CURRENT CONCEPTS IN DERMATOLOGY

Karthik Krishnamurthy, D.O., FAOCD
Activity Chair
Acknowledgement of Commercial Support

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Continuing Medical Education Statements

*This activity will change your practice and improve patient outcomes!*

**AOA Statement:**
The American Osteopathic College of Dermatology is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians. This activity anticipates being approved for 26 hours of AOA Category 1-A credit pending approval by the AOA CCME and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity. March 29-April 1, 2017

**AAD Statement:**
The American Osteopathic College of Dermatology Current Concepts in Dermatology (Program #698100) is recognized by the American Academy of Dermatology for 26 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology's Continuing Medical Education Award. March 29-April 1, 2017

**ACCME Statement:**
The American Osteopathic College of Dermatology is currently seeking accreditation by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. March 29-April 1, 2017
American Osteopathic College of Dermatology
Mission Statement &
Continuing Medical Education Needs Assessment

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

The 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 26 hours of AOA Category 1-A credit pending approval by the AOA CCME.

The American Osteopathic College of Dermatology Current Concepts in Dermatology (Program #698100) is recognized by the American Academy of Dermatology for 26 AAD Recognized Credit(s) and may be used toward the American Academy of Dermatology’s Continuing Medical Education Award.

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

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

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

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

Learners will be provided with information on identified COI from any of the above categories of persons that affect the content of CME, and that information will be positioned in course materials such that it is read by learners prior to the execution of the CME activity. Speakers for the AOCD will be required to provide disclosure information to meeting attendees during their introduction of their topic. Additionally, disclosure statements are provided in the program schedule given to each meeting attendee and is available online at www.aocd.org.
In accordance with the ACCME’s Standards for Commercial Support of Continuing Medical Education, the Policy on Collection of Financial Relationships and Resolution of Conflicts of Interest (COI) exists to provide guidance for staff, instructors, planners, reviewers and managers of CME activities sponsored by The American Osteopathic College of Dermatology, (AOCD). This policy addresses the underlying philosophy of disclosure to learners, mechanisms to collect disclosure information and the parties from whom financial disclosure shall be collected, the mechanisms to resolve COI, and requirements to make disclosure to learners prior to the start of an activity.

Professional Practice Gap Statement:
Physicians need to understand, update and manage changes in dermatology in order to provide optimal patient care. Dermatologists in private practice may not have immediate access to new updates in therapies and treatments. This activity will help to close gaps in physician’s areas of 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.

• Attendees will learn new treatment options for pediatric dermatology issues.
• Attendees will be able to recognize clues to determining the causes of localized contact dermatitis.
• Attendees will learn the epidemiology of HIV as it pertains to dermatology.
• Attendees will learn the cutaneous manifestations of HIV infection.
• Attendees will be able to identify what an ethical dilemma is and how it can be analyzed.
• Attendees will gain more knowledge about conflicts of interest and how they apply to in-office dermatopathology laboratories.
• Attendees will gain an understanding of the appropriate coding guidelines and concepts using easy to understand methodologies of code selection and application.
• Attendees will learn how to identify appropriate dermatology codes and correct use/application of such codes for services procedures performed in your practice to ensure accurate claim submission as well as proper code identification.
• Attendees will gain an understanding of the quality of life impact of hyperhidrosis.
• Attendees will learn the known pathogenesis and treatment of hyperhidrosis.
• Attendees will be able to correlate clinical manifestations of disease with rational treatment selection and progress monitoring.
• Attendees will gain an awareness of the current state of acne, rosacea, eczema, psoriasis in patients and correlate with management plan.

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
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  
Kirkville, 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

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, has published in prestigious journals and texts, including the Journal of Investigative Dermatology, the Journal of the American Academy 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.

Jeff Benabio, MD
Dr. Benabio grew up in a small Italian neighborhood in Rhode Island, where he developed a life-long love for the Red Sox, pasta and Dunkin Donuts. He earned a BA from Providence College and an MA from Brown University. After working in alcohol and addiction studies at Brown, he and his wife moved to North Carolina where he was project manager of a stroke study at UNC-Chapel Hill. In 2003, he graduated first in his class from Wake Forest University School of Medicine, where he also served as Class President, President of Alpha Omega Alpha and was the recipient of the prestigious Faculty Award. He completed his medical internship at Scripps Mercy Hospital in San Diego and his dermatology residency at UC Irvine, where he was named chief resident.

Currently, Dr. Benabio is Physician Director of Healthcare Transformation, at Kaiser Permanente in San Diego, CA. In addition to being a board-certified practicing dermatologist, he leads one of the country’s largest telehealth programs and is also a leading voice for using social technologies to benefit healthcare teams and to empower patients. He is a member of the Re-imagining Ambulatory Design (RAD), Health Information Process Transformation (HIPT) and Telehealth committee at Kaiser Permanente. He serves on several boards, including the External Advisory Board for the Mayo Clinic Center for Social Media and writes “Digital Doctor,” a monthly column about digital medicine published in Skin & Allergy News, Pediatric News, Hospitalist News, Rheumatology News, GI and Hepatology News and Family Practice News. He has been quoted in numerous publications including the Wall Street Journal, USA Today, CNN and O, The Oprah Magazine. Perhaps, most importantly, Glamour magazine named him “A Rock Star of Dermatology.”

Over the last five years, Dr. Benabio has given over 50 lectures and keynote addresses on topics including social networking, reputation management, patient empowerment, health information technology, healthcare design and telehealth. When he isn’t practicing medicine or blogging, he can found on a Southwest Airlines flight most likely reading a biography of Teddy Roosevelt or Winston Churchill on his kindle.

Managing Your Online Reputation
This lecture will be an overview of various social and reputational online platforms, explanation of why they are important and teaching best practices to manage them.
Objectives:
1. Help attendees assess their current online reputation
2. Help attendees differentiate between different social and reputational platforms
3. Review how to actively manage your reputation, including addressing bad reviews

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

References:
1. Why Physicians are Embracing Online Patient Reviews. Physicians Practice. 6 Jan 16.

Core Competencies: 4, 5

Disclosures: No disclosures provided by speaker

Larissa Chismar, MD
Dr. Larissa Chismar is a board-certified dermatologist and dermatopathologist.

Dr. Chismar earned her medical degree from Albert Einstein College of Medicine in Bronx, NY. She completed her residency training in dermatology and fellowship training in dermatology at Montefiore Medical Center in Bronx, NY.

Dr. Chismar is a member of American Society of Dermatopathology, American Academy of Dermatology, International Society of Dermatopathology, Alpha Omega Alpha Honor Medical Society, Atlanta Association of Dermatology and Dermatologic Surgery and American Medical Association.

Challenges in Dermatopathology
This lecture will discuss the importance of detailed communication between the dermatologist and dermatopathologist. We will then discuss challenging cases that require correlation with the clinical and histologic findings, focusing on examples of difficult melanocytic lesions, soft tissue tumors and inflammatory conditions.

Objectives:
1. Review what information is important to include on dermatopathology requisition forms and why dermatopathologists may encounter diagnostic difficulty without this information
2. Review challenges encountered by dermatopathologists in the interpretation of melanocytic neoplasms, soft tissue neoplasms and inflammatory conditions
3. Review diagnostic pitfalls that may arise with partial biopsies

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

References:

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

Disclosures: No disclosures provided by speaker
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:

Core competencies: 1, 3, 5, 6

Disclosures: No disclosures provided by speaker

Eugene Conte, DO, FAOCD

Dr. Eugene Conte earned his medical degree from Michigan State University College of Osteopathic Medicine. He completed his dermatology internship and residency at Pontiac Osteopathic Hospital.

Dr. Conte serves as Assistant Clinical Professor of Dermatology at Michigan State University, Ohio University College of Osteopathic Medicine and Wright State University. At Grandview Medical Center, he is Chairman of the Department of Dermatology.

Dr. Conte is a diplomate of the American Osteopathic Board of Dermatology and the National Osteopathic Board of Medical Examiners. With more than 25 years of experience, he is a Fellow of the American Osteopathic College of Dermatology and has served as President of this prestigious organization.

Osteopathic Dermatology Research and the Foundation for Osteopathic Dermatology

This lecture will discuss the current ongoing osteopathic dermatology research projects being funded by the FOD and discuss in detail the grants available to an osteopathic dermatologists and abstract presentations.

Objectives:
1. Discuss how the Foundation for Osteopathic Dermatology (FOD) supports osteopathic dermatology research
2. Discuss the multiple grants available to an osteopathic dermatologist who wants to pursue research
3. Present “abstracts” from ongoing research projects

Needs:
1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new technology
4. Advances in medical knowledge
John Coppola, DO, FAOCD
John C. Coppola, DO, is a board-certified dermatologist and skin cancer surgeon with advanced training in a wide array of skin conditions and cosmetic procedures. A Clearwater Floridian, Dr. Coppola earned his Bachelor of Science degree from the University of North Carolina at Chapel Hill. After receiving his medical degree with highest honors from Nova Southeastern University, he completed his dermatology residency at Michigan State University Botsford Hospital and served as chief resident his final year.

Dr. Coppola currently enjoys training the next generation of physicians as a clinical associate professor for Florida State University’s College of Medicine. His previous teaching appointments included serving as a clinical instructor of Michigan State University while in private practice in Michigan. He is the author of numerous published journal articles and is now active in dermatologic medical research.

His passion for personalized care focuses on three key tenets: preventing sun damage, educating his patients on skin health & vitality and getting to know his patients also as people (for military veterans, he is eternally grateful for their service). When not at work, he can be found most days spending time playing with his German shepherd “Grizzly”.

20 Tricks to Finishing Your Office Day On Time
This lecture offers a myriad of tips on running your medical and surgical dermatology practice patient schedule on time to improve patient satisfaction and reduce physician burn out.

Objectives:
1. Review how to incorporate health-based technology into your practice
2. Review how to improve office and patient flow to improve efficiency

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

References: Pending

Core Competencies: 3, 4, 5

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.
So Many Drugs, So Little Time
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. Review initial doses and follow up adjustments with several medications 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:

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

Salma Faghri de la Feld, MD
Dr. Salma Faghri de la Feld is a board-certified dermatologist.

Dr. Faghri de la Feld earned her medical degree from the Warren Albert School of Medicine at Brown University in Providence, RI. She completed her internship at Brown University/Rhode Island Hospital in Providence, RI. Dr. Faghri de la Feld completed her dermatology residency at University of Alabama School of Medicine in Birmingham, AL, where she served as chief resident. She is an Assistant Professor of Dermatology at Emory University.

Clues in Contact Dermatitis
This lecture will provide an overview of patch testing process and clinical clues to eyelid, lip and facial allergic contact dermatitis including common allergens and avoidance tips. Overview of systemic contact dermatitis with focus on nickel and balsam of Peru.

Objectives:
1. Provide attendees with an overview of patch testing and whether patients can be patch tested while on immunosuppressants
2. Help attendees recognize clues to determining the causes of localized contact dermatitis (specifically eyelid, lip and facial dermatitis)
3. Review causes of systemic contact dermatitis, including nickel and balsam of Peru

Needs:
1. Advances in medical knowledge

References:
2. Huyuh et al. (2012). The Dermatologists. 20(8).
Ron Feldman, MD
Dr. Ron Feldman is a board-certified dermatologist.

Dr. Feldman received a Bachelor of Science degree from College of Charleston in Charleston, SC. He earned his medical degree and a Ph.D from the Medical University of South Carolina in Charleston, SC. Dr. Feldman completed his dermatology residency at Cleveland Clinic in Cleveland, OH and an autoimmune blistering disease fellowship at the Center for Blistering Diseases in Boston, MA.

Bullous Disease as a Window Into the Body
This lecture will provide mechanisms of autoimmune bullous diseases with a unique perspective on how these diseases can provide insight into other systemic processes.

Objectives:
1. Define mechanisms of autoimmune bullous diseases
2. Help attendees understand how bullous diseases can provide insight into systemic disease
3. Review treatments for both bullous diseases and related systemic diseases

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

References:

Core Competencies: 2, 3

Disclosures: Consultant for Eli Lilly

Michelle Foley, DO, FAOCD
Dr. Michelle Foley is a board-certified dermatologist specializing in medical and surgical dermatology, with a passion for non-surgical aesthetics and facial rejuvenation. Her practice approach is to provide personalized care and education for each of her patients. Dr. Foley works with both men and women to help them look their best utilizing non-invasive techniques; combining injectables, topical agents, lasers and physician-strength skin care. “Best results are always achieved when you partner with your patient to build a treatment plan that is right for that individual. Cosmetic dermatology is not a one-size-fits-all world,” she explains.

Dr. Foley was born in Alabama and grew up on the west coast of Florida. After graduating Summa Cum Laude from Florida State University, she attended Nova Southeastern University College of Osteopathic Medicine in Ft. Lauderdale, FL. There she graduated with the highest of honors and received the Terry Internal Medicine Award for the highest achievement in academic and clinical internal medicine. Dr. Foley completed her dermatology training at Michigan State University/POH Regional Medical center in Detroit, Michigan where she served as the chief resident.

Locally, Dr. Foley is an Associate Clinical Professor for Florida State University College of Medicine and a volunteer educator for Halifax Hospital Family Medicine Program. She also serves as the Associate Editor for the Journal of the American Osteopathic College of Dermatology.
A Decade of Lessons Learned the Hard Way: Practical Knowledge for the Medical and Cosmetic Dermatologist and Practice Owner

This lecture will present and discuss the failure and success of treatment of difficult medical and cosmetic cases, as well as the failure and success of decisions facing the practice owner.

Objectives:
1. Present alternative therapies to treat difficult cases that previously failed common treatment or are easily misdiagnosed
2. Present a streamlined approach to cosmetic patients in your office that will increase both your profit margin and patient satisfaction
3. Present both tried, failed and successful strategies for growth of your medical and cosmetic practice

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

References:

Core Competencies: 1, 2, 3, 6

Disclosures: No disclosures provided by speaker

Adam Friedman, MD
Adam Friedman, MD, FAAD, is an Associate Professor of Dermatology and serves as Residency Program Director and Director of Translational Research in the Department of Dermatology at the George Washington University School of Medicine and Health Sciences.

Dr. Friedman completed his undergraduate training at the University of Pennsylvania and graduated with Distinction in Dermatologic Research at the Albert Einstein College of Medicine in New York. He completed his internship at New York Hospital Queens and returned to Einstein for his dermatology residency and was appointed chief resident during his final year.

Dr. Friedman joined the Einstein faculty after graduation from 2010-2015, during which time he was the Director of Dermatologic Research, Director of the Translational Research Fellowship and the Associate Program Director. Dr. Friedman is currently investigating novel nanotechnologies that allow for controlled and sustained delivery of a wide spectrum of physiologically and medicinally relevant molecules, with an emphasis on treating infectious diseases, accelerating wound healing, immune modulation and correcting vascular dysfunction. In line with his research interests, he serves as Vice President of the Nanodermatology Society. Dr. Friedman was recently appointed as President of the Dermatology Section of the New York Academy of Medicine.

Dr. Friedman is also committed to resident and medical education. He chaired the leadership workgroup of the American Academy of Dermatology Resident/Fellows Committee, currently serves on the Sulzberger Committee on Education and is the Senior Editor of the Dermatology In-Review Online Workshop. Dr. Friedman serves as the Dermatology Expert for healthguru.com and publishes a column on Everyday Health entitled “The Skin You’re In.”

Urticaria: Diagnosis and Treatment Considerations
This lecture will highlight the common condition many do not appropriately know how to manage.

Objective:
1. Review how to recognize urticaria and formulate appropriate workups

Needs:
1. New advances in dermatologic treatment
2. Availability of new medication(s) or indication(s)
3. Advances in medical knowledge
References:
2. The Diagnosis and Management of Acute and Chronic Urticaria, 2014 Update, *JACI.* 2014;133(3):1270-77.

Core Competencies: 1, 2, 3, 6

Disclosures: Speaker for Janssen Biotech, Inc.; Consultant for Galderma, Encore, Pfizer

Melinda Greenfield, DO, FAOCD
Melinda F. Greenfield is a board-certified dermatologist specializing in the diagnosis and treatment of the skin, hair and nails. Her additional areas of expertise include cutaneous surgery, Botox, fillers, leg vein treatment (sclerotherapy) and other cosmetic procedures.

Dr. Greenfield has been in Albany, GA since 2000 and has quickly become a local and regional expert in the field of dermatology. She is on the speaker’s board for several pharmaceutical companies and lectures for many local and regional groups. She especially enjoys educating the community on the dangers of the sun and skin cancer.

She is an Associate Clinical Professor at the Georgia Campus of the Philadelphia College of Osteopathic Medicine and the Georgia Health Sciences University (Medical College of Georgia). She is on the board of the Dougherty County Medical Society, as well as the Georgia Osteopathic Medical Association. She served as president of the Georgia Osteopathic Medical Association for the 2011-2012 term. She is also an Associate Editor of the *Journal of the American Osteopathic College of Dermatology.*

Dr. Greenfield received her Bachelor of Science degree from the University of Maryland and received her medical degree with honors from Nova Southeastern University in Ft. Lauderdale, FL. She completed a year of internal medicine at Sinai Hospital of Baltimore prior to her three year dermatology residency at St. Barnabas Hospital in Bronx, NY.

She lives in Albany, GA with her husband, Carl and two children, Nathan and Josie. In her spare time she enjoys cooking, reading, tending to her 8 cats and 1 dog and training for various running races and triathlons.

Fermentation, Civilization and the Microbiome
This lecture will review the history of fermentation and how it has contributed to the health of human civilization, introduce the human microbiome and emphasize the importance of understanding a healthy microbiome as a practicing dermatologist.

Objectives:
1. Review the process of fermentation and how it has contributed to the history and health of human civilization
2. Review the human microbiome and the importance of maintaining a healthy microbial ecosystem
3. Relate the healthy microbiome to the practice of dermatology

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

References:

Core Competencies: 2, 3
Charles Gropper, MD

Charles A. Gropper, MD, is a board-certified dermatologist who is a diplomate of the American Board of Dermatology and the National Board of Medical Examiners. Currently, Dr. Gropper is an Associate Clinical Professor of Dermatology at the Mount Sinai School of Medicine, as well as a dermatopharmacology peer reviewer for the *Lancet Journal*.

Dr. Gropper graduated with an Artium Baccalaureatus (A.B.) degree with magna cum laude honors from Brown University in Providence, RI. He attended the University of Pennsylvania School of Medicine where he received his medical degree. After completing his education, Dr. Gropper completed an internal medicine internship at the Mount Sinai Hospital followed by a residency in dermatology at Albert Einstein College of Medicine and a fellowship in dermatopharmacology at New York University Medical Center.

For over 18 years, Dr. Gropper has practiced medicine in hospitals and private practices in New York, Brooklyn and the Bronx. He has also held positions as Chief of Dermatology and Associate Clinical Professor of Dermatology. Currently, he is Chief of Dermatology at St. Barnabas Hospital in the Bronx. He has co-authored numerous professional articles and book chapters related to dermatology and dermatopharmacology. He has received over a dozen awards for significant contributions, teacher of the year, educating residents and exceptional service.

Dr. Gropper is a fellow of the American Academy of Dermatology, as well as a member of the American Medical Association, the International Society for Digital Imaging of the Skin and the Space Dermatology Foundation.

**HIV In Dermatology**

This lecture will be a review of epidemiology, clinical features and management strategies for a variety of infectious, inflammatory and neoplastic skin conditions associated with HIV. Special emphasis will be placed on the need to be aware that a variety of common and rare skin conditions can be markers of HIV infection.

**Objectives:**

1. Review epidemiology of HIV as pertains to dermatology
2. Review cutaneous manifestations of HIV infection
3. Review treatment options for various HIV-related skin conditions

**Needs:**

1. Advances in medical knowledge

**References:**


**Core Competencies:** 2, 3

**Disclosures:** No disclosures provided by speaker

**Cindy Hoffman, DO, FAOCD**

**Great Cases From Osteopathic Institutions**

**Objectives:**

1. Present interesting cases
2. Discuss treatment of the interesting cases

**Needs:**

1. New advances in dermatologic treatment
2. New methods of diagnosis or treatment
3. Development of new technology
4. Advances in medical knowledge
Beth McLellan, MD
Beth McLellan, MD is a board-certified dermatologist and researcher in Montefiore’s Division of Dermatology and with Montefiore Einstein Center for Cancer Care. She is also Director of Dermatology at Jacobi Medical Center. She is committed to improving oncology patients’ quality of life and preventing interruptions in their care.

Prior to joining Montefiore, Dr. McLellan served as a full-time faculty member at New York University where she saw all inpatient dermatology consults and developed an oncodermatology program. Her medical training includes an internship in internal medicine at Loyola Medicine and dermatology residency at Henry Ford Health System in Detroit, where she served as chief resident and initiated a supportive oncodermatology clinic. Dr. McLellan received additional oncodermatology training at Memorial Sloan Kettering Cancer Center and at the Institute Gustave Roussy in Paris. She has received awards from the Women’s Dermatology Society and the Dermatology Foundation. She regularly lectures at both dermatology and oncology meetings and is actively involved in teaching medical students and residents.

Dr. McLellan specializes in complex medical dermatology and has a special interest in supportive oncodermatology - the treatment of dermatologic diseases in cancer patients. She works closely with oncologists to prevent and treat skin, hair and nail-related side effects due to cancer therapies. Dr. McLellan has received a Career Development Award from the Dermatology Foundation to study hair loss in breast cancer patients on hormonal treatments. In addition to hair loss, her research interests include hand foot syndrome and radiation dermatitis.

Dr. McLellan has published numerous articles and textbook chapters related to supportive oncodermatology. She is regularly invited to speak at dermatology and oncology conferences including, the annual meeting of the American Academy of Dermatology, the South Beach Symposium and the International Symposium for Supportive Care in Cancer.

**Cases In Oncodermatology**
This lecture will review some common reactions to cancer therapies, as well as dermatologic problems in cancer survivors in case-based approach. Reactions covered will include: hand foot skin reactions, papulopustular eruption, onycholysis, cutaneous metastases, nummular dermatitis of the reconstructed breast and secondary skin cancers following radiation therapy.

**Objectives:**
1. Review how to recognize and manage common side effects from traditional and targeted chemotherapeutic agents, including hand foot skin reaction, papulopustular eruption and onycholysis
2. Help attendees improve communication with oncologists by using common terminology and grading systems for treatment-related toxicities
3. Review the importance of dermatologic care in cancer survivors, especially surveillance for secondary skin cancers

**Needs:**
1. Advances in medical knowledge

**References:**

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

**Disclosures:** Stockholder of Spruce Health; Advisor for Spruce Health; Consultant for Biopelle
Faith McNicholas, RHIT, CPC, CPCD, PCS, CDC

Faith C. M. McNicholas, RHIT, CPC, CPCD, PCS, CDC has a wide range of experience in various medical specialties, both solo and group practice settings ranging from cardiology to endocrinology to dermatology. Her passion however, lies in dermatology.

She is the Assistant Editor for Derm Coding Consult – a quarterly coding and regulatory newsletter published by the American Academy of Dermatology (AAD), a regular feature contributor to Association of Dermatology Managers/Administrators (ADA/M) Newsletter, Journal of Dermatology Nurses Association (JDNA). She has written extensively on coding, reimbursement and regulatory changes and how it affects the physician practice. She is also a known presenter at the AAD Annual and Summer Meetings, AAPC Regional Meeting, ADA/M Guest Key Note speaker and presenter, JDNA Annual meetings and AAD monthly webinars and regional symposia.

She is a Registered Health Information Technician (RHIT) and member of American Health Information Management Association (AHIMA) as well as a Certified Professional Coder (CPC) and member of the American Academy of Professional Coders (AAPC) with specialization in dermatology coding. Other qualifications include certification Medical Billing, medical coding, management of medical office and healthcare practice and a degree Health Information and Management Technology. She is a certified and approved ICD-10-CM/PCS Expert and Trainer.

She is a member of AHIMA Clinical Terminology & Classification Practice Council that monitors and provide AHIMA with expertise related to advocacy, member needs and best practices in clinical terminologies and classification systems, as well as a member of AAPC Chapter Association Board of Directors, a group of volunteers who advance coding education efficacy among coders.

She is currently the Manager of Coding and Reimbursement/Government Affairs at the AAD in Schaumburg, Illinois. She is also proprietor of Coracle – a medical coding, billing and practice management consulting firm.

Faith is also recipient of the 2014/2015 American Medical Association (AMA) Specialty Staff Liaison Excellence Award. She was awarded the 2015/2016 JDNA People’s Choice Award for her article on “Tips for Seamless ICD-10-CM Readiness.”

AAD Billing and Coding Update

Learn how to easily identify appropriate dermatology codes and correct use/application of such codes for services/procedures performed in your practice to ensure accurate claim submission, as well as proper code identification and application for more complex procedures to accurately reflect the services provided.

Objectives:
1. Review what’s new and revised in coding and regulatory updates pertaining to dermatology in 2017
2. Review the appropriate coding guidelines and concepts using easy to understand methodologies of code selection and application
3. Review how to easily identify appropriate dermatology codes and the correct use/application of such codes for services procedures performed in your practice to ensure accurate claim submission as well as proper code identification

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

References:
3. Center for Medicare and Medicaid Services Local Coverage Determination (CMS LCD).

Core Competencies: 3, 6, 7

Disclosures: No disclosures provided by speaker
Carlos Nousari, MD

Carlos Nousari, MD is nationally and internationally recognized as a leading authority in dermatoinmunology. He is a clinician, a researcher and a prolific author in the areas of dermatoinmunology, dermatopathlogy and immunofluorescence. In particular, he has conducted extensive research in autoimmune blistering diseases, connective tissue disorders and vasculitides.

Prior to joining Dermpath Diagnostics in June 2004, Dr. Nousari served as co-director of the Division of Immunodermatology at Johns Hopkins Medical Institute in Baltimore, MD and as chairman of the Department of Dermatology and Director of Dermatopathology and Immunodermatology at the Cleveland Clinic Florida in Weston. Dr. Nousari is currently the program director of the Broward Health Medical Center Dermatology Residency Program. He also serves as the Medical Director at Dermpath Diagnostics South Florida and the Director of the Institute for Immunofluorescence. Dr. Nousari is a Professor of Dermatology at the University of Miami, University of Florida and Nova Southeastern University where he runs an immunobullous clinic.

Photosensitive Disorders in Middle Age and Beyond

This lecture will explore the various photodermatoses potentially encountered in clinical practice. An emphasis will be placed on clinical diagnosis tips, how to interpret antibody results and the pathophysiology of the different disease processes.

Objectives:
1. Discuss the clinical presentations and histological features of various photodermatoses
2. Explore the pathophysiology of ultraviolet-mediated diseases
3. Understand how to interpret the antibodies tested in various photodermatoses

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

References:

Core Competencies: 2, 3

Disclosures: No disclosures provided by speaker

Leslie Potter Lawley, MD

Dr. Leslie Potter Lawley is a board-certified dermatologist and pediatric dermatologist.

Dr. Lawley earned her medical degree from Emory University School of Medicine in Atlanta, GA. She completed an internship and her dermatology residency training at Emory University Hospital in Atlanta, GA. She then completed a fellowship in pediatric dermatology at Northwestern University Medical School in Chicago, IL.

Dr. Lawley is a member of the American Academy of Dermatology, American Medical Association, Society of Investigative Dermatology, Society of Pediatric Dermatology, Women's Dermatologic Association.

Look-Alikes, Controversies and What's New in Pediatric Dermatology

This lecture will compare and contrast several pediatric dermatology diagnoses, including vascular birthmarks (specifically infantile hemangiomas and capillary malformations), forms of infected atopic dermatitis, and infantile cutaneous tumors (specifically nevus sebaceous, mastocytoma, and juvenile xanthogranuloma) and highlight recent literature applicable to these topics.
**Objectives:**
1. Distinguish clinical features of infantile hemangiomas and capillary vascular malformations (i.e. port wine stains) and understand systemic implications of each
2. Differentiate clinical features of secondary infections complicating atopic dermatitis including eczema, herpeticum, eczema coxsackium and impetiginized eczema
3. Review the current literature regarding the risks of tumor development within nevus sebaceous birthmarks

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

**References:**

**Core Competencies:** 2, 3

**Disclosures:** Content author for Up To Date

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**Don’t Sweat It: Treatments for Hyperhidrosis**
This lecture will discuss the large portion of patients that suffer from hyperhidrosis. There is an undeniable need for more practitioners that know how to diagnose and treat hyperhidrosis.

**Objectives:**
1. Review quality of life impact of hyperhidrosis
2. Review known pathogenesis of hyperhidrosis
3. Review treatment of hyperhidrosis

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

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


Albert E. “Bo” Rivera, DO, FAOCD
Dr. Albert E. “Bo” Rivera is a licensed physician and surgeon in Alabama, board-certified diplomat of the American Osteopathic College of Dermatology, a fellowship-trained member of the American College of Mohs Surgeons, as well as member of several dermatology and medical specialty organizations such as the American Society for Dermatologic Surgery, American Society for Mohs Surgery, American Academy of Dermatology, Skin Cancer Foundation and the Madison County Medical Society.

He was born and grew up in Haleyville, AL, graduating from Haleyville High School. Afterward, he completed his undergraduate education at Auburn University, earning a degree in premedicine and zoology. He completed his medical training at Kansas City University of Medicine and Biosciences in Kansas City, MO. His internship in general surgery was done at the University of Kentucky, in Lexington, KY, followed by an internal medicine residency at Northside Hospital and Heart Institute in Saint Petersburg, FL. At Northeast Regional Medical Center in Kirksville, MO, he completed both a dermatology residency as well as a dermatology research and laser fellowship under the direction of Lloyd J. Cleaver, DO. Upon completion of his residency, Dr. Rivera was nationally awarded the James Bernard, D.O. Residency Leadership Award based on integrity, respect, empowerment and initiative. The final honor in his training was completing a Mohs Micrographic Surgery subspecialty fellowship under the direction of Roger I. Ceilley, MD and Andrew K. Bean, MD in West Des Moines, IA. Over the years he has had the opportunity to publish several articles in national and international medical journals, as well as authoring chapters in medical textbooks and online. Dr. Rivera serves on the editorial board for the Journal of Clinical and Aesthetic Dermatology and the Journal of the American Osteopathic College of Dermatology, as well as serving on the AOCD Editorial/Public Relations Committee and as an American Academy of Dermatology Liaison. He has also given presentations at local, national and international venues to both non-medical and medical professionals throughout his medical career.

Dr. Rivera enjoys multiple aspects within dermatology but has specific interest and extensive training in the prevention and treatment of skin cancers. Personally, he enjoys traveling, educating others, general fitness, as well as participating in and viewing multiple sports. Also, away from work, he enjoys time with his wife, Stephanie, a daughter who was born in 2015 and their Labradoodle. Dr. Rivera has also been awarded the Doctor’s Choice Award in Dermatology for Madison.

A Play Yard of Dermatology Tips
This lecture will cover various accumulated tips relating to business, customer service, efficiency, medical dermatology, surgical dermatology and Mohs.

Objectives:
1. Discuss accumulated collection of business and customer service tips
2. Discuss accumulated collection of medical and surgical dermatology tips
3. Review and discuss the WAR (Webb and Rivera) Score

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

References: Pending

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

Advisory Board: Castle Biosciences

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.

Cutaneous Manifestations of Illegal Drug Use
This lecture will highlight the common and rare cutaneous manifestations of illegal drug use in the United States. It will also review the methods of drug use, the equipment utilized and the risk factors for these types of side effects.

Objectives:
1. Review common cutaneous physical exam signs and symptoms of illegal drug use
2. Review the common adulterants of drugs in the United States
3. Review the more exotic bacterial infections associated with drug use in the United States

Needs:
1. New advances in dermatologic treatment
2. Advances in medical knowledge
3. Legislative, regulatory, or organizational changes effecting patient care

References:
1. Bologna
2. Andrews
3. Duuvvier Atlas

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

Disclosures: No disclosures provided by speaker

George Schmieder, DO, FAOCD
George J. Schmieder, DO, FAOCD, FAAD, is a board-certified dermatologist and Mohs Skin Cancer Surgeon. Dr. Schmieder completed his dermatology residency at the esteemed University of Miami. He is a subject level expert in cosmetic and laser dermatology, as well. His dedication to his community and country is evidenced by his 20+ year commitment to the U.S. Navy. Dr. Schmieder has earned a stellar reputation for performing Mohs surgery in Jacksonville. He is devoted to teaching and recently began the Park Avenue Dermatology Residency program. Academic research has also been one of his personal endeavors demonstrated by the many past and present clinical research studies to explore the latest techniques and use of new pharmaceuticals for the treatment of a variety of skin conditions and skin-related disorders, such as acne, atopic dermatitis, psoriasis, pre-cancerous skin lesions and more.

Local Flaps and Mohs Reconstruction and When to Use Them
This lecture will involve the planning and execution of a flap repair following Mohs surgery, which varies from case to case. This lecture will show the audience different approaches on how to close Mohs defects when simple closure is not indicated.

Objectives:
1. Help attendees understand that the methods of reconstruction are dependent on the depth/thickness of the defect and the overall shape and size of the wound
2. Help attendees understand which method is chosen must be an inherent upon vascular supply
3. Help attendees understand that reconstruction must consider maximal horizontal stabilization with minimal vertical tension

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

References:

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

Disclosures: Owner of Park Avenue Dermatology, PA

Ben Stoff, MD
Benjamin Stoff, MD, holds a joint appointment as Assistant Professor in the Department of Dermatology and the Department of Pathology at Emory University School of Medicine. A board-certified dermatologist and dermatopathologist, Dr. Stoff specializes in the diagnosis and treatment of skin cancer and is a member of the multidisciplinary melanoma team at Winship Cancer Institute. He began practicing with Emory Healthcare in 2011.

Dr. Stoff is a fellow of the American Academy of Dermatology, the American Society of Dermatopathology and the Emory Center for Ethics. He is a member of American Academy of Dermatology, American Society of Dermatopathology, Emory University Hospital Ethics Committee, American Society of Bioethics and Humanities and Atlanta Society of Dermatology and Dermatologic Surgery.

Dr. Stoff attended medical school at the University of Texas Southwestern and completed his internship at Baylor University Medical Center. He then completed his residency in dermatology and fellowship in dermatopathology at Emory University School of Medicine. He is currently a student in the Masters in Bioethics Program at the Center for Ethics at Emory University.

Dr. Stoff’s research interests include bioethics, dermatopathology and melanoma. He is also interested in global health and has received the Skin Care in Developing Countries grant from the American Academy of Dermatology. He is a reviewer for the Journal of the American Academy of Dermatology and the Journal of Drugs in Dermatology.

Dr. Stoff has been elected Teacher of the Year in the dermatology department of Emory University School of Medicine for three consecutive years.

Contemporary Ethical Controversies in Dermatology
This lecture will define ethics, explain its importance to practicing dermatologists and apply ethical reasoning to contemporary controversies in dermatology.

Objectives:
1. Explain what an ethical dilemma is and how it can be analyzed
2. Describe conflict of interest and how it applies to in-office dermatopathology laboratories
3. Recount arguments in favor of and against free skin cancer screening events

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

Core Competencies: 5

International Volunteerism in Dermatology: Short-Term Travel, Long-Term Impact
This lecture will define global health and emphasize the importance of dermatology in global health. It will also dispel common myths about short-term global health volunteer work. This lecture will also discuss the qualities of short-term projects that make them successful at carrying out the goals of global health. It will close by showing tropical diseases relevant to dermatology and model organizations.

Objectives:
1. Explain what global health is and why dermatologists should participate
2. Describe educational interventions that can be carried out successfully by the short-term volunteer
3. List model organizations that facilitate short-term experiences in global health for dermatologists

Needs:
1. Advances in medical knowledge

References:

Core Competencies: 2, 3, 4, 5

Disclosures: No disclosures provided by speaker

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

Name That Nubbin!
This lecture will provide an overview of various bumps and spots on the skin in children.

Objectives:
1. Review treatment options for pyogenic granulomas
2. Review congenital cysts on the neck
3. Review treatment options for warts and molluscum

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

References:

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

**Pediatric Dermatology Update**
This lecture will give an overview of new treatments from common pediatric dermatology issues.

**Objectives:**
1. Review new treatment options for pediatric dermatology issues
2. Review new details about common pediatric rashes
3. Review JAK inhibitors

**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:**

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

*Disclosures: Speaker for Valeant, Bayer; Advisory Board of Sanofi Regeneron, Amgen, Allergan*

CORE/O’Bleness Memorial Hospital
**Speaker:** Jessica Hoy, DO

**Cutaneous Manifestations of Systemic Disease**

**Objectives:**
1. Review key clinical characteristics of nutritional dermatoses
2. Formulate a differential diagnosis for a patient presenting with a nutritional dermatosis
3. Review appropriate workup and treatment for zinc deficiency and its differential

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

**References:**

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

*Disclosures: No disclosures provided by speaker*
KCU-GMEC/Dermatology Residency of Orlando  
**Speaker:** Panyamol Kittipongdaja, DO  
*Papulosquamous, Lichenoid & Eczematous Dermatoses*

**Objectives:**
1. Review new treatment options (including investigational drugs) for psoriasis and eczema  
2. Review different types of PRP and unique characteristics of each  
3. Review most commonly tested contact allergens

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

**References:**

**Core Competencies:** 2

Disclosures: *Off-Label - We will be discussing investigational drugs for the treatment of psoriasis and eczema*

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KCU-GMEC/Tri-County Dermatology  
**Speaker:** Maren Gaul, DO  
*Psychodermatology*

**Objectives:**
1. Review how to recognize common neuropsychocutaneous disorders  
2. Review how to treat common neuropsychocutaneous disorders  
3. Review how to work up common neuropsychocutaneous disorders

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

**References:**

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

Disclosures: *No disclosures provided by speaker*

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LECOMT/St. John’s Episcopal Hospital  
**Speakers:** Anna Karp, DO; Stephanie Lasky, DO  
*Figurate Erythemas and Purpuras*

**Objectives:**
1. Review the diagnosis and treatment of erythemas  
2. Review the diagnosis, pathogenesis and treatment of purpuras

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

References:

Core Competencies: 2, 3

Disclosures: No disclosures provided by speakers

LECOMT/University Hospitals Regional Hospitals

Speakers: Rosanne Paul, DO; Madeline Tarrillion, DO

Acne & Related Disorders

Objectives:
1. Review the current guidelines of care for the management of acne vulgaris
2. Review the identification and management of acne-related dermatologic disorders
3. Review the application of osteopathic principles to acne vulgaris and related conditions

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

References:

Core Competencies: 1, 2, 3

Disclosures: No disclosures provided by speakers

MWU/OPTI/Advanced Desert Dermatology

Speaker: Jennifer Peterson, DO

Neonatal Dermatology

Objectives:
1. Review high-yield highlights of neonatal dermatology for board review
2. Review clinically relevant pearls for managing common skin conditions in the neonatal period
3. Review literature to stay current with evidence-based practices in neonatal dermatology

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

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

Disclosures: Off-Label - Acitretin/isotretinoin for harlequin ichthyosis and collodion baby IVIG for sclerema neonatorum

MWU/OPTI/Affiliated Dermatology
Speaker: Stephanie Blackburn, DO
Disorders of the Tongue and Nails

Objectives:
1. Review dermatologic mucosal membrane condition
2. Review dermatologic tongue disorders
3. Review dermatologic nail disorders

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

References:

Core Competencies: 2, 3, 6

Disclosures: No disclosures provided by speaker

NSUCOM/Broward Health Medical Center
Speakers: Jennifer Conde, DO; S. Brandon Nickle, DO; Brittany Smirnov, DO
Vasculitides and Vaso-Occlusive Disorders

Objectives:
1. Identify the clinical findings associated with small, mixed and medium-sized vessel vasculitis
2. Identify the histopathologic findings associated with small, mixed and medium-sized vessel vasculitis
3. Identify the disease states commonly associated with IgA vasculitis

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

References:

Core Competencies: 2

Disclosures: No disclosures provided by speakers
NSUCOM/Largo Medical Center
Speakers: Joseph Dyer, DO; Natalie Edgar, DO; Dawnielle Endly, DO

Viral Dermatoses

Objectives:
1. Review various dermatologic correlations to the herpes viruses
2. Provide an awareness of possible dermatologic conditions that may result from various human papilloma viruses
3. Review various childhood exanthems and their potential implications

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

References:

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

Disclosures: No disclosures provided by speakers

NSUCOM/Larkin Community Hospital
Speakers: Jennifer David, DO; Samuel Ecker, DO; Yuri Kim, DO

Vesiculobullous Diseases

Objectives:
1. Review the histology and immunofluorescence findings of various vesiculobullous diseases
2. Review the clinical presentation and epidemiology of various vesiculobullous diseases
3. Review the treatment of various vesiculobullous diseases

Needs:
1. Advances in medical knowledge

References:

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

Disclosures: No disclosures provided by speakers

NYCOMEC/Palisades Medical Center
Speakers: Lauren Keller, DO; Tanasha Simela, DO; Tyler Vukmer, DO

Cysts and Disorders of the Hair

Objectives:
1. Review the diagnosis of common disorders affecting the hair and scalp with treatment options
2. Review the technique for performing a scalp biopsy
3. Identify and describe the clinical and histopathologic features of cysts
Needs:
1. New advances in dermatologic treatment
2. Availability of new medication(s) or indication(s)
3. Advances in medical knowledge
4. New methods of diagnosis or treatment

References:

Core Competencies: 2, 3, 6

Disclosures: No disclosures provided by speakers

NYCOMEC/St. Barnabas Hospital
Speaker: Lacey Elwyn, DO

*Epidermal and Dermal Tumors*

Objectives:
1. Identify how to diagnose and treat benign epidermal tumors
2. Identify how to diagnose and treat benign dermal tumors
3. Identify how to diagnose and treat benign follicular and adnexal tumors

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

References:

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

Disclosures: No disclosures provided by speaker

OMNEE/LewisGale Hospital-Montgomery
Speakers: Gina Caputo, DO; Jacqueline Fisher, DO

*Granulomatous, Metabolic and Depositional Diseases*

Objectives:
1. Review the clinical presentation of granulomatous, metabolic and depositional diseases
2. Review the treatment options for granulomatous, metabolic and depositional diseases
3. Review high-yield board-relevant information pertinent to granulomatous, metabolic and depositional diseases

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

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

Disclosures: No disclosures provided by speakers

OPTI-West/Aspen Dermatology
Speaker: Chelsea Loy, DO

Pediatric Vascular Disorders

Objectives:
1. Review the pathogenesis of pediatric vascular disorders
2. Identify when a dermatologist should refer to other specialties in pediatric patients with vascular disorders
3. Review new treatment options available for pediatric disorders

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

References:

Core Competencies: 2, 3

Disclosures: No disclosures provided by speaker

OPTI-West/Silver Falls Dermatology
Speakers: Bryce Desmond, DO; Benjamin Perry, DO

Pediatric Dermatology: Pigmented Lesions

Objectives:
1. Identify common pediatric dermatoses
2. Identify the most common features of pediatric pigmented lesions
3. Differentiate between spitz nevus and melanoma

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

References:

Core Competencies: 2, 3, 6, 7

Disclosures: No disclosures provided by speakers
**PCOM/Lehigh Valley Health Network**  
**Speakers:** Huyenlan Dinh, DO; Elise Grigurich, DO  
**Premalignant and Malignant Non-Melanoma Skin Cancer**

**Objectives:**
1. Review basic knowledge regarding premalignant and malignant dermatologic lesions
2. Discuss up-to-date literature on staging and managing high risk squamous cell carcinoma
3. Evaluate new treatment modalities for premalignant and malignant lesions

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

**References:**

**Core Competencies:** 1, 2, 3, 6, 7

*Disclosures: No disclosures provided by speakers*

**PCOM/North Fulton Hospital Medical Campus**  
**Speaker:** Irina Milman, DO  
**Pediatric Dermatology: Tumors of Fat, Muscle and Bone and Epidermal, Appendageal and Dermal Tumors**

**Objectives:**
1. Identify the most common pediatric tumors of fat, muscle and bone
2. Identify the most common pediatric epidermal, appendageal and dermal tumors
3. Identify the most common syndromes associated with the above tumors

**Needs:**
1. Advances in medical knowledge

**References:**

**Core Competencies:** 1, 2

*Disclosures: No disclosures provided by speaker*
Genodermatoses

Objectives:
1. Review high-yield clinical findings for common genodermatoses
2. Review treatment options and appropriate referrals for genodermatoses patients
3. Match specific eye/ear findings unique to individual genodermatoses

Needs:
1. New advances in dermatologic treatment
2. Advances in medical knowledge

References:

Core Competencies: 1, 2, 3, 6

Disclosures: No disclosures provided by speakers

Pediatric Papulosquamous and Eczematous Dermatoses

Objectives:
1. Differentiate between the most common papulosquamous and eczematous eruptions in pediatric patients
2. Review etiologies of the most common papulosquamous and eczematous eruptions in pediatric patients
3. Review treatment options for the most common papulosquamous and eczematous eruptions in pediatric patients

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

References:

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

Disclosures: No disclosures provided by speakers
SCS/MSUCOM/Oakwood Healthcare System  
**Speaker:** Dustin Portela, DO  
**Pediatric Blistering Diseases**

**Objectives:**
1. Review the pathophysiology and presentation of pediatric bullous disorders  
2. Review board-relevant dermatopathology associated with pediatric bullous disorders  
3. Review advancements of treatment options for pediatric bullous disorders, including gene therapy  

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

**References:**

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

**Disclosures:** No disclosures provided by speakers

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**Still OPTI/Northeast Regional Medical Center**  
**Speakers:** Emily Kollmann, DO; Nicole Tillman, DO  
**Infectious Diseases: Fungal**

**Objectives:**
1. Review the characteristics of superficial fungal infections  
2. Review the characteristics of deep fungal infections  
3. Review the treatment of fungal infections  

**Needs:**
1. New advances in dermatologic treatment

**References:**

**Core Competencies:** 2  

**Disclosures:** No disclosures provided by speakers
Texas OPTI/South Texas Osteopathic Dermatology

Speaker: Dylan Alston, DO

Photo and Pregnancy Related Dermatoses

Objectives:
1. Review the differences between major pregnancy related dermatoses
2. Review photoprotection as it pertains to the treatment of photodermatoses
3. Review when to appropriately engage other specialists, including OB/GYN, during the evaluation and management of pregnancy dermatoses

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

References:

Core Competencies: 2, 3, 4, 6

Disclosures: No disclosures provided by speaker

Texas OPTI/UNTHSC

Speaker: Bridget McIlwee, DO

Eosinophilic and Neutrophilic Dermatoses

Objectives:
1. Review basic neutrophil and eosinophil biology and how these cells contribute to the pathophysiology of the disorders discussed
2. Review how to diagnose, evaluate and treat neutrophilic dermatoses and various dermatologically-significant neutrophilic disorders
3. Review how to diagnose, evaluate and treat eosinophilic dermatoses and various dermatologically-significant eosinophilic disorders

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

References:

Core Competencies: 2, 3, 7

Disclosures: No disclosures provided by speakers
**Wednesday, March 29, 2017**

<table>
<thead>
<tr>
<th>Time</th>
<th>Primary Pathway (Salon I/II)</th>
<th>Resident Pathway (Plaza Ballroom)</th>
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<tr>
<td>10:00 a.m. - 12:00 p.m.</td>
<td>Board of Trustees Meeting</td>
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<td>12:00 p.m. - 5:00 p.m.</td>
<td>Exhibitor Set Up</td>
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<tr>
<td>1:00 p.m. - 2:00 p.m.</td>
<td><em>Pediatric Dermatology Update</em></td>
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<td>Lisa Swanson, MD</td>
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<td>2:00 p.m. - 2:15 p.m.</td>
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<td><em>Pediatric Dermatology: Pigmented Lesions</em></td>
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<td>2:15 p.m. - 2:30 p.m.</td>
<td><em>Name That Nubbin!</em></td>
<td><em>Pediatric Vascular Disorders</em></td>
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<td>Lisa Swanson, MD</td>
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<td>2:30 p.m. - 2:45 p.m.</td>
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<td><em>Disorders of the Tongue and Nails</em></td>
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<td>2:45 p.m. - 3:00 p.m.</td>
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<td><em>Neonatal Dermatology</em></td>
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<td>3:00 p.m. - 4:00 p.m.</td>
<td><em>Cutaneous Manifestations of Illegal Drug Use</em></td>
<td>MWU/OPTI/Advanced Desert Dermatology</td>
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<td>Peter Saitta, DO, FAOCD</td>
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<td>4:00 p.m. - 5:00 p.m.</td>
<td><em>Osteopathic Continuous Certification Update</em></td>
<td>Sagis Diagnostics Dermpath Bowl</td>
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<td>Lloyd Cleaver, DO, FAOCD</td>
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<tr>
<td>5:00 p.m. - 7:00 p.m.</td>
<td>Program Director’s Committee Meeting</td>
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Peds Derm Updates
Now Even Updatier!

ELIZABETH (LISA) SWANSON, MD
ADVANCED DERMATOLOGY COLORADO
ROCKY MOUNTAIN HOSPITAL FOR
CHILDREN
LISASWANSONMD@GMAIL.COM

Disclosures

- Speaker
  - Valeant
  - Bayer
  - Aqua
- Advisory Board Representative
  - Sanofi Regeneron
  - Amgen
  - Allergan

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).

Pathogenesis of Atopic Dermatitis

- Skin barrier is “broken”
- Overactive immune system process
  - Reaction to normal staph on skin?
  - Result of a “bored” immune system?

Atopic Dermatitis: Standard Treatment

- Sensitive skin care
  - ALL free and clear detergent, no dryer sheets/fab soft
  - Dove sensitive skin or cetaphil soap
  - Vanicream/Vaseline/Aquaphor as moisturizers
  - Robathol bath oil
  - Bleach baths- ¼ cup bleach in full tub water
Atopic Dermatitis- Standard Treatment

- Topical steroids- always do OINTMENTS in little kids
  - HC 2.5
  - Triam 0.1
  - Fluocinonide 0.05
  - Clobetasol 0.05
- No need to “soak and smear”. Skin can be wet or dry (JAAD Aug 2016)

Atopic Dermatitis: Steroid Burst

- Topical steroid burst for severe eczema/significant flares
  - Clobetasol bid for 4 days
  - Fluocinonide bid for 10 days
  - Triamcinolone bid until clear or followup appt

Calcineurin Inhibitors

- Elidel (pimecrolimus) 1% ointment
- Protopic (tacrolimus) 0.1% ointment
- Great for areas like face and folds
- Can be used as part of a maintenance routine
- Black Box Warning
- Pimecrolimus study from Pediatrics
  - 2418 patients age 3-12 mos old
  - Pts followed for 5-10 yrs
  - Found no evidence of lymphoma, malignancy or immune system impairment
  - Concluded it was safe even in the younger age group

NEW Treatments- Crisaborole

- Boron based topical ointment
- Inhibits phosphodiesterase-4 activity (PDE4) and decreases production of proinflammatory cytokines
- Several studies showing its efficacy down to age 2
- 65% of patients in preliminary studies were clear/almost clear
- Early and sustained improvement in pruritus
- Well tolerated; 4.4% of patients had stinging/burning
- Safety studies so far look great
- FDA approved in Dec 2016; NOW AVAILABLE!

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 or every other week
- Scheduled for FDA approval soon
### Treatments on the Horizon - Dupilumab
- JAAD Sept 2016
- Phase IIB study
- 380 patients; international study
- Pts with mod-severe eczema; 18 and older
- Produced early and sustained patient reported and clinically relevant improvements in sleep, mental health and quality of life
- Tried different dosing regimens - 300 mg once a week and 300 mg every other week did the best

### 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 the baby, it reduces the risk of eczema in that baby by 20-30%

### 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
What’s New in Pediatric Allergic Contact Dermatitis?

- Either on the rise or being recognized more commonly
- 1 exposure to the triggering agent causes a rash for 3 weeks (patients cannot intermittently use their allergen)

Patch Testing Considerations in Kids

- TRUE test is helpful in kids
  - The causative agent was identified in 71% of kids with the TRUE test
  - Even though it can be helpful, it is not often pursued in children due to the inconvenience of it, cost of it, etc
  - Most of the time, we try to identify the culprit based on the pattern of the rash

Wet Wipe Contact Dermatitis

- Due to preservative MCI/MI (Kathon CG)
- Also think about it in cases of persistent facial dermatitis
- There are now 2 brands of wipes that don’t contain the allergen
  - Honest Brand
  - Earth’s Best Hypoallergenic

Nickel Contact Dermatitis
Nickel Contact Dermatitis

- Most common allergen
- Present in almost anything metal
  - Jewelry
  - Snaps on jeans
  - Belt buckles
- Strict avoidance is the only option
- [www.nonickel.com](http://www.nonickel.com)
- Dimethylglyoxime test
- Can trigger an id reaction

Id Reaction

- An id reaction is a sympathy rash to the primary problem
- Most commonly triggered by allergic contact dermatitis, but can be triggered by molluscum or tinea

Gianotti Crosti

- Also causes monomorphic skin colored to pink papules all over arms, legs and cheeks
- Check the ears
- Typically caused by EBV but several viruses can do it
- Can take up to 8 wks to resolve
- Topical steroids help if itchy
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

- Toilet Seat Dermatitis

- Either a reaction to a cleanser being used on the seat or to the components of the seat itself
- Characteristic distribution on the lateral buttocks and post thighs
- “Soft and Comfy” toilet seat covers- Amazon $5.99
- Treat with hydrocortisone or desonide

Toilet Seat Dermatitis

- What’s New in Pediatric Psoriasis?

- Plaque psoriasis
- Guttate psoriasis- triggered by strep
- Inverse psoriasis- nearly always mistaken for yeast/tinea cruris in kids/teens
- Check the nails, check the tongue
Pediatric Psoriasis - Topical Treatment

- Clobetasol cream/ointment - body
- Clobetasol foam (Olux/Olux E Foam) - scalp
- Taclonex suspension or Enstilar foam
- Elidel or Protopic - face and folds
- I personally don’t think calcipotriene alone or tazaroc is that helpful
- Light therapy

Psoriasis

- Topical steroids continue to be the mainstay for pediatric psoriasis
- Systemic therapy options have been largely limited to cyclosporine, acitretin, methotrexate
- Biologic therapy is difficult because of lack of FDA approval, lack of data
- Systemic effects of psoriasis are making it more advantageous to consider systemic therapy, even in children

Biologics in Kids

- Enbrel (etanercept) - NOW APPROVED FOR KIDS >6 YRS OLD!!
  - Approved in Europe for psoriasis in kids >6 yrs old
  - Approved in US for JIA in kids >2 yrs old
  - 1 study in US in children- 2008-211 patients age 4-17
    - 0.8 mg/kg/wk
    - 57% achieved PASI 75
    - This study has been continued to date and has great long term safety data (JAAD Feb 2016)

- Humira (adalimumab) - CURRENTLY PURSUING PED PSOR INDICATION
  - Approved in US for kids with JIA (>2 yrs old) and Crohn’s (>6 yrs old)

- Stelara (ustekinumab)
  - Several case reports of effectiveness and safety
  - 1 clinical trial: patients age 12-18, 110 patients
    - 80% reached PASI 75 at 12 wks (JAAD Oct 2015)
  - Large study outside US is in progress
  - I have several pediatric patients on it

Psoriasis is a Systemic Disease

- #1 association in children is obesity
- Talk to them about weight
- Ask kids about smoking and stress
- Consider checking blood pressure
- Still unclear if we should be screening for hypercholesterolemia or diabetes in kids with psoriasis, but they are associated

What’s New with Pediatric Rashes?
Perioral Dermatitis

- Always ask about steroid use - topicals, inhalers, nasal sprays, etc.
- Standard treatment
  - Elidel bid
  - Amoxicillin 30 mg/kg/day divided bid for a month

Perioral Dermatitis in Kids - Additional Treatment Options

- Tacrolimus 0.1% ointment
- Clindamycin lotion/wipes
- Metronidazole cream
- Sodium sulfacetamide products
- Aczone
- Gentamicin 0.3% ophthalmic ointment
- Longer antibiotics
  - Azithromycin
    - I have classically prescribed it MWF for a month
    - Some providers are using it for 5-7 days, then 2 wks off, then repeat
  - Make sure there are no steroids on the face

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 - Irritant Contact!
Diaper Rashes

- 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

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)
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

Herpes Zoster

- Since the chicken pox vaccine has been more regularly administered to children, cases of herpes zoster in children have been on the rise
- We don’t know why immunity seems different with the vaccine vs having the chicken pox
- Patient is contagious to people who have not had the chicken pox (can’t catch shingles from shingles)
  - Need to avoid unimmunized kids and pregnant women
- Treatment with Acyclovir 30-50 mg/kg/day divided TID (valtrex if old enough to take pills)

Pediatric Rashes- Herpes Zoster

What’s New with 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

Acne

- Acne in kids age 3-7
- Ask about inhaled steroid use- can be the cause
- Good idea to order labs and/or refer to peds endocrinology
  - Total/free testosterone
  - DHEA-S
  - LH/FSH
  - Bone age- plain film of left hand and left wrist

Mid Childhood Acne
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 antiinflammatory ways
  - 1% and 4% strength being studied
  - BID dosing, appears effective and tolerable
- SEB002- topical to work with blue light. Delivers light absorbing gold-coated silica microparticles that are absorbed into the pilosebaceous unit and then enhance the PDT (Practical Derm Oct 2015)

Oral Contraceptive Pills

- Given desire to decrease oral antibiotic use, the use of OCPs has become more appealing
- My counseling routine
  - How to start the pill
  - Weight gain, nausea, mood issues
  - Blood clots, heart attack, stroke
  - Health benefits
  - Timeliness is important

OCPs

- Retrospective review of 2147 patients on OCPs for acne (JDD June 2016)
  - All OCPs help with acne
  - Triphasics probably help a little more than monophasics
  - Non estrogen component matters for efficacy:
    - Best- Drospirenone (Yaz, Yasmin)
    - 2nd Best- Norgestimate/desogestrel (ortho tri cyclen, ortho cyclen/ micronette, desogen)
    - 3rd Best- 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 >20 yrs duration
- History of or current DVT/PE
- Major surgery with prolonged immobilization
- Ischemic heart disease or Valvular heart disease with complications
- History of CVA
- Headaches (migraine with focal neuro symptoms at any age or without aura if >35 yrs old)
- Active viral hepatitis
- Severe decompensated cirrhosis
- Liver tumor (benign or malignant)

### Other Hormone Tidbits

- Progesterone only methods of birth control tend to increase acne
  - Implanon
  - Mirena IUD
  - Progesterone mini pills
- Spironolactone can be helpful in the teenage population, especially if the patient has features of or a diagnosis of PCOS

### Infantile Hemangiomas

- Propranolol is still great!
  - Suspension is 20 mg/5 ml
  - 2 mg/kg/day divided TID
    - If you are doing the math correctly, the dose ends up being around 1 ml TID for most babies
  - Always give with food
  - To prevent hypoglycemia
  - Don’t be afraid- if the hemangioma needs it, use it!
  - Typically used during growth period (1st 8-12 mos of life), but can work even beyond the proliferative phase (SPD May/June 2015)
Which Hemangiomas Need Propranolol?
- Large hemangiomas
- Ulcerating hemangiomas
- Hemangiomas in functional locations that will interfere with crawling, walking, etc
  - Knees, hands, elbows
- Special site hemangiomas
  - Eyelids, nose, lips, parotid glands, genital area
- Dome shaped hemangiomas
  - Even when they involute, there is usually residual fibrofatty tissue

Infantile Hemangiomas
- Long term studies show no risk of developmental adverse effects or growth impairment at age 4 in pts treated with at least 6 mos of propranolol (JAAD July 2016)
- Topical timolol 0.5% gel forming solution can work for superficial hemangiomas- applied BID

What’s New with Hyperhidrosis?

Hyperhidrosis Treatment Options
- Drysol or OTC Certain Dri at bedtime
- Oral robinul- 1 mg daily, then 1 mg bid
- Iontophoresis- good for hands/feet
  - Fischer MD1A is the best unit- $6-800
- Botox
- Miradry- just for armpits

Hyperhidrosis- Other Options
- “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
- Topical botox- on the horizon
- Topical oxybutynin- on the horizon

More About Oxybutynin (Ditropan)
- SPD Sept/Oct 2015- oxybutynin for palmoplantar hyperhidrosis
  - 2.5 mg daily x 1 wk, then 2.5 mg bid x 2 wks, then 5 mg bid
  - Dry mouth
  - Available as 5 mg pills or 5 mg/ml solution
- SPD May/June 2016- Spain- kids/teens
  - Oral robinul not available in Spain
  - 2.5 mg daily and increase by 2.5 mg daily at 2 wk intervals until results are seen
  - Contraindications: bladder/intestinal obstruction, severe ulcerative colitis, glaucoma, myasthenia
  - No monitoring needed
  - Oropharyngeal xerosis is most common side effect
What’s New with Cooties?

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
  - 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

Post Scabetic Dermatitis

- Post scabietic dermatitis is very common
- Itchy, eczematous rash that waxes and wanes for up to 2-3 mos after the scabies has been treated
- Important to warn patients it will probably happen
- Schedule a followup visit
- Some of it can be a little bit psychological; important to examine and reassure
- Treat with topical steroids
What's New with JAK Inhibitors?

- Male patient with h/o arthritis and alopecia totalis
- Started on Tofacitinib (Xeljanz- JAK1/3 inhibitor) for arthritis
- All his hair regrew

JAK Inhibitors Appear Promising

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

JAK Inhibitors- JAAD Jan 2017

- Tofacitinib for alopecia areata in 90 adult patients
  - Severe alopecia areata, alo tot, alo univ
  - Clinical response in 77%
  - 58% had intermediate-complete response over 4-18 mos
  - Consider adding in pulse pred for nonresponders
  - After 10 yrs of complete scalp hair loss, pts are less likely to respond
  - No serious adverse events over 12 mos
  - When to stop treatment still unclear; probably indefinite

JAK Inhibitors- JAAD Jan 2017

- Tofacitinib for alopecia areata in 13 adolescents
  - Ages 12-17
  - Used 5 mg bid dose
  - Hair regrowth in 70% of patients
  - Safety questions- baricitinib being studies for treatment of interferon-mediated autoimmune syndromes in kids as young as 18 mos and URI appears to be the most common side effect in those kids

JAK Inhibitors

- Xeljanz (Tofacitinib) 5 mg bid
- Appears well tolerated- side effects include headache, GI upset
- Baseline labs
  - CBC with diff, CMP, lipid panel
  - TB test, Hep B, Hep C, HIV
- Repeat CBC with diff, CMP and lipid panel every month for 3 mos, then every 3 mos
- I have 2 patients currently on it for AA and 2 patients on it for vitiligo, doing well
- Topical versions probably still 2-3 yrs away
Miscellaneous Tips and Tricks for Kids
MAM Air Pacifier

- For kids that have persistent dermatitis around the mouth, drool and irritation from pacifiers are a common cause
- Recommend the MAM Air Pacifier which is more open than most

Buzzy

- www.buzzyhelps.com
- Vibrates and you can attach a reusable ice pack to add cold
- Distracts the nerve fibers so the child feels buzzy and minimizes the pain they feel
- Place it on the skin “between the brain and the pain”
- Comes in plain black, a bee, and a ladybug
- Costs $70
- Easy to wipe down with an alcohol swab

Prize Box

- If you see a lot of kids, it really helps to have a small prize box or sticker box
- Cheap to buy things to fill it (most of the items cost less than a $1)
- Can help serve as a distraction
- Can help make kids feel comfortable
- Can “make a negative a positive” after painful procedures
The End!

- Feel free to contact me with any questions
- lisaswansonmd@gmail.com
Nubbin: something that is small for its kind, stunted, undeveloped, or imperfect

Made Famous in a Friends Episode

- Chandler reveals his accessory nipple
- Joey: “I can’t believe you. You told me it was a nubbin.”
- Ross: “Joey, what did you think a nubbin was?”
- Joey: “I don’t know. You see something, you hear a word, I thought that’s what it was. Let me see it again.”

