Angioedema alone 20%
  • Urticaria alone 15%

Acute
• Common, 10-20% of general population experience transient symptoms 1-2 times in lifetime
• Often related to mast cell and basophil activation from multiple triggers
• Both IgE and non-IgE-mediated mechanisms responsible

Triggers
• Medications
• Foods
• Illness
• Inhalants
• Insects

Mechanism
• IgE-mediated process
  • Allergenic proteins cross-link IgE on mast cells/basophils leading to release of histamine/other mediators
Acute

- Diagnosis mostly based on history and physical exam
- Skin testing or limited labs if indicated
- Biopsy findings
  - Dilation of small venules and capillaries in superficial dermis
  - Widening of dermal papillae, flattening of rete pegs, and swelling of collagen fibers

Acute

- Treatment
  - Elimination of causative agent
  - First-line: Antihistamines
    - First-generation rapid onset and effective but sedative and can impair motor skills
    - Second-generation effective with minimal to no side effects
  - Oral corticosteroids use for poor response to A/H and for short duration

Chronic

- Prevalence estimated 0.5-5% of general population, incidence estimated 1.4% yearly
- Cause
  - Idiopathic in majority of cases
  - Rarely allergic trigger
  - Autoimmune – increased association with thyroid disease
    - 30-50% produce IgG antibodies to the Fc epsilon component of the IgE receptor and ≤ 10% produce IgG antibodies to IgE itself
  - Infection – ie hepatitis, mononucleosis, parasitic (comorbid eos)
  - Vasculitides/ connective tissue disease – ie SLE
  - Malignant neoplasm
  - Hormonal therapies - BCP

Chronic

- Evaluation
  - Description
    - Edematous pink or red wheals of variable size and shape with surrounding erythema and generally puritic
    - Painful or burning is not characteristic and suggests vasculitis
    - Individual lesions usually fade in 24-48 hours, new lesion may develop simultaneously at other sites
    - Vasculitis lesions are palpable and usually nonblanching, span several days and often have residual hyperpigmented changes
    - Angioedema typically is nonpruritic, brawny, nonpitting edema, without well defined margins and without erythema

Urticaria versus Vasculitis

Angioedema
Chronic

- Evaluation
  - History
    - Relationship of episodes to the following:
      - Ingestion (medication or food)
      - Time of day
      - Menstrual cycle
      - Physical stimuli
      - Exertion
      - Occupational exposure
      - Stress
        - Physical
        - Emotional/Mental

- Testing
  - Most often not indicated for chronic cases
  - Targeted labs based on clinical suspicion may include:
    - CBC with differential, sedimentation rate and/or C-reactive protein, liver enzyme, and thyroid-stimulating hormone level
    - Recurrent angioedema in absence of urticaria
      - Evaluate for hereditary angioedema, acquired C1 inhibitor deficiency, or ACE-I associated angioedema if clinically indicated

Physical Urticaria

- Subgroup of patients with tendency to have flares from environmental stimuli on inflammatory cells
- Mechanism of mast cell activation uncertain
- Estimated 0.5% of population is affected
- Lifetime prevalence 4-6%
- Comprises 20-30% of all cases of CU
- Variable resolution of disease
  - 13-16% at 1 year, 50% after 5 years
  - Dependent on subtype, age of onset, and severity

- Aquagenic
  - Rare condition, 0.3% of CU
  - Trigger is direct contact with any water source independent of temperature
  - Confirmed with 35°C water applied to skin for 30 minutes

- Cholinergic
  - 11% of young adults, 2-5% of CU
  - "pinpoint" (1-3mm) hives surrounded by larger flares associated with increased core body temperature
  - Common factors: exercise, sweating, emotion, hot baths/showers, saunas
  - Severity ranges from mild pruritus to severe life-threatening reactions

- Cold
  - 2% of CU
  - Pruritis and swelling with cold stimulus exposure
  - Systemic reaction associated with systemic cold exposure (aquatic activities)
    - Confirmed by applying cold stimulus to skin with wheal and flare appearing during skin re-warming
    - Treatment is avoidance, pharmacotherapy in some case (ie: epinephrine for systemic reaction history)

- Delayed-pressure
  - 1-2% of CU
  - Swelling, that can be painful, delayed onset 4-6 hours (occasionally 12-24 hours) after pressure exposure
    - Common factors: working with tools, sitting on a bench, constricting garments
  - Confirmed by 15# weight suspended over shoulder for 15 minutes
  - Often very difficult to treat, conventional antihistamine dosing frequently not efficacious
Physical Urticaria

- **Dermatographia**
  - Most common physical urticaria, 2-5% of general population, 10% of CU
  - Wheal and flare quickly with pressure applied to skin
  - Confirmed by stroking skin with firm object

- **Exercise-provoked**
  - Occur in two conditions
    - Cholinergic
      - Exercise-induced anaphylaxis – 2 types
        - Provoked by exercise
        - Exercise temporally related to food or medication (ASA) ingestion
      - Two subgroups – specific food trigger and non-specific
        - Wheat & celery most common
  - Management includes – avoiding exercise several hours after eating, carry injectable epinephrine, exercise with partner, and wearing medical ID jewelry
  - If symptoms begin, immediate cessation of activity

- **Solar**
  - 0.4-0.5% of CU
  - Quick appearance (generally 1-3 minutes) with sunlight exposure
  - Confirmed with phototesting with different wavelengths

- **Vibratory**
  - 0.1% of CU
  - Pruritis and swelling to vibratory stimulus
  - Can be familial
  - Confirmed by exaggerated response with skin exposure to a vortex mixer

Chronic

- **Management**
  - **Non-pharmacologic**
    - Avoidance of exacerbating triggers
  - **Pharmacologic**
    - Potent topical corticosteroids possibly effective for delayed-pressure urticaria
    - Step-care approach is mainstay
Chronic Management

- Step-care Approach
  - Step 1: Monotherapy with 2nd generation antihistamine
  - Step 2: One of more of following
    - Increased dose of Step 1 2nd generation antihistamine
    - Add another 2nd generation antihistamine
    - Add H2 antagonist
    - Add leukotriene receptor antagonist
    - Add 1st generation antihistamine at bedtime
  - Step 3: Dose advancement of potent antihistamine
  - Step 4: Add an alternative agent

Chronic Management

- Alternative agents used for refractory cases
  - Omalizumab
    - Efficacy supported by large double-blind randomized controlled trials
    - FDA-approved for ages 12 and older
    - Rarely induces remission without maintenance treatment
  - Cyclosporine
    - Greatest published experience for efficacy of other alternative agents
    - Requires frequent lab monitoring and follow-up visits
  - Other anti-inflammatory agents, immunosuppressants or biologics
    - Dapsone, sulfasalazine, hydroxychloroquine, and colchicine

Urticaria Differential Diagnosis

- Vasculitis
  - Overall low prevalence
  - Systemic symptoms may be present such as fever, arthralgia, arthritis
  - Lesions
    - >24 hours duration in same location
    - Less pruritic, more painful
    - Palpable purpura or petechiae
    - More prominent on lower extremities
    - Can leave residual pigmented changes
  - Obtain skin biopsy with any unusual presentation

Urticaria Differential Diagnosis

- Cutaneous T cell Lymphoma (CTCL)
  - Heterogeneous group of lymphoproliferative disorders
  - Characterized by accumulation of malignant clonal T-lymphocytes in skin
  - Incidence 12.7/1,000,000 M>F and AA>other races
  - Frequent, severe pruritis normally not relieved by emollients, topical steroids or oral antihistamines
  - Sezary syndrome
    - More aggressive form, generalized erythroderma and lymphadenopathy
    - Mycosis fungoides
      - Most common variant, mostly diagnosed 5th & 6th decades
      - Typically present as erythematous patches which may progress to plaques and tumors
      - Indolent course, progression over years to decades
      - Diagnosis confirmed by skin biopsy

Angioedema Differential Diagnosis

- Hereditary angioedema
- Acquired C1 inhibitor deficiency
- ACE-1 associated angioedema
Hereditary Angioedema


Not all that itches is urticaria, Ann Allergy, Asthma, & Immunol. 2012; 109:10-11

Course Description

- Urticaria and angioedema are common medical conditions seen by primary care providers as well specialists. Diagnosis and management can be challenging for the medical provider. Optimal management involves identifying possible underlying triggers as well as ruling out other diseases presenting in a similar fashion. This lecture is intended to help providers identify and optimally manage urticaria and angioedema.
With that said

- I have no true conflicts of interest with the content of this presentation

What is a dermoscope?

- Handheld instrument with magnifying objective & light source that removes surface glare & allows us to see structures that are not visible to the naked eye

What is dermoscopy?

- The analysis of the primary morphology of microscopic subsurface skin structures that are not visible to the unaided eye

- It is one of many methods used to study the primary morphology of lesions:
  - Clinical (gross) primary morphology (i.e., ABCDE)
  - Dermoscopic (microscopic) primary morphology
  - Confocal (fuzzy-cellular) primary morphology
  - Histopathology (cellular) primary morphology
There remains no doubt that dermoscopy improves overall diagnostic accuracy; however, skeptics question the effectiveness of dermoscopy for melanoma detection!

1. Is dermoscopy effective at detecting melanoma?
   - Multiple meta-analysis have shown that dermoscopy improves diagnostic accuracy.
   - Dermoscopy increases the sensitivity for diagnosing melanoma by 30% compared to the naked eye alone.
   - More than 2/3 of melanomas are misclassified as benign when using the clinical ABCD rule.

2. Does dermoscopy reduces the number of benign lesions biopsied?
   - Besides increasing the sensitivity for diagnosing melanomas, dermoscopy also improves specificity.
   - This results in a lower number of biopsies performed of benign lesions (unnecessary biopsies).
   - Thus, dermoscopy improves the benign to malignant ratio – More MM diagnosed with less benign lesions removed – Lower NNT (number needed to treat) is not occurring at cost of detecting more advanced cancers.

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Dermoscopy is more accurate than the naked eye alone for the diagnosis of melanoma
- Meta-analysis including 9 prospective studies
- Dermoscopy improves sensitivity and specificity compared to naked eye

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<th>Specificity</th>
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<td>Dermoscopy</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Naked Eye</td>
<td>71%</td>
<td>81%</td>
</tr>
</tbody>
</table>

Dermoscopy improves the benign to malignant ratio
- 36 dermatologists divided in 3 groups
  - Group A: no digital dermoscopy, less dermoscopy training
  - Group B: no digital dermoscopy, more dermoscopy training
  - Group C: digital dermoscopy (DD)
Let’s see what “Big data” reveals regarding this matter.

**Results:** The participating clinics contributed a total of 306,134 cases, including 37,172 melanomas and 265,163 malignant nevi. The overall NNE values achieved in SCs and SECs in the 10-year period were 6.7 and 28.8, respectively. The NNE improved over time in SECs from 6.7 (1991-1995) to 6.8 (2006-2010), but appeared unchanged in SCs. Most of the effect on NNE in SECs was due to a greater number of excised melanomas. Higher NNE values were observed at patients younger than 40 years and for lesions located on the trunk.

In era of cost containment: The powers to be should be helping to promote the use of dermoscopy!

- Non-dermoscopy users performed 2.7 x more biopsies on nevi & SK and found fewer melanomas.

<table>
<thead>
<tr>
<th></th>
<th>Non-dermoscopy users</th>
<th>Dermoscopy users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Sk: 75,713</td>
<td>Sk: 18,085</td>
</tr>
<tr>
<td></td>
<td>Nev: 206,860</td>
<td>Nev: 76,183</td>
</tr>
<tr>
<td>Melanoma*</td>
<td>7,262</td>
<td>9,910</td>
</tr>
<tr>
<td>Total</td>
<td>285,835</td>
<td>104,178</td>
</tr>
</tbody>
</table>

- Early detection is the most useful strategy to improve melanoma prognosis.
- Dermoscopy shown to detect melanoma earlier, especially in high-risk patients.

3. Does dermoscopy lead to the detection of thinner melanomas?

Dermoscopy is associated with thinner melanomas.

Dermoscopy is associated with thinner melanomas.
Melanomas diagnosed in clinics with dermoscopy are thinner

- The rate of melanoma in situ was lower in the group that came with a pre-made diagnosis of melanoma (MMC) rather than the cases newly diagnosed by the authors using dermoscopy

<table>
<thead>
<tr>
<th>Table 2.1:</th>
</tr>
</thead>
<tbody>
<tr>
<td>No dermoscopy</td>
</tr>
<tr>
<td>Melanoma detected</td>
</tr>
<tr>
<td>MMC</td>
</tr>
<tr>
<td>Diagnosis</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>Blank</td>
</tr>
</tbody>
</table>


No dermoscopy Dermoscopy


Dermoscopy

- Improves diagnostic accuracy!
- Improves the benign to malignant ratio!
- Leads to diagnosis of thinner melanomas!

To the skeptics:
- This is not a battle of dermoscopy vs clinical information but rather
- How the clinical findings inform dermoscopy and vise versa (abductive reasoning)
- Experts integrate all available information to render the most accurate diagnosis (management)
- The key is clinical-dermoscopy correlation (concordance vs discordance)

Let’s see what “Big data” reveals regarding this matter

Dermoscopy

<table>
<thead>
<tr>
<th></th>
<th>Users</th>
<th>Non-users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma ratio</td>
<td>1.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Melanoma outcome</td>
<td>50%</td>
<td>40%</td>
</tr>
<tr>
<td>Ratio (for every thick melanoma : number of thin MM)</td>
<td>1:2.3</td>
<td>1:1.7</td>
</tr>
</tbody>
</table>


Two-step diagnostic procedure

Step 1

Is the lesion a melanocytic tumor?
Two-step diagnostic procedure

Step 1

I. Any anatomical location
   1. Network
   2. Aggregated or peripheral rim of globules
   3. Streaks
   4. Homogeneous blue pigment

In addition:
II. On volar skin (palm/soles & nails) – parallel pattern
III. On face - Pseudo-network pattern

1. Network (lines)

- Pigment network (lines, reticular)
- Negative network (non-pigmented lines)
- Angulated lines (angled lines)

1a. pigment network (lines, reticular)

- Grid-like network composed of pigmented lines and hypopigmented “holes”.
- Network lines correspond to the rete ridges. They appear pigmented due to the superimposition of melanin pigment in keratinocytes & melanocytes along the vertical axis of the rete ridges (i.e., relative increase in melanin pigment per unit area).
- The “holes” correspond to tips of the dermal papillae (i.e., supra-papillary plate)
1b. Negative network, also known as reverse or inverse network (lines, reticular, white)

- serpiginous interconnecting hypopigmented lines that surround irregularly shaped pigmented structures, which resemble elongated and curvilinear globules.

1c. Angulated lines (lines, angulated, polygonal)

- Angulated lines forming zig-zag pattern and rhomboidal/polygonal structures also indicates that the lesion is melanocytic (one exception: pigmented AK).
Angulated lines

- Histopathology correlation:
  - Confluent melanoma cells at DE junction with melanophages in dermis

2. Globules (3-5, usually brown, not blue-gray)

Globules (clods, color)

- Symmetrical, round to oval, well demarcated structures
- > 0.1 mm diameter
- Nests of pigmented melanocytes at dermo-epidermal junction, or in dermis
- Brown, black, blue, white (red globules = vascular)
3. Streaks

- Encompasses radial streaming pseudopods

confluent junctional nests of pigmented melanocytes
4. Homogeneous blue pigmentation

Additional criteria

Volar & Nail Lesions
separate lectures

Facial & Mucosal Lesions
separate lectures
Two-step diagnostic procedure

Step 1

Is the lesion a melanocytic tumor?
If it has one of these features, then...

Step 2

Order of dx.
1. DF
2. BCC
3. SCC
4. SK
5. Angioma
6. CCA
7. Seb hyp
1. Dermatofibroma
   (clinical info is critical)
   Delicate network (exception)
   Central scar-like/crystalline
   Ring-like globules
   Vessels / blush in center

1. Dermatofibroma
   Central white patch
   Delicate peripheral network
   70% of DF’s have this pattern

Increased melanin in keratinocytes
Broadened rete ridges (dirty feet) appear as ring-like globules
NPD: appear as white scar-like area
PD: will appear with a pink hue with crystalline structures
Vessels within scar-like area (seen better with PD)

Specific structures must support interpretation of the global pattern

Stellate white (pink) streaks, white network (PD)
Almost exclusively seen under PD
4% in NPD
75% in PD

Blood extravasation / blood vessel dilation
Vessels within the scar-like area can be seen in:
NPD: gel, minimal pressure (50%)
PD: non-contact (80%)
70% of DF’s have network structures
40% of DF’s have ring-like globules

2. BCC

Positive features (At least one present):
- Large grey-blue ovoid nests
- Multiple grey-blue non-aggregated globules
- Leaf-like areas
- Spoke wheel areas (concentric globules)
- Arborizing "tree-like" telangiectasia
- Ulceration
- Shiny white blotches & strands (PD)

1. Leaf-like areas (lines, radial, connecting to a common base)

- Brown to blue-gray to pink discrete bulbous blobs or lines connecting at a common base
- Some can manifest “leaf-like” shapes
2. spoke-wheel-like structures
(lines, radial, converging to a central dot or clod)

- well circumscribed
- brown to gray-blue-brown
- radial projections
- meeting at a darker brown central hub

Concentric structures:
I consider them to be variants of spoke wheels

Concentric structures correspond on histopath to superficial BCC.
These structures are actually variants of the same feature.
Thus, it is not uncommon to see all 3 in same lesion.
3&4. blue-gray ovoid nests & non-aggregated globules (Clods, blue, small or large)

- circumscribed round to oval structures
- confluent blue-gray color
- Can resemble globules but they will not be arranged in an aggregated pattern

Non-Classical features:
1. Short fine superficial telangiectasia
2. Multiple small erosions
3. Concentric structures
4. Multiple in-focus blue/gray dots
5. arborizing vessels

- In-focus, red, branching vessels

6. shallow ulcerations (including multiple small erosions)

- Red to orange crust / erosions
• Ulcers (red, orange)

Multiple small erosions

Accuracy of dermoscopic criteria for discriminating superficial from other subtypes of basal cell carcinoma

Non-classical BCC features

* Multiple dots (in focus)
Concentric structure
* Short fine telangiectasia
Multiple erosions (serous crust)

Fine, sharply in focus brown/blue-gray dots in BCC (buckshot scatter)
Problem with Classical & non-classical criteria for BCC

- 4 of 6 criteria are only seen in pigmented variants of BCC (ovoid nest, blue-gray globules, leaf-like and spoke-wheel like structures)
- 2 of 2 features that are seen in amelanotic BCC (>90% of BCCs) are associated with nodular BCC (arborizing vessels & ulceration)
- With these criteria it will not be possible to dx the following lesion:

New criterion helpful in diagnosing many BCCs (including BCCs that lack the Menzies criteria)

65% of BCC lacking the classical and non-classical features of BCC could be diagnosed by SWS (blotches & strands)
7. Shiny white blotches & strands

- Structure is seen only with polarized light
- White blotches (clods) and strands

Non polarized BCC

3. SCC
Focally scaly/keratotic and rough

-glomerular vessels
  focally present at periphery
- Hairpin vessels
  usually with a white halo
- Keratin pearls & white circles
- Rosettes (strawberry pattern)
- Brown dots/globules aligned in a linear fashion

NB: Pigmented AK can also have structures seen in LMM!
Glomerular Vessels

- Morphology
  - Tightly coiled vessels
- Most commonly associated with
  - Bowen’s – PPV 62%
- Distribution
  - Bowen’s – focally in clusters at the periphery
  - Psoriasis – diffuse throughout
  - CCA – string of pearls
  - Stasis – in normal skin
  - Porokeratosis – diffuse throughout

Hairpin Vessels

- Morphology
  - Vessels with a sharp bend - creating a U shape
  - May twist upon its own axis
  - Surrounded by a white halo (background) in keratinocytic tumors
  - Surrounded by a pink halo (background) in melanoma
- Most commonly associated with
  - SK – PPV 70% (but if pink background think MM)
- Distribution
  - SK & MM – random (on ridges in SK)
  - KA – around perimeter
Rosettes

Rosette derives from the natural shape of a rosette in botany, formed by leaves radiating out from the stem.

NB: Only seen with polarized light.

Strawberry pattern
Polarized dermoscopy

Non-Polarized dermoscopy

Rosette structures (clover)

Few glomerular vessels

Focal brown dots aligned linearly at the periphery

Milia-like cysts

dots or clods, white

- round whitish or yellowish structures
- commonly seen in seborrheic keratosis
- can also be seen in congenital nevi & MM
- if pigmented, they resemble globules

Comedo-like openings

clods, brown or orange & circles

- commonly seen in seborrheic keratosis
- also seen in papillomatous melanocytic nevi
- keratin-filled invaginations of the epidermis

• Milia-like cyst
• Comedo-like opening
• Fissures & ridges (gyri & sulci)
• Fingerprint-like
• Hairpin vessels
• Moth-eaten borders

4. SK
seborrheic Keratosis

multiple milia-like cysts (3 or more) comedo-like openings (crypts)

Milia cyst are more conspicuous under non-polarized light

- Milia cyst (superficial & small) are not usually visible with polarized dermoscopy

Milia cyst important after BCC has been ruled out

The significance of structures is based on 2-step level

- Milia cyst not important (but helps in dx. CMN)
- Milia cyst important after BCC has been ruled out
FINAL DX: Melanoma 0.5mm with SK like features

Gyri & sulci (fissures & ridges)

- Confluent branching clefts
- Due to deep keratin filled invaginations of the epidermis
- Commonly seen in seborrheic keratosis
Fissures (sulci) & ridges (gyri) = cerebriform pattern

Fingerprint like network structures

- Seen in solar lentigines and early seborrheic keratosis
- Tiny ridges running in parallel & resembling fingerprints

Sometimes it is difficult to differentiate lentigo/SK from melanocytic lesions.
The ink test can...
Hairpin vessels with a white halo

- Looped vessels in papillary dermis
- White halo due to keratin

Hairpin blood vessels with a whitish halo

Seborrheic keratosis

Moth eaten borders

- Seen in solar lentigines and early seborrheic keratosis
- Resembles a moth-eaten garment
Moth-eaten Border

The significance of structures is based on 2-step level

Step 1

Melanocytic
Non-Melanocytic

BWV is a melanoma specific structure
BWV is not significant

What structures do you see?

Blue white veil

comedo

Fat finger like structures

7 globules

Few milia cysts

- B:M ratio in the hands of experienced dermoscopists is 5:1 (it is lesions like these that make up the bulk of the benign biopsies)

When dermoscopy morphology gives conflicting / mixed messages then R/O worst diagnosis.
Specific structures must support interpretation of the global pattern.

3. Left medial site, shave biopsy:
- Melanoma, at least in situ with adenoid extension, favor locally invasive to 0.4 mm, non-invasive. Malignant cells in a neovascular collarette with a retiform keratosis, see...