Nubbin

- I am going to use the term nubbin to mean a collection of spots in kids that represent a “miscellaneous” sort of category
Spider Angioma

- Small raised pink-red papule with radiating telangiectasia like legs on a spider
- Blanch with pressure from a glass slide
- Eventually resolve on their own
- Can be treated with vascular laser if bothersome

Pyogenic Granuloma

- “Little ball of capillaries”
- Common in kids and pregnant women
- Some people remember trauma to the area prior to its growth
- 2 Treatment Options
  - Shave removal
  - Topical timolol bid

Pyogenic Granulomas

- Initial study in March/April 2014 SPD journal using timolol 0.5% gel forming solution BID
- Great results with clearance after 2-3 mos
- Bleeding stopped relatively instantly
- Likely working by vasoconstriction
- Important to followup these patients to ensure improvement (spitz nevi, even melanoma in ddx)
**Juvenile Xanthogranuloma**
- Form of non-Langerhan’s cell histiocytosis
- Presents as an orange-yellow-brown dome shaped papule in a child
  - “color of the rising sun”
- Benign; will resolve spontaneously
- Recurs if it is removed

**Lichen Striatus**
- Causes a linear streak of raised flat topped skin colored to pink papules, typically down an extremity
- Can affect the nail on that extremity
- 10% of cases are bilateral
- Sometimes itchy, sometimes not
- Topical steroids or calcineurin inhibitors help for the itch
- Resolves on its own; typically takes 2-3 yrs

**Ring Phenomenon**
- Typically associated with cantharidin
- Can happen with liquid nitrogen
- The treated wart may or may not go away and then a ring of warts develops around the initial wart
- If you continue that treatment, the ring gets bigger
- I feel it is happening more and more commonly with cantharidin these days
Warts

- Countless treatment options
  - Liquid nitrogen
  - Cantharidin
  - OTCs
  - Candida
  - Squaric Acid (contact sensitizers)
  - Laser
  - Bleomycin
- Best Thing Ever- WartPeel!
  - Nucara Pharmacy- Iowa
  - Sal acid + 5FU
  - Magic in a bottle
  - Applied at bedtime under “sticky tape”
  - $89 and worth every penny!

WartPeel

- 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 73% had clearance
  - Avoid if bee allergy
- Valtrex 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 1 yrs, 80% by 4 yrs (SPD Sept/Oct 2015)

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)

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**Wart vs Callus/Corn - A Handy Trick**

- Press on top of it
  - If it hurts, it is a callus/corn
- Press on the sides of it (squeeze it)
  - If it hurts, it is a wart

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**Pseudofurunculoid Molluscum**

- Look like pimples/boils
- Due to body's immune system response
- Not infected, just inflamed
- BOTE sign - Beginning Of The End

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**Pseudofurunculoid Molluscum**

**PF Molluscum and Id Reaction**
**PF Molluscum and Id Reaction**
- Treat the Id Reaction with topical steroids
- Treat the PF molluscum with oral antibiotics or bleach baths
- F/u 2-3 wks
- Usually everything is “all better”

**Molluscum Contagiosum**
- Caused by a poxvirus
- Very common in kids- pretty much all kids get them
- Spread by direct contact and spread like crazy in water (including swimming pools)
- Treatment is not mandatory as they will go away with time
  - Can take up to 2 yrs to resolve on their own
  - Recent study of 170 kids- half treated, half not treated
  - Molluscum resolved in the same amount of time

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**Molluscum Treatment Options**
- Imiquimod/Zyclara
  - Apply MWF at bedtime x 8 wks
  - A little irritation = good; a lot of irritation = bad
- Zymaderm
  - All natural OTC product, botanical based
  - Applied BID
- Candida antigen injections
  - Injected into 1 of the molluscum every 3 wks
  - Tolerable, typically 3-5 treatments
  - Side effect profile
- Cantharidin
  - Never use it in the axilla
  - Blister can be bad
  - Opt resolution with each treatment is success
  - Hard to get these days
- Curettage
- Liquid Nitrogen
- Topical retinoids

**Molluscum Dermatitis**
- Some kids will get an eczema like rash around the molluscum
- Important to treat it as it itches so kids scratch and then spread the molluscum

**Accessory Tragus**
- Benign, harmless
- No associated issues with hearing, kidneys, etc
- Can be removed
- My preference is to have peds ENT do it as they can be a “top of an iceberg”
- Sometimes if it is small and clearly just fleshy without cartilage, I will numb it and snip it off
Solitary Mastocytoma

- Benign collection of mast cells
- Hives up when rubbed or irritated
- Will go away
- Not scary

Urticaria Pigmentosa

- Lots of solitary mastocytomas
- Not scary, but looks scary and parents are often freaked out
- Most kids outgrow it
- No reason to check serum tryptase
- No risk of mast cell leukemia
- Manage with topical steroids prn
- Antihistamines +/-

Dangerous Mast Cell Issues

- Bullous Mastocytosis - presents as blistering in a newborn; ddx includes EB
- Diffuse Cutaneous Mastocytosis - the skin is diffusely infiltrated by mast cells so it becomes yellowish and rubbery diffusely
- Only these 2 mast cell issues carry risk of mast cell leukemia and require systemic workup and hem/onc involvement
**Aquagenic Syringeal Acrokeratoderma**
- Causes swelling, papules, increased wrinkling on palms following immersion in water
- If occurring in a young child, they should be screened for Cystic Fibrosis
- If occurring in an older, clearly healthy child, then there is no concern
- Sometimes kids with this are heavy sweaters-treating that can help
- Kids outgrow it

**Gluteal Variant of Perioral Dermatitis**
- Consists of small pink papules and pustules on buttocks
- DDx includes keratosis pilaris and staph
- I typically culture at first visit to r/o staph
- Treatment:
  - Clindamycin wipes
  - Elidel
  - Amoxicillin (azithro if PCN allergic)

**Herpes Zoster**
- Since the chicken pox vaccine has been more regularly administered to children, cases of herpes zoster in children have been on the rise
- We don't know why immunity seems different with the vaccine vs having the chicken pox
- Patient is contagious to people who have not had the chicken pox (can't catch shingles from shingles)
  - Need to avoid immunized kids and pregnant women
- Treatment with Acyclovir 30-50 mg/kg/day divided TiD (valtrex if old enough to take pills)
Psoriasis

- This was a real “curbside” photo sent to me
- No other photos were sent
- Even with the limited info, this is clearly psoriasis, most likely guttate
- “Psoriasis” pink
- Koebner phenomenon

Bronchogenic Cyst

- Classically in the sternal notch
- Can look like a milia, cyst, divot
- Should be removed by a peds ENT or peds general surgeon
- “Tip of an Iceberg”

Other Neck Cysts in an Infant

- Sternal notch-bronchogenic cyst
- Midline upper neck-thyroglossal duct cyst
- Lateral neck-branchial cleft cyst
Nevus Anemicus

- Somewhat reticular hypopigmented-appearing area. Appears mottled
- Due to slight decrease in superficial cutaneous blood vessels
- Recently described as an association with NF-1
  - Typically on the chest

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

Bed Bugs

- Cause typical bug bite appearance, but often occurs in clusters of 3: “breakfast, lunch and dinner”
- Home needs to be evaluated by a professional exterminating service-no “DIY” projects
- Bed bugs know where to hide; they don’t want to be found
- Come out when CO2 levels in the air indicate that we are asleep
Pilomatricoma

- Subcutaneous firm plaque
- Skin colored and sometimes a bluish hue
- Demonstrates a positive "teeter totter" sign
- 2/3 resolve on their own
- Can be surgically excised

Tinea Corporis

- Ketoconazole 2% cream bid (apply to area and 1 inch around, cont treatment after clinical clearance)
- Oral meds if extensive
- Capitis (presents as redness, scaling and alopecia)
  - MUST USE ORAL MEDS
  - Griseofulvin 20-25 mg/kg/day divided bid for 6 wks. Must be given with fatty food.
  - 2nd line- either itraconazole or lamisil

Pediatric Onychomycosis

- It happens!
- Often there is family history
- Evaluate for tinea pedis
- Treat with terbinafine for 3 mos
  - <20 kg: 1.5 mg/dl divided bid
  - 20-40 kg: 15 mg/dl (30 pills)
  - >40 kg: 30 mg daily
- Terbinafine can be used in a pinch (comes in syrup)
  - Pulse dosing
- Liver function tests- to test or not to test
- Griseofulvin doesn't work
Hyperkeratotic Lichenoid Papules of the Elbows and Knees

- Very common in kids age 4-12, boys > girls
- Misdiagnosed as flat warts, molluscum, KP
- Probably a variant of KP
- Kids outgrow it
- Could treat it with AmLactin, Cerave SA, etc

Toddler (Infantile) Acne

- Kids age 6 mos- 3 yrs old
- Typically occurs on cheeks
- Small pink papules and pustules
- Sometimes comedones
- Can scar; important to treat
- 1st line- Topical clindamycin
- 2nd line- Topical adapalene
- 3rd line- Oral amoxicillin

Pigmented Purpuric Dermatoses

- 5 types of pigmented purpuric dermatoses
- Most common type in kids in studies appears to be Schamberg’s Purpura
- In my clinic, most common type is definitely Lichen Aureus
## Pigmented Purpuric Dermatoses
- Idiopathic
- These conditions present with petechial lesions (often pediatricians will panic)
- Schaumberg's purpura looks like specks of cayenne pepper
- Lichen Aureus looks like petechiae in a gold-brown patch
- Treatment is difficult, but it resolves on its own eventually
- Topical steroids and UV light might help

## Lichen Aureus

## Pediatric Spots- Lumbosacral Dysraphism
- Lesions overlying lumbosacral spinal cord can indicate a problem underneath- tethered cord, meningocoele, tumor

## Pediatric Spots- Lumbosacral Dysraphism- HIGH RISK
- $>2$ cutaneous stigmata
- Lipoma
- Acrochordon/pseudotail/tail
- Aplasia cutis
- Dermoid cyst or dermal sinus
- Infantile hemangioma $>2.5$ cm in size
- Must do an MRI

## Pediatric Spots- Lumbosacral Dysraphism- Intermediate and Low Risk
- Intermediate
  - Atypical dimple ($>5$ mm)
  - Hemangioma less than $2.5$ cm in size
  - Hypertrichosis
  - Can do ultrasound if child $<3$ mos old, MRI if older than $3$ mos old
- Low
  - Simple dimple
  - Hyperpigmentation/hypopigmentation
  - Congenital nevus
  - Port wine stain
  - No imaging needed

## A Couple of Tricky “Nubbins”
Jan 2016 - Mom’s Photo

Sept 2016 - 1st visit

1st Visit
- Ordered an MRI stat
- Ddx - vascular (atypical hemangioma, AVM), neoplasm
- MRI results showed findings consistent with a hemangioma
- Started the patient on Propranolol

Nov 2016

Biopsy
- Pathology revealed DFSP
- Pt underwent excision in 2 stages
- Considered pre treatment with Gleevec but the stain for the 9,22 translocation was negative
**Initial History**

- Rash was noticed for about 6 wks
- Asymptomatic
- OTC remedies had not been helpful
- History of episodes of constipation and diarrhea but no significant abdominal pain, no blood in stool, no hospitalizations for symptoms
- Family was using bubble baths, fab soft, dryer sheets, Gain detergent

**Initial Visit**

- Attempted treatment for contact dermatitis with sensitive skin care and hydrocortisone 2.5 ointment
- No improvement
- Attempted treatment for yeast with econazole cream bid
- No improvement

**Biopsy Under Anesthesia**

- Punch biopsy showed granulomatous dermatitis c/w cutaneous Crohn’s
- Patient was referred to peds GI for GI eval which questioned the diagnosis of Crohn’s
  - Labs were normal
  - Didn’t want to scope her
- Presented patient at Colorado Grand Rounds and every dermatologist agreed with me
- Treated with clobetasol bid x 3 wks and it cleared
- Now will just see what happens

**A Quick Thought on Burnout and “Mindfulness”**

“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
“Life moves pretty fast. If you don’t stop and look around once in a while, you could miss it.”

-Ferris Bueller

Mindfulness Defined
- Putting down your juggling balls for a little bit
- Embrace the beauty of monotasking
- Paying attention in a particular way: on purpose, in the present moment, and nonjudgementally

High Yield Mindfulness Tidbits
- Take a second to notice things
  - Raisin
  - Fingers
- Start a “Gratitude” journal
  - Write down 2 or 3 things every night that you are grateful for that day

Mindfulness Activities
- Anything that lets you “zone out” for a little bit
- Meditation apps that help teach a “non-hippy” how to meditate
  - Headspace
  - Calm
- Fly fishing
- Tai Chi
- Yoga
- Adult coloring books

High Yield Burnout Tips
- Breathe
- Music can change your mood quicker than anything
  - Make yourself different playlists
- You can’t give what you don’t have
  - Think of yourself as a car. You need to fill up your tank once in a while to keep running
  - Make time for the things that refill your tank
The End

- Feel free to contact me with any questions
- lisaswansonmd@gmail.com
Wednesday, March 29, 2017
Resident Pathway
Melanocyte Basic Science

- Neural crest origin
- Migrate to epidermis, dermis, leptomeninges, retina, choroid, iris, mucus membrane epithelium, inner ear, cochlea, vestibular system
- Embryology
  - First appearance at the end of the 1st trimester
  - Able to synthesize melanin at the beginning of the 2nd trimester
- Ratio of melanocytes to basal cells is 1:10 in skin and 1:4 in hair
- Equal numbers of melanocytes across different races
  - Type, number, size, dispersion, and degree of melanization of the melanosomes determines pigmentation

Nevus of Ota

- A.k.a. Nevus fuscoaeruleus Ophthalmomaxillaris
- Onset at birth (50-60%) or 2nd decade
- Larger than mongolian spot, does not typically regres spontaneously
- Often first 2 branches of trigeminal nerve
- Other involved sites include ipsilateral sclera (~66%), tympanum (55%), nasal mucosa (30%).
- ~50 cases of melanoma reported
- Reported rates of malignant transformation, 0.5%-25% in Asian populations
- Ocular melanoma of choroid, orbit, chiasma, meninges have been observed in patients with clinical ocular hyperpigmentation.
- Acquired variation seen in primarily Chinese or Japanese adults is called Hori’s nevus
- Tx: Q-switched ruby, alexandrite, and Nd:Yag lasers

Congenital dermal melanocytosis

- AKA: Mongolian Spot
- Usually apparent at birth or within the first few weeks of life
- Regresses in ~95% by age 18 years; more likely to persist in extensive or extra-sacral variants; most common in Asians and blacks
- Presents as a single or multiple, blue-gray patch(es) with indefinite borders; favors the lumbosacral area and buttocks > back
- Varies in size from a 2-20+ cm
- CALM and melanocytic nevi within Mongolian spots often have a ‘halo’ that lacks dermal melanocytes
- DDx: ecchymosis, child abuse, patch blue nevus, venous malformation
- Extensive lesions with phakomatosis pigmentovascularis (type 2, 4, or 5)

Nevus Fuscoaerulesus Acromiodeltoideus

- AKA: Nevus of Ito
- Bimodal age of onset:
  - 50-60% present at birth or before 1 year of age
  - 40-50% appear at or around puberty
- All persist lifelong
- More common in Asians and African Americans; females > males
- Involves areas of skin innervated by the posterior supraclavicular and lateral brachiocephathaneous nerves
- Typically unilateral

Disclosures

- We have no financial or conflicts of interest to report
Café-au-Lait Macule (CALM)
- Light to dark brown macule or patch
- 10-20% of normal population can have a single lesion
- Generally 2-5 cm in diameter
- Conditions associated:
  - Neurofibromatosis
  - McCune-Albright syndrome (coast of Maine)
  - Legius syndrome
  - LEOPARD syndrome
  - Noonan syndrome
  - LEOPARD syndrome
  - Fanconi anemia
  - Bloom syndrome
  - Ataxia telangiectasia
  - Tuberous sclerosis
  - MEN 1 and 2B
  - Piebaldism
  - More...

Ephelides
- Light brown macules in sun-exposed areas
- Onset typically within first 3 years of age
- If acquired after this, can be a marker for UV-induced damage
- Hist: NORMAL # of melanocytes, INCREASED pigment in keratinocytes

Lentigo Simplex and Oral Melanotic Macules
- Lentigo simplex
  - Common in younger patients
  - Increased numbers in childhood or puberty
  - Sometimes eruptive → lentiginosis
  - Not related to sun exposure
- Oral melanotic macules
  - Primarily in adults over 60
  - Multiple lentigines seen in association with several genetic disorders:
    - LEOPARD syndrome
    - Carney complex
    - Taj syndrome
    - Popliteal syndrome
    - Cronkhite-Canada syndrome
    - Morphea-like Reticulohistiocytosis
    - Basal cell nevus
    - Presumed familial
    - Pseudoxanthoma elasticum syndrome
    - More...

LEOPARD syndrome
- Gene: PTPN11, AD
- Lentigines
- ECG abnormalities
- Ocular hypertelorism
- Pulmonary Stenosis
- Abnormal genitalia
- Retardation of growth
- Deafness
- *** LEOPARD Syndrome has no mucosal involvement

LEOPARD syndrome
- Noonan Syndrome
  - AD, PTPN11
  - Wide set ears
  - Ulnerythema ophryogenes (keratosis pilaris rubra atrophicans faciei)
  - Webbed neck
  - Undescended testes
  - Low posterior neck hairline
  - Pulmonary stenosis
  - Lymphedema
  - Keloid formation
  - CALMs
### CARNEY Complex

**NAME**
- Nevus
- Atrial myxoma
- Myxomas (myxoid tumors)
- Ephelides & Endocrine
  - Pigmented melanotic schwannomas
  - Pigmented phylary adenomas
  - Cushingoid features

**LAMB**
- Lentigines
- Most common on lips, face, sclera and vulva.
- Atrial myxomas
  - Tumors of heart tissue, often originate in atria
  - May obstruct blood flow through the heart → fainting, shortness of breath, chest pain
- Mucocutaneous myxomas
  - Pigmented or radiate
  - Various anatomic sites: breasts, shoulders, oral mucosa and tongue
- Blue nevi – can be found anywhere on body

### Peutz-Jeghers

**AD, STK11/LKB1 gene mutation**
- Encodes serine-threonine kinase tumor suppressor
- Mucocutaneous melanotic macules
  - Oral: Buccal, lip, tongue, gingiva
  - Melanonychia
    - Longitudinal
    - Half
    - Complete
  - Genital melanosis
  - Neck
  - Trunk
  - Palms/soles
- Cutaneous pigmentation may fade over time, oral pigmentation often permanent
- No increased risk of cancer
- Dx of exclusion
  - Rx/Peutz-Jeghers, Addison's disease, SLE

### Laugier-Hunziker Syndrome

**Sporadic inheritance**
- Mucocutaneous melanotic macules
  - Oral: Buccal, lip, tongue, gingiva
  - Melanonychia
    - Longitudinal
    - Complete
  - Genital melanosis
  - Neck
  - Trunk
  - Palms/soles
- Cutaneous pigmentation may fade over time, oral pigmentation often permanent
- No increased risk of cancer
- Dx of exclusion
  - Rx/Peutz-Jeghers, Addison's disease, SLE

### Bannayan-Riley Ruvalcaba

**AD, PTEN mutation**
- Allelic to Cowden’s syndrome
- Genital Lentigines (penile > vulvar)
- Macrocephaly
- Intestinal polyposis
- Lipomas
- Hemangiomas
- Scoliosis
- Mental retardation

### CARNEY complex

**AD inheritance**
- PRKAR1A gene
- Encodes the type 1A regulatory subunit of protein kinase A
- Cell cycle regulation, growth, and/or proliferation
- Referral to cardiology and endocrinology
Spitz Nevus

- 2 mm to >2 cm well-circumscribed, dome-shaped, red or pigmented papule or nodule
- Comprises ~1% of excised melanocytic lesions
- Typically children or young adults (<40 yrs)
- Majority are acquired, up to 7% congenital
- M/c on the head or neck
- Histologically can mimic melanoma
  - Differentiate with S100A6, Ki-67, P16

Spitz Nevus

- Pathogenesis
  - No particular etiologic factors have been identified to correspond with Spitz nevi
  - Widespread eruptive Spitz nevi have been associated with many of the same triggers as for common nevi:
    - HIV infection
    - Addison’s disease
    - Chemotherapy
    - Pregnancy
    - Puberty
    - Trauma
  - Spitz nevi with pregnancy and puberty
  - Possible hormonally activated dormant nevi

- Atypical spitz nevus risk factors for metastasis: Ulceration, ↑ Breslow depth, atypical mitoses, H-RAS mutation

- Treatment: Full-thickness excision

Nevus Spilus (Speckled lentiginous nevus)

- Tan patch containing brown macules that develop over time
- Can contain atypical nevi and small and medium-sized congenital nevi
- Typically larger nevus spilus
- No gender predilection
- Small risk of cutaneous melanoma

Clinical Features and Associations

- More common on the trunk and extremities
- Tan patch persists, central nevi increase over time
- Cutaneous melanoma arising within a nevus spilus has been reported
- Associated syndromes involving nevus spilus include
  - Phakomatosis pigmentovascularis types III and IV
  - Phakomatosis pigmentokeratotica
  - “Speckled lentiginous nevus syndrome”
  - Ipsilateral dysesthesia, muscular weakness or hyperhidrosis in patients with nevus spilus

Halo Nevus (Sutton’s)

- Nevus with peripheral white halo
- Epidemiology
  - Most common in teenagers with multiple nevi
  - Median age is 15 years
  - Typically appears on the back
  - No Gender predilection
- Pathogenesis
  - Development thought to involve either:
    1. An autoimmune (cell-mediated and/or humoral) reaction against non-specifically altered nevomelanocytes
    2. An autoimmune (cell-mediated and/or humoral) reaction against dysplastic nevus cells
    - This theory is not supported by histologic evaluations
  - May have underlying vitiligo (~20%)
  - Can occur in the setting of melanoma (local or elsewhere)
  - More common in adults
  - Can develop in association with sunburn
- Histopathology
  - Residual melanocytes with heavy infiltration of lymphocytes and histiocytes
- Management
  - Full skin examination to r/o melanoma and vitiligo

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- May have underlying vitiligo (~20%)
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  - Full skin examination to r/o melanoma and vitiligo
Melanoma

- Malignant tumor that arises from melanocytes
- Leading cause of skin cancer death
- Incidence rates of melanoma have increased over the past four decades by three- to five-fold
- Mortality rates began to stabilize in the early 1990s
- Rare in pediatric population
  - However, 3% of all pediatric cancers are melanoma
  - The annual transformation rate of a single mole into melanoma is estimated at ≤0.0005% for individuals younger than 40 years.
- Malignant tumors arise in the partial or complete absence of underlying nevi
  - Age is a more important prognostic factor for pediatric patients than sentinel lymph node positivity
- Approximately 50% are found on the dorsal aspect of the hands and feet, with the face and scalp being other common sites

References

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Vascular Tumor vs Malformations
- Vascular tumors are true cellular proliferations of endothelial cells
  - Includes infantile hemangioma, later onset pyogenic granuloma
  - Less commonly: tufted angioma, kaposiform hemangioendothelioma
- Vascular malformations are due to defects in morphogenesis
  - True angiogenesis may occur leading to expansion and thickening
  - Subcategorized as fast flow or slow flow
- Slow flow: capillary, venous, and lymphatic malformations
- Fast flow: arteriovenous malformations

VASCULAR TUMORS

Infantile Hemangiomas
- Most common tumors in the neonatal period, 4-5% of infants, most often noted in the first several weeks of life
- Significant growth over the first several months*
- Spontaneous involution over the years – note: may be incomplete, may leave scarring* - involution distinguishes these lesions from malformations
- Risk factors include: female, Caucasian, low birthweight, premature, multiple gestation, older mothers
- Margileth and Museles reported a 10% familial incidence

Pathogenesis – Defects in Signaling Theory
- Several hypotheses with no single theory explaining all features
- Somatic mutations in genes involved in the VEGF Signaling pathway
  - Shift from VEGFR2 -> VEGFR1
- Germline mutations in VEGFR2 and TEM8 found in a small subset
- Familial cases linked to chromosome 5q – suggests involvement in genes at this locus

Pathogenesis – Placental Hypothesis and GLUT-1 Theory
- **Placental hypothesis**
  - Hemangiomas share an immunohistochemical phenotype with placental cells
  - Suggesting that hemangiomas are:
    1) of placental origin, via embolization
    2) undergo differentiation toward a placental microvascular phenotype
- **GLUT-1**
  - Expressed by infantile hemangiomas and placenta, not by other vascular tumors or malformations
  - Other vascular antigens expressed by hemangiomas include: merosin, Fc gamma RII, and Lewis Y antigen

Pathogenesis – Hypoxia Theory
- Supported by the occurrence of hemangiomas with hypoxic placental changes, prematurity, low birthweight, retinopathy of prematurity, and regional arterial insufficiency syndromes e.g. PHACE(S)
- Hypoxia upregulates GLUT-1 and VEGF mobilization of endothelial progenitor cells
- Hypoxia and estrogen have a synergistic effect on endothelial cell proliferation in vitro

Pathogenesis of the Transition From: Proliferation to Involution
- **Indoleamine 2,3-dioxygenase (IDO)** degrades tryptophan
- Starves T cells of tryptophan inhibits T cell activation
- Believed to protect the fetus from rejection, and as a secondary effect, protects proliferating hemangiomas from immune surveillance
- IDO highly expressed by macrophages, dendritic cells, and placenta
- Downregulation of IDO may lead to involution
- **DUSP5** involved in apoptosis; somatic mutations in this gene may play a role in proliferation and involution

Clinical Presentation
- **Superficial hemangiomas** in the superficial dermis (50-65%)
  - Bright red in color during the proliferative phase
  - Finely lobulated surface, 'strawberry hemangioma'
  - Often focal, but may be of the larger plaque type or segmental type (may have arteriovenous shunts e.g. PHACE(S))
- **Deep hemangiomas** in the deep dermis and/or subcutis (25-35%)
  - May not be evident in the first few weeks
  - Warm, ill-defined, blue to purple masses with no to minimal overlying changes
  - Often have a significant arterial supply and a bruit may be felt
- **Mixed** (15%)
  - 25% have multiple lesions and may have visceral involvement

Complications
- **Ulceration**
  - Can occur in up to 10%, on average at 4 months
  - Whitish discoloration may be a sign of impending ulceration
  - High risk areas include the lips, anogenital region, and skin folds (neck)
- **Bleeding** is a rarely significant and can be managed with firm pressure
- **Kasabach Merritt Phenomenon** – thrombocytopenic coagulopathy
  - Associated with kaposiform hemangioendotheliomas and tufted angiomas
  - Presents within the first few months to a year of life
  - Tumor becomes indurated, enlarged, with local pallor and purpura

Natural History
- **Proliferative Phase**:
  - Maximal rapid growth often established early on
  - 85% achieve final size by 1.5 months of age
  - Become warm and firm on touch, surface may appear tense
  - Deeper lesions tend to plateau for a month longer than superficial lesions
  - Deeper component may continue to proliferate after the superficial component has plateaued
  - Small subset of lesions without a proliferative phase

- **Involution**:
  - Begins in the first year and persists for several years
  - Changes from bright to a gray-purple with tethering, assumes fatty consistency
  - 30% by 2 years, 60% by 4 years, 70% by 7 years, and 80% by 9 years
  - May leave atrophic, fibrofatty, or telangiectatic changes
Complications

- Anogenital
- Breast
- Pinna
- Lip
- Nasal tip
- Periocular
- CNS hemangiomas
- GI tract
- Liver

If conductive hearing loss – and lead to breast asymmetry – interfere with feeding –

- Proptosis
  - May obstruct vision and invade the orbital
  - Can compress the lobe leading to pain and swelling

- Painful defecation

- Visceral Involvement

  - If 5 or greater lesions, recommend evaluation for visceral involvement
  - Liver: most commonly involved
    - Complications include high output cardiac failure, abdominal compartment syndrome, and hypothyroidism
    - Hemangiomas may produce type 3 hepatic hemangioendothelioma, which is most commonly involved with hepatic hemangiomas
  - GI tract involvement – bleeding
  - CNS hemangiomas are rare (1%), may present with hydrocephalus

Systemic Involvement

- Large segmental lesions often associated with visceral involvement
  - Cerebrovascular (91%), cardiovascular (67%), structural anomalies associated with PHACE(S) syndrome

- Breast region – possible lymphoid hemangiosarcoma
  - large hemangiomas are often associated, often in the subjacent plane
  - may present as noisy breathing, tachypnea, stridor
  - referral to ENT

- Midline lumbosacral region
  - Occult spinal dysraphism is seen in 30% of lesions ≥ 2 cm
  - Other cutaneous, vascular, skeletal, glial (tumors, hemangiomas, etc.)

- Large hemangiomas of the lower body may be seen in LUMBAR syndrome

Visceral Involvement

- If 5 or greater lesions, recommend evaluation for visceral involvement
  - Liver: most commonly involved
    - Complications include high output cardiac failure, abdominal compartment syndrome, and hypothyroidism
    - Hemangiomas may produce type 3 hepatic hemangioendothelioma, which is most commonly involved with hepatic hemangiomas
  - GI tract involvement – bleeding
  - CNS hemangiomas are rare (1%), may present with hydrocephalus

Evaluation

- MRI w/ contrast is best for evaluating the extent and tissue characteristics
  - If equivocal, or concerns for malignancy, consider a biopsy

Pathology – Infantile hemangiomas

- Proliferating phase: lobules of endothelial masses separated by fibrous septae with larger vessels within the septae
  - Striking lobularity with densely fibrotic stroma, stromal hemosiderin deposits, focal thrombosis and sclerosis of capillary lobules, lack of mitotic figures, decrease in # of vessels with fibro fatty tissue, reduced # mast cells
  - Increased number of mast cells
  - Mitotic figures and apoptotic bodies may be present

Pathology – Congenital hemangiomas

- Slow growing with lower mitotic rate, cellular hemosiderin stainable iron, lack of collagens to tissues, fewer mast cells, proliferating thin walled vessels associated with multiple the vessel vascular
- May demonstrate areas of sclerosis

RICH and NICH

- Congenital hemangiomas, fully developed at birth
- Distinct from infantile hemangiomas in that they are GLUT-1 negative

- Proliferating congenital hemangioma (RICH)
  - Significant initial rapid growth followed by little to no growth postnatally
  - May ulcerate, necrose, or bleed
  - May be associated with transient thrombocytopenia

- Non-involuting congenital hemangioma (NICH)
  - Unlike infantile hemangioma, grows proportionally with the child
  - May worsen with maturity and do not spontaneously involute

RICH: Spontaneous involution at 5 months

Lesion in a school aged child with no change since birth
Treatment – Topical Therapies

- **Goals:** prevent/reverse life-threatening complications, treat ulcerations, prevent disfigurement, avoid overly aggressive treatments that may lead to scarring
- **Non-intervention**
  - Appropriate for small hemangiomas
  - Important to discuss care for superficial bleeding and ulceration
- **Ulceration tx:** local wound care, pulsed dye laser, pain control

Local therapies
- IL corticosteroids, TAC 5-40 mg/mL have been used successfully
- Caution in periorbital area, consider potent class I topical steroid
- Beta blockers (e.g. topical timolol 0.5% gel, topical propranolol, etc.)
  - 4 weeks of topical timolol gel, 1 drop BID


Treatment – Systemic Therapies

- **Systemic Corticosteroids**
  - Individualize dosage and tapering regimen
  - Prednisone: 2-3 mg/kg/day to 3-5 mg/kg/day
  - Side effects: cushingoid facies, irritability, disruption of sleep, GI sx, decreased growth rate (with catch up), HPA axis suppression, immunosuppression
  - Live vaccines not recommended
  - Bactrim for PCP prophylaxis

- **Systemic Beta Blockers**
  - Binds B2 adrenergic-R on hemangioma endothelial cell → vasoconstriction and decreased expression of VEGF, bFGF → apoptosis
  - No consensus on dosage, 2-3 mg/kg used in studies, taper to prevent rebound tachycardia
  - Side effects: hypotension, bradycardia, hypoglycemia, bronchospasm, sleep disturbances
  - Baseline cardiac evaluation and pediatric cardiologist referral prior to therapy

- **Pulsed Dye Laser**
  - Consider for superficial hemangiomas, not effective for deeper lesions
  - May result in pigmentary alteration, atrophic scarring, and ulceration

- **Surgical Excision**
  - Best reserved for involuted lesions to remove fibro fatty tissue and redundant skin
  - Also consider in cosmetically sensitive areas such as the nasal tip or lip

PHACES

- Posterior fossa malformations
  - Dandy-Walker is the most common
- Hemangioma of the face
  - Usually plaque-like, more than one dermatome
- Arterial abnormalities
- Coarctation of the aorta
- Eye abnormalities
- Sternal nonunion
- Supraumbilical raphe

**Diffuse Neonatal Hemangiomatosis**

- Cutaneous and visceral hemangiomas
- Liver hemangioma may be complicated by obstructive jaundice
- Prognosis depends on which organ systems are involved
- If the patient has multiple cutaneous hemangiomas: US, UA, stool guaiac, CBC
- Mortality in severely affected infants may occur secondary to liver disease, GI bleeding, neurological problems, high output cardiac failure and respiratory compromise
- If no visceral involvement: benign neonatal hemangiomatosis

**PHACES**


**Diffuse Neonatal Hemangiomatosis**

Tufted Angioma

- Onset during infancy or early childhood
- Presents as ill-defined red-brown plaque or patch over the neck or upper trunk
- Plaque slowly extends over time
  - Typically does not regress

PELVIS Syndrome

- Perineal hemangioma
- External genital malformations
- Lipomyelomeningocele
- Vesicorenal abnormalities
- Imperforate anus
- Skin tags

Pyogenic Granulomas

- Presents as rapidly growing, friable skin or mucosa with frequent ulceration
- Common in children and young adults
- Associated with antecedent drama, pregnancy, oral medications (retinoids, inidinavir, and EGFR inhibitors)
Kaposiform Hemangioendothelioma

- Characteristics
  - Rare; usually occurring in children younger than 2
  - Male-female incidence equal
  - Presents as a rapidly growing vascular macule, plaque, nodule, or bulging indurated mass
  - Associated with Kasabach-Merritt phenomenon: life-threatening thrombocytopenia from platelet trapping within the tumor; likely caused by retroperitoneal tumors
- Pathology
  - Densely infiltrated nodules composed of spindle cells with minimal atypia and slit-like vessels containing hemosiderin; GLUT-1 negative
- Treatment
  - Corticosteroids are first-line; complete surgical excision if feasible; vincristine is the first-line treatment for Kasabach-Merritt phenomenon

Glomeruloid Hemangioma

- Characteristics
  - A type of hemangioma seen in POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin lesions) syndrome
  - Firm, red-to-purple papules on the trunk or the extremities
- Pathology
  - Appears similar to a renal glomeruli; dilated dermal vessels filled by small, well-formed capillary loops
- Treatment
  - Not required, but consider shave excision, cryosurgery, electrodessication, or pulsed dye laser surgery

Vascular Malformations

- Capillary malformation: a group of disorders that developed from changes in the blood/lymphatic channel formation
- Venous malformation (VM): recognized clinically as a well-demarcated patch or plaque with a blue hue with compressibility and ability to refill with dependency
  - Can be focal, segmental, or widespread
  - T2-weighted MRI is the best imaging modality
  - Cephalic VM: develop into cosmetic and function problems with time → distortion of facial features, sleep apnea (laryngeal VM), skull defects
  - Trunk and limb VM: spongy masses that can be emptied with elevation and massage; can involve muscles and joints
Vascular Malformations

- **Lymphatic malformation**: an abnormal proliferation of lymphatic channels

- Vascular malformations are further classified as “fast-flow” and “slow-flow”
  - Fast-flow: arteriovenous malformations (AVM)
  - Slow-flow: Capillary, venous and lymphatic malformations

Capillary Malformations

Port-Wine Stain

- Port-Wine Stains (PWS) are capillary malformations that are usually present at birth.
- Can be localized, segmental, or multifocal.
- PWS tend to grow with the child and do not regress.
- Facial PWSs are commonly located along the sensory trigeminal nerve: V1 (ophthalmic), V2 (maxillary), and V3 (mandibular).
- As the patient ages, PWSs tend to become darker and more violaceous, especially when located on facial V2-V3 distributions.
- **Nevus Simplex and Salmon Patches are NOT PWSs, rather congenital capillary stains.**
Phakomatosis Pigmentovascularis (PPV)
• The combination of a capillary malformation (Port-Wine Stain) with different melanocytic neoplasms
• Types:
  - Ia/b: PWS + epidermal nevus
  - IIa/b (Phakomatosis cesioflammea): PWS + Mongolian spot +/- nevus anemicus
  - IIIa/b (Phakomatosis spilorosea): PWS + nevus spilus +/- nevus anemicus
  - IVa/b (Phakomatosis pigmentovascularis): features of II + III or II + V
  - Va/b (Phakomatosis cesiomarmorata): Mongolian spot + cutis marmorata telangiectatica congenita

Sturge-Weber Syndrome (Encephalotrigeminal Angiomatosis)
• Sporadic neuroectodermal syndrome
• Characterized by
  - Port-wine stain at birth in trigeminal distribution
  - Greater risk of SWS – if PWS involves all (V1, V2, V3) branches, bilateral, both upper and lower eyelids
  - Leptomeningeal angiomatosis (ipsilateral to PWS)
  - Resultant seizures
  - Ocular involvement – 60% of SWS patients
    - Glaucoma most common, ocular AVMs, nevus of Ota, buphthalmos, and blindness.
  - Other features
    - Mental retardation, cerebral atrophy, tram-track cortical calcifications, enlarged choroid plexus

Klippel-Trenaunay Syndrome
• Sporadic disorder
  - Triad of Vascular malformations, venous varicosity, hyperplasia of soft tissue and bone.
  - MC vascular malformation is PWS (LE > UE)
  - Lesions of KT are usually all on same extremity
  - Parkes-Weber syndrome –
    - Includes Arteriovenous malformations.
Telangiectasias (Spider & Angioma Serpiginosum)

- Not true capillary malformations.
- May appear in infancy or early childhood.
- They are usually composed of small, punctate linear vessels distributed in either a segmental, unilateral nevoid, or diffuse pattern.
- Children sometimes develop so-called spider angiomias comprised of a brightly erythematous central punctum with radiating ‘spider-like’ telangiectasias. They are usually located on sun-exposed areas.
- Risk factors include fair skin and a history of minor skin injury at the site.
- These may disappear spontaneously or persist throughout life.

Spider Angioma

Telangiectasia (Spider & Angioma Serpiginosum)

- Angioma serpigenosum: Clusters of dark red puncta in a serpiginous pattern. Typically on an extremity and typically female.

Cutis Marmorata Telangiectatica Congenita (CMTC)

- Dark red to purple reticulated vascular pattern that is broad.
- Usually affects one or more limbs and the trunk.
- Often associated with telangiectasias +/- prominent veins.
- Persists upon warming.
- Often lightens in color over the first year of life.

CMTC

Neonate with CMTC (Photos one year apart)
Hereditary Hemorrhagic Telangiectasia (HHT)
- AKA: Osler-Weber-Rendu disease
- AD; ENG (endoglin) and ALK1 (activin receptor-like kinase 1) genes
- Multiple telangiectasias on mucosal and cutaneous surfaces.
- First manifestation: nose bleeds in children
- Telangiectasias typically appear in adolescence and adulthood.
- Internal organs may be affected and screening for pulmonary and CNS AVMs is imperative

Ataxia-Telangiectasia (Louis-Bar Syndrome)
- Multi system autosomal recessive disorder
- ATM gene defect (chromosome 11q)
  - Mild form ATM – due to MREII gene defect
- High rate of chromosomal breakage and sensitivity to ionizing radiation
- Characterized by
  - Truncal ataxia – as early as infancy
  - Other neurologic features include dysarthria, nystagmus, ptosis, cognitive abnormalities
  - Oculocutaneous telangiectasias – around 3-5 years old
  - Ocular/ocular conjunctivae and other sun-exposed sites
  - Profound humoral/vascular immunodeficiency
  - IgA, IgG, IgE decreased with chronic respiratory infections
- Other features:
  - Premature aging of skin and hair, non-infectious subcutaneous granulomas

Ataxia-Telangiectasia

Angiokeratoma (5 types)
- Angiokeratomas are essentially telangiectasias that have an overlying hyperkeratotic surface.
- 5 types:
  - Angiokeratoma circumscriptum
  - Angiokeratoma corporis diffusum
  - Angiokeratoma of Mibelli
  - Angiokeratoma of the scrotum (Fordyce)
  - Solitary angiokeratoderma

Angiokeratoma
- Angiokeratoma circumscriptum:
  - Malformation of dermal and subcutaneous capillaries and veins, and is variably classified as a capillary or venous malformation. The vascular malformation is congenital.
  - Superficial ablative therapy is typically followed by recurrence, regardless of whether ablation is performed by excision, laser, cryotherapy, or electrocautery.
Angiokeratoma

- **Angiokeratoma corporis diffusum – AKA Fabry Disease:**
  - Fabry disease is a rare X-linked lysosomal storage disease. It is caused by mutations in the alpha-galactosidase A (GLA) gene, leading to a deficiency in alpha-galactosidase A.
  - Angiokeratomas occur in 66% of males and 36% of females with Fabry disease. The average age of onset in males is about age 20; in females it is about 10 years later.
  - Lesions tend to occur in the “bathing trunk” area, from the umbilicus to the genitalia.
  - Telangiectasias occur in about 25% of male patients presenting around age 25 and in women around age 40. The vascular lesions can be treated with intense pulse light or various vascular lasers.

- **Angiokeratoma of Mibelli:**
  - Usually appear as 1–5 mm red vascular papules, which become hyperkeratotic over time.
  - The papules are dull red or purplish-black, verrucous, and rounded, and are usually situated on the dorsum of the fingers and toes, the elbows, and the knees. Frequently, these are called telangiectatic warts.
  - The patient often has cold, cyanotic hands and feet.
  - This is a rare genodermatosis with an autosomal-dominant trait for vascular lesions located over bony prominences and a family history of chilblains. The condition is most frequently discovered in prepubertal children.
  - Treatment includes electrocautery, fulguration, CO2 laser ablation, long-pulse vascular laser therapy, or cryotherapy, with fairly good results.

- **Fordyce Angiokeratoderma:**
  - Multiple small vascular papules that stud the scrotum and sometimes the vulva in middle-aged and elderly individuals.
  - There is often a diffuse redness of the involved area that may be a source of concern to the patient. Urethral or clitoral lesions may also be seen.
  - Treatment is best accomplished by shave excision, cautery, laser ablation, or fulguration of troublesome lesions. The primary therapy is reassurance.

- **Solitary Angiokeratoma:**
  - A single small, bluish-black, warty papule that occurs predominantly on the lower extremities.
  - It is not a hereditary lesion and probably follows trauma, with subsequent telangiectasia before the formation of the angiokeratoma.
  - The mode of acquiring this lesion, and its small size, solitary nature, and location, distinguish it from other forms of angiokeratoma.
  - Solitary angiokeratoma is to be considered in the differential diagnosis of seborrheic keratosis, melanoma, pigmented basal cell carcinoma, and ordinary hemangioma.
  - Treatment is by electrosurgery, laser ablation, or excision.
Venous Malformations

- MRI to determine extent of involvement
- Localized intravascular coagulopathy and treat accordingly
- Manage site-specific complications

Syndromes Associated with VMs

- Familial cutaneous and mucosal venous malformation (VMCM)
  - Autosomal dominant condition with VMs affecting skin, oral mucosa, and muscles; some visceral VM (intestines, lungs, CNS) noted
  - Mutation in the TEK gene
- Blue rubber bleb nevus syndrome (BRBNS)
  - Sporadic disease with dark blue papules and compressible protuberances
  - Gastrointestinal involvement can lead to bleeding and iron deficiency anemia
- Glomuvenous malformation (GVM)
  - Variant of VM with rows of glomus cells around venous channels
  - Solitary, blue-purple nodules usually without visceral involvement
  - Mutation in the glomulin (GLMN) gene
- Maffucci Syndrome
  - Sporadic condition with a combination of VMs and enchondromas most commonly on the extremities
  - PTHR1 gene

Syndromes Associated with VMS

- Blue Rubber Bleb Nevus Syndrome
- Glomuvenous Malformation
- Maffucci Syndrome
Glomangioma

- Glomuvenous malformations (GVM; formerly called ‘glomangioma’) may be solitary or multiple, and may be localized or involve a larger territory of skin.
- Cutaneous Findings: They are often bluish to purple, cobbledstoned or plaque-like in appearance.
- During childhood, they typically acquire a deeper blue hue and thicken, and become tender when palpated.
- Congenital plaque-like GVMs are usually pink at birth, with noticeable thickening and change in color to blue-purple during childhood.
- These plaque-like GVMs may arise sporadically, or occur as a manifestation of autosomal dominant GVM.

EXTRA CUTANEOUS: In addition to skin and mucosal involvement, VM can also involve deeper soft tissues, muscles, joints, and in severe cases, visceral sites such as the abdomen and pelvis.

DIAGNOSIS: Usually established by clinical features, but imaging may be used as well - ultrasonography, Doppler, MRI, and CT scans are useful for evaluating the extent of involvement.

TREATMENT: VMs can be treated with many different modalities including sclerotherapy, excision, endovenous laser ablation, cutaneous laser ablation or a combination of these modalities.
- Sclerotherapy has emerged as the mainstay of treatment for VMs, followed by surgical excision.
- The decision regarding when to treat is usually based on whether there is significant functional impairment or disfigurement.

Lymphatic Malformations

- Hyperplasia of the lymphatic network
- Can be superficial (skin, mucous membranes), deep (bone, muscle), or visceral
- Primary:
  - Abnormal development of lymphatic system
- Secondary:
  - Abnormal distribution of lymphatic channels

Lymphangioma

- Lymphatic Malformation – aka Lymphangioma – are slow-flow vascular anomalies.
- 4 types:
  - Macrocystic
  - Microcystic
  - Combined
  - Generalized (rare)
- Etiology is unknown – cases are sporadic.
**Lymphangioma**

- Cutaneous Findings are visible at birth and can even be found on prenatal US.
- They occur commonly on the neck and axilla and can be referred to as **Cystic Hygroma**
- Extracutaneous finding include intraoral involvement, mandibular and orbital locations as well as visceral and abdominal lesions.
- Treatment for these benign lesions is typically directed at managing complications or restoring anatomy.
- Treatment modalities include:
  - Sclerotherapy, compression, surgical resection and RF ablation

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**Resources**

- Neonatal and Infant Dermatology, 3rd edition. Eichenfield, Frieden, Mathes & Zaenglein
- Andrews’ Disease of the Skin, 11th edition. James, Berger, Elston
Disorders of the Tongue and Nails
Stephanie Blackburn, DO PGY 4
Affiliated Dermatology
Date: 3/29/2017

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None

Off Label Usage
None

Learning Objectives
- Review disorders of the tongue and oral lesions
- Discuss diagnosis and potential treatment options for dermatologic disorders of the tongue and disorders of the oral cavity
- Expand differential diagnosis in regards to tongue/oral lesions
- Review board relevant nail disorders

Introduction
- Diagnosis and treatment of dermatologic lesions of the oral cavity and tongue is challenging
- In a study from 2001, almost all (84%) hospital doctors in general and geriatric medicine felt that it was important to examine the patient's mouth, however less than one-fifth (19%) routinely performed such examinations [1]

Fissured Tongue
- Congenital disorder with enlarged tongue and plicate superficial or deep grooves
- Seen in Melkersson Rosenthal syndrome (facial paralysis/lip edema/scrotal tongue) and many patients with Down syndrome
- Occurs with geographic tongue in 50% of patients and both are commonly seen in psoriasis [2]
- No treatment is necessary, however recommending mouthwash to keep the fissures clean is important

Herpetic Geometric Glossitis
- May mimic fissured tongue
- Herpetic geometric glossitis is painful and affects predominantly immunocompromised individuals
- Centered on the back of the dorsal tongue
- Treat with antivirals: acyclovir, valacyclovir, famciclovir, etc, or foscarnet for acyclovir resistant HSV [3]

Disclosure

http://diseasespictures.com/fissured-tongue/
Geographic Tongue

- Sharply demarcated atrophic erythematous patches
- May be ischemic finding or manifestation of atopy
- Dorsal tongue
- The appearance changes day to day and there are periods of exacerbation and quiescence
- Two clinical variants:
  - Discrete annular "bald" patches of glistening, erythematous mucosa with absent or atrophic filiform papillae
  - Prominent circinate or annular white raised lines that vary in width up to 2 mm
- May be associated with increased severity of psoriasis
- Treatment is not necessary if asymptomatic, but use of 0.1% solution of tretinoin applied topically has shown clearing within 4-6 days

Annulus Migrans

- Geographic tongue associated with psoriasis and/or reactive arthritis

Black Hairy Tongue

- On the dorsum of the tongue anterior to the circumvallate papillae
- The "hair" is due to benign hyperplasia of the filiform papillae
- Associated with smoking, use of oral antibiotics, psychotropic drugs, and Candida
- Differentiated from oral hairy leukoplakia due to clinical location. Hairy leukoplakia is on the lateral tongue
- Treatment: exfoliation of the tongue with toothbrush alone or with 1-2% hydrogen peroxide. May use urea, tretinoin or papain (meat tenderizer)
- Discontinue predisposing factors (smoking) and increase oral hygiene

Atrophic Glossitis

- Bald tongue/smooth tongue
- Painful
- Results from atrophy of the filiform and fungiform papillae
- Moeller/Hunter glossitis-B12 deficiency
- Iron deficiency,pellagra, malabsorption syndrome, anorexia nervosa, alcoholism
- Treat underlying cause

Eruptive Lingual Papillitis

- Acute self limiting inflammatory stomatitis
- Affects children with seasonal distribution (Spring)
- Fever (40%), difficulties in feeding (60%), and intense salivation (60%) are common
- Inflammatory hypertrophy of the fungiform papillae on the tip and dorsolateral sites of the tongue
- Spontaneous resolution in a mean of 7 days
- Viral infection with 50% transmission among family members

Median Rhomboid Glossitis

- Shiny oval or diamond-shaped elevation on the dorsum in the midline immediately in front of circumvallate papillae
- No change in size and no link to cancer
- May result from abnormal fusion of the posterior portion of the tongue, but it is nearly always chronically infected with Candida
- Histologically there is chronic inflammation with fibrosis
- Eosinophilic ulcer of the oral mucosa may look similar
- Treat with oral antifungals
Granular Cell Tumor

- 1/3 of reported cases of granular cell tumor occur on the tongue (1/3 skin, 1/3 internal organs) [2]
- About 2/3 of patients are black and 2/3 are women [2]
- Well circumscribed, solitary, firm nodule ranging from 5-30 mm
- Histologically distinct with sheets of large polygonal cells with abundant eosinophilic granular cytoplasm with central nucleus [11]
- Pustulo-ovoid bodies of Milian—discrete round eosinophilic giant lysosomal granules
- Overlying PEH [12]
- S100+
- Complete excision is advisable due to potential difficulties distinguishing between malignant granular cell tumor

White Sponge Nevus

- Spongy, white plaque
- Most common site is buccal mucosa
- Autosomal dominant disorder with mutations in mucosal keratin pair K4 and K13
- HPV-16 DNA has been identified in some patients [2]
- Treatment with antibiotics may give improvement, including tetracycline 5mL swished in the mouth for 1 minute twice daily

Leukoplakia

- Presents as whitish thickening of the epithelium of the mucous membranes
- White pellicle is adherent to underlying mucosa, attempts to remove result in bleeding
- Benign form is usually in response to irritation
- If progresses to carcinoma, follows a 1 to 20 year lag time, unless patient is immunosuppressed
- Associated with tobacco, alcohol and poorly fitting dentures
- Treatment: surgery or destruction, fulguration, excision, cryosurgery, CO2 laser ablation

Oral Hairy Leukoplakia

- Distinctive condition strongly associated with HIV/immunosuppression
- HHV4/Epstein-Barr virus
- In immunosuppressed patients there is continuous shedding of EBV virus in oral secretions
- If noted, a workup for immunosuppression is recommended

Squamous Cell Carcinoma

- Presents as an ulcer or mass that does not heal, often with associated pain
- Most common oral malignancy
- The majority of cases develop from leukoplakia or erythroplakia
- Up to 2/3 of patients with primary tongue lesions have nodal disease
- Biopsy any persistent papule, plaque, erosion or ulcer
- It is estimated that the use of alcohol and tobacco account for up to 80% of SCC of head/neck [1]. However, alcohol alone has not been shown to be an independent risk factor [2]
- A subset of oropharyngeal SCC is associated with HPV-16 (Proliferative verrucous leukoplakia)
- Survival rate is 50% due to late diagnosis and metastasis
Lichen Planus of Nails

- The reported incidence of nail involvement varies from less than 1% to 10% [2]
- Twenty nail dystrophy may be the sole manifestation
- This is characterized by nail coarseness affecting all fingernails and toenails because of excessive longitudinal ridging
- Dorsal pterygium is one of the characteristic findings and may be present in the classic form [16, 17]
- Treatment is unsatisfactory. Intralesional steroids may be of some benefit

Koilonychia

- Thin and concave, with everted edges.
- May be due to faulty iron metabolism
- Defect in plate/matrix
- May be seen in: LEOPARD, ectodermal dysplasia, trichothiodystrophy, nail-patella syndrome
- May be acquired in Plummer-Vinson syndrome, hemochromatosis and neonatal (physiologic)

Beau’s Lines

- Transverse furrows that begin in the matrix and progress distally as the nail grows
- Temporary arrest of function of the nail matrix
- Specific associations may include childbirth, measles, paronychia, acute febrile illnesses, high altitude exposure and drug reaction

Nail Patella Syndrome

- Absence or hypoplasia of the patella and congenital nail dystrophy
- Hyperpigmentation of the pupillary margin of the iris (“Lester iris”) is characteristic
- 60% of patients have renal abnormalities and 20% suffer from renal failure [2]
- Mutations in LMX1B gene

Darier’s Disease

- V-shaped distal nicking
- Alternating red and white longitudinal bands with subungual hyperkeratosis
- AD inheritance
- Mutation in ATP2A2 gene encoding SERCA2, calcium ATPase

Pachyonychia Congenita Type 1

- AD
- Defect in K6α, K16
- Focal PPK
- Benign oral leukokeratosis
- Nail dystrophy with significant subungual hyperkeratosis
Pachyonychia Congenita Type II

- AD
- Defect in K6b, K17
- Nail dystrophy
- Steatocystomas
- Eruptive vellus hair cyst
- Natal teeth
- Pili torti

Half and Half Nails

- Proximal ½ with white zone
- Distal ½ with red/brown zone
- Due to chronic renal disease and nail bed edema

Meuhrcke’s bands

- Transverse white bands parallel to lunula
- Disappear with squeezing of nail
- Due to hypoalbuminemia, nephrotic syndrome, liver disease, malnutrition and chemotherapy

Terry’s nails

- Proximal 2/3 white nail color
- Distal 1/3 brown-pink band
- Cirrhosis, hypoalbuminemia, diabetes, cardiac disease

Mee’s Lines

- Transverse lines of entire nail breadth in all nails
- Grows out with nail growth
- Due to parakeratosis of the ventral nail plate
- Arsenic poisoning, trauma, medications, severe illness

Tumors Affecting the Nail

- Myxoid Cyst:
  - Smooth, soft nodule most commonly adjacent to the DIP joint
  - May cause longitudinal grooving in the nail plate
  - Contains clear yellow viscous fluid
- Glomus Tumor:
  - Small reddish-blue tender subungual tumor
Tumors Affecting the Nail

• Acquired Digital Fibrokeratoma:
  – Firm excrescence on the finger or toe
  – Pathology: collagen with no prominent nerves

• Accessory digit:
  – Firm excrescence on the finger or toe, most commonly at proximal portion of 5th digit
  – Pathology: Collagen with prominent nerve fascicles

Resources


Thank You

• Affiliated
  - Kevin Miller DO
  - Sarah Belden DO
  - Jason Barr DO
  - (Program Director)
  - Stephanie Blackburn DO
  - Dylan Howard DO
  - Dustin Mullens DO
NEONATAL DERMATOLOGY

Jennifer Peterson
Kevin Svancara
Jonathan Bellew

Advanced Desert Dermatology

DISCLOSURES

- No relevant financial relationships to disclose
- Off-label use of acitretin in ichthyoses will be discussed

PHYSIOLOGIC

- Vernix caseosa
  - Creamy biofilm
  - Present at birth
  - Opsonizing, antibacterial, antifungal, antiparasitic activity
- Cutis marmorata
  - Reticular, blanchable vascular mottling on extremities > trunk/face
  - Response to cold
  - Disappears on re-warming
  - Associations (if persistent)
    - Down syndrome
    - Trisomy 18
    - Cornelia de Lange syndrome

- Milia
  - Hard palate – Bohn’s nodules
  - Oral mucosa – Epstein pearls
  - Associations
    - Bazex-Dupre-Christol syndrome (XLD)
    - BDCA, follicular atrophoderma, hypohidrosis, hypotrichosis
    - Rombo syndrome
    - BDCA, verruciform atrophoderma, teleangiectasias
    - One-facial-digital syndrome (type 1, XLD)
    - Basal cell- nevus (Gerlin) syndrome
    - Brocq-Spiegler syndrome
    - Pachyonychia congenita type II (Jackson-Lawler)
    - Atrichia with popular lesions
    - Down syndrome
    - Secondary
      - Porphyria cutanea tarda
      - Epidermolytic hyperkeratosis

- Miliaria
  - First weeks
  - Eccrine gland obstruction due to heat, moisture, occlusion
  - Crystalina
    - Clear vesicles on head, neck, upper trunk
  - Rubra
    - Erythematous papules in intertriginous areas
  - Profunda
  - Sucking blister
    - Solitary blister on hand, wrist, lip

PHYSIOLOGIC

- Transient neonatal pustular melanosis
  - Birth
  - Pustules → hyperpigmented macules with collarette of scale
  - Resolve within 4 weeks
  - Neutrophils
  - Erythema toxicum neonatorum
    - Full term
    - 24-48 hours
    - Erythematous macules, papules, pustules, wheals
    - Eosinophils
  - Neonatal acne (neonatal cephalic pustulosis)
    - First 30 days
    - Malassezia globosa & sympoidalis overgrowth

- Erythema neonatorum
  - Neutrophils
  - Eosinophils

- Neonatal transient erythema
  - Neutrophils

TRANSIENT, NON-INFECTIOUS

- Transient neonatal pustular melanosis
  - Birth
  - Pustules → hyperpigmented macules with collarette of scale
  - Resolve within 4 weeks
  - Neutrophils
  - Erythema toxicum neonatorum
    - Full term
    - 24-48 hours
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- Erythema neonatorum
  - Neutrophils
  - Eosinophils

- Neonatal transient erythema
  - Neutrophils

TRANSIENT, NON-INFECTIOUS
Subcutaneous fat necrosis of newborn
- Healthy infants
- Perinatal hypoxemia, hypothermia, hypoglycemia
- 1st week
- Localized, indurated subcutaneous nodules
- Cheeks, shoulders, back, buttocks, thighs
- Hypercalcemia
- Monitor x 1 month after clinical resolution
- Panniculitis, necrosis, needle-shape clefts, prominent inflammation

Sclerema neonatorum
- Ill/premature infants
- 1st week
- High mortality rate
- Diffuse woody induration
- Spares genitalia, palms, soles
- Panniculitis, necrosis, needle-shape clefts, minimal inflammation

Candida infection
- Irritant contact dermatitis
- Allergic contact dermatitis
- Seborrhoeic dermatitis
- Atopic dermatitis
- Miliaria
- Granuloma gluteale infantum
- Jacquet’s erosive dermatitis
- Perianal pseudoverrucous nodules & nodules
- Biotin/multiple carboxylase deficiency
- Cystic fibrosis
- Langherans cell histiocytosis
- Kawasaki disease
- Perianal Strut
- Vulvovaginal impetigo
- Scabies
- Congenital syphilis

Granuloma gluteale infantum
- Granulomatous nodules
- Secondary to inflammation, maceration, Candida infection, halogenated topical steroids
- Jacquet erosive dermatitis
- Rare
- Erythematous, papular & erosive with elevated borders
- Pain with urination
- Secondary to irritant dermatitis, moisture, Candida, Hirschsprung disease
- Perianal pseudoverrucous nodules
- Urinary/fecal incontinence

Acrodermatitis enteropathica
- Eczematous & erosive patches/plaques, flaccid bullae
- Also periorificial & acral
- Zinc deficiency
- Relative hypoparathormonidism
- Healthy, breastfed infants
- Low zinc level in maternal milk
- Upon weaning from breast milk
- Premature infants
- Infected form (AR)
- Acquired form
- Inadequate nutrition
- Poor absorption
- Biotin/multiple carboxylase deficiency
- Neonatal form (AR)
- Holocarboxylase synthetase deficiency
- Acquired & erythrodematous
- Fatal if untreated
- Infantile form
- Biotinidase deficiency
- Aplasia, incontinence, hearing loss
- Treated with Biotin
**DIAPER DERMATITIS**
- Langerhans cell histiocytosis
- Hashimoto-Pritzker disease
- Subcutaneous distribution
- Kawasaki disease
- Tender
- Desquamation
- Perianal Strep
- Well demarcated perianal erythema
- Preceding Strep URI
- Bullous impetigo
- Honey-colored crusts, fissured bullae
- Scales
- Congenital syphilis
- Red-brown, papulosquamous
- May be erosive/bullous

**CONGENITAL INFECTIONS**
- Toxoplasmosis
  - Truncal “Blueberry muffin” lesions
  - Red-blue papulonodules
  - Due to dermal hemopoiesis
  - Ocular & CNS abnormalities
  - Thrombocytopenia
  - Intracranial calcifications
- Rubella
  - Blueberry muffin lesions
  - Cataracts, deafness
  - Congenital heart disease
  - CNS abnormalities
  - Hepatosplenomegaly
  - Maternal infection during first 12-16 weeks of gestation

**CMV**
- Most common infectious cause of deafness & MR
- Blueberry muffin lesions, petechiae
- Oer’s eye intranuclear inclusion bodies

**HSV**
- Vesicles, erosions, scarring
- Temporal lobe encephalitis
- Microcephaly, chorioretinitis
- Mostly perianal HSV-2
- 50-75% mortality if untreated

**Varicella**
- Congenital
  - Cicatricial skin lesions
  - First 20 weeks gestation
  - Neonatal
  - 5 days before to 2 days after delivery

**Syphilis**
- 14+ weeks gestation
- Early (birth to 2 years)
  - Rhagades
  - Papulosquamous macules/papules
  - Bullous lesions
  - Snuffles
  - Lymphadenopathy
  - Splenomegaly
- Late
  - Parrot’s lines
  - Hutchinson’s teeth
  - Mulberry molars
  - Hageman’s sign
  - Saddle nose
  - Interstitial keratitis
  - Gummas
  - Tabes dorsalis

**RASHES REQUIRING WORKUP & TREATMENT**
- Staph scalded skin syndrome
  - Group 2 phage Staph aureus
  - Exfoliative toxin A/B → cleave desmoglein 1
  - Immature renal function, lack of specific immunity
- Ophthalmia
  - Periumbilical erythema, edema, tenderness, focal purulent discharge
- Mastitis
  - Term infants
  - 3 weeks
  - Neonatal breast abscess due to S. aureus

**OTHER INFECTIONS**
CONGENITAL NEVI & DEFECTS

- Nevus sebaceous
  - Waxy, yellow-orange-tan, hairless plaque on face/scalp
  - Most prominent in neonates & again in puberty
  - Tumor development
    - Trichoblastoma, syringocystadenoma papilliferum
    - BCC

- Epidermal nevus
  - Bullosous congenital ichthyosiform erythroderma risk in offspring
  - Accessory tragus
    - First branchial arch
    - Associated with oculoauriculovertebral (Goldenhar) syndrome
  - Supernumerary nipples
    - Occur along embryological milk lines

CONGENITAL NEVI & DEFECTS

- Aplasia cutis congenita (ACC)
  - Ovoid erosion/ulceration/scar/membranous defect
  - Hair collar sign
  - Associations
    - Adams-Oliver syndrome
    - Scalp ACC, SMTC, lung & cardiac defects
    - Bart syndrome
    - Lower extremity ACC, dominant dystrophic EB
    - Seiltes syndrome
      - Bilateral temporal ACC, loose fisures, abnormal lashes,
        spindel staring brow
    - Scalp
      - Vesicles, dystrophic nails, guttate
    - Yin & Yang, ectodermal dysplasia, annular band syndromes
    - Extensive – increased AFP

CONGENITAL NEVI & DEFECTS

- Collodion baby
  - Lamellar ichthyosis
  - Congenital ichthyosiform erythroderma
  - Self-healing collodion baby
  - Harlequin fetus (AR)
    - ABCA12 gene
  - Universally fatal historically
  - Supportive care
    - Acitretin
  - Increased survival
  - Improved mobility
    - Encourages softening & shedding of encasement
    - Eclabium – able to latch & feed
  - Start early (by day 7) – significant improvement in 1 month

GENODERMATOSES PRESENTING IN NEONATAL PERIOD

- Epidermolysis bullosa
- Incontinentia pigmenti
  - Oculocutaneous albinism
- Neurofibromatosis type 1
- Cuts laxa
- Ehlers-Danlos syndrome
- Hereditary palmoplantar keratodermas
- Piebaldism
- Congenital erythropoietic porphyria
- Ectodermal dysplasias
- Multiple lentigines syndromes
- Phakomatosis pigmentovascularis

IMMUNOLOGIC

- Neonatal lupus erythematosus
  - Birth to first few weeks
  - SCLE lesions perioretally & on extremities
  - Transplacental exposure to maternal antibodies
    - Anti-La
    - Anti-U1RNP
  - Congenital heart block (50%)
    - CKG
    - 2/3 require permanent pacemaker
    - 20% mortality
  - Thrombocytopenia, neutropenia, transaminitis
  - Cutaneous lesions resolve in 6-8 months
- Neonatal pemphigus
- Langerhans cell histiocytosis
- Immunodeficiency syndromes
REFERENCES


*Images courtesy of Jain (see above) & DermNet New Zealand (http://creativecommons.org/licenses/by-nc-nd/3.0/nz/).
<table>
<thead>
<tr>
<th>Time</th>
<th>Primary Pathway (Salon I/II)</th>
<th>Resident Pathway (Plaza Ballroom)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6:30 a.m. - 7:30 a.m.</td>
<td>Lilly USA, LLC Product Theater: Clinical Insights on Taltz Eugene Conte, DO, FAOCD Held in Plaza Ballroom (No CME Awarded)</td>
<td></td>
</tr>
<tr>
<td>7:30 a.m. - 8:30 a.m.</td>
<td>Local Flaps and Mohs Reconstruction and When to Use Them George Schmieder, DO, FAOCD</td>
<td></td>
</tr>
<tr>
<td>8:30 a.m. - 9:30 a.m.</td>
<td>Fermentation, Civilization and the Microbiome Melinda Greenfield, DO, FAOCD</td>
<td>Genodermatoses RMOPTI/Colorado Dermatology Institute</td>
</tr>
<tr>
<td>9:30 a.m. - 9:45 a.m.</td>
<td></td>
<td>Benign Epidermal and Dermal Tumors NYCOMECS/St. Barnabas Hospital</td>
</tr>
<tr>
<td>9:45 a.m. - 10:00 a.m.</td>
<td></td>
<td>Figurate Erythemas and Purpuras LECOMT/St. John's Episcopal Hospital</td>
</tr>
<tr>
<td>10:00 a.m. - 10:15 a.m.</td>
<td>Osteopathic Dermatology Research and the Foundation for Osteopathic Dermatology Eugene Conte, DO, FAOCD</td>
<td>Cysts and Disorders of the Hair NYCOMECS/Palisades Medical Center</td>
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<tr>
<td>10:15 a.m. - 10:30 a.m.</td>
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<tr>
<td>10:30 a.m. - 11:00 a.m.</td>
<td>Break with Exhibitors</td>
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<tr>
<td>11:00 a.m. - 11:15 a.m.</td>
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<td>Premalignant and Malignant Non-Melanoma Skin Cancer PCOM/Lehigh Valley Health Network</td>
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<tr>
<td>11:15 a.m. - 11:30 a.m.</td>
<td>20 Tricks to Finishing Your Office Day On Time John Coppola, DO, FAOCD</td>
<td>Photo and Pregnancy Related Dermatoses Texas OPTI/South Texas Osteopathic Dermatology</td>
</tr>
<tr>
<td>11:30 a.m. - 11:45 a.m.</td>
<td></td>
<td>Eosinophilic and Neutrophilic Dermatoses Texas OPTI/UNTHSC</td>
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<tr>
<td>12:00 p.m. - 1:00 p.m.</td>
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<td>Infectious Diseases: Fungal Still OPTI/Northeast Regional Medical Center</td>
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<tr>
<td>1:00 p.m. - 1:15 p.m.</td>
<td></td>
<td>Pediatric Papulosquamous and Eczematous Dermatoses SCS/MSUCOM/Botsford Hospital</td>
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<tr>
<td>1:15 p.m. - 1:30 p.m.</td>
<td>A Decade of Lessons Learned the Hard Way: Practical Knowledge for the Medical and Cosmetic Dermatologist and Practice Owner Michelle Foley, DO, FAOCD</td>
<td>Pediatric Blistering Diseases SCS/MSUCOM/Oakwood Healthcare System</td>
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<tr>
<td>1:30 p.m. - 1:45 p.m.</td>
<td></td>
<td>Cutaneous Manifestations of Systemic Diseases CORE/O’Bleness Memorial Hospital</td>
</tr>
<tr>
<td>1:45 p.m. - 2:00 p.m.</td>
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<tr>
<td>2:00 p.m. - 3:00 p.m.</td>
<td>Urticaria: Diagnosis and Treatment Considerations Adam Friedman, MD</td>
<td></td>
</tr>
<tr>
<td>3:00 p.m. - 3:30 p.m.</td>
<td></td>
<td>Break with Exhibitors</td>
</tr>
<tr>
<td>3:30 p.m. - 4:30 p.m.</td>
<td>A Play Yard of Dermatology Tips Albert E. “Bo” Rivera, DO, FAOCD</td>
<td></td>
</tr>
<tr>
<td>3:30 p.m. - 4:30 p.m.</td>
<td>Student Members Forum</td>
<td></td>
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<tr>
<td>4:30 p.m. - 5:30 p.m.</td>
<td>Photosensitive Disorders in Middle Age and Beyond Carlos Nousari, MD</td>
<td></td>
</tr>
<tr>
<td>5:30 p.m. - 7:00 p.m.</td>
<td></td>
<td>Sagis Diagnostics Dermpath Bowl</td>
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</tbody>
</table>
Thursday, March 30, 2017
Primary Pathway
Local Flaps and Mohs Reconstruction

GEORGE J. SCHMIEDER D.O., FACEP

My Disclaimer
- I've been doing Mohs surgery since 2002
- I have no conflict of interest with any drug companies.
- This lecture is a review of Local Flaps in Facial Dermatologic Surgery.
- This lecture is not designed to teach you how to do various Advancement Flap techniques, rather to refresh and explore just how complex Dermatologic Surgery has become over the past 20 years.
- There are various ways to approach closures, as many different Mohs surgeons sitting in the audience may agree.
- I want to review with you some of the risks and benefits of doing different closures.
- My hope is this lecture will assist our residents and some of you who are seeking re-certification with some board review gimmie's!

Introduction
- Understanding Flap Repair status post Mohs surgery is a dynamic process and varies from patient to patient.
- There are many different ways to approach repairing the surgical defect and I am not suggesting my way is the only way.
- I always evaluate the risks and benefits of all repair options in every surgery case.
- This allows me to maximize each repair success by going over the benefits and risks of the procedure with the patient and family as needed.

Flap Design
- When simple closure is not an ideal repair – due to size, tension, or poor cosmetic result.
- In this case, I suggest an “Adjacent Tissue Transfer” procedure, such as a flap.
- A Local Skin Flap is simply a portion of full thickness skin and variable subcutaneous tissue transferred from an adjacent donor site into the surgical defect.
- Nothing can be stressed more than communicating with your patient about the closure you are proposing to them. Have them sign consent forms for large defect repairs.
- Complicated repairs are always important to go over again; have an additional signature and acknowledge an additional family member or spouses approval.

K.I.S.S. Principle
“Keep It Simple Stupid”
- This may be my best advice to every person in the room when it comes to surgery, whenever possible; use the K.I.S.S. Principle.
- There are many risks to Dermatology surgery and flap repair.
- Risks include: pain, bleeding, infection, bruising, dehiscence and poor outcome scars. Every one of these and more should be listed in your consent form.
- I cannot stress going over your consent with every patient. Just do it! With each patient one on one. In a court of law this will save you!

Mohs Consent
**K.I.S.S. Principle**

“Keep It Simple Stupid”

- This is the simply the best advice I can give you as an experienced Mohs surgeon. Always have a trusted staff to help ensure you are obtaining the patient’s consent to surgery.
- Always take a time out and be sure the consent form has been signed before you start every surgery. Remember, as the surgeon, the consent is your responsibility no matter how busy you become.
- Never start a surgery without checking the consent being signed and at least briefly going over with your patient.
- Don’t be afraid to take a time out before you MAKE the excision. 60 seconds is all it takes!

---

**Pre-Test**

Before we get started lets take a look at one of my cases and think of how you might approach closing this case.

A. Transposition Flap
B. Rotation Flap
C. Secondary Intention
D. Advancement Flap
E. Interpolation Flap

---

**Pre-op BCC**

---

**4 stage immediate post-op**

---

**Pre-Test**

Before we get started lets take a look at one of my cases and think of how you might approach closing this case.

A. Transposition Flap
B. Rotation Flap
C. Secondary Intention
D. Advancement Flap
E. Interpolation Flap

---

**4 week post-op**
Before we get started, let's take a look at one of my cases and think of how you might approach closing this case.

A. Transposition Flap
B. Rotation Flap
C. Xenograft/Secondary Intention
D. Advancement Flap
E. Interpolation Flap
Before we get started, let's take a look at one of my cases and think of how you might approach closing this case.

A. Transposition Flap
B. Rotation Flap
C. Xenograft/Secondary Intention
D. Advancement Flap
E. Interpolation Flap

Day of surgery after completion of Xenograft
Advancement Flaps

- A Rotation Flap is a random pattern flap where the motion or movement is in a rotating fashion.
- The primary movement of an Advancement Flap is the one dimensional sliding of tissue directly into a defect. This helps redistribute the excess tissue.
- Advancement Flaps have many variations which we will go over in the following slides. They include Single and Bilateral Advancement Flaps as well as Island Pedicle flaps.

- A large single Advancement Flap is often performed on the cheek. These are used to repair medium to large defects of the medial cheek and lateral portion of the nose.
- The next patient has a large defect on the lateral portion of the nose. The incision is placed in the alar crease and nasal labial fold by removing tissue above and below the defect to allow the cheek to advance into the Nasolabial sulcus.
- Depending on the size of the defect sometimes it is necessary to take down the Flap to the periosteum of the nasal sidewall-cheek junction to take pressure off the leading edge and recreate the natural concave surface of the face, which helps prevent webbing in the nasolabial fold.
Immediately after Closure

Infiltrative BCC
Left alar crease

2 stage
Post Mohs

Closure
Nasal sulcus left open to heal by secondary intention

Close up
Helical Rim Advancement Flap

- Used to repair defects of the Helical Rim.
- This is an incredible flap for mid and lower Helical rim defects.
- This may be my preferred closure for the Helical Rim.
- Of course, remember the K.I.S.S. principle so a complex closure is always considered first by trying to undermine surrounding tissue and pull the edges together but, when the defect is too large for a complex closure on the helical rim.
- Then the Helical Rim Advancement Flap is the winner!

Micronodular BCC Lower Helical Rim

Closure after 3 stages of Mohs

Closure after 2 stages of Mohs SCC

Bilateral Advancement Flap or H-Plasty

- Not one of my favorite Flaps.
- I've only used them on large scalp and forehead defects. Sometimes they can be very successful when used on the eyebrows.
- Cosmetically it's really difficult to hide this flap on the forehead and scalp and should be one of your last resorts.
- Use it only when having a difficult time in moving tissue.
Crescentic Advancement Flap

- It's two primary functions are to repair the upper lip and with many nose defects to preserve the Ala.
- So that the superior scar line is placed in the perinasal sulcus.
- This is a complicated difficult repair and I wouldn't recommend this for anyone who doesn't have a great deal of surgical experience. This is time consuming and carries with it more risk.
- This flap is particular useful for the repair of the upper lip, as I will show in the next slide.
- Also useful in the Perialar area with large defects.
Island Pedicle Flap

- Referred to as V to Y Advancement Flap.
- This has become a coding nightmare and CMS wants a named artery when using this closure. Including detailed photos of course! Example, when doing an Island Pedicle Flap in the nasolabial fold you need to name the superior labial artery.
- The Island Pedicle Flap is most commonly done on nasal and perinasal closures where free margins are at risk for distortion.
O-T/O-L Advancement Flap

- An L-plasty or what we commonly refer to as an O to L Advancement is a single tangent flap.
- An incision is made at one end of the defect, extending outward for some length. The mobilized tissue is then advanced into the defect.
- Tissue redundancy is created on the side of the defect opposite the Flap Incision and must be removed or carefully sewn out.
- I use this with large distal nasal sidewall defects.
East-West Advancement Flap

- Modified burrow advancement flap
- This is used extensively for small nasal tip defects to disrupt the straight line effect and create a more natural wave in the closure.
- Almost all of my older men will require some follow-up Dermabrasion or Fraxel laser resurfacing.

East-West Advancement Flap
Right bridge of nose
Pre surgery

East-West Advancement Flap
Right bridge of nose
Post surgery

East-West Advancement Flap
Left alar crease
Closure

East-West Advancement Flap
Left mid forehead/Left upper forehead medial
SCC Pre-surgery

East-West Advancement Flap
Left mid forehead/Left upper forehead medial
Combined Closure
East-West Advancement Flap
Left mid forehead/Left upper forehead medial
Combined Closure

Rotation Flap
- Rotation Flap is a random pattern flap.
- The primary movement of the Rotation Flap is the sliding of tissue about a pivot point into the defect.
- This will help redistribute wound tension as well as tissue redundancy.
- There are several variations including Single and Bilateral Rotation Flaps as well as Dorsal Nasal Flaps.

Dorsal Nasal Rotation AKA The Rieger Flap
- This Flap is used to repair nasal defects involving the nasal dorsum or nasal tip.
- The tissue reservoir of the nasal root and glabella allows for the movement of the dorsal nasal skin superior to the defect.
- A long sweeping arc is created that extends into the nasolabial sulcus and terminates in the glabella.
- A back cut in the glabella improves the rotational mobility of this flap and is termed a Hatchet Flap.
- If the arc of the Flap is not long enough there will be too much tension and you will see elevation of the nasal tip.

Rotation Flap/ AKA Rieger Flap
Mid tip large nodular BCC

Dorsal Nasal Rotation AKA The Rieger Flap

Rotation Flap/ AKA Rieger Flap
Mid tip large nodular BCC Close up
Rotation Flap/ AKA Rieger Flap

At close

Close up

Surgery if flared nostrils

Transposition Flaps

- Primary movement of a Transposition Flap is not merely sliding but picking up the flap and transposing over the intervening tissue, redistributing tension vectors.
- There are several versions of Transposition Flaps. The most commonly used in my daily surgery clinic are Bilobed Flaps.
- The other Rhombic and Banner will be discussed briefly.

- Simply put, Transposition Flaps transpose loose adjacent skin over an island of normal skin to the site of the Mohs defect.
- Transposition Flaps are usually smaller than advancement and rotation flaps.
- The resulting scars are geometric broken lines that may be less noticeable than longer linear closures.
- One of the biggest advantages of Transposition Flaps is that they utilize adjacent skin and provide excellent color and texture match.
- This is particularly true on the nose where a Bilobed Flap can have a far better outcome than a graft from a distant site.
Bilobed Flaps

- Although this is a frequently used flap in our clinic, I consider this flap a highly technical and skill-oriented Transposition Flap.
- Consists of two Transposition Flaps executed in succession which follow the same direction of rotation over intervening tissue.
- Basic premise is to fill the defect with the primary lobe, while filling the secondary defect with the secondary lobe which leaves a triangular shaped tertiary defect to be closed primarily.
Banner Flaps
- A Random pattern finger shaped cutaneous flap that, like other transposition flaps, tap into adjacent skin to borrow laxity and fill a defect.
- Most commonly planned as a melolabial transposition to repair defects of the nasal ala or from the pre or post auricular area to close defects on the ear.
- To minimize risk of vascular compromise the Flaps are typically designed to rotate through an angle of 60-120° instead of the originally described 180°

Bilateral Rotation Flap
- Sometimes due to the size of the defect or the potential tension, the flap mandates a Bilateral Rotation Flap.
- Where tissue is rotated into a defect from two opposite sides.
- The vectors of rotation often may be mirror images of each other.
- This is often used in large defects on the scalp, as I will show you.
- When the vectors of movement are in opposition, this creates an O to Z flap.
Bilateral rotation flaps

Large SCC scalp

3 stage Mohs
Immediate post-op

The rotation vector
drawn out

Undermining tissue

Closure of defect
Bilateral Rotation Flaps

- Besides being useful for scalps, let me show you some examples of the lips.

Right mid upper lip
Post surgery

Right mid upper lip
Closure

Rhombic Flaps

- Designed by conversion of the primary defect into a four-sided parallelogram with each side of equal length and tip angles of 60° and 120°.
- This rhombus forms the recipient site for the flap as well as the template on which to plan the flap incisions.
Rhombic Flaps

- Import pedicle tissue from a site distant to the defect.
- These are considered Axial Flaps that can support a larger mass of tissue compared to the other random flaps.
- These Flaps are used to repair defects distant from the donor site.
- The vascular pedicle must be temporarily left in place to ensure adequate blood supply.
- This means it requires more than one stage to complete the repair.

Interpolation Flap

- Many interpolation flaps may be classified as axial flaps if their vascular pedicle is based on a large, named artery.
- The 1st stage of an interpolation flap involves the design and creation of the flaps.
- The 2nd stage involves the takedown of the flap in which the pedicle is incised and removed, while the residual tissue is sewn into the defect and the donor site is closed primarily.

Paramedian Forehead Flap

- Paramedian forehead flaps are useful to repair large deep nasal defects.
- Tissue is mobilized from the forehead based on one of the supratrochlear arteries.
- Then transposed to the large distal nasal defect with the pedicle remaining attached in the glabellar region.
- It takes 2-3 weeks until the pedicle is separated from the brow.
- Many Mohs surgeons do these in the office setting.
- I personally prefer a surgical center with IV conscious sedation.

Paramedian Forehead Flap
Nasolabial Interpolation Flap

- This flap is utilized to repair defects of the ALA, particularly in instances where cartilage grafting is required to restore the structural integrity of the alar rim.
- This flap is harvested from the medial cheek and nasolabial fold and is based on branches of the angular artery.

ABBE Flap

- Also known as the lip-switch flap and is reserved for repair of large, deep defects, typically of the upper lip.
- Particularly useful for defects that involve up to half of the lips without crossing the midline.
- The flap is harvested from the ipsilateral lower lip and is based on the inferior labial artery.
- The artery is located deep to or within the orbicularis oris muscle and runs along the mucosal aspect of the vermillion border.

- This defect should be full thickness including muscularis and oral mucosa.
- It is rotated upon a vascular pedicle that makes up the lateral aspect of the flap.
- The inferior labial artery will be visualized as it is transected at the mobilized edge of the flap.
- The donor site is undermined and closed first to facilitate freeing up the flaps.
- This should be closed in layers such as one would do in a wedge resection: mucosa, muscularis, subcutaneous, then cutaneous.

- Lastly the flap will be rotated superiorly and also inset with a layered closure.
- The key to this closure as is any closure around the mouth is the alignment of the vermillion borders both at the donor site and defect.
- As with other interpolation flaps, the pedicle will remain in place for at least 3 weeks.
The ABBE Flap is:
- Also a 2-stage interpolation flap used for large defects of the helix.
- Defects in this location typically involve the perichondrium are not suitable for grafts.
- Considered a Random Flap as it is not based on a large named artery.
- It is harvested from the richly vascularized skin of the postauricular scalp and is advanced over intervening intact skin to fill the helical defect.
- Like all interpolation flaps the pedicle remains attached to the posterior scalp for 3 weeks.
- This Flap often comes with post-op bleeding and much discomfort. Never do this flap on a Friday afternoon.

The Retroauricular Flap is:
- The donor site is not repaired until pedicle take-down and often, due to its inconspicuous location, is left to heal secondarily.
- Meticulous postoperative wound care is necessary to ensure an optimal outcome.
- Verbal and written instructions regarding home wound care should be reviewed and then provided in writing to the patient.
- Every Interpolation Flap needs a pressure dressing should be applied and left intact for 48 hours.
- We have everyone change the bandage after 48 hours and reinforce the importance that the wound must be kept clean, moist and covered until sutures are removed.
- This promotes epithelialization, reduces the chances of infection and will help eliminate desiccation.
- Most importantly it will aid in hemostasis.

Complications:
- Bleeding
- Hematoma
- Pain
- Infection
- Flap necrosis
- Hypertrophic scar/keloid
- Erythema
- Telangiectasia
Before we get started, let's take a look at one of my cases and think of how you might approach closing this case.

A. Transposition Flap
B. Rotation Flap
C. Secondary Intention
D. Advancement Flap
E. Interpolation Flap
Before we get started, let's take a look at one of my cases and think of how you might approach closing this case.

A. Transposition Flap
B. Rotation Flap
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A. Transposition Flap
B. Rotation Flap
C. Secondary Intention
D. Advancement Flap
E. Interpolation Flap
Post-Test

Before we get started, let's take a look at one of my cases and think about how you might approach closing this case.

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B. Rotation Flap
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D. Advancement Flap
E. Interpolation Flap
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D. Advancement Flap  
E. Interpolation Flap
FERMENTATION, CIVILIZATION AND THE MICROBIOME

MELINDA F. GREENFIELD, DO
ADVANCED DERMATOLOGY AND COSMETIC SURGERY
PONTE VEDRA BEACH, FL

Fermentation

- Fermentation is a metabolic process in which an organism converts a carbohydrate, such as starch or a sugar, into acid, gas or alcohol.

Two Fermentation Processes

**Ethanol Fermentation**
- Beer, Wine, Bread
  - Yeast and certain bacteria perform ethanol fermentation where pyruvate (from glucose metabolism) is broken into ethanol and carbon dioxide.

**Lactic Acid Fermentation**
- Yogurt
  - The pyruvate molecule from glucose metabolism is fermented into lactic acid.
  - Lactic acid fermentation is used to convert lactose into lactic acid in yogurt production.
  - It also occurs in animal muscles when the tissue requires energy at a faster rate than oxygen can be supplied.

Fermentation’s Effects

- It’s believed that the establishment of fermentation facilitated the shift from a hunter/gatherer society to an agricultural society because it allowed people to settle in one area and preserve food vs. following the food sources.

Fermentation of Food

- For over 6000 years, humans have been preserving foods with the process of fermentation:
  1. Preserved food= improved food safety
  2. Degradation of toxic components and anti-nutritive factors (phytic acid)
  3. Enriching of diet with amino acids, vitamins, probiotics
  4. Enhancing the bio-availability of nutrients
  5. Enriching the sensory quality of foods
  6. Multiple health benefits
**Health Benefits-Fermentation/probiotics**

- Manufacture of vitamins
- Support and increase the rate of metabolism
- Detoxification of chemicals
- Promote cell growth including RBC
- Enhance immune and nervous system function
- Increase production of enzymes improving food assimilation and absorption of nutrients
- Crowd out pathogenic organisms

**All Things Fermented…**

- **Bean-based:** Cheonggukjang, doenjang, miso, natto, soy sauce, stinky tofu, tempeh, oncom, soybean paste, Beijing mung bean milk, kinama, iru
- **Dough-based:** Proofing-sourdough
- **Grain-based:** Batter made from rice and lentil prepared and fermented for baking idlis and dosas, Amazake, beer, bread, choujiu, gamji, injera, kvass, makgeolli, murri, ogi, rejuvelac, sake, sikhye, sourdough, sowans, rice wine, malt whisky, grain whisky, idli, dosa, vodka, boza
- **Vegetable-based:** Kimchi, mixed pickle, sauerkraut, Indian pickle, gundruk, tursu

**All Things Fermented…**

- **Fruit-based:** Wine, vinegar, cider, perry, brandy, atchara, nata de coco, burong mangga, asinan, pickling, višnátá, chocolate, raki
- **Honey-based:** Mead, mehteglin
- **Dairy-based:** Some cheese also, kefir, kumis (mare milk), shubat (camel milk), cultured milk products such as quark, flimjölk, crème fraîche, smetana, skyr, and yogurt
- **Fish-based:** Baguun, fasekh, fish sauce, Garum, Hákarl, jaotgal, rakfisk, shrimp paste, surströmming, shidal
- **Meat-based:** Chorizo, salami, sucuk, pepperoni, nem chua, som moo, saucisson
- **Tea-based:** Pu-erh tea, Kombucha

**Let’s Explore………**

- How does fermentation and it’s effects make us healthier?

**Microbiome**

- Describes all the organisms that live in and on our bodies (bacteria, viruses, fungi, protozoa, helminths) along with their genes
- Considered a counterpart to the human genome

**Microbiome**

- During birth baby is colonized by bacteria- thus begins the evolution of our individual microbiome
- Our unique microbial footprint develops over our lifetime and is altered by just about everything: C-section, vs vaginal delivery, breast milk vs bottle, food, hygiene, exposure to chemicals, pets, farm animals, toxins, medications and even emotions
Was this you growing up?

Microbiome

- The end result of our individual microbial salad is so unique and distinctive that it’s more specific than our own DNA
- We have about 23,000 human genes and 8,000,000 microbial ones
- Some studies suggest that gut bacteria play a critical role in carbohydrate metabolism, enzymatic detoxification and even determining whether or not a disease you are genetically predisposed to actually develops
- This may explain why identical twins with inherited diseases don’t always manifest the disease; the genes may be the same but the microbes are different

Or this??

Microbiome

- Disruption of the microbial ecosystem can cause disease
- As adults there are ways we can keep our microbiome healthy
- As physicians, it is our duty to keep our patients’ healthy microbiome in mind

The Human Microbiome Project

- Established in 2008
- Funded by NIH
- Goal: characterize the human microbiome and analyze its role in human health and disease
DERMATOLOGY WORLD

- Certain diseases carry with them certain types of bacteria
- Healthy skin shows a balance of bacteria
- Dysbiosis causes an imbalance and results in a pro-inflammatory state
- This leads to dysregulation of the immune system
- NIH is currently evaluating trial of skin autologous microbiome transplant to decrease S. aureus colonization
- ‘The option of rebalancing and rediversifying the skin microbiome, instead of eliminating pathogens randomly will add to the arsenal of treating skin diseases’

Microbiome-studies

- Study Nature, 2006 “An obesity-associated gut microbiome with increased capacity for energy harvest” found that germ free mice colonized with the gut flora of obese mice became obese
- They correlated this to fewer Bacteriodetes than Firmicutes in gut flora
- It’s postulated that the flora in obese mice is more efficient at extracting energy from food

Microbiome

- In a similar study (published in Science in 2013) researchers at Washington University in St. Louis took gut bacteria from identical twins, one was lean and one was obese, and transplanted them into germ-free mice
- Within a few weeks, the mouse that received the microbes from the obese twin became obese and the one who received them from the lean twin remained lean
- What happens when you put the lean mice with the fat mice? Or vice versa?

Microbiome

- As stated in the book, The Microbiome Solution, by Dr. Robynne Chutkan, “the microbiome has one of the biggest impacts on our genes, turning them on and off and determining which ones are ultimately expressed as disease”
- She goes on to discuss how the study of “epigenetics” evaluates how the environment affects heritable traits without actually changing the DNA material in our genes, and suggests that the gut bacteria you inherit might be far more important than the genes you inherit

Microbiome

- Studies have shown that children prescribed large amounts of antibiotics are at higher risk of obesity later in life
- Antibiotic exposure before birth can affect children the same way
The word antibiotic literally means “against life” from its Greek roots. And, that’s exactly what this form of medicine is designed to do; antibiotics stop or slow down the growth of microscopic organisms (bacteria, fungi, and some parasites), in turn treating potentially dangerous infections.

Antibiotics and the microbiome

- 2016, Genome Med, “The effects of antibiotics on the microbiome throughout development and alternative approaches for therapeutic modulation”
- Antibiotics influence the function of the immune system, our ability to resist infection, and our capacity for processing food, and storing energy
- Now more important than ever to revisit how we use antibiotics
- We have a better understanding of the long term effects on diseases such as malnutrition, obesity and diabetes

Antibiotic Overkill

- Between 2000-2010 world wide use of antibiotics has increased by 35%
- US ranks #1 in per capita consumption
- Average American child receives 17 rounds of antibiotics by their 18th birthday
- Incidence of antibiotic resistant infections rising sharply-2015-over 50,000 deaths in US and Europe- expected to rise to 10 million worldwide by 2050
- The resultant antibiotic resistance and the superbugs created are killing more Americans each year than murders and car accidents combined
- One round of antibiotics can kill off over 30% of the bacteria in the gut and create an imbalance that can take months to years to recover from

How does the microbiome effect the immune system?

- The relationship between the mammalian host and its microbiota is symbiotic, and this shapes the host’s immune system
- There exists a type of ‘cross-talk’ between the two via the exchange of chemical signals
- This allows the immune system to recognize bacteria that are ‘harmful’ and find ways to remove them while allowing the good bacterial to remain intact
- It is thought that the microbiome directly influences immune reactivity and targeting

How does the microbiome effect the immune system?

- It is suggested that connections between the microbiome and a growing number of diseases exist, including:
  - Crohn’s disease
  - UC
  - Irritable bowel syndrome
  - Type 1 & 2 diabetes
  - Rheumatoid Arthritis
  - Periodontal disease
How does this affect dermatology?

- **Am J Gastroenterol. 2010-** authors DJ Margolis, etal suggested that while the risk of IBD from Isotretinoin appears to be minimal, it appears that there is a potential association between the oral tetracycline class of drugs used to treat acne and inflammatory bowel disease.
- They also found a hazard ratio of 2.25 for the development of Crohn’s disease with the use of doxycycline, with the risk evident only after 2 months of use.

- **JAAD, February 2017, Patterns of antimicrobial resistance in lesions of hidradenitis suppurativa,** Fisher, et al sought to determine the frequency of antimicrobial resistance in HS lesions from patients on antibiotic therapy.
- Cross-sectional analysis on 239 patients with HS seen at Johns Hopkins from 2010-2015.
- Concluded that antibiotic therapy for HS treatment may be inducing antibiotic resistance.
- Raised the question regarding the balance of antibiotic use versus potential harms associated with antibiotic resistance.

- **SKIN THERAPY LETT. 2013 JUL-AUG;18(5):1-4.**
  - A controversial proposal: no more antibiotics for acne!
  - Muhammad M, Rosen T
  - Use of antibiotics, often for prolonged periods, has become the de facto standard of care for acne (and rosacea). However, the world is now facing a health crisis relating to widespread antibiotic resistance.
  - The authors provide current evidence to suggest that dermatologists should consider a radical departure from standard operating procedure by severely curtailing, if not outright discontinuing, the routine and regular use of antibiotics for acne.

- **J Drugs Dermatol. 2010 May;9(5):519-24**
  - Trends in the treatment of acne vulgaris: are measures being taken to avoid antimicrobial resistance?
  - Kinney MA, Yentzer BA, Fleischer AB Jr, Feldman SR.
  - CONCLUSION: The development of antibiotic resistance is of concern. Greater awareness of retinoid use for maintenance therapy, using topical benzoyl peroxide to prevent resistance, and limiting use of oral antibiotics to as short a time period as possible are measures to contribute to better eco-responsible acne treatment.


- Systematic review of Propionibacterium acne resistance to systemic antibiotics.
- Cooper AJ
- Research since 1978 has suggested an association between poor therapeutic response and antibiotic-resistant propionibacteria. The overall incidence of P. acne antibiotic resistance has increased from 20% in 1978 to 62% in 1996. Resistance to specific antibiotics varied and was most commonly reported with erythromycin and clindamycin, tetracycline and doxycycline, and trimethoprim. Resistance to monochloride is rare.
- CONCLUSIONS:
  - In many patients with acne, continued treatment with antibiotics can be inappropriate or ineffective. It is important to recognize therapeutic failure and allow treatment accordingly. The use of long-term rotational antibiotics is outdated and will only exacerbate antibiotic resistance.

What do we do???

- Figuring out how to undo the damage done by antibiotics and an unhealthy lifestyle might be the answer to undo the damage.
How do we build a better biome and improve our general health?

It's never too late to get dirty....

7 ways to embrace more microbes

- Stay away from hand sanitizers
- Exposure yourself to the great outdoors
- Stop destroying your personal army of microbes
- Make your microbes flourish with greens
- Get rid of artificial sweeteners and other chemicals
- Discover prebiotics- non digestible short chain fatty acids that help your bacteria flourish- artichokes, garlic, beans, oats, onions and asparagus
- Protect your microbiome with probiotics

Probiotics

- Evidence-based reviews indicate that certain strains of probiotics help to balance the microbial colonies in the gut
- The inhibition of pathogenic bacteria may be due in part to pH as well as antimicrobial activity of the probiotic colonies (good guys vs bad guys)
- Touted for an array of diseases: eczema, acne, IBS, autism, food allergies, etc.
- In the US the products are unregulated and not subject to FDA oversight
- Very difficult to find products with consistent strains, dosages and populations of bacteria
- Nearly 40 billion dollar industry

Benefits of Probiotics-Eczema

- 2012 *Journal of Allergy and Clinical Immunology*, Infants whose mothers took probiotics during pregnancy and breastfeeding were less likely to develop eczema
- 23 randomized, placebo-controlled studies examining the effects of probiotics on the development of eczema and food allergies- 60% of these studies show a favorable outcome during first year of life

Benefits of Probiotics- Antibiotic Associated Diarrhea (AAD)

- May 2013, review in the Cochrane Database of Systematic Reviews, looked at 23 studies testing a total of 3938 children 2 weeks to 17 years of age who received a probiotic along with an antibiotic
- Probiotic usage was associated with a significant 64% reduction in the risk of AAD
Probiotics Affect Brain Activity?

- June 2013, *Gastroenterology*, utilized a functional MRI that demonstrated women who consume probiotic-containing yogurt on a regular basis have altered activity in the regions of the brain that control central processing of emotion and sensation.
- Not yet determined if these effects are beneficial according to the lead author, Kirsten Tillisch, MD.
- Study funded by Danone Research.

Probiotics and The Skin

- Gut-brain-skin axis originally proposed over 70 years ago by dermatologists John H. Stokes and Donald M. Pillsbury.
- Many studies show acne and rosacea patients are at higher risk for GI and emotional issues.
- Theory: anxiety ↔ GI issues → alter gut microbial flora → promotes local and systemic inflammation.
- As early as 1961 there were published case reports showing the benefits of probiotics for the treatment of acne.
- One study showed 80% clinical improvement when patients consumed a probiotic.
- Other studies from Italy and Russia have also shown improvement.

Probiotics and the Skin

- 2008 study published in *Clinical Gastroenterology and Hepatology* noted that SIBO (small intestinal bacterial overgrowth) was 10 times more prevalent in rosacea patients, and correction of SIBO led to marked improvement in rosacea.
- Other recent studies are looking at the topical application of probiotics for acne and rosacea.

Looking to the future…

- Our control over microbial disease is diminishing.
- Pathogens are outsmarting every new antibiotic we develop.
  1. Anti-quorum sensing
  2. Anti-toxin production
  3. Enhancing microbiota
  4. Fecal transplants
  5. Phage therapy
  6. Probiotics
Disclosure
Speaker Faculty
• Abbvie
• Lilly
• Janssen Biotech
• Celgene

Learning Objectives
• To understand how The Foundation for Osteopathic Dermatology supports research.
• Learn about the multiple grants available to a Dermatologist who wants to pursue a research project.
• Present "Abstracts" from ongoing research projects that the Foundation is supporting.

History
• The Foundation for Osteopathic Dermatology was founded in 2002 by 10 members of the AOCD as a unique extension of the Osteopathic Dermatology community.

Mission Statement
• To improve the standards of the practice of Osteopathic Dermatology by raising awareness and supporting research through grants and awards given to those promising applicants who are devoted to research in all areas of Dermatology under the jurisdiction of an Osteopathic Dermatologist including providing public health information and charitable events.
The Foundation for Osteopathic Dermatology Research Grants

What are the Research Grants Available by Category

The Foundation for Osteopathic Dermatology Resident Research Grant
- This grant is awarded to a Dermatology “RESIDENT” in an AOA/ACGME accredited Dermatology program.
- The purpose of this grant is to foster research in dermatology conducted by residents at a graduate level and supervised by an attending dermatologist.

The Foundation for Osteopathic Dermatology Young Investigator Grant
- This grant is awarded to an Osteopathic dermatologist who is a “GRADUATE” of an AOA/ACGME program and is practicing in a clinical and or research setting.
- The purpose of this grant is to foster research among young dermatologists and is awarded to promising physicians researchers meeting this criteria.

The Foundation for Osteopathic Dermatology Physician Investigator Grant
- This grant is awarded to an established osteopathic dermatologist who is certified in dermatology and conducting research in a clinical setting at an accredited institution. The purpose of this grant is to sponsor or co-sponsor research in any area of dermatology.

The “FOD” Institutional Grant
- This grant is awarded to the “INSTITUTION” where an Osteopathic Dermatologist is currently conducting their clinical or bench research. The research may be clinical, diagnostic and or therapeutic as it relates to the specialty of Dermatology.
Foundation Grants Awarded 2015 - 2016

Karthik Krishnamurthy, D.O., FAOCD, FAAD

- Genomic Characterization of Melanomas in the Hispanic Population by Single Nucleotide Polymorphism (SNP) Analysis
  - The FOD Physician Investigator Grant

Alexis Stephens, D.O.
- Dermoscopy Research “To establish unique dermoscopic features in patients of Skin of Color”
  - The FOD Resident Research Grant

Huyenlan Dinh, D.O
- Frontal Fibrosing Alopecia: A Cross-Sectional Survey
  - The FOD Resident Research Grant

Frontal Fibrosing Alopecia: A Cross Sectional Survey

Lanny Dinh, D.O.
Lehigh Valley Health Network/PCOM
Department of Dermatology
AOCD

Investigators
- Principal Investigator: Tanya Ermolovich, DO
- Sub-Investigators: Nektarios Lountzis, MD, Lanny Dinh, DO, and Veronica Rutt, DO
- Biostatistician: Jennifer Macfarlan, MPH
Background

- Frontal Fibrosing Alopecia (FFA)
  - Scarring alopecia that is a clinical variant of lichen planopilaris
  - 1994
    - Incidence on the rise
    - Seen more in postmenopausal females
    - Premenopausal females
    - Men

Background

- Etiology
  - Unknown
  - Hormonal
  - 2016: Leave on facial products
    - Sunscreen use

Background

- Treatment
  - Symptomatic
    - Topical/Intralesional corticosteroids
    - Oral anti-inflammatories
    - Finasteride
    - Pioglitazone

Study Objective

- Hypothesis generated, exploratory study
- Cross-sectional survey
  - 40-50 patients from the Lehigh Valley area
  - Characterize the disease

Study Criteria

- Inclusion criteria
  - 18 years or older
  - Physical exam findings consistent with scarring alopecia on the scalp in a band-like frontal or frontal temporal distribution
- Exclusion criteria
  - History of chemotherapy or radiation therapy to the scalp or body
Survey

- Duration of the disease
- History of lichen planus on the skin or mucosal surfaces
- History of hair loss in other areas
- History of shingles or trauma to the scalp and/or face
- History of hormonal imbalance
- History of surgery to the scalp and/or face
- All past medical and surgical history
- Current medications

Survey

- History of hypothyroidism/hyperthyroidism
- History of smoking
- History of an autoimmune disease
- Family history of hair loss
- Race/Ethnicity
- Current or history of hair care products
- Hair care grooming practices (dyes, straighteners, curlers, perms)
- Facial leave on products

Progress

- Network Office of Research and Innovation (NORI)
- IRB expedited process
- Update at the next AOCD

Thank you

- Tanya Ermolovich, DO
- Nektarios Lountzis, MD
- Veronica Rutt, DO
- Jennifer Macfarlan, MPH
- AOCD Foundation Grant
- Lehigh Valley Health Network

Matthew Zarrago, D.O.

- “A Randomized, Double-blind, Multicenter Study of the Efficacy and Safety of AbobotulinumtoxinA Reconstituted up to 10 Weeks Prior to Injection.”

The FOD Resident Research Grant

Gregory R. Delost, D.O.

- “Autoimmunity in Primary Cutaneous Lymphoma and Pseudolymphoma”

- The FOD Resident Research Grant
Adolescent and young adult cutaneous lymphomas:
Clinical spectrum and autoimmunity
Foundation for Osteopathic Dermatology
Gregory R. Delost, DO
University Hospitals Cleveland Medical Center
Department of Dermatology

Background: AYA and Autoimmunity
- Adolescent and young adult (AYA) cancer may behave differently.
- Many autoimmune diseases share similar clinical, histological, and pathophysiological features with cutaneous lymphomas.
- Previous research:
  - Young patients (<30) with MF/SS in general have a favorable outcome1
  - Many autoimmune diseases especially when diagnosed at younger ages, were associated with higher risk of NHL2
  - Subcutaneous panniculitis-like T-cell lymphoma has upregulation of autoimmunity-associated genes3

Objectives
- To validate the University Hospitals Multidisciplinary Cutaneous Lymphoma Program cohort against the national Surveillance, Epidemiology, and End Results (SEER)-18 database
- Characterize pediatric, AYA, and adult population distributions of subtypes of lymphoma at a level of specificity not recorded by SEER
- Determine if the incidence of concomitant autoimmunity differs between healthy and cutaneous lymphoma AYA and adult populations

Methods
- Retrospective chart review
- Validate with the SEER-18 database
- Compare our ANA positivity rate (≥ 1:80) with that of the National Health and Nutrition Examination Survey (NHANES)
Conclusions

- UH cohort closely reflected SEER
- Female CTCL peak of incidence occurred 1-2 decades before males
- Male CBCL peak of incidence occurred 1-2 decades before females
- Autoimmunity may be a driver in cutaneous lymphoma
- Future direction: For the pediatric and AYA patients, do certain genes confer a risk for developing cutaneous lymphoma?

Acknowledgements

- Foundation for Osteopathic Dermatology
- Dr. Kevin Cooper: PI
- Dr. Jeffrey Scott: SEER
- Dr. Gene Conte

Frontal Fibrosing Alopecia: A Cross-Sectional Survey

- Principal Investigator: Tanya Ermolovich, DO
- Sub Investigator’s: Nektarios Lountzis, MD, Huyenlan Dinh, DO, Veronica Rutt, DO, Jennifer Macfarlan, MPH

The FOD Young Investigator Research Grant/
The FOD Resident Research Grant

How Are The Foundation for Osteopathic Dermatology Research Grants Supported

“Pledges and Gifts to the Foundation” from

- AOCD Members
- AAD Members
- Business and Industry
- General Public
- Osteopathic Medical Schools
- Planned Giving
- Silent Auctions (Donations to the Auction)
The Future : My Opinion

- Let me start by “stating that what I am about to say is “My Opinion”.
- Some of the Foundation Officers my not agree with me regarding the issue I am going to discuss.
- However with the changes that are taking place in our Osteopathic Profession and the future ACGME collaboration I feel that all involved need to be informed.

The Dermatology Foundation
December 15, 2016

On or about December 15, 2016 as an AAD member I received a “Dear Colleague” letter from Michael D. Tharp, M.D. the President of The Dermatology Foundation. This letter included a “Pledge Response” urging me to become a DF member or to consider pledging to the “Leaders Society” of the DF. After considering his request regarding a donation I decided to write him a letter and ask one simple question.

A SIMPLE QUESTION

- Dear Dr. Tharp;
- Before I make my decision regarding a donation to The Dermatology Foundation can you please tell me in the last 20 years or even the last 10 years how many Osteopathic Dermatology Residents and or Researchers have ever received a Grant from The Dermatology Foundation?

“THERE WAS”
“NO”
“RESPONSE”
“TO MY LETTER”

DID I MAKE A DONATION

“NO”

THE FUTURE

For those who wish to support Osteopathic Dermatology Research in The Future Consider The Foundation for Osteopathic Dermatology
LEVELS OF SUPPORT

Pinnacle Table                      $ 25,000  
Ulbrich Circle                        $ 10,000  
Koprince Society                  $   1,000  
Leaders of Osteopathic Dermatology                         $     500  
Scholars Circle                       $     250  
Residents Forum                   $     100

The Foundation for Osteopathic Dermatology is one of the fastest growing Foundations in Osteopathic Medicine.

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Foundation for Osteopathic Dermatology
Grant Information and Application can be obtained by writing:
Foundation for Osteopathic Dermatology
P.O. Box 7525  
Kirksville, Missouri 63501-7525

Thank You
20 Tips To Running On Time*
*and maintaining your sanity

JOHN COPPOLA, DO  FAOCD, FAAD
ASSISTANT CLINICAL PROFESSOR - FSU COLLEGE OF MEDICINE
FACULTY - ORANGE PARK MEDICAL CENTER DERM RESIDENCY
PARKS DERMATOLOGY CENTER
ORMOND BEACH - PORT ORANGE - PALM COAST - ORANGE CITY

Why does running on time matter?
- Finishing your day 15 minutes late, 5 days a week for 48 weeks a year for 20 years:
  - 50 EXTRA full days (24 hours) spent at work
  - That’s 150 EXTRA work days (based on 8 hr workday)
- Finishing an hour behind?
  - 200 full days
  - That’s 600 EXTRA work days!

Why does running on time matter?
- Era of Health Grades
  - Online patient reviews are becoming a part of the future of reimbursements, contracts, reputations, and future career opportunities
- Bottom Line to your business
  - Over time pay
  - Office morale and cuts back on staff turnover
  - To have your lunch time to do what you need to
  - So you can get home to your hobbies, dogs, kids, or spouse!
  - (not necessarily in that order)
Our Practice
- 9 Providers
  - 2 MDs, 2 DOs
  - 4 PAs, 2 ARNPs
- 58 employees
- 5 Locations
- Aesthetic, Surgical, and Medical
- 800-900 phone calls on Mondays

Typical busy Florida practice
- 35-45 patients a day with 3-6 surgeries daily
- 25-35 biopsies daily
- 8am-4pm Mon-Thurs, 8am-12pm Fri
- 10 min slots for both new and established patients
- 5-12 new patients daily
- 80% of all 10 min slots are FSEs with all necessary biopsies, LN2 of Aks, discussion of 5FU treatments, or minor rashes done at that appt as well
- 30 min slots for surgical procedures
  - (occasionally adjusted to 20 or 40m)

My Patient Demographics
- Mostly 50-90 yo Fitzpatrick Type I-III
- Retired, middle class
- Very little pediatric derm
- Not a medicaid provider
- Weaned out cosmetic patients

Not every tip will apply to you
- Payor Mix
- Demographics
- Procedure Mix
- Employee vs Practice Owner
- May require fundamental change to your patient flow to implement
  - Some won't happen overnight – 7th year in practice, 5th as an owner implementing changes
  - Better title would be “Tips on running practice ergonomically”

Tip # 1
GET TO THE OFFICE 20 MIN EARLY
- Get through your mail
- Approve any refills you need
- Sign off on lab & path reports
- See your first patient 10 min early if they are there
  - You are now 10 min ahead!
**TIP # 2**
WRITE MORE GENERICS AND REFILLS

- Cuts down on interruptions during your day to you, but more importantly to your desk nurses
- Teach patients up front, give good pharmacy directions if you are concerned about overuse

**Tip # 2**
- Too many call backs on generic doxycycline
  - Rx: doxycycline hyclate 100mg BID x 5 days
  - Pharmacy note in EMA: monohydrate/tablets if less expensive
- Too many call backs on generic class 1 steroids
  - Rx: clob prop .05% ointment BID x 7 days
  - Pharmacy note in EMA: beta diprop .05%/Fluocinonide ointment/cream if less expensive
- Too many call backs on prior auths in general
- Make the patient call their insurance/pharmacy and figure out what they can be on

**TIP # 3**
SCHEDULED TIMES FOR DRUG REPS

- No one at the last hour before lunch or end of day
- No more than 3 a day in the office
- Utilize your mid levels for sample sign offs
- Be honest and upfront
  - Are you ever going to write their drug?
  - New info?
  - Regular prescriber?
- Be polite – they have a hard job and play an important role, but these rules are not hard to implement
Tip # 4
DON’T HAVE DRUG LUNCHES
&
BRING YOUR OWN LUNCH

Tip # 4
- Lunch and Learns for staff for specific reasons
- Buy lunch for your staff yourself on occasion
- Biweekly pot lucks
- Allows you to have the time for yourself to catch up or close charts

Tip # 5
STANDING ORDER IN PMS FOR COMPLICATED PATIENTS

Tip # 6
SURGERY BEFORE LUNCH AND LAST APPT OF DAY

Tip # 6
- If you need to squeeze in an emergency, this is when you do it
- If doing enough surgeries, make last 2 appts of day surgical

Tip # 7
DON’T WAIT FOR THE PAPERWORK TO BE COMPLETED TO BRING THE PATIENT BACK
TIP # 8
TAKE THE PAPERWORK AWAY IN THE EXAM ROOM

TIP # 9
MAKE YOUR INTAKE PAPERWORK MIRROR YOUR SOFTWARE

TIP # 10
DON’T CALL BACK BENIGNS/DON’T SEND BENIGN LETTERS

Tip # 10
- “No news is good news”
- MAs reiterate
- Still have to know? Use your patient portal
- FREE UP YOUR STAFF

TIP # 11
EVERYONE NEEDS A MICHELLE R.

Tip # 11
- Practice implementation & management of all regulatory programs
- Medicare E.H.R. Incentive program, PQRS, Quality Payment Program and Physician Compare
- Manage all of the regulatory submissions
- Analyzing and interpreting new and revised regulations, policies and procedures
- Maintain up-to-date knowledge and understanding of all MIPS Performance categories and their associated measure technical specifications
- Raise quality scores through ongoing medical record audits; identify issues and trends in data abstraction, diagnosis coding and clinical documentation;
- Provide quarterly reports assessing practices’ performance gaps and incentive payment readiness; create communication tools and workflow improvement strategies for helping clinical support staff and providers achieve incentive goals.
Tip # 11
- Bachelor Degree in Business Administration & Health Information Management
- Certified Medical Coder – RHIT, RHIA, CCS
- Extensive knowledge of healthcare industry, medical terminology, CPT & ICD9/10 coding, clinical documentation, billing and medical office ops, Medicare/commercial insurance guidelines
- Knowledge of managed care data reporting and analysis such as HEDIS, Medicare Risk Adjustment, quality of care studies and benchmarking
- Ability to proficiently read and interpret medical records.
- Understanding of clinical documentation guidelines.
- Extensive experience with Microsoft Excel, Access and/or SQL helpful.

Tip # 11
- You are not too small to have a Michelle R band together.

Tip # 12
- MANAGEMENT STAFF NEEDS TO BE TRAINED...OVER AND OVER
- Invest in your staff
  - Biannual retreats for managerial staff
  - ADAMS training
  - http://www.ada-m.org
  - Local university managerial and leadership seminars
  - Bimonthly MA meetings
  - Quarterly Provider and Department Head Meetings
  - Quarterly Share Holder Meetings
  - Lawyer and CPA

Tip # 13
- YOUR STAFF HAS REALLY GOOD IDEAS
TIP # 14
DON’T ROTATE YOUR MAs

Pay a little more if you need to for them to travel with you
Builds loyalty and synergy in your patient flow
Can anticipate your needs (and quirks) better

TIP # 15
CROSS TRAIN EVERYONE

TIP # 16
GET RID OF BAD APPLES AND DON’T HIRE MEDIOCRITY

Tip # 16
Harvard Business Review estimates that up to 80 percent of employee turnover is due to bad hiring decisions
Do working interviews and be able to not extend a job offer after 90 days

TIP # 17
BE IN THE MIDDLE OF EVERYTHING & DON’T WALK FAR
Tip # 18

- Sunday morning path sign outs
- Refills in a flash
- Path logs maintained/logged out with a fraction of the work involved previously
- Using the best software for your practice?
- Allergan Practice Consultant
- Using the newest updates of EMA
  - Photos now linked to paths/Protocols
  - Email reminders/text reminders
“I can’t take a day off for that”

- Pick up just one tip that saves you 30 seconds in the room.
- 40 patients a day / 5 days a week for 1 year
  - 9 full workdays worth of time
  - If you are cheap, you can even write off the trip

Tip # 20

TIP # 20
DON’T SEE PATIENTS THAT ARE LATE

Tip # 20

- 10 minute window
- Patients that habitually miss appts are deferred to mid levels or dismissed from practice
- Hard to implement until you can run on time yourself
- “Dr C runs on time” - at points of contact

• Once you do, it’s a game changer for your schedule and your reputation
  - Pts will come to you just because you run on time
  - For every one patient that gets upset over this in my office, there are 30 that actually thank me and refer patients because of it.
A Decade of Lessons Learned the Hard Way
Michelle W Foley, DO, FAOCD

Background
- No disclosures
- Narrative through in-office “teachable moments”
- Learned the most when things don’t go as expected
- No one died or got sued in the making of this presentation
- Practice in a predominately retirement community with a practice that is 65 percent general and surgical derm, 35 percent cosmetics

Case 1
- 45 y/o female (CPA) with weeks hx of intense itching. Many visible excoriations. Only takes occasional Advil for headache.
- Seen by PA for this. PA does full H and P and due recent travel to Arizona, scabies prep that is negative. Bx done that day
- Pt sent home with topical steroid
- Bx showed acantholytic dermatosis, no evidence of scabies or inflammatory cells

Case 1
- Pt treated for Grovers with some mild improvement.
- RTC to see me due to failure to improve after 5 weeks
- Still with predominate excoriations on arms, legs, and back and few on abdomen. Scattered urticarial-like lesions noted especially on her thighs
- Biopsy done that day

Lesson 1
- Oh boy - not what I was expecting
- Started on prednisone
- Labs ordered
- Elevated glucose and neuts, ANA neg, RF neg
- Hep panel, Complement, Cryoglobulins all pending
- Referral to Mayo Clinic - Jacksonville
- Diagnosis:....................

Lesson 1
- Go back to basics - take your own history
- Form an ORIGINAL differential diagnosis
- Don’t get lost in the details
- Information bias and overload is a REAL thing
Case 2

• It's May in Florida
• Pt is in his garden daily
• Does NOT recall injury but spots have been present for 6 weeks
• Neighbor is a retired dermatologist from NY and made him come in
• Punch biopsy taken and tissue culture sent

Case 2

• Punch biopsy: Suppurative and granulomatous dermatitis suspicious for infection. All stains negative.
• Culture: (isolated from enrichment broth only) Staph aureus
• Quest Labs contacted
• Pt c/o new lesions
• Empiricitraconazole started suspecting sporotrichosis

Case 2

• Pt is not improving after 4 weeks of therapy and, in fact, has new lesions.
• Dose increased to 200 mg bid and second tissue culture taken.

Case 2

• Quest: (isolated from enrichment broth only) Staph aureus
• NO WAY !!!
• Quest manager: “I’m sorry for the inconvenience”
• Call ID friend for help
• Quant gold is positive

Case 2

• 3rd tissue sample for culture taken
• Pt aware I am using a possible “out of network” lab for culture this time and is agreeable
• Hospital lab contacted and currier picks up tissue

Finally!!

Correct diagnosis made in October
Lesson 2

- Be persistent
- Be willing to discuss why a higher cost or out of network provider may be needed. (this is not always easy given time constraints and patients budgets)
- This may be the case with labs, pathologists, surgeons, consultants
- Phone a friend
- Quantiferon TB Gold can be positive in non-TB cases due to similar peptide antigens located on region of difference(RD1)

Case 3 and 4

- 77 y/o male with extensive sun damage and hx XRT to head and neck for throat cancer. Tough personality
- Active tennis player
- Hx of “laser” treatment to large “sun spot” on top of head
- Old records obtained
- Multiple sessions of IPL to treat unwanted spots on face and scalp, many of which were returning due to daily outdoor tennis etc.

Case 3

- MMIS in all scout biopsies
- Pt refused Mohs at Mayo Clinic
- Underwent wide local excision x 3 to clear all margins. No invasive component identified. Large grafts placed
- Remains clear today

Case 4

- 51 y/o Caucasian female
- Biopsy proven eruptive-type granuloma annulare
- Poor response to topical steroid, but excellent response to 21 day prednisone taper
- Clear for over 10 months
- Called for a refill on oral prednisone when new flares occurred.
- I wanted patient to be seen. Could not come in because of conflicting schedules but crying on phone because she can’t sleep secondary to the itching.
- Refilled her script and saw pt 6 weeks later
- Pt had just undergone hip surgery for aseptic necrosis

Lesson 3

- You are the expert in your office. Act like it!!
- Patients want what is easy, painless and convenient.
- They can’t be bothered with rules, guidelines or protocol
- This many times conflicts with our duty as physicians
- Stand up for what you know or believe is right
Lesson 4

- Each patient is a unique individual
- Varying degrees of health and co-morbidities
- Forced to think outside the box and sometimes vary from classic standard of care

The lower extremity SCC

- Extremely common in my patient population
- Very often pathergy related
- Many recurrent cases after EDC and or surgery

Lesson 4

- Definitive treatment is not always possible
- Take the entire patient into consideration
  - Age, Immunosuppression, general health, wound care compliance
  - Recognize pathergy when it’s happening, inform other doctors about it
    - JAAD 2009 Nov 61(5):892-7
  - First, do no harm

Cosmetic Lessons

- Educate your cosmetic patients ad nauseam
- ALWAYS - photos and consents
- Document, Document, Document
  - I do mention “off label use”
  - Unpredicted outcomes will happen
  - Know when to say “NO”
  - Be confident and hold their hand

Education

- Have staff that are specifically trained to deal with cosmetic patients (consults, scheduling, follow-up questions)
- Review patient photos or consults prior to scheduling procedures
- Be honest with patients and NEVER promise and outcome

Photos and Consent

- Most cosmetic suits do NOT end in judgement against the doctor
- Informed consent does not prevent lawsuits
- Photos (before and afters) are life-savers
- Most patients that feel disappointed with outcome are more positive after reviewing their photos
- Sometimes its not about what they say its about
Document

- Make note of bruises and expected swelling. Pt will call.
- If patients ask for new Botox pattern, I document that this was at their request
  - Frozen foreheads, heavy brows

Off-label Use

- My patient population is older
- Effects and risks may be “unknown”
- Outcome may be less predictable
- Go slow and bring the patient back
- Rome wasn’t built in a day

Unpredicted Outcome

- The Bio-film
- Erythema and swelling 6 weeks after 66 y/o female had HA filler for ML.
- Dental work 4 days before swelling started
- Responded well to Doxy and low dose prednisone.
- FISH
- Consider asking about upcoming or planned dental procedures

To Refund or Not Refund?

- Received a letter from a patient in 2016
  - 3 pages hand-written with recent photos
  - Pt last seen by me in 2011 (5 yrs and 8 months prior) for filler
    - (Radiesse and Juvederm)
  - Pt was requesting all money be refunded with interest or she would be seeking representation
  - Contacted our attorney
    - Ignore urge to be right
    - Do not engage
    - Did NOT refund

Practice Lessons

- You can’t prepare for everything, but do your best
- Death via Medicare
- Natural disasters (Hurricane Matthew)
- Line of credit in place for unexpected times

Life Lesson

- Freeze your credit!! Do it now, do it today!!
- Bureau of Justice Statistics 17.6 million Americans were victims of identity theft in 2014
- 3 out of 4 partners in my practice have had their identity stolen
- As a physician, your SS# is everywhere. Every agency, insurance company, governing body and your staff may have access to it.
  - HOURS of time spent on the phone
Urticaria: Diagnostic and Treatment Considerations

Adam Friedman, MD, FAAD
Associate Professor of Dermatology
Residency Program Director
Director of Translational Research

Urticaria: The Basics

- Affects 20% of population
- Occurs across the age spectrum
- Sometimes possible to identify a trigger such as food, drug, insect sting or infection
- More than 2/3 of cases are self-limiting

Characteristics: The Basics

- Pruritic
  - Burning
- Erythematous
  - Often exhibit central pallor
- Oval, round or irregular shape or plaques
- Plaques “move” to different locations over minutes to hours
  - < 24 hours
- Typically leaves no PIPA/scarring
  - Other than from scratching

Pathophysiology: What we actually know

- Reaction mediated by activated mast cells and basophils in superficial dermis
  - When activated release histamine --> vasodilators
Histamine and Pruritus: A Simple Relationship

- Histamine receptors located on C-fiber neurons
- Histamine binding triggers an itch impulse

Histamine and Pruritus: A bit more complicated...

Histamine and Pruritus: So where are we?

Histamine and Pruritus: Do you have the right diagnosis?

Patients call everything “hives”

Histamine and Pruritus: Diagnosis and Work up of Urticaria
**Differential Diagnosis**

- Insect Bites (papular urticaria)
- Atopic dermatitis
- Erythema multiforme
- Bullous pemphigoid
- Urticaria pigmentosa
- Vasculitis
- SLE
- Morbilliform drug eruptions
- PUPPP
- Erysipelas
- Cellulitis
- Contact dermatitis
- Dermatitis herpetiformis
- Photodermatitis
- Familial cold autoinflammatory syndrome

**Pruritus: Itch without Rash**

- Xerosis
- Uremia
- Cholestasis
- Malignancy
- Non-Hodgkins Lymphoma
- Polycythemia vera
- Thyrotoxicosis
- Multiple sclerosis (dysesthesias)
- Iron Deficiency Anemia
- Diabetes (autonomic dysfunction)
- Medications
- Psychiatric illness

**Classification**

- Acute versus Chronic Urticaria
  - Acute episodes < 6 weeks
    - More likely to have an identifiable trigger
  - Chronic episodes last > 6 weeks
    - “Chronic spontaneous vs inducible”
    - Less likely to have an identifiable trigger
    - ~70% cases have unknown etiology
    - Longer duration = lower chance of identifying cause
Acute Urticaria: Common Causes

- Overall, identify cause in acute urticaria 20% - 90% cases
- Acute Urticaria - “infection, medication, food”
  - Foods/food products most commonly milk, egg, peanut, wheat and soy in kids
  - Tree nuts, peanuts and shellfish in adults
  - Yellow food dye annatto
  - Red food dye carmine
  - Contact with raw fruits or vegetables, animal saliva, certain detergents or perfumes

Common Causes (cont)

- Viral or bacterial infection especially in children
  - Mycoplasma
  - Adenovirus, enterovirus, rotavirus, respiratory syncytial virus, Epstein-Barr virus and CMV
- Parasitic infections
  - Blastocystis hominis, Plasmodium falciparum and Anisakis simplex
- Medications (especially antibiotics)
  - Stinging insects
    - Bees, wasps, hornets, imported fire ants
- Latex products
  - Cross reacts with passion fruit, banana, avocado, chestnut, kiwi

And yes....