5. Vascular lesion

**Lacunae** *(Clods, red)*

- red, maroon, blue, black lagoons (clods)
Hemangioma
Lacunae (saccules)

**Pearl:**
Caution if you see ill defined lacunae that are not separated by:
- Septae
- BWV

Well defined lacunae
- Septae separating lacunae
- Lacunae surrounded by BWV

Thrombosed Angiomas
Blackest of Black

Angiokeratoma

Thrombosed angioma
6. Clear cell acanthoma

- Morphology/Distribution/Arrangement
  - Dotted or glomerular vessels distributed in a serpiginous pattern (string of pearls)
7. Sebaceous Hyperplasia

- **Morphology/Distribution/Arrangement**
  - Serpentine and arborizing vessels that are a bit out of focus and come from periphery and migrate towards the center of the lesion but do not cross the midline (crown/corona vessels).
  - The center of the lesion has popcorn-like appearance.

Two-step diagnostic procedure

**Step 1**

If it has no melanocytic features & it has no features seen in one of the 4 (+2) common non-melanocytic lesions, then…
Vascular Structures

1. Morphology

2. Distribution (focal, throughout, peripheral, central, random, not random)

3. Arrangement (string of pearls, crown)

In hypomelanotic / amelanotic lesions:
1. Analyze the morphology, distribution and arrangement of blood vessels
2. Look for additional clues such as milia/comedo to confirm your diagnosis!
3. Remember: Context, context, context!

Vessels in non-melanocytic lesions

- Hairpin – keratinizing tumors
- Arborose – BCC
- Dotted in serpiginous distribution – CCA

Vessels in melanocytic lesions

- Milky red area
- Elongated looped vessels
- Multi-pronged looped vessels

Poroma

1. Elongated looped vessels
2. Multi-pronged looped vessels
Vessels in non-melanocytic lesions

- Hairpin – keratinizing tumors
- Arborizing – SCC
- Irregular hairpin or serpentine – CCA

Vessels in melanocytic lesions

- Comma – DN
- Dotted – MM & Spitz & DN
- Linear & polymorphous – NM
- Milky red areas – BCC

Irregular hairpin or serpentine vessels

Two-step diagnostic procedure

Step 1

Melanocytic

Non-melanocytic

Vascular patterns

Melanocytic

Non-melanocytic

Non-specific (structureless/featureless):

- While some of these lesions are truly structureless, some may in fact display structures but the presence or absence of any one of these structures cannot be relied upon to differentiate melanocytic from non-melanocytic lesions. However,...
- Some of these structures can assist in diagnosis when present in the correct context (e.g., extra criteria in BCC: dots, short fine vessels)
- Many of these structures are important in step 2 of the 2-step algorithm (differentiating nevi from melanoma: blotches, regression structures, BWV, etc)

Structures that do not help in differentiating melanocytic from non-melanocytic lesions

- Dots
- Shiny white structures
- Blotch
- Regression structures
- Blue-white veil
Two-step diagnostic procedure

**Step 1**
- **Melanocytic** Skin Lesion
  - Benign: DF, SK, CCA, angioma, seborrheic keratosis
  - Malignant: BCC, SCC

**Step 2**
- Vascular patterns
  - Non-specific (structureless) lesion

**R/O Melanoma:**
1. Biopsy or
2. Digital monitoring (STMM) – but never for raised lesions!

**Rate of growth of melanoma subtypes:**
- Median melanoma growth in mm per month:
  - **SSM:** 0.00
  - **LMM:** 0.10
  - **NM:** 0.20
  - **SM:** 0.30
  - **MM:** 0.40
  - **LMM:** 0.50
  - **HMM:** 0.60


**Change over 4 months**

"Short term mole monitoring" helps detect melanoma based on change (sensitivity high) and helps confirm biologically senescent (indolent) lesions (increases specificity)

This is a:
1. Melanocytic lesion
2. Non-melanocytic lesion
This is a:
1. Melanocytic lesion
2. Non-melanocytic lesion
This is a:
1. Melanocytic lesion
2. Non-melanocytic lesion
This is a:
1. Melanocytic lesion
2. Non-melanocytic lesion

My eyes are just as good !!!
Your visual abilities “are just as good” for finding what?

Clinically detected cancers

Dermoscopically detected cancers

Important principle:
If you only look at lesions that are of clinical concern to you then dermoscopy can only help improve your specificity.
To improve your sensitivity for detecting skin cancer requires that you look at lesions that clinically do not look concerning to you.
Nevus (DN) vs. Melanoma

The “Beauty and the Beast” sign
- Benign nevi (DN) tend to adhere to one of ten recurrent patterns (finite #).
- These patterns all fit the definition of beauty, demonstrating symmetry of pattern, structure, and color.

The most common benign patterns are:
1. Diffuse network pattern

Diagnosis: Benign nevus

2. Patchy network pattern

Diagnosis: Benign nevus

3. Peripheral network with central hypopigmentation

Diagnosis: Benign nevus
4. Peripheral network with central hyperpigmentation

5. Homogeneous

6. Peripheral globules
Peripheral globules with central network pattern

Periostial fibro-epithelial plexus

Diagnosis: Benign enlarging nevus

Starburst pattern with tiered globules

Peripheral globules & Starburst patterns are manifestations of the same biologic process – radial growth!

Starburst with radial streaming

Starburst with pseudopods
7. Reticulo-globular pattern

8. Globular pattern

Diagnosis: Benign nevus
The “Beauty and the Beast” sign

- Melanoma, symbolized by the beast, is a melanocytic lesion that deviates from the benign patterns (infinite # of patterns).
- Melanomas almost invariably display some degree of asymmetry of pattern, color, and structure, which elicits a sense of unease in the viewer.
Melanoma Patterns:
- Deviate from global benign patterns
- Have at least one of the melanoma specific features listed below

<table>
<thead>
<tr>
<th>MM SPECIFIC STRUCTURE / FEATURE</th>
<th>SENSITIVITY (highest reported)</th>
<th>SPECIFICITY (highest reported)</th>
<th>ODDS RATIO (highest reported)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical network</td>
<td>77%</td>
<td>88%</td>
<td>9.5</td>
</tr>
<tr>
<td>Streaks</td>
<td>23%</td>
<td>98%</td>
<td>5.8</td>
</tr>
<tr>
<td>Negative network</td>
<td>22%</td>
<td>98%</td>
<td>2.8</td>
</tr>
<tr>
<td>Crystalline (shiny white lines)</td>
<td>5%</td>
<td>98%</td>
<td>9.7</td>
</tr>
<tr>
<td>Atypical dots &amp; globules</td>
<td>98%</td>
<td>97%</td>
<td>4.8</td>
</tr>
<tr>
<td>Atypical blotch</td>
<td>36%</td>
<td>98%</td>
<td>9.1</td>
</tr>
<tr>
<td>BWV</td>
<td>51%</td>
<td>98%</td>
<td>13</td>
</tr>
<tr>
<td>Regression structures</td>
<td>46%</td>
<td>94%</td>
<td>8.5</td>
</tr>
<tr>
<td>Atypical vessels</td>
<td>63%</td>
<td>98%</td>
<td>12.5</td>
</tr>
<tr>
<td>Peripheral brown structureless areas</td>
<td>63%</td>
<td>98%</td>
<td>29</td>
</tr>
</tbody>
</table>

Melanoma specific structures
1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

Pigment network

Network
- Nevus
  - Typical / regular network
  - Network symmetrically distributed with minimal variability in line thickness, color & hole sizes. Network is sharp, & usually without any gray colors.

- Melanoma
  - Atypical / irregular network
  - Increased variability of line thickness and color (*gray). Variability of hole size. Network distributed asymmetrically & disrupted forming branched streaks. Often the lines are smudged.

Typical vs atypical is defined relative to the network quality within the rest of the lesion (degree of variability).

### Network:
- Pigment network
- Negative network
- Angulated lines

### Melanoma specific structures
1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

### Angulated lines (lines, angulated, polygonal)
- Angulated lines joining to create zig-zag lines & polygons (rhomboidal structures)

### Angulated lines creating a zigzag pattern &/or polygonal / rhomboidal structures
Confluent junctional nests of pigmented melanocytes:
- Reflection of radial growth.
- In MM it is associated with the superficial spreading type.

**Melanoma specific structures**

1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peeping, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

**Negative network (reverse network)**

Serpiginous interconnecting hypopigmented lines that surround irregularly shaped pigmented structures, which resemble elongated and curvilinear globules.

This structure can be seen with both polarized and non-polarized dermoscopy.
Nevus

Rare in benign nevi except for some CMN & Spitz. Usually symmetrically distributed (ordered). In CMN also see rounded brown structures.

Brown structures are more elongated & curvilinear in appearance. Present focally in asymmetric distribution.

Melanoma

Negative network

Negative pigment network: An additional dermoscopic feature for the diagnosis of melanoma

Conclusion: The overall morphologic pattern of SNP, such as the negative distribution and the peripheral location of SNP, along with the multicomponent pattern and the asymmetric pigmentation, could be used as an additional feature in distinguishing melanoma from Spitz nevi and other benign lesions. (J Am Acad Dermatol 2013;69:955-60.)

However,.........

“White” network in Spitz nevi and early melanomas lacking significant pigmentation

(88.5%) and 24 (92.3%) Spitz nevi

10 (25.6%) and 8 (20.5%) cases of 39 melanomas

Conclusion: Although white network occurs at significantly higher frequency among hypopigmented nevus, it is not exclusively seen in Spitz nevi. Thus, evision of melanocytic tumors showing this pattern is mandatory. (J Am Acad Dermatol 2013;69:955-60.)

Negative network can be seen with both PD & NPD

NPD

PD
Melanoma specific structures

1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

Crystalline (Shiny white lines)

- Short, white, linear lines that can only be seen with polarized dermoscopy.
- The lines are often oriented in an orthogonal fashion, one to the other.
- Due to birefringent properties of collagen, causing polarized light to randomize its polarization rapidly. Also explains angular dependence.

Non-polarized Dermoscopy
Polarized Dermoscopy

Crystalline structures can be seen in Spitz Nevi. Often seen in melanoma.

Nevus
Can be seen in Spitz
Melanoma
Often seen in melanoma
Study: 11,225 consecutive prospectively examined lesions (JAAD)

<table>
<thead>
<tr>
<th>Melanocytic lesions with crystalline:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1 / 9860</td>
<td>DN</td>
</tr>
<tr>
<td>0 / 91</td>
<td>CMN</td>
</tr>
<tr>
<td>0 / 15</td>
<td>blue nevi</td>
</tr>
<tr>
<td>2 / 182</td>
<td>EN</td>
</tr>
<tr>
<td>3 / 3</td>
<td>Spitz</td>
</tr>
<tr>
<td>16 / 17</td>
<td>invasive melanomas</td>
</tr>
<tr>
<td>0 / 5</td>
<td>MMS</td>
</tr>
</tbody>
</table>

In melanocytic tumors the presence of crystalline is highly suggestive of invasive melanoma (or Spitz).

OR for melanoma in biopsied lesions is 9.7.

229 consecutively diagnosed “melanomas” (retrospective review)

-65 of 110 (41%) invasive MMs had crystalline/chrysalis
-20 of 119 (17%) in situ MMs had chrysalis/crystalline

Invasive melanomas with chrysalis/crystalline were significantly thicker as compared to those without chrysalis/crystalline (0.68 vs. 0.43mm)

• Predictors of thicker MM >0.75mm:
  - blue gray areas
  - vessels
  - abrupt cutoff
  - > 4 colors
  - blue white veil
  - > 2 structures

• Predictors of thicker MM & +SLNB (negative predictor: atypical network)
  - Blotch
  - ulceration

• Predictors of thicker MM & distant metastasis
  - Shiny white streaks
  - Milky red areas

Melanoma specific structures

1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (B/W over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

Dots (clods, small)

• black dots = pigment in the stratum corneum and the upper part of the epidermis
• brown dots = small nests at or near the DEJ or in epidermis (below stratum corneum)
• blue-gray dots = free melanin in dermis or in macrophages
• red dots = dotted vessels

Collagen XVII is expressed in malignant but not in benign melanocytic tumors and it can mediate antibody induced melanoma apoptosis

These results suggest that the accumulation of collagen XVII endodomain in melanocytic tumors is associated with malignant transformation to be a potential marker of malignancy and a target for antibody-induced melanoma apoptosis.
Nevus:
- Dots located centrally
- Situated on network lines
- Situated in hole of network

Melanoma:
- Atypical / irregular dots
- Dots distributed asymmetrically, located focally at the periphery & not associated with network lines

Regular black or brown dots:
- Centrally located
- Overlying network lines (even if found at periphery of lesion)

Dots:
- Melanoma
- Typical / regular dots
- Atypical / irregular dots

Important to determine if dots are on the network or not.

Also important to determine if dots are within hole of network.

Figure 1. Schematic representation of the normal pigment network. The lines of the network represent melanin along the rete ridges while the holes correspond to the dermal papillae. A brown dot on the network.
Pigment network mesh centered by a brown globule

Situated in hole of network = target globules

Regular black or brown dots

Irregular black or brown dots

Not associated with network lines, or in hole of network, or in center.

They tend to be distributed asymmetrically and are often located towards the periphery of the lesion.

Brown (or black) dots not on the network lines

While black dots can often be tape stripped off, they are still significant if located off the network lines.

**globules**

- symmetrical, round to oval well demarcated structures, >0.1mm in diameter
- brown - nests at or below DE-junction in papillary to upper reticular dermis (most common)
- black - heavily melanized nests
- blue - nests in deeper dermis
- white - balloon cell nests
- red - vascular structures
Nevus

Typical / regular globules
Globules of uniform size, shape and color. Symmetrically distributed
- throughout the lesion
- at periphery
- or centrally

Melanoma

Atypical / irregular globules
Globules are asymmetrically distributed, often aggregated focally. When reddish in color, highly suggestive of melanoma.

Globules

Globules of relative uniform size, shape and color located throughout the lesion

Melanoma specific structures

1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

Irregular Globules

Globules of differing shapes, sizes, and colors. Also, tiered globules.

Globules asymmetrically distributed, often aggregated focally. Also includes tiered globules & globules at periphery.

Melanoma

Globules of relative uniform size, shape and color located centrally and surrounded by a network

Globules of relative uniform size, shape and color located around the entire perimeter of the lesion

Blotch

- Large concentration of melanin pigment
- Throughout epidermis (with or without melanin in dermis)
- Visually obscuring the underlying structures

*NB: large concentrations of melanin in the stratum corneum is called a black lamella. A lamella can resemble a blotch.*

Melanoma
Melanoma specific structures

1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

Blue white veil

- Bluish blotch with overlying white ground—glass haze
- Not associated with scar-like depigmentation or peppering/granularity
- Associated with palpable (raised) portion of the lesion

Blue-white veil

compact orthokeratosis
BWV due to orthokeratosis is more conspicuous with NPD.

Homogeneous BWV (hue) throughout entire lesion (NPD). However, it may appear more heterogeneous with PD!

Heterogeneous BWV (with PD or NPD). Often focally and asymmetrically located but can also encompass the entire lesion.

**Melanoma specific structures**

1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

**Regression structures**

Peppering/granularity (dots, gray) consists of fine gray particles.

Depigmented area/scar like depigmentation (structureless zone, white) is a structureless area that is white in color. Thus, it is lighter in color as compared to the lesion and the background skin color.

The combination creates a BW color or veil (on palpation it will be macular / flat).

Papillary dermis thickened by fibrosis – note a few melanophages.
Peppering (uncommon to have scarring) that is usually symmetrically located & involving <10% of lesion area

Peppering (+/- scarring) that is asymmetrically located & involves >50% of lesion area

**Regression structures = peppering &/or scar like depigmentation (BWV overlying macular areas)**

**Melanoma specific structures**
1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
3. Negative pigment network
4. Shiny white lines or Crystalline structures (only with PD)
5. Atypical dots & globules
6. Irregular blister
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

**Vascular Structures: Nodular lesions**

**Nevus**

**Melanoma**

**Vascular Structures: Flat lesions**

**Nevus**

**Melanoma**

**Dotted, globular, serpentine/linear polymorphous, milky-red**

**Monomorphous dotted "target network" vessels (in CMN can be polymorphous), milky-red**

**Comma vessels (IDN, CMN)**

**Dotted, globular, serpentine/linear, milky-red (polymorphous)**

---

**Dermoscopic Evaluation of Amelanotic and Hypomelanotic Melanoma**

---

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

<table>
<thead>
<tr>
<th>Negative feature (if present, non-melanoma)</th>
<th>Positive features (if any 1 present then melanoma)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 Milia-like cysts</td>
<td>Irregularly sized or distributed brown dots/globules</td>
</tr>
<tr>
<td>Multiple blue-gray dots</td>
<td>Irregularly shaped depigmentation</td>
</tr>
<tr>
<td>Blue-white veil</td>
<td>&gt;1 Shade of pink</td>
</tr>
<tr>
<td>Predominant central vessels</td>
<td>Dotted and linear irregular vessels</td>
</tr>
</tbody>
</table>

Dotted vessels

NPD

PNCD

Linear irregular (hairpin) serpentine vessels

Amelanotic 1.65mm melanoma arising in DN
Polymorphous = Dotted & linear irregular

Melanoma specific structures
1. Atypical network
2. Irregular streaks (pseudopods &/or radial streaming)
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6. Irregular blotch
7. Blue-white veil over raised areas
8. Regression structures (BWV over flat, peppering, scar)
9. Atypical vascular structures
10. Peripheral tan/brown structureless areas

Histologically – flattening of rete ridges at DEJ, melanocytes arranged predominately as solitary units + lea melanin, pagetoid scatter of melanocytes
Tan to brown structureless areas

Nevus
Tan, symmetric & homogeneous structureless (hypopigmented) area in center of lesion.

Melanoma
Brown structureless area(s) at periphery of lesion.

Light brown structureless area towards center
Light brown structureless area towards periphery

Remodeling of the Dermoeocdermal Junction in Superficial Spreading Melanoma
Insights Gained From Correlation of Dermoscopy, Reflectance Confocal Microscopy, and Histopathologic Analysis

Slow-growing melanoma: a dermoscopy follow-up study
British Journal of Dermatology 2010 162, pp267–273

Any melanocytic lesion on any anatomical site that reveals any of the 10 melanoma specific dermoscopic structures should be viewed with suspicion.
In addition, additional melanoma specific structures exist for lesions on volar skin, nails, mucosal surfaces and on the face.
- Pseudo-network pattern (face)

- Parallel pattern (volar skin = palms/soles)

- Parallel ridge pattern

- Malignant pattern

- Multi-component pattern (75%)

- Homogenous pattern (25%)
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Peripheral network
Central hypopigmented and structureless area

Does this lesion manifest any MM specific structures?
1) yes
2) no
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no

- Atypical globules
- Atypical network
- Milky red area

Melanoma
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no

Negative network

Melanoma
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no

- Focal streaks
- Milky red area
- Peripheral tan structureless areas

Melanoma
0.15mm
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no

BWS - regression
Structureless areas

Melanoma in situ
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no

Negative network
Dotted vessels
Crystalline structures

DN with focal severe atypia & with minor Spitzoid features
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Cobblestone globules

Does this lesion manifest any MM specific structures?
1) yes
2) no
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Does this lesion manifest any MM specific structures?
1) yes
2) no

Focal peripheral globules

Atypical dots

DN with focal severe atypia

Melanoma
Does this lesion manifest one of the 10 benign nevus patterns?
1) yes
2) no

Pseudopods - starburst

Spitz nevus

Does this lesion manifest any MM specific structures?
1) yes
2) no

Spitz nevus

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

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

Insights gained from teaching experience
- SK, hemangioma & DF are usually easy to identify (for dermoscopists) and should be excluded from entering algorithm
- Clear cut benign or malignant lesions should be excluded from entering algorithm
- Only lesions for which the diagnosis is unknown enter the algorithm

Insights from UDA study by IDS
- While many structures have the power to discriminate nevi from melanoma, most have extremely poor inter-observer agreement.
- The most powerful discriminator was "architectural disorder" (disorganized/dermoscopic asymmetry) with an OR of 6.6.
- The feature with highest inter-observer agreement was also "architectural disorder" (the subjective view had higher agreement than the objective view)
You do not need to be able to identify the individual objects on the table to know if the desktop is organized or disorganized.

Put it all together.
Triage
Amalgamated
Dermoscopy
Algorithm

STEP 1
If the lesion is NOT a clear-cut SK, DF or Angioma then what's next?

Symmetry of SHAPE
(but disorganized pattern)

Definition of:
Symmetry (organized) / Asymmetry (disorganized)
Symmetry of SHAPE
(but disorganized pattern)
Organized PATTERN
(but asymmetry of shape)

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

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

Examples
Pizza Margherita
SYMMETRY (organized)

Pizza Quattro Stagioni
ASYMMETRY (disorganized)

Starburst Pattern
SYMMETRY (organized)
ASYMMETRY (disorganized)

Symmetric Cancers
- Nodular MM
  - blue, black, gray
- Spitzoid MM
  - negative network or starburst pattern
- Amelanotic cancers
  - SWS, vessels, ulceration

If the lesion does NOT manifest a disorganized or starburst pattern, what’s next? (these are all symmetric lesions!)
Symmetric lesion

Sharply demarcated borders

Symmetric lesion
Symmetric lesion

SCC in situ / KA

All others get “monitored”
How did TADA perform

<table>
<thead>
<tr>
<th>Method</th>
<th>Overall Sensitivity</th>
<th>Overall Specificity</th>
<th>Malignancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three Points</td>
<td>90.8</td>
<td>79.5</td>
<td>Melanoma, pBCC</td>
</tr>
<tr>
<td>Chaos and Clue</td>
<td>90.6</td>
<td>82.7</td>
<td>Melanoma, pBCC, pSCC</td>
</tr>
<tr>
<td>Skin Black Rule</td>
<td>78.2</td>
<td>80.5</td>
<td>Melanoma</td>
</tr>
<tr>
<td>AI Rule</td>
<td>92.0</td>
<td>82.0</td>
<td>Melanoma</td>
</tr>
<tr>
<td>TADA</td>
<td>93.8</td>
<td>72.8</td>
<td>Melanoma, pBCC, pSCC</td>
</tr>
</tbody>
</table>

TADA results by lesion type and dermoscopic training

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma (MM, MMIS, AMM, NM)</td>
<td>94.3</td>
<td>-</td>
</tr>
<tr>
<td>BCC</td>
<td>96.0</td>
<td>-</td>
</tr>
<tr>
<td>SCC</td>
<td>96.0</td>
<td>-</td>
</tr>
<tr>
<td>Seborrhoeic Keratosis</td>
<td>81.0</td>
<td>-</td>
</tr>
<tr>
<td>Dermatofibroma</td>
<td>93.0</td>
<td>-</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>73.0</td>
<td>-</td>
</tr>
<tr>
<td>Nevi</td>
<td>63.0</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure: Triage Amalgamated Dermoscopic Algorithm (TADA)

*This algorithm is based on the use of polarized dermoscopy*

- Unequivocal SK, DF or angioma
- Asymmetric distribution of colors or structures or starburst pattern
- Blue-black or grey color
- White structures
- Negative network

Biopsy/refer

Reassure/Monitor
Saturday, September 17, 2016

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

7:00 a.m. - 8:00 a.m.  The Physics of Perfect Skin: Enhancing the Integument Through Laser
E. Victor Ross, MD

8:00 a.m. - 9:00 a.m.  Lasers: Lessons Learned
E. Victor Ross, MD

9:00 a.m. - 10:00 a.m.  Updates in Pediatric Dermatology
Lisa Swanson, MD

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

10:30 a.m. - 11:30 a.m.  Lessons Learned from 10 Challenging Cases
Lisa Swanson, MD

11:30 a.m. - 12:30 p.m.  Image Guided Superficial Radiation Therapy (IG-SRT)
Daniel Ladd, DO, FAOCD

12:30 p.m. - 1:30 p.m.  Tips and Techniques to Improve from a Dermatopathology Point of View
Whitney High, MD

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

2:00 p.m. - 3:00 p.m.  Male and Female Pattern Hair Loss
Craig Ziering, DO, FAOCD

3:00 p.m. - 4:00 p.m.  Osteopathic Continuous Certification Update
Lloyd Cleaver, DO, FAOCD

4:00 p.m. - 5:00 p.m.  Allergan Product Theater (No CME awarded)
What’s New in Atopic Dermatitis?