Urticaria After Ingestion of Alcoholic Beverages

F Rebeiro, N Sousa, J Carrapatosa, A Sogere Luís
Immunology Department, Coimbra University Hospital, Coimbra, Portugal

Non-immunologic, Direct Mast Cell Activation

- “PROMS”
  - Polymyxin B
  - Radiocontrast media
  - Opiates
    - Codeine, morphine, meperidine
  - Muscle relaxants
  - Salicylates
- Other
  - NSAIDS (kids)
  - Vancomycin (remember “Red Man Syndrome”)
  - Dextran (in IVs and eye drops)
  - Neuromuscular blocking agents (D-tubocurarine)
  - Stinging nettle
  - Sympathomimetics (amphetamine, ephedrine, phenylephrine)
  - Tomatoes and strawberries

Contact Urticaria

- 30-60mins after exposure
- Nonimmunologic
  - MC, no prior sensitization
  - Plants/nettles, animals/caterpillars, jellyfish, meds/DMSO, bacitracin
  - Others cobalt, chloride, benzoic acid, cinnamic aldehyde, cinnamic acid and sorbic acid
- Immunologic- IgE mediated rxn
  - Latex rubber, bacitracin, potato, apple, henna
- Dx: good hx, contactant test, pr crab test for food, RAST for immunologic contact urticaria

Chronic Urticaria: Physical aka Inducible Urticarias

- Reproducible by environmental factors
  - Physical stimuli
- Subtype of Chronic Urticaria: 20-30%
- Most frequently in young adults
- **DISTINGUISHING FEATURE:** Attacks are brief, lasting only 30-60 mins versus few hours to days for typical urticaria
  - Exception: pressure urticaria, swelling lasts hours
- Episodic and often limited to areas of inciting stimulus
- Unresponsive to corticosteroids
- Less likely to spontaneously resolved
Examples of Physical Urticaria

- Dermatographism*
- Cholinergic
- Heat
- Exercise-induced
- Cold
- Aquagenic
- Solar Urticaria
- Vibratory

Features of Physical Urticaria

<table>
<thead>
<tr>
<th>Type</th>
<th>Age (yrs)</th>
<th>Clinical Features</th>
<th>Angio-</th>
<th>Diagnostic Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatographism</td>
<td>20-50</td>
<td>Linear lesions</td>
<td>No</td>
<td>Light stroking of skin; + transfer factor</td>
</tr>
<tr>
<td>Cold (primary vs. secondary)</td>
<td>10-60</td>
<td>Itchy, pale lesions (5% with cryos)</td>
<td>Yes</td>
<td>3-10 minute ice-cube test; + transfer factor</td>
</tr>
<tr>
<td>Cholinergic (heat bumps)</td>
<td>10-50</td>
<td>Itchy, monomorphic pale or pink lesions</td>
<td>Yes</td>
<td>Exercise or hot shower; + transfer factor</td>
</tr>
<tr>
<td>Pressure</td>
<td>20-50</td>
<td>Large painful or itchy lesions</td>
<td>No</td>
<td>Dermographometer; application of pressure to skin</td>
</tr>
<tr>
<td>Solar</td>
<td>20-50</td>
<td>Itchy pale or red swelling</td>
<td>Yes</td>
<td>Irradiation by a solar simulator; + transfer factor</td>
</tr>
</tbody>
</table>
Dermatographism Misnomers

- "Red Dermographism"
  - Response to rubbing, not stroking, the skin
- "White Dermographism"
  - Blanching response seen in patients with atopic dermatitis
  - Not a form of urticaria
- "Black Dermatographism"
  - Black line associated with metal contact

Black Dermatographism

Natural History of Chronic Urticaria

- Chronic Urticaria:
  - 50% are free of lesions within 1 year
  - 20% continue to experience episodes for more than 10 years (not necessarily continuous)

The natural history of chronic urticaria in childhood:
A prospective study

- 92 children 4 to 15 years of age with CU
  - Median duration of 4.3 years (range 2.5-5.8 years).
  - Remission rates at 1, 3, and 5 years after the onset of CU symptoms were 18.5%, 54%, and 67.7%

Urticaria: The Evaluation

1. Onset (e.g. timing of symptoms with any change in medication or other exposures).
2. Frequency, duration, severity, and localization of wheals and itching.
3. Dependence of symptoms on the time of day, day of the week, season, menstrual cycle, or other pattern.
4. Known precipitating factors of urticaria (e.g. physical stimuli, exertion, stress, food, medications).
5. Relation of Urticaria to occupation and leisure activities.
6. Associated angioedema, systemic manifestations (headache, joint pain, gastrointestinal symptoms, etc.)
7. Known allergies, intolerances, infections, systemic illnesses or other possible causes.
8. Family history of urticaria and atopy.
11. General physical examination.
Urticaria Diagnostic Evaluation

- History & Physical Exam Short Cut
  - Diary
    - Any unusual exposures immediately prior to the episode
  - Does the patient have pictures?
    - Iphone, galaxy, etc
  - Family hx
    - HLA-DR4, HLA-DRB4 53, HLA-DQ8
  - Provocative tests for physical causes

Provocative Testing

<table>
<thead>
<tr>
<th>Physical Urticaria</th>
<th>Testing Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold</td>
<td>Ice cube test</td>
</tr>
<tr>
<td>Localized heat</td>
<td>Test tube of water at 44C</td>
</tr>
<tr>
<td>Cholinergic</td>
<td>Exercise for 15-20 min or leg immersion in 44C bath</td>
</tr>
<tr>
<td>Delayed pressure**</td>
<td>Sand bag test: 15 lb weight for 15 min</td>
</tr>
<tr>
<td>Dermatographism</td>
<td>Stroking the skin firmly</td>
</tr>
<tr>
<td>Solar</td>
<td>Specific wavelength of light exposure</td>
</tr>
<tr>
<td>Aquagenic</td>
<td>Water compress</td>
</tr>
<tr>
<td>Vibratory</td>
<td>Vortex for 4 min</td>
</tr>
</tbody>
</table>

- Laboratory tests:
  - No routine labs
  - ** New European guidelines for chronic spontaneous urticaria: ESR/CRP and blood differential
  - Other potential labs: LFTs, HepB, ANA, Stool, U/A, Thyroid function, anti-thyroid antibodies
  - Complements (if + angioedema)
    - Screen with C3 and C4 levels → C4 low, C3 normal in angioedema
    - C1q level low in acquired, but normal in hereditary
  - Skin tests
    - Allergy testing if specific trigger can be implicated

Skin biopsy?

- Generally, not helpful

Indications:
- Lesions lasting more than 24 to 48 hours
- Atypical?
- Scarring
- Purpura
- Suspicion of Urticaria pigmentosa
- Refractoriness to therapy
Therapeutic Approach: An Overview

- Avoiding triggers
  - Known antigens
  - Potentiating factors
    - Alcohol, narcotics, non-steroidal anti-inflammatory drugs/asa, "pseudoallergens"
    - Loose fitting clothing, temperature control, photoprotection
  - Underlying conditions: Thyroid, H.pylori, dental abscess

- Inhibiting mast cell mediators/release
  - H1 antihistamines
    - Prefer 2nd gen, non-sedating, long-acting antihistamines
    - Combination of therapies
  - Treating the inflammatory response
    - Ex: Omalizumab, cyclosporine, dapsone, methotrexate, colchicine, mycofenolate mofetil, hydroxychloroquine

Table 1. Key concepts in urticaria management in children

- Avoidance elimination of underlying causes and/or eliciting triggers is important.
- Second-generation H1-antihistamines are the mainstay of pharmacological treatment aimed at providing symptom relief
  - Up-dosing has not been validated in children
  - First-generation H1-antihistamines should be avoided, mostly due to relevant side-effects
  - Difficult cases may require other therapeutic interventions, the risk-benefit ratios being carefully analysed as there is hardly any evidence supporting it in children.
  - Corticosteroids should be avoided whenever possible and strictly used for short periods only (3-7 days), given the unacceptable side-effects from long-term use.

Urticaria in Children

1st Line: H1 Antihistamines

- H1 antihistamines
  - First generation:
    - Diphenhydramine, Chlorpheniramine, Hydroxyzine
    - Hydroxyzine only one specifically contraindicated in pregnancy
  - PEDS considerations
  - Second generation (non-sedating):
    - Cetirizine, Loratadine
  - Second generation derivatives:
    - Desloratadine, Levocetirizine, Fexofenadine
  - Go with non-sedating
    - NO Cetirizine and Levocetirizine in severe renal impairment (CC <10ml/min)
    - Loratadine and Desloratadine with caution

H1 Antihistamines in Peds

GO UP TO 4-FOLD DOSE

Pregnancy & lactation

- No H1 antihistamines are class A
  - Loratadine and cetirizine are B
  - Diphenhydramine long track record of safety
  - Tx for nausea!
- Current data indicates that administration during lactation has no detrimental effect on breast-fed infant
1st Line: H2 Histamine Antagonists

- Basophils have H2 receptors that mediate histamine release
- Safe toxicity profile
  - Paucity of clinical data
- Cimetidine, Ranitidine, Famotidine
- Famotidine ~ diphenhydramine
  - Twenty-five patients in an emergency department setting.
- Off-label indication
- Dosing
  - Ranitidine: 1-2 mg/kg q 12h
  - Cimetidine: 20-40 mg/kg/d split q6h

42 adult subjects

- High-dose (4000 IU) vs low-dose (600 IU) x daily for 12 weeks.
  - All triple drug therapy of ranitidine, montelukast and a high dose of cetirizine.
  - 33% reduction in total urticaria severity score (USS) at 1 week post-enrollment in both treatment groups
  - ~40% reduction in total USS in subjects treated with high-dose

2nd line: Doxepin

- Very potent H-1 and H-2 antihistaminic properties
- Small studies: N = 16-50 pts
- Dosing: 10-25 mg BID to TID
  - Largest study: 10 mg TID vs diphenhydramine 25 mg TID
  - 43% vs 5% total and 74% vs 10% partial clearance
- AE: sedation, xerostomia
- Not in pts with recent MI or hepatic dysfunction
- Start 10 mg qhs and increase slowly

2nd line: Leukotriene Receptor Antagonists

- Leukotrienes are signaling molecules from the arachadonic acid inflammatory pathway
  - Receptors on mast cells
- Dosing is daily; low AE rate
  - Response 30 to 50 percent
- All the same?
  - Most not effective as monotherapy
  - Zileuton 600 mg four times daily for one week > Zafirlukast 20 mg twice daily for one week
  - Synergy with H1 antihistamines
    - Loratidine 5mg + Montelukast 10 mg daily

2nd line: Nifedipine

- Mast cell stabilizing properties
- Doses range:
  - 5 to 10 mg three times daily
  - 30-60 mg daily in extended-release form
  - Can titrate up 5 mg based on clinical response and appearance of side effects.
- Study example: 10 patients; Nifedipine 10 mg three times daily
  - 7/10 patients reports + improvement
- Dizziness and reflex tachycardia
- Clinical pearl: Grapefruit juice increases serum levels of nifedipine
**GW 3rd line: Omalizubab**

- Humanized monoclonal antibody of IgG1k type that binds free IgE in the blood
- 150-375 mg SQ q2-4 weeks
- Initial dosing is based on pre-treatment serum IgE levels and weight for maximum of 150 mg per injection site
  - Multiple injections may be required for each administration.
- The most significant AE is anaphylaxis*.
  - Blackbox warning
  - Administration in a medical facility, followed by patient observation for a period of time.
  - ~two hours after initial injection and 30 minutes for subsequent injections.
  - Less likely: serum sickness-like reaction

---

**GW Dosing schedule**

- **MOA unknown**
- May work by:
  - Down-regulating IgE receptors on mast cells
  - Rapid reduction of plasma IgE might down-regulate mast cells independent of IgE receptor density
  - Prevention of FcεRI dependent-secretion of mast cell cytokines by unknown method

---

**GW Feeling lazy?**

- “After reconstituting and swirling for 1 minute, gently swirl the vial for 5 to 10 seconds approximately every 5 minutes in order to dissolve any remaining solids. The lyophilized product takes 15 to 20 minutes to dissolve. If it takes longer than 20 minutes to dissolve completely, gently swirl the vial for 5 to 10 seconds approximately every 5 minutes until there are no visible gel-like particles in the solution. Do not use if the contents of the vial do not dissolve completely by 40 minutes.”

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**GW Original Article**

**Omalizumab for the Treatment of Chronic Idiopathic or Spontaneous Urticaria**

- Phase 3, multicenter, randomized, double-blind study,
  - Moderate-to-severe chronic idiopathic urticaria recalcitrant to H1 blockers
- 323 patients; 3 SQ injections (4 weeks apart)
  - Doses of 75 mg, 150 mg, or 300 mg or placebo,
  - 16-week observation symptomatic
- Reduction of sx: −8.1±6.4 in the 150-mg group (P=0.001), and −9.8±6.0 in the 300-mg group (P<0.001)

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**GW Complicated**

- For patients with IgE levels between 30 and 700 IU/mL and body weight between 66 and 130 lb.

http://www.xolair.com/hcp/determining-the-dose.html
3rd Line: Cyclosporin A

- 3-5mg/kg/day benefit about 2/3 of patients with antihistamine recalcitrant CU
- Example of studies:
  - Cyclosporin 5mg/kg/day for 8 weeks, then 4mg/kg/day for 8 weeks
  - 82.5% controlled week 1
  - 50% relapse rate by month 9 but short lived/easily controlled
  - Double-blind RCT; N = 99
  - 82.5% controlled week 1
  - 50% relapse rate by month 9 but short lived/easily controlled
- Long term cyclosporin
  - 3 mg/kg for 3 months, 1 to 2 mg/kg for 8 to 14 months, then 1 to 1.5 mg/kg for 60 to 120 months
  - 25% resolution, 22.5% improvement
  - No malignancy or abnormal renal function; 16% drop out due to AE

3rd line: Dapsone

- Inhibits PMN chemotaxis/ Anti-MPO
- Dapsone 25mg daily + cetirizine 10mg daily
  - 9 urticaria controlled within 3 months and maintained for 1 further month 2 improved with dapsone 50mg daily no flare when dapsone was discontinued
  - Dapsone 50 mg + desloratadine 10 mg
  - Dapsone + desloratadine > desloratadine (p<0.001)
  - Three-months follow-up
  - 9/38 complete response, 27/38 partial response, 2/38 no response
- Titrated slowly: check g6pd, CBC/ retic

3rd line: Colchicine

- Inhibits PMN chemotaxis
- Biopsy specimens with neutrophils and eosinophils
- Study example:
  - N=7
  - Prednisone 20 to 40 mg daily for 5 days, H1 antihistamines plus colchicine 0.6 mg, twice daily
  - 5/6 controlled

3rd Line: Methotrexate

- More effective in patients with functional auto-antibodies to FcεRIα and/or IgE?
- Study example:
  - N=10
  - Methotrexate 5 to 15 mg weekly (cumulative dose 15 to 60 mg)
    - 1 clear (no symptoms, off glucocorticoids, on antihistamines)
    - 4 considerable benefit (improvement with glucocorticoid reduction)
    - 3 some benefit (fewer wheals but no glucocorticoid reduction)
    - 2 no benefit
  - Relapse within weeks of d/c
- Clinical pearls: X Trimethoprim, the sulfonamides, and dapsone
  - Tetracyclines increase serum [].
- AE: Bone marrow suppression, teratogenicity, hepatic toxicity, gastrointestinal intolerance, interstitial pneumonitis, pulmonary fibrosis

3rd Line: Mycophenolate Mofetil

- ? inhibiting the production of autoantibodies to the high-affinity IgE receptor and/or IgE
- Studies:
  - N=9; patients on prednisone and antihistamines
    - 1 gm BID x 12 weeks
    - By week 4 prednisone decreased
    - All patients off prednisone by week 12
    - No rebound after 6 months
  - Retrospective chart review: n=19
    - Autoimmune and idiopathic CU
    - Dose: 1000 to 6000 mg divided twice daily
    - Improved both types of CU (91% vs. 88%)
    - Complete control higher in the autoimmune group (70% vs. 41%)
- AE: GI and hematologic.

3rd line: Sulfasalazine

- Efficacy and safety of sulfasalazine in patients with chronic idiopathic urticaria
  - Retrospective chart review 39 patients with sulfasalazine-treated CU
    - Initiated at a dosage of 500 mg/d and increased by 500 mg each week based on clinical tolerance/labs.
    - Titrated up weekly until a dose of 2,000 mg/d was achieved
    - Weekly labs until stable on 2g/d (CBC, LFTs)
    - 83.9% improvement in symptoms within the first 3 months,
    - 51.6% of patients asymptomatic within the first 6 months of starting sulfasalazine
    - Serious AE leading to drug discontinuation occurred in 6.5% of patients
      - Drug-induced leukopenia; one with rhabdomyolysis.
      - AE rates ~ cyclosporin and omalizumab (high dose)
• Unclear mechanism - decrease the release of histamine from either mast cells and/or basophils
• Example of Studies (small; 14-88 patients)
  – 3 treatments weekly (median number 22)
    • 9 week
    • 30% resolved, 20% moderate improvement, 29% marked improvement
  – 3 treatments weekly (median number 31.4)
    • Clearance in 10 patients (45%), marked improvement in five (22%), and moderate improvement in seven (31%) patients
    • Relapses controlled with antihistamines

Practice parameter

The diagnosis and management of acute and chronic urticaria: 2014 update

Chief Editors: Jonathan A. Fertigstein, MD, David M. Long, MD, and David A. Khan, MD

STEP 1
  • Monotherapy with second generation antihistamine
  • Avoidance of triggers (e.g., NSAIDs) and relevant physical factors if physical urticaria/angioedema syndrome is present.

STEP 2
  One or more of the following:
  • Dose advancement of 2nd generation antihistamine used in Step 1
  • Add another second generation antihistamine
  • Add H2-antagonist
  • Add leukotriene receptor antagonist
  • Add 1st generation antihistamine to be taken at bedtime

STEP 3
  Dose advancement of potent antihistamine (e.g., hydroxyzine or doxepin) as tolerated
Not so simple - Treatment of Physical Urticarias

- **Dermatographism**: nifedipine, broad-band UVB phototherapy, narrow-band UVB phototherapy, PUVA phototherapy, omalizumab
- **Delayed-pressure urticaria**: NSAIDs, montelukast, colchicine, dapsone, sulfasalazine, systemic glucocorticoids, danazol, stanozolol, chloroquine, tranexamic acid, intravenous immunoglobulin, etanercept, infliximab, omalizumab
- **Cold urticaria**: zafirlukast, montelukast, cyclosporin, mizolastine, stanozolol, omalizumab, anakinra
- **Cholinergic urticaria**: danazol, stanozolol, scopolamine butylbromide, omalizumab
- **Solar urticaria**: β-carotene, hydroxychloroquine, cyclosporin, phasmapheresis, photopheresis, broad-band UVB phototherapy, ultraviolet A phototherapy, PUVA phototherapy, intravenous immunoglobulin, omalizumab
- **Aquagenic urticaria**: stanozolol, PUVA phototherapy
- **Adrenergic urticaria**: propranolol

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In Short…

- It’s all in the history…sometimes
  - Should guide w/u
- Climb the (therapeutic) ladder
  - High ceiling on antihistamines
  - Combo is King

"I must say, Mr. Jennings, you have the worst case of Hives I’ve ever seen."
A Play Yard of Dermatology Tips
2017 AOCD Spring Current Concepts in Dermatology Meeting
March 29 – April 1, 2017
Atlanta, Georgia

Albert E. “Bo” Rivera, DO
Southeastern Skin Cancer & Dermatology
Madison, Alabama

Disclosures
- No financial conflicts
- Published WAR Score that is to be discussed
- Credit is given when able to those I’ve learned from (when slides obtained, it is selective and out of context from original author lecture)
- Relative rookie, not a certified medical or business expert by any means – this works for me
- Currently looking to hire a physician

Objectives
1. Discuss an accumulated collection of business and customer service tips
2. Discuss an accumulated collection of medical and surgical dermatology tips
3. Review and discuss the WAR (Webb and Rivera) Score

Have a Mission Statement
- What guides you?

Always treat others as you would have them treat you. The mission of Southeastern Skin Cancer & Dermatology will constantly be guided by these words. Our practice is created for and focused on those with skin concerns at any age, with specific expertise for individuals with cancers of the skin. For our family of patients, we continually strive to provide optimal care and establish relationships that will surpass those expected from the typical medical provider. Your care will always be offered in a current yet established, detailed, efficient and respectful manner, always including the human touch. In addition, tremendous importance is placed on integrity and rapport with other healthcare providers, medical business associates and the community which we service. Regardless of the condition, venue or nature of interaction, our efforts are not complete until you are completely satisfied.
Ask your staff: What makes us special or different? - Do you know? Do they know?

Office Tips – Patient Satisfaction
Credit: Charles N. Ellis, MD

Patient satisfaction
“Research indicates that better patient care experiences are associated with higher levels of adherence to recommended prevention and treatment processes, and better clinical outcomes....”
and higher patient QoL

Office Tips – Patient Satisfaction
Credit: Charles N. Ellis, MD

Patient Perspective of Quality
- Timeliness
- Attitudes of all staff
- Information & explanations
- Body language, physical touch
- Sights, sounds, smells
- Sociability, supplies, smooth operations
- evidence shows that all these factors affect patient's experience of care.

Office Tips – Hiring
Credit: Charles N. Ellis, MD

Staff critical to success
- Hire the right people!
- Can't emphasize this point enough
- Interview process includes our philosophy and Gold Service Card
- Never, EVER "SETTLE" when hiring
- Better an open spot than wrong person
- You can teach skills; you can't teach attitude, compassion, smiling

Office Tips – Customer Service
Presentation by local Chick-fil-A owner

Welcoming from the Start
- Open Counter
  - elevated to protect privacy (info out of sight)
- No windows or barrier
- Always acknowledge
  - as entering OR
  - as approach counter
Office “Feel” and Function
- Open spaces, not claustrophobic
  - Does create “wasted space” per some
    - Depends on local market and willingness
  - Not “wasted” if makes for better day and life
- Consistent, duplicated rooms
  - Exam table
  - Cabinets
  - Supplies
  - Consider flow from patient perspective
    - door to door

Patient Interaction
- Personal greeting
  - avoid “JONES!”
- Engage the patient
- Do you or the patient want to be here?
- Care about plan and pt understanding
  - one size doesn’t fit all

Positive Attitude
- Recommend find lecture by Disney executives
  - “always in character when on stage”
  - leave problems at door
- Chick-fil-A
  - “my pleasure”
- Regularly motivate and appreciate
  - “thank you” and mean it
  - group outings
  - benefits

Words Matter to Patients
- “Thank you” for...
  - seeing us, trusting us, your time, your effort
- “I’m sorry” that....
  - you’re not better, it was difficult, this isn’t as expected
- “We”
  - pts don’t want to disappoint you, create team effort
- “I don’t know”, “I’m not sure”
- “Lobby”
  - people WAIT in a waiting room

Our Requirements
- Efficient
  - “achieving maximum productivity with minimum wasted effort or expense”
  - “working in a well-organized and competent way”
  - “preventing the wasteful use of a particular resource”
- Consistent
  - “acting or done in the same way over time, especially so as to be fair or accurate”
  - “unchanging in nature, standard, or effect over time”
- Timely
  - avoid overbooking (two day prior reminder)
  - be honest with yourself

Get Reviews
- People will talk
  - be proactive (negative more motivated than positive)
- Choose positive/favorable patients
- Overwhelm the unrepresentative minority
- The reality is already here
  - casually online and government requirements
Office Tips – Patient Satisfaction

Mentioned by Dr. Ellis that we already do also:
- Say “thank you” to staff
  - And patients for using meds, teamwork, choosing you, etc
- No clock in reception area
- You are always “on stage” (Disney)
- Sit down (7 minute increased estimate by pt)
- Don’t interrupt
  - exam while pt talking

Business and Billing

How we do it: Passing MIPS

- Pathology
  - we call if abnormal, portal for normal
- Online registration (most) required
  - create login
  - have patient test it or enter info

Flap vs Primary Closure

- Primary Closure
  - Primary Closure is defined as closure of all tissue levels during the original surgery, regardless of the presence of wires, wicks, drains, or other devices or objects extruding through the incision. This category includes surgeries where the skin is closed by some means, including incisions that are described as being “loosely closed” at the skin level. Thus, if any portion of the incision is closed at the skin level, by any manner, a designation of primary closure should be assigned to the surgery (CDC)

- Patients now accepting of portal results
  - especially normal
  - Many like personal for abnormal results
Flap vs Primary Closure

- Adjacent Tissue Transfer (Flap)
  - Skin taken from an adjacent area and moved to fill the surgical defect. A flap is transferred with an intact blood supply and remains connected to its origin. (NZDerm)
  - At least three sides must be removed from original blood supply (maybe argue two sides plus a tip if rotation)

* BR supplemental definition

Primary Closure

Flap vs Primary Closure

- Primary closures are NOT to be billed as flaps
- Regardless of undermining area, layers, depth, tension, special sutures, etc
- Pulling straight or curved edges together is a primary closure only
- Fraudulent or ignorant billing puts you at risk
- Don't do it

Flaps (adjacent tissue transfer)

CPT 99024

- Postoperative follow-up visit, normally included in the surgical package, to indicate that an evaluation and management service was performed during a postoperative period for a reason(s) related to the original procedure.
- Applies to surgeries with 90 and 10 day global periods.
- Indicates that a required postoperative visit has been provided.
- Zero dollar amount associated with 99024. Payment has already been received through the single global surgical payment.

Credit: URMC Compliance Office
Billing denials
- Challenge or resubmit if you know you are correct
  - Document accurately
- More effort on purpose
  - Payers want to recoup $.
- My rookie experience
  - Accepting every denial very costly.

Patient Compliance

Compliance
- We all want the best for the patient
- Correct diagnosis and treatment
- Patient must follow instructions

Monitoring Compliance Electronically
Credit: Steven Feldman, MD, PhD

Pearl #3
Patients lie
Credit: Steven Feldman, MD, PhD

Pearl #8: Some teens don’t listen to mom
Credit: Steven Feldman, MD, PhD
Compartments

Tanning beds don’t clear psoriasis
Credit: Steven Feldman, MD, PhD

If you put 10 psoriasis patients in your light box
If you see 10 patients with psoriasis who tried a tanning bed for their psoriasis

Office UVB 80% effective
You see 8 clear
Tanning Bed 80% effective
You see 0 clear

Color Perception
Credit: Steven Feldman, MD, PhD

Context and Perception
Credit: Steven Feldman, MD, PhD

Compartments Affect Context, and Context Affects Perception

Referring Physicians
- Don’t know what they are doing? Selection bias?
The “Other” Dermatologist
- Always botching things? What about the good results?

Compliance
- Know your patient (the “whole patient”)
  - requires adequate interaction
- Be aware of biases
  - know your compartment
- Team with patient
  - common goal
- Verify patient understanding
  - we say and do “our part” daily

Severe Dermatoheliosis, Field Cancerization and Skin Cancers
Severe Dermatoheliosis or Field Cancerization or both?

Dermatoheliosis - “Photoaging”; “characteristic changes to skin induced by chronic ultraviolet exposure”
- typically refers to visible
Field Cancerization - “biological process in which large areas of cells at a tissue surface or within an organ are affected by a carcinogenic alteration(s)”
- typically refers to microscopic
Field Cancerization

Off-label Topical Management

Credit: Stuart Brown, MD (1930-2015)

- 2 or 3 days on, rest remainder of week (5FU)
- week out of each month (imiquimod)
- patient cycled
  - Use as long as tolerated
  - Rest until feel OK to restart
  - multiple variations of "continual stimulation"

Field Cancerization

Oral Nicotinamide

A Phase 3 Randomized Trial of Nicotinamide for Skin-Cancer Chemoprevention

METHODS

In this phase 3, double-blind, randomized, controlled trial, we randomly assigned, in a 1:1 ratio, 398 participants who had had at least two nonmelanoma skin cancers in the previous 5 years to receive 500 mg of nicotinamide twice-daily or placebo for 12 months. Participants were evaluated by dermatologists at 3-month intervals for 19 months. The primary end point was the number of new nonmelanoma skin cancers.

Non-Melanoma Skin Cancer

Credit: Anokhi Jambusaria MD, MSCE

How I do it

- Divide tumor into quadrants
- Inject 0.1 ml 5-fluorouracil into each quadrant
- Max dose per session: 2 cc
- Repeat in 4-6 weeks as needed
- Note: Can shave toeventId (may decrease number of treatments)
Non-Melanoma Skin Cancer
Credit: Anthony Rossi, MD

SSC-KA – How I do it

- Intralosional MTX injections (range 1 to 3 injections) separated by two weeks apart in an effort to reduce tumor burden, morbidity, and surgical defect
- Methotrexate: 12.5 mg/ml or 25 mg/ml - 1 ml in total injected
- 4 injection points – quadrants at the base of the lesion
- Can shave the lesion flat – send for pathology

Skin Cancer Management Options
Credit: Anthony Rossi, MD

- SCC-KA
- Mohs Micrographic Surgery
- Standard Excision
- Radiotherapy
- PDT
- Topical 5% Imiquimod
- Cryosurgery

Oral Retinoids

- Usually 10–30 mg daily

Skin Cancer Management Options
Credit: Anthony Rossi, MD

- Imiquimod
  - British Association of Dermatologists recommendations
  - topical imiquimod appears effective in primary small superficial SCC
  - Imiquimod may possibly have role in treatment of primary nodular SCC

Skin Cancer Management Options
Credit: Anthony Rossi, MD

- Imiquimod associated with histological clearance
- 25% randomized trials associating treatments for primary SCC
- 75% BCC, success rate of histological clearance for initial treatment of superficial SCC after paramuroid flap
- Imiquimod only for 6 weeks at 7.5 mg/week success rate for superficial BCC
- Lower rates of early treatment failure (due to lack of histological clearance) in analysis of 5 trials with 1146 patients
- High dose imiquimod compared to low dose Imiquimod (0.05 mg, 0.18 mg, 0.24 mg)
- No significant difference in treatment failure for superficial or nodular BCC

Skin Cancer Management Options
Credit: Anthony Rossi, MD

- Imiquimod
  - Topical 5% Imiquimod
  - Lower rates of early treatment failure (due to lack of histological clearance) in analysis of 5 trials with 1146 patients

Skin Cancer Management Options
Credit: Anthony Rossi, MD

- Low-Dose Retinoids in the Prevention of Cutaneous Squamous Cell Carcinomas in Organ Transplant Recipients

A 16-Year Retrospective Study

Catherine A. Hansard, MA, PHD, MRCGP; Mary Leadham Green, MA, Irene M. Legh, MRCGP, FRCGP

Interventions
- Continuous systemic retinoids at doses of 0.2 to 0.4 mg/kg per day for a minimum of 12 months

Conclusions
- Low-dose systemic retinoids significantly reduce SCC development in DPTs for the first 3 years of treatment, and this effect may be sustained for at least 8 years, with a generally well-tolerated side-effect profile. Studies are now

Acne Medications
Antibiotics and OCPs

Spironolactone and Cancers

Spironolactone Lab Value Monitoring

Isotretinoin

Depression and IBD
Isotretinoin Lab Value Monitoring

- Baseline
- Within first 8 weeks
- As needed based on patient and results

Miscellaneous Therapeutics

N-Acetylcysteine for Neurotic Excoriations

N-Acetylcysteine in the Treatment of Excoriation Disorder
A Randomized Clinical Trial

N-Acetylcysteine, a Glutamate Modulator, in the Treatment of Trichotillomania
A Double-blind, Placebo-Controlled Study

N-Acetylcysteine for Trichotillomania

N-Acetylcysteine for Aphthous Ulcers

Zinc for Aphthous Ulcers

Zinc Citrate – 34% elemental
Zinc Sulfate – 22% elemental
Zinc Gluconate – 13% elemental
Zinc Monomethionine – 21% elemental

80-120 mg elemental zinc x 1-4 months
- Prolonged can decrease calcium, magnesium, zinc
Zinc for Viral Warts

Read the article to learn more about zinc for viral warts.

Zinc for Molluscum

Efficacy comparison between cimetidine and zinc sulphate in the treatment of multiple and recalcitrant warts

Methods: A randomised double blind prospective study. Eighteen patients with multiple warts were divided into two groups: one took 375 mg/kg/day of cimetidine (maximum 1200 mg/day) and the other 15 mg/kg/day of zinc sulphate (maximum 600 mg/day) for three months.

Results: Among the 18 patients who participated in the study, nine took cimetidine and nine zinc sulphate. Just one patient in the zinc sulphate group did not complete treatment due to nausea and vomiting. None patients who were treated with zinc sulphate were vomiting and all did not show modifications in lesions. Among the group who was treated with cimetidine, nine did not show modifications in lesions and four showed decrease from baseline lesion 50%.

Conclusions: 10 mg/kg/day zinc sulphate dose seems to be more effective than cimetidine for the treatment of children and adults with multiple and difficult to handle warts. However, the small number of patients did not allow any definitive conclusion.

Anthralin for Alopecia Areata

Tolerated by pediatric patients as well.

Fexofenadine for Alopecia Areata

Supplement 180 mg daily.

Simvastatin/Ezetimibe for Alopecia Areata

- baseline lipids
- simvastatin 20mg daily only
- oppose study just cited
- coverage issues
- personal N = 4, all with success (none universalis)
Surgical Tips

Pregnancy and Surgery
Credit: Keith Harrigill, MD, MBA, MPH/TM, FAAD

- American College of Obstetricians and Gynecologists’ (ACOG) Committee on Obstetric Practice

- ACOG is referring to major surgeries such as laparoscopies, laparotomies, appendectomies, cardiac catheterizations, etc. What we do (excisions and Mohs) is considered "minor surgery" by ACOG.

Pregnancy and Surgery
Credit: Keith Harrigill, MD, MBA, MPH/TM, FAAD

- Consensus Recommendations
  - A pregnant woman should never be denied indicated surgery, regardless of trimester (MM, PG, aggressive CA)
  - Elective surgery should be postponed until after delivery
  - Non-urgent surgery should be performed in the second trimester when possible
  - Additional Recommendation
    - When possible, involve the patient’s obstetrician before a significant surgery. They may offer specific advice for that patient and that situation (fetal monitoring, for example).

My Derm Surgery Approach
- Biopsy anything that is clinically suspicious for malignancy, at any gestational age.
- I use lidocaine 1% with epinephrine
- For anything other than biopsies, shave removals, or simple excisions, collaborate with the OB of record
- Extensive cases at advanced gestational ages may require intraoperative monitoring. The OB will coordinate this.
- Up to 20 weeks, position without regard to the pregnancy. After 20 weeks, place in the lateral decubitus position (IVC).

Bent Needles
- Ergonomic positioning of wrist
- Prevents reuse of contaminated needle
- Care with handling as usual

Mohs marking
- Before sample is numbed or removed
- In addition to skin nicks
- 100% prevents mistaken orientation
Mohs Surgery

- Surgical excision of cutaneous malignancies
- 100% margin control
- Uncertainty of defect
- Creativity of repair
- "Gut feeling" of case even at biopsy

Mohs Surgery

- NO system to quantify cases when written
- Predictors of advanced reconstruction
- Correlation of treatment delay to defect size
- Predictors of extensive subclinical spread


WAR Score Goals
- Uncomplicated
- Dependable
- Reproducible
- Quantitative
- Preoperative assessment
- Predict
  - Complexity
  - Associated time

WAR Score Abstract

Mohs Surgery WAR (Webb and Rivera) Score

<table>
<thead>
<tr>
<th>Greatest Dimension Size</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 0.9 cm</td>
<td>0 points</td>
</tr>
<tr>
<td>1.0 – 1.9 cm</td>
<td>1 point</td>
</tr>
<tr>
<td>2.0 – 2.9 cm</td>
<td>2 points</td>
</tr>
<tr>
<td>&gt; 3.0 cm</td>
<td>3 points</td>
</tr>
</tbody>
</table>

Recurrent tumor: 1 point
Primary tumor: 0 points
Nose, Eyelid, Ear or Lip: 1 point
Other anatomic locations: 0 points
Aggressive tumor type/subtype: 1 point
Nonaggressive tumor type/subtype: 0 point

Total WAR Score: ___ points

WAR Score Study Design
- Sept 2009 – June 2010
- Random selection
- Self reported questionnaire
- 21 physicians (22% response)
  - Name, location, years in practice
  - Mohs College and Mohs Society
- 10 consecutive cases (211 total)

Score Inclusion Considerations
- Age
- Mental /physical condition
- Comorbidities
- Race
- Medications/Allergies
- Immunosuppression
- Patient experiences
- Greatest dimension/Area
- Duration of tumor presence
- Previous treatment(s)

Choose greatest dimension, area, location, age/condition, comorb...
### WAR Score General Statistics

<table>
<thead>
<tr>
<th>Mohs College</th>
<th>Mohs Society</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respondents</td>
<td>12/21</td>
<td>9/21</td>
</tr>
<tr>
<td>Stages</td>
<td>1.7 ± 0.8</td>
<td>1.5 ± 0.8</td>
</tr>
<tr>
<td>Time (h)</td>
<td>2.45 ± 1.37</td>
<td>2.20 ± 1.17</td>
</tr>
<tr>
<td>WAR Score</td>
<td>1.2 ± 1.0</td>
<td>1.2 ± 0.9</td>
</tr>
</tbody>
</table>

### WAR Score Results Summary

- **Recurrence**
  - Predicts stages
  - Predicts time
- **Location**
  - Predicts stages
  - Does NOT predict time
  - Choice of repair
- **Aggressiveness**
  - Predicts stages
  - Predicts time
  - Does NOT predict stages or time
- **Greatest Dimension**
  - Variable subclinical spread
  - Predicts time
  - Area
  - Variable subclinical spread
  - Predicts time
  - Experience
  - Does NOT predict stages or time

### Summary of Variables Analyzed

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>p-value (stages)</th>
<th>p-value (time)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max. Dimension (cm)</td>
<td>1.19 ± 0.89</td>
<td>0.10</td>
<td>0.002</td>
</tr>
<tr>
<td>Area (cm²)</td>
<td>1.73 ± 0.46</td>
<td>0.10</td>
<td>0.0005</td>
</tr>
<tr>
<td>Ear, Nose, Eyelid, Lip</td>
<td>1.8 ± 0.9</td>
<td>0.10</td>
<td>0.0005</td>
</tr>
<tr>
<td>Other Anatomic Locations</td>
<td>1.4 ± 0.7</td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>Time (h)</td>
<td>2.05 ± 0.40</td>
<td></td>
<td>0.051</td>
</tr>
<tr>
<td>Recurrent Tumors</td>
<td>3.03 ± 1.21</td>
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<td>0.001</td>
</tr>
<tr>
<td>Time (h)</td>
<td>2.25 ± 1.28</td>
<td></td>
<td>0.0005</td>
</tr>
<tr>
<td>Primary Tumors</td>
<td>2.25 ± 1.28</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Time (h)</td>
<td>2.22 ± 1.18</td>
<td></td>
<td>0.051</td>
</tr>
<tr>
<td>Aggressive Tumors</td>
<td>2.3 ± 0.6</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Time (h)</td>
<td>2.3 ± 0.6</td>
<td></td>
<td>0.001</td>
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<tr>
<td>Nonaggressive Tumors</td>
<td>2.29 ± 1.25</td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>Time (h)</td>
<td>2.25 ± 1.25</td>
<td></td>
<td>0.001</td>
</tr>
</tbody>
</table>

### WAR Score Statistical Significance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rho value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stages</td>
<td>0.41</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time</td>
<td>0.34</td>
<td>&lt;0.0001</td>
</tr>
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### Mohs Surgery WAR (Webb and Rivera) Score

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<tr>
<td>Nonaggressive tumor type/subtype</td>
<td>0 points</td>
</tr>
</tbody>
</table>

**Total WAR Score:** 

---

Albert E. Rivera, DO – Southeastern Skin Cancer & Dermatology
59yo, BCC (1 point)
1 Stage, Primary Closure

28yo, BCC (2 points)
1 Stage, Bilobed Flap

52yo
Infiltrative BCC (4 points)

2 Stages
Wedge Primary Repair

74yo Nodular BCC
Recurrent (3 points)

2 Stages
Nasolabial Interpolation Flap
Central Flap Necrosis
Good Final Result

WAR Score Practice Relevance
- Time management
- Operative day planning
- Anticipation (avoid "surprises")
- Average daily workload

Example:
- 6 cases – one or less 3+ point
  two or less 2 point
  three or more 0-1 point

WAR Score Training Relevance
- Resident training
  - Increase case complexity with experience
  - Standardize Mohs experience within/between programs

In Conclusion.....
- The WAR (Webb and Rivera) score is a minimal effort, efficient, reproducible tool to be used in preoperative Mohs surgery planning.
  - Improves office efficiency, predictability, case load, resource allotment, and organization
- The components of the score include maximum tumor dimension, recurrence, location and aggressiveness with each being assigned a numerical value that is totaled, resulting in a final quantitative score.

Mohs Surgery WAR (Webb and Rivera) Score

<table>
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<td>0</td>
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<tr>
<td>1.0 – 1.9 cm</td>
<td>1</td>
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| Aggressive tumor type/subtype: | 1 point|
| Nonaggressive tumor type/subtype: | 0 point|

Total WAR Score: ___ points

Summary
1. Shared an accumulated collection of business and customer service tips
2. Shared an accumulated collection of medical and surgical dermatology tips
3. Reviewed and discussed the WAR (Webb and Rivera) Score: a preoperative Mohs surgery assessment tool
Thank You!
Questions?

Rivera@SoutheasternSkin.com
Thursday, March 30, 2017
Resident Pathway
Genodermatoses

Rocky Vista University/Colorado Dermatology Institute
Jon Bielfield, DO – PRG-3
George Brant, DO – PRG-3
Michelle Elway, DO – PRG-2

Ichthyosis Vulgaris

- M/C sx of cornification
  - 1/200 prevalence
- Impaired cornified keratinocytes, increased TEWL, inflammation from irritants/allergens
- Aut semidominant
  - Mild with heterozygous filagrin mutation
  - Severe if both alleles mutated
- Extensors, scalp, forehead
- Hyperlinear palms, KP, AD

Treatment
- Emollients
- Ceramides
- Humectants
- Keratolytics
  - Urea, lactic/salicylic acids

Pathology
- Thin to absent granular layer, orthokeratosis

X-Linked Recessive Ichthyosis

- X-linked recessive
  - 1/5,000 male births
- Deletion of STS gene (arylsulfatase C)
- Steroid sulfatase deficiency
  - Increased cholesterol
  - Decreased cholesterol
  - Low/lack of estrogens in amniotic fluid
- Failure of labor to progress
- Mild erythroderma, large translucent scales
  - Evolves to brown "flecky" scales over extremities, trunk, neck
  - Spares palms, soles, face
- A/W comma-shaped corneal opacities, cryptorchidism (increased risk of testicular CA), increased risk of ALL, rare neurological sx

X-linked Ichthyosis

- Dx: FISH, molecular gene testing
- Tx: Humectants, keratolytics, retinoids

Financial Disclosures

We have no financial disclosures
Jon Bielfield, DO
George Brant, DO
Michelle Elway, DO
Lamellar Ichthyosis/Nonbullous Congenital Ichthyosiform Erythroderma

- AR, mutation in TGM1 or ABCA12
- Abnormal cross-linking of structural proteins in epidermis, leads to defective differentiation and desquamation
- Collodion membrane at birth and erythroderma
  - Large, brown plate-like scales, prominent flexural involvement
  - Generalized, except ‘bathing suit ichthyosis’ in South African variant
  - A/W ectropion, eclabium, scarring alopecia (peripheral scalp), PPK, nail dystrophy, heat intolerance

Treatment
- Acitretin for severe dx
- Topical retinoids and keratolytics limited used secondary to irritation
- Possible problematic systemic absorption if keratolytics applied to an extensive area

Epidermolytic Hyperkeratosis/Bullous CIE

- AD, Keratin 1 and Keratin 10 mutations
- Occasionally offspring of parent with epidermal nevus sx
- EHK changes in epidermal nevi
- Erythroderma, peeling skin, erosions at birth
- Can have sepsis, dehydration, electrolyte imbalances
- Gradually evolve to widespread hyperkeratosis with corrugated ridges on flexures
- Cobblestone pattern on extensors
- Episodic blistering, secondary infections, body odor, PPK

EHK/EI/Bullous Congenital Ichthyosiform Erythroderma

- Massive orthokeratosis, cytolysis of suprabasal/granular layers, clumped tonofilaments

Treatment
- Neonates
  - Protective isolation, emollients, and monitoring
- Children and adults
  - Emollients, humectants
  - Mechanical exfoliation of hyperkeratosis
  - Bleach baths
  - Antimicrobials prn
  - Avoid widespread use of salicylic acid
  - Possible toxicity

DDx in neonates
- Epidermolysis bullosa
- SSSS
- Superficial EI
- Ichthyosis hystrix
- Sjogren-Larsson
- KID sx

Sjogren-Larsson Syndrome

- AR, FALDH mutation
- Defective conversion of fatty alcohols to fatty acids
- Important for epidermal lipid synthesis, and catabolism of phospholipids/sphingolipids in CNS myelin
- Generalized ichthyosis w/erythroderma
  - Evolves to darker scale w/out erythema
  - Flexures, lower abdomen, neck
  - Spasticity, scissor gait

Lamellar Ichthyosis

- Acitretin for severe dx
- Topical retinoids and keratolytics limited used secondary to irritation
- Possible problematic systemic absorption if keratolytics applied to an extensive area
Sjogren-Larsson Syndrome
- Atypical retinitis pigmentosa with glistening white dots
- Pruritus is unique
- Responds to Zileuton
- Variable prognosis dependent on CNS complications/mobility
- Physical therapy can prevent spasticity progression

Netherton Syndrome
- AR, SPINK5 mutation
- Serine protease inhibitor may be associated with downregulating inflammatory pathways
- Congenital erythroderma, failure to thrive
- Classic triad
  - Ichthyosis linearis circumflexa - serpiginous plaques with double-edged scale
  - Trichorrhexis invaginata - “bamboo hair”
  - Examine eyebrow/eyelash hair if scalp hair sparse
- Atopic diathesis

Netherton Syndrome
- Topical calcineurin inhibitors for pruritus and erythema
- Limit use, potential for high absorption and toxicity
- Oral retinoids
  - Often have adverse effects
- Allergy referral
- May improve at puberty

Nevoid Basal Cell Carcinoma Syndrome (NBCCS)
- AKA Gorlin Syndrome
- Autosomal dominant
- Due to mutations in PTCH or PTCH1 gene
  - Most due to premature termination & production of shortened gene product or long arm deletions on chromosome 9q22
  - Some people carrying the genetic mutation do not meet diagnostic criteria
- Diagnosis based on major and minor criteria (varies by source)
  - 2 Major
  - 1 Major + 2 Minor
  - 1 Major + molecular confirmation

Major Criteria
1. Development of multiple BCC’s (>5) or a BCC before age 30
2. Odontogenic keratocysts of the jaw - mandible or maxilla
3. Pitted depressions of hands and feet (palmar plantar pits) 2 or more
4. Lamellar calcification of the falx <20 YOA
5. 1st degree relative with NBCCS

1) Skin Tumors--BCC
- Usually appear between ages 17-35
- Marked tendency towards central facial area
- Type I: fair skin & prior UV exposure particularly prone to multiple BCC’s
  - 1-10mm, hyperpigmented or skin-colored, dome-shaped papules
- Striking resemblance to typical compound or intradermal nevi, polypoid bcc or acrochordon-like BCC in childhood.
2) Jaw Cysts
• Occur in ~ 90% of patients
• Occur as early as age 5, rarely after 30
• Both mandible (2x mc) and maxilla show cystic defects on x-ray
• Occur as painless swelling
• Have a keratinized lining but uncommonly a cyst may be an ameloblastoma

3) Pits of Palms & Soles
• Unusual pitting of palms and soles is distinguishing feature of Gorlin's
• Occurs in 87% of pts
• Usually apparent in 2nd decade
• Hist: basaloid proliferation, but lesions don't progress or behave like BCC

4) Lamellar calcification of falx

5) 1st degree relative

Minor Criteria
• 1. Childhood medulloblastoma
• 2. Lympho-mesenteric or pleural cysts
• 3. Macrocephaly (97th percentile)
• 4. Cleft lip/palate (5% of patients)
• 5. Vertebral/rib abnormalities—bifid, fused, missing or splayed ribs; scoliosis; kyphosis
• 6. Preaxial or postaxial polydactyly
• 7. Ovarian/cardiac fibromas
• 8. Ocular abnormalities

Gorlin Syndrome
Clinical findings are dependent on 2 characteristics:
• Race
• Form of the mutation (point mutation vs deletion)
  • Pts with NBCCS due to deletions of chromosome 9q22 have all stigmata of typical NBCCS and in addition often have severe MRI, hyperactivity, overfriendliness with strangers, short stature, and less commonly neonatal hypotonia, epicanthic folds, short neck, scoliosis, and epilepsy.
Further Consultations/Work-up

• Ophthalmology—numerous ocular findings
• X-rays—oral, spine
• Genetic counseling
• Oral surgeon
• Routine skin checks/surveillance

Management

• Genetic counseling
• Strict sun avoidance and maximum skin protection
• Avoid ionizing radiation (radiation tx for medulloblastoma, BCC or other CA)
• Regular monitoring and biopsy of suspicious lesions
• Topical tazarotene or imiquimod to prevent and treat superficial tumors
• Oral retinoids may reduce frequency of new BCCs & slow growth of small BCC’s
  • However, once D/C’d, lesions again begin to grow

• Vismodegib—hedgehog pathway inhibitor
  • Reduces BCC tumor burden & prevents growth of new BCCs
  • Poor tolerability leads to high d/c rate
  • Topical smoothened inhibitor appears effective & better tolerated
• Surgical tx used for most lesions—Mohs, Excision or ED&C
  • Megaseessions—general anesthesia with removal of several lesions
  • PDT—beneficial to tx areas that have had multiple BCC’s in the past

Gorlin Syndrome

• Can be physically and emotionally devastating
• Support groups
• Conferences for patients

Other syndromes with multiple BCCs

• Bazex-Christian-Dupre Syndrome
• Rombo Syndrome
• Brooke-Spiegler Syndrome
• Xeroderma Pigmentosum
• Schöpf-Schulz-Passarge Syndrome
• Infundibulocystic BCC syndrome
• Unilateral nevoid BCC with comedones
Bazex-Christian-Dupre Syndrome
- X-linked dominant
- Multiple BCCs of face at early age
- Follicular atrophoderma of extremities
- Hypotrichosis and localized/general hypohidrosis of face & head

Rombo Syndrome
- Multiple BCCs
- Atrophoderma vermiculatum
- Hypotrichosis
- Milia

Infundibulocystic BCC syndrome
- AD inheritance
- Palmar pits and jaw cysts with multiple trichoepitheliomas
- Skin-colored pearly papules affecting central face and accentuated in nasolabial folds
- Unilateral nevoid BCC with comedones
  - Linear arrangement of close-set papules sometimes interspersed with comedones
    - Present at birth.
  - Bi reveal basal cell epitheliomas which don't increase in size with age of patient

Neurofibromatosis Type I
- AKA Von Recklinghausen’s disease
- AD inherited syndrome manifested by nervous system, bones and skin.
- NF-1 (neurofibromin) responsible for 85% of cases
  - Neurofibromin-1 protein that negatively regulates signals transduced by Ras proteins
  - High rate of spontaneous postzygotic mutation
  - Both alleles must be affected for pt to grow a neurofibroma
  - Early post-zygotic mutation affecting the 2nd allele in fetal life resulting in LOH affecting entire Blaschko segment
  - Gene locus 17q11.2; 50% are new mutations
  - Birth incidence 1/3000

Diagnostic criteria = 2 or more of the following:
- > 6 café au lait macules (> 5mm prior to puberty or > 15mm after puberty)
- 2 or more NFs or 1 plexiform NF
- Pathognomonic “button-hole” sign
- Axillary or inguinal freckling (Crowe’s sign)
- 2 or more Lisch nodules
- Optic gliomas
- Osseus lesion: Sphenoid wing dysplasia, thinning of long bone cortex with or without pseudarthrosis
- First degree relative with NF-1
** Nevus anemicus (neck & upper chest), xanthogranuloma (cephalic or genital), and glomus tumors are strongly a/w NF-1. Prevalence is high during first 2 yrs of life, when other diagnostic criteria may be absent.

Café-au-lait macule and axillary freckling
- Oval-shaped light-brown patch
- Multiple small 1–2 mm lentigines in the axilla
- Crowe’s sign
Cutaneous Neurofibromas

- Small, soft, skin-colored to pink polypoid papules that characterize NF1
- Can be pressed down into the panniculus by light pressure and spring back when released
- “button-holing"

Lisch nodules

- Multiple yellow-brown papules on iris
- Late finding, usually seen in older patients

Plexiform Neurofibromas

- Soft tissue swelling of the left hand, note the overlying hyperpigmentation
- Feels like "bag of worms"

Neurofibromatosis Type II

- NF-2 resembles NF-1 but it has Bilateral Acoustic Neuromas and the affected gene is MERLIN or SCHWANNOMIN, mutation in SCH gene on 22q11-q13
- NF-3 (mixed) and NF-4 (variant) have higher risk of optic neuromas, neurilemmomas, meningiomas
- NF-5 segmental (dermatomal)
- NF-6 only café au lait, no neurofibromas
- NF-7 late onset

Neurofibromatosis II Diagnosis

Requires either of the following:
- Bilateral 8th cranial nerve masses, seen on CT or MRI
- 1st degree relative with NF-2 and either unilateral 8th nerve mass or two of the following:
  - A neurofibroma, meningioma, glioma, schwannoma, and juvenile posterior subcapsular lenticular opacity

Neurofibromatosis TX

- Treatment of NF requires a team approach
  - Neurology
  - Ophthalmology
  - Dermatology
  - Endocrinology
  - Orthopedics
  - Oncology
- Neurofibromas that are bothersome can be excised
- Progressive deterioration w/ loss of hearing, ambulation, & sight. Death resulting from CNS tumor.
- Recommended screening:
  - CT or MRI at diagnosis in high-risk patients
  - Yearly exam with problem focused workup
- Trials of targeted therapy to reduce the growth of cutaneous NFs are ongoing
Disorders of pigmentation

- Oculocutaneous Albinism
- Chédiak-Higashi Syndrome
- Hermansky-Pudlak Syndrome
- Griscelli Syndrome
- Hypomelanosis of Ito
- Incontinentia Pigmenti
- Piebaldism
- Waardenburg Syndrome

Oculocutaneous albinism

- Seven genetic forms
  - Main types are 1-4
  - Most common is OCA2
- All are autosomal recessive
- Variable pigmentary dilution of skin, hair, and eyes

Oculocutaneous albinism type 1

- Accounts for around 40% of OCA worldwide
  - Prevalence – 1:28,000 blacks; 1:39,000 Caucasians
- Presents at birth
- Divided into two types: 1a and 1b
- Pathogenesis
  - Mutations in the TYR gene on chromosome 11q
  - Leads to an absence (OCA type 1a) or reduction (OCA type 1b) of tyrosinase activity (and therefore melanin biosynthesis)

OCA type 1a

- Complete loss of tyrosinase function = no melanin
- White hair and skin
- Pink irides, turn blue-grey over time
  - Decreased visual acuity (20/400)
  - Photophobia
- No pigmented lesions develop

OCA type 1b

- Retain some tyrosinase function
- May develop some pigment over time
- Eyes can turn tan or light brown
- Hair can turn yellow
- Pigmented lesions can develop
- Visual acuity not as severely affected as type 1a
- Temperature sensitive variant
  - Enzyme with limited activity below 37°C and none above
  - Melanin pigment only in cooler areas (ie acral)
OCA type 2
- “Yellow mutant albinism”
- Accounts for about 50% of OCA
- Tyrosinase positive
- Defect in OCA2 gene (previously P gene)
  - Decreased eumelanin synthesis
- Mild to moderate pigment dilution
  - Light brown hair and skin
  - Develop pigmented nevi/lentigines over time

OCA type 3
- More common in South Africa
- Mutation in tyrosinase-related protein 1 (TYRP1) gene
  - Important in maintenance of melanosomes and cell structure
  - Affects melanocyte proliferation and cell death
  - Essential cofactor for tyrosinase activity
- Patients have red hair and reddish brown skin
  - AKA “rufous” or red OCA
  - Decreased visual acuity, but may be minor/undetectable

OCA type 4
- Very rare, except in Japan (where it accounts for 25% of OCA)
- SLC45A2 mutation (formerly MATP)
- Resembles OCA2
  - Distinguished by molecular studies

Chédiak-Higashi Syndrome
- AR; lysosomal transport (LYST) gene defect
- Presents in infancy with pigmented dilution (sun-exposed sites may be hyperpigmented) and “silver hair”
- Immunodeficiency
- Bleeding diathesis
- Neurologic degeneration
- Death typically by age 10 from infection or an accelerated lymphoma-like phase

Hermansky-Pudlak syndrome
- AR; 9 associated gene defects described
- Most common in Puerto Rico, especially HSP1
- Main features
  - Tyrosinase-positive OCA
  - Bleeding diathesis
  - Absence of dense bodies in platelets
  - Lysosomal ceroid accumulation
  - Pulmonary fibrosis, cardiomyopathy, granulomatous colitis, renal failure
  - Immunodeficiency (HSP2)
Incontinentia pigmenti
• X-linked dominant (lethal in males)
• NFκβ essential modulator (NEMO) gene mutation
• 4 stages:
  • Vesicular
  • Verrucous
  • Hyperpigmented
  • Hypopigmented
• Cutaneous lesions follow lines of Blaschko

Vesicular stage
• Occurs in 87% of cases
• Onset within first 6 weeks of life
• Vesicles in linear or whorled erythematous plaques

Verrucous stage
• Onset age 2-6 months
• Usually resolve within first year of life
• Some cases reported to last several years

Hyperpigmented stage
• Onset after age 6 months
• Linear/whorled hyperpigmentation following lines of Blaschko
• May last years then fade with no sequelae

Hypopigmented stage
• May be seen in some adults
• Subtle hypochromatic or atrophic linear lesions

Other cutaneous manifestations
• Patchy alopecia
• Atrophic changes of hands
• Onychodystrophy, painful subungual keratotic tumors
Extracutaneous manifestations

- Teeth (90%): delayed eruption, partial anodontia, microdontia, peg- or cone-shaped teeth
- Bones (40%): syndactyly, skull deformities, dwarfism, spina bifida, etc.
- Eyes (35%): strabismus, cataracts, retinal detachment
- CNS (33%): seizures, mental retardation, spastic paralysis, microcephaly

Histology

- Varies with clinical stage

Genodermatoses with EYE Findings

- Richner-Hanhart Syndrome—Painful keratitis, dendritic corneal ulcers (pseudoherpetic)
- Waardenburg Syndrome—heterochromia iridis (2 different eye colors in same individual)

Genodermatoses with EYE Findings

- KID syndrome - photophobia, severe keratitis, neovascularization, blindness
- Pseudoxanthoma elasticum (& lead poisoning) - angioid streaks

Genodermatoses with EYE Findings

- Homocystinuria - ectopia lentis(lens dislocation), downward
- Marfan Syndrome - ectopia lentis, upward

Genodermatoses with EYE Findings

- X-Linked Ichthyosis—comma-shaped corneal opacities
- Fabry disease—whorl-like corneal opacities
- Gardner Syndrome—congenital hypertrophy of retinal pigment epithelium (CHRPE)
Genodermatoses with EYE Findings

- Goltz Syndrome - coloboma (defect in iris)
- Neurofibromatosis - Lisch nodules (pigmented hamartomatous nevi in iris)
- Tuberous Sclerosis - retinal phakomas (hamartomas)
- Sjogren-Larsson syndrome - perifoveal glistening with white dots in ocular fundus
- Cockayne syndrome, Refsum disease - retinitis pigmentosa (salt/pepper)

Genodermatoses with NOSE & EAR Findings

- Trichorhinophalangeal syndrome - bullous pear-shaped nose
- Rubinstein-Taybi syndrome, progeria - beaked nose
- Beckwith-Wiedemann Syndrome - circular depression (posterior rim of helices), ear lobe crease
- Congenital contractual arachnodactyly - crumpled ears
- Hyper-IgE Syndrome - broad nasal bridge

Hyper-IgE Syndrome

- broad nasal bridge
Benign Epidermal and Dermal Tumors
St. Barnabas Hospital Dermatology Residency Program, Bronx, NY

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Disclosures
• No conflicts of interest to disclose

Outline
• What makes a tumor benign?
• Benign Epidermal Tumors
• Benign Dermal Tumors
  • Clinical Overview
  • Diagnostic Pearl
  • What’s new?
    -- Literature Highlights
    -- Syndrome Associations?

Tumor
• Signals
  • Proliferation
  • Differentiation
  • Cell death
• Triggers
  • Blood supply
  • Matrix-cell
  • Cell-cell

Benign Tumor
• Mass of cells that lack ability to invade neighboring tissue
• Slower growth rate
• More differentiated
• Surrounded by fibrous sheath of connective tissue or remain within epithelium
• Do not recur when completely excised
• May compress surrounding tissue

Epidermis
Benign Epidermal Tumors

1. Seborrheic Keratosis
2. Clear Cell Acanthoma
3. Epidermolytic Acanthoma
4. Parakeratosis
5. Inverted Follicular Keratosis
6. Warty Dyskeratoma
7. Lichen Planus Like Keratosis
8. Epidermal Nevus

Seborrheic Keratosis – Clinical Overview

• Pathogenesis: AD with Incomplete Penetrance
• Clonal expansion of a mutated epidermal keratinocyte
• More than 80% of seborrheic keratoses have at least one mutation
• 45% have more than one mutation in an oncogene such as FGFR2, FGFR3, PIK3CA, KRAS, EGFR

Sign of Leser-Trélat

• Abrupt increase in size or number is a cutaneous sign of internal malignancy
• 60% of neoplasms are adenocarcinomas (primarily of GI tract)
  • Others: lymphoma, breast cancer, SCC of lungs
• May be accompanied with:
  • Acanthosis nigricans
  • Tripe palms

Diagnostic Pearl

Dermoscopy

- Milia-like cysts
- Irregular crypts
- Fissures/ridges
- Blue-gray lobules
- Light brown fingerprint-like parallel structures
- Fat fingers (the calf of a cerebriform surface)

Seborrheic Keratosis - Diagnostic Pearl

Dermoscopy

- Multicomponent (n = 32; 19.9%) (Combination of 3 or more distinctive dermoscopic structures)

Malignancy

• Instances of malignant neoplasms arising within and adjacent to SKs were reported as early as 1932
• Likely coincidental, although it is possible that the various cell types present in an SK could develop into their respective neoplasms
  • Spinous cells
    • Invasive SCC
    • KA
    • SCCIS
  • Basaloid cells
    • BCC: Most frequent neoplasm seen in association with SKs
    • SKs and BCC derived from the infundibular portion of the hair follicle
Seborrheic Keratosis – Diagnostic Pearls
Borst-Jadassohn Phenomenon

- Morphologic pattern:
  - Nested atypical keratinocytes situated within normal epidermis
  - Clonal Bowen Disease
  - Hidroacanthoma Simplex
  - Clonal Seborrheic Keratosis

Seborrheic Keratosis – What’s new?
6 Histologic Types

- Acanthotic SK
- Hyperkeratotic SK
- Reticulated SK
- Clonal SK
- Melanoacanthoma SK
- Irritated SK

Seborrheic Keratosis with Pseudorosettes and Adamantinoid Seborrheic Keratosis: Two New Histopathologic Variants

- One lesion showed abundant intercellular mucin, closely resembling to adamantinoma, and therefore was named **adamantinoid seborrheic keratosis**
- The other one exhibited a peculiar distribution of the basaloid keratinocytes, which were arranged radially around small central spaces, resulting in pseudorosette formation

Clear Cell Acanthoma – Diagnostic Pearl
Dermoscopy

- Blood vessels lined up - “string of pearls”

2. Clear Cell Acanthoma (Pale Cell Acanthoma, Degos Acanthoma) – Clinical Overview

- Morphology/Distribution
  - Mild erythematosus nodule with a collarette
  - Measures 1-2 cm
  - Most commonly on legs
  - Eruptive form - produce up to 400 lesions
- Histology
  - Discrete acanthoma with overlying parakeratosis
  - Distinct transition between normal epidermis and pale cells in stratum spinosum
  - Excess glycogen in the cells accounts for their clear appearance and is due to a defect in phosphorylase
  - Peppered with neutrophils

3. Epidermolytic Acanthoma – Clinical Overview

- Pathogenesis: theories include...
  - Exogenous factors: UV, Viral, Trauma
  - Increased keratinocyte metabolic activity
  - Aberrant keratin gene expression
- Morphology/Distribution
  - Pigmented keratotic papules
  - Solitary or disseminated
  - Mainly trunk
Epidermolytic Acanthoma – Diagnostic Pearl

- Histology
  - Often crateriform
  - Epidermolytic hyperkeratosis
  - Granular layer is thick and contains irregularly shaped keratohyalin granules and cytoplasmic borders are indistinct

Case of isolated epidermolytic acanthoma: Genetic and immunohistochemical analysis

- Histologic findings of that of isolated epidermolytic acanthoma (IEA) is also noted in Bullous Congenital Ichthyosiform Erythroderma (BCIE) which is caused by genetic mutations in K1 and K10
- Authors examined lesional cytokeratin via immunohistochemical microscopy which showed reduced staining of CK1 and CK10
- Based on histological similarity with BCIE and reduced staining of CK1 and CK10, somatic mutation of K1 and K10 has been hypothesized to be pathogenesis of IEA

Epidermolytic Acanthoma – What’s new?

4. Porokeratosis – Clinical Overview

- Pathogenesis:
  - Reed theorized lesions represent expanding mutant clone of keratinocytes in genetically-susceptible individuals
  - Induced by triggering factors (UV exposure, immunosuppression)
  - SCC in lesions of all porokeratosis (except punctate) reported
  - Lesions in older patients, those of long standing duration, and linear variants all have higher rates of malignant degeneration

Porokeratosis – Clinical Overview

1. Classic Porokeratosis of Mibelli
2. Disseminated superficial actinic porokeratosis (DSAP)
3. Linear Porokeratosis
4. Porokeratosis Palmare et Plantaris Disseminata (PPPD)
5. Punctate Porokeratosis

- DSAP: Most common type of all porokeratosis
  - Multiple thin papules
  - Most commonly on the legs of adult women
  - SART3, SSH1, and ARPC3 are possible gene mutations
  - Lowest risk of malignant conversion

Porokeratosis – Diagnostic Pearl

- Cornoid Lamella - thin column of tightly packed parakeratotic cells extending from an invagination of epidermis through the adjacent stratum corneum
- Granular layer is absent or markedly attenuated
- Dyskeratosis and pyknotic keratinocytes with perinuclear edema in the spinous layer

Porokeratosis – What’s new?

Craniosynostosis, anal anomalies, and porokeratosis (CDAGS syndrome): case report and literature review

- Craniosynostosis
- Large open fontanelles
- Hearing loss
- Anal anomalies
- Genitourinary malformations
- Porokeratosis (erythematous plaques on face and extremities)
- JAB - No molecular defect has been identified
5. Inverted Follicular Keratosis – Clinical Overview

- Pathogenesis
  - Derived from infundibulum of hair follicle

- Morphology/Distribution
  - Firm, white-tan to pink papule
  - 85% occur on the face

Inverted Follicular Keratosis – Diagnostic Pearl

- Histology
  - Endophytic
  - Squamous eddies
  - Lack of epithelial dysplasia

Inverted Follicular Keratosis – Associations

- Associated with:
  - Cowden’s Syndrome

6. Warty Dyskeratoma – Clinical Overview

- In 1954, Helwig coined “Isolated Darier’s”
- Also follicular dyskeratoma

- Pathogenesis:
  - Acquired ATP2A2 gene mutation → lack SERCA2 → malunion and keratinization of epithelial cells

- Morphology/Distribution:
  - Verrucous papule with central keratotic plug
  - Solitary, rarely multiple
  - Often involving the face, scalp, or back
  - Measure <1-2 cm

Warty Dyskeratoma – Diagnostic Pearl

- Histology:
  - Endophytic growth
  - Corps ronds and grains
  - Parakeratotic crust

Acantholytic Dyskeratosis
Differential Diagnosis
- Warty Dyskeratoma
- Darier’s Disease
- Grover’s Disease

Warty Dyskeratoma – What’s New Dermoscopy

- White homogeneous area with 3 yellow clods with intervening hair follicles
7. Lichen Planus-Like Keratosis – Clinical Overview

- **Pathogenesis:**
  - Inflammation of a benign lentigo, actinic keratosis, or seborrheic keratosis
  - Theory: increased number of Langerhan cells process an unidentified epidermal antigen → infiltration of lymphocytes
  - At least half are related to “precancerous” actinic keratosis
- **Morphology/Distribution:**
  - Initially pink-to-red
  - Upper chest, forearms
  - Over time, melanin deposited to form a gray hue
- **Histology:**
  - Lichenoid infiltrate of mainly lymphocytes with scattered histiocytes

8. Epidermal Nevus – Clinical Overview

- **Pathogenesis:**
  - Originate from pluripotent cells in basal layer of embryonic epidermis
  - Genetic mosaicism implicated involving KRT1, KRT10, PIK3CA

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**Epidermal Nevus – Diagnostic Pearls**

- Develop within first year of life
- Single linear lesion of well-circumscribed hyperpigmented, papillomatous papules or plaques in linear array along Blaschko’s lines
- Acanthosis, papillomatosis, hyperkeratosis
- Nevus verrucous has a warty appearance
- Nevus unius lateris - extensive unilateral plaques
- Ichthyosis hystrix - variant with extensive bilateral involvement
- Epidermal Nevus Syndrome - occur in combination with developmental anomalies
  - Neurologic
  - Musculoskeletal

**Associations - Epidermal Nevus Syndromes**

- Schimlpenning syndrome (PTCH)
  - Multiple sebaceous and eccrine glandular anomalies, acral (palmoplantar), and musculoskeletal anomalies
- Phacomatosism pigmentokeratotica (PTCH)
  - Multiple sebaceous and papular epidermal nevus, seborrheic, hypothyroidism, vitamin D-resistant rickets
- Proteus Syndrome (AKT1)
  - Type 2 Segmental Cowden disease (Proteus-Like Syndrome, SOLAMEN Syndrome) (PTEN)
  - Becker nevus syndrome
  - CHILD syndrome (NSDLH)
  - Nevus comedonicus syndrome (FGFR2)
  - Angora hair nevus syndrome
  - Garcia-Hafner-Happle syndrome

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**Lichen Planus-Like Keratosis – What’s new? Differentiating Regressed Melanoma from Regressed Lichenoid Keratosis**


**Results**

- 40% regressed melanomas demonstrated complete / near complete loss of melanocytes within the epidermis with Melan-A and MiTF immunostaining, while 8% of regressed LPLK exhibited this finding
- Necrotic keratinocytes were seen in the epidermis in 33% regressed melanomas as opposed to all of the regressed LPLK
- A dense infiltrate of melanophages in the papillary dermis was seen in 40% of regressed melanomas, a feature not seen in regressed LPLK
PTEN Hamartoma Syndromes

Cowden Disease - AD
- Trichilemmomas
- Mucosal neuromas
- Sclerotic fibromas
- <10% patients have CALMs
- Hamartomas AND carcinomas of the breast, thyroid, and colon

PTEN (Cowden Epidermal Nevus Syndrome (Proteus-Like Syndrome (SOLAMEN))
- Segmental overgrowth
- Lipomatosis
- Arteriovenous malformations
- Epidermal Nexi
- Features of Cowden Disease/Banayan-Riley-Ruvalcaba Syndrome

Benign Dermal Tumors

- Tumor origins:
  - Neural
  - Fibrohistiocytic
  - Vascular
  - Adipose
  - Polilocular
  - Eccrine
  - Apocrine
  - Sebaceous

Benign Dermal Tumors of Neural Differentiation

1. Neuroma
2. Schwannoma
3. Neurofibroma
4. Granular Cell Tumor

Neural Tumors - Peripheral Nerve Sheath Tumors

- Hamartomas
  - Neuromas
  - PEN
  - Traumatic
- True Nerve Sheath Neoplasms
  - Schwannomas
  - Neurofibromas
  - Neurothekeomas
- Miscellaneous
  - Granular cell tumor

Neuroma – Clinical Overview

- Pathogenesis:
  - Hamartoma
  - Proliferations of neural tissue: axons and Schwann cells are in equal numbers
  - Traumatic: Regenerative proliferation of axons and Schwann cells with fibrous tissue
- Clinically:
  - Solitary skin colored to erythematos, firm, papules or nodules, sometimes painful
  - Traumatic: seen at sites of nerve injury
  - PEN: seen on face or mucocutaneous junction

Neuroma – Associated Syndromes

- Mucosal neuromas
  - MEN2b
  - Cowden disease
  - Banayan-Riley-Ruvalcaba syndrome
2. Schwannoma (Neurilemmoma) - Clinical Overview

- Pathogenesis:
  - True nerve sheath neoplasm of schwann cells
- Clinically:
  - Subcutaneous skin colored papulonodule on the flexural aspect of an extremity, along a peripheral nerve
  - May be painful (BENGAL)
- Description: Well circumscribed, encapsulated deep dermal or subcutaneous tumor consisting of two areas:
  - Antoni A: cellular areas consisting of spindle cells with palisaded nuclei arranged in parallel rows with intervening acellular areas (Verocay bodies)
  - Antoni B: hypocellular myxoid areas
  - S100+, EMA+, NF- (Axons are usually absent)

Schwannoma - Associated Syndromes

- Associations
  - NF2 (bilateral acoustic neuromas, meningiomas)
  - Familial Schwannomatosis (INII/SMARCB1)

Not to be confused with...
Psammomatous Melanotic Schwannoma

- Carney Complex, AD:
  - PRKAR1A gene
- NAHERLS:
  - Rani, retinal hamartomas, myxoid neurofibromas, epithelioids
  - Carney, retinal hamartomas, mucocutaneous myxomas, blue nevi
- Endocrine neoplasia:
  - Adrenal glands
  - Pituitary gland (GH secreting tumors)
  - Testes (Sertoli cell tumors)

3. Neurofibroma – Clinical Overview

- Pathogenesis:
  - Proliferation of the entire neuromesenchyme: Schwann cells, endoneurial fibroblasts, perineurial cells, mast cells
- Clinical/Histology: “Buttonhole Sign”
  - Usually solitary, skin colored, soft, rubbery papulonodule
  - Plexiform Neurofibroma: subcutaneous mass “bag of worms” on palpation
  - Unencapsulated nodular proliferation in dermis consisting of spindle cells with wavy nuclei, pale stroma and few mast cells
  - NF+, S100+, EMA-

Associations: Neurofibromatosis-1 (von Recklinghausen Disease)

- 2 or more of the following:
  - 6+ Cafe-au-lait macules
  - >5mm pre-pubertal
  - >15mm post-pubertal
  - 2+ Neurofibromas
  - 1 Plexiform Neurofibroma
  - Melanin in the soles (Crowe sign) and groin
  - 2+ optic hamartomas (Lisch nodules)
  - Café-glace
  - Sphenoid wing dysplasia (Sphenoid wing dysplasia)
  - First degree relative with NF-1

Sphenoid Wing Dysplasia

Diagnostic Pearl: Strain Patterns
Neurofibromatosis-1 Highlights

- Patients with NF-1 have increased risk of tumors:
  - Protein product of NF1 gene, neurofibromin, is involved in negative regulation of RAS signaling
  - Juvenile myelomonocytic leukemia
  - Optic gliomas
  - Malignant peripheral nerve sheath tumors
  - Pheochromocytoma
  - CNS tumors

- NF-1 + JXG + JML = “Triple Association”:
  - 18% of children with NF-1 are diagnosed with one or more JXGs within the first 3 years of life
  - Children with NF-1 have 500-fold greater risk of developing JML compared to general pediatric population
  - Risk of JML is 30 times higher if JXGs are present

4. Granular Cell Tumor – Clinical Overview

- Pathogenesis:
  - Neural crest derived with peripheral nerve-related cellular differentiation

- Clinically:
  - Adult, women, African American
  - Solitary asymptomatic skin colored/brown sessile dermal or subcutaneous papulonodule often on the:
    - Head and neck (70%)
    - Breast (5-15%)
    - Proximal extremities

Granular Cell Tumor Histology – Diagnostic Pearl

- Description: Poorly demarcated nodule in dermis made of large pale cells with granular cytoplasm (accumulation of lysosomal granules), and centrally located nuclei
- PAS -, Diastase-resistant, S100+, CD57+ (neuronally expressed adhesion molecule)
- Intracytoplasmic granules named Pustulo-Ovoidal Bodies of Milan

Granular Cell Tumor – What’s New?

- Histologically may be confused with SCC due to marked pseudoepithelial hyperplasia
- May need immunohistochemical studies to differentiate
  - S-100, vimentin, CD68, p53, Ki-67, E-cadherin, collagen IV and cytokeratin AE1/AE3 antibodies
  - Strong staining of S-100 protein, CD68, vimentin, E-cadherin and low proliferative activity observed with Ki-67 expression confirmed the diagnosis of a granular cell tumor

Benign Dermal Tumors of Fibrohistiocytic Differentiation

1. Angiofibroma
2. Dermatofibroma
3. Sclerotic Fibroma
4. Keloid

1. Angiofibroma – Clinical Overview

- Clinically: Skin colored firm papules
  - Face, esp nose (fibrous papule)
  - Periungual (koenen’s tumor)
  - Penis (pearly penile papules)
Angiofibroma – Associated Syndromes

- Tuberous sclerosis (adenoma sebaceum)
- MEN-1 Syndrome
- Birt-Hogg-Dube Syndrome

Angiofibroma – What’s new?

Topical sirolimus for the treatment of angiofibromas in tuberous sclerosis

Indian J Dermatol Venereol Leprol. 2017 Jan-Feb;83(1):27-32

- Sirolimus is an immunosuppressive and anti-cancer agent, known as mammalian target of rapamycin (mTOR) inhibitors
- It inhibits cancer cell induced angiogenesis and proliferation. For this reason, it has been used for the treatment of angiomyolipomas, lymphangioleiomyomatosis and angiofibromas

Initial Presentation

2. Dermatofibroma – Clinical Overview

- Common pigmented or pink firm, dome shaped papule with central induration
- +Dimple sign, F>M
- Possibly caused by injury

Dermatofibroma (Benign Fibrous Histiocytoma) – Associated Syndromes

“S.A.P.I.”

Multiple DFs found in:
- SLE
- Atopic dermatitis
- Pregnancy
- Immunosuppression

3. Sclerotic Fibroma – Clinical Overview

- Clinically
  - Solitary or multiple on skin or mucous membranes
  - Pearly papule or nodules
  - Develop during adulthood
- Histology
  - Well circumscribed, dome shaped, dermal hypocellular nodules composed of collagen that is arranged in short intersecting stacks in a parallel arrangement and separated by spaces containing connective tissue matrix
  - Spindle cell with occasional cytoplasm and small nuclei
  - Vimentin, Muscle-Specific Actin, CD34

Sclerotic Fibroma – Associated Syndromes

- Cowden Disease
4. Keloid – Clinical Overview

- Clinical / Histology:
  - Commonly on chest, back and earlobes, darker skin and skin wounds
  - Collagen III
  - Firm, smooth, papule or plaque
  - May be painless or pruritic
  - Broad, haphazardly arranged brightly eosinophilic collagen bundles, increased fibroblasts and atrophic epidermis

- Current standard recommend avoiding surgical procedures for 6-12 months after taking oral isotretinoin
- Avoidance includes: Chemical peels, dermabrasions, lasers
- Study shows only one case of keloid development out of 504 surgical patients who used isotretinoin
- Isotretinoin causes atrophy of the pilosebaceous unit, which is where reepithelialization originates

Keloid – Associated Syndromes

- Rubinstein–Taybi Syndrome (CREB binding protein)
- Keloids are apt to develop spontaneously in adolescence or early adulthood
- Microcephaly
- Mental retardation
- Beaking of the nose
- Characteristic broadening of the terminal phalanges of the thumbs and first toes
- Multiple pilomatrixomas

Keloid – Updates From The Literature

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Outline

- What makes a tumor benign? ✓
- Benign Epidermal Tumors ✓
- Benign Dermal Tumors ✓
  - Clinical Overview ✓
  - Diagnostic Pearls ✓
  - What’s new? ✓
    - Literature Highlights ✓
    - Syndrome Associations ✓

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Notes:
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References
References


Thank You

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Figurate Erythemas and Purpuras

Figurate Erythemas

Erythema Annulare Centrifugum

- Introduction
  - Superficial and deep forms.
  - More common in adults.
  - Peak incidence in 5th decade of life.
  - Duration: days to months, often self-limiting
  - Most commonly idiopathic, but can be related to infection or other exposures.
  - Reaction pattern or “hypersensitivity” reaction to one of many antigens

Disclosures

- None

Objectives

- Discuss the following figurate erythemas and treatments
  - Erythema Annulare Centrifugum
  - Erythema Marginatum
  - Erythema Migrans
  - Erythema Gyratum Repens
- Discuss the different types of purpuras and their etiologies
  - Review basic methods of coagulation
  - Review specific purpuric syndromes
  - Discuss treatment modalities

Pathogenesis

- Infectious causes:
  - Dermatophytes (Tinea Pedis)
  - Fungal: Candida, Penicillium in blue cheese.
  - Viruses (e.g. poxvirus, EBV, varicella-zoster virus, HIV)
  - Parasites and Ectoparasites (e.g. Phthirus pubis).
- Drug induced: diuretics, NSAIDs, antimalarials, gold, finasteride, amitriptyline, etizolam
- Other: Pregnancy, certain foods, autoimmune endocrinopathies, hyper-eosinophilic syndrome and occasionally, lymphomas and leukemia.
Clinical Features

- Initial lesions begin as firm pink papules that expand centrifugally and then develop central clearing.
- Can enlarge to greater than 6 cm.
- Favors upper legs, hips and trunk.
- In the superficial form, lesions are minimally elevated, and there is desquamation at the inner margin, i.e. “trailing scale.” +/- pruritus.
- In deep gyrate erythema, the advancing edges are indurated and raised, and there is usually no scale. Non-pruritic.
- As lesions resolve, PIH is common.

Pathology

- Superficial lesions: mild spongiosis, focal parakeratosis, superficial perivascular lymphohistiocytic infiltrate
- Fairly tight aggregates around vessels, the so-called “coat sleeve” anomaly.
- Rarely eosinophils. Edema in the papillary dermis.
- Deep lesions: lymphocytic infiltrate with a sharply demarcated perivascular arrangement is present primarily within the mid and lower dermis.

Differential Diagnosis

- Tinea Corporis
- Annular Psoriasis
- Annular Urticaria
- Erythema Marginatum
- Allergic Urticarial Eruption
- Autoimmune disorders, including linear IgA bullous dermatosis, Sjögren’s syndrome and lupus erythematosus, can also have erythematous annular, arciform and polycyclic lesions.

Treatment

- If EAC is due to an underlying disorder, the skin lesions will usually resolve once the disease has been successfully treated
- Usually self-limited.
- Topical corticosteroids.
- Topical anti-pruritics and sedating antihistamines for pruritus.
- Systemic corticosteroids, however recurrence is common after discontinuation.
- Case Reports: Empiric use of antibiotics, anti-fungal agents, topical tacrolimus, topical calcipotriene, oral metronidazole, subcutaneous etanercept and subcutaneous interferon-alpha.

Erythema Marginatum

- Cutaneous manifestation of Rheumatic Fever
- ~3% of patients with untreated group A β hemolytic Streptococcal infections can develop acute rheumatic fever
- Latency period of 2-5 weeks before development of rheumatic fever
- Rash occurs in less than 10% of patients with acute rheumatic fever
- Higher incidence in children, peak age 5-15 years.
- Associated findings: Jones Criteria: Carditis, Migratory Polyarthritis, Sydenham’s chorea, fever and subcutaneous nodules.
Clinical Features

- Lesions begin as erythematous macules that spread peripherally and become patches or plaques, can be polycyclic, with NO scale.
- Usually asymptomatic.
- Migrates over a period of 12 hours (by 2–12 mm).
- Lasts from a few hours to a few days – usually transient. Can recur over a few weeks.
- Most commonly on the trunk, axillae and proximal extremities, spares face.

Erythema Marginatum

Differential Diagnosis

- Annular urticaria
- Annular erythema of infancy
- Neutrophilic figurate erythema of infancy
- EAC
- Erythema Gyratum Repens
- Hereditary periodic fever syndromes (particularly TNF receptor-associated periodic syndrome (TRAPS))
- Kawasaki disease

Treatment

- Treat underlying rheumatic fever disease.
- No specific treatment for the rash.
- Lesions usually resolve spontaneously.
- Treatment of rheumatic fever does not usually affect the rash.

Erythema Migrans

Clinical Features

- Initial cutaneous presentation of Lyme disease in 60-90% of cases
- Lyme disease infection is caused by the spirochete *Borrelia burgdorferi* and transmitted by species of the *Ixodes* tick
- Lyme disease is most prevalent in US and in Europe (Scandinavia and central Europe)

- Typically 1-2 weeks after tick detachment
- Erythematous annular plaque with light-colored central area of a bull’s eye appearance
- Favors trunk, axilla, groin and popliteal fossa
- Untreated, usually last four weeks
- Disseminated EM – EM and satellite oval-shaped widespread patches due to spirochtemia
Erythema Migrans
• Early Localized disease – EM, flu like symptoms, regional lymphadenopathy
• Early Disseminated disease – neural involvement (facial nerve common), migratory joint pain, carditis, conjunctivitis
• Chronic Disease – acrodermatitis chronica atrophicans, persistent neurologic and rheumatologic symptoms

Clinical presentation AND either history of exposure or laboratory evidence of infection
• PCR, culture, serological evidence
• Borrelia antibodies detection in serum might not be specific as peak specific IgM response is 3-6 weeks into infection
• Serologic tests will stay positive for months to years

Diagnosis

Pathology
• Superficial and deep perivascular and interstitial infiltrate of lymphocytes, sometimes with abundant plasma cells and eosinophils
• Warthin-Starry stain is positive in 50% showing spirochetes

Differential Diagnosis
• Arthropod assault
• Erysipelas
• Cellulitis
• Non-pigmented fixed drug eruption
• Allergic contact dermatitis

Treatment
Erythema Gyratum Repens

- Rare, males=females, Caucasians
- Gyrate polycyclic rapidly growing erythematous plaques with a trailing scale
- Migrates up to 1cm/day
- Wood grain resemblance due to “rings within rings” pattern
- Can be pruritic
- Additional findings: acquired ichthyosis, palmoplantar keratoderma and hypereosinophilia

Erythema Gyratum Repens

- Unknown etiology, malignancy association >80% cases, i.e. the most specific paraneoplastic syndrome
- 1/3 patients= lung cancer, 8% esophageal cancer, 6% breast cancer
- The figurative eruption can precede, occur concurrently or appear after the diagnosis of the neoplasm
- Non-paraneoplastic cases: TB, CREST syndrome, pregnancy, bullous dermatosis

Differential Diagnosis

- Erythema annulare centrifugum
- Erythema migrans
- Resolving pityriasis rubra pilaris
- Erythrokeratoderma variabilis

Erythema Gyratum Repens

- Treatment: identify and treat underlying malignancy

Purpuras
**Definition**

- Visible hemorrhage into the skin or mucous membranes.
- Divided into 6 subsets:
  - Petechiae
  - Macular Purpura
  - Macular ecchymoses
  - Palpable purpura
  - Non-inflammatory retiform purpura
  - Inflammatory retiform purpura

- **Petechiae** (<4 mm red-purple hemorrhagic macules):
  - Seen in: ITP, TTP, DIC, Platelet function defects, Aspirin/NSAID use, trauma, valsalva maneuver, etc.

- **Macular Purpura** (5-9 mm red-purple hemorrhagic macules that don’t blanch):
  - Seen in: Hypergammaglobulinemia of Waldenstrom, thrombocytopenia

- **Macular Ecchymoses** (>1 cm red-purple-green patch due to bleeding in skin):
  - Seen in: Anticoagulant use, hepatic insufficiency, Vitamin K deficiency, DIC, Actinic purpura, steroid use, Vitamin C deficiency, Ehlers-Danlos disease, platelet function diseases, etc.

- **Palpable Purpura** (raised, non-blanching inflammatory purpura with erythema):
  - Seen in: Idiopathic, infection IgG/IgA/IgM complexes, Hypergammaglobulinemia purpura of Waldenstrom, Urticarial vasculitis, Mixed cryoglobulinemia, Rheumatic vasculitis, ANCA associated diseases, etc.

- **Non-inflammatory retiform purpura** (mottled lace-like livedo reticularis pattern causing a purple-ish discoloration):
  - Seen in: Heparin necrosis, thrombocytosis, TTP, cryoglobulinemia, ecthyma gangrenosum, Protein C/S deficiency, warfarin necrosis, livedoid vasculopathy, cholesterol emboli, etc.

- **Inflammatory retiform purpura** (visible hemorrhage into skin or mucous membranes in the livedo reticularis pattern):
  - Seen in: IgA vasculitis, mixed cryoglobulinemia, polyarteritis nodosa, chillblains, Wegener’s granulomatosis, livedoid vasculopathy, etc.

- **Livedo Reticularis**
  - Seen due to blood flow regulation in dermal and subcutaneous vessels and shows a net like pattern
  - Retiform purpura is due to occlusion of vessels in the case of livedo reticularis, distinguish the 2 by presence or absence of purpura.

**Coagulation**
Coagulation

- Primary hemostasis consists of the formation of a platelet plug that is sufficient for minor injuries to the microvascular system.
- If the size of the vessel or injury is too large, secondary hemostasis with clot formation is necessary.
- Too little clotting → death by hemorrhage.
- Too much clotting → thrombosis, embolus, necrosis.
- Requires extensive regulation and balance between procoagulant, anticoagulant, and fibrinolytic pathways.

Coagulation Related Pathways

Dermatology. 3rd Edition, Bolognia.

Platelet Plug (Primary Hemostasis)

http://www.sharinginhealth.ca/multimedia/images/hemostasis_Kathryn_Dorman.jpg

Thrombin (factor II)

- Generated in small amounts from primary clot.
- Activates platelets, leads to binding of procoagulant factors.
- Also stimulates release of factor V from platelet granules.
- Activates tissue factor Vila.
- Activates Factor IX to IXa and Factor X to Xa.

Anticoagulant pathway

- Initiation phase of clotting is down-regulated by tissue factor pathway inhibitor (TFPI) and antithrombin III (ATIII).
- Both bound to heparin sulfate molecules on endothelial cells.
- Capture activated clotting factors and prevent them from leaving the vicinity.
- TFPI can inactivate factor Xa; ATIII can neutralize thrombin, factor IXa, Xa, XIIa.
- Thrombomodulin/protein C/protein S.
- Important in large vessels.
- Thrombin from clot bind to thrombomodulin, and thus loses its ability to cause procoagulatory effects.
- Activates protein C → inactivates Factor Va, VIIIa.
Tests for Coagulation

- Thorough history and physical exam
- Labs: Platelet count, PT, and APTT
- If PT or APTT prolonged, can repeat testing using 1:1 mixture of pt plasma and normal plasma. If time normalizes, then there is a factor deficiency.
- Prolonged PT + normal APTT: Factor VII deficiency or use of PO anticoagulant
- Prolonged APTT + normal PT: use of Heparin, lupus anticoagulant, acquired factor VIII deficiency, or von Willebrand Disease
- Prolonged PT + APTT: fibrinogen deficiency, prothrombin, factor V or Factor X deficiency

Pigmented Purpuric Eruptions

- Diseases characterized by petechial hemorrhage likely due to capillaritis
- Minimal inflammation and hemorrhage of superficial papillary dermal vessels
- Source of inflammation unknown and no coagulation abnormalities
- Several variants

Schamberg's Disease

- Yellow-brown patches with an oval to irregular outline, pinpoint petechiae
- Most common form, peak frequency in middle aged to older men
- Usually involves lower extremities
- Stasis purpura clinically has more hemosiderin and less petechiae

Purpura annularis telangiectodes of Majocchi

- Uncommon, adolescents, young adults, especially women
- 1-3 cm annular plaques that slowly expand, punctate telangiectasia and petechiae within border, possible yellow center
- Trunk, proximal lower

Rare Variants

- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum: Schamberg like- purpuric red-brown lichenoid papules
- Eczematid-like purpura of Doucas and Kapetanakis: Scaly petechial or purpuric macs, paps and patches, usually pruritic
- Lichen aureus: solitary patch, color varies from golden to rust to purple brown

Lichen Aureus

http://www.cortesedermatology.com/dermatitis-images.html
Histology
- Red cell extravasation, endothelial swelling, perivascular lymphs, and hemosiderin containing macrophages
- Lichen aureus and Gougerot-Blum variants are characterized by lichenoid infiltrate
- Eczematid like purpura of Doucas and Kapetanakis often has spongiosis, patchy parakeratosis

Treatment
- Topical steroids especially if pruritic
- PUVA, NBUVB
- Ascorbic acid 500 mg BID with Rutoside 50 mg BID
- Cyclosporine

Hypermagammaglobulinemic Purpura of Waldenstrom
- Associated with a hypergammaglobulinemia
- Presence of small circulating immune complexes containing IgG or IgA rheumatoid factor
- IgG and IgA rheumatoid factors are highly soluble, which may explain the speed with which lesions appear and resolve
- Can be primary or secondary
- In younger patients, it is usually primary, but eventually patients may develop an autoimmune connective tissue disease (usually Sjogren’s)
- Complications include the development of a monoclonal gammopathy, lymphoma, or multiple myeloma
- Differential Dx: classic cutaneous small vessel vasculitis syndromes

Pathology
- Histopathology may show hemorrhage, a mild perivascular infiltrate, or a leukocytoclastic vasculitis
- Image shows dilated superficial capillaries, extravasation of red blood cells, and sparse mononuclear infiltrate without evidence of vasculitis

Hypermagammaglobulinemic Purpura of Waldenstrom
- Usually affects women
- MK purpura, tingling, or burning may precede the presence of purpura
- Symptoms are exacerbated by prolonged standing, tight fitting garments, and heat
- Petechiae or larger purpuric macules on lower extremities is the most common presentation
- Labs: Polyclonal hypergammaglobulinemia, elevated ESR, anti-RO and anti-LaAbs are usually present and may predict a higher likelihood of developing an autoimmune connective tissue disease

Treatment
- Limited treatment options
- Aspirin
- Support stockings
- Avoidance of triggers such as alcohol, prolonged standing
Mondors Disease:
• First described in 1939 by Henri Mondor
• Superficial thrombosis (SVT)
• Self limited
• Most commonly seen in patients aged 30-60 year old
• Female > male; 3:1

Predisposing factors include:
• Increased coagulation state
• Thoracic surgical procedures
• Breast surgery
• Tight clothes
• Mammary infections
• Pendulous breast
• Chronic inflammatory disease states
• Presents as a fibrous painful cord, with or without skin retraction, and with or without local inflammation.
• Can present on the chest wall, involving other venous areas, and following breast disease

Clinical Presentation

Work up
• Complete history and physical
• Ultrasonographic to confirm
• Mammography if suspicion of breast cancer

Most cases are idiopathic
• In a pool analysis of the four largest and most recent series:
  • Idiopathic (32.5%)
  • Breast Cancer (6.3%)
  • Iatrogenic (11.9%)
  • Inflammation (4.8%)
  • Trauma (32.5%)
    • Including: injury, muscular, heavy load, tight support, thrombophilia, hormone therapy

Treatment
• Mondor’s on chest wall: Spontaneous resolution in 2-8 weeks
• Other locations: less known, can consider anticoagulation and etiologic management if known. Surgery in persistent cases.
• Mondor’s after breast surgery: This is not a thrombotic process. Reports suggest that manual rupture of the fibrous bands ensures immediate functional recovery and pain relief.
• Penile Mondor’s: conservative treatment.
• There is approximately 13% recurrence

• There is approximately 13% recurrence

Conclusion
• Reviewed the four “classic” figurate erythemas: erythema annulare centrifugum, erythema marginatum, erythema migrans, and erythema gyratum repens
• Reviewed specific purpuric syndromes and treatment modalities
• Provided practical applications for these dermatological conditions
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Thank You
Cysts and Disorders of the Hair

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No Conflicts to Disclose

Hair Anatomy

Keratins 6a, 16 are expressed in outer root sheath

Hair Anatomy

Hair Anatomy – Vertical Section
**Hair Anatomy – Vertical Section**


**Hair Anatomy – Transverse Section**


**Hair Anatomy Regions**


- **Infundibulum**: epidermis to the insertion of the sebaceous gland
- **Isthmus**: opening of the sebaceous glands to attachment of arrector pili muscle

**Hair Anatomy Regions**


- **Infundibulum**: keratinizes with granular layer
- **Isthmus**: contains region known as the "bulge"; keratinizes with absence of granular layer = trichilemmal keratinization; inner root sheath is lost at this level; outer root sheath develops a corrugated, dense pink cornified layer

**Regions of Importance**

- **Bulge** = segment of outer root sheath at the arrector pili insertion; epithelial stem cells reside here
- **Bulb** = melanocytes generate hair color; location of inflammatory infiltrate in alopecia areata
- **Critical line of Auber** = widest diameter of lower portion of hair follicle; below line of Auber is where the bulk of mitotic activity occurs

**Anatomy of Hair Growth Cycle**

Androgenetic Alopecia

- Androgen-dependent, resulting from the conversion of scalp terminal hairs into miniaturized vellus hairs in a characteristic pattern.
- Type II 5-alpha reductase enzyme activity and DHT levels are increased in AGA.
- Histology shows normal number of follicles, increased vellus and telogen hairs, no significant inflammation.
- Treat with minoxidil, finasteride, dutasteride, or hair transplantation.
Telogen Effluvium
• Caused by pregnancy, malnutrition and other stressors that trigger a large numbers of hairs to enter the telogen phase simultaneously.
• Most common drug causes: retinoids, anticonvulsants, antithyroid medications, anticoagulants, lithium, interferons, and β-adrenergic blocking agents.
• Hair loss begins about 3 months after a definable precipitating event.
• Hair pull positive for 2 or more telogen hairs.

Trichotillomania
• More common in females and in children.
• Hair is pulled causing patchy or full alopecia; often have bizarre shapes, irregular borders, and contain hairs of varying lengths.
• Histology shows trichomalacia, pigmented hair casts, and empty follicles.
• Treat with behavioral modification.
• Clomipramine first line pharmacologic.

Alopecia Areata
• Presents as round or oval, non-scarring patches of hair loss; other presentations include totalis, universalis, and ophiasis patterns.
• Exclamation point hairs and yellow dots on trichoscopy.
• Most common nail change is pitting.
• Histology shows lymphocytic inflammation in "swarm of bees" pattern around lower portion of follicle.
• Treatment: ILK, minoxidil, topical anthralin, and combination therapy.
Temporal Triangular Alopecia

- Present at birth or acquired usually within the first decade of life.
- Clinically, lancet shaped patch of alopecia, usually in the temporal region(s).
- Very fine vellus hairs can be seen with magnification

Anagen Effluvium

- Sudden onset loss of anagen hairs.
- Triggered by chemotherapy, radiation, or chemicals (thallium, arsenic)

Other Non-Scarring Alopecias

- Post-operative (pressure induced): related to prolonged pressure, usually on the occipital scalp during surgery.
- Psoriasis associated alopecia: occurs with the shedding of thick psoriatic plaques; may also be related to TNF alpha inhibitors.

Scarring Alopecias

- Central Centrifugal Cicatricial Alopecia
  - Follicular degeneration from premature desquamation of inner root sheath
  - Often seen in African-American women, with follicular loss on the crown or vertex of the scalp, expanding in a symmetric, centrifugal fashion
  - Pathology: Premature desquamation of IRS, mononuclear infiltrate at isthmus, eccentric epithelial atrophy, concentric lamellae fibroplasia of affected follicles
  - Treatment: Doxycycline; potent topical corticosteroid

Central Centrifugal Cicatricial Alopecia

- Pathology images

**Lichen Planopilaris**
- Related to lichen planus; etiology remains unknown
- >50% associated with cutaneous or oral LP
- Scattered foci of hair loss associated with perifollicular erythema, follicular spines and scarring; often pruritus and tenderness
- Pathology: Band-like lichenoid interface dermatitis of superficial follicular epithelium, affecting upper portion of hair follicle
- Treatment: Antimalarials, topical/intralesional/oral corticosteroids

**Discoid Lupus Erythematosus**
- Alopecia with erythema, epidermal atrophy, dilated and plugged follicular ostia
- Pathology: Vacuolar interface of epidermis and follicular epithelium, superficial and deep inflammation with dermal mucin
- Treatment: Oral antimalarials, topical/intralesional/oral corticosteroids
- 50% of patients with DLE have scalp involvement

**Acne Keloidalis**
- Possible foreign body reaction to hair fragments or ingrown hairs
- Follicular papules/pustules that can progress to keloidal papules with surrounding alopecia on occiput scalp/posterior neck
- Pathology: Lymphocytic/plasmacytic inflammation at isthmus/lower infundibulum with lamellar fibroplasia and loss of sebaceous glands; total follicular destruction in advanced disease
- Treatment: Topical steroids, oral antibiotics, surgical excision

**Dissecting Cellulitis of the Scalp**
- Firm nodules on vertex and upper occiput develop into boggy oval and linear ridges with purulent, foul-smelling drainage though minimal associated pain
- Pathology: Perifollicular lymphocytic/neutrophilic inflammation affecting lower half of dermis and subcutis; end stage with loss of follicles
- Treatment: Oral isotretinoin, intralesional corticosteroids, oral antibiotics, TNFα inhibitors, surgery

**End-Stage Traction Alopecia**
- Prolonged traction
- Commonly seen in African American women with scarring alopecia of bitemporal and frontal scalp
  - Lag period of a decade or more exists between traction and hair loss
- Pathology: Total number of hairs markedly decreased, persistent sebaceous glands, columns of connective tissue replacing former follicles
- Treatment: adopt alternative hair practices, topical minoxidil, ILK, hair transplant
Pseudopelade of Brocq

- Not a distinct disease - pattern of end stage alopecia of other various forms of cicatricial alopecia
- Leads to asymptomatic, irregularly shaped, atrophic patches of alopecia
- Pathology: Atrophy, loss of sebaceous epithelium, fibrosis with absent hair follicles
- No successful treatment

Other Cicatricial Alopecias

- Aplasia Cutis Congenita: disruption of intrauterine skin development causing congenital absence of skin/subcutis leading to atrophic, coin-sized alopecia
- Keratosis Folicularis Spinulosa Devalcans: X-linked recessive disorder of abnormal follicular keratinization seen in childhood with alopecia of scalp, eyebrows and eyelashes; remits in puberty

Biopsy Techniques of the Hair

Hair/Scalp Biopsy - Indications

- A common procedure used to evaluate the histopathologic processes that can present in many clinical ways.
- May be used to assist with the diagnosis of scarring and non-scarring alopecias, effluvium conditions, infectious diseases of the hair and scalp, hair shaft abnormalities, and many others.
- Most often achieved by a “punch” biopsy technique, but in certain conditions the hair shafts can be:
  - Pulled/Plucked – Telogen/Anagen Effluvium
  - Cut – Nits, Hair shaft anomalies (trichorrhexis nodosa, pili torti, trichothiodystrophy, etc.)

Hair/Scalp Biopsy – Lesion Selection

- As a general rule with any biopsy, the area selected for sampling should be from fresh, but well-developed lesional tissue.
  - For inflammatory conditions involving the hair, areas of active inflammation, erythema, or edema should be chosen.
  - For scarring conditions of the hair or scalp, the peripheral edge of the involved tissue is more likely to provide meaningful pathological changes.
  - For non-inflammatory conditions (i.e. androgenetic alopecia), any involved tissue may be sampled.
  - For chronic diseases, older lesions should be selected

Hair/Scalp Biopsy – Lesion Selection

- On the face, there are a few areas that should be recognized as potentially dangerous. These areas correspond to arteries that lie superficially and may be transected during the procedure.
  - Temple – lateral to the eyebrow (temporal artery)
  - Supraorbital notch – medial brow (supraorbital artery)
Hair/Scalp Biopsy Techniques: Skin Preparation and Local Anesthesia

- After site selection, the area must be adequately prepped and anesthetized.
- Local skin preparation can be achieved with alcohol, chlorhexidine gluconate, and iodine formulations.
- Lidocaine is the most commonly used local anesthetic for skin biopsy, usually delivered by local infiltration.
  - For scalp biopsies especially, lidocaine mixed with epinephrine may offer better hemostasis than plain lidocaine.
  - Approximately 10 minutes should be given after local infiltration of lido + epi to maximize the epinephrine’s vasoconstrictive effects.
- EMLA achieves ~5mm depth after 2 hours of occlusion.

Punch Biopsy: Considerations and Technique

- Care must be taken to ensure that enough tissue is sampled to show representative changes.
  - In conditions affecting the hair, this often requires sampling down to the subcutaneous fat, as many of the inflammatory processes involve the hair bulb.
  - The necessary depth depends on anatomic site, age of the patient, nature of the disease, etc.
  - Occasionally a 6mm punch is required to obtain the subcutaneous fat.
- The punch should be pushed into the skin and rotated in one direction, as back-and-forth twisting may shear the epidermis completely off.
- Once the subcutaneous plane has been reached, the clinician should feel a decrease in resistance in the downward direction.

Punch Biopsy: Considerations and Technique

- Once the punch has been advanced to the appropriate depth, care must be taken to ensure the specimen:
  - 1. contains sufficient deep tissue
  - 2. is not damaged by forceps during removal
- To accomplish these, the following may be employed:
  - 1. use fine, sharp surgical scissors to carefully separate the base of the punch from the underlying tissue (subcutis).^2
  - 2. gently, use smooth-tipped forceps to grasp the specimen (teeth on forceps may cause crush artifact).
  - 3. use the lidocaine needle to “spear” the specimen and retract it from the base

What is Crush Artifact?

- Aggressive handling of the biopsy specimen during extraction can damage the tissue, rendering the histologic evaluation difficult or impossible to interpret.

[^2]: “Spear” technique using needle from lidocaine syringe – minimizing crush artifact.
Punch Biopsy Technique – Hemostasis and Closure

- After the specimen has been obtained and placed in the correctly labeled container, the defect may require:
  - Hemostasis (electrocautery, aluminum chloride, Monsel’s solution) – care should be taken to minimize the amount of epidermis damaged by electrocautery, which may cause scarring.
  - Closure (usually for punch biopsy sites > 2-3mm)
    - Simple interrupted sutures usually suffice.
    - A horizontal mattress suture may be used to stop bleeding.
    - A vertical mattress suture may help to draw edges together in larger (i.e. 6-8mm) defects if there is little tissue mobility.
    - On the scalp, prolene 3-0 to 4-0 is usually sufficient, and the blue color makes the material easier to identify against a background of hair (nylon can be difficult to find).

HAIR SHAFT ABNORMALITIES

Hair Shaft Abnormalities WITH Increased Fragility

- Trichorrhexis Nodosa: Incomplete fracture with frayed ends resembling two paintbrushes against each other.
  - Seen in Menkes disease (ATP7a mutation), trichothiodystrophy (ERCC2, ERCC3 mutation), Netherton’s syndrome (SPINK5 mutation), arginosuccinic aciduria (argininosuccinate lyase deficiency), Citrullinemia (argininosuccinic acid synthetase deficiency)
  - Most common hair shaft defect

- Trichothiodystrophy: Sulfur-deficient hair with alternating light and dark bands under polarizing light
  - Seen in trichothiodystrophy

- Trichorrhexis Invaginata: Ball & socket or collapsible telescope; “bamboo hair”.
  - Seen in Netherton’s syndrome

- Pili Torti: Hair fibers flattened and twisted at 180 degree angles.
  - Seen in Bjornstad syndrome (BCS1-like protein deficiency), Crandall syndrome, Menkes disease, Netherton’s syndrome

- Monilethrix: Beaded appearance of hair due to periodic thinning of hair shaft.
  - AD/hHB6, hHB1
  - AR/Desmoglein 4
  - Patients normal at birth, but develop short, brittle hair within a few months

Hair Shaft Abnormalities WITHOUT Increased Fragility

- Pili Trianguli et canaliculi: Premature keratinization of a triangular-shaped internal root sheath; “spun-glass hair”.
  - Persistent longitudinal groove along the long axis of the hair
  - Seen in Uncombable Hair Syndrome. Hair appears dry, dull, frizzy, short, and light in color, unmanageable
Hair Shaft Abnormalities WITHOUT Increased Fragility

- Pili Annulati: Alternating light and dark bands seen with reflected light
  - Light bands due to abnormal air-filled cavities
- Loose Anagen Hair: Anagen hairs without inner root sheath; ruffled proximal cuticle
  - Seen in loose anagen hair syndrome - hair is easily pulled from the scalp
- Wooly hair: Tightly curled hair; may see axial twisting, breaks, and splitting.
  - Seen in Naxos disease (Plakoglobin mutation), Carvajal syndrome (Desmoplakin mutation), Wooly hair and skin fragility syndrome, Diffuse partial wooly hair syndrome (mutations), Diphtheria pertussis (pertussis toxin)
  - Curly hair: Large loose spiral hair
- Curly hair: Loose spiral hair
- Trichoptilosis: Longitudinal splits in hair shaft due to trauma
- Trichonodosis: Knots develop in curly hair due to combing/rustling of hair
- Pili bifurcati: Two hairs, which occupy the same follicle, bifurcate and then rejoin
- Pili multigemini: Multiple hair shafts from one papilla

Cysts

- A cyst is a walled-off sub-epidermal cavity filled with fluid, keratin, or mucin
- Cysts can be classified by anatomic location, embryologic derivation or histologic features
  - 3 categories for classification:
    - Stratified squamous epithelium
    - Non-stratified squamous epithelium
    - Absence of epithelium

Derivation

Cysts with an Epithelial Lining
Epidermal Inclusion Cyst
- Common cyst found mostly on face and upper trunk
- Arises from the follicular infundibulum
- There is a possible genetic predisposition: Gardner’s Syndrome, Nevoid Basal Cell Carcinoma Syndrome, Pachyonychia Congenita
- Lined by stratified squamous epithelium with granular layer and contains lamellated keratin

Milia/Milium
- Arises from vellus hairs
- Common in children
- Common on face
- Widespread distribution found in hereditary Trichodysplasia (Marie-Unna Hypotrichosis); Oral-Facial-Digital Syndrome Type 1; Rombo Syndrome; and Bazex Syndrome

Pilar Cyst
- Clinically similar to EIC, but located on the scalp
- May be inherited as an autosomal dominant trait
- Frequently multiple
- Lined by stratified squamous epithelium with no granular layer; cyst contains homogenized keratin

Proliferating Trichilemmal Cyst
- Slow-growing nodule on scalp
- May increase in size
- Well-circumscribed nodule in the deep dermis with cystic and solid patterns; neoplastic cells with mitotic figures; tumor with pushing margins

Vellus Hair Cysts
- Commonly found on the trunk/chest as dome-shaped skin-colored to pigmented papules
- May be inherited in an AD manner
- DCR: eruptive vellus hair cysts
- May be seen in the setting of Pachyonychia Congenita type 2
Lined by squamous epithelium with granular layer with contents lamellated keratin and vellus hairs

Steatocystoma
- Lined to colored to yellow nodule that may drain oily fluid
- Common on chest, axilla, and groin
- Can be inherited as an autosomal dominant condition called Steatocystoma Multiforme
- Seen in conjunction with eruptive hair cysts and in Pachyonychia Congenita
- Cyst lined by stratified squamous epithelium with granular layer with thin, corrugated eosinophilic cuticle with adjacent sebaceous lobules

Dermoid Cyst
- Congenital cyst most often found on the face (lateral eyebrow)
- Lined by squamous epithelium with granular layer with cysts contain lamellated keratin; multiple pilosebaceous units near cyst lining

Hidrocystoma
- Skin colored to translucent or even blue cysts on the face
- Can be classified as Eccrine or Apocrine
- Associated with Ectodermal Dysplasia; Schopf-Schulz-Passarge Syndrome
- Cyst lined by layers of epithelial cells

Bronchogenic Cyst
- Most commonly found in the suprasternal notch at birth
- Formed from trapped respiratory epithelium of the trachea during embryologic development
- Lined by pseudostratified ciliated columnar epithelium with goblet cells; cyst lining often surrounded by smooth muscle, cartilage, mucous glands, or lymphoid follicles

Thyroglossal Duct Cyst
- Represent failed migration/remnant of the thyroglossal duct
- Commonly found on the midline neck
Lined with cuboidal, columnar, or stratified squamous epithelium containing characteristic thyroid follicles in cyst wall

Branchial Cleft Cyst
- Often present in the second or third decades of life
- Occur along the SCM, preauricular area, or the mandible
- Due to incomplete involution of branchial cleft structures
- Consider CT or MRI before removal

Branchial Cleft Cyst
- Lined by stratified squamous epithelium or pseudostratified ciliated columnar epithelium surrounding lymphoid tissue
- Common on the thighs of young women
- Can be found on the buttocks
- Epithelial lining is cuboidal or columnar with cilia on the surface and collagen and vessels deep to the wall

Cutaneous Ciliated Cyst
- Occur on the ventral penis near the glans in young men
- Thought to be a remnant of the urethral epithelium

Median Raphe Cyst
- Pseudostratified columnar epithelium with or without mucinous cells
Other

- Pigmented follicular
- Follicular Hybrid
- Ciliated Cyst of the Vulva

Cysts without an Epithelial Lining

Digital Myxoid Cyst

- Most commonly found on the dorsal distal phalanx of the fingers
- Drain clear gelatinous material if punctured
- Can have an underlying connection to a joint space
- Often traumatizes the nail matrix causing nail changes

Pseudocyst of the Auricle

- Usually presents as a painless swelling of the scaphoid fossa in middle-aged men

Pilonidal Cysts

- Not a true cyst since it is devoid of lining; consists of a large pool of mucin-containing spindle/stellate fibroblasts
**Mucocele**
- Caused by a disruption of the minor salivary gland ducts
- Commonly located on the lower labial mucosa
- Accumulation of mucinous material

**Ganglion Cyst**
- Large mucinous filled cysts attached to a tendon sheath or joint capsule but not communicating with the joint space
- Mucin is thought to be produced from fibroblasts
- Found on volar wrists, dorsal wrists, fingers, feet or knees

**Metaplastic Synovial Cyst**
- Occurs at sites of trauma or surgery
- May be lined by reactive cuboidal or epithelioid cells
- Villous projections into cystic cavity
- Frequently connected to the epidermis through fistulous tracts

**References**
- Bolduc, Chantal, MD, Leonard Sperling, MD, and Jerry Shapiro, MD. "Primary Cicatricial Alopecia." Journal of the American Academy of Dermatology 75.6 (2016): 1081-111. Print. (2)

THANK YOU!
Premalignant and Malignant Non-Melanoma Skin Cancer

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Objectives

• Briefly review disease pathogenesis, presentation, and treatment options
• Discuss updates in the literature in regard to the various premalignant and malignant lesions
• Introduce ongoing research and future studies in the field of non-melanoma skin cancers

Premalignant Lesions

Actinic Keratosis

• Most common precancerous lesion
  • Can progress to SCC
  • 0.1-0.6% per lesion-year
• Treatment options:
  • Cryotherapy
  • Topical treatments:
    • 5-FU (5-5.5%)
    • Imiquimod 5% cream
    • Ingenol mebutate
    • Diclofenac
  • Photodynamic therapy
  • Destructive/Surgical management

5-FU, imiquimod, ingenol mebutate and diclofenac are similarly efficacious but have different adverse effects and cosmetic outcomes.

Use dependent on patient preferences, prior physician and patient experience, and cost.
**Actinic Keratosis**

- Single course of 5% fluorouracil cream effectively reduces AK counts and need for spot treatment for longer than 2 years
- Fewer hypertrophic AKs in the treatment group at 6 months

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**Basal Cell Carcinoma**

- Most common type of skin cancer
  - 2 million Americans affected every year
- Metastasis is extremely rare
  - 0.0028-0.55% metastatic rate
  - 50% of deaths from BCC result from direct extension into vital structure rather than metastasis

**Pathogenesis**

- Arise from pluripotent cells associated with hair follicle
- Mutations that activate hedgehog signaling pathway
  - Sonic hedgehog
  - Patched 1 - most common
  - Smoothened
Basal Cell Carcinoma

Pathogenesis
- Arise from pluripotent cells associated with hair follicle
- Mutations that activate hedgehog signaling pathway → cell growth
  - Sonic hedgehog
  - Patched 1 - most common
  - Smoothened

Treatment options:
- Surgical
  - Excision
- Mohs Micrographic surgery (MMS)
- Curettage and electrodessication
- Radiation
- Topical treatments: Imiquimod, 5-FU
- Hedgehog pathway inhibitors (HPIs)

Follow up of 104 patients with locally advanced or metastatic BCC from the pivotal ERIVANCE study
- Median duration of vismodegib exposure was 12.9 months
- Increased response rates:
  - Metastatic disease - 30.3% to 33.3%
  - Locally advanced - 42.9% to 47.6%
- Median duration of response improved from 7.6 - 9.5 months for locally advanced disease
- No change in side effect profile or new emerging safety signals

8 articles (704 patients) systematically reviewed to evaluate clinical experience with hedgehog pathway inhibitors
- Vismodegib
  - Significant, consistent effect on locally advanced and metastatic BCC
  - Superior responses for metastatic BCC compared to traditional treatments
- Not enough data to review sonidegib since its approval in 2015
Basal Cell Carcinoma

- Treatment options:
  - Surgical
    - Excision
  - Mohs Micrographic surgery (MMS)
  - Curettage and electrodesiccation
  - Radiation
- Topical treatments: Imiquimod, 5-FU
- Hedgehog pathway inhibitors (HPIs)
  - Vismodegib (2012) and sonidegib (2015)
  - Itraconazole

29 patients enrolled in open-label study
- Cohort A: 200mg twice daily x 1 month
- Cohort B: 100mg twice daily x 2.5 months

- Reduced tumor size and promoted re-epithelialization in 8 patients
- None of the BCCs completely cleared
- Average tumor reduction with lower dosage (Cohort B) was comparable to higher dosage (Cohort A)

Squamous Cell Carcinoma (SCC)

- Second most common skin cancer in the United States
- 700,000 cases annually

Stage Union for International Cancer Control (UICC) 2010 Brigham and Women’s Hospital (BWH) 2013

T1 Tumor < 2 cm in greatest dimension 0 high-risk factors*
T2 Tumor > 2 cm in greatest dimension 0 high-risk factors*
T2a 1 high-risk factors*
T2b 2-3 high-risk factors*
T3 Tumor with invasion of deep structures (muscle, cartilage, bone) > 4 high-risk factors* or bony invasion
T4 Tumor with invasion of axial skeleton or direct perineural invasion of skull base

* BWH high-risk factors: tumor diameter > 2cm, poorly differentiated histology, perineural invasion > 0.1mm, tumor invasion beyond fat

- National comprehensive cancer network (NCCN) high-risk features:
  - Tumor location- mucosal surfaces, genitalia, periorbital, nose, lips, chin, ears, temples, sites of prior burn scars or radiation
  - Tumor diameter > 2cm
  - Tumor depth > 2mm (Clark level IV)
  - Perineural invasion
  - Lymphovascular invasion
  - Poorly differentiated histopathology
  - Immunosuppression
  - Solid organ transplant (particularly kidney) > bone marrow transplant
Squamous Cell Carcinoma

- National comprehensive cancer network (NCCN) high-risk features:
  - Tumor location: mucosal surfaces, genitalia, periorbital, nose, lips, chin, ears, temples, sites of prior burn scars or radiation
  - Tumor diameter > 2 cm
  - Tumor depth > 2 mm (Clark level ≥ IV)
  - Perineural invasion
  - Lymphovascular invasion
  - Poorly differentiated histopathology
  - Immunosuppression
    - Solid organ transplant (particularly kidney) > bone marrow transplant

- Additional management considerations for high risk SCC:
  - Sentinel lymph node biopsy (SLNB)
    - 2015 meta-analysis recommends considering SLNB for patients with T2 lesions
  - Radiographic imaging to assess disease burden for high risk patients
    - CT, MRI, PET
  - Biomarkers for characterization of aggressive SCC
    - Matrix-metalloproteinases, p300, nuclear IKK

- Immunotherapy for metastatic SCC
  - Metastatic SCC has elevated expression of epidermal growth factor receptor (EGFR)
  - Cetuximab - EGFR inhibitor
  - Panitumumab - monoclonal antibody against EGFR
  - Combination therapy of cetuximab, fluorouracil, carboplatin, or cisplatin
  - PD-1 inhibitors
  - CTLA-4 inhibitor

Chemoprevention
- 2 or more NMSC + 10 or more AKs
  - Acitretin – 0.2-0.4 mg/kg/day
  - 4 month up taper
  - CBC, CMP, lipids, LFTs q3mo
  - Continued indefinitely
- Nicotinamide (niacinamide or nicotinic acid) – 500mg BID
  - 23% fewer people had NMSC
  - Lower side effect profile and no lab monitoring

Cutaneous T-Cell Lymphoma

- T cell non-Hodgkin’s lymphomas
- Average of 6 years from presentation to diagnosis
  - Clinically and histopathologically can resemble benign inflammatory disorders including psoriasis and atopic dermatitis

- High-throughput TCR sequencing (HTS) detected T cell clones in 46/46 CTCL patients
  - More sensitive and specific than TCRγ PCR
  - Successfully discriminated CTCL from benign inflammatory diseases
  - Demonstrated hematogenous spread of small numbers of malignant T cells in patients with new skin lesions
Cutaneous T-Cell Lymphoma

- High-throughput TCR sequencing (HTS)
- Accurately assessed responses to therapy and facilitated diagnosis of disease recurrence
- Diagnosed CTCL in all stages
- Provided insights into the cell of origin and location of malignant CTCL cells in skin

- Largest cohort of patients with advanced MF/SS from 29 international sites
- 1,275 patients
- Identifies prognostic values to help stratify advanced-stage patients

- Interleukin (IL-31), Th2 cytokine
- Increased in serum of CTCL patients
- Found in IL-31 may play a role in CTCL pruritus by exerting indirect effects on sensory nerves through epidermal neoplastic T cells and keratinocytes to transmit itch

Merkel Cell Carcinoma

- Neuroendocrine carcinoma
- Linked to UV exposure and Merkel cell polyomavirus
- In the United States, the age-adjusted incidence is estimated at 0.24 per 100,000 person-years

- Review of Treatment
  - Wide local excision is the mainstay of tx (NCCN) + SLN
  - Immunotherapy with PD-1/PD-L1 inhibitors is a promising treatment option for advanced or metastatic disease
  - Clinical trials are currently in progress to further evaluate these novel therapeutic agents
Merkel Cell Carcinoma

- A case of metastatic MCC with a significant response to nivolumab—humanized IgG4 monoclonal PD-1 inhibitor

Merkel Cell Carcinoma

- 26 adults with advanced Merkel-cell carcinoma without previous systemic treatment
- Pembrolizumab, PD-1 inhibitor, dosed at 2mg/kg for 3 weeks
- Objective response rate was 96%, 4 patients had a complete response, and 10 had a partial response

Summary

- Topicals remain a viable option for chemoprevention and treatment of AKs
- Hedgehog pathway inhibitors, especially irtraconazole, continue to be studied for advanced BCC
- Staging for invasive SCC continues to be utilized to help determine prognosis
- High throughput sequencing is a new diagnostic tool for CTCL
- PD-1 inhibitors may be a potential treatment option for MCC in the future

References (AKs and BCC)


References (SCC)

References (EMPD)

• Azmahan, Abdullatif et al. Androgen receptor, androgen-producing enzymes and their transcription factors in extramammary Paget disease. Human Pathology. 49(11), 1682 - 1689.
• Plaza, Jose et al. HER-2/neu expression in extramammary Paget disease: A clinicopathologic and immunohistochemical study of 47 cases with and without underlying malignancy. Journal of Cutaneous Pathology. 2009; 36(7), 729-733.

References (MPD)


References (CTCL)


References (MCC)


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  - Carl Barrick, D.O.
  - Claire Dorfman, D.O.
Photo and Pregnancy Related Dermatoses

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2017 AOCD Spring Meeting
March 30, 2017 – 11:15 – 11:30 AM

Photo and Pregnancy Related Dermatoses

Disclosures
I have no actual or potential conflicts of interest in relation to this program and presentation.

Photodermatoses

Outline
• Photo-induced and photo-exaggerated dermatoses
  • Polymorphic Light Eruption
  • Actinic Prurigo
  • Hydroa Vacciniforme
  • Chronic Actinic Dermatitis
  • Solar Urticaria

PMLE

• Most common of the photodermatoses
  Onset: Non-scarring, pruritic, erythematous papulovesicles develop on exposed skin minutes to hours after UVR exposure
  Course:
  • Days to weeks, delayed-type hypersensitivity
  • Spring/early Summer
  • Juvenile Spring Eruption- Young Boys on helix of ear

PMLE

Diagnosis:
• Superficial & deep perivascular infiltrate, composed primarily of T-cells
• Papillary dermal edema, sometimes leading to bulla formation
• Interface dermatitis is absent
**PMLE Differential**

LE: (-) ANA/anti-Ro/La antibodies  
EPP: PMLE is not painful; (-) RBC protoporphyrin levels  
EM: No interface dermatitis on path  
Solar urticaria: shorter time course (1-2 hours)

**PMLE**

Treatment:  
- UV protection  
- Prophylactic low-dose UV sensitization x 4-6 wks  
Other meds:  
- Antimalarials  
- Beta-carotene  
- Potent topical corticosteroid  
- Oral steroid burst at onset  
- Niacinamide (with zinc)

**Actinic Prurigo**

Synonyms:  
- Hutchinson’s summer prurigo  
- Familial PMLE of American Indians  

Onset/Course:  
- Erythematous papulonodules w/ hemorrhagic crusts on exposed sites,  
- Cheilitis and conjunctivitis are common in native American sufferers but otherwise rare  
- Healed facial lesions may leave minute linear or pitted scars

**Actinic Prurigo**

Diagnosis:  
- Early acanthosis, spongiosis, perivascular infiltrate & edema; later w/ crusts, lichenification

**Actinic Prurigo**

Treatment:  
- Similar to PMLE with photoprotection, sunscreens, NB-UVB hardening  
- Thalidomide (50-100 mg qhs) for very resistant disease…then adjusted to lowest possible dose for maintenance  
- Niacinamide
**Hydroa Vacciniforme**

- **Onset**: Childhood, often resolving later in life
- **Course**:
  - Intermittent clustered, pruritic or burning erythematous macules
  - Followed by tender papules & coalescent hemorrhagic vesicles & bullae with scarring
  - All exposed sites (face and dorsal hands)
  - Appears within hours of summer sunlight

**Diagnosis**:
- Histology is pathognomonic
- Prominent keratinocyte degeneration
- Intraepidermal vesicles
- Epidermal & dermal necrosis

**Treatment**:
- Hydroa vacciniforme is almost always refractory
- Restriction of UVR exposure, broad-spectrum sunscreens and clothing until remission eventually develops in most cases
- In those patients with more severe disease, courses of low-dose, broad- or narrow-band UVB phototherapy orPUVA administered as for PMLE may occasionally help

---

**Chronic Actinic Dermatitis**

- **Onset**: older men w/ Fitz 1, more severe during the summer
- **Course**:
  - Persistent pruritic UV-light evoked eczema of the uncovered and to a lesser extent covered skin
  - Probably represents a DTH response against photo-induced endogenous allergen
  - Clinically resembles allergic contact dermatitis to exogenous allergens (airborne, sunscreens, plants)
  - Both broad-spectrum and monochromatic radiation are causative at levels far below MED

---
Chronic Actinic Dermatitis

**Diagnosis:**
- Histologically resembling allergic contact dermatitis

**Treatment:**
- Careful avoidance of UVR exposure & contact allergens is of primary importance
- Topical or intermittent oral corticosteroid and emollient therapy
- For refractory disease, prolonged courses of low-dose PUVA, or oral immunosuppressive therapy are needed
- Azathioprine often very effective over several months

Dermatoses of Pregnancy

**Outline**
- Pemphigoid Gestationis
- Pruritic Urticarial Papules and Plaques of Pregnancy
- Impetigo Herpetiformis
- Atopic Eruption of Pregnancy

Pemphigoid Gestationis

- AKA Herpes Gestationis
- **Onset:** 2nd or 3rd trimester
- **Course:** Abrupt onset of self-limited bullae
  - Can temporarily affect the skin of newborns
  - 25% manifest immediately postpartum
  - 75% flare within hours of labor
  - Tendency to recur with subsequent pregnancies
  - Neonatal disease due to transplacental transfer of maternal antibodies

Diagnosis:
- Histopathology
  - Classic subepidermal blister
- Immunofluorescence
  - DIF - In ALL patients, linear deposition of C3 at the BMZ
  - Salt-Split Skin: ROOF stains positive

Prognosis & Treatment
- Spontaneous resolution over wks-month’s s/p delivery
  - Typically within 3 months of delivery
- Generally requires initial doses of prednisone 0.5 mg/kg QD
  - Anticipate significant flares at time of delivery that necessitate high dose prednisone
  - Refractory cases treated with plasmapheresis
  - Topical corticosteroids & antihistamines may be effective

Pemphigoid Gestationis

- **Diagnosis:**
  - Histopathology
    - Classic subepidermal blister
- Immunofluorescence
  - DIF - In ALL patients, linear deposition of C3 at the BMZ
  - Salt-Split Skin: ROOF stains positive

Pruritic Urticarial Papules & Plaques of Pregnancy

- **Onset:** 3rd trimester, associated with maternal weight gain and twin pregnancy
- **Course:** Erythematous and edematous papules and plaques appear first in abdominal striae, with periumbilical sparing
- **Diagnosis:**
  - PUPPP remains a diagnosis of exclusion
  - Typical clinical presentation
  - Normal laboratory tests
  - Negative DIF/IIF
  - Non-specific H&E
**Pruritic Urticarial Papules & Plaques of Pregnancy**

**Prognosis & Treatment**
- Resolves spontaneously in about 4 weeks
- No flares postpartum
- Benefit from topical steroids and antihistamines
- Systemic steroids in refractory cases

---

**Impetigo Herpetiformis**

**Prognosis & Treatment**
- AKA “Generalized Pustular Psoriasis of Pregnancy”
- Onset - 3rd trimester
- Course - Acute onset of erythematous patches, on the abdomen & flexural areas that develop 2-3 mm pustules along the periphery
- Typically occurs in patients with NO prior history of psoriasis
- Diagnosis - ↑ WBC count ↑ ESR, Negative DIF/IIF
  - Hypocalcemia
  - Hypoalbuminemia

---

**Impetigo Herpetiformis**

**Prognosis & Treatment**
- Maternal Risks
  - Can be life threatening due to complications of hypocalcemia → seizures, tetany, delirium, cardiac arrhythmias
  - Fetal Risks
  - Placental insufficiency
  - Disease usually resolves postpartum
  - Often recurs with subsequent pregnancy with earlier onset & more severe course

---

**Impetigo Herpetiformis**

**Prognosis & Treatment**
- Systemic corticosteroids are 1st line treatment
- Starting doses up to 60mg prednisone QD
- Careful management of hypocalcemia & hypoalbuminemia
- Consider use of PUVA
- In life threatening cases, early delivery of the baby may be necessary

---

**Atopic Eruption of Pregnancy**

**Onset:** 1st trimester
**Course:** Two clinical variants
- Eczematous (E-type) – eczematous lesions in flexures
- Prurigo (P-type) – Papular eruption on trunk and extremities
- 80% have no history of atopic dermatitis

**Diagnosis:**
- Clinical diagnosis
- Biopsy shows non-specific mild acanthosis, parakeratosis and erosions
- 70% of cases with elevated IgE
Atopic Eruption of Pregnancy

Prognosis & Treatment
• Resolves following delivery
• But sometimes may persist for weeks to months
• Recurrence in subsequent gestations is common
• Treat symptomatic pts with medium potent topical steroids & antihistamines
• Also Urea 10%, UVB, menthol

Table 27.1 Dermatoses of pregnancy – fetal risk and involvement of newborn skin.