- Eczema causes stress, sleeplessness, 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 anxiety, ADHD, injuries (likely due to distraction), and infections (Cutis June 2016).

Sensitive skin care:
- ALL free and clear detergent, no dryer sheets/fab soft
- Dove sensitive skin or cetaphil soap
- Vanicream/Vaseline/Aquaphor as moisturizers
- Robathol bath oil
- Bleach bath- ¼ cup bleach in full tub water

Topical steroids- always do OINTMENTS in little kids:
- HC 2.5
- Triam 0.1
- Fluocinonide 0.05
- Clobetasol 0.05

No need to “soak and smear”. Skin can be wet or dry (JAAD Aug 2016)
Calcineurin Inhibitors
- Black Box Warning
- Pimecrolimus study from Pediatrics
  - 2418 patients age 3-12 mos old
  - Found no evidence of lymphoma, malignancy or immune system impairment
  - Concluded it was safe even in the younger age group

Treatments on the Horizon- Crisaborole
- Boron based topical ointment
- Inhibits phosphodiesterase-4 activity (PDE4) and decreases production of proinflammatory cytokines
- Several studies showing its efficacy down to age 2
- 65% of patients in preliminary studies were clear/almost clear
- Well tolerated
- Safety studies so far look great
- Progressing to phase 3 trials

Treatments on the Horizon- Dupilumab
- Blocks IL-4 and IL-13 (decreases the TH2 inflammatory response)
- 12 wk phase 2 study
  - 85% of patients achieved at least 50% improvement
  - 40% of patients were clear/almost clear
- Very tolerable
- Good side effect profile
- 300 mg subcutaneously once a week
- Scheduled for FDA approval in Q3 of 2016

Treatments on the Horizon- JAK Inhibitors
- Approved for dog eczema in 2013
- JAAD Sept 2015; 6 patients age 18-55
  - Tofacitinib 5 mg bid
  - Increased risk of herpes zoster
  - Check CBC, LFTs, and lipids
  - There has been increased rates of solid organ malignancy and lymphoma in RA patients on JAK inhibitors

Atopic Dermatitis Natural Therapy
- Coconut oil
  - Has good antibacterial properties, but doesn’t seem to help the eczema itself
- Sunflower seed oil
  - Does appear to help with eczema- difficult to find a good preparation
  - Aroma Workshop in Chicago
  - hello@aromaworkshop.com
  - Patients can call 773-871-1985
  - 8 oz spray bottle for $22 plus $5.50 shipping

Atopic Dermatitis Prevention
- Probiotics
  - Taken by a child with eczema appear to have no impact
  - But if a pregnant woman takes probiotics 2 weeks prior to having a baby and for 3 mos after having this baby, it reduces the risk of eczema in that baby by 20-30%
- Vitamin D
  - Some studies in the past suggested that vitamin D supplements could help eczema
  - One study looked at staph colonization and correlation with serum 25(OH)D level
  - Patients with low vitamin D had more staph colonization (SPD July/Aug 2015)
  - More recent study showed that serum vitamin D levels were NOT associated with the severity of the eczema (SPD May/June 2016)
**Atopic Dermatitis Prevention**
- Transepidermal Water Loss (TEWL)
- TEWL in first weeks of life associated with increased risk of eczema
- Families with h/o eczema should be managing their new baby with the same sensitive skin care strategies to try to prevent the eczema
- 50% reduction in eczema by simply using sensitive skin care in first weeks of life

**Eczema and Peanut Allergy**
- Early peanut exposure in severe eczema patients actually DECREASES the rate of peanut allergy (New Eng J Med)
- Consensus statement in SPD Jan/Feb 2016 showed an 11-25% reduction in risk of peanut allergy in high risk infants when peanuts were introduced between 4 and 11 mos of age

**Pityriasis Alba**
- Recent study compared topical steroids with topical calcineurin inhibitors for Pityriasis Alba
- Concluded that protopic/elidel work better than topical steroids (SPD Nov/Dec 2015)
- Could also consider treatment with calcipotriene or excimer laser

**Keratosis Pilaris Rubra**
- Pulsed dye laser has emerged as a very effective therapy for this condition (SPD July/Aug 2016)

**What’s New in Contact Dermatitis?**
- TRUE test is helpful in kids
  - The causative agent was identified in 71% of kids with the TRUE test
- Don’t use Finn chambers- contain Aluminum
  - Aluminum is in a lot of vaccines and some kids are sensitized to it
  - Use IQ chambers in kids less than 10 yrs old
- 1 exposure to the triggering agent causes a rash for 3 wks

**Patch Testing Considerations in Kids**
- TRUE test is helpful in kids
  - The causative agent was identified in 71% of kids with the TRUE test
- Don’t use Finn chambers- contain Aluminum
  - Aluminum is in a lot of vaccines and some kids are sensitized to it
  - Use IQ chambers in kids less than 10 yrs old
- 1 exposure to the triggering agent causes a rash for 3 wks
Allergic Contact Dermatitis - Wet Wipes

- Due to preservative MCI/MI (Kathon CG)
- There are now 2 brands of wipes that don’t contain the allergen
  - Honest Brand
  - Earth's Best Hypoallergenic

Shin Guard Dermatitis

- Can be irritant or allergic
- First step is to try the following steps:
  - Drysol (or OTC Certain Dri) applied to shins
  - Shin guard liners
  - Shin guards
  - Fluocinonide or clobetasol to treat
- Patch testing if initial plan doesn’t work

Shin Guard Contact Dermatitis

- Possible allergens
  - P-tert butylformaldehyde resin (PTBFR) is #1
  - PPD
  - Diakylthioureas
  - Disperse dyes

What’s New in Pediatric Psoriasis
Psoriasis

- Topical steroids continue to be the mainstay for pediatric psoriasis
- Systemic therapy options have been largely limited to cyclosporine, acitretin, methotrexate
- Biologic therapy is difficult because of lack of FDA approval, lack of data
- Systemic effects of psoriasis are making it more advantageous to consider systemic therapy, even in children

Biologics in Kids

- Enbrel (etanercept) - CURRENTLY PURSUING PED PSOR INDICATION
  - Approved in Europe for psoriasis in kids >6 yrs old
  - Approved in US for JIA in kids >2 yrs old
  - 1 study in US in children: 2008-2011 patients age 4-17
    - 0.8 mg/kg/wk
    - 57% achieved PASI 75
  - This study has been continued to date and has great long-term safety data (JAAD Feb 2016)
- Humira (adalimumab) - CURRENTLY PURSUING PED PSOR INDICATION
  - Approved in US for kids with JIA (>12 yrs old) and Crohn's (>6 yrs old)
- Stelara (ustekinumab)
  - Several case reports of effectiveness and safety
  - 1 clinical trial: patients age 12-18, 110 patients
    - 80% reached PASI 75 at 12 wks (JAAD Oct 2015)
  - Large study outside US is in progress

Psoriasis is a Systemic Disease

- #1 association in children is obesity
- Ask kids about smoking and stress
- Talk to them about weight
- Consider checking blood pressure
- Still unclear if we should be screening for hypercholesterolemia or diabetes in kids with psoriasis, but they are associated

What’s New with Pediatric Rashes?

Diaper Rashes

- Most common causes are irritant contact derm and yeast
- Symmetrical, moist appearing pinkness with satellite pustules suggests yeast
- Dermatitic like symmetrical rash that involves contact with soiled areas, frictional creases suggests irritant contact
- Regardless, I suggest zinc oxide barrier cream (Desitin) with each diaper change
- Pick one (go with your gut) and treat
  - Hydrocortisone 2.5% ointment bid
  - Econazole 1% cream bid

Diaper Rashes

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- Pick one (go with your gut) and treat
  - Hydrocortisone 2.5% ointment bid
  - Econazole 1% cream bid
Diaper Rashes- Irritant Contact!

- Diaper rashes are less common in breastfed babies
- Buying “superabsorbent” diapers reduces the risk for diaper rashes
- Cloth diapers can cause diaper rashes that are more vesicular with bullae and erosions
- Interestingly, candida is more common in babies that are being treated with wet wipes
- SPD May/June 2016

Diaper Rashes- Yeast!

Diaper Rashes- Yeast again!

Hand Foot and Mouth Disease

- Causes somewhat annular red-purple-gray patches on hands, feet, and around the mouth sometimes with intraoral lesions
- Previously coxsackie A16 and enterovirus 71 were the most common causes
- Coxsackie A6 has emerged over the past 2-3 yrs as the primary causative agent
- Produces more severe rash with prominent diaper area involvement
- Adults have been getting it
- Commonly produces onychomadesis 1-2 mos later (SPD July/Aug 2016)

Hand, Foot and Mouth Disease
### HFMD and Onychomadesis

- A petechial and purpuric rash has been reported in babies carried in “legs out, forward facing” carriers
- Tends to be on the medial thighs where the pressure is
- Appears that children with a low grade virus are more susceptible - increased capillary fragility
- Not dangerous (JAMA DERM June 2016)

### Tinea Versicolor

- If topicals fail, oral fluconazole 300 mg Q wk x 2 doses is very helpful
- DO NOT USE ORAL KETOCONAZOLE
  - Liver side effects, adrenal gland side effects, medication interactions

### Baby Carrier Rashes

- A petechial and purpuric rash has been reported in babies carried in “legs out, forward facing” carriers
- Tends to be on the medial thighs where the pressure is
- Appears that children with a low grade virus are more susceptible - increased capillary fragility
- Not dangerous (JAMA DERM June 2016)

### Baby Carrier Rashes

- Probably doesn’t go away for most prepubertal girls
- Maintenance treatment is better than as needed treatment (SPD July/Aug 2015)
- My regimen:
  - Clobetasol ointment bid for 2 wks, then once daily for 2 wks, then followup
  - Repeat that course if needed until clear
  - Then clobetasol MWF once daily or elidel once daily for maintenance
  - I see the girls every month until they are clear and then at minimum every 6 mos on maintenance

### Lichen Sclerosus

- Probably doesn’t go away for most prepubertal girls
- Maintenance treatment is better than as needed treatment (SPD July/Aug 2015)
- My regimen:
  - Clobetasol ointment bid for 2 wks, then once daily for 2 wks, then followup
  - Repeat that course if needed until clear
  - Then clobetasol MWF once daily or elidel once daily for maintenance
  - I see the girls every month until they are clear and then at minimum every 6 mos on maintenance

### What’s New with Acne?
Acne

- Happening younger and younger
- Used to be abnormal before age 9, now abnormal before age 7
- Most acne medicines are technically approved for age 12 and up (Epiduo approved age 9 and older)
- Helpful to work through the mail order pharmacies in these situations
  - GenRx- Prugen products
  - YourRx- Allergan products

Food and Acne

- Skim milk appears to be associated with increased acne, but not other milk or dairy
- Diet with a high glycemic index (high carb, high sugar) appears to worsen acne

Changes in Isotretinoin Monitoring

- A number of studies have shown that we have been “over monitoring” with labs for isotretinoin
- New recommendations are to check lipids and LFTs at baseline and then at 2 mos into therapy. If normal, that is all that is necessary.
- No need to check CBC

Topical Acne Meds on the Horizon

- DRM01- topical sebum inhibitor
- FMX101- topical minocycline foam
  - 4%, applied once daily, studies in Israel
- SB204- topical nitric oxide releasing gel that works in antimicrobial and anti-inflammatory ways
- SEB002- topical to work with blue light. Delivers light absorbing gold-coated silica microparticles that are absorbed into the pilosebaceous unit and then enhance the PDT (Practical Derm Oct 2015)

Oral Contraceptive Pills

- Given desire to decrease oral antibiotic use, the use of OCPs has become more appealing
- My counseling routine
  - How to start the pill
  - Weight gain, nausea, mood issues
  - Blood clots, heart attack, stroke
  - Health benefits
  - Timeliness is important

OCPs

- Retrospective review of 2147 patients on OCPs for acne (JDD June 2016)
  - All OCPs help with acne
  - Triphasics probably help a little more than monophasics
  - Non estrogen component matters for efficacy:
    - Drospirenone (Yaz, Yasmin)
    - Norgestimate/desogestrel (Ortho Tri Cyclen, Ortho Cyclen/Mircette, Desogen)
    - Norethindrone/levonorgestrel (Loestrin, Ortho Novum/Seasonale)
**OCPs**

- Typically want to try to avoid OCPs in girls less than 14 yrs old or girls that have had their period for less than 2 yrs
- Rifampin and Griseofulvin are the only antiinfectives that definitely decrease the efficacy of OCPs when preventing pregnancy
- Risk of clots is greatest when a patient is first starting the pill

**Contraindications to OCPs (W.H.O.)**

- Pregnancy
- Current breast cancer
- Breastfeeding <6 wks postpartum
- Age >35 yrs and a heavy smoker
- HTN
- Diabetes with end organ damage
- Diabetes >10 yrs duration
- History of or current DVT/PE
- Major surgery with prolonged immobilization
- Ischemic heart disease or Vascular heart disease with complications
- History of CVA
- Headaches (migraine with focal neuro symptoms at any age or without aura if >75 yrs old)
- Active viral hepatitis
- Severe decompensated cirrhosis
- Liver tumor (benign or malignant)

**Other Hormone Tidbits**

- Progesterone only methods of birth control tend to increase acne
  - Implanon
  - Mirena IUD
  - Progesterone mini pills
- Spironolactone can be helpful in the teenage population, especially if the patient has features or a diagnosis of PCOS

**What’s New with Hemangiomas?**

- Propranolol is still great!
  - 2 mg/kg/day divided TID
  - Always give with food
  - Don’t be afraid if the hemangioma needs it, use it!
  - Typically used during growth period (~8-12 mos of life), but can work even beyond the proliferative phase (SPD May/June 2015)
- Long term studies show no risk of developmental adverse effects or growth impairment at age 4 in pts treated with at least 6 mos of propranolol (JAAD July 2016)
- Topical timolol 0.5% gel forming solution can work for superficial hemangiomas- applied BID

**Infantile Hemangiomas**

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Post Propranolol Recurrences

- Recurrence rate post propranolol is about 25%
- Increased recurrence risk if propranolol is stopped before age 1 and in girls
- Growth hormone treatments can result in recurrences of hemangiomas in late childhood

Other Beta Blockers

- Propranolol vs captopril
  - Propranolol is much better
  - Captopril is not as effective and has increased cardiac side effects
- Propranolol vs nadolol
  - Nadolol 2 mg/kg/day once a day
  - Appropriate to switch to nadolol if child has sleep disturbances with propranolol

What’s New with Hyperhidrosis?

- “Secure” Robinul (glycopyrrolate) wipes
  - Available via an online Canadian pharmacy
- Oral oxybutynin
  - Start with 2.5 mg daily and increase by 2.5 mg daily at 2 wk intervals. Max 12.5 mg daily
- Iontophoresis- Fischer MD1A is best unit
- Topical botox- on the horizon
- Topical oxybutynin- on the horizon

More About Oxybutynin (Ditropan)

- SPD Sept/Oct 2015- oxybutynin for palmpoplantar hyperhidrosis
  - 2.5 mg daily x 1 wk, then 2.5 mg bid x 2 wks, then 5 mg bid
  - Dry mouth
  - Available as 5 mg pills or 5 mg/ml solution
- SPD May/June 2016- Spain- kids/teens
  - Oral robinul not available in Spain
  - 2.5 mg daily and increase by 2.5 mg daily at 2 wk intervals until results are seen
  - Contraindications: bladder/intestinal obstruction, severe ulcerative colitis, glaucoma, myas gravis
  - No monitoring needed
  - Oropharyngeal xerosis is most common side effect

What’s New with Cooties?
Scabies

- In infants, it tends to present as a widespread “dirty” appearing rash with various morphologies-pink papules, urticarial papules, pustules, eczematous patches
  - Check palms and soles for pustules- very typical
- In older kids, presents more typically with increased involvement in webspaces and groin area
- If itch is out of proportion to the rash, consider scabies

Scabies Treatment

- **Permethrin 5% cream**
  - Apply neck down tonight, wash off in am. Repeat in 1 wk
  - All family members have to do it simultaneously
  - Safe down to any age and safe in pregnant women
- **Ivermectin 0.2 mg/kg**
  - Take one dose today and another dose in 1 wk
  - I will use it if rash is extensive, affects face/scalp, or has failed permethrin
- **Precipitated Sulfur-10% in white petrolatum at compounding pharm**
  - Apply bid for 3 days
  - Very stinky, but no resistance has been seen (Winter Clinical Jan 2016)
- Wash all towels, clothes, sheets in hot water
- Vacuum carpet and upholstery
- Anything that can’t be washed should be placed in a closed plastic garbage bag and tied closed for 72 hrs

Warts

- Countless treatment options
  - Liquid nitrogen
  - Cantharidin
  - OTCs
  - Candida
  - Laser
  - Bleomycin
- **Best Thing Ever - WartPeel!**
  - Nucara Pharmacy-Iowa
  - Sal acid + 5FU
  - Magic in a bottle
  - Applied at bedtime under “sticky tape”
  - $89 and worth every penny!
WartPeel

Warts - Alternative Therapies
- Zinc sulfate 10 mg/kg/day (max 600 mg) x 2 mos
  - Complete clearance in 75% of patients
  - Nausea is really bad
- Propolis daily x 3 mos
  - 135 patients - 75% had clearance
  - Avoid if bee allergy
- Valtrix 1 gm daily x 60 days - just 2 cases (JDD Feb 2016)
- Picato: couple case reports on using it for genital warts and epidermodysplasia verruciformis
- Just wait: 200 kids - 65% resolved by 2 yrs, 80% by 4 yrs (SPD Sept/Oct 2015)

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

HPV Vaccines
- 3 approved HPV vaccines
- Some concern about reports of MS, optic neuritis, transverse myelitis
- 10 cases of regional pain syndrome
- 4 reports of premature ovarian failure (possibly an autoimmune reaction from vaccine)

Wart vs Callus/Corn - A Handy Trick
- Press on top of it
  - If it hurts, it is a callus
- Press on the sides of it (squeeze it)
  - If it hurts, it is a wart

What's New with Alopecia Aretata and Vitiligo?
Alopecia Areata

- JAK Inhibitors still appear promising
- JAMA Derm April 2016
  - Topical ruxolitinib 0.6% cream bid case report: hair seen at 12 wks
  - Oral tofacitinib for nail dystrophy associated with alopecia areata
    - 5 patients. Nails improved in all. Hair regrew in 1/3
- Derm News July 2016 - Tofacitinib
  - 10 patients. 6/10 had alopecia totalis/universalis
  - 10/10 had regrowth, 7/10 had >50% regrowth
  - Recurrence is an issue
- SPD Meeting 2016 - Poster - Tofacitinib
  - 13 pts aged 12-17. 5 mg bid
  - 9/13 had clinically significant regrowth; well tolerated
- Ustekinumab has been mentioned
- Simvastatin/ezetimibe (Vytorin)
  - Small 10 patient study showed success (Winter Clinical Mtg Jan 2016)
- Topical ruxolitinib 0.6% cream bid case report - hair seen at 12 wks
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Vitiligo

- 50% of vitiligo patients develop it by age 20
- 25% of vitiligo patients develop it by age 10
- Early onset before age 3 has worse prognosis
- Children are more likely to have segmental vitiligo and they have decreased risk of associated autoimmune conditions
- UVA1
- Red light
- Photocil
- Micrografting
- Gingko biloba 40-60 mg 2-3 times a day 10 mins before a meal
- Xtrac
- Calcineurin inhibitors is better than Xtrac alone (JAAD May 2016)
- Bimatoprost 0.03 (Latisse
- Topical Photocil-activated by sunlight to administer only nbUVB
- Afamelanotide (with nbUVB)
- Simvastatin
- Orencia
- Xeljanz (JAK Inhibs)
- Bimatoprost 0.03%

What’s New with Nevi in Kids?

- JAK Inhibitors
  - Case report of Tofacitinib working (JAMA Oct 2015)
  - Case report of ruxolitinib working for pt with alopecia areata and vitiligo (JAAD Feb 2016)
- Xtrac + calcineurin inhibitors is better than Xtrac alone (JAAD May 2016)
- Bimatoprost 0.03 (Latisse
  - Prostaglandins seem to help by stimulating melanocyte dendricity
  - Study excluded face
  - Low study completion rate (58%) but overall good efficacy with or without mometasone
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

What’s New in General Skin Education for Kids?

- Going to a tanning bed ONCE increases the risk for skin cancer by 40%
- Going to a tanning bed more than 10 times increases the risk for skin cancer by 100%
- If you start going to a tanning bed before the age of 35, you increase the risk for skin cancer by 59% (SPD July/Aug 2015)

Kids Post Transplant

- The number of children undergoing stem cell transplant for various reasons is growing
- Kids post stem cell transplant tend to develop more moles and have higher risk for atypical moles
- They need a FBSE every year

Mosquito Repellants

- CDC recommends getting a spray with one of the following ingredients:
  - DEET
  - Picaridin
  - IR3535
  - Oil of Lemon Eucalyptus
  - Pacamenthane-diol
Mosquito Repellants

- DEET is considered the most effective
- DEET is considered safe in 20-50% strength
- American Academy of Pediatrics recommends using DEET <30% for kids and reapply every 4-5 hrs
- OFF! Deep Woods VIII is the most recommended- contains 25% DEET

Mosquito Repellants

- Picaridin is considered 2nd best to DEET
- 2 products that contain it:
  - Sawyer Picaridin Insect Repellant
  - Natrapel 8 Hour

The End!