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Fetal risk</th>
<th>Newborn skin involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational pemphigoid</td>
<td>Increased risk of prematurity</td>
<td>Lesions of gestational pemphigoid in up to 10%</td>
</tr>
<tr>
<td>Pruritic urticarial papules</td>
<td>None</td>
<td>Single report to date</td>
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<tr>
<td>of pregnancy</td>
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<td>Prolact of pregnancy</td>
<td>None</td>
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<tr>
<td>Cholestasis of pregnancy</td>
<td>Increased risk of prematurity</td>
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<tr>
<td></td>
<td>labor, meconium staining, fetal</td>
<td></td>
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<tr>
<td></td>
<td>distress, and fetal death</td>
<td></td>
</tr>
</tbody>
</table>

Photo and Pregnancy Related Dermatoses

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DISCLOSURES

Neither I, nor the members of our residency program, nor any of the contributors to this presentation have any relevant disclosures to declare.

Neutrophil biology

- Neutrophils are a crucial defense against microbes
  - Neutrophils: like eos, basophils
  - Contain numerous granules – oxidative and non-oxidative
  - Enable destruction of target organisms

Neutrophil maturation and biology

- >5–10 × 10^9 neutrophils produced daily in bone marrow
- Differentiation from pluripotent stem cells requires 7–10 days
- Bone marrow upregulates neutrophil production in response to stress (e.g., infection)
- Mature neutrophils circulate in peripheral bloodstream for 3–12 hours
- They then migrate into tissues, surviving 2–3 days further

Neutrophil biology

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- Mature neutrophils circulate in peripheral bloodstream for 3–12 hours
- They then migrate into tissues, surviving 2–3 days further
Neutrophilic pathophysiology

- Neutrophils move at up to 30µm/min – fastest cell in the body
- Among first cells to arrive at sites of inflammation
- Neutrophils contain potent defense mechanisms
  - Destroy not only microbes and necrotic debris, but also normal tissue
- Release of lysosomal enzymes, ROS, prostaglandins and leukotrienes into the extracellular space → endothelial injury and tissue damage
- Neutrophils contribute to many acute and chronic diseases of skin, body
  - Varied diseases
  - Similar pathogenesis and histopathology → similar therapy

Sweet’s syndrome

- Acute febrile neutrophilic dermatosis
- Epidemiology
  - Occurs aged 20-50 years
  - Peak incidence 30-60 years
- Clinical presentation
  - Tender papules or nodules
  - Rash
  - Fever
  - Headache
  - Fatigue
  - Signs of inflammation
  - Oral ulcers
- Variants
  - Classical
  - Atypical
  - Drug-induced
  - Drug neutral

Pyoderma gangrenosum

- Epidemiology
  - Occurs aged 20-50 years
  - Peak incidence 30-60 years
- Clinical presentation
  - Tender papules or nodules
  - Rash
  - Oral ulcers
  - Fever
  - Headache
  - Fatigue
  - Signs of inflammation
- Pathology
  - Pustules
  - Ulcers
  - Granulomas
  - Fibrinous deposition

Sweet’s syndrome – diagnostic criteria

- Major criteria: must demonstrate both
  - Although several cutaneous lesions consistent with typical Sweet’s syndrome
  - Histopathology consistent with Sweet’s syndrome
- Minor criteria
  - Presence of associated systemic findings, such as infections, pregnancy, drugs, malignancy or other hematologic disorders
  - Glomerulonephritis
  - Scoliosis
  - Leukocytosis
  - Excellent response to systemic corticosteroids
- Associated laboratory abnormalities:
  - Elevated white blood cell count
  - Elevation of erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)

Pyoderma gangrenosum – common variants

- PAPA
  - PAPA syndrome
  - Pyoderma gangrenosum
  - Arthritis
  - Uveitis
  - Colitis
  - Scleritis
  - Cataracts
  - Polyarteritis nodosa
  - Pseudotumor cranii

[^266]:
Pyoderma gangrenosum: proposed diagnostic criteria

**Major criteria (must have all 2):**
1. Rapid progression of painful, necrotic ulcer with irregular, violaceous, undermined border
2. Ulcer occurrence in the setting of a chronic inflammatory disorder
3. Ulcer recurrence after excision

**Minor criteria (must have ≥2):**
- History of systemic disease associated with PG
- History of systemic disease associated with PG
- Rapid treatment response to systemic corticosteroids
- Histopathologic findings of PG
- Recurrent aphthous stomatitis
- Pyoderma gangrenosum: oral ulcers
- Behavioral changes, arthritis, skin lesions, positive pathergy test

**Simplified diagnostic criteria:**

1. Oral ulcers
2. Skin manifestations
3. Vascular lesions

**Behçet’s disease**

- **Epidemiology:** Rare, multi-systemic, recurrent polyarthritis, eye inflammation
- **Peak age of onset:** 20-35 years
- **Common:** Japan, Middle East, Turkey
- **Frequency:** 1 in 10,000

- **Treatment:**
  - **Oral:** Dapsone, mycophenolate mofetil
  - **Intralesional:** Intralesional corticosteroids
  - **Topical:** Calcineurin inhibitors
  - **Systemic:** Azathioprine, cyclophosphamide, mycophenolate mofetil

**Bowel-associated dermatosis-arthritis syndrome**

- **Characterized by:** Skin lesions, arthritis, and diarrhea with resultant malabsorption
- **Criteria:**
  - Arthritis
  - Skin lesions
  - Diarrhea
  - Positive pathergy test
- **Simplified diagnostic criteria:**
  - ≥2 episodes of skin alteration post GI surgery
  - ≥1 episode of skin alteration post GI surgery
  - Absence of skin alteration post GI surgery
  - Arthritis
  - Skin lesions
  - Diarrhea
  - Positive pathergy test

**Histopathology:**
- Diffuse secondary to variable nature and multi-organ involvement
- Cutaneous lesions:
  - Acneiform or follicular lesions
  - Papulopustules
  - Drug reaction
  - Drug rash
  - Drug eruption
  - Drug eruption with eosinophilia

**Behçet’s disease**

- **Diagnosis of Behçet’s requires score ≥2 points**
  - Oral aphthous
  - Skin manifestations
  - Vascular lesions
- **Plus 2:**
  - ≥3 episodes of oral ulceration
  - ≥3 episodes of skin alteration
  - ≥3 episodes of vascular lesion

**Pyoderma gangrenosum**

- **Histopathology:**
  - Ulcer, abscess, granuloma, necrotizing vasculitis
  - Bacterial, fungal, mycobacterial, necrotizing vasculitis
  - Granuloma, necrotizing vasculitis
- **Treatments:**
  - Antibiotics
  - Antifungals
  - Antimycobacterial therapy
  - Surgical excision
- **Complications:**
  - Wound care
  - Avoid debriding tissue
  - Oral, topical corticosteroids
  - Calcineurin inhibitors
  - Corticosteroids
  - Azathioprine, cyclophosphamide, mycophenolate mofetil
  - B-cell depletion therapy
  - TNF inhibitors
Eosinophil biology

- Found in tissues only during inflammatory responses
- Exceptions: GIT, tract, lymph, bone marrow
- Eosinophils guided into tissues by:
  1. Chemokines
     • Eotaxin-1
     • RANTES—regulated on activation, normal T-cell expressed and secreted
  2. Cytokines
  3. Surface adhesion molecules
     • VLA-4
     • CD11b/CD18 (MAC)

Eosinophil granule contents

- Major basic protein 1 (MBP-1)
  - Potent parasite toxin
  - Damages helminths
  - Stimulates mast cell secretion
  - Potent histamine releaser
- Cationic protein (ECP/Kcancel)
  - Potent protein toxin
  - Eosinophil-derived neurotoxin (EDN)
  - Eosinophil peroxidase (EPO)
  - Eosinophils macrophages in presence of
  - Stimulates mast cell secretion
  - Toxic to tumor cells
- Eosinophilic pathophysiology

- IL-5, other inflammatory cytokines
  - Allergic inflammation
  - MBP-1
    - Damage to various mammalian cells
    - Exudation of bronchial cells
    - Toxic to tumor cells
  - EPO and MBP-1
    - Antiparasitic effect
    - Release of 5-hydroxytryptamine (serotonin)
    - Promotes clotting
- Eosinophilic cationic protein, IL-1
  - Cytokines
  - Act as APCs
  - Promote the Th2 and acquired immunity

- Eosinophilic dermatoses
  - Hypereosinophilic syndrome
  - Periodic fever syndromes
  - Medium vessel vasculitis
  - Small vessel vasculitis (LCV), including
    - Neutrophilic dermatosis of the dorsal hands
    - Neutrophilic urticaria
    - Neutrophilic eccrine hidradenitis
  - Toxic to tumor cells
  - Damages various mammalian cells
  - Allergic inflammation
  - Promotes clotting
  - Stimulation of cell secretion

- Eosinophil biology
  - Core
    - Major basic protein 1 (MBP-1)
    - Eosinophil cationic protein (ECP/RNaseA)
      - Potent protein toxin
    - Eosinophil-derived neurotoxin (EDN)
    - Eosinophil peroxidase (EPO)
  - Matrix
    - Stimulates neutrophils, superoxide, lysosome
  - Stimulation of cell secretion
  - Toxic to tumor cells
  - Damages various mammalian cells
  - Allergic inflammation
  - Promotes clotting
  - Stimulation of cell secretion
**Granuloma faciale**
- **Etiology**: idiopathic inflammatory dermatosis
- **Epidemiology**: predominantly affects middle-aged white men
- **Pathophysiology**: Precise etiology remains unknown
- **Presentation**: symmetric flat-topped, red-brown, pruritic papules
- **Characteristically spare the skin folds** → bands of uninvolved skin called “deck-chair sign”

**Papuloerythroderma of Ofuji**
- **Etiology**: unknown
- **Epidemiology**: Approximately 100 cases reported
- **Elderly Japanese men**
- **Male:female ratio of 7:1**
- **Pathophysiology**: unknown
- **Presentation**: recurrent edematous plaques on extremities; may resemble cellulitis
- **Lesions typically preceded by itching, burning**
- **Pathophysiology**: exact pathogenesis unknown
- **Possible hypersensitivity reaction**
- **Febrile "Vigors"** - myeloproliferative disorders, drugs, insect bites, infections including dermatophytes, viruses, and Toxocara canis
- **Activated eosinophils play a major role in the disease process.**

**Well's syndrome (eosinophilic cellulitis)**
- **Etiology**: unknown
- **Epidemiology**: Over 200 cases have been reported to date
- **Affects head and neck region**
- **Presentation**: recurrent edematous plaques on extremities; may resemble cellulitis
- **Lesions typically preceded by itching, burning**
- **Pathophysiology**: exact pathogenesis unknown
- **Possible hypersensitivity reaction**
- **Febrile "Vigors"** - myeloproliferative disorders, drugs, insect bites, infections including dermatophytes, viruses, and Toxocara canis
- **Activated eosinophils play a major role in the disease process.**

**Treatment**
- First-line therapy: intralesional triamcinolone, 2.5-5mg/ml
- Disease often resistant to treatment
- Many other treatment options have been proposed

**Histology**: non-specific
- **Laboratory testing**: Peripheral eosinophilia, lymphopenia, elevated eosinophils
- **Treatment**: Systemic corticosteroids usually effective
- **PUVA alone or combined with systemic retinoids**
- **Associated diseases**: T-cell lymphomas, gastric carcinoma
- **Medications**: topical corticosteroids, antibiotics, antihistamines, antimalarials

**Hypereosinophilic syndrome**
- **Histopathology**: extracellular eosinophilic granules are present in the dermis forming the characteristic “bone-figures”
- **Laboratory testing**: Eosinophilia, peripheral eosinophilia, lymphopenia
- **Treatment**: Oral corticosteroids, antipruritic agents
- **Topical**
- **For mild cases, potent topical steroids.**
Hypereosinophilic syndrome

- **Etiology**: Myeloproliferative disorder characterized by persistent eosinophilia and end-organ damage.
  - L-HES (lymphocytic HES)
  - M-HES (myeloproliferative HES)
- **Epidemiology**:
  - Lymphocytic form: equal gender distribution
  - Myeloproliferative form: typically affects males (80%)
- **Pathophysiology**
  - Eosinophils cause end-organ damage
  - Lymphocytic HES: Chronic T-cells produce IL-5 → recruitment of eosinophils
  - Myeloproliferative HES: FIP1L1-PDGFRA fusion gene → constitutively active tyrosine kinase

- **Clinical presentation**
  - Cutaneous lesions: nonspecific; >50%
  - Pruritic enanthemus macules, papules, and nodules or urticaria, angioedema
  - Extravasation: Heart, lungs, CNS, PNS, liver
  - Features of myeloproliferative HES
    - Fever, weight loss, fatigue, increased serum vitamin B12 and tryptase
    - Endomyocardial fibrosis → restrictive cardiomyopathy
    - Oral, angular ulcers may occur

- **Laboratory testing/safety monitoring**
  - Evaluate abnormal peripheral T-cell population:
    - Flow cytometry, T-cell receptor gene rearrangement analysis
  - Screen for FIP1L1-PDGFRA fusion gene
  - Monitor for development of endomyocardial fibrosis by periodic echocardiogram
  - Endomyocardial disease may worsen during first several days of immunosuppressive therapy:
    - Serum creatinine and NT-proBNP levels

- **Treatment**
  - Lymphocytic HES
    - Glucocorticoids +/- IFN-α
  - Novel therapies:
    - Midostaurin and nilotinib (MEK inhibitors) against IL-5→ decreased Th-2 cytokines in trials
  - Myeloproliferative HES
    - If FIP1L1-PDGFRA gene rearrangement not present, imatinib (TK inhibitor) is drug of choice
    - Oral: Starting weekly to daily
    - Maintenance therapy required to avoid relapse
    - If FIP1L1-PDGFRA gene rearrangement present, tyrosine kinase inhibitor is prednisone 1mg/kg/day

- **Diagnosis**
  - **Clinical criteria**
    - Persistent eosinophilia of >1.5 x 10^9/L for at least 6 months
  - **Histology**
    - Non-specific; eosinophils are not always present
  - **Diagnostic criteria**
    1. Peripheral blood eosinophil count > 1.5 x 10^9/L in at least two separate blood samples
    2. Lack of evidence for parasitic, allergic or other recognized causes of eosinophilia
    3. Symptoms and signs of end-organ system involvement

Eosinophilic folliculitis

- **Epidemiology**
  - AIDS-associated
  - Eosinophilic pustular folliculitis
  - Eosinophilic fasciitis
- **Clinical presentation**
  - Pruritic follicular papules erupting on face, scalp, trunk
  - Treatment: HAART (increase CD4 count), phototherapy, topical corticosteroids +/- oral antihistamine
- **Histology**
  - Eosinophils around follicles; exocytosis of eosinophils and lymphocytes into follicular epithelium
Angiolympohid hyperplasia with eosinophils

- **Etiology:** unknown
- **Epidemiology:** young to middle-aged adults; no gender predilection
- **Clinical presentation:** red, pink, or brown papules/nodules, classically periauricular or on the scalp/forehead; may be painful
- **Histology:** vascular proliferation with "robin's" endothelial cells, surrounding eosinophils.
- **Treatment:** surgical excision; >30% recur

Kimura’s disease

- **Etiology:** unknown; benign condition
- **Clinical presentation:** hypereosinophilia, anemia, thrombocytopenia
- **Clinical presentation:** painless LAD/mass of head and neck
- **Pathology:** abnormal proliferation vascular endothelium with lymphoid follicles; eosinophilic infiltrate
- **Treatment:** mild/curettage; recurrence common
  - Oral steroids
  - Intranasal or oral estrogens
  - Surgical excision

Episodic angioedema associated with eosinophils (Gleich syndrome)

- **Diagnosis requires tried of:**
  1. Hypereosinophilia
  2. Recurrent angioedema
  3. Good response to systemic glucocorticoids
- **Prognosis:** good
- **No organ involvement
- **Treatment:** systemic glucocorticoids to control flares

Eosinophilic fascitis

- **Laboratory:** hypergammaglobulinemia, elevated ESR, peripheral eosinophilia
- **Associated diseases:** Chronic GVHD, panhypoponemia, anemia, thrombocytopenia; myeloproliferative disorders
- **Associated malignancies:** hematological malignancies reported
  - Unexplained anemia → biopsy
- **Treatment:** prompt; to preserve function
  - End tic: oranisoids, doses tapered 5-24m
  - Improvement may take several months

Toxic oil syndrome

- **1981 – affected more than 25,000 individuals in Spain**
- **600 died; 300 others left permanently disabled**
- **Aniline-processed rapeseed oil → systemic inflammatory response**
- **Genetically-susceptible individuals**
- **Signs and symptoms**
  - Morphelliform eruption → LE, morpheaform, or sclerodermoid presentation
  - Flu-like – fever and headache → inflammation in CNS, lungs, salivary glands
Eosinophilia-myalgia syndrome

- 1989 - contaminated batches of L-tryptophan in the United States
- >1500 individuals affected; 30 died

Clinical presentation
- Severe myalgias, fever, dyspnea
- Edema
- Macular exanthem
- Peripheral eosinophilia

Chronic phase
- Diffuse, deep sclerodermoid induration of extremities
- Progressive peripheral neuropathy, myopathy

Other categories of disease featuring prominent eosinophils
- Drug reactions
- Arthropod assault
- Bullous dermatoses (bullous pemphigoid)
- Urticaria
- Eosinophilic vasculitis (Churg-Strauss)

References

Infectious Diseases: Fungal Infections
Northeast Regional Medical Center
Emily Kollmann, D.O.
Nicole Tillman, D.O.

Classification of Fungal Diseases
• Superficial
  – Do not have the ability to invade hair, skin, nails
• Cutaneous
  – Dermatophytes
• Deep
  – Localized subcutaneous (implantation or dermal spread)
  – Dimorphic systemic (hematogenous spread)
  – Opportunistic (immunocompromised patients)

Disclosures
• No financial relationships exist with commercial interests

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<tr>
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Superficial Fungal Infections

- Pityriasis Versicolor
- Tinea nigra
- Black piedra
- White piedra

Pityriasis versicolor

- Malassezia furfur & M. globosa, yeast phase of Pityrosporum orbiculare
- Halo or hyperpigmented coalescing scaly macule commonly presents on the trunk/upper arms
  - Decreased pigmentation secondary to the inhibitory effects of dicarboxylic acids on tyrosinase (acids result from metabolism of surface lipids by the yeast)
  - Increased pigment due to PIPA
- Favors oily areas of skin and more common in summer time
- A/w seb derm, AD & neonatal cephalic pustulosis (M. sympodialis)
- Dx with KOH- "spaghetti and meat balls"
- Tx with topical or oral antifungals.
  - Terbinafine & griseofulvin ineffective
  - Do not use oral ketoconazole - hepatotoxicity

Tinea nigra

- Hortaea werneckii - a black yeast found in hot humid environments
  - Common in tropics and the gulf coast
  - One or several brown/black patches on palms or soles
  - Pigment confined to stratum corneum and scrapes off easily
  - KOH prep. - hyphae appear brown/gold
  - Culture to identify organism
  - Topical antifungals (clotrimazole, miconazole, ketoconazole) are effective
  - Griseofulvin not effective

Black and White Piedra

- Hyphae, arthropores and bacteria adhere to each other to form nodules or 'stones' along hair shaft
  - Hair breakage may occur
  - Black Piedra - Piedraia hortae - Firm adherent nodule on the face and scalp
  - White Piedra - Trichosporon ovoides or T. inkin - Soft, less adherent nodules in the axilla & pubic hair
  - Can cause fungemia, fever, lung infiltrates, renal failure, necrotic skin lesions in immunosuppressed
  - Tx: shaving hair
  - Oral and topical antifungals
    - Black Piedra - Oral & topical terbinafine
    - White Piedra - Oral Itraconazole
    - Topical Imidazoles
    - Ciclopirox olamine
    - Selenium sulfide
    - Chlorhexidine solutions
    - Zinc pyrithione
    - Amphotericin B lotion

Dermatophytoses

- Fungal infections caused by three genera of fungi (Dermatophytes)
  - Unique ability to invade and multiply within keratinized tissue (hair, skin and nails)
    - Trichophyton
    - Microsporum
    - Epidermophyton
  - “Tinea” precedes the Latin name for the involved body site
    - Capitis, faciei, barbae, corporis, cruris, pedis, manus, unguium
  - Scaly annular plaques that spread centrifugally from the point of skin invasion
    - Initially eroded and then may become serpiginous

Tinea corporis

- Any dermatophyte can potentially cause tinea corporis
  - MC: T. rubrum, T. mentagrophytes
- Tinea imbricata - E. floccosum
- Lesions can also be vesicular, granulomatous or verrucous in appearance

Majocchi’s Granuloma

- Usually caused by T. rubrum
- Represents a deep dermatophyte folliculitis in which the wall of the follicle is disrupted
- Perifollicular papulopustules or granulomatous
Tinea Cruris

- Inguinal region, upper thighs
  - Occasional extension onto the abdomen and buttocks
  - Scrotum is usually spared (candidiasis if involved)
- MC: *E. floccosum, T. rubrum and T. mentagrophytes*
- Check feet for T. pedis or onychomycosis

Tinea Mannum

- Usually non-inflammatory and often unilateral
  - Harm to foot hyperkeratosis of the palms and soles that fails to respond to emollients
  - Moccasin-type tinea pedis is often present
  - There are clinical features such as chronicity and hyperkeratosis
  - "Two feet and one hand syndrome" = dermatophytid (id) reaction
  - Other presentations include exfoliative, vesicular and papular variants

Tinea Pedis

- Soles and interdigital web spaces
- MC: *T. rubrum, T. mentagrophytes, E. floccosum*
- Four major clinical types of tinea pedis
  - Moccasin, interdigital, inflammatory, and ulcerative

Tinea Capitis

- Common in children
  - Predilection for African descent
- MC: *T. tonsurans > M. canis*
- Alopecia with or without scale is the most common presentation
  - Discrete patches or involve the entire scalp
  - "Comma", "corkscrew", and dystrophic broken hairs
  - Posterior cervical and posterior auricular lymphadenopathy
  - Alopecia is reversible with treatment

Kerion

- Boggy, purulent plaques with abscess formation and associated alopecia
  - Variant of endothrix
  - Can result in permanent scarring

Favus

- MC: *T. schoenleinii, T. violaceum, M. gypseum*
- Thick, yellow crusts composed of hyphae and skin debris ("scutula")

Diagnosis

- KOH (potassium hydroxide)
- Culture
  - Sabouraud Dextrose Agar (SDA): gold standard
  - Modified SDA (Mycosel or Mycobiotic): SDA + cycloheximide + chloramphenicol
- DERM (dermatophyte test media)
  - Peptones, dextrose, cycloheximide, phenol red, chlortetracycline, and gentamicin
  - Dermatophytes turn media from amber to red color due to alkaline by-products
  - Non-dermatophytes cause media to turn yellow (or stay amber-colored)
- H&E
  - Gomori methenamine silver (GMS): outlines fungal elements black
  - Periodic acid-Schiff (PAS): outlines fungal elements magenta with green background
  - Fontana-Masson: stains dematiaceous fungi

Treatment

- Uncomplicated tinea corporis, cruris, pedis
  - Topical antifungals 1-2x/day 2-4 weeks

- Oral medications
  - Ketoconazole, econazole, terbinafine
  - Baseline LFTs for terbinafine
  - Fluconazole contraindicated with coadministration of drugs that cause QT prolongation
  - Itraconazole contraindicated with congestive heart failure

- Tinea capitis, kerion, majocchi’s granuloma
  - Need oral medication due to involvement of the hair follicle
  - Griseofulvin: 20-25 mg/kg/day (microsize suspension) for 6-8 weeks, terbinafine
  - Both are considered very safe
  - Zeasorb AF powder can be used for prevention
  - Feet and body folds
4 Types of Onychomycosis

1. Distal Subungual Onychomycosis
   - T. rubrum is most common cause
   - Begins distally, involves nail bed, nail plate, and hyponychium
2. White Superficial Onychomycosis (WSO)
   - T. mentagrophytes is most common cause
   - Organisms invade surface of toenail plate
   - T. rubrum is more common in HIV positive patients
3. Proximal White Subungual Onychomycosis
   - T. rubrum is most common cause
   - Organisms enter the cuticle; leukonychia in the proximal nail plate near lunula
   - May be a sign of HIV infection
4. Candida onychomycosis
   - Erosion of nail and massive nailbed hyperkeratosis
   - Usually in patients with mucocutaneous candidiasis

Onychomycosis Diagnosis

- No single method gives 100% accurate results
- KOH of clippings or curettings of subungual debris
  - Chlorazol black E can be added to improve sensitivity
- Histopathologic examination with PAS stain
- Culture
  - Sabouraud agar with chloramphenicol & cycloheximide (mycosel) agar
  - May be a sign of HIV infection

Onychomycosis Treatment

- Many patients do not seek treatment
  - Patients with diabetes or peripheral neuropathy should be treated
- Topical treatment ciclopirox nail lacquers: modestly effective
  - Thymol in EtOH
- Efinaconazole (Jublia, 14 alpha demethylase inhibitor) or Tavaborole (Kerydin, inhibits aminoacyl-tRNA synthetase) daily for 48 weeks
- Oral therapy: better cure rate, especially if all nails involved
  - Terbinafine
    - 250mg/day for 6-8 weeks (fingernails) and 12-16 weeks (toenails)
    - Monitor liver function
  - Potential for SCLE development
  - Itraconazole
    - Pulsing is recommended
    - Associated with CHF and drug interactions (strong CYP3A4 inhibitor)

Candidiasis

- C. albicans
  - Common inhabitant of GI, GU, and skin
  - Oral (Thrush)
    - Affects: Newborns, children
    - Side effect of immunosuppressants and corticosteroids
    - Oral Thrush
    - Side effect of immunosuppressants and corticosteroids
    - Side effect of immunosuppressants and corticosteroids
  - Perleche (angular cheilitis)
    - May be due to ill-fitting dentures or from exaggerated skin folds
    - Riboflavin/nutritional deficiencies
  - Intertrigo
    - Chronic paronychia
    - Topical antifungals
    - May combine with mild topical steroid for short duration
    - Iodoquinol and hydrocortisone
  - Chronic paronychia
    - Oral fluconazole if refractory
    - Avoid moisture and irritants
  - Diaper dermatitis
    - Oral nystatin if recurrent
    - Compounding with zinc oxide for barrier

Candida Diagnosis

- KOH prep
  - Spores and pseudohyphae under microscope
- Gram stain
  - Dense, gram positive oval bodies
- Histopathology
  - Budding yeast and pseudohyphae in stratum corneum
  - Intraepidermal budding
  - Pseudohyphae; vertically or horizontally oriented
  - Pseudohyphae in stratum corneum
  - Hyperkeratosis and crusting
- Culture on sabouraud glucose agar

Candidiasis Treatment

- Terbinafine not effective
- Oral Thrush
  - Fluconazole
  - Ketoconazole
  - Fluconazole
- Perleche
  - Iodoquinol
  - Hydrocortisone
  - Ibuprofen
  - Antifungal
- Intertrigo
  - Topical antifungals
  - May combine with mild topical steroid for short duration
  - Oral fluconazole
  - Avoid moisture and irritants
  - Diaper dermatitis
  - Oral nystatin if recurrent
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Sporotrichosis

- Etiology
  - Chronic, granulomatous, subcutaneous inflammatory disease
  - Begin as small, pink, scaly papule
  - Due to direct inoculation of organism from penetrating trauma
  - Affects the lower extremities

- Chromoblastomycosis (Chromomycosis)
  - Caused by
    - Fonsecaea pedrosii - MC
    - Rhinocladiella aquaspersa
    - Cladosporium carrionii
    - Malassezia furfur
  - Involves bones, joints, meninges, pulmonary, genitourinary tract
  - Slowly progressive
  - Farmers account for 75% of cases

Mycetoma (Madura Foot, Maduromycosis)

- Etiology
  - Caused by
    - Madurella grisea, M. Mycetomatis, Leptoshaeria senegalensis, Exophilai
    - Nocardia, Actinomadura, and Streptomyces
    - Fonsecaea compacta
    - Rhinocladiella aquaspersa
    - Cladosporium carrionii
    - Fusarium monoliforme
    - Nocardia asteroides, Actinomadura jeaneselmei, Phialophor verrucosa, C. geniculate, Pseuduallescheria boydii
  - Increased prevalence in Mexico, Central/South America, India, and Africa

- Mycetoma
  - Histology
    - Actinomyces
      - Microaerophilic with neutrophils (mature, opaque discoid formations)
      - Granules with capillary loops
      - Granules of fermenting bacteria
    - Eumycetoma- more resistant
      - Mycelial tangles
      - Mycelial bodies, cigar-shaped
      - Cat-scratch disease, lymphocutaneous
  - Treatment
    - Surgical removal, voriconazole, itraconazole
    - Rifampicin/cotrimoxazole, or imipenem
    - Actinomyces- penicillin
    - Extensive lesions- itraconazole 200-400mg/day x 6-12 months
    - Small lesions- excision, cryotherapy
  - Radiographs will show bone involvement
  - MRI may show “dot in a circle” sign = grains
  - Grains made of filamentous bacteria
  - Grains with suppurative foci
  - Sinus tracts with neutrophils (resembles stellate abscesses)
  - Smooth splendore-hoeppli phenomenon at periphery
  - Grains made of fungal hyphae
  - Grains with suppurative foci
  - Sinus tracts with neutrophils
  - Smooth splendore-hoeppli phenomenon at periphery

- Chromoblastomycosis
  - Histologically
    - Pseudopelletomatous hyperplasia with intradermal pseudopods
    - Nodules, with scarring
    - Lymphogranuloma venereum
    - Cat-scratch disease
    - Lymphogranuloma venereum
    - Cat-scratch disease
  - Treatment
    - Itraconazole, terbinafine, potassium iodide
  - Histology
    - Yeast cell with surrounding eosinophilic fringe (represents reaction between host and fungus)
    - Asteroid bodies
    - Stellate abscess (CLATS)
    - Cigar shaped yeast in tissue (rarely seen)
    - Sclerotic bodies (medlar bodies, copper pennies)
    - Dermal granulomatous reaction
    - Pseudopeitheliomatous hyperplasia with intraepidermal proliferation
  - Terbinafine, cryotherapy, CO2, PDT, Amphotericin/itraconazole combination
**Keloidal Blastomycosis**
- **Lacazia loboi**
  - Central/South America- acquired from water, soil, vegetation
  - Associated with dolphins
- Ears, face, upper extremities
- Painless, smooth surface nodules
- Keloid like lesions
- Increase in size with invasion of surrounding skin or lymphatics

**Histology**
- Organisms are thick walled, refractile, spherules
- Attached to one another with narrow connections- “brass knuckles” or “chain of coins” “pop beads”

**TX**
- Surgical excision treatment of choice
- Itraconazole 100mg/day, clofazimine 100mg/day
- Combination therapy with excision and itraconazole or cryotherapy

**Blastomycosis**
- **Gilchrist Disease**
  - Blastomyces dermatitidis
  - Epidemiology:
    - Endemic to North America (Mississippi/Ohio river valleys/Great Lakes)
    - Found mainly in soil
  - Pathogenesis:
    - Inhalation of organisms

**Histology**
- Broad-based bud
- Thick double-contoured wall
- Pseudo epitheliomatous hyperplasia with intraepidermal pustules

**Clinical Variants**
- Primary pulmonary infection:
  - Typically asymptomatic/self limited, can resolve fill or progress
  - Infant cases with dissemination to skin
- Cutaneous Manifestations:
  - Typically after pulmonary infection
  - Nodule presenting papulopustules, well-demarcated verrucous plaques with crusting and pustules especially at borders
  - +/- central ulceration, healing begins centrally and heals with cobblestones pattern
- Treatment: oral antifungal
  - Severe or progressive: Amphotericin B
  - Mild: Itraconazole, Ketoconazole, Fluconazole

**Histoplasmosis**
- Darling’s disease, Cave disease, Ohio valley disease, taphosporine endocarditis
- Found in soil, frequently in bat/ground nests
- Transmission via inhalation of airborne spores
- Southeastern or central US

**Histology**
- Lacks a true capsule- surrounded by pseudocapsule
- Organisms within histiocyte
- *P. marneffei* (Histoplasmosis)
- *H. capsulatum* (Histoplasmosis)
- *G. inguinale* (Rabdosia)
- *R. sclearoma* (Leishmaniasis)
- *L. donovani* (Leishmaniasis)

**Treatment:**
- Spontaneous healing/itraconazole, amphotericin B
Atopic Dermatitis

• Epidemiology:
  - Most common in infants and children
  - Afflicts 15-30% of children, ~1% of adults
  - 85% begin during the first year, 95% before 5 years
  - Up to 70% spontaneous remission before adolescence
  - Prevalence of 15-30% in industrialized nations during early childhood

• Pathogenesis:
  - Atopic dermatitis is a chronic, relapsing, intensely pruritic condition that is often associated with allergic rhinitis and/or asthma, often referred to as the "atopic march.
  - Involves a skin barrier breakdown in addition to dysfunctional innate and adaptive immune response, including:
    - Unbalanced increase in T-helper 2 cells and hyperimmunoglobulinemia E.
    - T-helper 2 cells stimulate the production of immunoglobulin E and eosinophilia by releasing interleukin-4, -5, and -13, as well as decreasing protection against bacterial superinfection by releasing interleukin-10.

• Complications:
  - Bacterial infections: most commonly Staphylococcus aureus
  - Viral infections: HSV, molluscum contagiosum, HPV, eczema herpeticum, eczema coxsackium, eczema vaccinatum
  - HRQL impairment in generalized AD – exceeds that in asthma, epilepsy, and diabetes – comparable to that in renal disease or cystic fibrosis – equals (child) or exceeds (parent) that in psoriasis

• More than 50% develop Asthma
• About 75% develop Allergic Rhinitis
Psoriasis

- **Infantile psoriasis:**
  - Guttate psoriasis
  - New mechanisms
  - Biologics: Recent Treatment Advances

- **Treatment:**
  - After an URI
  - Raindrop-like

- **Psoriasis in infancy typically involves the diaper area and face.**
  - Nail findings of pitting, onycholysis, oil spots, and subungual hyperkeratosis are present in 10% of affected infants.
  - Not typically pruritic

- **Nevertheless, most patients will go on to develop chronic psoriatic disease several years later.**

- **The prognosis in children is typically better than in adults, with many children spontaneously clearing within several weeks to months.**

- **Psoriasis incidence has a bimodal pattern, with one peak in childhood and a second peak in adulthood.**

- **It occurs most frequently in individuals of Northern European descent.**

- **Psoriasis affects about 2% of the world’s population and can develop at any age.**
  - **Etiology:** aberrant T-cell function and keratinocyte responses are believed to be major culprits in the pathogenesis of psoriasis.
  - **Psoriasis is a polygenic disease:** HLA-Cw6 influencing early onset and can develop at any age and in both sexes.

- **Epidemiology:**
  - Psoriasis affects about 2% of the world’s population and can develop at any age and in both sexes.
  - **Psoriasis incidence has a bimodal pattern, with one peak in childhood and a second peak in adulthood.**
  - **It occurs most frequently in individuals of Northern European descent.**

- **Psoriasis is a chronic, intermittently relapsing inflammatory disease characterized by sharply demarcated erythematous, silvery, scaly plaques and papules on the scalp, elbows, knees, and other prominent sites of movement include the nails, hands, feet, and face.**

- **Recent Treatment Advances**
  - **Biologics:**
    - Crisaborole, an oral, selective phosphodiesterase 4 (PDE-4) inhibitor is applied topically twice daily as a 2% cream, effective in moderate to severe plaque psoriasis and approved for patients 2 years of age and older.
    - Dunlopilumab, a human monoclonal antibody that inhibits signaling of IL-4 and IL-13, showed efficacy in a phase 3 study of adult patients with moderate to severe plaque psoriasis.
    - Apremilast (Otezla), an oral PDE-4 inhibitor is applied topically twice daily as a 2% cream, effective in moderate to severe plaque psoriasis.
    - Inflammatory bowel disease may flare or initiate during therapy.
    - Reportedly both safe and effective, with the majority of patients clear or almost clear after one month of use.

- **Systemics: Anti-histamines, cyclosporine, mycophenolatemofetil, azathioprine, methotrexate, vedolizumab.**

- **UV-therapy:** safe and highly effective for this condition.

- **Topical corticosteroids, topical calcineurin inhibitors, tar, emollients.**

- **Environmental triggers, such as heat, humidity, inappropriate bathing habits, latex allergy, and nickel allergy occur more often in persons with atopic dermatitis.**

- **Topical corticosteroids** may be effective in improving lesion area and severity as well as pruritus.

- **Auspitz sign:** the phenomenon in which trauma, including acupuncture, may induce local plaques of psoriasis (the Koebner phenomenon). Patients may interpret these lesions as “slow-healing wounds.”

- **Ixekizumab, an IL-17A inhibitor** 300 mg by subcutaneous injection for weeks 0, 1, 2, 3 and 4, followed by 300 mg every 4 weeks.
  - In a phase 3 study in patients with moderate to severe plaque psoriasis, ixekizumab demonstrated significant improvements in PASI 90 response rates at weeks 12 and 52.
  - The FDA is expected to approve ixekizumab in HLA-B27 positive patients in the United States in 2018.

- **Dupilumab, a human anti-IL-4 receptor a monoclonal antibody** demonstrated efficacy in reducing eczema area and severity as well as pruritus in adults with moderate to severe atopic dermatitis.

- **Titzer: improved symptoms within 4 weeks and 12 weeks of treatment.**

- **Secukinumab, an IL-17A inhibitor** is given on week 0 followed by 80 mg on weeks 2, 4, 6, 8, 10, 12. After week 12, 80 mg is given every 4 weeks.

- **Baricitinib, a reversible JAK1 / JAK2 inhibitor** 1% of infants by 1 year of age and 2% of infants by age 2.

- **Ponesimod** is an oral, selective, reversible modulator of sphingosine 1-phosphate receptor 1, effective in moderate to severe psoriasis.

- **Removal of scale:** psoriatic arthritis **• Aupehla sign**

- **Dupilumab was reported to be effective in reducing eczema area and severity as well as pruritus, depression and anxiety, and improving quality of life.**

- **Auspitz sign:** the phenomenon in which trauma, including acupuncture, may induce local plaques of psoriasis (the Koebner phenomenon). Patients may interpret these lesions as “slow-healing wounds.”

- **Latex allergy and nickel allergy occur more often in persons with atopic dermatitis.**

- **UV-therapy:** safe and highly effective for this condition.

- **Topical corticosteroids, topical calcineurin inhibitors, tar, emollients.**

- **Environmental triggers, such as heat, humidity, inappropriate bathing habits, latex allergy, and nickel allergy occur more often in persons with atopic dermatitis.**

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- **Auspitz sign:** the phenomenon in which trauma, including acupuncture, may induce local plaques of psoriasis (the Koebner phenomenon). Patients may interpret these lesions as “slow-healing wounds.”
Pityriasis Rosea

- **Etiology**: Is controversial, but likely due to a viral pathogen with a flu-like prodrome.
  - +/- HHV6 and HHV7
- **Commonly begins** with a solitary pink-flesh colored scaly plaque “herald patch” followed by oval patches and plaques with a fine ‘collarette’ scale along the Langer’s lines of cleavage.
- **Typically the face, scalp and distal extremities are spared.**
- **Inverse and papular patterns** are more common in younger and darker-skinned individuals.
- **Self-limited and usually clears within 6 weeks.**

- **Supportive treatment** includes topical corticosteroids and anti-histamines. UV light is thought to hasten resolution and reduce pruritus.

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Lichen Planus

- **Etiology**: Unknown but viruses, medications and contact allergens have been proposed
  - Autoimmune T cells attack basal keratinocytes.
  - Hepatitis C has not been associated in the U.S. with pediatric cases, but cases have been described after hepatitis B vaccination.
  - Drugs causing LP-like reactions include: ACEi, beta-blockers, thiazides, anti-malarials, griseofulvin, NSAIDs, tetracycline, carbamazepine, phenytoin, and penicillamine.
- **Clinical**: Purple, planar, polygonal, and pruritic papules commonly on the flexures, ankles, wrists and genitalia. White papules forming an annular or lace-like patterns may be found on the buccal mucosa but are less common in pediatric cases.
- **Patients may spontaneously resolve in several months, or — more likely — follow a chronic course.**
- **Treatment**: Limited disease can be treated with topical corticosteroids and anti-histamines. For extensive or recalcitrant cases, the addition of a 2- to 6-week course of systemic corticosteroids (1 mg/kg per day) can be helpful, phototherapy, methotrexate, ciclosporin, and systemic chelating agents may also be used.

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Pityriasis Rubra Pilaris

- **Etiology**: Unknown, but likely a disorder of abnormal keratinization
- **Clinical**: PRP starts as small follicular papules which coalesce into yellowish-pink, scaly plaques with islands of sparing.
  - Hyperkeratosis of the elbows, knees, ankles, and Achilles tendon commonly affects pediatric cases.
  - Types III-V occur in children with type IV being the most common.
  - Clinical course is variable.
- **Treatment**: Topical Emollients, Corticosteroid, retinols and keratolytics for limited disease. If extensive consider systemic retinoid therapy, UVB or vitamin A (100-000 U/day).
Cutaneous T-cell Lymphoma

- Epidemiology
  - Lymphoma cutis is rare in children but the most common form is cutaneous T cell lymphoma (CTCL)
  - 0.5-5% of cases occur in childhood
  - Better outcomes in children secondary to limited disease at the time of presentation

- Clinical
  - Most commonly presents as erythematous, scaly patches, papules, and plaques on the scalp and buttocks
  - Lesions can morph into a variety of shapes and become scaly
  - Hypopigmented CTCL is the most common subtype in children

- Pathology shows a predominance of CD8+ T cells in contrast to classic CTCL

- Differential:
  - psoriasis, atopic dermatitis, tinea corporis, contact dermatitis, and seborrheic dermatitis
  - If seemingly benign conditions are refractory to standard treatment, a biopsy (or a series of biopsies) is warranted


Paller AS, Mancini AJ. Hurwitz clinical pediatric dermatology: a textbook of skin disorders of childhood and adolescence. Elsevier Health Sciences; 2015 Sep 25. Figures 2.19, 3.4 and 3.35

Seborrheic dermatitis

- Clinical
  - Characterized by well demarcated erythematous plaques with overlying yellow, greasy scale and crust
  - Typical locations: scalp, face, postauricular, pre-sternal, and intertrigenous areas

- Epidemiology
  - Most common in infants (3rd-4th month) and adolescents. If infant seborrheic dermatitis persists past 6-12 months, concomitant atopy is more likely

- Etiology:
  - Large unknown, but linked to sebaceous gland activity
  - Increased incidence during times of heightened hormonal control
  - Adult disease is more closely linked to Pityrosporum ovalis (Malassezia ovalis)

- Leiner’s Disease ‘phenotype of immunodeficiency’:
  - Severe seborrheic dermatitis, failure to thrive, and diarrhea

- Treatment:
  - Infantile seborrhea will heal in 3-4 weeks without treatment.
  - If thick scale is present, the use of "no tears" shampoo and baby oil along with a gentle brush for exfoliation will suffice.
  - For non-scalp areas, low potency steroid cream and topical antifungals can be used.
  - Traditional anti-seborrheic shampoos are favored for adolescent cases. Monitor for secondary candida or bacterial infection and treat appropriately

Lymphomatoid Papulosis

- Benign, recurrent disorder with histologic features similar to lymphoma

- Clinical:
  - Presents with widespread papules, papulovesicles, or even nodules with necrotic centers
  - Lesions will typically resolve within a few months, however the disorder can last for years
  - Up to 9% of pediatric patients go on to develop Non-Hodgkin’s Lymphoma, which makes long-term monitoring important

- Histopathologic:
  - Heavy CD30+ T cell infiltrate is seen that can resemble Hodgkin’s disease (Type A), mycosis fungoides (LB), or anaplastic large T cell lymphoma

- Treatment:
  - Often unsatisfactory, but includes corticosteroids (topical and systemic) pulse therapy and PUVA/NBUVB
Pityriasis Lichenoides

- Idiopathic, papulosquamous eruption marked by two overlapping forms, which exist on a spectrum
  - Pityriasis Lichenoides et Varioliformis Acuta (PLEVA)
    - Acute form with widespread papulovesicles that ulcerate and can occasionally occur with constitutional symptoms
  - Pityriasis Lichenoides Chronica (PLC)
    - Scaly papules and plaques that can arise from PLEVA or de novo that can last 6 months to 2 years; lesions heal with dyschromia
- Etiology:
  - Idiopathic. Both believed to be a reactive lymphoproliferative disorder with a possible viral trigger
- Treatment
  - Systemic antibiotics (azithromycin), NBUVB (most effective), and topical corticosteroids mainly for control of pruritus

Reactive Arthritis

- Etiology:
  - Most common after enteric infections in children (Salmonella, Yersinia, Shigella)
- Clinical:
  - Reactive disorder most commonly presenting due to abnormal immune response following infection of certain antigenic pathogens
  - Complete triad of conjunctivitis, urethritis, and arthritis rarely seen
  - Skin manifestations include circinate balanitis, keratoderma blenorrhagica, and geographic tongue
  - Arthritis most often asymmetric and affects weight bearing joints of hip, knee, ankle, sacroiliac involvment rare in children despite most being HLA-B27 positive
- Prognosis in children is better than adults and most resolve with administration of NSAIDS and bed rest.
- Treatment:
  - Systemic immunosupressants including methotrexate and cyclosporine for resistant cases.
  - Ophthalmology and rheumatology referrals recommended.

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Overview
• Infectious Disease
• Drug Related Disorders
• Hereditary Disorders
• Autoimmune Conditions
• Miscellaneous Disorders

INFECTIOUS

Staphylococcus Scalded Skin Syndrome

• Clinical Presentation
  • Fever, skin tenderness and erythema in groin folds, axillary regions, nose, that leads to a generalized superficial exfoliative dermatitis and bullae
  • Nikolsky sign. Perioral crusting and fissuring

Staphylococcus Scalded Skin Syndrome

• Pathogenesis
  • Staphylococcus aureus group 2 phage (71) infects child at a distant site
  • Exfoliative toxins/Epidermolytic toxins A and B (ET-A, ET-B) bind to desmoglein-1 → superficial bullae within the granular layer (subcorneal)
  • ET is a unique serine protease that shows lock and key specificity to desmoglein-1

• Diagnosis
  • History Clinial
  • Culture of the bullae will be NEGATIVE. Must culture site of initial infection

• Treatment
  • Supportive care: IV fluids
  • Dicloxacillin
Bullous Impetigo

**Clinical Presentation**
- Flaccid bullae which rupture and leave honey colored crust behind
- No surrounding erythema
- Can have systemic manifestations such as malaise, diarrhea

**Pathogenesis**
- Often secondary to Staphylococci group 2 phage type 71 at the site of the lesion
- Exfoliative toxins A and B bind to desmoglein 1 forming superficial bullae within the granular layer (subcorneal)

**Diagnosis**
- Mainly clinical, but can culture site of infection

**Treatment**
- Topical mupirocin
- There is no clear preference among systemic treatment: antistaphylococcal penicillins (dicloxacillin), amoxicillin/clavulanate, cephalosporins (cephalexin), and macrolides, although resistance rates to erythromycin are rising.

Bullous Tinea

**Clinical Presentation**
- Tense multilocular bullae with surrounding erythema and scale often located along the arch of the foot
- Common to see interdigital fungal involvement
- May serve as a portal of entry for superinfection and cellulitis

**Pathogenesis**
- Most common dermatophyte: *Trichophyton mentagrophytes*
- Most commonly due to chronic disease that has not been treated or incorrectly treated

**Diagnosis**
- KOH scraping, fungal culture, biopsy

**Treatment**
- Topical antifungals
- If extensive, can use oral terbinafine up to 250 mg once daily for 2 weeks

Eczema Herpeticum

**Clinical Presentation**
- AKA Kaposi varicelliform eruption
- Itchy, umbilicated vesiculopustules that erupt in a disseminated pattern. These often become hemorrhagic and crusted
- Seen in children with atopic dermatitis

**Pathogenesis**
- Reactivation of HSV 1 predominantly
- Other viruses indicated in literature: Coxsackie A 16, vaccinia, and varicella zoster

**Diagnosis**
- Mainly clinical
- Tzanck smear, viral culture, direct fluorescent antibody, biopsy

**Treatment**
- Acyclovir (10-15 mg/kg/day), intravenous or oral
- Oral valacyclovir has a higher bioavailability than oral acyclovir
- In acyclovir resistant cases, can use foscarnet or cidofovir
**Blistering Distal Dactylitis**

**Clinical Presentation**
- Tense vesicles filled with purulent fluid and surrounding erythema on the dorsal surface of distal fingers and toes
- Can involve the proximal nail fold

**Pathogenesis**
- Group A B-hemolytic Streptococcus, S. aureus, S. epidermidis are the responsible organisms

**Diagnosis**
- Rare, but mainly a clinical diagnosis. Can culture

**Treatment**
- I&D
- Dicloxacillin or first generation cephalosporin (cephalexin)

**Varicella Virus**

**Clinical Presentation**
- A congenital infection of the newborn
- Greatest risk at first 20 weeks gestation
- Presents as cicatricial erythematous vesicles with crust
- Chorioretinitis, cataracts, cortical atrophy, psychomotor retardation and hypoplastic limbs

**Pathogenesis**
- Transplacental infection
- Maternal rash within 5 days before to 2 days after delivery, varicella-associated antibodies are not transferred to the baby → severe rash

**Diagnosis**
- Clinical
- Can get viral titer to confirm

**Treatment**
- Live attenuated vaccine has lowered incidence
- Acyclovir (10–15 mg/kg/day)
**Herpes Simplex Virus**

**Clinical Presentation**
- Erythematous vesicles with erosions and scarring in a localized or disseminated manner
- Temporal encephalitis

**Pathogenesis**
- Results from fetus contact with active maternal genital herpes lesions during delivery
- Majority HSV 2

**Diagnosis**
- Clinical
- Can swab maternal lesions prior to delivery to check for viral shedding

**Treatment**
- Acyclovir (10–15 mg/kg/day)
- Mothers with active HSV-2 genital lesions should have c-section

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**Stevens Johnson Syndrome & Toxic Epidermal Necrolysis**

**Clinical Presentation**
- Patients with fever, severe mucosal/conjunctival ulcerations and occasional GI and/or GU involvement
- Dusky erythematous or purpuric macules, papules, patches or plaques → flaccid bullae with epidermal detachment and necrosis
- Nikolsky and Asboe-Hansen seen in most cases

**Pathogenesis**
- Almost always drug related, rarely infection (Mycoplasma pneumoniae most common) or immunization
- Anticonvulsants (1st), antibiotics and non-steroid anti-inflammatory drugs

**Diagnosis**
- Clinically, eruption begins 7-21 days after initiation of drug
- Biopsy: full epidermal thickness necrosis

**Treatment**
- D/C offending agent!!
- Supportive care in ICU or burn unit: IVF, wound care, electrolyte and nutritional supplement
- IVIG

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**Drug Related**

**Acute Generalized Exanthematous Pustulosis**

**Clinical Presentation**
- An eruption of multiple sterile pustules with surrounding erythema, appearing first on face and intertriginous areas, then spreading to trunk and extremities
- Edema of the face and sometimes hands

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AGEP

- **Pathogenesis**
  - Most frequently mentioned drugs: antibiotics (beta lactams, macrolides), antifungal agents (itraconazole, fluconazole), anticonvulsants (carbamazepine and phenobarbital).

- **Diagnosis**
  - History (especially drug intake)
  - Biopsy: shows subcorneal pustule with neutrophil and eosinophil infiltrate.

- **Treatment**
  - Discontinue drug.
  - Use topical steroids for symptomatic relief.

Bullous Fixed Drug Eruption

- **Pathogenesis**
  - Lesions appear 1-2 weeks after first exposure. May recur with re-exposure.

- **Clinical Presentation**
  - Sharply circumscribed erythematous to violaceous patches with central vesicles and bullae.

- **Causes**
  - Sulfa, NSAIDs, Tetracyclines, Aspirin, Acetaminophen, Metronidazole.

- **Histopathology**
  - Superficial and deep interstitial and perivascular infiltrate with lymphocytes. There may be necrotic keratinocytes in the epidermis and dermal melanophages.

- **Treatment**
  - Discontinue offending agent.

Hereditary Bullous Disorders

- **Epidermolysis Bullosa Simplex**
  - Blistering in the epidermis/dermis/sublamina densa.
  - Types:
    - Dowling-Meara: onset at birth, widespread bullae, mucosal involvement, early death.
    - Koebner: generalized bullae at birth, heal without scarring, mucosal involvement.
  - Mutations in Keratins 5 and 14.

- **Junctional Epidermolysis Bullosa**
  - Blistering in the lamina lucida.
  - Types:
    - Dystrophic: blistering in the dermis/sublamina densa.
    - Kindler Syndrome: multiple cleavage planes possible.

- **Dystrophic Epidermolysis Bullosa**
  - Blistering in the dermis/sublamina densa.
  - Types:
    - Distichiasis: pigmented bullae.
    - Weber-Cockayne (localized).
    - Rieger Syndrome: localized.

- **Kindler Syndrome**
  - Multiple cleavage planes possible.
  - Early death.

Epidermolysis Bullosa Simplex (EBS)

- Keratin 5/14 subtypes continued:
  - EBS with mottled pigmentation
    - mainly associated with KRT5 mutation
  - Autosomal recessive EBS
    - Mutation in KRT14 or occasionally BPAG1
  - Subtypes with mutations in Plectin (links filaments to the plasma membrane and crosslinks hemidesmosomal proteins)
    - EBS with muscular dystrophy
    - EBS with pyloric atresia
    - EBS ogna type
      - Acral blistering, generalized bruising

Junctional Epidermolysis Bullosa (JEB)

- Autosomal recessive inheritance
- Enamel hypoplasia is linked with multiple types of JEB
- Subtypes
  - JEB non-Herlitz type
    - Laminin 5 or BPAG2 mutation
    - Bullae heal with atrophic scarring, may also have scarring alopecia and nail dystrophy
    - Rarely improves
    - Condition improves over time
  - JEB Herlitz type
    - Laminin 5 mutation
    - Diffuse skin healing bullae
    - Early death
    - Retinal atroctusion tissue
    - JEB with pyloric atresia
    - Integrin α6β4 mutation

Dystrophic Epidermolysis Bullosa (DEB)

- All caused by mutation in collagen VII
- Recessive DEB:
  - Hallopeau-Siemens:
    - Severe bullae that heal with scarring
    - Mitten deformity
    - Fatal squamous cell carcinomas
  - Non-Hallopeau-Siemens:
    - Localized to acral prominences
    - Less severe than above
- Dominant DEB:
  - Cockayne-Touraine
  - Recurrent infections
    - Rooster with mild scarring
  - Rare variant
    - Hypoaggregated perifollicular papules

Epidermolysis Bullosa Continued

- Treatment:
  - Day to day management includes avoiding mechanical trauma, loose clothing, non-adhesive dressings, bleach baths
  - Prompt treatment of secondary infections
  - Close monitoring for squamous cell carcinoma development
  - Multispecialty involvement
    - Dystrophic Epidermolysis Bullosa Research Association of America (DEBRA)
    - http://www.debra.org/research-trials
    - Information on the latest stem cell transplant, protein replacement and gene therapies that are currently being tested

Kindler Syndrome

- Rare autosomal recessive inherited subtype of epidermolysis bullosa
- Usually caused by a loss of function mutation in the gene FERMT1 (KIND1)
- Encodes a protein kindlin-1, involved in keratinocyte adhesion
- Characteristics:
  - Congenital blistering
  - Trauma induced skin fragility
  - Atrophic/aneurysm skin
  - Pseudolymphoma
  - Pernioglandular hyperkeratosis
  - Pseudosyndactyly
  - Periodontal disease
  - Phimosis
  - Pseduoainhum

Kindler Syndrome

- Histology:
  - Atrophic epidermis
  - Vascular changes at basement membrane
  - Giant intercellules
  - Decreased immunostaining of anti-kindlin-1 antibody
- Treatment:
  - Need multidisciplinary team (dentist, urologist, ophthalmologist)
  - Skin protection from trauma and sun
  - Close monitoring for squamous cell carcinoma development
  - Prompt treatment of secondary infections
  - Blistering improves with age, but pseduoainhum is progressive
**Bullous Congenital Icthyosiform Erythroderma (BCIE)**
- AKA Epidermolytic Hyperkeratosis or Epidermolytic Ichthyosis
- Autosomal dominant inheritance
- Gene defect in Keratins 1 (KRT1) and 10 (KRT10)
- Expressed in spinous and granular layer of epidermis
- Presents with diffuse erythema at birth in addition to vesicles and erosions
- Overtime has less erythema and more verrucous plaques, especially over flexural areas
- Other characteristics:
  - Malodorous plaques
  - Palmoplantar keratoderma (KRT1)
  - Nail dystrophy

**Histology:**
- Acanthosis, hyperkeratosis
- Expanded granular layer
- Large keratohyalin granules
- Vacuolar change and intracellular edema at spinous/granular layers
- Clumped keratin filaments seen on electron microscopy

**Treatment:**
- Mainly supportive, wound care and emollients for blistering
- Use of antiseptic soap to decrease bacterial colonization
- Oral or topical retinoids can be of benefit

**Incontinentia Pigmenti (Bloch-Sulzberger Syndrome)**
- Inherited X-linked dominant
- Usually lethal in males
- Gene mutation of NEMO (NF-kB essential modulator); also known as IKBKG gene
- Normal function is to protect against apoptosis
- Four stages follow the lines of Blaschko
  - Vesiculobullous lesions
    - Neonatal period
  - Verrucous and hyperkeratotic lesions
    - 2-6 months
  - Hyperpigmented patches
    - Toward the end of infancy
  - Hypopigmentation and atrophic lesions
    - Early adulthood

**Histology**
- Vesicular stage: Eosinophilic spongiosis with intraepidermal bullae
- Verrucous stage: Hyperkeratosis, acanthosis, and dyskeratotic cells
- Hyperpigmented stage: Pigment incontinence
- Hypopigmented stage: Atrophic epidermis with loss of adnexal structures

**Other characteristics:**
- Alopecia
- Pegged teeth
- Eye abnormalities
- Nail dystrophy
- Seizures
- Delayed development

**Treatment:**
- Multispecialty coordination (Neurology, dentistry, ophthalmology, geneticist)
- Early ophthalmologic screenings for infants for retinopathy and strabismus evaluation
- Prompt referral to neurology if any CNS abnormality

**Linear IgA Bullous Dermatoses of Childhood**
- Immune-mediated, subepidermal, vesicobullous dermatosis with clinically unique features in children. Also called “chronic bullous disease of childhood”
- Epidemiology: Mean age of 4.5 years
- Autoantigen: 97 kDa Ag (LAD-1/LABD97)
- Histology: subepidermal bullae with neutrophils in dermal papillae
- DIF: linear IgA (+/- C3) deposition at BMZ
- Treatment: dapsone (first line) 1-2 mg/kg or sulfapyridine. Second line agents include; oral corticosteroids, colchicine, and nicotinamide
- Childhood disease remits within 2-4 years

**Clinical:** Annular and herpetiform bullae with preference for flexural areas of lower trunk, extensors, thighs, and groin. “Crown of Jewels” configuration.
Dermatitis Herpetiformis

- Cutaneous manifestation of gluten sensitivity. (90% of DH patients have gluten-sensitive enteropathy, 20% have intestinal symptoms of celiac disease)
- F>M in children, HLA-DQ2 (strongest association)
- Autoantigen: epidermal transglutaminase (TG-3), tissue transglutaminase (endomysial)
- Chronic pruritic erythematous grouped papules/vesicles on elbows, knees, and buttocks.
- Excoriation of vesicles common.
- Associated with gluten-sensitive enteropathy (wheat, barley, rye), NOT in rice, corn, oats
- Labs: anti-gliadin (DH)/anti-endomysial (celiac disease)
- Associations: increased risk of enteropathy-associated T cell lymphoma (refer to GI), Hashimoto's thyroiditis, insulin dependent diabetes mellitus.
- Treatment: Dapsone (skin improvement 24-48 hrs) 0.5 mg/kg, gluten-free diet

Histology: neutrophilic microabscesses in dermal papillae
DIF (normal appearing skin): granular IgA > C3 in dermal papillae

Bullous Systemic Lupus Erythematosus

- Rare blistering eruption that consists of vesicles and bullae. Clinically may look like BP or EBA with histopathology usually resembling DH. May be more common in African Americans.
- Antigen: Type VII collagen
- Clinical: Non-inflamed bullae/vesicles (hx of SLE usually)
- Based on 5 main criteria: (1) acquired vesiculobullous eruption, (2) subepidermal bullae with neutrophils, (3) DIF with linear or granular deposition of IgG (+/- IgA, IgM, etc), (4) type VII antibodies, (5) response to dapsone
- Should also fulfill criteria for American College of Rheumatology for SLE ( positive ANA, decreased complement, arthralgia, leukopenia, proteinuria, thrombocytopenia, elevated ESR may be seen).
- Treatment: Dapsone, PO corticosteroids, anti-malarials, azathioprine, mycophenolate mofetil

Histology: subepidermal bullae neutrophils in dermal papillae (similar to DH)
DIF/SSS: Linear IgG, IgM, IgA, C3, fibrinogen at BMZ, dermal side

Epidermolysis Bullosa Acquisita

- Rare, acquired, subepidermal immune-mediated bullous disease with antibodies directed against Type VII collagen (170 kDa)
- Rarest subepidermal bullous diseases in Western Europe (may be more common in Korean/Asian and African-American populations)
- Treatment: Unsatisfactory and difficult to treat. Dapsone and prednisolone may be of benefit for the childhood form.

Non-inflammatory bullae with fragile skin in areas easily traumatized (elbows, hands, knees, toes).
Heals with scarring +/- mucous membrane involvement.
Childhood EBA overlaps with childhood BP and linear IgA bullous dermatosis.
Systemic diseases may occur in association (inflammatory bowel disease, SLE, RA, thyroiditis, and DM).
Epidermolysis Bullosa Acquisita

Histology: subepidermal separation without acantholysis, variable infiltrate (neutrophils or non-inflammatory).

DIF/IIF: linear IgG (-/+ C3, fibrinogen, IgA, IgM) at BMZ, bind dermal side of SSS (floor).

Bullous Pemphigoid

- Rarely occur in children.
- Autoantigen: BPAG2 (collagen XVII) 180 kDa NC16A domain, BPAG1 230kDa, cytoplasmic plaque protein.
- Clinical.
- RF: SSS shows binding to epidermal side of split (roof).
- Treatment: Oral/topical corticosteroids, steroid-sparing (azathioprine, mycophenolate mofetil), tetracycline +/- nicotinamide, dapsone.

Histology: subepidermal bulla with eosinophils and lymphocytes in papillary dermis, +/- neutrophils.

Bullous Pemphigoid

Often with initial urticarial lesions which evolve into tense bullae, +/- pruritus.

Individual lesions in infants and older children look like elderly but sites of involvement may vary.

Infants-bullae first appear acrally, then generalize (including face). Involvement of the genital region and other mucosal sites may occur in children.

DIF: linear IgG (C3) at BMZ.

Pemphigus

- Group of autoimmune blistering diseases of the skin and mucous membranes.
- Includes:
  - Vulgaris:
    - Potentially fatal disease, can be seen in newborns (neonatal pemphigus) but rare.
  - Foliaceous:
    - More superficial and less severe than PV.
  - Drug Induced:
  - Paraneoplastic:
    - Less commonly due to an underlying malignancy in children.
  - IgA:
    - Characteristic histologic deposit.