- Feel free to contact me with any questions
- lisaswansonmd@gmail.com
Case #1
- 5 month old female presents with new rash on left lateral chest wall and left upper inner arm
- Appears asymptomatic
- Rash consists of teeny monomorphic pink papules on left upper inner arm and left lateral chest wall
- Initial diagnosis: Unilateral laterothoracic exanthem
- Recommendations: Observation and f/u in 3 wks

Case #1
- Pt follows up 3 wks later and rash has become more widespread- torso, proximal extremities
- Still appears asymptomatic
- Nothing on palms and soles
- Rash consists of teeny pink papules and some larger pink papules with a superficial pustule on top
- Revised diagnosis: Viral exanthem vs Eosinophilic Pustular Folliculitis (EPF)
- Recommendations: Clobetasol bid as spot treatment and f/u in 3 wks

“Dermatology? Jeez, the whole profession is ah, just put some aloe on it.”
- Seinfeld

Disclosures
- Speaker
  - Valeant
  - Bayer
- Advisory Board Representative
  - Ranbaxy/Sun
  - Allergan

Lesson Learned from 10 Challenging Cases
Elizabeth (Lisa) Swanson, MD
Advanced Dermatology Colorado
Rocky Mountain Hospital for Children

“Dermatology? Jeez, the whole profession is ah, just put some aloe on it.”
- Seinfeld

Case #1:
“A bruise is a lesson... and each lesson makes us better”
- George R.R. Martin, A Game of Thrones
Case #1
- Pt follows up 3 wks later and rash has continued to get worse- now extensive on torso, arms and legs
- Still seems asymptomatic
- Still consists of pink papules with some larger pink papules with a superficial pustule
- Still nothing on palms and soles
- Diagnosis: EPF
- Recommendations: Biopsy to confirm diagnosis given lack of response to Clobetasol

Pt follows up and rash has continued to get worse- now extensive on torso, arms and legs
- Still seems asymptomatic
- Still consists of pink papules with some larger pink papules with a superficial pustule
- Still nothing on palms and soles
- Diagnosis: EPF
- Recommendations: Biopsy to confirm diagnosis given lack of response to Clobetasol

Biopsy shows changes consistent with eosinophilic pustular folliculitis
- Changes were so classic that dermatopathologist requested permission to use the slides for his teaching deck
- Diagnosis: EPF
- Recommendations: Trial of several different topical steroids
- Clobetasol
- Betamethasone Dipropionate
- Dermasmoothe

Diagnosis: EPF
- Recommendations: Trial of several different topical steroids
- Clobetasol
- Betamethasone Dipropionate
- Dermasmoothe

Pt follows up and rash is unchanged
- Now patient seems itchy and she is failing to gain weight
- Diagnosis: EPF
- Recommendations: Consider trying prednisolone

While we were considering oral pred, the pt’s family sought out a 2nd opinion
- Upon exam, it was obvious to the other provider that the patient had scabies
- Rash resolved completely with permethrin

Don’t let a biopsy result “blind you” and prevent you from considering other diagnoses and properly reevaluating the patient
- If a patient isn’t responding as expected (clobetasol typically works quite well for EPF), the first step is to reconsider the diagnosis. Try to look at it with fresh eyes.
- Learn from the experience. Let it haunt you for a little while. But be better the next time a similar situation presents itself.

“When you hear hoofbeats, think of horses, not zebras”

*Medical Proverb, 1925*
Case #2
- 17 month old healthy boy with h/o eczema presented with 1 wk history of rash on his torso
- Asymptomatic, child was feeling well
- Mom describes the rash as looking “like a cheetah”
- Pt’s rash had a mixture of morphologies. He had some 3-4 mm blue grey macules mixed with 3-5 mm somewhat indented skin colored areas
- Some of the indented skin colored areas had a pinpoint pink papule within them
- Mom said that 2 wks prior, pt had a rash on his torso that was typical of his “dairy rash” that he gets whenever he accidentally has dairy. It only lasted a day.
- DDx included weird viral exanthem, weird PIH/anetoderma reaction to “dairy rash”, atypical lichen planus, PLEVA

Labs done by PCP were normal including:
- CBC
- CMP
- Uric acid
- LDH
- CRP
- PT/PTT
- ESR

Pt followed up 1 week later and rash was unchanged
Skin biopsy was performed

Pathology was read out as “distorted follicle with neutrophilic and lymphocytic inflammation and associated dermal whirled morpheaform collagen thickening”
Case #2
- Given the follicular involvement, I opted to treat it as a weird folliculitis
- Started patient on keflex
- Within 3 days, the rash was clear!

Case #2: Lessons Learned
- Common things are common and can present atypically
- Don’t “psych out” your dermatopathologist

Case #3:
“Sometimes the best diagnostic test is the followup visit.”
- 12 yr old girl presented with 1 yr history of rash on her lower legs
- The spots appear, turn bruise-like, then resolve
- Asymptomatic
- Really worsened after climbing the “Incline” at Pike’s Peak
- On exam, the patient had nontender reticular erythematous-violaceous patches on lower legs and thighs with some violaceous areas that were slightly palpable

Case #3
- Pt complained of mild joint pains in shoulders and knees but no h/o inflammatory changes
- Was having a lot more fatigue which was unusual for her
- Complained of “tingling” sensations in legs but no numbness or nerve issues with arms
- No GI issues

Case #3: Photos
Case #3 - Histopathology
- Had been seen by different dermatologists and had 2 previous biopsies
- Both showed vague changes- superficial and mid dermal perivascular dermatitis without features of panniculitis or vasculitis
- I did an additional biopsy (making sure to sample one of the palpable lesions) which showed the same

Case #3 - Labs
- CBC and CMP normal
- CRP and sed rate normal
- ANA, RF, cANCA, pANCA, antiphospholipid antibody, and cryoglobulins negative
- U/A normal
- PT/PTT/INR normal
- ASO normal

Case #3
- Her rash seemed so characteristic of PAN, but nothing else was supporting that in terms of labs and pathology
- Patient had a thorough eval by peds rheum and peds hematology and everything was normal
- We opted to take a “wait and see” approach

Case #3
- 1.5 yrs after I met the patient (and 2.5 yrs into the rash), the patient came to followup with new whitish skin changes around her left ankle
- The changes were clearly consistent with atrophie blanche and allowed us to diagnose this as livedoid vasculopathy
- Patient was started on baby aspirin daily and compression stockings and all of her lesions have cleared
- She has had recurrence when she stops the baby aspirin so she has had to continue it

Case #3 - Lessons Learned
- If you do an appropriate workup that turns up nothing, it is ok to watch and wait
- Often conditions will declare themselves over time or simply resolve
Case #4

“Never say never.”

- 32 yr old female presented with 2 month history of rash on forehead and scalp
- Previously treated with elidel and fluocinonide by another provider but only worsened
- On exam, the pt had erythematous scaly annular patches on bilateral forehead and extending into left temporal scalp
- Exam was consistent with tinea faciei/tinea capitis

Case #4

- Given that the tinea was involving the face and scalp, the area had been previously treated with fluocinonide, and the patient was an inpatient peds oncology nurse (dealing with immunosuppressed patients), I prescribed Griseofulvin 500 mg bid
- Went over griseofulvin counseling

Case #4 - Labs

- Patient was admitted and monitored by GI/Hepatology service
- Eventually the LFTs started to trend down
- T Bili was slower to trend down
- Nausea persisted for several weeks
- Predicted that it will take 8 wks for her LFTs to normalize
- Ultrasound and hepatitis serologies were done
- Conclusion was that this was Griseofulvin induced liver toxicity
- 1 in a million

Case #4

- Patient returns for followup 4 wks later
- Rash is improved by about 75%
- Patient reports nausea, epigastric pain, and poor appetite for the past 5 days
- Given symptoms, I ordered labs
- Patient was admitted and monitored by GI/Hepatology service
- Eventually the LFTs started to trend down
- T Bili was slower to trend down
- Nausea persisted for several weeks
- Predicted that it will take 8 wks for her LFTs to normalize
- Ultrasound and hepatitis serologies were done
- Conclusion was that this was Griseofulvin induced liver toxicity
- 1 in a million
The remaining dilemma is how to treat the patient. Her tinea is improved, but not clear. We can’t use griseofulvin and we can’t use any oral -azoles or terbinafine with her current liver status. Typically topicals do not work for tinea faciei/tinea capitis, but I opted to try Extina (ketoconazole) foam hoping that it will be effective.
Never say never
- Rare reactions happen
- Evaluate what happened and the decisions you made
- Would you do the same thing again?
- You can’t not use valuable medicines just because these rare things happen

16 yr old male presented for evaluation of acne on face, chest and back
- Also has eczema on his scalp
- Pt has h/o autism spectrum disorder and won’t use anything on his skin because he doesn’t like the way it feels
- Won’t even moisturize or wash his face

The number of children “on the spectrum” is growing every day
- A lot of these children have tactile sensitivity that can make it difficult to manage their skin conditions
- These patients simply will not use some conventional “go to” therapies because of their sensitivities
- Through trial and error, I have figured out several products that pts with tactile sensitivity like

- HPR Plus Foam
- Desonate gel
- Olux E foam
- Enstilar foam
- Kenalog “no touch” spray
- Finacea foam
- And sometimes it’s easier to opt for oral medications

Understand a patient’s sensitivities and try to come up with a treatment plan that they are going to use and be ok with
- If they don’t like the feel of the medicine, they are just not going to use it
Case #6

“IT is common sense to take a method and try it. If it fails, admit it frankly and try another. But above all, try something.”

 Franklin D. Roosevelt

Case #6

- 8 yr old male presented for 2 yr history of skin tightening
- Pt has h/o ADHD, mild autism, fetal alcohol syndrome
- Comes in with his adoptive parents
- Originally started on right inguinal crease and right thigh. Now spreading to right buttock, left post upper arm.
- Sometimes painful
- On exam, pt had several patches of skin that were as firm as granite. No overlying hyperpigmentation
- Family had recently moved from Texas
- Thorough workup including skin biopsy had been done in Texas
- Conclusion was stiff skin syndrome
- Pt had no features of scleroderma, no history suggestive of nephrogenic fibrosing dermopathy, and pathology differentiated it from morphea profunda
- Pt was on MTX at the time of our 1st visit. Family had not found it helpful
- Was trying to do physical therapy

Case #6

- Stiff skin syndrome is quite rare- around 44 reported cases since 1970
- No good treatment besides physical therapy to promote mobility and range of motion
- SPD Meeting 2013 I asked for advice from anyone and everyone that talked to me and I got a few suggestions
  - UVA
  - Gleevac
  - Xeljanz
- After discussion and working with a peds hem/onc colleague, we started gleevac
- Pt was on it for about 1 1/2 yrs. Seemed to slow down the progression, but hard to tell
- Developed peripheral neuropathy due to the gleevac so we stopped it
- Patient relatively rapidly developed new areas of involvement over 3 mos
- Started him on dasatinib July 2015 - similar to gleevac but no risk of peri neuropathy
- At last visit, he had noticeable improvement in previously affected areas
Case #6 - Lessons Learned
- When a condition has no known treatment, just try something that makes sense
- Discuss the pros and cons with family, but usually families are willing to think “outside the box” with these rare conditions

Case #7
- 4 yr old boy with lamellar ichthyosis presented for evaluation of a facial rash
- He had been managing his lamellar ichthyosis with another peds derm provider, but when the facial rash didn’t improve they wanted another opinion
- Rash had been going on for a few months
- Consisted of eczematous patches and pustules
- A previous culture had been positive for staph
- Pt had been treated with keflex x 7 days, azithro x 7 days, nystatin/triam mix, metronidazole cream without success

Case #7
- Even with the changes of the lamellar ichthyosis, it was clear that the facial rash involved the areas around the eyes, nose and mouth
- It was consistent with periorificial dermatitis
- It has responded to oral antibiotics, but recurrence has been a struggle

Case #7 - Lessons Learned
- Just because someone has a rare genetic skin disease, doesn’t mean that they can’t have a very common skin disease superimposed
- If you take the lamellar ichthyosis changes out of it, the diagnosis was relatively simple

“Everyone gets so much information all day long that they lose their common sense.”
Gertrude Stein
Case #8

“Crying helps me slow down and obsess over the weight of life’s problems”.

- Solzhenitsyn's Inside Out

Case #8

- 14 yr old male with severe acne that has failed oral antibiotics and several topical meds
- Starts isotretinoin
- At 2 month followup, pt complained of some “short fuse” like symptoms, but denied symptoms of depression and said that overall he was feeling good on the medicine

Case #8

- 2 wks later the patient’s mom calls in a panic
- The pt has become increasingly more distant and depressed
- He has become more angry
- Mom found on his phone that he texted a friend that he wanted to kill himself

Case #8 - Accutane and depression

- The association between isotretinoin and depression became a big deal when a senator’s son committed suicide while on accutane in 2000
- Since then the association between the two has been somewhat unknown and ambiguous

Case #8 - Accutane and Depression

- From 2005-2015, I had not seen true depression on accutane
- I have seen patients with “short fuse syndrome”
- I had gotten to the point where I was mentioning the possible association with mood issues, but I was downplaying it

Case #8 - Accutane and Depression

- During 2015 and 2016, I have had 3 male patients become severely depressed on accutane. None of them had h/o mood issues prior.
- Appears to happen acutely
- All 3 admitted that they felt the symptoms early on, but had lied to me about it because they saw the improvement the accutane was having with their skin
- 2 of them were cutting themselves unbeknownst to their friends and family
- All 3 of them expressed suicidal ideation
- 1 of them was admitted to the hospital on a psych hold
- All 3 of them stopped the accutane and their mood returned to normal
Case #8 - Lessons Learned

- There is an association between accutane and depression, albeit rare (3 cases in 10 yrs)
- I now always examine the chest and arms in patients on accutane to evaluate for cutting
- Seems there is a bit more risk with males

Case #9

- "Don't waste your energy trying to change opinions...Do your thing, and don't care if they like it."
- - Tim Kev, Bossypants

Case #9

- 4 y/o female with history of skin lesions that started 2 yrs ago
- Initially presented as 1 patch on the left upper arm
- Saw a dermatologist in CO Springs several times and 2 biopsies were done which showed granulomatous inflammation suggestive of infection, but no stains were positive for infection
- Pt was referred to peds ID for further eval and screening bloodwork which showed abnormalities with several immunoglobulins
- Immunology workup at Natl Jewish revealed positive genetic testing for Ataxia Telangiectasia and the patient was diagnosed with AT
- Since the diagnosis of AT, the patient's skin lesions have progressed
- The initial patch on left upper arm has gotten bigger and she has developed a large patch on right leg and smaller patches on chest and left dorsal foot
- Newest patch is on the left lateral canthus and mom is quite concerned that this is appearing on her face

Case #9

- The pt was evaluated at Children's Derm and an additional biopsy was done which also showed granulomatous inflammation with negative infectious stains
- Pt was empirically treated with oral azithromycin for 3 mos and topical ketoconazole without any improvement
- When I saw patient in April, I opted to try treatment with clobetasol on body and elidel to lesion on face
- On exam, pt does not have prominent telangiectasia on the conjunctiva, cheeks or lips (she is only 4 so presumably they will develop in the future)
- She has 2 round pink-purple somewhat firm, somewhat scaly well demarcated plaques on left upper arm and right leg
- 2 pink papules on left dorsal foot and chest
- 5 mm circular pink scaly patch on left lateral canthus
CO Springs biopsies showed granulomatous inflammation concerning for infection

- PAS negative
- AFB was read as positive based on a clump of 30 organisms, however it was suspicious for false positive or contaminant given the "clump" and the fact that there was a similar clump on the edge of the tissue outside of the cells
- IHC was done with lymphoma workup panel including CD1a, 20, 30, 4 and 8. CD1a was slightly low, probably due to underlying immunodeficiency and suspicion for lymphoma based on stain results was low

Biopsy from Children's Derm showed perivascular and interstitial granulomatous dermatitis. No microorganisms seen.

The pt was referred to me because the immunology team wanted more biopsies done for special infectious disease tests

I felt that enough biopsies had been done on this 4 yr old

I felt this was simply cutaneous granulomas that can occur in patients with Ataxia-Telangiectasia

I did not want to do more biopsies on the patient

It can be difficult to go against the "orders" from a referring provider or team, but you have to do what you feel is right

I did end up having the patient attend a dermatology grand rounds and the entire room agreed with me

Even though other doctors treat kids with skin disease, we are the skin specialists for a reason

No one knows dermatology as well as dermatologists

Stand up for your knowledge and your experience (even if you are a young physician)

Practice medicine the way YOU feel comfortable
Case #10
“A pessimist sees the difficulty in every opportunity; an optimist sees the opportunity in every difficulty.”
—Winston Churchill

Case #10
Currently 10 yr old girl with history of psoriasis
- Has had psoriasis since age 5
- Started on scalp
- Now involves scalp, arms, legs, private area
- Has only worsened over time
- Has been treated with topical steroids, elidel, and light therapy

At several points, I mentioned systemic therapy

The treatment of pediatric psoriasis is 10 yrs behind the treatment of adult psoriasis

Discussed systemic options with pt and parents
- Methotrexate
- Enbrel
- Humira
- Stelara

When I mentioned stelara, the pt herself said loudly “That’s what I want”

Parents took some convincing but agreed

Insurance covered it (!)

The patient is a small 10 yr old so she is receiving 22.5 mg stelara every 3 mos

She is 100% clear and she and her family are so happy
She went to camp for the first time
She can go to sleep overs
Friends don’t ask her about all the scaling

Case #10—Lessons Learned
- See the opportunity in a difficult situation to change a person’s life for the better
- Listen to your patients, even the kids!
- Be willing to take a (responsible) leap of faith!

Overall Lessons
- When it comes down to it, we are all just trying to do our best every day
- We all make mistakes, as much as we hate to admit it
- The important thing is that we try hard, we do what we think is right, and we learn from our mistakes and missteps
- Always try to put yourself in the patient’s shoes
“Keep your feet on the ground, and keep reaching for the stars.”

- Casey Kasem, American Top 40

Quotes that I Loved but Couldn’t Fit

- “I like you...you have the boldness of a much younger woman” – Jack Donaghy, 30 Rock
- “Saving lives? She’s one step above working at the Clinique counter” – Seinfeld
- “Some people are worth melting over” – Olaf, Frozen
- “These people are members of a community that care about where they live. So what I hear when I’m being yelled at is people caring loudly at me” – Leslie Knope, Parks and Rec
Image Guided Superficial Radiation Therapy (IG-SRT)

Daniel J. Ladd Jr, DO, FAOCD, FAAD
General Dermatologist, Mohs Surgeon
Tru-Skin Dermatology, Austin, TX

Financial Disclosure
- Medical Director Sensus Center of Excellence
- Chief Medical Officer, SkinCure Oncology

Depths of “Image Guided” technology
- Photography (0.1 mm)
- Reflect.Confocal Microscopy (0.2 - 0.5 mm)
- Optical Coherence Tomography (< 2 mm)
- Epiluminescent Dermoscopy (2 mm)
- High Frequency Ultrasound (5 mm)

Why should we care about IG-SRT?
- Because this is a straightforward new level of care for our patients
- New non-invasive way to “look below the surface” with patients.
- Works well for BCC and SCC
- Accurate Staging of each tumor is now possible before a biopsy is performed or a treatment is chosen

Why should we care about IG-SRT?
- We are the skin cancer experts!
- We love images!
- Mohs is the gold standard for surgical cure.
- Disadvantage: Mohs requires excision to obtain an image of the tumor margins
- SRT is the gold standard for non-surgical cure
- SRT coupled with Sonographic imaging is new

IGSRT enhances patient understanding
- Sharing these images with patients is a powerful tool in bringing patients into the curative process
- Reduces “minimization of skin cancer” by patients.
- Often tumor looks flat after biopsy, patients don’t “see” anything with naked eye and can’t feel much by palpation
IGSRT enhances patient compliance

- Helps patient to “see” the problem in relation to normal skin.
- Becomes a visual guide that SRT or surgery is working or has worked.
- Can use imaging prior to Mohs to assist in planning.
- Improves compliance with treatment.
- This reduces pt refusal to accept treatment.

Overview of imaging depths

- Reflect. Confocal Microscopy 0.2 - 0.5 mm
- Optical Coherence Tomography < 2 mm
- Ultrasound/Sonography 5 mm

Reflect. Confocal Microscopy (0.2 - 0.5 mm)

R. Confocal Microscopy - diagnostic aid, minimal depth/penetration (0.2/0.5mm)

Optical Coherence Tomography (< 2 mm)
Problem: There are no reimbursement codes for OCT. That’s why we really only see it in major research and academic centers.

- R. Confocal Microscopy - 0.2 – 0.5 mm
- Optical Coherence Tomography < 2 mm

Reflective Coherence Microscopy will be reimbursed by MC in 2017!

- 96931 - RCM, subcellular imaging of the skin
- 2017 payment amount $157.41
- Also 96932, 96933, 96934, 96935, 96936
- AADA to comment on undervaluation of this code because compared to 88305, RCM requires more work, time and intensity than 88305.
- Source: AAD Member to Member, Mark Kaufmann, MD, Proposed CMS fee schedule: How will it impact the specialty? Online as of August 26, 2016

RCM Devices approved* by FDA

- MelaFind FDA pre-market approval in Fall 2011*
- Use: Melanocytic lesions, Cost: $7,500
- Non-invasive, painless, performs analysis
- Allows tracking changes in mole
- Measures morphological disorganization
- Offers treatment plan: Positive or Negative
- *FDA 5 year limitation, study re: accuracy

Vivascope 3000, Cost is $50,000 to $60,000

- FDA approved in 2008
- “for review by physicians to assist in forming a clinical judgement”
- Previously contraindicated for use as “a primary means of diagnosis”
- “Handheld microscope”
- We do 40-50 biopsies to detect one melanoma

Literature on US for NMSC

Bobadilla et al, Pre-surgical high resolution ultrasound of facial basal cell carcinoma: correlation with histology, Cancer Imaging, 2008, Sept 22;8:163-72
US reported morphology and thickness of tumors prior to surgery.
Tumor thickness on US and histology was very good (intraclass correlation coefficient) (0.9)
US useful in BCC surgery planning, it can recognize lesions, layers of involvement and vascularity patterns in a non-invasive way.
Literature on US for NMSC

- US can show primary tumor and provide detailed anatomic data. Sonography is currently unmatched by any other imaging technology.

Literature: High-Risk Cutaneous SCC of the Head and Neck

- High Risk Factors for patients with SCC:
  - SCC Skin lesion measures >2 cm
  - SCC Thick or deeply invasive > 4 mm deep
  - Recurrent SCC
  - High grade or desmoplastic SCC
  - Perineural invasion/lymphovascular invasion
  - Near Parotid (ear, temple, forehead, ant. Scalp)
  - Immunosuppressed

Why is SCC depth not taken into account in TNM staging?

Staging happens BEFORE surgery. Our only method to achieve this is punch biopsy. Deep tumor lacks tissue integrity, so deeper punches the specimen can break apart, reducing your accuracy. So the only accurate way to evaluate is with a surgical excision specimen, which occurs AFTER staging. Why should we use US to improve this process?