Pemphigus Vulgaris (PV)

- Rare in pediatric patients, but can be seen in the newborns (neonatal pemphigus) whose mothers have pemphigus vulgaris.
- Due to passive transfer of maternal IgG to fetus.
- Autoantibody:
  - Desmoglein 3 (mucosal)
  - Desmoglein 1 (mucocutaneous).
- Clinical:
  - Vesicles and erosions trunk and extremities, mucosal involvement uncommon in neonatal form. (+) Nikolsky and Asboe-Hansen sign.
Drug Induced Pemphigus
- Particularly rare in children
- Sulphhydryl group containing medicines are implicated, most common being penicillamine and captopril
- Sulphhydryl groups thought to interact with the sulphhydryl groups in desmogleins 1 and 3, thus modifying the antigenicity of the desmoglein.
- Clinical:
  - Initially, a nonspecific morbilliform, annular, or urticarial eruption may be seen, eventually evolving after a variable latency period into the blistering process.
- Treatment:
  - Removal of offending agent if known
  - Corticosteroids if necessary

Paraneoplastic Pemphigus
- General:
  - In adults, commonly due to underlying malignancy (non-Hodgkin’s lymphoma most common)
  - In children, the most common causes include:
    - Castleman’s disease
    - Giant lymph node hyperplasia
    - Benign giant lymphoma
    - Sarcoma
- Autoantibody:
  - Desmoglein 3, periplakin, envoplakin, desmoplakin I, BPAG1, plectin, 170 kDa Ag, rarely desmoglein 1
- Clinical:
  - Intractable stomatitis, ocular involvement common, bullous or lichenoid lesions

Pemphigus Foliaceous (PF)
- Endemic (fogo selvagem) is more common in pediatric patients
- Seen in rural Brazil after a bite from black fly (Simulium nigrimanum)
- Sporadic PF is rare in children, but if present, shows a dramatic pattern of crusted plaques and erosions with an arcuate, circinate, or polycyclic morphology on the face and scalp.
- Autoantibody:
  - Desmoglein 1
- Clinical:
  - Crusted plaques and erosions in polycyclic distribution on face and scalp

Paraneoplastic Pemphigus
- Histology
  - Suprabasilar acantholysis, ± acinar basal layer damage associated with lymphocytic infiltrate, and necrotic keratinocytes
  - DIF: intercellular IgG/C3 along BMZ
  - IIF: intercellular IgG, best substrate is rat bladder epithelium
- Prognosis & Treatment
  - Poor prognosis, respiratory failure due to bronchiolitis obliterans more common
  - Treatment of malignancy, palliative immunosuppression

PV
- Histology
  - “tomb stone row” suprabasal split with acantholytic keratinocytes (possible follicular involvement), perivascular lymphocytes and eosinophils
  - DIF: intercellular IgG4 > C3, netlike pattern in epidermis
  - IIF: monkey esophagus, correlates with disease severity
- Prognosis and Treatment
  - Self resolving within weeks

Pemphigus Foliaceous (PF)
- Histology
  - Subcorneal acantholysis with acantholytic cells seen on blister roof (cling-ons), neutrophils can be seen in blister cavity (resembling impetigo)
  - DIF: same as PV, however, more pronounced in upper layers
  - IIF: best substrate is guinea pig esophagus
- Treatment:
  - First line: Systemic corticosteroids
  - Steroid-sparing therapies reported: Azathioprine, mycophenolate mofetil, IVIG, plasmapheresis, methotrexate, cyclophosphamide
  - Biologics: Rituximab

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  - Treatment of malignancy, palliative immunosuppression
IgA Pemphigus
• Blistering disease with intraepidermal IgA deposits
• Two types: Subcorneal pustular dermatosis (SPD), Intraepidermal neutrophilic type (IEN)
• There is no difference in the clinicopathologic features and prognosis of the disease between adults and children
• Autoantibody:
  - desmocollin 1 (SPD), ± desmoglein 1/3 (IEN)
• Clinical:
  - SPD: serpiginous vesicles or pustules; may be associated with underlying IgA gammopathy
  - IEN: flaccid pustules and bullae involving intertriginous locations which enlarge forming annular or polycyclic (sunflower-like) arrangement
• Histology:
  - intrapidermal pustule or vesicles containing neutrophils, no acantholysis
• DIF: intercellular IgA deposition
• IIF: (+) in 50%, intercellular IgA
• Treatment: Dapsone, oral corticosteroids

Herpes Gestationis
• Aka Pemphigoid gestationis (PG), is an autoimmune bullous dermatosis of pregnancy.
• Common in the 2nd or 3rd trimester, or immediately postpartum
• Neonatal disease is observed in up to 10% of children born to mothers with PG
• Autoantibody:
  - anti-BPAG2 (BP180, NC16A site)
• Clinical:
  - Erythematous urticarial or vesicular rash, but yellowish plaques on erythematous base and frank bullae have also been reported
  - Fingernail lesions in the newborn are due to a passive transfer of Ig
• Histology:
  - papillary dermal edema resulting in subepidermal bulla with eosinophil rich infiltrate, ± keratinocyte necrosis, perivascular infiltrate
• DIF: linear C3 deposition ± IgG at basement membrane
• IIF: epidermal base (roof of blister like BP)
• Treatment:
  - The disease is generally mild and resolves spontaneously in the course of days to weeks after onset.

Subcorneal Pustular Dermatosis
• Aka Sneddon-Wilkinson
• Etiology still unknown, but certain associations have been seen including a benign monoclonal IgA gammopathy and pyoderma gangrenosum
• Clinical:
  - annular or polycyclic lesions, usually commencing in the flexures, with holoma superficial (subcorneal) sterile pustules
  - Has a cyclic course, as the pustules resolve they are replaced by superficial scaling and then new pustules form
• Histology:
  - Perivascular inflammatory infiltrate with neutrophils and occasional eosinophils
  - Neutrophils migrate through the epidermis, without forming spongiform pustules, to collect beneath the stratum corneum in subcorneal pustules
• Treatment: Dapsone

Chilblains
• Abnormal inflammatory response to cold, damp, non-freezing conditions
• Common in the UK and northwestern Europe, particularly in those whose homes lack central heating
• Unknown pathogenesis, but thought to have a vascular origin
• Clinical:
  - Lesions are red-purple and usually macular, papular or nodular
  - Develop symmetrically on acral skin, in particular the fingers and toes, but can occur elsewhere
• Histology:
  - Nonspecific, consisting of dermal edema plus a superficial and deep lymphohistiocytic infiltrate (mainly T cells) with peri-eccrine accentuation
• Treatment:
  - Adequate clothing and avoidance of cold, damp conditions are important preventive measures. As are keeping feet dry and avoidance of smoking
• In a Double-blind, placebo-controlled trial, nifedipine (20 to 60 mg daily) was found to be efficacious for the treatment of pernio

Phytophotodermatitis
• Pathogenesis: A phototoxic eruption, commonly caused by a topical or oral photosensitizing agent followed by exposure to UVR
• Members of 2 plant families are common causes: Apiaceae and Rutaceae. The common photosensitizer is furocoumarins
• Clinical presentation: Random configurations of erythema, edema and bullae after sun exposure
Erythema Multiforme

- Clinical Presentation: Typical target lesions with at least three distinct zones. There is usually a central bullae and the lesion resembles a target.
- Pathogenesis: Occurs in predisposed individuals, often in the setting of HSV or Mycoplasma pneumonia infection.
- Histopathology: Spongiosis and focal vacuolar degeneration of basal keratinocytes with dermal edema and a perivascular infiltrate of mononuclear leukocytes and T lymphocytes.

Bullous Mastocytosis

- Some infants with urticaria pigmentosa or diffuse cutaneous mastocytosis may develop bullous lesions.
- Thought to be due to increased mast cell serine proteases.
- Often resolves by age 3-5y.
- Manage as you would for other child mastocytoses with increased attention to wound care for eroded lesions.

Porphyria

- Inherited or acquired disorders due to enzyme deficiency causing increased production of photosensitizing porphyrins or their precursors during heme synthesis.

Table from: Photosensitivity and Photoreactions in Hurwitz Clinical Pediatric Dermatology, Mancini AJ, Paller AS. Elsevier 2011. p 449
Porphyria

- Congenital Erythropoietic Porphyria (CEP) [AR]
- Occurs in infancy through 1st decade
- Extreme photosensitivity, hyperthermia, erythroderma
- Erythropoietic Porphyria [AD]
- Occurs between 1-4yo
- Photosensitivity with burning, galstones, hepatic damage
- Hepatoerythropoietic Porphyria [AR]
- Usally manifests before 2 years of age
- Dark urine is most common initial finding
- Acute Intermittent Porphyria [AD]
- No skin findings
- Neurologic and psychiatric findings with abdominal pain

Friction Blisters

- Occur most commonly on the soles and heels.
- Caused by repeated friction
- Blistering occurs just below the stratum granulosum

Burns and Scalds

- Can be accidental or intentional (child abuse)
- Careful history and physical examination with care to note child caregiver interactions
- In inflicted wounds there is often a delay in seeking care from the time of injury
- Look for lesions in various stages of healing

References

References

Cutaneous Manifestations of Systemic Disease: Nutritional Deficiencies

Jessica Hoy, D.O.
OhioHealth O’Bleness Hospital Dermatology Residency
AOCD Spring Meeting
March 30, 2017

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- Dr. Gabriela Maloney, PGY-4
- Dr. Alyson Rispath, PGY-2

Objectives
- Case presentation
- Review select nutritional deficiencies and the differential diagnosis
  - Clinical presentation
  - Work-up
  - Treatment
  - Pathology

- No disclosures

[Image of skin condition]
Medications
• Pantoprazole
• Paroxetine
• Furosemide
• Methylphenidate
• Warfarin
• Docusate sodium
• Ferrous sulfate

Patient BB
• Past medical history
  • HIV
  • Seizures
  • Anxiety
  • Depression
  • DVT

• Past surgical history
  • Gastric bypass in 2003 (Guinea pig?)
  • Cholecystectomy

Differential diagnosis
• Nutritional deficiencies
  • Acrodermatitis enteropathica
  • Pellagra
  • Riboflavin
  • Acanthosis
  • Essential fatty acid
  • Biotin

• Necrotic acral erythema
• Necrotic migratory erythema
• Acrokeratosis paraneoplastica
Work up
- CBC with diff
  - Hb 9.0 g/dL
- MCV 93.6
- CMP
  - Na 134 mmol/L
  - K 4.8 mmol/L
  - Ca 9.3 mmol/L
  - Albumin 3.9 g/dL
  - Total protein 4.0 g/dL
- B12 501 pg/mL
- Folate 74.8 ng/mL
- Vit D 25-OH 35 ng/mL
- Niacin 2.16 mg/dL
- Zinc 0.40 mcg/mL (ref 0.65-1.10)
- ANA <40

Acquired acrodermatitis enteropathica
- Supplemented with Zinc 50mg PO daily (0.5-1mg/kg/day)
- Supplemented with Niacin 50mg daily
- Refer to GI for workup of chronic diarrhea and likely malabsorption in setting of prior gastric bypass surgery

Follow up at 4 weeks

Zinc deficiency
Acquired acrodermatitis enteropathica
- Clinical features
  - Symmetrical exuberant or vesiculobullous lesions located perioral
  - Oral erosions
  - Grossoles, angular cheilitis, alopecia, diarrhea
- Risk factors
  - IBG, malabsorption, anorexia, HIV, alcoholics

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Zinc deficiency

Acrodermatitis enteropathica
- Triad: periorificial dermatitis, alopecia and diarrhea present in 20% of patients
- Occurs in 4 clinical scenarios:
  1. Premature infants (poor absorption and ↑ requirement of zinc) when weaned off breast milk
  2. Inherited form (AR) manifests when weaned off breast milk
  3. Mutation in zinc transporter gene SLC39A4
  4. Healthy infants if low zinc level in maternal milk
- Acquired form if malabsorption or inadequate nutrition

Differential diagnosis
- Nutritional deficiencies
- Acrodermatitis enteropathica
- Pellagra
- Riboflavin
- Pyridoxine
- Essential fatty acid
- Biotin
- Necrolytic acral erythema
- Necrolytic migratory erythema
- Acrokeratosis paraneoplastica

Zinc Deficiency

Acrodermatitis enteropathica

B vitamin deficiencies
- B-complex vitamins serve as coenzymes in many metabolic pathways that are functionally closely related
- A lack of one of the vitamins has the potential to interrupt a chain of chemical processes, including reactions that are dependent on other vitamins
- Many vitamin deficiency dermatoses share similar clinical features
Vitamin B2 (Riboflavin) Deficiency

• AKA Oral-ocular-genital syndrome
• Riboflavin is a water soluble vitamin that is absorbed in the small intestine by the human riboflavin transporters RFVT1 and RFVT3
• It functions in intracellular oxidation-reduction reactions related to:
  • Energy production
  • Enzyme functions
  • Normal fatty acid and amino acid synthesis
  • Reproduction of glutathione

Clinical features
• Angular cheilitis
• Atrophic, sore, magenta-colored tongue
• Seborrheic dermatitis-like changes (nose, mouth, eyes)
• Angular cheilitis
• Photophobia
• Seborrhea
• Anemia due to bone marrow hyperplasia
• Mental retardation in infants

Vitamin B2 (Riboflavin) Deficiency - Oral-ocular-genital syndrome

Vitamin B3 (Niacin) Deficiency

• AKA Pellagra
• Involved in reduction-oxidation reactions, tryptophan precursor amino acid

Clinical features
• 6 D’s
  • Photosensitive dermatitis
    • Primary finding - 38%
  • Dementia
  • Diarrhea
  • Death
  • Angular cheilitis
  • Perianal dermatitis
Vitamin B3 (Niacin) Deficiency

- Risk factors
  - Malnourished diet
  - Malabsorption
  - Kidney disease
  - Isoniazid
  - Post-celiac disease
- Hemochromatosis can present with a pellagra-like dermatosis
  - GI CCK
  - Aminoaciduria and cryptophan deficiency

Vitamin B6 (Pyridoxine) Deficiency

- Ubiquitous in all foods
- Role in amino acid and fatty acid metabolism

- Clinical Hallmarks:
  - Seb Dermatitis
  - Periungual Dermatitis
  - Peripheral neuropathy
  - Sideroblastic anemia

- Relevant Associations
  - Cirrhosis
  - Uremia
  - Isoniazid: requires B6 supplementation
  - OCD
  - Malnutrition

Essential Fatty Acid Deficiency

- Unsaturated fatty acids:
  - Linoleic
  - Linolenic
  - Arachidonic acid (can be metabolized from linoleic acid)
- Must be obtained from an exogenous source
- Constitutes up to one quarter of the fatty acids of the stratum corneum

Essential Fatty Acid Deficiency

- Clinical features
  - Erythema, widespread eczematous dermatitis, and an intertriginous weeping eruption
  - Nail becomes lighter in color with diffuse atrophy
  - Poor wound healing, growth failure, and increased risk of infection may occur
- Risk factors
  - Parenteral nutrition without EPA, aggressive low-fat diet, GI abnormalities, low-birth-weight infants, cystic fibrosis
Essential Fatty Acid Deficiency

Vitamin B7 (Biotin) Deficiency

Vitamin B7 (Biotin) Deficiency
- Universally available and produced by intestinal bacteria
- Multiple carboxylase deficiency, AR
  - Retinol carboxylase deficiency-neonatal form
  - Biotinidase deficiency-juvenile form
- Permanent neurologic sequelae if delay in treatment

Biotin Deficiency
- Clinical features
  - Keratotic dermatitis
  - Alopecia
  - Seborrheic dermatitis
  - Fissures may be prominent on the feet, face and the perianal area
  - Neonatal-acrocyanoderma
  - Juvenile—resembles acne-dermatitis enteropathica
  - Neurologic: Depression, seizures, paresthesias
- Risk factors
  - Short gut, malabsorption, ingestion large amount of raw egg whites, anticonvulsants

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<thead>
<tr>
<th>Vitamin or Trace Mineral</th>
<th>Recommended Lab Test</th>
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<tr>
<td>Vitamin B1 (Thiamin)</td>
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<td>Vitamin B6 (Pyridoxine)</td>
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Vitamin or trace mineral Treatment of deficiency

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Differential diagnosis

- Nutritional deficiencies
  - Acrodermatitis enteropathica
  - Pellagra
  - Riboflavin
  - Pyridoxine
  - Essential fatty acid
  - Biotin
- Necrolytic acral erythema
- Necrolytic migratory erythema
- Acrokeratosis paraneoplastica

Necrolytic Acral Erythema

- Fewer than 100 cases worldwide since it was first described in 1996
- Clinical features
  - Hyperkeratotic pink to violaceous plaques involving acral sites, particularly lower extremities
  - Blisters and erosions are common
  - May be painful or pruritic
- Associations
  - Human Immunodeficiency Virus
  - Presence of NAC in HIV is ~1%
  - Zinc deficiency has rarely been reported

Necrolytic Acral Erythema

- Treatment options
  - Therapy for underlying HCV
  - Interferon alone or in combination with ribavirin
  - Supplementation with zinc may improve NAC even in the absence of zinc deficiency
  - Variable success
Necrolytic Migratory Erythema

- AKA Glucagonoma Syndrome
- NMF + weight loss + adult-onset DM + colitis
- Clinical features
  - Eroded, erythematous patches and plaques involving intertriginous areas, face (particularly perioral) and distal extremities
  - May be painful or pruritic
  - Recurs over weeks to months
- Associations
  - Glucagon-secreting tumor of the pancreas (pallid tumor)
  - Severe liver disease

Necrolytic Migratory Erythema

- Treatment involves addressing the underlying cause
  - Surgical resection of pancreatic tumor
  - Replacement therapy for deficiency states
Acrokeratosis Paraneoplastica

- **Clinical features**
  - Erythematous plaques with desquamative erythematos lesions
  - Lesions are typically located symmetrically on the oral surfaces
  - Palmoplantar keratosis
  - Hands and feet are affected in 60% and 75% of patients respectively
  - Blisters of hands and feet is common in African-American patients

Acrokeratosis Paraneoplastica

- Bazex syndrome can progress in three stages
  - (a) cutaneous lesions in ears, fingers and nails
  - (b) palmoplantar keratosis
  - (c) involvement of knees, elbows and torso

- The primary tumor tends to become symptomatic during the stage of palmoplantar keratosis

Pathology

- Acute lesions
  - Patellar, upper 1/3 of bones
  - Ballooning or vacuolar degeneration
  - Dermal vascular dilatation
  - Confluent keratinocyte necrosis
  - Seen in Acrokeratosis enteropathica, keratoactinic acral erythema, Necrolytic migratory erythema

Acrokeratosis Paraneoplastica

- Bazex syndrome
  - Primarily affects Caucasian males over 40 years of age
  - Associations
    - Squamous cell carcinomas of the head and neck
    - Liposarcoma, bladder, prostate and breast cancer has also been reported
    - In 67% of cases reported, cutaneous manifestations preceded the diagnosis of cancer by approximately one year
    - In 18% of patients, cutaneous lesions and cancer are diagnosed concomitantly and in 15% of the cases the diagnosis of cancer occurs first

Acrokeratosis Paraneoplastica

- Acquired acrodermatitis enteropathica: case report of an atypical presentation.
Chronic or resolving lesions
- Psoriasiform hyperplasia
- Confluent parakeratosis
- Hypogranulosis
- Minimal to absent epidermal pallor

In summary
- Cutaneous findings often the first signs of nutritional deficiency, therefore the dermatologist can play a key role in diagnosis
- Common dermatoses not responding to conventional therapy should alert the clinician to search for nutritional deficiencies
- Initiating treatment can often provide diagnostic information as lab work-up can be unreliable

Acknowledgements
- Dr. Dawn Sammons
- Co-residents
  - Dr. Hoch Winkelmann
  - Dr. Tyler Sokoloff
  - Dr. Gabriela Maloney
  - Dr. Alyssen Ridpath

References
References

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<td><em>Cases In Oncodermatology</em></td>
<td>Granulomatous, Metabolic and Depositional Diseases</td>
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<td>11:30 a.m. - 12:30 p.m.</td>
<td>Abbvie Product Theater: <em>Milestones in the Treatment of Hidradenitis Suppuritiva</em></td>
<td>Pediatric Dermatology: Tumors of Fat, Muscle and Bone and Epidermal, Appendageal and Dermal Tumors</td>
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<tr>
<td>12:30 p.m. - 1:30 p.m.</td>
<td><em>HIV In Dermatology</em></td>
<td>PCOM/North Fulton Hospital Medical Campus</td>
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<td>1:30 p.m. - 2:30 p.m.</td>
<td><em>Managing Your Online Reputation</em></td>
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<td>2:30 p.m. - 3:00 p.m.</td>
<td>Break with Exhibitors</td>
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<td>3:00 p.m. - 4:30 p.m.</td>
<td><em>AAD Billing and Coding Update</em></td>
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<tr>
<td>5:00 p.m.</td>
<td>Presidential Reception</td>
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Friday, March 31, 2017
Primary Pathway
Challenges in Dermatopathology
Larissa A. Chismar, MD FAAD
3/31/17

Overview
- Communication between the dermatologist and dermatopathologist
- Melanocytic lesions
- Soft tissue lesions
- Adnexal lesions
- Inflammatory lesions

Communication
- Communication between the dermatologist and dermatopathologist is essential for a successful relationship
- The dermatopathology requisition form is the primary way that dermatologists communicate information to the dermatopathologist
- Including more information on the requisition form helps your dermatopathologist make the best diagnosis for your patient

The Dermatopathology Requisition Form: Attitudes and Practices of Dermatologists
- Larissa A. Chismar, MD, Nicole Umanoff, BS, Blair Murphy, BS, Kate V. Viola, MD, MHS, Bijal Amin, MD
- Journal of the American Academy of Dermatology
  - Volume 72, Issue 2, Pages 353-5 (February 2015)

Disclosures
- Employee of Atlanta Dermatopathology, A PathGroup Company
- No conflicts of interest

What Did We Want to Know?
- Demographic information
- Who fills out form?
- Estimate of time spent on form
What Did We Want to Know?

- How important do you think it is to include various pieces of information?
  - Location, color, size, duration, clinical DDx, treatment history, Fitzpatrick skin type, ethnicity, history of malignancy, history of organ/bone marrow transplant, history of HIV, history of Hepatitis B or C, other past medical history, history of melanoma
- How often do you include the above pieces of information?

What Did We Want to Know?

- How strongly do you agree with the following statements?
  - I am reluctant to add clinical information because I do not want to bias the dermatopathologist
  - I believe the dermatopathologist should be able to make a diagnosis without any clinical information

What Did We Want to Know?

- How strongly do you agree with the following statements?
  - I am reluctant to add clinical information because I do not want to bias the dermatopathologist
  - I believe the dermatopathologist should be able to make a diagnosis without any clinical information

Attitudes Toward Requisition Forms

- Clinical information biases pathologist
- Pathologist should make diagnosis without clinical information
Looked at clinical information provided and microscopic diagnosis for 100 consecutive melanocytic lesions
• Important information not always included on requisition form
  – Clinical morphology provided in 33%
  – No mention of any ABCDE criteria in 55%
  – Lesion size provided in 22%
  – Partial vs. complete sampling of lesion specified in 0%
  – Only information on form “r/o X” in 29%

Some Information is Important to Include?
• Lesion location
• Patient age
• Clinical impression/differential diagnosis
• Partial versus complete sampling
• Duration of lesion
• Lesion morphology
• Clinical symptoms
• Previous treatments
• Known clinical diagnoses
• Previous dermatopathologic diagnoses (like history of melanoma)
• Clinical photographs

Remember...
• The information you supply on the requisition form becomes a part of the patient’s medical record!
Challenges with Melanocytic Lesions

- Partial biopsies

Partial Biopsies for Suspected Melanoma

- 31% of US dermatologists (Survey 1995)
- 27% of cases in Victoria, Australia (2000)
- 30% and 22% of cases referred by GPs and dermatologists, respectively, to a UK surgical unit (2008)


Impact of Partial Biopsy on Histopathologic Diagnosis of Melanoma

- Increased odds of false negative diagnosis in partial versus excisional biopsies
  - Shave: odds ratio 2.6%
  - Punch: odds ratio 16.6%

Concordance with Excision Specimen

- 96% of shave biopsies
- 71% punch biopsies


Most Diagnostic Criteria to Distinguish Nevus from Melanoma Rely on Excisional Biopsies
Criteria for the Diagnosis of Melanoma

- Architecture—Asymmetry of
  - Silhouette
  - Lateral junctional borders
  - Distribution of melanocytes and nests at the junction
  - Distribution of pigment within the lesion
  - Distribution of inflammatory response
  - Epidermal alteration
  - Cytologic details
- Architecture—Other
  - Large dimension of the lesion
  - Poor delimitation of the lesion
  - Large confluent nests
  - Expansile nodules and solid growth pattern
  - Consumption of the epidermis
  - Lack of maturation
- Cytologic and other criteria
  - Cellular atypia
  - Cellular pleomorphism and mitotic figures
  - Pagetoid spread
  - Sun damage


It Can Be Easy

- Utilization of known criteria

Challenges with Melanocytic Lesions

- Partial biopsies
  - It is possible to diagnose melanoma through the utilization of known criteria in a partial biopsy
  - It is not possible to exclude melanoma!
    - Sampling error
CASE

- 55 y/o F
- Left posterior shoulder
- “R/O nevus with increased pigment”

Diagnosis: “Nevus”

10 years later: Metastatic melanoma
Challenges with Melanocytic Lesions

- Partial biopsies
  - It is not possible to exclude melanoma!
- Sampling error
  - Melanoma arising in association with a nevus

CASE

- 69 y/o F
- Right lateral malar cheek
- “Irregular brown macule”
- “Atypical nevus versus melanoma versus benign nevus”
Diagnosis: “Pigmented solar keratosis and solar lentigo”

Diagnosis: “Pigmented solar keratosis and solar lentigo”

Keep looking
Partial biopsies
- It is not possible to exclude melanoma!
  - Sampling error
    - Melanoma arising in association with a nevus
    - Contiguous lesions in lentigo maligna

Contiguous Pigmented Lesions
- Present in 48% of LM specimens
  - Solar lentigo (30%)
  - Pigmented actinic keratosis (24%)

CASE

- 60 y/o M
- Right preauricular
- “SK vs. lentigo vs. lentigo maligna”
Challenges with Melanocytic Lesions

- Partial biopsies
  - It is not possible to exclude melanoma!
    - Sampling error
      - Melanoma arising in association with a nevus
      - Contiguous lesions in lentigo maligna
      - Skip areas or regression in MMIS

“… a partial biopsy may result in a partial diagnosis which may be a misdiagnosis.”


Surgical Pathology Claims to a US Medical Indemnity Provider

- False-negative dx of melanoma - single most common reason for filing a malpractice claim against a pathologist
- Partial bx was responsible for over 50% of false-negative melanoma misdiagnoses


Size of the lesion

Single most important piece of clinical information when submitting a pigmented lesion!

Usually known to the clinician, but not always communicated


Pigmented Lesion Subcommittee Consensus Statement

- Preferred bx technique for evaluation of a lesion highly suspicious for melanoma: narrow excisional biopsy with 1- to 3-mm margins ...
- …via saucerization/shave, punch, or elliptical biopsy...

AAD and the NCCN clinical practice guidelines for melanoma
Vague DDx on requisition can be challenging – Let your pathologist know when you're really worried!

Clinical photographs can be helpful

Challenges with Melanocytic Lesions

- Vague DDx on requisition can be challenging
  - Let your pathologist know when you're really worried!
- Clinical photographs can be helpful
CASE

- 66 y/o F
- 5th right toe
- “R/O atypia”

Final diagnosis: Acral nevus
CASE

- 56 y/o F
- 5th left toe
- "R/O DN vs wart vs hematoma"
Final diagnosis: Acral lentiginous melanoma

Challenges with Soft Tissue Lesions

- Large number of soft tissue tumor types
- Relative rarity of most types
- Subtle histological differences between them
- Inflammatory lesions may mimic sarcomas
- Malignant soft tissue tumors may mimic benign lesions → often misdiagnosed

Classification of Soft Tissue Tumors

1. Adipocytic
2. Fibroblastic/ Myofibroblastic
3. So-called Fibrohistiocytic
4. Smooth Muscle
5. Pericytic (perivascular)
6. Skeletal Muscle
7. Vascular
8. Chondro-osseous
9. Tumors of Uncertain Differentiation
Classification of Soft Tissue Tumors

- Biological Potential
  - Benign
  - Intermediate (locally aggressive)
  - Intermediate (rarely metastasizing)
  - Malignant (= sarcoma)

CASE

- 49 y/o F
- Left shoulder
- “R/O neoplasm”
Repeat biopsy:
Diagnosis: Dermatofibrosarcoma protuberans

- Fibrohistiocytic neoplasm of intermediate malignancy (rarely metastasizing)
- Young and middle-aged adults, but also in infants and children
- Trunk > proximal extremities, head & neck
- Slowly growing firm plaque → (multi-) nodular
- Average size at time of excision 4-5 cm!
- Recurrence rate 20-50%
- May metastasize 0.5% - 4%

DFSP Immunophenotype

<table>
<thead>
<tr>
<th>DF</th>
<th>DFSP</th>
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<tbody>
<tr>
<td>FXIIa +</td>
<td>FXIIa -</td>
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<tr>
<td>CD34 -</td>
<td>CD34 +</td>
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</tbody>
</table>

CD34 Positive Soft Tissue Tumors

- Spindle cell lipoma
- Neurofibroma
- Solitary fibrous tumor
- Pleomorphic fibroma
- Kaposi sarcoma and other vascular tumors
- MPNST
- Epithelioid sarcoma
- Gastrointestinal stromal tumor

Dermatofibrosarcoma Protuberans Variants

- Sclerosing
- Granular
- Myoid nodules
- Atrophic / Plaque-like
- Myxoid
- Pigmented (Bednar tumor)
- Giant cell fibroblastoma-like
- Fibrosarcomatous

Challenges with Soft Tissue Lesions

- History can be misleading
CASE

- 35 y/o F with a non-healing lesion on the palm noticed after injury
- Previous biopsy at outside institution was suspicious for an infectious process
Diagnosis:
Epithelioid sarcoma

Epithelioid Sarcoma
- Malignant sarcoma of uncertain differentiation
- Young adults age 10-39 years
- M > F
- Extremities, especially flexor surfaces of hands, wrists and forearm > lower extremity
- Slow growing painless plaque or nodule
- May have multifocal involvement at presentation
- History of trauma in 20%

Epithelioid Sarcoma
- Aggressive sarcoma that propagates along fascial planes, tendons, and nerve sheaths
- Local recurrences in up to 77%
- Metastases in 40% (regional LN, lungs, skin of scalp), usually after multiple recurrences
- 70% of patients die of the disease
Challenges with Soft Tissue Lesions

- History can be essential for diagnosis

CASE

- 66 y/o M
- Right superior parietal scalp
- "Tumor"
Diagnostic Considerations

- Neural tumor – malignant peripheral nerve sheath tumor
- Spindle cell malignant melanoma with loss of some melanocytic markers

Outside Consultation

- Prominent soft tissue expert
- Favored diagnosis of spindle cell malignant melanoma
  - Tumor close to the overlying epidermis without evidence of pre-existing neurofibroma
  - Staining for H3K27me3 was positive
  - Loss highly specific for MPNST (homozygous PRC2 (polycomb repressive complex 2) inactivation results in loss of histone H3K27 trimethylation)
    - 51% MPNST in series of 100 tumors negative for H3K27me3
    » 49% sporadic tumors, 70% NF 1-associated tumors, 100% radiation-associated

Additional History

- Patient with history of NF1
- MPNST on right upper back (dx 2013)
- Metastasis of MPNST to right lower lobe of lung (dx 2014)
- Metastasis to liver (dx 2016)
New Diagnostic Considerations

- History makes MPNST more likely
  - ? Metastatic lesion
  - ? New primary

Excision:
Final Diagnosis

• MPNST arising in NF

CASE

• 65 y/o F
• Right posterior scalp
• "Firm white nodule. R/O BCC vs SK vs cyst."
Diagnosis:
Surface of cystic proliferation with focal poroid features

Excision
1.5 x 1.1 cm ellipse:
Diagnosis:
Malignant adnexal neoplasm, favor solid carcinoma

Solid Carcinoma
- Thought to be a variant of microcystic adnexal carcinoma
- Innumerable small, solid aggregates of neoplastic cells extending throughout the dermis, often into the subcutis (infiltrative growth pattern)
- Larger aggregates of neoplastic cells than MAC
- Cells are cytologically bland, mitoses are rare (usually absent)
- Has been reported on the scalp (Lai et al, Am J Dermatopathol 2014;36(11):925-7.)

Challenging Inflammatory Lesions
Challenging Inflammatory Lesions

- Patient’s history may be misleading

CASE

- 38 y/o M
- Right occipital scalp/posterior neck
- “Confirm tick bite”
Diagnosis: Varicella zoster virus folliculitis

Varicella Zoster Virus Folliculitis

- Varicella zoster virus affecting hair follicle/sebaceous unit ("sebaceitis")
- Often not evident in initial sections (need deeper levels!)
  - Mimics robust inflammatory process and easily misdiagnosed
- Could be completely missed with shave biopsy
- Patient history may be misleading

Challenges Can Affect Every Case!

- Partial biopsies can be misleading even for very basic diagnoses
CASE

- 65 y/o F
- Right dorsal hand
- “R/O carcinoma”

Diagnosis:
Hyperplastic solar (actinic) keratosis

Note: The atypical epithelial changes are transected at the base. If the lesion fails to respond to conservative therapy, an additional biopsy is recommended.

Repeat biopsy performed at follow-up visit:
Diagnosis:
Invasive squamous cell carcinoma

Conclusions
- Good dermatologist-dermatopathologist communication is essential to make the best diagnosis for your patient
- More clinical information is better
- Beware of partial biopsies (and always alert your dermatopathologist!)
- Carefully read your pathology report – always consider repeat biopsy or call to your dermpath if something seems unusual or doesn’t fit well with clinical findings

References
HIV and the Skin

Charles A. Gropper, M.D.
Chief of Dermatology
St. Barnabas Hospital, Bronx, NY

The Bronx

Arthur Ave
- New York Botanical Garden
- Bronx Zoo
- Yankee stadium
- Wave Hill
- Horace Mann School
History of HIV

• July 1981
  – 26 initial cases of young men with unusual presentation of dermatologic findings reported by NYU
    • KS: not classical type
    • Oral Candidiasis
    • Chronic HSV
  – Now more likely to present with other STD such as syphilis

HIV Facts and Figures

• More than 60 million people infected with HIV and more than half have died since epidemic began
HIV Facts and Figures

- Annual number of new HIV infections has remained stable
- New infections remain high: Estimated 56,300 Americans get infected each year
- More than 18,000 people with HIV die each year in the US

http://www.cdc.gov/hiv/resources/factsheets/us.htm

Prevalence of Undiagnosed HIV Infection


Prevalence of Undiagnosed HIV Infection

GLOBAL
- Living with HIV: 37 x 10^6
- Incidence: 2 x 10^6
- Cumulative AIDS mortality: 36 x 10^6
- Once diagnosed only 43% engage in care

USA
- Living with HIV: 1.2 x 10^6
- Cumulative AIDS mortality: 68,000
- Once diagnosed only 40% engage in care

HIV: Still a Problem

HIV: USA, 2016

United States Department of Health and Human Services

Prepared by: AIDS United


- 20% Rise in Unprotected Sex from 2005-2011
- People are “sero-sorting”
- Better treatment and bad economy lead to risky behavior
- New infections still about 50,000/year
- Government goal to decrease to 30,000/year
HIV Transmission: Variable Laws

- **California** – Felony punishable by up to 8 years in prison
- **Missouri** – Class B felony to expose a person to HIV. If complainant becomes infected, the charge is a class A felony. The use of a condom is not a defense
- **New York** – Reckless endangerment in the first degree for engaging in conduct which creates a grave risk of death to another person
- **Texas** – Aggravated assault laws whereby a person “intentionally, knowingly, or recklessly... uses or exhibits a deadly weapon as part of an assault”. Saliva of an HIV infected person is considered a deadly weapon

HIV Discrimination

Primary vs Secondary HIV Skin Conditions

<table>
<thead>
<tr>
<th>Classification of HIV-Related Skin Pharyngitis</th>
<th>Secondary Skin Pharyngitis</th>
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<tbody>
<tr>
<td>Erythematous Macules</td>
<td>Erythematous Papules</td>
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<tr>
<td>Pustules</td>
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<tr>
<td>Ulcers</td>
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<td>Vesicles</td>
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HIV AND THE SKIN

- Prevalence of cutaneous abnormalities approaches 100% in patients with HIV
- Some cutaneous conditions are unique and pathognomonic for HIV
  - Example: Kaposi’s Sarcoma
- Skin findings may be marker of disease stage
  - Example: EPF usually occurs in pts with T Cell Count <200

KEY POINT:
DERMATOLOGISTS SHOULD STILL CONSIDER HIV INFECTION IN PATIENTS PRESENTING WITH BOTH COMMON AND RARE SKIN ABNORMALITIES

Correlation of CD4 Count with HIV-Associated Dermatologic Disorders

<table>
<thead>
<tr>
<th>CD4 Count</th>
<th>Acute retroviral syndrome</th>
<th>Oral hairy leukoplakia</th>
<th>Vaginal candidiasis</th>
<th>Seborrheic dermatitis</th>
<th>Kaposi’s sarcoma</th>
<th>Eruptive atypical melanocytic nevi and melanoma</th>
<th>Kaposi’s sarcoma</th>
<th>Eosinophilic folliculitis</th>
<th>Seborrheic dermatitis, refractory</th>
<th>Molluscum, extensive</th>
<th>Miliary TB, disseminated</th>
<th>Cryptococcosis, disseminated</th>
<th>Histoplasmosis, disseminated</th>
<th>Coccidioidomycosis, disseminated</th>
<th>Botryomycosis</th>
<th>Non-Hodgkin lymphoma</th>
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<tr>
<td>&gt;500 CD4+ cells/mm³</td>
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CATEGORIES OF SKIN PROBLEMS IN HIV

- INFECTIOUS
- INFLAMMATORY
- NEOPLASTIC
Viral Infections with HIV

- Acute HIV Morbilliform Rash
- Herpes Simplex
- Syphilis
- Varicella/Zoster
- HPV
- Oral Hairy Leukoplakia

INFECTIONOUS

- HERPES SIMPLEX VIRUS
  - CDC Defined Index Infection in making AIDS. Dx
  - Clinical findings similar to non HIV patients if immune system relatively intact
  - Once immunosuppressed, HIV patients often develop chronic painful ulcer
    - Perianal, perioral, perungual

Treatment of HSV in HIV patients

- Acyclovir, Famiclovir, Valacyclovir
- Acyclovir-Resistant HSV Infection
  - Thymidine-kinase-negative, acyclovir resistant HSV-2
  - IV: foscarnet and cidofovir
  - Topical: trifluridine, cidofovir, and imiquimod

HSV in HIV

Syphilis

- Concurrent Primary + Secondary Lues = HIV+

HZV in HIV

- Herpes Zoster often precedes thrush and oral hairy leukoplakia
  - May be early sign of HIV
  - Duration, pain and amount of scarring may be more severe in HIV patients
  - Recurrences in up to 25%
  - Dissemination with widespread ulcers or hyperkeratotic, verrucous lesions may occur
HZV

Disseminated HZV

HPV

- HPV infection more common in immunocompromised patients
- Cervical dysplasia is common in HIV infected women
- Increased risk of anal warts and anal carcinoma in homosexual men

HPV

Anal HPV

Acute HIV Exanthem and Enanthem

- Maculopapular rash which sometimes resembles P. rosea
- Upper trunk, proximal limbs, palms, and soles
- Oral erythema or erosions may be present
- Usually resolves in 1-2 weeks
- Patients may seronegative and most infectious at time of rash
HIV Acute Rash

ORAL HAIRY LEUKOPLAKIA
- Develops in about 25% of infected individuals
- Predictor of rapid decline and AIDS progression
- White plaques with hair like progressions
- No malignant potential
- May regress with antiretroviral therapy

Molluscum Contagiosum
- Extragenital molluscum contagiosum occurs almost exclusively in HIV-infected or immunocompromised patients
- The following infections resemble molluscum-like lesions:
  - Coccidioidomycosis
  - Cryptococcus
  - Histoplasmosis
  - Aspergillosis

Deep Fungal Infections
- Cryptococcus
  - Presents with meningitis
  - May present as molluscum-like lesions on the face and neck
Cryptococcus

Deep Fungal Infections

• Histoplasmosis
  – May represent reactivation of previous infection
  – Cases seen in NYC mostly in patients who lived previously in an endemic area
  – Variable skin lesions: pustules, acneform, ulcerations and plaques
  – May be fatal syndrome with sepsis, DIC, and pulmonary, CNS and renal failure

Histoplasmosis

Mucocutaneous histoplasmosis in HIV with an atypical eczema like presentation
Vandana Mehta, Abhishek De, C Balachandran, Puja Monga Dermatology Online Journal 15 (4): 10

HISTOPLASMOSIS

Deep Fungal Infections

• Sporotrichosis
  – Asymptomatic pulmonary infection that spreads to the skin
  – Widespread ulcers and SQ nodules
Deep Fungal Infections

- **Aspergillus**
  - May be primary or secondary
  - Primary from local skin injury
  - Red plaques with pustules and ulcers or molluscum like lesions
  - Treatment with amphotericin B or itraconazole

**INFECTIONOUS**

- **BACILLARY ANGiomatosIS**
  - Bartonella henselae or B. quintana
  - Differential Dx: Kaposi’s Sarcoma

**Sporotrichosis in HIV**

**Aspergillus**

**Bacillary Angiomatosis**

**BACILLARY ANGiomatosIS**
Onychomycosis in HIV

- 4 Types of Onychomycosis
  - Distal and Lateral Superficial (DLSO)
    - T. rubrum and T. mentagrophytes most common
  - Proximal Subungual (PSO)
    - Marker of HIV
  - Superficial White (SWO)
    - T. mentagrophytes
  - Total Dystrophic (TDO)

Proximal Subungual Onychomycosis

Norwegian Scabies

INFLAMMATORY

- Xerosis/Ichthyosis
- Seborrheic dermatitis
- Psoriasis
- Reiter’s Syndrome
- Papular Pruritic Eruption of AIDS
- Eosinophilic Folliculitis
- Erythema Elevatum Diutinum
- Photosensitivity

XEROSIS AND ICHTHYOSIS

- Xerosis most prominent on lower legs
- HIV pts often have refractory pruritus
- Similar to asthenetic eczema seen in elderly
- Worse in patients with atopic diathesis
- Acquired ichthyosis is seen in advanced HIV (CD4+ <50)
- Treatment with moisturizers and topical steroids
  - Often unsatisfactory
SEBORRHEIC DERMATITIS
• Affects ~5% of Non-HIV population
• Most common skin disorder to affect HIV pts, up to 85% incidence
• Usually affects the scalp and central face
• With HIV, can be widespread or inverse
• If exaggerated, sudden onset, or acute worsening, consider HIV infection

PSORIASIS and HIV
• Overall incidence not increased with HIV
• Similar clinical features with or without HIV
• With HIV, may have increased intertriginous involvement and more dramatic presentation
• Significant nail dystrophy and arthritis may be seen
• Not uncommon to develop psoriatic erythroderma
• Worsens with declining immune status

REITER’S SYNDROME
• All pts with newly diagnosed Reiter’s should have HIV testing
• Commonly occurs in HIV pts with HLA-B27 after GU or GI infection
• Palms and soles develop pustules and form keratotic papules.
  – coalesce until soles are thickened and scaled = keratoderma blennorrhagicum
• Nails, groin & axilla, and oral (erosions, geographic tongue) & genital (circinate balanitis) regions often affected
• Histo is identical to psoriasis and same Tx for both diseases

PAPULAR PRURITIC ERUPTION (PPE)
• Marked pruritus
• Symmetrical, non-follicular papules, with secondary changes
• May be secondary to peripheral eosinophilia, hyperreactive mast cells, or neural irritation from direct HIV infection
• May be on spectrum which includes eosinophilic folliculitis or response to arthropod Ag’s
Patient with itchy Rash

- 40 YO Hispanic Man with 2 week h/o itchy bumps on his face, chest, back
- PMH: HIV/AIDS: CD4 31
- Recent stay at hotel with “bed bugs”

Eosinophilic Pustular Folliculits

- Treatment with Betamethasone Valerate cream, erythromycin 2% solution, and ketoconazole cream
- Much improved at 2 week followup
Eosinophilic Pustular Folliculitis

- Highly pruritic, follicular papulopustular eruption of the face, neck, trunk, and extremities
- Cultures are negative
- Peripheral eosinophilia may be present
- CD4+ usually <200
- One of most characteristic pruritic dermatosis associated with HIV
- May be exaggerated reaction to Malassezia yeast

Eosinophilic Pustular Folliculitis

- Treatment with Betamethasone Valerate cream, erythromycin 2% solution, and ketoconazole cream
- Much improved at 2 week followup

Kaposi’s Sarcoma

- Chronic form of cutaneous LCV
- CD4+ count <200
- Necrotising vasculitis with firm red-brown papules, plaques, or nodules, symmetrically on extensor surfaces
- Asymptomatic or painful itching/burning (worse after exposure to cold)
- Tx: Dapsone

Patient with spots on the back

- 34 year old female
- Spots on back for one month
- CD 4 4
- On HAART, bactrim
Photosensitivity

- May be symptom of HIV or drug side effect
  - In some reported cases, photosensitivity was the first clinical sign of HIV
  - Occurs in 5.4% in sero-positive patients
  - More common in individuals of African descent

- Most HIV patients are UVB sensitive
  - The most severely affected individuals are both UVB and UVA sensitive

Photosensitivity

- Reported cases of of Photodermatitis with subsequent Vitiligo-like Leukoderma

  - Theories:
    - HIV triggers immune dysregulation leading to autointimmunity against the skin
    - Viral-mediated melanocyte destruction
    - Koebner phenomenon induced by photodermatitis in susceptible people.

KAPOSI’S SARCOMA

- Neoplasm of endothelial cells
- Closely associated with HHV-8 infection
- Predominantly seen in MSM
- Initially red-brown macules. Small violaceous papules, large plaques, ulcerated nodules also seen
- Internal involvement in 72%, usually in GI tract and lymphatics → secondary lymphedema
- Poor prognosis, avg survival time of 18 months

KAPOSI’S SARCOMA

- 23 cases of KS in HIV infected persons
- 7/23 had CD4>300
- 5/23 had never had any prior treatment with HAART
- These cases can not be directly attributed to immune reconstitution syndrome
- Conclusion: All patients with HIV should be screened for KS
LYMPHOMAS

- CD4+ counts <200
- Pink – violaceous papules, often ulcerate
- In patients with HIV:
  - Most are non-Hodgkin B-cell type
  - Younger age of onset
  - Extranodal (esp. CNS) involvement at presentation
- HIV+ children ↑ incidence of MALT lymphomas
- Decreased incidence lymphomas with HAART

LIPODYSTROPHY
aka Fat Redistribution Syndrome

- HIV patients treated with HAART may have lipohypertrophy, lipoatrophy or a mix of both
- Commonly have hypertriglyceridemia and insulin resistance
- Lipoatrophy associated with:
  - Duration of tx with thymidine analogues

LIPOHYPERTROPHY

- Enlarged dorsocervical fat pad
- Circumferential expansion of the neck
- Breast Enlargement
- Abdominal Visceral Fat Accumulation

Lymphoma of Skin

Lipodystrophy

- HIV patients being treated with antiretrovirals may have
  - Lipohypertrophy
  - Lipoatrophy
  - Mix of both

Lipoatrophy associated with:
  - Duration of tx with thymidine analogues

LIPOHYPERTROPHY

- Enlarged dorsocervical fat pad
- Circumferential expansion of the neck
- Breast Enlargement
- Abdominal Visceral Fat Accumulation
LIPOATROPHY

- **LIPOATROPHY IN HIV**
  - Peripheral fat wasting with loss of SQ tissue in face, arms, legs and buttocks
  - Face involvement is most common
  - May have social stigma

**Stavudine (NRTI) a/w higher risk**
- Substituting non-thymidine analogue for stavudine ➔ gradual improvement
- Tx: Pravastatin, pioglitazone for peripheral lipoatrophy; cosmetic sx

**LIPOATROPHY GRADING SCALE**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No facial lipoatrophy.</td>
</tr>
<tr>
<td>1</td>
<td>Mild flattening or shadowing of one or more facial regions. No prominent bony landmarks.</td>
</tr>
<tr>
<td>2</td>
<td>Intermediate point between grade 1 and grade 3.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate concavity of one or more facial regions. Prominence of bony landmarks. May have visibility of underlying musculature.</td>
</tr>
<tr>
<td>4</td>
<td>Intermediate point between grade 3 and grade 5.</td>
</tr>
<tr>
<td>5</td>
<td>Severe indentation of one or more facial regions. Severe prominence of bony landmarks. Clear visibility of underlying musculature.</td>
</tr>
</tbody>
</table>

**SOURCE:** Levy, et al. JAAD. Vol 59, Issue 6: 923-933

**Immune Reconstitution Inflammatory Syndrome (IRIS)**
- Occurs with sudden increased CD4 count or decreased viral load
- Flare of skin conditions with improved immune function
- Often follows start of HIV medications.
- Skin Conditions which flare: EPF, KS, HSV, HZV

**Immune Reconstitution Inflammatory Syndrome (IRIS)**

- The initiation of antiretroviral treatment for individuals with HIV may be accompanied by
  - a paradoxical flare of underlying inflammatory diseases
  - the recurrence of dormant infections
  - worsening of prior treated opportunistic infections

**Idiopathic Pyoderma Gangrenosum as a Novel Manifestation of the HIV Immune Reconstitution Inflammatory Syndrome: A Report of Three Cases**

*J Assoc Physicians India. 2015 Jul;63(7):72-6*
Pyoderma Gangrenosum: IRIS

Medication Reactions

- Patients with HIV have an increased incidence of cutaneous drug eruptions
- Risk for TEN is 1000x greater in AIDS patients

Drug-Induced Hyperpigmentation

- Azidothymidine (zidovudine, AZT)
  - Causes hyperpigmentation of mucous membranes and nails in 10%
  - Typically occurs after 4-6 weeks of therapy
  - Increase in melanin in basal layer and dermal melanophages
  - Fades after discontinuation

Eruptive Dermatofibroma

- Common benign fibrous nodule that often arises on the lower legs
- Multiple eruptive DF is rare but frequently associated with underlying immunocompromising disease

- Chief Complaint:
  - Numerous mildly itchy nodules x6 months
- HPI:
  - 28 year old African-American woman with PMH of AIDS and hypercholesterolemia who presents with a 6 month history of pruritic hyperpigmented papules and nodules on the trunk and extremities
  - Lesions are not painful
  - Occurred rapidly over the course of a few months while off antiretroviral therapy (ART)
  - Has recently restarted ART
  - No prior treatment
• **PMH:**
  - AIDS, diagnosed 2011, 2/2 blood transfusion, CD4 16 at presentation, now 61
  - Homozygous familial hypercholesterolemia
  - HPV with low grade squamous intraepithelial lesion (LSIL)
  - Chronic anemia of unclear etiology, multiple transfusions as child
  - Hepatic leiomyoma, s/p bx, benign but with elevated LFTs

• **PSH:**
  - MRSA lung abscess s/p thoracotomy and numerous blood transfusions in 2014

• **Allergies:**
  - Bacitracin (anaphylaxis); cephalosporins (angioedema)

• **Medications:**
  - Emtricitabine/tenofovir disoproxil (Truvada)
  - Dolutegravir (Tivicay)
  - Dapsone
  - Atorvastatin (Lipitor)
  - Exetimibe (Zetia)
  - Mipomersen (Kynamro)

• **Family Hx:**
  - No cancer, skin or autoimmune diseases
  - Strong family history of early coronary artery disease

• **Social Hx:**
  - Single, 2 children
  - Denies smoking, drinking, drug use
  - Not currently sexually active

• **Review of Systems:**
  - Denies fever, chills, cough, weight loss, recent travel outside the country

• **Labs**
  - CBC shows mild pancytopenia
    - Hb 9.1, WBC 4.2, Plt 134
  - CMP unremarkable except AST 39
  - Total Cholesterol 299, LDL 251, Triglycerides 45
  - CD4 61, Viral Load undetectable
  - RPR negative
  - Quantiferon gold negative
  - Hepatitis B SAb, SAg, CAb, Hepatitis C Ab all negative
  - TSH 1.15

**Physical Exam**

**Physical Exam**
Physical Exam

Differential Diagnosis
- Epidermal inclusion cyst
- Melanocytic or blue nevus
- Nodular melanoma
- BCC, esp pigmented
- Prurigo nodules
- Keloid or hypertrophic scar
- Schwannoma
- Pilomatrixoma
- Cold abscess

Neurofibroma
Kaposi sarcoma
Cutaneous metastasis
Dermatofibrosarcoma prolubersa
Dermatofibroma
Dermatomyofibroma
Leiomyoma
Sarcoidosis

Dermatopathology

Patient PW

Specimen Source:
A. Right Upper Arm; Skin biopsy:
**DIAGNOSIS**

**A. Right Upper Arm; Skin biopsy:**
- CELLULAR FIBROUS HISTIOCYTOMA (CELLULAR DERMATOFIBROMA), EXTENDING TO ALL MARGINS.

Comment: The tumor cells are positive for Factor XIIIa and negative for CD34, HHV8, and ERG. There is entrapment of fat by tumor cells within the superficial subcutis, which is an unusual finding. Although these tumors typically follow an indolent clinical course, there is an increased risk for local recurrence. Re-excision is recommended. Multiple levels have been examined.

**Cellular Dermatofibroma**

- **Introduction**
  - Dermatofibroma – 2nd most common fibrohistiocytic tumor of the skin
  - First described in 1994, one of many subtypes of DF
  - Considered to be locally aggressive and have potential for metastasis
- **Epidemiology**
  - Rare, ~5% of all DF
  - Occur in young to middle age adults, male predominance
  - Overall rate of metastasis is unknown but thought to be very rare
  - No reported cases in HIV or AIDS patients

Pathogenesis

- Unknown, possibly trauma however newer literature debates this reactive origin
- Eruptive DF associated with immunosuppression
- Potential for recurrence and metastasis
- Association with multiple chromosome abnormalities
- DF of all types known to be eruptive in: autoimmune disorders, atopic dermatitis, immunosuppression (e.g. HIV)
- No reports of eruptive cellular DF in HIV or AIDS patients

References:
Malignant dermatofibroma: clinicopathological, immunohistochemical, and molecular analysis of seven cases

- Examined 4 aggressive or metastatic cellular DF along with mixed type DFs
- All showed marked chromosomal abnormalities
- Recurrence occurred between 8 months and 9 years
- Metastasis occurred between 3 months and 8 years after diagnosis
- 2 patients died of their disease

Examined 5 metastatic cellular DF using array based comparative genomic hybridization analysis

- Compared above to 5 non-metastatic cellular DF and normal DNA
- Showed that increased chromosomal abnormalities associated with metastatic potential
- Acknowledge that chromosome analysis is currently too costly to perform on all cellular DF
- Recommend cautious management of patients with large cellular DF

DNA copy number changes in tumors within the spectrum of cellular, atypical, and metastasizing fibrous histiocytoma

- Published in JAAD 2014
- Examined 5 metastatic cellular DF using array based comparative genomic hybridization analysis
- Compared above to 5 non-metastatic cellular DF and normal DNA
- Showed that increased chromosomal abnormalities associated with metastatic potential
- Acknowledge that chromosome analysis is currently too costly to perform on all cellular DF
- Recommend cautious management of patients with large cellular DF

Cellular Dermatofibroma

- Clinical Features
  - Appear clinically similar to benign DF
  - Occur in upper extremities and non-classical locations – face, ears, hands and feet
  - Diagnosis made by biopsy
  - Per published case series, most are larger (3+ cm)

Pathology:
- High cellularity, minimal intracellular collagen, abundant mitosis, extension into the subcutis and no cellular atypia or nuclear pleomorphism
- Central necrosis or infarction has been reported.
- Variable expression of smooth muscle actin, seen much more frequently than in ordinary dermatofibroma.
- Positive for factor XIIIa, negative for CD34
- Focal, peripheral expression of CD34 and desmin reported

Cellular Dermatofibroma

- Treatment:
  - All literature recommends complete excision, no consensus on margins
  - 1 publication reported 0.5 mm margin with fatal outcome
  - Recurrence rate of 26-64% depending on source
  - Rare reports of metastasis to lymph nodes, lungs, soft tissue, brain
  - No consensus on treatment of metastatic disease beyond complete excision if possible
  - Metastatic disease fatal in 32% of reported cases (7/22)

- Published in American Journal of Dermatopathology 2014
- Recommend complete excision and careful surveillance especially for local recurrence
  - Multiple local recurrence associated with metastasis
  - If large primary or local recurrence recommend chest X-ray and ultrasound lymph node exam
  - Repeat CXR if any pulmonary symptoms develop

Follow Up and Treatment Options

- Patient has 2 large biopsy proven cellular DF
- Next step is to remove these 2 lesions
- As our patient’s CD4 count increased and her viral load decreased many of her previously nodular lesions have become macular
  - Should these be biopsied?
- With >10 lesions, 2 biopsy proven cellular DF, is biopsy and excision of all lesions feasible without causing extensive disfigurement?

Conclusion

- Many skin findings are associated with HIV
- The prevalence of HIV is still high even as the incidence has waned
- Dermatologists should be aware of HIV associated skin conditions and consider HIV testing when there is suspicion of infection

THE END

• THANK YOU!
How do patients choose?

• Other’s opinions
• Marketing

How do patients choose?

• Marketing – easy to ignore
• Other’s opinions – easier than ever!
62% used online reviews to learn about doctors
How does Yelp filter reviews?

$y = \text{out}_0 + \gamma + \sum_{j=1}^{n} \beta_j x_j + \epsilon$

<table>
<thead>
<tr>
<th>Table 1: Characteristics of filtered reviews.</th>
</tr>
</thead>
<tbody>
<tr>
<td>($\beta$)</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Has the_{adjective} level in story</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>log(Review length)</td>
</tr>
<tr>
<td>log(User review count)</td>
</tr>
<tr>
<td>User has photo</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data + Yelp Advertiser</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data</td>
</tr>
<tr>
<td>Yelp Advertiser</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>log(Review length)</td>
</tr>
<tr>
<td>log(User review count)</td>
</tr>
<tr>
<td>User has photo</td>
</tr>
</tbody>
</table>

R²: 0.43

Notes: One observation variable in the linear multiple regression analysis was omitted as collinear with other variables. All variables are centered at their mean. Business level effect. Controls for variables in the labeled feature [not] are shown in parentheses.
Choose Based on Positive Review

Choose Based on Negative Review

Choose Based on Malpractice Suit

9.3 out of 10

“I waited an hour for a 5 min appt!”

“I waited an hour for a 5 min appt!”
Service = Quality

Reach out
Repair
Redact

I'm sorry. Please call 619-922-9727 so we can help you.

"There were dead plants in the waiting room."

"There was a dead person in the waiting room."

Reach out
Repair
Redact
We can’t discuss specifics about your comments. However, we are committed to high quality care and we take your feedback seriously.

Reducing wait has been a challenge for our practice, so we just hired a consultant to help us improve scheduling.

When responding:
It’s better to be fast than complete
HIPAA always applies
Never argue

Summary
• Reputation will only become more important
• Reach out, Repair, Redact
• It’s the waiting room, stupid
• We all have bad reviews ....

Shake it off, shake it off.

-T. Swift
2017 Dermatology Coding Updates

2017 Spring Current Concepts in Dermatology Seminar
American Osteopathic College of Dermatology
March 31, 2017

Faith C M McNicholas, RHIT, CPC, CPCD, PCS, CDC
Manager, Coding and Reimbursement
American Academy of Dermatology
fmcnicholas@aad.org

2017 CPT News

<table>
<thead>
<tr>
<th>CPT Code/Modifier</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Telemedicine: Appendix P</td>
<td>Lists current CPT codes with evidence of some payer approval for use when provided via an integrative audio and video telecommunication system</td>
</tr>
<tr>
<td>*99201 - *99215</td>
<td>*E/M codes included in this list</td>
</tr>
<tr>
<td>Modifier 95</td>
<td>Indicates a service generally reported as a face-to-face service was performed via a real-time interactive audio and video telecommunication system</td>
</tr>
<tr>
<td>0419T (will sunset January 2022)</td>
<td>Destruction of neurofibroma, extensive (cutaneous, dermal extending into subcutaneous); face, head and neck, greater than 50 neurofibromas</td>
</tr>
<tr>
<td>04120T (will sunset January 2022)</td>
<td>Trunk and extremities, extensive, greater than 100 neurofibromas</td>
</tr>
</tbody>
</table>

2017 Medicare Part B Premium and Deductible

• 2017 Part B premium standard is $134
  • Average is $109, up from $104 in 2016
• Low Social Security cost of living adjustment of 0.3%.
  • “Hold harmless” provision designed to protect seniors prevented a larger increase
• 2017 Part B Deductible is $183, up from $166 in 2016
  • Co-insurance remains 20% of Medicare Physician Fee Schedule (MPFS) allowed amount
• File Medicaid claim prior to billing patient
Medicare Beneficiary Identifier Revision

By April 2019 Medicare beneficiaries, Social Security ID numbers will be replaced with random identifiers

CMS requests provider’s assistance

• Check your patient’s address
• Ask the patient to update the Social Security Office directly if any changes

https://faq.ssa.gov/supportKBAnswer.asp?questionID=1704

Administrative Law Judge (ALJ) and Federal Claim Appeal Increase

ALJ and Federal District Court amount in controversy increase for 2017

<table>
<thead>
<tr>
<th>Appeal Claim Total Required</th>
<th>Administrative Law Judge</th>
<th>Federal District Court</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>$150</td>
<td>$1,500</td>
</tr>
<tr>
<td>2017</td>
<td>$160</td>
<td>$1,560</td>
</tr>
</tbody>
</table>

*Total may encompass a single claim or the accumulation of claims

Medicare Drug Waste Modifier

Medicare Change Request CR 9603

JW - Drug amount discarded/not administered to any patient.
Documentation must be available if requested

• Beginning January 1, 2017
• Reporting unused drug and biological portions require JW modifier to identify discarded drugs and biologicals when processing Part B claims.
• Do not use JW modifier to report Competitive Acquisition Program (CAP) drugs and biologicals.
Medicare Drug Waste Modifier

Documentation must include:
- Date and time the drug was discarded
- Amount discarded
- Reason for wastage
- Who wasted the drug
- Check local Medicare contractor for provider requirements for reporting of drug wastage

For more information see:
- Derm Coding Consult, Spring 2015, Billing for Drugs and Biologicals in your Practice

Medicare Payment Revision

Non-face-to-face prolonged E/M service

- Must be:
  - Tied to an E/M service
  - Time spent by billing physician only
  - Not within the scope of clinical staff
  - No other CPT to report this work

- Document:
  - Time
  - Summary of non-face-to-face work

Prolonged E/M Service

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Global</th>
<th>CMS work RVU</th>
</tr>
</thead>
<tbody>
<tr>
<td>99358</td>
<td>XXX</td>
<td>2.10</td>
</tr>
<tr>
<td>99359</td>
<td>XXX</td>
<td>1.00</td>
</tr>
</tbody>
</table>
2017 Medicare Fee Schedule Overview

• Published on 11/15/2016
• Very little impact on dermatology payments overall
• CMS estimates the CY 2017 PFS conversion factor (CF) to be $35.8887, a slight increase over the 2016 CF of $35.8043.