- Study lower lip SCC
  - In node negative patients avg. depth = 4.2 mm
  - In node positive patients avg. depth = 11.5 mm

Depth matters! 3 SCC studies...Lip, H&N

<table>
<thead>
<tr>
<th>Depth/Thickness of SCC</th>
<th>Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 4 mm</td>
<td>17%</td>
</tr>
<tr>
<td>More than 4 mm</td>
<td>83%</td>
</tr>
<tr>
<td>Less than 5 mm</td>
<td>4%</td>
</tr>
<tr>
<td>More than 5 mm</td>
<td>17.5%</td>
</tr>
<tr>
<td>Less than 4 mm</td>
<td>6.7%</td>
</tr>
<tr>
<td>More than 4 mm</td>
<td>45.7%</td>
</tr>
</tbody>
</table>

TNM Staging and depth, Veness article

- “The current TNM staging system for cSCC does not incorporate important prognostic factors...such as thickness/depth of invasion when assigning T stage.
- Size alone (ie T1 ≤ 2 cm) is the main criterion used.
- With emerging data on high risk cSCC and the risk associated with other factors there is a need to investigate an improved and more prognostic staging system.”

This is exciting stuff because

- SRT-100 Vision could be our window into a better, more precise TNM staging system for SCC
- Tumors can be measured BEFORE they are biopsied
- Shave biopsy reduces our SCC THICKNESS measurement
- Wouldn’t it be more accurate to measure the tumor volume (3 D) prior to biopsy?
- If this was melanoma, where depth is everything, wouldn’t we always want pure unaltered depth measurements?
SRT-100 Vision is first device to bring ultrasound to the office setting

- FDA approved for NMSC and Keloids
- Reimbursement codes already exist
- US Field Placement 77280
- US Tumor measurement G6001
- This changes skin cancer treatment discussions with our patients for the better...

Clinical BCC on L chin

Dermoscopy of the same tumor...

HD Ultrasound image of the same BCC

And another that is measuring exact size

Biopsied BCC clinical photograph
Dermoscopy of biopsied BCC, D. Ladd

SRT-100 Vision sonography of same biopsied BCC - depth measured & documented

SRT-100 Vision combines documentation of tumor volume with EHR documentation of SRT treatments, hence the term IGSRT or Image Guided SRT
BCC

More IGSRT...

Yes, even more images...

Nasal Tip BCC - Ximena Wortsman, MD

Irregular BCC, Ximena Wortsman, MD

“Butterfly” Ximena Wortsman, MD
No other FDA approved device combines radiation & ultrasound (or any other kind of) imaging for NMSC

Other commercial devices that offer imaging or radiation of NMSC
- Sonography Devices - probes are not designed for evaluation of skin because they are for imaging inside the body.
- MPTflex - European
- MelaFind - melanocytic positive or negative
- Vivascope 3000 - assist in clinical judgements
- Esteya, Electronic Brachy
- Axxent, Electronic Brachy
MelaFind Vivascope 3000

- Sorts Melanocytic lesions into "positive" or "negative" categories of disorganization
- "To assist in forming a clinical judgement"
- Previously contraindicated as a primary means of diagnosis

Axxent - EBx

Esteya - Ebx
Summary of IG-SRT

- Ultrasound allows us to evaluate the depth of SCC and BCC prior to biopsy, surgery or SRT.
- Real time visual images bring the patient into the skin cancer staging process.
- US could improve our TNM staging of SCC.
- Depth imaging makes us more comfortable in recommending SRT over surgery.
- Depth imaging makes us more comfortable in preparing our patients for Mohs surgery.
- Offering pts a non-invasive option is the right thing to do.

The End

drladd@tru-skin.com
“Dermatopathologist”
• One of just two ABMS-recognized subspecialties in Dermatology

Board Certified Dermatologist

Board Certified General Pathologist

Dermatopathology Fellowship

Varies with program & background

“Dermatopathologist”

Interesting Trends

Nine geographic areas of USA (1986-2001):
biopsy rate ↑ 2.5x (for those > 65 y/o)
melanoma ↑ 2.4 x

General Practice of Dermatopathology
Crudely Simplified
Biopsy Performed & Fixed in Formalin

Accessioned at Lab

“Grossed In”

“Processing”

- Water and fat removed with successive washes of:
  - EtOH to remove the water
  - xylene to remove the EtOH
Embedding
• Voids in tissue are replaced with paraffin so tissue may be sectioned

Cutting the Block
• Cut into thin (3.5 micron) sections
• Allow light to pass through

Autostainer & Coverslipper
• Makes final H&E stained slide that is ready to “read”

Normal Skin
Epidermis
Stratum Corneum

Dermis
Hair & Seb Glands

Chain of Dependency
• Biopsy
• Courier
• Logging/Intake
• Grossing
• Embedding
• Cutting
• Labeling
• Analysis
• Typing
• Issued Report
• Distribution

Potential for error exists at each point.
You need to provide as many “clues” to the correct diagnosis as you possibly can!

Prevent An Error Before it Transpires
• “Crap in = Crap out”
  – “r/o melanoma” on everything
  – “r/o cancer” on everything
  – “rash” or “D48.5” on everything
• Multiple specimens in the same bottle
• Curetting of a pigmented lesion
• Mismarking shaves, punches, excisions
We use bar codes and rotating ink to prevent tissue misidentification.

I might even promote doing biopsies in "3D":
- Description (or what was Done)
- Diameter (size or extent)
- Diagnosis

Basic Histology
BCC and SCC

“Rule out BCC vs. SCC”
(no other data provided)

How confident would you be, if you were the doctor examining this case?

“Always punch the thickest part of the lesion.”

Pariser et al. DOJ 1999; 5(2):4
The biopsy contained:

An intradermal nevus.

The patient died of - the adjacent melanoma.

Impact of Partial Samplings

- Odds of misdiagnosis on biopsy:
  - Punch Biopsy vs. Excision (OR=16.6, P=.001)
  - Shave Biopsy vs. Excision (OR=2.6; P=.02)

- Misdiagnosis with adverse event:
  (local persistence/recurrence/mets prior to correct dx)
  - Punch Biopsy vs. Excision (OR=20, P=.001)
  - Shave Biopsy vs. Excision (OR=2.4; N.S.)

4 mm Punch Biopsy by Volume
- Assume 4 mm cylinder
  Volume of punch is = 50.3 mm³
- Assume is two 3.5 um ‘silhouettes’ on slide
  “Volume” inspected is = 0.112 mm³

The dermatopathologist is inspecting 1/450th of the overall punch sampling in these terms!!!!

5 cm Excision by Perimeter Analysis
- Assume excision is 1:3.5 ratio (common)
  Circumference is = 11.55 cm
- Assume grossed into 7 pieces each 3.5 um thick
  “Circumference” inspected is = 0.005 cm

The dermatopathologist is inspecting 1/2300th of the overall circumference of the lesion!!!!

TIP: Choosing the wrong biopsy technique may confound results
Case

Dermatofibroma with overlying basaloid induction

Fibrotic and cellular ("busy") dermis above subcutis

Fibrohistiocytic cells intercalated between collagen bundles

Peripheral palisading of nuclei (looks like BCC)

Imagine if a shave biopsy would have been performed to "r/o BCC."

Special Techniques

For Special Situations
Verrucous Carcinoma

- Endophytic
- Unremarkable cytology
- Malignant status derived from behavior and architecture

Verrucous Carcinoma

- Special subtype of SCC
- Mucosa, acral skin, and genitalia
- Eponyms based upon location:
  - Oral – Ackerman tumor
  - Genital – Buschke-Lowenstein tumor
  - Acral – epithelioma cuniculatum
- Medicolegal conundrum if insufficiently sampled (HELP!!!)

Mycosis Fungoides

- Form of cutaneous T-cell lymphoma (CTCL)
- Early forms = thin patches or plaques in “double-protected” areas
- Early disease is difficult to diagnose by histology alone (“patch stage”)

Mycosis Fungoides

- Dx REQUIRES clinicopathologic correlation
- No single test establishes a diagnosis MF
- Average time from onset to diagnosis is 6 years (and ≥3 biopsies)

**TIP:** shave biopsy maximizes DEJ available for inspection - may be useful in early mycosis fungoides!
Bullous Pemphigoid

- #1 immunobullous disease
- Elderly with multiple comorbidities
- Subepidermal blister
- Eosinophils present in the blister cavity

TIP: You can shave off the entire blister and makes examination easier

Prominent spongiosis

- Eosinophilic spongiosis
- Eosinophils in upper dermis and aligned along dermoepidermal junction

Biopsy of Bullous Disease

Immunofluorescence Studies

- “Direct immunofluorescence” (DIF)
  - uses patient tissue and lab antibodies
  - can only be performed on fresh tissue or tissue fixed in Michel medium
  - placement in formalin ruins the tissue

- Useful to study:
  - blistering conditions
  - connective tissue disease
  - vasculitis
Panniculitis

- Inflammation of the deep fat
- Diseases include:
  - erythema nodosum (#1)
  - erythema induratum
  - pancreatic fat necrosis
  - factitial disease (surreptitious injection)
  - other rare diseases

Typical Clinical Image

Erythema nodosum

Markedly widened subcuticular septae

Widened septae with granulomatous inflammation

“Rule Out Panniculitis”

What can you really say in this situation?!?!?!
Stacked Punch Biopsy for Panniculitis

“Rule out alopecia.”

Don’t even get me started.

ALOPECIA PROCESSING

TIP: Don’t shave the hair just trim it short! (it allows the tissue to be oriented easily)

Beware of “Crush Artifact”

TIP: Very nearly all tissue removed from a human being should be sent for analysis

(in my humble opinion)

Lymphoid Proliferations

• B-cell lymphoma often presents as:
  – red to purple nodules
  – middle-aged to elderly
  – single or few lesions on the head/neck

TIP: Very nearly all tissue removed from a human being should be sent for analysis

(in my humble opinion)

TIP: Lymphocytes, especially malignant ones, are sensitive to lateral pressure, and “crush” may render the biopsy useless.
Melanoma was found in 61 cases (0.66%).

One Half is SK
Other Half is Melanoma

5 of 1335 “skin tags” contained a malignancy – 4 BCC, 1 SCC – compared to 6 malignancies in 697 “moles” – is this a reason to require submission of all tissue?

Biopsy from posterior neck of a 34 year old woman.

“Rule out tag.”
This ink can be used in clinical settings as well (and not just Mohs).

Simple Things…

• 10% Neutral Buffered Formalin
  – “fixes” the specimen
  – cross-links lysine residues in proteins
  – CANNOT be used for immunofluorescence specimens

**TIP:** volume 10% NBF should be 10x the specimen volume

Lab Boxes for After Hours Pickups

<table>
<thead>
<tr>
<th>Component</th>
<th>% by Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formaldehyde</td>
<td>37</td>
</tr>
<tr>
<td>Methanol</td>
<td>13</td>
</tr>
<tr>
<td>Sodium Hydroxide (deionized)</td>
<td>5</td>
</tr>
<tr>
<td>Sodium Nitrate</td>
<td>0.7</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>0.4</td>
</tr>
<tr>
<td>Silica</td>
<td>0.4</td>
</tr>
</tbody>
</table>

10% NBF begins to freeze at 31.8°F and is entirely solid at 23.1°F.

**TIP:** Be careful where you position the pick-up box in cold weather!!!!

“Turn Around Time…”

• Research in pharmacy, nursing and medicine demonstrates that errors are associated with:
  – hectic work environments
  – interruptions and distractions

The effect is *independent* of the experience of the practitioner.
Now sit back and wait for your path report!

More tips to follow…

Initial Check

• Is this my patient?
• Does the gross information & technique match?
• Was my history and clinical impression accurate?
• Is this a plausible diagnosis?

No Path Report is Beyond Reproach

No stone tablet.
No burning bush.

This is MELANOMA.
If any other diagnosis returns, it should be treated with great suspicion.

Ultimately, the diagnosis was ALMM 1.6 mm deep.

Sites of Important Information

• Diagnosis
• Comments
But also…
• Gross desc.
• Micro desc.
What are levels or step sections?

- Cutting deeper into the paraffin block
- Allows for inspection of a different area of sample (usually done in sets of 3)
- Useful when one questions the "representative" nature of the sections

Level 1
"r/o NMSC"

Level 3
"r/o NMSC"

Level 3 – Higher Magnification
"r/o NMSC"

BCC

Use of Levels Should be Documented

- Didn’t get expected diagnosis, but levels were performed → maybe reassuring
- Didn’t get expected diagnosis and levels weren’t performed → perhaps they should be!

Step Levels Critical in Detecting the Malignancy
Use of Immunostains or Special Stains

- Immunostains bind immunologic epitopes on tissue that are, in turn, bound by a chromagen.
- Special stains utilize other means to mark tissue:
  - PAS for fungus
  - GMS for fungus
  - Gram stain (Brown Brenn) for bacteria
  - Fite or AFB stains for acid fast bacilli
  - Colloidal Fe stain for mucin

Case
- 79 year-old man
- “r/o NUB” on chest

Is this basal cell carcinoma?

Melan A stain for melanocytes

Immunohistochemical Staining

BerEp4

Immunohistochemical Staining

BerEp4

Cytokeratin 7
First Stage - Mohs’ (Frozen Section)

Re-Excision

Re-excision IHC Studies

Re-excision IHC Studies

Special Stains for Infection

• Insensitive for some infectious disease:
  – sporotrichosis (organisms rarely seen)
  – cellulitis (organisms rarely seen)

In most situations a culture is more sensitive. Best to do both if infection is a possibility.

• Special stains showed NO organisms
• Culture grew a dimorphic fungus
Where do you find stains reported in a histology report?

Margins

There are important things understand regarding limitations that exist in the analysis of margins.
Where do you find information on margin status?

- Usually present in several places upon a report (diagnosis, micro, comments)

Oriented Specimens

- Suture or nick marks a specific position
- Examiner can provide a more specific location of any residual tumor

Complete extirpation should not be "assumed" particularly when the margins are reported to be narrow.

Providing actual measurements is emerging as the preferred standard.

"Breadloaf" Sections

Allow for inspection of well less than 1% of the overall margin.

Thank you.
Male and Female Pattern Hair Loss

Craig L. Ziering, DO, FAOCD, FISHRS
Beverly Hills, CA
AOCD Fall Meeting
September 17, 2016

Causes of Male Pattern Hair Loss

• DHT, a key factor in male pattern hair loss, is a substance found in the body that may contribute to shortening the growing phase of hair, causing hair follicles to get smaller and smaller, until there are fewer visible hairs left.

Disclosure

• R & D for Restoration Robotics

Causes of Female Hair Loss

• Anemia
• Thyroid Disease
• Excess Androgens
• Psychological Stress
• Traction Alopecia
• Crash Dieting
• Enlarged Prostate
• Surgery Stress
• Auto-Immune Disorders
• Severe Illness
• Genetics

Types of Female Hair Loss

Ludwig I-1: The central parting of a woman with no hair loss.
Ludwig I-2 I-3 I-4: The width of the parting gets progressively wider indicating thinner hair along the center of the scalp.
Ludwig II-1 II-2: Diffuse thinning of the hair over the top of the scalp.
Ludwig III: A woman with extensive diffuse hair loss on the top of the scalp, leaving thin strands above the crown.
Ludwig Advanced: A woman with extensive diffuse hair loss on the top of the scalp, leaving thin strands above the crown.
Ludwig Frontal: A pattern of female hair loss that is described as "frontal accentuated." This means there is more hair loss at the hair parting instead of just in the top middle of the scalp.
Hair Restoration Options:

Non-Surgical and Surgical

Hair loss is progressive. If we are going to add hair surgically, we still need to understand the importance of keeping your native hair.

Non-Surgical Options

1. Oral Tablet: Finasteride (5mg available for post-menopausal females)
2. Topical Foam or Liquid: Minoxidil
3. Scientific: Laser Therapy (LLLT)
4. Natural Supplement: Viviscal Professional
   • ACell/PRP and SMP

Finasteride

Z-Pro: Finasteride 1mg

- Finasteride is a prescription drug that prevents the conversion of testosterone to dihydrotestosterone (DHT) in the body.
- Specifically used to treat hair loss and male pattern hair loss on the vertex and the anterior mid-scalp area.
- Suitable for men and post-menopausal females

Less than 1.8% have shown minimal sexual side effects within the first 2 to 3 weeks

Minoxidil 5%

SUGGESTED USE:
- Apply Minoxidil solution twice daily
- Towel dry or blow dry hair before application
- Apply directly onto the scalp
- Wash hands after application
- Apply 5 minutes before using styling aids
- Do not shampoo or swim for 4 hours after application
- Let solution dry before going to bed

Topical Hair Loss Treatment Studies show that at 48 weeks of use, Minoxidil hair loss medication stabilizes hair loss in over 70% of men and approximately 80% of women.

Acts as a Vasodilator that helps increase blood circulation to the hair follicle.

* During the first 2-4 weeks of use, excess shedding may occur
3  Laser Therapy
LLLT

Low Level Laser Therapy technology harnesses light energy and emits it from a laser diode that penetrates the scalp and invigorates the cells that deliver nutrients and oxygen to hair follicles.

The scientific term for the process is called "photobiostimulation" (PBS).

1) An increase in ATP (Adenosine Triphosphate) and protein synthesis,
2) Improved cell proliferation and eliminates oxygen free radicals,
3) Reinvigorates the sebaceous gland and strengthens the erector pili muscle
4) Increased blood circulation

3 Laser work to stimulate the scalp and provide energy to the follicles in the resting and shedding phases of the hair cycle. Improved respiration at the cellular level revitalizes hair to grow thicker and healthier.

Lasers work to energize dormant and miniaturized hair follicles. This type of laser has been thought to increase blood circulation, improve cellular activity, and reverses the normal deterioration of cells. Hair follicles with improved circulation of blood receive more nutrients, resulting in healthier hair.

SUGGESTED USE:
- Months 1-6: 3 times per week for 30 minutes each
- Months 7-12: 2 times per week for 30 minutes each
- After 1 year: 1 time per week for 30 minutes

Results and time frames may vary per patient, so increase usage with additional shedding or for increased effectiveness.

4  Viviscal Professional

Viviscal Professional 100% drug free supplements are scientifically formulated with the proprietary marine protein complex AminoMar and the important nutrients Biotin and Apple Extract to nourish thinning hair and promote existing hair growth from within.

"Viviscal" strengthens and replenishes vital nutrients in thinning hair. It is a natural dietary supplement, safe for both men and women, with clinical studies that support its use for promoting existing growth. I find it particularly useful for my patients who want to bring their hair back in balance during periods of everyday stress.” - Dr. Craig L. Ziering, DO, FAOCOD

Proof Positive:
- 75% of studied participants observed a significance decrease in hair loss
- 92% of alopecia patients showed re-growth of permanent hair after 6 months
- 83% of alopecia totalis patients showed re-growth of permanent hair after 4 months
- 15% of study participants showed partial re-growth
- 93% of customers would recommend it to a friend
- 125% increase in terminal hairs after 6 months
- 75% saw an increase in overall hair volume
- Baseline 0-90 day subjects showed a significant increase in the number of terminal hairs and diameter

4  Viviscal Professional

The only OTC product with clinical studies to back up data

Viviscal Professional

The only OTC product with clinical studies to back up data

Before / After 6 Months:
Viviscal Professional and Laser Cap Treatment

Combined Non-Surgical Therapy

Before After 6 Months:
Viviscal Professional and Laser Cap Treatment
What is SMP?

- Similar to a tattoo but with different ink and smaller needles
- Gives the appearance of 2D hair follicles “shaven hair follicle”
- Can be used in patients:
  - With various forms of alopecia
  - Using hair system or hair concealers (Toppik, SureThik)
  - Previous transplant scars (both FUT/FUE)
  - Male or female pattern hair loss

SMP - Scalp Micro Pigmentation

ACell / PRP (Platelet Enriched Plasma)
Surgical Options

Trichosculpture

- The artistic arrangement and redistribution of hair utilizing the most advanced technology and surgical techniques in combination with the classical principles of art to create a natural, aesthetically pleasing hair restoration result

Trichosculpture

- Involves recognizing the entire three-dimensional qualities of the head and face
- Combines classical principles of design with a patient’s unique bone and facial structure to create a custom hair restoration that extends way beyond the simple transfer of hair used by other hair restoration techniques
- Gives you more balance, symmetry, volume, and depth to the crown
- Makes the absolute most of the patient’s donor hair

Ziering Zones

Hairline
- 800-1200 grafts
- Approx. Area = 30 cm²

Frontal 1/3
- 1500-1800 grafts
- Approx. Area = 70 cm²

Frontal 1/2
- 2000-2500 grafts
- Approx. Area = 100 cm²

Hairline and Temporal Peaks
- 1200-1500 grafts

Male Zones 1-4

Complete Crown
- 1400-1750 grafts
- Approx. Area = 80 cm²

Partial Crown
- 800-1250 grafts
- Approx. Area = 50 cm²

Expanded Crown
- 1800-2250 grafts
- Approx. Area = 100 cm²

Posterior 2/3
- 2300-2750 grafts
- Approx. Area = 130 cm²

Male Zones 5-8
Ziering Zones

Female Zones 1-3

Mild
800-1200 total grafts

Moderate
1500-2000 total grafts

Severe
2000-2500 total grafts

Female Zones 4-6

Ziering Zones

4 Surgical Steps

1 - Donor Harvesting
2 - Micro-Dissection
3 - Recipient Site Creation
4 - Graft Placement

Treatment Area Design

• Recipient Plan
• Donor Plan

Treatment Area Design is An Art

1 - Donor Harvest Options

• Microscopic Follicular Unit Transplantation (STRIP)
• Follicular Unit Extraction (FUE)
• Robotic FUE
The Ziering Tunnel Technique eliminates tension on the donor closure area. A strip of tissue is removed from the donor zone in the back of your head where your hair is genetically programmed to grow for life and then the individual follicular units are dissected underneath a Ziering Scope®.

Perform by the Doctor

Donor Harvest
STRIP / MFUT

High-resolution digital imaging of each follicular unit for rapid, micron-level targeting accuracy

Image-guided robotic alignment for speed and precision beyond manual techniques

Minimally invasive dissection Delivers clean, accurate, healthy, intact grafts every time with nearly undetectable harvest sites

Computer sensors monitor patient breathing and movements.

Alternative FUE Donor Styles:
Hair Above Previous Scar Untrimmed

Alternative Donor Styles:
Midriff Cut

No Linear Scarring with FUE

Total Grafts: 2017
Total Grafts: 2263

Alternative FUE Donor Styles:
Midriff Cut

Microscopic Dissection of the Grafts

The Ziering Scope was developed to gain the best yield from the patient's finite donor area, ensuring that these grafts remain healthy and vital while the ZM Hair Technicians separate them into their natural, transplantable follicular units of 1 to 4 hairs.

(On average, person has 2.4 hairs per follicular unit graft)

Natural follicular unit grafts
1, 2, 3 and 4 hair follicular unit grafts

Are your grafts “Ziering Certified”?-

All patient grafts are carefully dissected under a microscope by a Certified Ziering Technician. Whether it is FUT (Strip) or FUE, all grafts are certified before being placed into your scalp.

Ziering Certified Grafts:
Healthy surrounding tissue still intact

Ziering Certifid Technicians have the most combined years of experience than any other hair transplant practice in the world.

Recipient Site Creation

Ziering Blade

- Allows grafts to be placed closer together, giving GREATER DENSITY in one session.
- Diamond shaped design allows wide center recipient sites which PROTECTS the grafts and prevents compression of the grafts.
- Smaller incisions for diminished scabbing & quicker healing.
- UNPARALLELED PRECISION and gives control over the ANGLE, DIRECTION & ORIENTATION of each incision.

Recipient Site Creation

Male Patient: Immediate Post-Op

Graft Placement

Our staff have been hand selected and trained by a Ziering Certified Doctor.

Post Op Healing

2,175 Follicular Units (5 days Post Op)

Recovery times vary from patient to patient, redness of the scalp can last between 5-10 days. There is a less than 10% chance of swelling, which normally occurs between days 3 and 5.

The optional Ziering Post Operative Package includes:

- Complete Graftcyte Kit
- Reusable Ice Pack
- Comfort Pillow
- 6 Laser Healing Sessions which can help speed up the recovery time, thus getting you back to your normal everyday activities sooner.
The Award Winning
ZIERING Whorl*
• The Ziering Whorl is a hair pattern classification system and an advanced surgical technique for restoring bald spots based on a scientific study with 534 patients.
• There are 5 discernible hair growth patterns: S, Z, Double S, Double Z and Diffuse.
• Once the pattern is identified, the recipient sites are made, recreating a patient’s natural whorl pattern and working from the inside of the whorl outward to prevent the common and dated bull’s eye results.
• This technique gives a patient a denser, more natural looking result and represents the new standard for bald spot restorations.

*Dermatological Surgery Journal, August 2004

Hair Growth Progress
2,515 Follicular Units
Before 4 Months Post-Op 10 Months Post-Op

Hair Growth Progress
2,705 Follicular Unit Grafts
Before 3 Months After 9 Months After

Hairline Restoration
5 Months Post-Op: 1,924 Follicular Units

Hairline Restoration
Before After
12 Months Post-Op: 3,000 Follicular Units

Hairline Restoration

Female Restoration
Traction Alopecia
4.5 Months Post-Op: 2,657 Follicular Unit Grafts

Female Restoration

Bi-Temporal Recession occurs in approximately 80% of females with pattern hair loss.

6 Months Post-Op:
1,856 Follicular Unit Grafts

Female Restoration

9 Months Post-Op: 2,724 Follicular Units PLUS Finasteride

Ziering Whorl
4 Months Post-Op: 1,500 Follicular Units

Ziering Whorl

14 Months Post-Op: 2,669 Follicular Units

Hairline & Crown Restoration

3 Months Post-Op: 2,724 Follicular Unit Grafts PLUS Finasteride

Ziering Whorl

Before After

Before After

Before After

Before After

Before After
Osteopathic Continuous Certification (OCC)

American Osteopathic Board of Dermatology
Lloyd J Cleaver, DO, FAOCD
September 17, 2016

Disclosures
- No Financial Disclosures

Learning Objectives
After this presentation, you will:
- Identify which AOA body oversees the certification and recertification policies and procedures.
- Evaluate why continuous physician assessment is needed.
- Review OCC’s goals and its components, which only includes one new component.

Bureau of Osteopathic Specialists (BOS)
- Organized in 1939
- Official certifying body of the AOA
- All certification is granted by the AOA
- Oversees and implements all certification and recertification policies and procedures
- Oversees development and implementation of OCC

AOA Specialty Certifying Boards
- Anesthesiology (1956)
- Dermatology (1945)
- Emergency Medicine (1980)
- Family Physicians (1972)
- Internal Medicine (1942)
- Nuclear Medicine (1974)
- Neuromusculoskeletal Medicine (1977)
- Neurology & Psychiatry (1941)
- Obstetrics & Gynecology (1942)
- Otolaryngology & Ophthalmology (1940)
- Orthopedic Surgery (1978)
- Pediatrics (1940)
- Pathology (1943)
- Preventive Medicine (1982) – Most Recent
- Physical Medicine & Rehabilitation (1964)
- Proctology (1941)
- Radiology (1939) - First
- Surgery (1940)
Types of AOA Board Certifications

- Primary (General) Certification
- Certification of Special Qualifications (CSQ)
  - CSQ becomes primary or DO can maintain both primary and CSQ certifications
- Certification of Added Qualifications (CAQ)
  - Must maintain primary and CAQ
  - DERMPATH, MOHS, PEDS DERM

AOA Certifications

- Primary Certifications Offered: 28
- CSQs Offered: 22
- CAQs Offered: 37
- 18 Boards

Standards Review Process

Through the process, the BOS provides:

"the public with a dependable mechanism for identifying practitioners who have met particular standards"*

*Standards for Educational and Psychological Testing, American Psychological Association, 1985

Influencing Factors on the Development of OCC

- Allopathic MCC
- AOA CAP Program
- Performance Improvement Initiatives
- CMSS Conjoint Committees
- IOH Reports on Quality Care
- FSMB and MOL
Institute of Medicine Reports

ABMS - Current

22 Boards
MOC
Current discussion regarding MOC

Patient Expectations of Physicians
Gallup Survey

Maintenance of Licensure

• Federation of State licensure Boards
• "Top of your head" survey
• State legislature develop laws
• CMS recommends

Why OCC / MOC?

• Responsibility of the profession to the public
• Maintain competence
  – Continuous improvement
• Practice performance activities will encourage physicians to reflect, assess, and learn, improving their practice
• Assessment drives learning

Continuous Certification Goals

• Ensure high standards for patient care
• Provide physicians with the means to continually assess and improve their abilities
• Assure stakeholders that physicians are being assessed by reliable and valid measures
• Transparent to public and communicate information about physicians' competence
## Terminology

- Consistency in terminology is important.
- For example:
  - Time-Dated Certificate
  - Non Time-Dated Certificate
  - No such thing as “Lifetime” Certificate

## Non-Time-Limited Certifications

- OCC is voluntary
- Extra credential
- Certificate show above and beyond
- Will NOT lose your certification, even if you don’t pass
- Will NOT lose your licensure
- States May Require MOC or OCC

## AOBD OCC PLAN

- Certified physicians are committed to lifelong learning, higher standards and to practicing the highest quality patient care. The health care system in the United States is evolving, and the requirement that physicians maintain certification by passing a regular examination model is no longer the competitive standard, or the standard demanded by the public.
- With the advent of more rigorous quality models, the American Osteopathic Association (AOA) and its entire associated specialty certifying boards, under the direction of the Bureau of Osteopathic Specialties (BOS) has developed Osteopathic Continuous Certification (OCC) to help meet new and evolving industry and regulatory requirements.
- The BOS has mandated that the AOBD implement OCC for Dermatology by January 1, 2013. Diplomates holding a time-dated certification will be required to participate in all components of OCC to maintain certification beginning January 1, 2013.
- Diplomates holding a non-time-dated (formerly referred to as lifetime) certification will not be required to participate in OCC at this time. However, they are strongly encouraged to participate in OCC, particularly as more states begin to require an ongoing certification process to maintain licensure.
- The AOBD uses a 10 year OCC complete cycle, with 3 year CME cycles.
- Non-compliance with OCC may lead to a loss of board certification.

## OCC Philosophy

- The AOBD recognizes the following:
  1. A continuous quality improvement process in patient care promotes the identification of opportunities to improve patient care, the development of methods to address identified quality gaps in patient care, and the implementation of plans to improve and re-measure patient care.
  2. Augmenting the certification process with a continuous quality improvement process provides physicians with the opportunity to evaluate and improve their knowledge base, facilitating the incorporation of evidence-based medicine into their practices.
  3. There is a growing expectation by public governmental agencies, licensure bodies, health plans and employers for an Osteopathic continuous certification process.
  4. Osteopathic continuous certification will ultimately provide better patient care and a consistent method for the evaluation of osteopathic dermatology care nationally.

## OCC Components

- Certified osteopathic dermatologist with time-date certificate
  - five (5) components of OCC to maintain certification
    1. Unrestricted Licensure;
    2. Lifelong Learning/CME;
    3. Cognitive Assessment (re-certification examination);
    4. Practice Performance Assessment and Improvement (OCAT);
    5. Continuous AOA Membership
- As a board certified dermatologist, you are already participating in four of the five components.
- Component 4 – Practice Performance Assessment and Improvement is the only NEW requirement for maintaining certification through OCC.

## Osteopathic Continuous Certification (OCC)

- As of Jan. 1, 2013, all AOA boards have implemented a continuous certification process for diplomats (OCC)
### Osteopathic Continuous Certification (OCC)
- Required for all diplomates with time-limited certifications
- Uniquely osteopathic
- Flexible to meet your unique practice needs
- Nationally recognized
- Five components, with core competencies integrated throughout

### Core Competencies
Incorporated into each Board's OCC Process
- Osteopathic Philosophy/Osteopathic Manipulative Medicine
- Medical Knowledge
- Patient Care
- Interpersonal and Communication Skills
- Professionalism
- Practice-Based Learning and Improvement
- Systems-Based Practice

### CMS Conditional Acceptance of OCC
- CMS conditionally qualifies the American Osteopathic Association for participation in the 2012 Physician Quality Reporting System Maintenance of Certification Program Incentive.
- CMS will be “Conditionally Qualifying” boards pending verification that technical requirements are met.

### CMS Requirements
**Physician Quality Reporting**
- Quality measures
- Submit data for 12 month reporting period
- Either as individual or member of selected group practice

**AND…**

### CMS Requirements
**…AND**
- More frequently than is required to qualify for or maintain board certification:
  - Participate in OCC/ MOC Program
  - Successfully complete a qualified OCC/ MOC Program practice assessment

### OCC Component 1
- **Unrestricted Licensure**
  - Valid unrestricted license to practice medicine in one of the 50 states or Canada
  - Adhere to the AOA’s Code of Ethics
**Component 1: Unrestricted Licensure**

- AOA board certified dermatologists must hold a valid, unrestricted license to practice medicine in one of the 50 states or territories.
- Adherence to the AOA’s Code of Ethics is required.
  - Candidates will attest to meeting this requirement once in each three year CME cycle. This is done by registering with the board every 3 years in Canvas and uploading necessary forms.

**OCC Component 2**

- **Lifelong Learning**
  - Minimum of 120 credits of CME during each three-year cycle (two boards require 150 credits)
  - Minimum of 50 specialty credits must be in the specialty area of certification
    - As applicable, 25% of specialty credits must be in each CAQ subspecialty focus area

**CME**

- 50 hour specialty specific CME is required by AOA and AOBBD
- 25 of those credits must be obtained through the AOCD per 3 year cycle
- 120 hours is a requirement of the AOA to continue membership which is needed to continue certification

**AOA CME Requirements**

- 120 CME Credits
- 30 1-A Credits
- 60 Specialty CME Credits 25 must be AOCD
- CAQ Specialty CME Credits (as applicable)

**OCC Requirements for Diplomate**

- Component 2
- Lifelong learning/continuing medical education
  - Fulfill a minimum of 120 hours of CME credit during each 3-year CME cycle
    - 50 credit hours must be in dermatology
    - 25 credit hours must be through the AOCD
    - CAQ’s have 50% requirement or 25hrs.
    - If you hold more than 1 CAQ this is reduced to 13hrs./CAQ
    - Specialty CME must be presented by AOA or ABMS certified in the specialty topic being presented
    - CME has been removed from AOA membership requirements

**OCC Component 3**

- **Cognitive Assessment**
  - At least one psychometrically valid and proctored examination through the period of certification
  - Must assess a physician’s specialty medical knowledge as well as core competencies in the provision of health care
Component 3: Cognitive Assessment

- Every 10 years, time-dated certificate holders participating in OCC must successfully complete the AOBD OCC Cognitive Assessment Examination (recertification examination).
  - Psychometrically valid exams
  - Assess dermatology knowledge
  - Assess core competencies in the provision of health care.

OCC Component 4

- Practice Performance Assessment (PPA) and Improvement
  - Diplomates must engage in continuous improvement through comparison of personal practice performance measured against national standards for his or her medical specialty

OCC Component 4

- Practice Performance Assessment (PPA) and Improvement
  - Has been challenged in the MOC by class action suit and currently the ABIM has put it’s PPA on hold for two years.
  - The AOBD supports removal of the PPA requirement and if the BOS continues this requirement will request changing format and avoid O-CAT

Component 4 library

- Different vendors offer PPAs — Costs vary by vendor
- Designed to be relevant to your individual practice. Some examples:
  - Atopic dermatitis
  - Melanoma
  - Acne

General Process for Component 4

- Physician submits data
- Quality improvement data (CAP, Hospital, etc.)
- Patient surveys
- Board reviews
- Data against national benchmarks
- Physician receives report with recommendations for improvement

Component 4: Practice Performance Assessment and Improvement (PPA)

- Each physician in OCC must engage in continuous quality improvement through the evaluation of their personal practice performance and development of quality improvement plans.
- The AOBD has several different, chart based, online modules available through the AOA O-CAT program. The completion of one PPA module will be required every 5 years in the cycle (i.e. one PPA module completed during years 1-5 and one PPA module completed during years 6-10).
- Participants will also be required to complete one Communication module (available through AOA O-CAT) every 5 years in the cycle (i.e. one communication module completed during years 1-5 and one communication module completed during years 6-10).
OCC Requirements for Diplomate

- Component 4:
  - Practice performance assessment and improvement (O-CAT, self-assessment, education thru CME, AAD MOC Modules, patient survey, Physician survey)
    - Requires diplomates engage in continuous improvement through comparison of personal practice performance measured against national standards for his or her medical specialty.

CME for OCC

- CME Credit given for
  - Completion of 4 phases of a PPA Module (10 CMEs)
  - Completion of Communication Module (10 CMEs)
  - Recertification Exam

OCC Component 5

- Continuous AOA Membership
  - Membership in the professional osteopathic community provides physicians with online technology, practice management assistance, national advocacy for DOs and the profession, professional publications and CME activity reports and programs

Limited Scope Practice

- Diplomates devoting 90% or greater of time in clinical practice areas outside their primary certifications may propose and submit practice performance (Component 4) data specific to their area of clinical practice

  - The format of the data for the module relative to clinical practice must be submitted for the certifying board approval prior to participation.

AOBD OCC PHASE IN

<table>
<thead>
<tr>
<th>Certification Expiring</th>
<th>Component 4 Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013-2016</td>
<td>No Component 4 Requirements</td>
</tr>
<tr>
<td>2017-2019</td>
<td>One Activities Each: One Practice Performance Assessment and One Communication Module on OCAT</td>
</tr>
<tr>
<td>2020 and Beyond</td>
<td>Two Activities Each: Two Practice Performance Assessment and Two Communication Module on OCAT</td>
</tr>
</tbody>
</table>
Core Competencies

1. Osteopathic Philosophy and Osteopathic Manipulative Medicine
2. Medical Knowledge
3. Patient Care
4. Interpersonal and Communication Skills
5. Professionalism
6. Practice-Based Learning and Improvement
7. Systems-Based Practice

Interpersonal & Communication Skills

- Physicians are expected to demonstrate
  - interpersonal and communication skills
  - establish and maintain professional relationships with patients, families, and other members of health care teams.

OCC is NOT Pass/Fail

- It is about practice performance and excellence
- How your clinical practice compares to national benchmarks and your peers
- Designed to help direct your self-learning

Communication

- Most people think they communicate well
- Always room for improvement

Research shows

The longer a physician is in practice the more his or her communication skills deteriorate.

Communication

Affects:
- Patient Safety
- Patient Care
- Patient Retention
- Patient Referral
- Risk Management
- Malpractice
- Staff performance
Failure in Communication
Can occur at many levels
• physician to patient
• staff to patient
• physician to physician/healthcare team
• patient to physician/staff
• third-party payor to healthcare team

OCC Pathways
• There are three (3) pathways in which a diplomate may meet this requirement based on their professional activity.
  • Full Scope Clinical Practice
  • Limited Scope Practice (must provide documentation to board verifying limited practice)
  • Clinically Inactive Physicians

Limited Scope Practice
• Diplomates devoting 90% or greater of time in clinical practice areas outside their primary certifications may propose and submit practice performance (Component 4) data specific to their area of clinical practice
• The format of the data for the module relative to clinical practice must be submitted for the certifying board approval prior to participation.

Component 4 Vendors
• OCAT
• Other options that AOBD is pursuing
• Write your own PPAs (Practice Performance Assessment Modules)

O-CAT
Program Goals:
• To embed knowledge, hone skills, apply behavior
• Online training takes place over a minimum of 6 months
• Series of short "module-ettes"
O-CAT Topics

- Fundamentals of Communication
- Medical Motivated Sequence
- Listening
- Patient Safety and Communication
- Improving Patient Compliance
- Health Literacy
- Ask Me Three
- What a Difference a Word Makes

O-CAT Topics

- Emotional Labor
- Projecting Empathy
- Language and Culture
- Difficult Topics
- Statistical Literacy
- Diagnostic News Delivery
- Communicating Osteopathic Philosophy

Clinically Inactive Practice

- Physicians eligible:
  - See NO clinical patients OR
  - Do not supervise residents on patient management OR
  - Unemployed
- Attestation required
- Board will offer different Component 4 criteria
- AOA will report clinically inactive status to 3rd parties (employers, credentialers, etc.)

Clinical Performance Assessment Tool

- Fulfill Component 4 utilizing AAD’s module
  - OCAT
  - Modules include:
    - Acne
    - Atopic Dermatitis
    - Melanoma
    - Biopsy PI CME

Patient and Peer Surveys

- AAD has surveys available to be utilized through their systems
  - Patient Communication Survey
  - Peer Communication Survey

Create your own survey
Self Assessment Modules

SRC was asked to provide the criteria for an acceptable Self Assessment Module.

SAMs are:
• Objective
• Time framed
• Measureable
• Reportable
• Actionable for improvement

Performance Improvement Module
Requirements of ABMS Board & AOCD

• Evaluation of practice performance completed twice in ten year
  – Peer and communication survey
    • At five years
    • At 10 years
  – Practice Assessment/quality improvement
    • Twice per ten-year cycle—at 5 years and 10 years
    • Chart abstractions sent in to sponsoring organization for feedback

Quality Reporting Systems

• AAD PQRS (Physician’s quality reporting system)
• AOA PQRS/O-CAT
  – Eligible for bonus for 2011 and 2012 reporting measures
  – 2015 will be penalized for not meeting measures

Measures

• Melanoma: Continuity of Care Recall System (#137)
• Melanoma: Coordination of Care (#138)
• Overutilization of Imaging Studied in Stage 0-1A Melanoma (#224)
Est. Anticipated Physician Cost for OCC

- $1800 fee for examination per 10 year cycle
- CME cost varies
- O-CAT cost $295/2 years 2 times/10years
- Yearly PQRS may require more
- Maintenance of Certification Fee $300 per 3 years or $900 for 3 cycles or 9 years
  - Late fees if not registered on time (April 15)
  - Non AOCD members fees are more

Questions / Concerns?

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Frequently Asked Questions

- Who is required to participate in OCC?
  - All time-limited certificate holders will be required to participate in OCC.

- Can I remain certified if I do not participate in OCC?
  - No. By choosing not to participate in OCC you are voluntarily foregoing the rights to your board certification.

- Do I need to register in order to participate?
  - Yes. Every diplomate must complete a registration application as provided by the AOBD, submit a registration fee, and be approved before proceeding with the OCC process. Separate application and fees are required for the Cognitive Assessment Examination (Component 3).

- What happens if I hold a time limited certificate and I choose NOT to participate in OCC?
  - No. If an individual is required to participate in OCC (i.e., has a certification with an expiration date), and he or she does not comply with the process, their certification is at risk. There is an appeal process and a remediation process, but ultimately, failure to comply may lead to a loss of certification, just as failure on the re-certification examination would lead to loss of board certification.
Frequently Asked Questions

• I have a "lifetime" (not time dated) board certification. Must I register for AOBD OCC?
  – No. If you have a non-time-limited certification, you will not be required to participate in OCC at this time. However, the AOA strongly encourages your voluntary participation. The Federation of State Medical Boards (FSMB) has agreed to accept OCC for Maintenance of Licensure (MOL). If you do not participate in OCC, you may have additional requirements for MOL as prescribed by the state(s) where processed.
• I have a restricted license. What happens to my AOA board certification?
  – Your certificate will expire December 31 of the tenth year after issue (e.g. a 2004 certificate expires 12/31/2014). You must PASS the examination no later than the year of expiration of your certificate. You MAY take the examination one year before the expiration of your certificate. You must take the re-certification examination within the last two years of your OCC cycle (i.e. year 9 or 10).
• I don't currently practice in my field of certification. How can I meet the OCC requirements?
  – The AOA has developed an online platform that will be accessed through Osteopathic.org in order to track the progress of an OCC cycle. There will be an OSCAT subscription fee of $295 for 3 years.

Frequently Asked Questions

• What components need to be completed before I can take the exam?
  – Prior to completion of the Cognitive Assessment Examination (Component 3), the following components must be completed:
    – Component 1: unrestricted licensure, must be current and verified
    – Component 2: Lifelong Learning/Continuing Medical Education, is a continual CME process required of all diplomates. CME requirements.
    – Component 4: Practice Performance Assessment and Improvement, must be completed by the AOBD for the practice performance assessment modules. Lifelong Learning/Continuing Medical Education, is a continual CME process required of all diplomates. CME requirements.
    – Component 5: continuous AOA membership in good standing, must be current and verified.
  – What if I miss a step and don’t complete all of the requirements by the deadlines?
    – If the modules are not completed and prevent a diplomate from completing the cognitive assessment exam prior to the expiration of their current certificate, certification will be inactivated and so noted on the AOA Physician Profile. The diplomate will be noted as being non-compliant with OCC.

Frequently Asked Questions

• Limited-scope family medicine
  – Limited-scope and non-clinical practice dermatologists will have to develop and complete two Practice Performance Assessment and Improvement modules in topic areas relative to their current activities as well as complete two communication modules. Diplomates will have to identify or develop an assessment tool that provides performance data that demonstrates practice performance improvement in an area relative to the activity. These non-standard modules will have to be approved in advance by the AOBD.

Frequently Asked Questions

• I don’t currently practice in my field of certification. How can I meet the Component 4 requirements?
  – There are three professional activity pathways:
    – Full-scope clinical practice
    – Limited-scope family medicine
    – Non-clinical practice
  – Limited-scope and non-clinical practice dermatologists will have to complete two Practice Performance Assessment and Improvement modules in topic areas relative to their current activities as well as complete two communication modules. Diplomates will have to develop and complete an assessment tool that provides performance data that demonstrates practice performance improvement in an area relative to the activity. These non-standard modules will have to be approved in advance by the AOBD.

Frequently Asked Questions

• I have a CAQ in addition to my primary. What must I do for OCC?
  – A minimum of 13 of your 50 specialty credits/3-year cycle must be obtained in the CAQ specialty area
  – Practice performance assessment components will be developed at the CAQ level

Frequently Asked Questions

• How many Practice Performance Assessments (PPA) will be required?
  – Newly certified dermatologists are required to complete 2 clinical modules and 2 professionalism modules during their year certification cycle. One clinical and one communication module must be completed in years 1-5. A second clinical and one communication module must be completed in years 6-10.

Frequently Asked Questions

• What if I miss a step and don’t complete all of the requirements by the deadlines?
  – If the modules are not completed and prevent a diplomate from completing the cognitive assessment exam prior to the expiration of their current certificate, certification will be inactivated and so noted on the AOA Physician Profile. The diplomate will be noted as being non-compliant with OCC.
Frequently Asked Questions

• I’m dually certified through the AOA and ABMS. What must I do for OCC?
  – Must fully participate in all five (5) Components of OCC
  – Potential pathway still evolving through the AOA, BOS and the specialty certifying boards

• I am dually boarded through two AOA specialty certifying boards. What must I do for OCC?
  – You will need to complete OCC for each certification, including passing an examination and completing practice performance activities (OCC Components 3 and 4)
  – Example: Internal Medicine and Dermatology

• I’m not board certified. May I participate in OCC to fulfill my state’s MOL requirement?
  – Still under discussion at the BOS
  – Working on a pathway for non-certified DOs

• Who is required to participate in OCC?
  – All time-limited certificate holders will be required to participate in OCC.

• Can I remain certified if I do not participate in OCC?
  – No. By choosing not to participate in OCC you are voluntarily suspending the rights to your board certification.

• Do I need to register in order to participate?
  – Yes, every diplomate must complete a registration application as provided by the AOBD, submit a registration fee, and be approved before proceeding with the OCC process. Separate application and fees are required for the Cognitive Assessment Examination (Component 3).

• Can I remain certified if I don’t participate in OCC?
  – No. By choosing not to participate in OCC you are voluntarily suspending the rights to your board certification.

• What happens if I hold a time limited certificate and I choose NOT to participate in OCC?
  – If an individual is required to participate in OCC (i.e. has a certification with an expiration date), and he or she does not comply with the process, their certification is at risk. There is an appeal process and a remediation process, but ultimately, failure to comply may lead to a loss of certification, just as failure on the re-certification examination would lead to loss of board certification.
Frequently Asked Questions

I have a "lifetime" (not time dated) board certification. Must I register for AOBD OCC?
- No, if you have a non-time-limited certification, you will not be required to participate in OCC at this time. However, the AOA strongly encourages your voluntary participation. The Federation of State Medical Boards (FSMB) has agreed to accept OCC for Maintenance of Licensure (MOL). If you do not participate in OCC, you may have additional requirements for MOL as prescribed by the state(s) where processed.

I have a time limited board certification. When must I take the re-certification examination (Component 3 – OCC Cognitive Assessment)?
- Your certificate will expire December 31 of the tenth year after issue (e.g., a 2005 certificate expires 12/31/2015). You must PASS the examination no later than the year of expiration of your certificate. You MAY take the examination one year before the expiration of your certificate. You must take the re-certification examination within the last two years of your OCC cycle (i.e., year 9 or 10).

What components need to be completed before I can take the exam? Prior to completion of the Cognitive Assessment Examination (Component 3), the following components must be completed:
- Component 1: unrestricted licensure, must be current and verified
- Component 2: Lifelong Learning/Continuing Medical Education, is a continual CME process required of all diplomates – CME requirements
- Component 4: Practice Performance Assessment and Improvement, must be completed at least one year prior to the expiration of your certificate and may be approved in advance by the AOBD
- Component 5: continuous AOA membership in good standing, must be current and verified.

What if I miss a step and don’t complete all of the requirements by the deadlines?
- If the module are not completed and prevent a diplomate from completing the cognitive assessment exam prior to the expiration of their current certificate, certification will be inactivated and so noted on the AOA Physician Profile. The diplomate will be noted as being non-compliant with OCC.

It seems like I am already meeting OCC requirements through CME, licensure, AO/AOCD membership and recertification exam. Are there any additional requirements that I am not already completing?
- Yes, Component 4 is Practice Performance Assessment and Improvement (PPA). You will be required to complete two clinical (PPA) modules and two communications modules during the 10 year cycle. Each module in years 1-5 and one in years 6-10. The PPA and communication modules will be available online from Osteopathic CAT (http://osteopathic-cat.com). There will be an OCC subscription fee of $235 for 3 years.

How many Practice Performance Assessments (PPA) will be required?
- Newly certified dermatologists are required to complete two clinical modules and two professionalism modules during their year certification cycle. One clinical and one communication module must be completed in years 1-5. A second clinical and one communication module must be completed in years 6-10.

The issuance date of a current certificate will determine the transition schedule for the number of modules to be completed by currently certified diplomates. The transition schedule is located here: http://aobd.org/advisor/occ/practice-performance-assessment-modules-o-cat/

I don’t currently practice in my field of certification. How can I meet the Component 4 requirements?
- There are three professional activity pathways:
  - Full scope clinical practice
  - Limited scope clinical practice
  - Non-clinical practice
- Limited-scope and non-clinical practice dermatologists will have to develop and complete two Practice Performance Assessment and Improvement modules in topic areas relative to their current activities as well as complete two communication modules. Diplomates will have to identify or develop an assessment tool that provides performance data that demonstrates practice performance improvement in an area relative to the activity. These non-standard modules will have to be approved in advance by the AOBD.
Table 2: Comparison of “Active” US MD Seniors/Graduates with “Active” US DO Seniors/Graduates in 2016 Matched in NMP & SOAP

<table>
<thead>
<tr>
<th>Type of Applicant</th>
<th># of Applicants</th>
<th>Matched</th>
<th>% Matched</th>
<th>Unmatched</th>
<th>% Unmatched</th>
</tr>
</thead>
<tbody>
<tr>
<td>US MD 3rd/4th</td>
<td>19,989</td>
<td>28,306</td>
<td>94.6</td>
<td>1,183</td>
<td>6.0</td>
</tr>
<tr>
<td>US DO Sen/Grad</td>
<td>2,082</td>
<td>2,531</td>
<td>84.8</td>
<td>454</td>
<td>15.2</td>
</tr>
<tr>
<td>Totals</td>
<td>22,071</td>
<td>30,837</td>
<td>92.8</td>
<td>1,637</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Table 3: All DO Seniors/Graduates Oligarchs Applying for the 2016 NMP Match

<table>
<thead>
<tr>
<th>Status</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdraw before match</td>
<td>1,208</td>
<td>15.9</td>
</tr>
<tr>
<td>No rank list</td>
<td>188</td>
<td>4.4</td>
</tr>
<tr>
<td>Matched in NMP</td>
<td>2,396</td>
<td>16.0</td>
</tr>
<tr>
<td>Matched in SOAP</td>
<td>132</td>
<td>3.1</td>
</tr>
<tr>
<td>Unmatched without Oligarch status</td>
<td>654</td>
<td>10.6</td>
</tr>
<tr>
<td>Totals</td>
<td>4,278</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4: Application of ACME-DOA Accredited Postdoctoral Training for ACGME Pre-Accreditation Status as of July 30, 2016

<table>
<thead>
<tr>
<th>Type of Program</th>
<th>Number</th>
<th>Applied</th>
<th>Approved</th>
<th>Matched</th>
<th>unmatched</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internship</td>
<td>90</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Residency</td>
<td>663</td>
<td>113</td>
<td>12.1</td>
<td>100</td>
<td>51</td>
</tr>
<tr>
<td>Fellowship</td>
<td>260</td>
<td>5</td>
<td>2.3</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Totals</td>
<td>989</td>
<td>122</td>
<td>12.6</td>
<td>101</td>
<td>52</td>
</tr>
</tbody>
</table>

Table 5: Projected Range of DO Seniors/Graduates Who Will Not Match in the 2020 NMPB SOAP in 2020 and be Unable to Obtain PGY-1 Positions

<table>
<thead>
<tr>
<th>Scenario</th>
<th>#Applicants</th>
<th>% Matched</th>
<th>% Unmatched</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best Case</td>
<td>7,000</td>
<td>90.7</td>
<td>651</td>
</tr>
<tr>
<td>Worst Case</td>
<td>7,000</td>
<td>77.4</td>
<td>1,582</td>
</tr>
</tbody>
</table>

Table 6: Comparison of US MD Seniors/Graduates with US DO Seniors/Graduates in Obtaining PGY-1 Surgical Residencies in 2020 NMP Match

<table>
<thead>
<tr>
<th>Residency</th>
<th>Total Matched Positions</th>
<th>MD</th>
<th>DO</th>
<th>NOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopedic</td>
<td>105</td>
<td>699</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>Otorhinolaryngology</td>
<td>191</td>
<td>290</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Plastic Surgery</td>
<td>145</td>
<td>144</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Neurology</td>
<td>35</td>
<td>33</td>
<td>2</td>
<td>5.7</td>
</tr>
<tr>
<td>Vascular Surgery</td>
<td>52</td>
<td>50</td>
<td>2</td>
<td>3.8</td>
</tr>
<tr>
<td>Surgery-Peds</td>
<td>167</td>
<td>156</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Surgery-Cid</td>
<td>1,999</td>
<td>1,041</td>
<td>58</td>
<td>5.2</td>
</tr>
<tr>
<td>Ob/Gyn</td>
<td>1,141</td>
<td>1,013</td>
<td>128</td>
<td>11.2</td>
</tr>
<tr>
<td>Totals</td>
<td>4,593</td>
<td>3,804</td>
<td>129</td>
<td>5.7</td>
</tr>
</tbody>
</table>

Table 7: ACGME-OOA Accredited Surgical Residency Programs, Filing for ACGME Pre-Accreditation & Determination of Status for Initial Accreditation

<table>
<thead>
<tr>
<th>Residency</th>
<th>Number</th>
<th>Filled</th>
<th>Approved</th>
<th>Initial Accred.</th>
<th>Failed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurosurg.</td>
<td>11</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Ob/Gyn</td>
<td>34</td>
<td>11</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Orthopeadics</td>
<td>44</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Orthopedics</td>
<td>25</td>
<td>14</td>
<td>12</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Ob/Gyn</td>
<td>20</td>
<td>10</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Surgery</td>
<td>59</td>
<td>33</td>
<td>14</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>Totals</td>
<td>192</td>
<td>87</td>
<td>38</td>
<td>8</td>
<td>30</td>
</tr>
</tbody>
</table>
Summary

- OCC
  - Assures high standards for patient care
  - Demonstrates commitment to continuous improvement
  - Is practice-relevant
  - Ensures osteopathic excellence

The End
Sunday, September 18, 2016

7:00 a.m. - 8:00 a.m. Breakfast with Exhibitors

8:00 a.m. - 9:00 a.m. Medicolegal Issues in Dermatology and Dermpath
Whitney High, MD

9:00 a.m. - 10:00 a.m. The Culture of Your Wound Culture
Derrick Adams, DO, FAOCD

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

10:30 a.m. - 11:30 a.m. Osteopathic Dermatology
Reagan Anderson, DO, FAOCD

11:30 a.m. - 12:30 p.m. Therapeutic Update
James Q. Del Rosso, DO, FAOCD
I have no relevant disclosures

Malpractice in Dermatopathology—Principles, Risk Mitigation, and Opportunities for Improved Care for the Histologic Diagnosis of Melanoma and Pigmented Lesions

Whitney A. High, MD*
Department of Dermatology, University of Colorado Health Science Center, P.O. Box 4710, Mail Stop P700, Aurora, CO 80045, USA

Derm and Dermpath in USA?
Good News! NEJM 2011

- Examined claims:
  - 40,000 doctors
  - 6 year period
  - Overall 7.4%/year were sued
  - Medical specialty - 55% sued by 65 y/o
  - Surgical specialty - 74% sued by 45 y/o

N=23,371 cases asserted* 2009-2013
- Cases were clinically coded by specialty
- Just 272 (1.2%) identified with a responsible service of “dermatology”
- Total incurred amount of $20M
- Represented just 0.5% of all incurred costs among all specialties ($4.1B)

N=272 CBS MPL cases asserted 09-13 with a primary responsible service of Dermatology by major allegation

<table>
<thead>
<tr>
<th>Allegation Category</th>
<th># cases</th>
<th>Total Incurred Amt</th>
<th>% of cases</th>
<th>% of total incurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Tx</td>
<td>122</td>
<td>$5,992,279</td>
<td>45%</td>
<td>30%</td>
</tr>
<tr>
<td>Diagnosis-Related</td>
<td>66</td>
<td>$9,377,865</td>
<td>24%</td>
<td>47%</td>
</tr>
<tr>
<td>Medication-Related</td>
<td>37</td>
<td>$3,047,116</td>
<td>14%</td>
<td>15%</td>
</tr>
<tr>
<td>Surgical Tx</td>
<td>21</td>
<td>$729,496</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Communication</td>
<td>13</td>
<td>$239,521</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Safety &amp; Security</td>
<td>5</td>
<td>$271,239</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Discrimination</td>
<td>3</td>
<td>$49,447</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>PT Monitoring</td>
<td>2</td>
<td>$62,335</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Anesthesia-Related Tx</td>
<td>1</td>
<td>$129,290</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Hosp Policy &amp; Proc</td>
<td>1</td>
<td>$78,480</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Provider Behavior</td>
<td>1</td>
<td>$10,375</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Sum:</td>
<td>272</td>
<td>$19,987,444</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

N=272 CBS MPL cases asserted 09-13 with a primary responsible service of Dermatology by injury severity

<table>
<thead>
<tr>
<th>Severity Category</th>
<th># cases</th>
<th>Total Incurred Amt</th>
<th>% of cases</th>
<th>% of total incurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>50</td>
<td>$787,929</td>
<td>18%</td>
<td>4%</td>
</tr>
<tr>
<td>Medium</td>
<td>179</td>
<td>$7,008,445</td>
<td>66%</td>
<td>35%</td>
</tr>
<tr>
<td>High</td>
<td>43</td>
<td>$12,191,069</td>
<td>16%</td>
<td>61%</td>
</tr>
<tr>
<td>Death</td>
<td>20</td>
<td>$4,956,576</td>
<td>7%</td>
<td>25%</td>
</tr>
<tr>
<td>Permanent significant</td>
<td>16</td>
<td>$5,486,482</td>
<td>6%</td>
<td>27%</td>
</tr>
<tr>
<td>Permanent major</td>
<td>4</td>
<td>$1,738,277</td>
<td>1%</td>
<td>9%</td>
</tr>
<tr>
<td>Permanent grave</td>
<td>3</td>
<td>$9,735</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Sum:</td>
<td>272</td>
<td>$19,987,444</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

N=272 CBS MPL cases asserted 09-13 with a primary responsible service of Dermatology by top contributing factors

<table>
<thead>
<tr>
<th>Contributing Factors Code</th>
<th># cases</th>
<th>% of cases</th>
<th>Top Clinical Judgment Factors</th>
<th># cases</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>CJ - clinical judgment</td>
<td>102</td>
<td>38%</td>
<td>CJ1021 - pt assess-failure/delay in ordering diagnostic test</td>
<td>30</td>
<td>11%</td>
</tr>
<tr>
<td>TS - technical skill</td>
<td>101</td>
<td>37%</td>
<td>TS4008 - technical performance—possible technical problem</td>
<td>56</td>
<td>21%</td>
</tr>
<tr>
<td>BR - behavior</td>
<td>97</td>
<td>35%</td>
<td>CJ2009 - selection/management therapy—other</td>
<td>10</td>
<td>4%</td>
</tr>
<tr>
<td>CO - communication</td>
<td>73</td>
<td>27%</td>
<td>CJ2013 - selection/management therapy—medical</td>
<td>14</td>
<td>5%</td>
</tr>
<tr>
<td>DO - documentation</td>
<td>52</td>
<td>19%</td>
<td>TS4009 - technical performance—poor technique, other</td>
<td>22</td>
<td>8%</td>
</tr>
<tr>
<td>CS - clinical systems</td>
<td>52</td>
<td>19%</td>
<td>CJ3001 - inappropriate utilization equipment (overuse)</td>
<td>3</td>
<td>1%</td>
</tr>
</tbody>
</table>

N=272 CBS MPL cases asserted 09-13 with a primary responsible service of Dermatology by final diagnosis

<table>
<thead>
<tr>
<th>Category of Case</th>
<th># Cases</th>
<th>Sum of Total Incurred Amt</th>
<th>% of cases</th>
<th>% of total incurred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>47</td>
<td>$2,369,778</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>Cancer of skin</td>
<td>46</td>
<td>$4,605,782</td>
<td>17%</td>
<td>23%</td>
</tr>
<tr>
<td>Poisoning</td>
<td>36</td>
<td>$2,930,022</td>
<td>13%</td>
<td>15%</td>
</tr>
<tr>
<td>Burns</td>
<td>32</td>
<td>$1,177,033</td>
<td>12%</td>
<td>0%</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>29</td>
<td>$679,219</td>
<td>11%</td>
<td>3%</td>
</tr>
<tr>
<td>Other skin disorders</td>
<td>22</td>
<td>$368,378</td>
<td>8%</td>
<td>2%</td>
</tr>
<tr>
<td>Cancer; other primary</td>
<td>8</td>
<td>$5,810,260</td>
<td>3%</td>
<td>20%</td>
</tr>
</tbody>
</table>
Laser "accidents" 2
Cosmetic filler 1
Isotretinoin complications 3
Missed melanoma 6
Chloroquine 1
TEN/SJS 1
NMSC 1
Potent steroids 2
Light therapy 1
Connective tissue disease 1
Cryosurgery 1
Merkel cell 1
Balanitis obliterans with SCC 1

Litigation Within Dermatology & Dermatopathology

- **Misdiagnosis** of melanoma is a key problem
- The Doctors Company (1990-2001)
  - “skin cancer” and/or “melanoma”
    - 8.6% of all claims against pathologists
    - 14.2% of all claims against dermatologists

Too much litigation versus too many errors?

- Harvard Medical Practice Study (1990)
  - 31,000 medical records examined
  - “Negligence” only by consensus
  - 1 out of 25 harmed by medical error
  - Only 4% of injured actually made claims

Half Full or Half Empty

- 90% of suits involved actual medical injury
- Courts “right” ~ 75%
- Only 0.4% of claims “frivolous”
  - “Careful & Deliberate”

- 10% of claims without injury
- 75% is a “C”
- ~ $52,000 & 5 yrs to adjudicate
  - “Wasteful & Fickle”

Purpose of Malpractice Law

“To identify a party injured because of substandard care and compensate the party, so as to make them whole.”

- Malpractice is tort law
- It is a civil action
  - “Preponderance of the evidence” (>50%)
Elements of Malpractice

Six elements of a *prima facie* case

1. Duty
2. Standard of Care
3. Breach of Duty
4. Cause in Fact
5. Proximate Cause (Legal Cause)
6. Damages

(failure to prove a single element is fatal)

Simple Pyramidal Structure

Duty To Act

**Negligent Action or Inaction**

**Damages from Negligent Action/Inaction**

Duty

- “Contractual” agreement to provide care with proper professional skill
- Opposed to “curbside,” “hallway,” or “sidewalk” consultations
- Courts traditionally reluctant to assign duty to those with only tangential relationship
- Use of “images” (telederm) or actual patient materials (slides) may make one liable

Varying Standards of Care

- Some states:
  - “reasonably prudent physician” of same background, training, experience
- Other states:
  - knowledge and skill common to members in good standing
  (conformity to “customary practice” but also with consideration of a “respectable minority”)

Causation

- Concept of contributory negligence
- Cause in Fact (“But for,” causation)
  - Determined by jury
  - Did that actions actually lead to the result?
- Proximate Cause (legal causation)
  - Determined by the judge
  - Was the result foreseeable?
  - Is it “reasonable” to hold the party accountable?

Standard of Care is ALWAYS Established *de novo*

- Expert testimony (difficult to secure & expensive)
- P’s costs often fronted by the attorney
  - in exchange for a ~1/3 interest in any award
- Trial expenses ~ $50,000 - $100,000
- ~ 500 hours of prep = $75,000 - $100,000

“Investment” in jeopardy - $125,00 to $250,000

Baker KD, The Federation of Defense & Corporate Counsel
http://www.thefederation.org/documents/baker-sp02.htm

Notes
- The outcome does NOT have to be favorable!
- You do NOT have to be “correct”!
**Show Me the Money!**

**Compensatory Damages**
- **Special damages**
  - medical bills (past, present, future)
  - lost wages (past, present, future)
- **General damages**
  - pain & suffering (*per diem* vs. lump sum)
  - loss of enjoyment/consortium

*RARELY PUNITIVE DAMAGES!*

**US Attorneys Not Really Interested in “Close Calls”**
- Average cost of lawsuit
  - Plaintiff's Atty. = $125-250k
- "Where's Waldo" cases
  - some pigmented lesions are difficult for *ALL* experts
- Farmer, et al. (1996)
  - 37 "classic" melanomas & 11 "expert" dermpaths
  - unanimity for "melanoma" in just 11 cases (30%)

"The first thing we do, let's kill all the lawyers".

"Chilling not only to physicians, but to patients, and *sobering* to lawyers for plaintiffs."

- A.B. Ackerman, 1996

**The Doctor's Defense**
- Attack *validity* of the required elements
  - "there was no breach the standard of care"
- Assert an *affirmative defense*
  1. Conflicting legal duty (psychiatrists)
  2. Consent (most often employed defense for procedures)
  3. Statute of Limitations (variable length)

Do we really want to eliminate lawyers?
Statute of Limitations

- Time period when a suit must be filed
- Varies from state-to-state
- Tolled in children until a certain age
  - age of “majority,” simply a specified age
- Point of argument in many situations:
  - begins when one is *reasonably* alerted to an injury and not simply “date of service”

Anonymous Pt v. Anonymous Derm
Virginia 1997

- Plaintiff sought care for mole upon leg
- Derm biopsied → interpreted as benign
- Two years later → pt. visited a surgeon
- Surgeon requested medical records
- Derm then re-assessed slide and amended the path report → “melanoma”

*Was suit timely?*

Court Decision

- SOL *did not* begin at misdiagnosis
- RULING: SOL began 2 years from when the melanoma “moved from epidermis into the dermis”

(When the *heck* was that?)

**Important point:**
The SOL may begin when an injured party *should have been reasonably aware* that an injury had transpired.

What are the issues discussed with damage caps…

are such caps ethical?
are such caps legal?

Do Caps Save Money

- Both economic and non-economic damage caps exist
- Conflicting evidence over whether:
  - non-economic damage caps save money
  - economic damage caps are ethical

For states/entities with damage caps there may be an even *greater disincentive* to sue.

Would you risk $125,000 for a 1 in 5 shot at $150,000?

TITLE 24. GOVERNMENT—STATE
ADMINISTRATOR
ARTICLE 10. GOVERNMENTAL IMMUNITY

24-10-19. Limitations on judgments

(1) The maximum amount that may be recovered in any single occurrence, whether from one or more public entities and public employees, shall be—

(a) For any injury to one person in any single occurrence, the greater of one hundred thousand dollars.

(b) For any injury to two or more persons in any single occurrence, the sum of one hundred thousand dollars, except that, in such instance, no person may recover in excess of one hundred thousand dollars.

For states/entities with damage caps there may be an even greater disincentive to sue.
“Defensive” medicine costs continue to increase.

Oregon’s Unique Situation

- Clarke v OHSU
  - $12M+ damages
  - state was substituted for MDs/RNs
  - result - $200k remedy
  - law was unconstitutional “as applied” to case

Structure of US Court System

- United States Supreme Court
- State Supreme Court
- Federal Circuit Court
- State Appellate Court
- Federal District Court
- State District Court

“That $250,000 wouldn’t pay for my medication for the rest of my life,” [the patient] responded. “$250,000 for my kind of injury, it’s nothing. It’s a pittance.”

Apology Laws

- Now exist in 29 states
- Protect doctor against use of certain statements in situation of:
  - “perceived” medical error
  - negative outcome
- Vary from state to state

Colorado Apology Law

- Broadest in the nation
- C.R.S. 1-25-13
  - protects “any and all statements, affirmations, gestures, or conduct expressing apology, fault, sympathy, commiseration, condolence, compassion, or a general sense of benevolence…”
- Doctor can apologize, describe in detail any mistakes and the information is inadmissible
Texas Apology Law

- Narrower than Colorado’s apology law
- TCP&R Code Sec 18.061(a)(1):
  - protects statements that “expresses sympathy or a general sense of benevolence relating to the pain, suffering, or death of an individual involved in an accident.”
- However, unlike Colorado’s law, it does not bar a doctor’s admission of liability or fault

How might this work…

- Imagine after a procedure the following statement is made:
  
  “I am sorry for your pain. I mistakenly failed to close your wound properly and that failure caused your pain and suffering.”

- Colorado – entire statement protected
- Texas – only “I am sorry…” is protected.

**Physician-Patient Communication: The Relationship With Malpractice Claims Among Primary Care Physicians and Surgeons**

Levinson, W, Roter, DL, Mullooly JP, Dull VT, Frankel RM

*JAMA* Volume 277(7), 19 February 1997, pp 553-559

- Doctors with fewer claims:
  - used more orientation/education
  - laughed and used more humor
  - spent slightly longer in routine visits (mean 18.3 vs. 15.0 min)

*Sometimes when your first you are last.*

**Dermatology & Dermatopathology Litigation**

- The Doctors Company
  - 1998 to 2001: 144 pathology claims
  - 23 (16%) were misdiagnosis of melanoma (second only to breast cancer for litigation potential)

**Medico-legal Aspects of Error in Pathology**

Dermatology & Dermatopathology
davidbtraut, MD

- Melanoma: 13% of all pathology claims (44/335)
- False negative 95% (42/44) but false positive 5% (2/44)

(2006 ACS estimates: 63k melanomas, 217k breast cancers)
“Breakdown” of 42 False Negative Claims

- Erroneous “diagnoses” involved:
  - Spitz nevus: 3 cases
  - Dysplastic nevus: 3 cases
  - Spindle cell SCC: 3 cases
  - Atypical fibroxanthoma: 1 case
  - Missed desmoplastic melanoma: 2 cases

No explanation for the other 30 cases.
No case details or information regarding financial outcomes.

“It’s unlikely you will ever be sued…”

Each year 1.5 M animals cross the Serengeti…

Continued Evolution is a Certainty
Five things to make sure of…

1. Make sure the sample is adequate
2. Make sure the history/tissue is right
3. Make sure the report is tight
4. Biopsy books must be run regularly
5. Make sure communication lines are open to between the dermatologist and the dermatopathologist

1. The sample

Alas, this product does not exist…

Case

- 52 year-old VA patient
- 2004 - “dark lesion” on L neck
- Punch biopsy performed
- Diagnosis: irritated junctional nevus
- 2006 - lesion persisted and worried him
- Rebiopsy – Melanoma 0.65 mm

Clinical Presentation

Methods of Sampling

- **Shave** – inadequate for true “r/o melanoma”
- **Punch** – specialized use with difficult lesion
- **Saucerization** – gaining acceptance
- **Excision** – preferred where safe & practical
Punch the thickest area?

Study of Saucerization
(Pariser et al. DOJ 1999; 5:4)

Level 1
"r/o NMSC"

Level 3
"r/o NMSC"

Level 3 – Higher Magnification
"r/o NMSC"

BCC
4 mm Punch Biopsy by Volume
- Assume 4 mm cylinder
  Volume of punch is = 50.3 mm³
- Assume is two 3.5 µm ‘silhouettes’ on slide
  “Volume” inspected is = 0.112 mm³
  The dermatopathologist is inspecting 1/450th of the overall volume of the sampling!!!!

TIP:
Secure a representative biopsy
(pssst – medicolegally, this is ALWAYS the clinician’s obligation)

If the problem is truly the sample itself, eventually the error will be discovered….

2. Make sure the clinical history and the tissue are right

  • 65 year woman
  • chest
  • “rto NUB”
Prevent An Error Before It Occurs

- "Crap in = Crap out"
  - "r/o melanoma" on everything
  - "r/o cancer" on everything
  - "rash"
  - "238.2" for everything
- Multiple specimens in the same bottle
- Curetting of a pigmented lesion
- Mismarking shaves, punches, excisions

Can't be successful with this attitude:

Not my job!

Everyone involved is a target…

“throw them all against the wall, see who sticks!”

When a error leads to a lawsuit…

"throw them all against the wall, see who sticks!"

I might even promote doing biopsies in "3D":
- Description (or what was Done)
- Diameter (size or extent)
- Diagnosis
Chain of Dependency

- Biopsy
- Courier
- Logging
- Grossing
- Embedding
- Cutting
- Labeling
- Reading

Potential for error exists at each point.

You need to provide as many “clues” to the correct diagnosis as you possibly can!

Ultimately, P09-41107 was a BCC but tissue placed on the slide was spongiotic dermatitis.

Not including a REALISTIC clinical impression decreases error detection (as does mismarking punch/shave, etc.)

Ultimately, P09-41109 was spongiotic dermatitis but the tissue placed on the slide was BCC.

• 5 of 1335 “skin tags” contained a malignancy
  – 4 BCC, 1 SCC
  – compared to 6 malignancies in 697 “moles”
  – is this a reason to require submission of all tissue?
Biopsy from posterior neck of a 34 year old woman.

"Rule out tag."

This ink can be used in clinical settings as well (and not just Mohs).

3. Make sure the report is tight

Initial Check

- Correct patient?
- Does biopsy technique & gross size match?
- Was history and clinical info accurate?
- Is the final assessment plausible?

No Path Report is Beyond Reproach

No stone tablet.
No burning bush.

No stone tablet. No burning bush.
This is MELANOMA.
If any other diagnosis returns from the dermatopathologist, it should be treated with great suspicion.

Ultimately, the diagnosis was ALMM 1.6 mm deep.

4. Keep a biopsy book and run it routinely to look for “drops”

A Real Case
• 23 y/o woman with lesion upon the leg
• Punch biopsy at FM clinic
• Biopsy to local dermpath, who issues a “placeholder” dx, but requests consultation
• University dermpath recognizes it as difficult melanocytic process:
  – performs stains,
  – solicits FISH studies
  – take to University Consensus Conference
• Ultimately, evidence favors melanoma

• University issues report = melanoma
  – copy of report marked “received” at local lab
  – it existed on servers at lab for 3 years
• Dermpath who requested the consultation never updates “placeholder” report
• Neither FM doc nor patient ever make any inquiries in to matter
• 3 years later:
  – pt develops recurrence, + lymph node in groin
  – metastatic disease

Two of the Best Instruments for Safer Medical Care

Thank you
The Culture of Your Wound Culture

Derrick Adams, DO, FAOCD
Private Practice
Vita Dermatology
Red Bluff, CA

No Conflicts of Interest

Today’s Topics
• Problem
• Hx of culture/techniques
• Colonization vs Infection
• Microbiome
• Sequence testing vs Wound Cultures
• Chronic wounds
• Culture technique

The Problem Scenarios
• My antibiotic dilemma
• “Your culture was negative. There is no infection.”
• “It just grew normal skin flora”
• “You should be really sick or dead based on your culture result”

Bacterial Cultures
• Standard since 1800’s
• Detect roughly 1% of bacteria in chronic wounds
• Select for bacteria that thrive in nutritional and physical parameters set by a lab
• These organisms may not be relevant
• Reported organism - outcompetes others
• Anaerobes cultivation is problematic
• Ignores all other life forms

The Great Plate Count Anomaly

• Observation that most environmental microorganisms seen in the microscope cannot be grown under laboratory conditions

Your Aerobic Wound Culture

• Gram stain
• Blood Agar
• Chocolate Agar
• CNA (gram +)
• MAC (gram -)
• Thiol

Your Anaerobic Wound Culture

• Gram stain
• Brucella blood agar
• CNA
• Laked Blood agar

*Both cultures – 24, 48, 72 hour reads

Wound Swabs

• Cotton, calcium alginate, Dacron-Rayon
• Collect < 0.1ml
• Tend to retain collected specimen
• Sterile loop is diluted (+1,+2,+3,+4)
• More testing = less material (aerobic, anaerobic, mycobacterial, and fungal)
• Transport dilemmas
Colonization vs Infection

- Infection is **your diagnosis**. Not the lab’s
- Organisms cultured from wounds do not define infection
- Antibiotics can have lasting effects

C. Diff Risk with Antibiotic

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Odds of CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroquinolones</td>
<td>2.8-5.2</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>2.8-20.3</td>
</tr>
<tr>
<td>3rd Gen Cephal</td>
<td>3.2-4.8</td>
</tr>
<tr>
<td>Penicillins</td>
<td>1.75</td>
</tr>
<tr>
<td>Macrolids</td>
<td>1.4</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>1.78</td>
</tr>
<tr>
<td>Proton inhibitors</td>
<td>1.7-2.2</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>0.91</td>
</tr>
</tbody>
</table>

*J. Antimicrob Chemother (2014)69(4)881-2*

Healthy Skin

Chronic Wounds

Infection/Inflammation
Sequenced Based Testing
16S rRNA

- "gold standard" among microbiologists
- >500,000 in public database (NCBI)
- Reportedly > 2 million in private database
- GreenGenes, EZ-Taxon e, Ribosomal Database Project, SILVA

16S rRNA

- 16S rRNA present in prokaryotes
- Encodes part of a ribosome
- Allows for identification and amplification (PCR)
- Slow rate of evolution

Pros and Cons of DNA/RNA sequencing

Pros
- Eliminates bias of culture techniques
- Not limited to bacteria
- Microbial load
- Microbial diversity
- Identifies “Pathogens”
- Cost is reasonable
- Primer tailored

Cons
- Possible human contamination
- Viable vs non-viable
- ID’d organism may not be clinically relevant
- “Chain of Evidence”
- Primer bias*
Mycobacteria (acid-fast)

- Good for slow growers
- Rapidly growing mycobacteria (RGM)- 65-KDa heat shock protein and RNA polymerase Beta subunit genes*

*Differentiate between *M. abscessus*, *M. chelonae*, *M. bolletii*, and *M. massiliense*.

Yeast & Molds

- Phenotypic testing can be difficult
- Phenotypic variation within species*
- Can take weeks
- 26S ribosomal RNA (rRNA) and Internal Transcribed Spacer 1 and 2 regions (ITS1 & ITS2)

Culture-based and Sequence-based

- Who is there?
- Not what’s going on

Skin & Soft Tissue Infections (SSTI) by Real-Time PCR

- *Bacteroides fragilis*, 
- *Enterococcus faecalis*, 
- *Escherichia coli*, 
- *Group A Streptococcus*, 
- *Group B Streptococcus*, 
- *Klebsiella* 
- *Prevotella Groups 1 & 2*, 
- *Proteus mirabilis*, 
- *Pseudomonas aeruginosa*, 
- *Staphylococcus aureus*, 
- *MRSA*

PRIMER BIAS!
We are...

- 2 -5 lbs of bacteria
- 90% bacteria, 10% human by cell count
- 99% bacteria, 1% human by genes
- Largely ignorant of our microbiome
- 99.6% of human microbiome species cannot be cultured

Square CM of Your Skin

- Hundreds of distinct species
- Estimated 1 million bacteria
- Very site specific
- Quite resilient to change (*forehead licking)
- May affect immunity
- May affect physiology of keratinocytes

Human Microbiome

- 2007 NIH
- 242 healthy adults
- Gut
- Genitourinary
- Skin
- Spatial niches

Top 4 Skin Phyla

- Actinobacteria
- Firmicutes
- Bacteroidetes
- Proteobacteria
Top 4 Skin Phyla

- **Actinobacteria** – *Propionibacterium*, *Mycobacterium*, *Corynebacterium*, *Nocardia*
- **Firmicutes** – *clostridium, staph, strep*
- **Bacteroidetes** – *b.fragilis, prevotella*
- **Proteobacteria** – *e.coli, pseudomonas*

Palm Microbiome

- 51 healthy subjects
- 4742 distinct species
- Average 158 species coexisting on single palm

The Belly Button Biodiversity Project

- *Propionibacterium* – sebaceous areas
- *Staphylococcus* – moist areas/intertriginous
- *Corynebacterium* – same as staph
- Antecubidal fossa – highest diversity among subjects
- Partially occluded sites (axilla/inguinal) – more stable

Surprise!

- Gram-negatives found in dry areas (forearm and legs)
- Not always fecal contaminant
- Low-abundance species may be “linchpins” of the skin ecosystem (soil fungal studies)

**Generalities**

- *Propionibacterium* – sebaceous areas
- *Staphylococcus* – moist areas/intertriginous
- *Corynebacterium* – same as staph
- Antecubidal fossa – highest diversity among subjects
- Partially occluded sites (axilla/inguinal) – more stable

**Phylogenetic Diversity**

- Baldrain, et al. Active and total microbial communities in forest soil are largely different and highly stratified during decomposition. ISME J 2012;6:248-58
- Chen, et al. Soil fungal communities in forest soil can largely differ and highly stratified during decomposition. ISME J 2012;6:248-58

• “Culture Everything!”
• Microbial Load
• Sensitivity Data
• Biofilm analysis
• Reasonable cost

Wound culture: Pseudomonas

Wound culture: "normal skin flora"
**Finegoldia magna**

- Normal skin flora

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**Top 5 Nail Fungus by Next Gen Sequencing**

- Trichophyton Rubrum 38%
- Leptosphaerulina chartarum 17%
- Cladosporium uredinicola 14%
- Epicoccum nigrum 13%
- Malassezia restricta 9%

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**National Human Genome Research Institute (fungal studies)**

- Heel – largest fungal diversity, 80 species
- Nail clippings – 60 species
- Toe web – 40 species
- (Head and trunk hosted between 2-10)


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**“Normal Skin Flora?”**

- Propionobacterium acnes – orthopedic and neurosurgery infections
- Elaborate biofilms in nonunion open fractures
- Very difficult to culture


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**100 Adults Toe Web Spaces**

- Candida albicans
- Rhodotorula rubra
- Torulopsis and Trichosporon cutaneum
- Microsporum gypseum,
- Trichophyton rubrum
- Rhiadopus stolonifer
- Trichosporon cutaneum
- Fusarium
- Scopulariopsis brevicaulis
- Curvularia
- Alternaria alternata
- Paecilomyces
- Aspergillus flavus
- Penicillium

Two Faces of Same Microbe

**Planktonic**
- Acute infections
- Grows easily

**Biofilm**
- Chronic infections
- Difficult to grow & treat
- Express a radically different phenotype than planktonic
- Only diagnostic tool is molecular

Top 10 Chronic Wound Genera

- “Garbage in, Garbage out”
- Surface or deep?
- Are they on antibiotics?
- Immune status?
- How old is the wound?
- What are you looking for?
- Who is taking sample?

Wound Swab (FYI – no standardized technique)

- Deep-tissue or punch biopsy
- Needle aspiration
- Swab culture (levine’s vs “Z” technique)
- Sequence based swab/tissue


Tissue Biopsy for Culture
• Debride and clean superficial area
• Resect viable tissue with aseptic technique
• Aerobic & Anaerobic orders

Needle Aspiration for Culture
• Disinfect overlying tissue
• Use 18-22 gauge needle to aspirate fluid
• Aerobic & Anaerobic orders

Superficial Swabs
• Carefully swab surface of wound
• Throw swab into garbage can

Sequencing Sample Collection
• Swab the deck!
• Throw everything in!
• Try to give as much as possible
• Remember: a chronic wound is an ecosystem
• Topical lidocaine will degrade DNA

Summary
• Infection is a clinical diagnosis and not a culture diagnosis
• Most wounds will culture something
• Choose your culture/sequence technique wisely
• Comprehensive sequencing is available
• Today’s dogma is tomorrow’s heresy

- Ehrlich G. D., Domeo P. The problem of culture negative infections. Biofilm Infections. Springer series on biofilm 7. DOI 10.1007/978-3-642-29554-6_1
- Bowler PG, Davies BJ. The microbiology of infected and non infected leg ulcers. Int J of Dermatol 38:573-6
Osteopathic Principles

- Human being is a dynamic unit of function (body, mind, spirit)
- Self-regulatory mechanisms that are self-healing in nature
- Structure and Function are interrelated at all levels
- Rational treatment is based on these principles

Actinic Keratosis

- The body is a unit; the person is a unit of body, mind, and spirit
- Appearance affects spirit
- Consider whole region/unit affected for treatment

Actinic keratosis

- Structure and function are reciprocally interrelated
- Sun-damaged skin
- P53 mutation

Actinic keratosis

The body is capable of self-regulation, self-healing, and health maintenance.

**Field Therapy**

**Observe**

**Cryotherapy**

**Light Therapy**

---

Actinic keratosis Treatment

**Cryotherapy**

- Low 1-year clearance rate - 28%
- Isolated lesions vs. diffuse involvement

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Actinic keratosis Treatment

**Imiquimod**

- 73% 1-year clearance rate
- 54% 1-year clearance rate

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Actinic Keratosis Treatment

**Imiquimod**

- Immunomodulator - best MOA for self-healing
- Activator of Toll-like receptor 7
- Induces TNF-alpha, INF-gamma, ......
- Minimal systemic absorption

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Actinic Keratosis Treatment

**5-FU**

- Flourinated pyrimidine analog with cytotoxic effects
- 6% systemic absorption

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Actinic Keratosis Treatment

Diclofenac
64% 90 day clearance rate when combined with cryosurgery
- Prostaglandin synthesis
- Prostaglandins ↑ in sun damaged skin


Actinic Keratoses Holistic Approach

Consider the whole patient
- Isolated vs. broad area
- Economics
- Ability to self-heal
- Immunomodulators

Psoriasis

Structure and function are reciprocally interrelated.

Immune dysregulation
- T-helper 1 cells
- T-helper 17 cells
Psoriasis

Psoriasis

The body is a unit, the person is a unit of body, mind, and spirit.

Psoriasis Comorbidities

Obesity

Leptin

Increased in psoriasis patients

Stimulates TNF-α and IL-6

Weight loss


Psoriasis Comorbidities

Cardiovascular

Hypertension

Increased renin and ACE levels

Adiponectin

Decreased in psoriasis patients

Anti-inflammatory and anti-atherogenic

Psoriasis

The body is capable of self-regulation, self-healing, and health maintenance.

Stress

Activates HPA axis

Athers immune function

Impairs ability to self-regulate, self-heal

Coping strategies


Osteopathic Treatment

The body is a unit, the person is a unit of body, mind, and spirit.

Individualized

Extent of disease

Comorbidities

Lifestyle

Availability (distance from treatment facility)

Comprehensive
Psoriasis Treatment

Topical
- Emollients
- Keratolytics
- Corticosteroids
- Calcineurin inhibitors
- Vitamin D analogs

Psoriasis Treatment

Topical corticosteroids
↓ number of antigen presenting cells and cellular receptors
↓ neutrophil adhesion to vascular endothelium


Psoriasis Treatment

Calcineurin inhibitors
FK506 binding protein
Binds calcineurin
Blocks IL-2
Inhibits T cell activation
More appropriate for thin skin

Psoriasis Treatment

Calcineurin inhibitors
FK506 binding protein
Binds calcineurin
Blocks IL-2
Inhibits T cell activation
More appropriate for thin skin

Psoriasis Treatment

Vitamin D analogs
- Inhibits keratinocyte proliferation/differentiation
- Inhibits IL-2, IL-6, IFN-γ
- Inhibits cytotoxic T-cells and NK cells


Psoriasis Treatment

Systemic
- Steroids
- Retinoids
- TNF-α inhibitors
- Other immune modulators

Psoriasis Treatment

Oral Retinoids
- Bind nuclear factor receptors
- Stabilize inflammation
- Cellular differentiation
- Apoptosis
- Acitretin
- Etretinate
- Half life 80-160 days
Psoriasis Treatment

Rational treatment is based upon an understanding of the basic principles of body unity, self-regulation, and the interrelationship of structure and function.

Acne - Pathophysiology

Structure and function are reciprocally interrelated.

Follicular hyperkeratinization
Proliferation + desquamation
Microcomedone

Acne - Treatment

Structure and function are reciprocally interrelated.

Treat the structural problem - microcomedone
Function will return to normal.

Acne - Treatment

• Maintenance therapy with a topical agent
• Treats comedones (structural issue)
• Acne clears (normal function of skin returns)

Acne

The body is capable of self-regulation, self-healing, and health maintenance.
Acne and Antibiotics

The body is capable of self-regulation, self-healing, and health maintenance.

Limit antibiotic use to 3-6 months


Acne and Diet

The body is a unit; the person is a unit of body, mind, and spirit.

Low glycemic index

Dairy has testosterone precursors that are converted to active forms when ingested and act on the pilosebaceous units

Stimulate insulin-like growth factors


Acne Scarring

Severe acne can result in deep pitting scars, which are cosmetically undesirable.

Significant psychological impact and decreased quality of life


Acne Scarring

The body is capable of self-regulation, self-healing, and health maintenance.

Many treatment options take advantage of the body’s ability to self-heal in order to achieve results. In addition, treating patients as a whole person requires taking their psychological well-being into consideration.

Acne Scarring

A comprehensive, Osteopathic approach to managing acne should not only include treating the acute presentation, but also long-term sequelae such as disfiguring scarring. There are many treatment options available that take advantage of the body’s ability to self-heal in order to achieve results. In addition, treating patients as a whole person requires taking their psychological well-being into consideration.

Upcoming Meetings:

2017 AOCD Spring Meeting
Ritz-Carlton Atlanta
Atlanta, GA
March 29 - April 2, 2017

2017 AOCD Fall Meeting
Intercontinental New Orleans
New Orleans, LA
October 25 - October 28, 2017

2018 AOCD Spring Meeting
Hilton
West Palm Beach, FL
March 21 - March 24, 2018

2018 AOCD Fall Meeting
Westin San Diego - Gaslamp Quarter
San Diego, CA
October 9 - October 13, 2018