Relative Value Units and Related Information Used in CY 2017 Final Rule

<table>
<thead>
<tr>
<th>2017 CPT/HCPCS Mod Description</th>
<th>Global</th>
<th>2016 Payment Amount</th>
<th>2017 Payment Amount</th>
<th>% Payment Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>11100 Biopsy skin lesion</td>
<td>000</td>
<td>$104.91</td>
<td>$105.15</td>
<td>0.24%</td>
</tr>
<tr>
<td>11300 Shave skin lesion 0.5 cm/c</td>
<td>000</td>
<td>$98.46</td>
<td>$99.77</td>
<td>1.31%</td>
</tr>
<tr>
<td>11400 Exc tr-excision lesion 0.5 cm/c</td>
<td>G00</td>
<td>$135.33</td>
<td>$136.93</td>
<td>0.80%</td>
</tr>
<tr>
<td>11600 Exc tr-excision lesion 0.5 cm/c</td>
<td>G01</td>
<td>$194.42</td>
<td>$196.96</td>
<td>0.78%</td>
</tr>
<tr>
<td>12031 Intermediate surgery 2.5 cm/c</td>
<td>G01</td>
<td>$240.60</td>
<td>$241.89</td>
<td>0.53%</td>
</tr>
<tr>
<td>17000 Destruct premalign lesion</td>
<td>G00</td>
<td>$67.67</td>
<td>$67.83</td>
<td>0.24%</td>
</tr>
<tr>
<td>17311 Mohs stage 1/intrag 0.5 g</td>
<td>XXX</td>
<td>$673.12</td>
<td>$674.35</td>
<td>0.18%</td>
</tr>
<tr>
<td>96910 Phototherapy with uv-b</td>
<td>XXX</td>
<td>$72.32</td>
<td>$72.34</td>
<td>0.26%</td>
</tr>
<tr>
<td>96930 Phototherapy with uv-b</td>
<td>XXX</td>
<td>$34.37</td>
<td>$39.84</td>
<td>15.39%</td>
</tr>
<tr>
<td>97313 Office/outpatient visit</td>
<td>XXX</td>
<td>$73.40</td>
<td>$73.93</td>
<td>0.72%</td>
</tr>
</tbody>
</table>

2017 Medicare Fee Schedule - overview

• Reflectance Confocal Microscopy (RCM) 96931-96936 assigned new assigned values.

• No more Physician Quality Reporting System or EHR Meaningful Use reporting.

• Instead, MACRA Quality Payment Program (QPP) with a Merit-based Payment Improvement System (MIPS) and Alternate Payment Models (APMs).
Two Tracks: MIPS and Advanced APMs

Here is all I know….

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

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

**MACRA Timeline**

- 2017 is a Transition Year — Pick Your Pace

**Test Pace: Avoid Penalties**
- Test MIPs of the following:
  - One measure in the quality performance category at least once
  - One activity in the improvement activity category
  - Five required measures making up the base score of the advancing care information (ACI) category

**Partial Participation: Small Incentive**
- Partial participation of the following:
  - More than one quality measure in the quality performance category
  - More than one improvement activity
  - More than the five required measures in the ACI category

**Full Participation: Larger Incentive**
- Full participation of the following:
  - Six quality measures in the quality performance category
  - One high-weighted improvement activity or two medium-weighted improvement activities
  - Five required measures making up the base score of the ACI category

**Excluded from program if you:**
- Are in the Medicare program for the first year
- Have less than $30,000 in allowed charges to Medicare Part B per year
- See less than 100 Medicare Part B patients per year

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

Here is all I know….
Review of Codes with 10 and 90 Day Global Days

- Physicians in Florida, Kentucky, Louisiana, Nevada, New Jersey, North Dakota, Ohio, Oregon and Rhode Island will be expected to report post-procedure visits using CPT 99024 beginning July 1.
- **North Carolina** – exempt but can volunteer
- Practices with fewer than 10 providers are exempt.
- Codes reported annually by more than 100 practitioners and reported more than 10,000 times, or allowed charges in excess of $10 million annually
- No penalty for not reporting, no payment for reporting
Review of Codes With 10 and 90 Day Global Periods

- CMS survey practitioners to gain information regarding post-op visits may occur in mid-2017
- CMS will collect data from Pioneer and Next Gen ACOs on the “activities and resources involved in and around surgical events”

ICD 10 Updates

- Code specificity required as of October 1, 2016
- No specific dermatology code changes. However, 2017 Guideline changes may impact your practice
- Review Derm Coding Consult for more information

2017 ICD-10 Guidelines

- Clinical Criteria and Code Assignment
- Excludes1
- Bilateral Conditions
- Etiology/Manifestation
- Terms – With, Use additional code
- Episode of Care
- Complications of Care
Clinical Criteria / Code Assignment

- Diagnosis codes reported are NOT selected based on clinical criteria used to establish the diagnosis.
- Physician’s statement alone that the condition is present supports reporting of the ICD-10 code.

Excludes

- Listed with mutually exclusive codes:
  - Two conditions cannot be reported together
    - Clinically
    - Coding rule

- Clarification provided by CMS in October 2015
  - If unrelated, report both conditions

Example

<table>
<thead>
<tr>
<th>Pathology Report</th>
<th>ICD codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1 specimen from abdomen – Lentigo maligna</td>
<td>D03.59 Melanoma in situ of other parts of trunk</td>
</tr>
<tr>
<td>#2 specimen from back – Malignant melanoma</td>
<td>C43.59 Malignant melanoma of other parts of trunk</td>
</tr>
</tbody>
</table>

Report both codes

Documentation must reflect separate sites within same anatomic location – per ICD grouping
Bilateral conditions

- When available, report bilateral conditions with bilateral codes
- Even when only unilateral treatment is provided

<table>
<thead>
<tr>
<th>Bilateral Condition Is:</th>
<th>Treatment is:</th>
<th>Code as:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present bilaterally</td>
<td>Unilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Present bilaterally</td>
<td>Bilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Present unilaterally – Previously treated side is healed or no longer present</td>
<td>Unilateral</td>
<td>Unilateral – list side treated if applicable; History of code for previously treated side</td>
</tr>
</tbody>
</table>

Patient presents with swelling and pain of both ears. On exam, manipulation of auricle causes pain and a furuncle is present at left pre-auricle area. Gentle debridement of both ears and neomycin applied.

Assessment: otitis externa cellulitis
Rx: hydrocortisone drops
ICD-10-CM: H60.13 Cellulitis of external ear, bilateral

Patient returns in follow-up of otitis externa cellulitis. Patient states right side is better, left still hurts. Exam shows condition is resolved on right. Left side ear canal is red, swollen, and littered with moist, purulent debris.

Rx: Continue hydrocortisone drops
Ciprofloxacin 500 mg po bid for 10 days
ICD-10-CM: H60.12 Cellulitis of left external ear

Etiology / Manifestation

Condition with underlying etiology and manifestations
- Sequencing rules apply
  - Underlying condition or cause is listed first
  - Manifestation of this condition or cause is listed second

- Code first/Use additional code
  - Links cause or etiology to condition being treated
  - May help to show complexity of care needed
Directional Terms - Updated

• Watch for “code first” and “use additional code” guidance
  L51 – Erythema multiforme
  Use additional code for adverse effect, if applicable, to identify drug
• “if applicable” was added to guidance for 2017

Example

Combination Code

75 year-old Type 1 diabetic female patient presents with small raised, yellow and somewhat waxy lesions on lower part of her legs.

Final Diagnosis: Necrobiosis lipoidica diabeticorum

ICD-10-CM code: E10.620 Type 1 DM with diabetic dermatitis

Example

One Condition / Two Codes

Patient presents for follow-up of non-pressure chronic ulcer of right ankle secondary to Type 1 diabetes. Breakdown of ulcer is limited to skin. Diabetes is followed by primary care.

Final diagnosis: non-pressure ulcer, DM type 1

ICD-10-CM codes:
  E10.621 Type 1 Diabetes mellitus with foot ulcer
  L97.311 Non-pressure chronic ulcer of right ankle limited to breakdown of skin
  Code first any associated underlying condition
Directional Term Updates

• With – as listed in code title or Alphabetic index
  L05.01 Pilonidal cyst with abscess
• May be documented as "associated with" or "due to"
• Presumes causal relationship of linked terms
• Even in absence of documentation linking conditions
• If unrelated – Document as not related

Example

28 year old male presents with painful, swollen lesion in the sacrococcygeal region. Review of systems is negative for fever, chills or drainage at lesion site. No abscess is present at this time. Patient states that he had a similar lesion in the area approximately one year ago that disappeared spontaneously.

Final Diagnosis: Pilonidal cyst

ICD-10-CM Code: L05.91 Pilonidal cyst without abscess

Episode of Care - Clarification

• Initial care – A
  • Each encounter where active care is provided
• Subsequent care – D
  • Encounters occurring after active treatment is completed

Initial care includes

• Initial visit for the condition
• While patient is receiving active treatment for the condition
• Surgical treatment, emergency department encounter
Documentation Should Reflect Episode

Follow up patient for second degree caustic burns on back of right hand from drain cleaner. Doing well on steroids and topical medication. No signs of infection. Continue on current medications. Dressing changed, patient to return in two days for dressing change.

ICD-10-CM Codes: T23.661D Corrosion of second degree of back of hand, right

T54.3X1D Toxic effect of corrosive alkalis and alkali-like substances, accidental

Complications of Care

- Based on documented relationship between condition and previous care or procedure
- Not all conditions occurring during or after procedures or treatment are considered complications
- Documentation must reflect cause-and-effect relationship
- Complication codes may reflect episode of care
- Active treatment – treatment of the condition described by the code

Example

Patient returns 5 days after punch biopsy with infection at biopsy site.

ICD-10-CM Code: T81.4XXA Infection following a procedure, initial encounter
Active Local Coverage Determination (LCDs)

- Allergy Testing
- Application of Bioengineered Skin Substitutes to Lower Extremity
  Chronic Non-Healing Wounds
- Debridement of Mycotic Nails
- Moh’s Micrographic Surgery
- Removal of Benign Skin Lesions
- Surgical Treatment of Nails
- Treatment of Varicose Veins and Venous Stasis Disease of the
  Lower Extremities
- Wound Care

List is not conclusive – based on MAC
**LCD Utilization and Limitations Guidelines**

- Guidelines set out by Medicare
  - Discuss the conditions affected by the policy
  - List the conditions covered under the policy
  - Describe what constitutes medical necessity
  - Describe what can cause claim payment denial

- Usually found on the first page of the LCD
  - Under Coverage Guidance

---

**Novitas Solutions Inc. (MAC)**

**Local Coverage Determination (LCD): Removal of Benign Skin Lesions (L34938)**

**Policy applies to**
- SKs, Skin Tags
- Milia, Molluscum contagiosum
- Seb. Acne (epidermoid) cysts
- Moles (nevi)
- Acquired hyperkeratosis (keratoderma)
- Viral warts (excluding condyloma acuminatum)

**Reasons for non-coverage**
- Skin lesions that do not pose a threat to health or function is considered cosmetic.
- Skin lesions that do not meet medical necessity, and not covered by the Medicare program.

**Reasons for Coverage**
- Lesion has one or more of these characteristics: bleeding, intense itching, pain.
- Physical evidence of inflammation, e.g., purulence, oozing, edema, erythema.
- Obstructs an orifice or clinically restricts vision.
- In an anatomical region subject to recurrent physical trauma.
- Wart removals will be covered under all the above.
- In addition, if periocular wart, must be associated with chronic recurrent conjunctivitis.
- Evidence of spread from one body area to another, particularly immunocompromised patient.

**Documentation**

- Documentation in the medical record is critical in coding to ensure that every aspect of the patient condition and care is captured.
- Use of the utilization and limitations guidelines can help improve your MR documentation.
- Consider including words like:
  - Bleeding
  - Intense itching
  - Pain
  - Physical evidence of inflammation, e.g., purulence, oozing, edema, erythema
  - Obstructs an orifice or clinically restricts vision
  - Anatomical region subject to recurrent physical trauma
Documentation Example 1

A 17 yo girl has a 1.1 cm raised brown nevus on her mid back that rubs on her bra. You remove it using a shave technique. Pathology report shows a benign compound nevus, and the lateral and underlying dermal margins are clear, confirming complete removal of the nevus.

You report:

11302 – shaving of epidermal or dermal lesion, single lesion, trunk, lesion diameter 1.1 – 2.0cm

- Complete removal of this lesion does not make this an excision.

Documentation Example 2

82 yo female patient presents with linear, splayed, vertical patterns of lesions on her chest. States over time, they have increased, get caught in neck chain, are inflamed and causing pain. They started off light tan in color, but have progressed to becoming dark brown.

You report:

17110 – Destruction (eg, laser surgery, electrosurgery, cryosurgery, chemosurgery, surgical curettement), of benign lesions other than skin tags or cutaneous vascular proliferative lesions; up to 14 lesions

Documentation Example 3

A 1.2 cm flesh-colored polypoid nodule on the upper thigh of a 45 yo man is irritated by his clothing. It is removed at the base with scissors, exposing underlying fat, and hemostasis is achieved with electrocautery. Pathology confirms a benign fibrofatty polyp.

You report:

11402 - Excision, benign lesion including margins, except skin tag, excised diameter 1.1 – 2.0 cm
### Removal of Benign Lesion LCD

The LCD further states the following will allow coverage:

- If clinical diagnosis is uncertain, particularly where malignancy is a realistic consideration based on lesional appearance (e.g. non-response to conventional treatment, or change in appearance).
- Prior biopsy suggests or is indicative of lesion malignancy or premalignancy.

### Documentation Example 4

50 yo boater has discreet but irregular 8mm shiny red flat lesion on his back. Clinical diagnosis is probable superficial BCC and a specimen is obtained for pathology with curettage as a definitive procedure with therapeutic intent to cure. Pathology confirms a benign diagnosis.

You report:

17110 – Destruction (eg, laser surgery, electrosurgery, cryosurgery, chemosurgery, surgical curettlement), of benign lesions other than skin tags or cutaneous vascular proliferative lesions; up to 14 lesions

- If pt presented with more than 15 lesions, you would report 17111 – Destruction of benign lesions; 15 or more lesions

### Novitas Solutions, Inc. (MAC)

Local Coverage Determination (LCD): MOHS Micrographic Surgery (MMS) (L34961)

<table>
<thead>
<tr>
<th>Policy Applies to</th>
<th>Reasons for non-coverage</th>
<th>Reasons for Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOHS Micrographic Surgery (MMS)</td>
<td>Requires a single physician to act in 2 separate and distinct capacities (surgeon and pathologist)</td>
<td>Requires a single physician to act in 2 separate and distinct capacities (surgeon and pathologist)</td>
</tr>
<tr>
<td>CPT Codes</td>
<td>Qualifications of the physician and office/facility team</td>
<td>If either of these responsibilities is delegated to another physician or other qualified health care professional who reports the service(s) separately, the MMS code should not be reported</td>
</tr>
<tr>
<td>17311 - 17315</td>
<td>Characteristics of the lesion (per procedure)</td>
<td>The qualifications of the performing physician must be verifiable if requested by the Contractor</td>
</tr>
<tr>
<td><em>See AAD Appropriate Use Criteria (AUC)</em></td>
<td>Documentation of the Medical Necessity</td>
<td>Providers of MOHS surgery are limited to MD or DO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The AUC provides necessary consideration of MOHS micrographic surgical treatment of a lesion;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>See LCD Documentation Requirements section</td>
</tr>
</tbody>
</table>
Medicare on Mohs

- After careful review, Medicare Jurisdictions adopted coverage for Mohs in accordance with the 2012 Appropriate Use Criteria (AUC) for Mohs Micrographic Surgery as published in JAAD Volume 67, Issue 4, pp 531-550, October 2012.
- MMS appropriate only when:
  - Superficial (lateral) or deep margins of the cancer lesion are uncertain clinically.
  - Likelihood of surgical cure and reconstruction would be compromised without use of immediate microscopic examination of the surgical margins.
- The medical records should clearly show that MMS was chosen because of the complexity (e.g. poorly defined clinical borders, possible deep invasion, prior irradiation), size or location (e.g. maximum conservation of tumor-free tissue is important).

CMS MLN Matters® Number: SE1318
Guidance To Reduce Mohs Surgery Reimbursement Issues
(Appplies to all Medicare carriers)
- Documentation should support the medical necessity for Mohs procedure
- Operative notes and pathology documentation must clearly indicate:
  - That Mohs was performed using accepted MMS technique;
  - That physician acted in two integrated, but distinct, capacities as surgeon and pathologist;
  - That the location, number, and size of the lesion(s) treated;
  - That the number of stages performed; and
  - That the number of specimens per stage.

Medicare Documentation Requirements
- Describe histology of the specimens taken in the first stage. Description should include:
  - Depth of invasion;
  - Pathological pattern;
  - Cell morphology; and, if present,
  - Perineural invasion or presence of scar tissue.
- Subsequent stages: note pattern and morphology of the tumor (if still seen) is as described for the first stage
- Or, if differences are found, note the changes
Documentation Requirements Cont’d

- ICD-10-CM/CPT code(s) submitted must be supported in the medical record.
- Documentation (pre-procedure E/M note and/or post-procedure operative notes) must address:
  - Why the lesion will not be (was not) managed by standard excision or destruction technique and (when applicable)
  - Why (when utilized or referred to a plastic surgeon) procedures for complex repair, adjacent tissue transfer or rearrangement, flap, or graft codes are employed.

Documentation Requirements Cont’d

- Diagnosis is appropriate for MMS and that it is the appropriate choice for treating a particular lesion.
- The primary procedure options and repair options were discussed with the patient and clearly noted in the pre- or post- procedure documentation.
- Document why the lesion will not be (was not) managed by excision or destruction technique.
- MMS was performed using accepted MMS technique, in which the physician acts in two integrated and distinct capacities: surgeon and pathologist (therefore confirming that the procedure meets the definition of the CPT code(s)).

Documentation Requirements Cont’d

- Operative Note: document location, number, and size of the lesion(s); number of stages performed; number of specimens per stage
- Histology Note:
  - First stage: if tumor present, depth of invasion; pathological pattern of the tumor; cell morphology; if present, note perineural invasion of scar tissue
  - Subsequent stages: if the tumor characteristics are the same as in the first stage, note this fact only. If the tumor characteristics are different from the first stage, describe the differences.
Mohs Micrographic Surgery
Appropriate Use Criteria

Why was it developed?
- Utilization of Mohs increased over 400% between 1995 and 2009
  - 1 in 4 skin cancers are treated with Mohs
- Variation in use across the country
- Allows specialty to ‘self-regulate’ and preserve the procedure for patients/tumors where benefit felt to be greatest;
- More AUC may be forthcoming
- Oversight AUC Cmte proposed
- Collaborative effort between AAD, ASDS, ACMS, & ASMS
- Over 75 physicians involved balance of COI, practice type, geographic location
- Payer representatives invited to participate
  - Fink Coast
  - Noridian
- Took 13 months to complete
- Co-published in JAAD and Dermatological Surgery

AAD Appropriate Use Criteria

- 270 indications
  - BCC
  - SCC
  - Lentigo maligna
  - Other rare cancers
- 3 Areas of the Body
  - H—M—L
  - Based on risk for recurrence and surgical difficulty

https://www.aad.org/practice-tools/quality-care/appropriate-use-criteria

AAD Definition of Appropriate

An appropriate treatment modality is one in which the anticipated clinical benefit combined with clinical judgment, exceeds the possible negative consequences for a specific indication.

- Anticipated clinical benefits of MMS may include high cure rate related to total margin assessment, low rate of recurrence, small defect size, range of reconstructive possibilities, retention of functional capacity, and low morbidity and mortality.
- Negative clinical consequences of MMS may include the possible risks of an extended surgical procedure under local anesthesia, risk of incorrectly interpreted margins, and risks associated with office-based surgery.
So What is Appropriate?

- Tumors in Area H and M are generally appropriate
- Smaller tumors in Area L (trunk & extremities) may not be appropriate
- Immunocompromised patients generally appropriate
- Recurrent tumors also generally appropriate in any location

Area H
- Face, genitalia, hands, feet, nail units, ankles, nipples/areola
- Central face, eyelids, eyebrows, nose, lips

Area M
- Cheeks, forehead, scalp, neck, jawline, pretibial surface

Area L
- Trunk and extremities
- Excludes pretibial surfaces, hands, feet, nail units and ankles

Immunocompromised
- HIV/AIDS, organ transplant, hematologic malignancy or pharmacologic suppression

Genetic Syndromes
- BCC nevus syndrome, xeroderma pigmentosa or other syndromes at high risk for skin cancer

Healthy
- No inflammatory process, no prior radiation therapy to affected area, no previous radiation to skin
- No immunocompromised, no genetic syndromes that predispose to skin cancer

Prior Radiated Skin
- Previously treated therapeutic radiation or prior radiation therapy to affected area

Aggressive Features
- Skin cancers having one or more of the following features have a higher incidence of local recurrence and regional metastasis such that minimal margin excision may not be in the beneficiary’s best interest:
Mohs Takeaway

- The physician (MD/DO) performing Mohs micrographic surgery must be specifically trained and highly skilled in MMS techniques and pathologic identification.
- If a surgeon performs an excision using Mohs surgical techniques but does not personally provide the histologic evaluation of the specimen(s), the CPT codes for MMS shall not be used.
- Instead standard excision codes should be chosen for such medically necessary services (e.g., 11600 – 11646).
- Medicare is aware that a biopsy of the skin lesion for which Mohs surgery is planned may be necessary in order for the physician to determine the exact nature of the lesion(s) to be removed. Occasionally, that biopsy may need to be done on the same day that the Mohs surgery is planned.
- In order to allow separate payment for a biopsy and pathology on the same day as Mohs surgery, the -59 modifier is appropriate. The 59 modifier is also appropriate when a separate skin lesion, other than the lesion for which Mohs surgery is performed, is biopsied on the same day that the Mohs surgery is performed.

Mohs Takeaway

- If a prior biopsy of the site undergoing Mohs surgery has been previously performed within the last 60 days, the surgeon should make a reasonable effort to obtain those results rather than repeating the biopsy.
- Reporting both Mohs Micrographic Surgery CPT codes 17311-17315 and Surgical Pathology CPT® codes 88302-88309 on tissue used for margin evaluation during Mohs surgery is inappropriate and will indicate that true Mohs surgery was not done. Such claims for Mohs surgery (17311-17315) will be denied. There are occasional clinical situations in which tissue separate from the tissue examined during Mohs surgery is appropriately submitted for subsequent formalin fixed processing and histopathologic examination. The submitted tissue is not the same tissue that was processed during the Mohs surgery. It may constitute a tissue margin beyond that evaluated with Mohs surgery or it may involve a totally unrelated tissue specimen. In such situations both the Mohs surgery and the histopathology are subject to coverage. In such cases the clinical record must clearly show the reasoning for the histopathologic specimen and interpretation.
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Coding Questions

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Friday, March 31, 2017
Resident Pathway
Psychodermatology

- Cutaneous disorders psychiatric in nature, with absence of organic dermatologic causes.

Delusions of Parasitosis

- Firm fixation that he/she has parasitic infection.
- Female: Male 2:1, middle to older age.
- "ziplock sign" patient will often bring in epithelial debris in ziplock as proof.
- Associated with schizophrenia, depression, anxiety, drug/alcohol abuse, dementia and obsessive states.
- May experience sensations of biting, crawling or stinging.
- Practitioner needs to distinguish delusion from substance-induced formication.
- Skin Findings range from none to excoriations, lichenification, prurigo nodularis and/or frank ulcerations.

Delusions of Parasitosis: Management

- Establish rapport with the patient and to address the chief complaint seriously, making sure to do a thorough dermatologic examination.
- Diagnosis of exclusion, rule out infestation, underlying dermatologic condition.
- Consider biopsy and laboratory workup to rule out organic etiology.
- Present antipsychotic medication in pragmatic manner.

Disclosures

- No relevant financial relationships or conflicts of interest to disclose.
Psychogenic (neurotic) excoriations
- Unconscious compulsive habit of picking at themselves, so persistent that excoriations develop.
- Typical on contralateral side of hand dominance.
- Could be ritualistic or random areas.
- Most common in middle-aged women.
- Different degrees of healing and scarring.
- Most commonly associated with depression, obsessive-compulsive disorder, and anxiety.

Neurotic Excoriations - Management
- Treatment is difficult, psychiatric and behavioral intervention can be very useful.
- IL corticosteroids, flurandrenolide tape for old lesions.
- Treatment of choice is doxepin.
- If major depression is present use antidepressant dose 100mg/day. 50-75mg or 10-20mg per day for elderly also works.
- If underlying OCD component, consider SSRIs.
- A case study of treatment-resistant excoration disorder found that the addition of aripiprazole to venlafaxine resolved her disorder.

Acne Excoriee
- Frequently seen in young women.
- Subset of neurotic excoriations.
- Ritualistic picking of acne lesions.
- Tx: Doxepin and SSRIs.

Factitious dermatitis (dermatitis artefacta)
- Self-inflicted cutaneous lesions often induced by foreign objects with intent to elicit sympathy, escape responsibility, or collect financial benefit.
- F:M 3:1, typically midlife.
- Most suffer from borderline personality disorder.
- Dermatologic findings that do not match history.
  - Typically located in areas that are easily reached by the hands.

Factitious Dermatitis - Management
- Wound care.
- Exclude possible primary skin disorder.
- Recognize signs of anxiety disorder and signs of depression.
  - Psychiatry, psychotherapy, antidepressant, antianxiety or antipsychotic medications.
Gardner-Diamond syndrome

- Factitial disorder.
- Clinically presents with painful swollen ecchymoses at sites of trauma.
- Women with underlying psychiatric disorder.
- Treatment: difficult, psychiatry.

Trichotillomania (trichotilloss or neuromechanical alopecia)

- Neurosis characterized by abnormal urge to pull out hair.
- Commonly affecting the scalp, eyebrows, eyelashes, pubic hair, and the beard.
- On the vertex crown it is known as the “friar tuck” form.
- Nails may show onychophagy.
- Occasionally, trichophagy: patients may eat the hair causing intestinal obstruction with a trichobezoar.
- Rapunzel syndrome: When the benzoar develops a hair extending too and obstructing the small intestine.

Trichotillomania

- Look for hairs of varying lengths.
- In some patients an area can be shaved to watch hair regrowth.
- Epidemiology:
  - 8 yo boys, 12 yo girls
  - F:M 5:1
  - Population prevalence 0.6%

Pathology:

- Presence of pigmented hair casts (also seen in traction alopecia).
- Perifollicular lymphocytes, plasma cells and neutrophils are usually sparse or absent.
- Perifollicular hemorrhage occasionally found in early lesions.
- Perifollicular fibrosis - late change.
- If the follicle is destroyed, a vertical fibrous tract often remains at the site.
- DDx: Alopecia areata, tinea capitis

Treatment:

- Cognitive-behavioral therapy.
  - Self-monitoring, teaching the patients to do something else whenever they are feeling the urge to pull their hair, relaxation techniques and positive reinforcement.
- Pharmacotherapy with clomipramine and SSRIs.
  - Olanzapine or N-acetylcysteine also show promise.
  - Effects of inositol are currently being studied.

Dermatothlasia

- Cutaneous compulsion to pinch and rub skin until bruising.
- Often a defense to pain at a different location.
Bromidrosiphobia
- Delusion of bromhidrosis.
  - Patient is convinced his/her sweat is creating a repugnant odor keeping people away, despite contrary evidence.
- Male: Female 3:1, average age 25.
- Atypical antipsychotics pimozide may be beneficial.
- Can be an early sign of schizophrenia.

Body dysmorphic disorder
- Excessive preoccupation with having an ugly body part.
  - 10-14% of dermatology patients.
- Starts commonly in early childhood.
- Patient is preoccupied with slightest defects in appearance.
- Associated with compulsive, ritualistic behaviors.
- Frequently centered around nose, mouth, genitalia, breasts and hair.
- Commonly present for cosmetic surgery evaluation.
- Presence of varying degrees of insight (in contrast to psychosis, where, by definition, there is essentially no insight).
- Associated with depression, somatoform disorder and social isolation.

Body Dysmorphic Disorder - Management
- Two categories:
  - Obsessive compulsive – display OCD behaviors, come in for multiple visits.
    - Tx: SSRIs (first line)
  - Delusional – no insight on their condition.
    - Tx: Antipsychotics
  - Both categories are never satisfied with their surgeries.
- Treatment includes cognitive-behavioral therapy.

Scalp dysesthesia
- A subset of “cutaneous dyesthesia syndromes”.
- Characterized by pain and burning sensations without objective findings.
- Primarily women middle-age to elderly.
- Associated with cervical spine degenerative disc disease.
- Hypothesized to be from chronic tension on the occipitofrontalis muscle and scalp aponeurosis.
- Treatment is gabapentin and low dose SSRIs.

Burning mouth syndrome (glossodynia, burning tongue)
- A subset of “cutaneous dyesthesia syndromes”.
- Burning sensation of oral mucosa without objective skin findings.
- Frequently postmenopausal women.
- Diagnosis of exclusion, rule out other causes.
- Treatment include topical lidocaine, capsaicin, doxepin, and alpha-lipoic acid as well as oral medications (SSRIs, TCA and gabapentin).
- Low level laser therapy has shown some promise with larger studies needed.

Vulvodynia
- Si/sx: Vulvar discomfort; burning pain; lasts 3 mo or longer.
- Provoked by physical contact.
- Subtypes: localized and generalized.
- Epidemiology: Typically nulligravid woman in late 30s.
- Underlying causes must be ruled out (candido, endometriosis, neoplasia, contact dermatitis, hypoestrogenism, neurological etiologies).
Vulvodynia

- Tx: Pt education, psychological support, lubricants, elimination of irritants, antidepressants (SSRIs or TCAs), gabapentin, pregabalin.
- Topical analgesics are also a treatment option with a recent study supporting treatment with compounded creams (baclofen 5% & autacoid palmitoyl ethanolamide 1%).

Trigeminal trophic lesions

- Interruption of peripheral or central sensory pathways of trigeminal nerve, resulting in a slowly enlarging anesthetic unilateral ulcer on nasal ala or adjacent cheek.
- Nasal tip is spared.
- Biopsy to exclude tumor or infection.
- Etiology: ulcer is typically due to self-inflicted trauma to anesthetic skin.

- Tx: Prevention by occlusion and psychotrophic medicine.
- Carbamazepine has also been investigated as a potential treatment option.
  - A recent case report displayed successful treatment of TTS with a thermoplastic dressing.

References

- Dermatology Bologna 3rd edition Chapter 7
- Andrew’s Dermatology 12th edition Chapter 4
- Sima Jain Dermatology 2012 p. 151

Acknowledgements

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ACNE & RELATED DISORDERS

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Disclosures

• We do not have any relevant disclosures.

Overview

• Acne Vulgaris
  – Pathogenesis
  – Clinical Features
    • Variants
    • Treatments
• Rosacea
  – Pathogenesis
  – Classification & clinical features
    • Rosacea-like disorders
  – Treatment

• Folliculitis & other follicular disorders

Acne vulgaris

• Pathogenesis
• Multifactorial
  • Genetics – role remains uncertain
  • Sebum – hormonal stimulation
  • Comedo
  • Inflammatory response
  • Propionibacterium acnes
  • Hormonal influences
  • Diet

Acne vulgaris

- Clinical Features
  - Face & upper trunk
  - Non-inflammatory lesions
    - Open & closed comedones
  - Inflammatory lesions
    - Pustules, nodules & cysts
    - Post-inflammatory hyperpigmentation
    - Scarring
    - Pitted or hypertrophic

Acne variants

- Acne fulminans
- Acne conglobata
  - PAPA syndrome
- Solid facial edema
- Acne mechanica
- Acne excoriée
- Drug-induced
**Acne variants**

- Occupational
- Chloracne
- Neonatal acne (neonatal cephalic pustulosis)
- Infantile acne
- Endocrinological abnormalities
- Apert syndrome

**Acne variants**

- Acneiform eruptions
- Tropical acne
- Radiation acne
- “Pseudoacne” of the transverse nasal crease
- Idiopathic facial aseptic granuloma
- Childhood flexural comedones

**Treatment**
**Rosacea**

- **Pathogenesis**
  - Unknown and remains controversial
  - Dysregulation of the innate immune system
  - Increased expression cathelicidiin (LL-37), AMP, kallikrein 5 (KLK5)
  - Microorganisms
    - *Demodex folliculorum*, *Staphylococcus epidermidis*, *Helicobacter pylori*, *Bacillus oleronius*
  - UV light radiation
  - Neurogenic dysregulation
  - Abnormal barrier function

**Rosacea**

- **Classification & clinical features**
  - Erythematotelangiectatic (ETR)
  - Papulopustular (PPR)
  - Phymatous
  - Ocular

**Rosacea-like disorders**

- Lupus miliaris disseminata faciei
- Roscea fulminans
- Morbihan’s disease
- Periorificial dermatitis
- Rosaceiform dermatitis
- Steroid-induced rosacea
- Pityriasis follicularum
- Haber’s syndrome
Treatment

- Educate patient on the chronic and intermittently flaring nature of this skin condition
- Based on subtype and severity
  - ETR
  - PPR
  - Phymatous
  - Ocular

Treatment of rosacea-like disorders

- Morbihan’s Disease
- Periorificial dermatitis
- Rosaceiform dermatitis
- Steroid-induced rosacea
- Pityriasis folliculorum
Folliculitis

- Superficial folliculitis
- Eosinophilic folliculitis
- AIDS-associated eosinophilic folliculitis
- Eosinophilic pustular folliculitis of infancy
- Disseminated and recurrent infundibulofolliculitis

Treatment

- Superficial folliculitis
- Eosinophilic folliculitis
- AIDS-associated eosinophilic folliculitis
- Eosinophilic pustular folliculitis of infancy
- Disseminated and recurrent infundibulofolliculitis

Folliculitis

- Deep folliculitis
- Sycosis
- Pseudofolliculitis barbae
- Acne keloidalis
- Follicular occlusion tetrad
- Hidradenitis suppurativa
Treatment

• Deep folliculitis
• Sycoisis
• Pseudofolliculitis barbae
• Acne keloidalis
• Follicular occlusion tetrad
• Hidradenitis suppurativa

Other follicular disorders

• Disorders of follicular keratinization
  • Erythromelnosis follicularis faciei
  • Keratosis pilaris atrophicans
  • Lichen spinulosus
  • Phrynoderma
  • Trichostasis spinulosa

#ClevelandAgainstTheWorld
VASCULITIDES & VASO-OCCCLUSIVE DISORDERS

Broward Health Medical Center
Dermatology Residency Program
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Disclosure
• We have no financial interests or relationships to disclose.

CUTANEOUS SMALL-VESEL VASCULITIS

A. Hypersensitivity Vasculitis/Leukocytoclastic Vasculitis
B. Henoch-Schonlein Purpura
C. Acute Hemorrhagic Edema of Infancy
D. Urticarial Vasculitis
E. Cryoglobulinemic Vasculitis
F. Erythema Elevatum Diutinum

• All ages & sexes, MC in adults
• Etiology: immune complex deposition
• Presentation: palpable purpura, erythematous papules, urticarial lesions involving dependent areas
  – Koebner phenomenon
  – Fever, weight loss, myalgias with flares
• Pathology:
  – H&E: LCV, karyorrhexis, extravasated RBC
  – DIF: C3, IgM, IgA and/or IgG granular deposits in vessels

HYPERSENSITIVITY VASCULITIS / CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS (LCV)


• MC children
• Etiology: bacterial & viral infections
• Presentation: palpable purpura, arthritis, abdominal pain, renal disease
• Pathology:
  – H&E: LCV
  – DIF: IgA vasculitis
• Treatment: systemic corticosteroids, immunosuppressants, ACE-I
• Prognosis: monitor for chronic renal insufficiency

HYPERSENSITIVITY VASCULITIS / CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS (LCV)

• Secondary LCV
  • Idiopathic (50%)
  • Infection (15-25%)
  • Inflammatory Disorders (15-20%)
  • Drug Exposure (10-15%)
  • Neoplasms (2-5%)
  • Genetic Disorders (Rare)
• Treatment:
  – Acute
    • Often resolves without treatment
    • Avoid trigger
    • Supportive care
  – Chronic (>4 wks)
    • Ciclosporine, dapsone, corticosteroids
• Prognosis: monitor for chronic renal insufficiency

HENOCH-SCHONLEIN PURPURA

ACUTE HEMORRHAGIC EDEMA OF CHILDHOOD

- Children < 2 yrs
- Etiology: likely infectious
- Presentation: cockade, annular, purpuric plaques involving the face, ears, distal extremities
  - No systemic findings
- Pathology:
  - H&E: LCV
  - DIF: IgA vasculitis
- DDx: Child abuse, urticaria, urticarial vasculitis, erythema multiforme
- Treatment: Resolves spontaneously in 1-3 weeks

URTICARIAL VASCULITIS

- Adults, peak 50s, F>M
- Etiology: unknown
- Variants:
  - Normocomplementemic
  - Hypocomplementemic
- Associations:
  - CTD (Sjögren’s, SLE)
  - Serum sickness
  - Cryoglobulinemia
  - Infections (HBV, HCV, EBV, Lyme)
  - Medications
  - Hematologic & solid malignancies: colon & renal cell cancer

CRYOGLOBULINEMIC VASCULITIS

- Vasculitis is ONLY seen with types II and III
  - Type I can present with vasculopathy
- Small & medium-sized vessels, but preferentially involves small vessels
- Association with HCV & HBV infections

URTICARIAL VASCULITIS

- Diagnosis: skin biopsy
  - H&E: < 48 hours in onset
  - DIF: < 24 hours in onset
- Pathology:
  - H&E: LCV + neutrophilic infiltrate
  - Hypo DIF: C3 granular pattern in BV & BM
- Treatment:
  - 1st line: antihistamines, NSAIDs
  - Alt: colchicine, hydroxychloroquine, dapsone
  - Systemic: steroids, azathioprine, mycophenolate mofetil, rituximab
- Prognosis:
  - Chronic and benign - 3 years
**CRYOglobulinemic Vasculitis**

- **Laboratory Evaluation:**
  - Often falsely negative, need to test multiple times
  - Blood samples should be kept at 37°C (98.6°F) while being transported to lab
- 70% are RF (+); 20% are ANA (+)
- Low C4 levels - do not correlate with disease activity
- **Treatment:** treat underlying disease!
  - Hep C (+): new antivirals (i.e Harvoni), Ribavirin, Interferon
  - Plasma exchange or cyclophosphamide with corticosteroids may be needed for severe renal or neurological involvement
  - Rituximab

**Erythema Elevatum Diutinum**

- Symmetric red-violet to red-brown papules & plaques
- Persistent lesions that develop on extensor surfaces/small joints
  - Trunk generally spared
  - A/e infections, hematologic, rheumatologic diseases
- Limited to skin
- **Pathology:** LCV with fibrinoid necrosis
- **Treatment:** typically responds promptly to Dapsone or sulfapyridine

**Medium-Vessel Vasculitis**

A. Polyarteritis Nodosa (benign & systemic)

**MIXED (MEDIUM & SMALL) VESSEL VASCULITIS**

A. Connective Tissue Disease Associated (usually rheumatoid vasculitis)
B. Septic Vasculitis
C. ANCA-Associated
  1. Microscopic Polyangiitis
  2. Granulomatosis with Polyangiitis
  3. Allergic Granulomatosis (Churg-Strauss)

**Polyarteritis Nodosa**

- Cutaneous variant has chronic, more benign course
  - Often a/w strep infection in children
- HBV, HCV, infections, inflammatory diseases, malignancies (hairy cell leukemia) & medications
- **Pathology:** Segmental necrotizing vasculitis in subcutaneous tissue
- **Treatment**
  - Classic PAN – systemic corticosteroids (1 mg/kg/day of prednisone)
  - Cutaneous PAN – topical or intratresional steroids, may need systemic steroids if progressive or extensive

**Polyarteritis Nodosa**

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- **Treatment**
  - Classic PAN – systemic corticosteroids (1 mg/kg/day of prednisone)
  - Cutaneous PAN – topical or intratresional steroids, may need systemic steroids if progressive or extensive

**Rheumatoid Vasculitis**

- Rare, late complication in patients with longstanding, severe, deforming RA
- High morbidity and mortality
- **Risk Factors**
  - Smoking, HLA-DRB1 (familial epitope), uncontrolled RA, high RF titer and anti-CCP, PVD
- **Presentation**
  - Purpura, cutaneous ulcers (upper or lower ex), rheumatoid nodules, digital infarcts, nail fold infarcts
  - Extracutaneous: seveoire erosive arthritis, scleritis, retinal vasculitis, pulmonary, renal, GI, & CNS findings
- **Treatment**
  - No established guidelines to help guide therapy, high-dose glucocorticoids + cyclophosphamide has shown promising results

**Mixed (Medium & Small) Vessel Vasculitis**

A. Connective Tissue Disease Associated (usually rheumatoid vasculitis)
B. Septic Vasculitis
C. ANCA-Associated
  1. Microscopic Polyangiitis
  2. Granulomatosis with Polyangiitis
  3. Allergic Granulomatosis (Churg-Strauss)
**MICROSCOPIC POLYANGIITIS**

- Presentation: purpuric papules, macules, red-purple purpura, cutaneous ulceration, livedo, rarely urticaria
  - Systemic: fever, weight loss, myalgias, arthralgias, segmental necrotizing and crescentic glomerulonephritis, soft pulmonary involvement, pulmonary capillaritis, vasculitis, neuropathy, eye disease
- Pathology: necrotizing LCV
- Laboratory findings: ANCA + (70%), p-ANCA > c-ANCA
- Treatment: systemic corticosteroids
  - Generalized: MTX + CS
  - Organ involvement: cyclophosphamide then MMF, MTX, or azathioprine, IVIG and anti-TNF

**GRANULOMATOSIS WITH POLYANGIITIS**

- Rare, potentially life-threatening PR3-ANCA associated necrotizing vascultis of small to medium-sized vessels and extravascular necrotizing granulomatous inflammation
- F/M peak age 45-65 years
  - 1) Necrotizing granulomatous inflammation of upper & lower respiratory tracts
  - 2) Glomerulonephritis
  - 3) Necrotizing small to medium-vessel vasculitis
- Presentation:
  - Papulo-purpuric eruption followed by oral ulcerations: “strawberry gingiva”
  - Perifollicular papules, scalp, firm non-tender purpuric papules of fingertips, urticaria
- Labs:
  - c-ANCA in 80-90%
  - ANCA + (70%), p-ANCA > c-ANCA
- Pathology: LCV-like changes, palisading granulomas, granulomatous vascultis surrounding foci of basophilic necrosis
- Treatment:
  - Corticosteroids + cyclophosphamide
  - = 75% remission
  - Corticosteroids + rituximab may be equally effective

**CHURG-STRAUSS SYNDROME**

- Laboratory findings: peripheral eosinophilia, p-ANCA (anti-myeloperoxidase) positive, c-ANCA (anti-PR3) sometimes positive
- Pathology: small and medium LCV, Wells syndrome with flame figures, palisaded granulomas lacking giant cells with central eosinophil
- Treatment: corticosteroids, cyclophosphamide with corticosteroids if neuro, renal, myocardial, or gastrointestinal involvement
  - MTX or other steroid-sparing agents can be used to maintain remission

**BEHÇET'S DISEASE**

- HLA-B51
- Presentation: palpable purpura, subcutaneous nodules of extremities and scalp, firm non-tender purpuric papules of fingertips, urticaria
- 3 phases:
  1. Initial: allergic rhinitis, nasal polyps, asthma (35 yo)
  2. Secondary: 2-12 years later: fever, eosinophilia, with pneumonia and gastrointestinal
  3. Tertiary: diffuse angiitis of the liver, spleen, kidneys, CNS lesions (MS-like)
- Medication triggers: vaccination, desensitization, leukotriene inhibitors, azithromycin, nasal fluticasone, rapid d/c desensitization, leukotriene inhibitors
- Treatment:
  - Predominantly neutrophilic infiltrate
  - Vasculitis may involve small and medium vessels
    - Predominantly neutrophilic infiltrate
  - Treatment:
    - Colchicine, dapsone, thalidomide, TNF-inhibitors
Thank You
Vesiculobullous Diseases
Larkin Community Hospital/NSU-COM
Presenters: Yuri Kim, DO, Sam Ecker, DO, Jennifer David, DO, MBA
Program Director: Stanley Skopit, DO, MSE, FAOCD, FAAD

• We have no relevant disclosures

Topics of Discussion
• Subcorneal Vesiculobullous Disorders
  - Pemphigus foliaceous
  - Pemphigus erythematosus
  - Subcorneal pustular dermatosis (Sneddon-Wilkinson Disease)
  - Acute Generalized Exanthematous Pustulosis

• Intraepidermal Vesiculobullous Disorders
  - Pemphigus vulgaris
  - Pemphigus vegetans
  - Hailey-Hailey Disease
  - Darier’s Disease
  - Grover’s Disease
  - Paraneoplastic Pemphigus
  - IgA Pemphigus

Topics of Discussion (Continued)
• Pauci-inflammatory Subepidermal Vesiculobullous Disorders
  - Pemphigus gestationis
  - Porphyria Cutanea Tarda (PCT)
  - Epidermolysis Bullosa Acquisita (EBA)

• Inflammatory Subepidermal Disorders
  - Bullous Pemphigoid
  - Cicatricial Pemphigoid
  - Dermatitis Herpetiformis
  - Linear IgA

Subcorneal Vesiculobullous Disorders
• Pemphigus foliaceous
• Pemphigus erythematosus
• Subcorneal pustular dermatosis (Sneddon-Wilkinson Disease)
• AGEP

Pemphigus Foliaceous
• IgG Ab to desmoglein 1 (Dsg-1, 160 kDa)
• Peak onset middle age, no gender preference
• Endemic form – Fogo selvagem in Brazil and other parts of South America
• Pemphigus erythematosus- Localized variant of pemphigus foliaceous with features of lupus erythematosus
**Pemphigus Foliaceous**

- Topical and systemic steroids
- Mycophenolate mofetil
- Azathioprine
- Dapsone
- Rituximab
- IVIG

**Subcorneal Pustular Dermatosis**

- Aka, Sneddon-Wilkinson Disease
- Etiology unclear
- Cultures from the pustules are sterile
- More common in women and >40 y/o
- Some cases are associated with a monoclonal gammopathy (usually IgA)
Subcorneal Pustular Dermatosis

- Negative – if positive, most likely IgA Pemphigus

Subcorneal Pustular Dermatosis

- Treatment of choice: Dapsone
- Alternatives: retinoids, NBUVB, colchicine, topical steroids, cyclosporine

Acute Generalized Exanthematous Pustulosis (AGEP)

- Acute febrile pustular eruption
- Causes: Drugs, Hg ingestion, bacterial/viral infection
- Pustules begin on face/intertriginous areas — widespread within a few hours
- B/W reveals marked neutrophilia; pustules may show heavy S. aureus on culture
Intraepidermal Vesiculobullous Disorders

- Pemphigus Vulgaris
- Hailey-Hailey
- Darier’s Disease
- Grover’s Disease
- Paraneoplastic Pemphigus
- IgA Pemphigus

Pemphigus Vulgaris

- Ab against desmoglein 1 and/or 3
- Drug-induced: thiol drugs (penicillamine, captopril, enalapril, lisinopril, piroxicam), pyrazolone derivatives (phenylbutazone, oxyphenylbutazone), antibiotics (penicillin derivatives, cephalosporin, rifampicin)
- Pemphigus Vegetans - Rare vegetative variant of Pemphigus Vulgaris (Neumann and Hallopeau type)

AGEP

- Negative

AGEP

- Symptomatic treatment
- Antihistamines
- Topical tx of St. aureus with mupirocin
- Reassurance
Pemphigus Vulgaris

• Treatment:
  – Oral corticosteroid
  – Methotrexate
  – Azathioprine
  – Mycophenolate mofetil
  – Plasmapheresis
  – IVIG
  – rituximab

Hailey-Hailey

• Benign familial pemphigus
• AD, ATP2C1 gene (encodes Golgi-associated Ca2+ ATPase hSPCA1), results in abnormal intracellular calcium signaling
• Onset typically 2nd to 3rd decade
• Presents with flaccid vesicles initially on erythematous base over intertriginous areas, ruptures easily, and gives rise to macerated or crusted erosions
**Hailey-Hailey**

- Negative DIF

**Treatment**
- Avoid triggers (sweating, friction, tight clothing)
- Topical corticosteroids
- Topical antibiotics (clindamycin, mupirocin)
- Topical calcineurin inhibitors
- Oral antibiotics (tetracycline, minocycline)
- Anticholinergics (glycopyrrolate)
- Intra-lesional corticosteroids
- Botulinum toxin
- Lasers (CO2, Er:YAG, PDL)

**Darier’s Disease**

- AD, ATP2A2; SERCA2 calcium-dependent ATPase
- Impaired cell cohesion, increased apoptosis
- Onset puberty (6-20 yrs)
  - Chronic & unremitting
  - Exacerbated by sun, heat, lithium therapy
  - Superinfection- bacterial, fungal, HSV
- Kaposi’s varicelliform eruption - vesicular eruption w/ fever
Darier’s Disease

- Intensely pruritic papulovesicular eruption occurring as scattered eroded lesions usually on the trunk of a well-appearing male > 40 years old.
- Self limited variant (transient acantholytic) vs chronic relapsing variant (persistent acantholytic)
- Associated with AD, ACD/ICD, and asteatotic eczema
- Exacerbated by heat, friction and sweat

Treatment:
- Light-weight clothing and sunscreen
- Antimicrobial cleanser, keratolytics
- Topical steroids, topical retinoids
- Isotretinoin and acitretin
  - Very effective however relapse when stopped
- Prompt oral acyclovir or valacyclovir (HSV)

Grover’s Disease

- Intensely pruritic papulovesicular eruption occurring as scattered eroded lesions usually on the trunk of a well-appearing male > 40 years old.
- Self limited variant (transient acantholytic) vs chronic relapsing variant (persistent acantholytic)
- Associated with AD, ACD/ICD, and asteatotic eczema
- Exacerbated by heat, friction and sweat

Treatment:
- Negative DIF
Grover’s Disease

• Negative DIF

Treatment
• Avoidance of exacerbating factors, loose clothing, topical steroids, topical antibiotics, calcipotriol, urea, zinc oxide, antihistamines
• Refractory cases may respond to dapsone, isotretinoin, oral corticosteroids, PUVA or NBUVB

Paraneoplastic Pemphigus

• First sign: Severe stomatitis
• Erosions and ulcerations can affect oropharynx and extend onto vermilion lip
• Palm and soles involvement is common
• Pseudomembranous conjunctivitis
• Bronchiolitis obliterans

Overview

• Associated underlying neoplasms
  – Non-Hodgkin lymphoma (40%)
  – CLL (30%)
  – Castleman’s disease (10%)
  – Malignant and benign thymomas (6%)
• Autoimmunity
  – IgG autoantibodies target members of the plakin family and desmogleins
  – Autoantibodies detected by indirect immunofluorescence on rodent urinary bladder epithelium

Clinical H&E DIF Treatment
Paraneoplastic Pemphigus
- Resistant to most therapies
- Treatment is aimed at the underlying malignancy
- Reduction in antibodies
  - Corticosteroids, azathioprine, cyclosporine, photopheresis, mycophenolate mofetil, IVIG
- Rituximab
  - CD20 monoclonal antibody, has been used to treat cases with an underlying CD20+ lymphoma

IgA Pemphigus
- Intraepidermal IgA deposits, 2 clinical types
  - Subcorneal pustular dermatosis (SPD) variant
    - IgA ab to desmocollin 1
  - Intraepidermal neutrophilic (IEN) type
    - IgA ab to desmoglein 1 or 3
- Avg onset 6th decade, slight female predominance
IgA Pemphigus

- Oral and topical corticosteroids
- Dapsone
- Isotretinoin/acitretin
- Mycophenolate mofetil
- Adalimumab

Subepidermal vesiculobullous disorders: pauci-inflammatory subepidermal conditions

- Porphyria cutanea tarda
- Epidermolysis bullosa acquisita

Porphyria cutanea tarda (PCT)

- Acquired (T I) or AD (T II)
- Deficiency of uroporphyrinogen decarboxylase in the heme biosynthetic pathway (enzyme 5 of 8)
- Liver disease major causative/contributing factor
- Skin lesions develop due to sun exposure (400-410 nm)
- Urine "glows" - orange-red fluorescence with acetic acid/10% HCl
PCT

• Sun avoidance/ Zinc Oxide or Titanium Dioxide
• Eliminate ETOH
• Serial phlebotomy +/- chelation therapy
• Antimalarials: hydroxychloroquine

Epidermolysis Bullosa Acquisita (EBA)
• Rare acquired autoimmune blistering disease to NC-1 domain of collagen VII
• Non-inflammatory or pauci-inflammatory tense bullae affecting trauma-prone extensor skin surfaces
• Lesions heal with significant scarring and milia
• Resembles the inherited form of dystrophic epidermolysis bullosa with lack of family history
• Exclusion of all other bullous diseases
EBA
- Supportive care
- Systemic steroids
- Dapsone
- Imuran
- Cellcept
- IVIG, cyclosporine, methotrexate, rituximab, colchicine, photopheresis & anti-TNFα biologics for severe or recalcitrant disease

Pemphigoid Gestationis
- Self-limited, rare: 1 in 50,000 pregnancies
- Typically 3rd trimester or immediate postpartum period
- Antibody: anti-BPAg2 (NC16A domain of BP 180)
- HLA-DR3, HLA-DR4 associations
- Maternal risk: Grave’s disease
- Fetal risk: prematurity, small gestational age, up to 10% risk of skin involvement

Overview
Clinical
H&E
DIF
Treatment

Pemphigoid Gestationis
- 0.5 mg/kg of prednisolone daily; taper as soon as blister formation suppressed
- Delivery usually precipitates flare → increase dose
- Cyclosporine
- Mild cases: potent topical steroids + emollients & antihistamines (usually ineffective)

Overview
Clinical
H&E
DIF
Treatment
Inflammatory Subepidermal Conditions

- Bullous pemphigoid
- Cicatricial pemphigoid
- Dermatitis herpetiformis
- Linear IgA dermatosis

Bullous Pemphigoid

- Most common autoimmune bullous disorder with chronic nature
- Typically seen in patients over age 60
- Autoantigens: BPAG2 (180 kDa) and BPAG1 (230 kDa)
- 10-35% with oral involvement
- Drug-induced: furosemide, NSAIDs, PCN-derivatives, phenactin, gold, potassium iodide, captopril, enalapril, D-penicillamine, sulfasalazine

Bullous Pemphigoid

Overview

Clinical

H&E

DIF

Treatment

- Oral corticosteroids
- Steroid sparing agents
  - Azathioprine
  - Mycophenolate mofetil
  - Thalidomide
  - Methotrexate
  - Cyclophosphamide
- Tetracycline + nicotinamide
- Dapsone
- IVIG for refractory cases
Cicatricial Pemphigoid

• Rare autoimmune disease involving the mucous membrane → scarring

• Autoantigens:
  – **BPAG2** (180 kDa): mucosa & skin
  – β4 (subunit of α6β4): pure ocular form
  – **Laminin 5** (epiligrin): increased risk of malignancy

Overview

Clinical

H&E

DIF

Treatment

Cicatricial Pemphigoid

• Drug-induced (similar to BP)
  – Thiol-containing drugs
    – Captopril, gold thiosulfate, D-penicillamine
  – NSAIDS (Indomethacin)
  – β-blockers (practolol)
  – Clonidine
  – Sulfadoxine

Overview

Clinical

H&E

DIF

Treatment

Cicatricial Pemphigoid

• Treatment of choice:
  – Dapsone

• Alternatives:
  – Topical/intralesional/oral corticosteroids
  – Cyclophosphamide
  – Azathioprine

Overview

Clinical

H&E

DIF

Treatment
Dermatitis Herpetiformis

- Aka: Duhring’s Disease
- Recurrent pruritic chronic disease associated with gluten-sensitive enteropathy
- Gluten: storage proteins found in wheat, rye, barley
  - Gluten: glutin: soluble fraction; likely antigenic component
- Autoantigen: epidermal transglutaminase (TG-3), tissue transglutaminase (endomysial)
- Labs: anti-gliadin/anti-endomysial antibodies

Overview

Clinical

H&E

DIF

Treatment

Dermatitis Herpetiformis

- Dapsone
- Sulfapyridine
- Gluten-free diet
- Referral to Gastroenterology: gluten-sensitive enteropathy and increased risk of small bowel lymphoma
- Referral to Endocrinology: increased incidence of thyroid disease (Hashimoto’s thyroiditis) and IDDM

Overview

Clinical

H&E

DIF

Treatment

Linear IgA Bullous Dermatosis

- Rare; likely identical to chronic bullous disease of childhood
- Autoantigens:
  - LAD-1 is cleaved and yields LABD97
- Drug-induced
  - Vancomycin, captopril, cephalosporin, PCN, NSAIDs, phenytoin, sulfonamide

Overview

Clinical

H&E

DIF

Treatment
Linear IgA Bullous Dermatosis

- Dapsone
- Sulfapyridine
- Prednisone
- Azathioprine
- Mycophenolate mofetil

Conclusion

- Vesiculobullous diseases can be inherited or acquired
- These conditions may be antibody or cell-mediated
- The involved intracellular adhesion molecules determine subcorneal, intraepidermal or subepidermal splitting
- Direct immunofluorescence and salt splitting can help determine diagnosis
Psoriasis

Pathogenesis

• Hyperproliferation disorder, driven by complex cascade of inflammatory mediators
  • Mixed T-helper (Th-1) and Th17 inflammatory disease
  • T cells and cytokines play pivotal role
  • Overexpression of Th1 and Th17 cytokines, along with IL-8 leads to accumulation of neutrophils
  • Main signal for Th1 development: IL12 which promotes IFN-gamma
  • In animals, shifting from Th1 to Th2 improves psoriasis

Main T-helper cell(s) involved?
Th-1 and Th-17

• HLA Cw6 (strongest)
• HLA B17: early onset
• HLA B27: psoriatic arthritis

Drugs that exacerbate psoriasis
• Withdrawal of systemic corticosteroid
• Lithium
• B-blocker
• Antimalarial
• ACEi
• G-CSF

Psoriatic arthritis
• Asymmetrical oligoarthritis (70%)
Pustular Psoriasis (localized)

- Palmoplantar pustulosis
  - Localized form
  - Tense sterile pustules on palmoplantar surfaces with yellow-brown macules
  - Maybe associated with SAPHO syndrome
    - Synovitis, Acne (conglobata), Pustulosis, Hyperostosis, Osteitis
  - Inquire about sternoclavicular tenderness and/or back pain
- Acrodermatitis continua of Hallopeau
  - Limited to fingertips or digit
  - Pustules on the fingertips and within nailbed, often with subsequent nail shedding

Small Molecules

- Apremilast (Otezla)
  - PDE-4 inhibitor → increase cAMP
  - Dosage adjustment in severe renal impairment
  - Strong CYP3A4 inducer
  - e.g. rifampin, phenytoin, phenobarbital, carbamazepine
  - Adverse events
    - Nausea
    - Deposition (1.3%), weight loss (10%)
- Tofacitinib (Xeljanz)
  - Inhibits JAK1 and 3 > 2
  - JAK-STAT pathway → decrease cytokine gene transcription
  - Tofacitinib 10 mg BID was non-inferior to etanercept
  - Increase risk of serious infections including opportunistic infections and malignancy in RA patients

IL-17 inhibitors

- Secukinumab (Cosentyx) / Ixekizumab (Taltz)
  - Human IL-17A antagonist
  - Adverse events
    - Exacerbation of inflammatory bowel disease
    -Transient and self-limiting neutropenia
    - Mucocutaneous candidiasis

New Biologics: IL-23 inhibitors

- Guselkumab
- Rizankizumab
- Tildrakizumab

Miscellaneous

• Etanercept approved for pediatric moderate to severe plaque PSO (Nov 2016)
  • Age 4 and up
  • not approved for IBD, unlike the other TNF-α inhibitors
• Methotrexate - should not be used concomitantly with TMP/SMX
  • Avoid pregnancy for 3 months
• Acitretin - half-life 2 days but can re-esterify to etretinate, which is highly lipophilic (120 days half-life)
  • Avoid pregnancy for 3 years
• Calcipotriene - inactivated by acidic pH

Contact Dermatitis

Which is the most frequent preservative used in cosmetics?
Parabens
(Not commonly a cause of ACD)

Which is the most common preservative in cosmetics to cause a positive patch test?
Quaternium 15

Contact Allergens

• Formaldehyde-releasing preservatives
  • Quaternium-11 - #1 cause
  • 2-bromo-2-nitropropane-1,3-diol (Bronopol) - #2 culprit
  • Diazolidinyl urea
  • Methyldibromo glutaronitrile (DMDM) - #3 culprit
• Other preservatives
  • Methylisothiazolinone (Kathon CG) – biocidal preservatives added to bubble solutions, baby wipes
  • Thimerosal – mercury-containing compound
  • Formaldehyde-releasing preservatives
  • Parabens – most common preservative overall, but very low rate of irritancy and allergenicity

• Rubbers
  • Thiuram – cross-reacts with disulfiram
  • Mercaptothiazoles – shoe dermatitis
  • Carbos – “bleached rubber syndrome

• Metals
  • Nickel – most prevalent allergen (17% worldwide). Beware of technologies containing nickel
  • Cobalt – cross-reacts with nickel
  • Vitamin B12 injection
  • Potassium dichromate – cement, tanned leather
Atopic Dermatitis

Plant Allergens
- Urushiol
  - Poison ivy, poison oak, poison sumac
  - May cross-react with cashew, mango, Japanese lacquer tree, Indian marking nut, jingko
  - Start to appear in a number of personal care products
- Sesquiterpene lactone
  - Chrysanthemum, ragweed, sunflower, artichoke, arnica, daisy, marigold
  - May cross react with permethrin

Pathogenesis
- T-helper 2 cells and related cytokines
  - All stages of the disease
  - IL-4 and IL-13 predominantly
  - IL-4 is also responsible for B cell class switching to IgE
- T-helper 1 cells and related cytokines
  - Chronic disease
  - IFN-γ, IL-12
- T-helper 17 and 22 recently implicated

Emerging therapies for AD
- Crisaborole
  - Topical PDE-4 inhibitor → increase cAMP
  - Mild to moderate AD in adults and children age 2 year and up
- Dupilumab
  - α subunit of IL-4R → IL-4, IL-13 blockade
  - Adults with moderate to severe AD
  - Headache and nasopharyngitis were more common in Dupilumab group compared to placebo

Atopic dermatitis and ACD

Recent consensus group statement published

- When to patch test:
  - Hand or foot eczema
  - Other very localized distributions
  - Worsens with topical therapy
  - Allergy to topical steroids or propylene glycol
  - Refractory cases
  - May suggest persistent allergenic trigger
  - Adults- or adolescent-onset AD
  - Whenever considering systemic immunosuppressant
  - Consider reversible option first


Thank you
Viral Dermatoses

Program Director:
Richard Miller, D.O., F.A.O.C.D.

Senior Residents:

Disclosures
• No relevant financial relationships or conflicts of interest to disclose

Objectives
• Discuss human papillomavirus, including its oncogenic potential
• Discuss herpes viruses with an emphasis on the Epstein-Barr virus
• Discuss other viral exanthems, including associations of hand-foot-and-mouth disease

Human Papillomaviruses

Joseph Dyer, DO

Human Papillomavirus (HPV)
• A dsDNA, non-enveloped virus that infects epithelia of skin or mucosa
• Causes an exciting array of warts in different size, shapes, colors...
• ...and anatomic locations

Awesome clinical spectrum of warts...
• Because > 130 subtypes of HPV
**Pathogenesis**

Abrasion in skin allows HPV to reach basal keratinocytes, where it replicates.

Viral binding to skin cells requires L1, the major capsid protein.

HPV genes are transcribed:

- **E1 + E2** are first, allowing transcription of the rest.
- **E6 + E7** promote proliferation and amplify viral DNA.

→ hyperproliferation of keratinocytes.

**Oncogenic potential**

- **E6 + E7** have a darker side.
  - **E6** is an oncogene → degrades p53
  - **E7** is an oncogene → binds RB

When p53 is degraded and RB is bound, uncontrolled cell cycling may ensue. This may cause carcinogenesis in certain subtypes of HPV.

**Verruca vulgaris**

- HPV 1, 2, + 4

**Myrmecia**

- HPV 1

From the Greek word for ant hill, referring to the clinical appearance of these plantar or palmar warts.

**Verruca plana**

- HPV 3 + 10

**Epidermodysplasia verruciformis**

- HPV 5 + 8

Clinically, 2 types of skin lesions:

- Tinea versicolor-like macules
- Verruca plana-like papules

TV-like

- SCC

VP-like

TV condition 2/2 mutation in EVER1/TMC6 or EVER2/TMC8

→ susceptibility to certain HPV subtypes

Clinically, 2 types of skin lesions:

- Tinea versicolor-like macules
- Verruca plana-like papules

→ later develop SCC.
Condyloma acuminatum

- HPV 6 + 11

Condyloma in children always brings up the issue of sexual abuse. That risk is highest in kids > 3 years old. Infants < 1 year old probably acquired HPV through vertical transmission. Children 1–3 years old may be referred to child protective services on a case-by-case basis.

Verrucous carcinomas

- Verrucous carcinomas are low-grade squamous cell carcinomas, occurring in different locations:
  - Genitals — Buschke-Lowenstein tumor
  - Soles — Epithelioma curuculum
  - Oral mucosa — Oral florid papillomatosis
  - Shins — Papillomatosis cutis carcinoides
- Avoid radiation, may cause frank malignant degeneration

Laundry list of wart treatments

- Watchful waiting
- Cryotherapy every 1–3 weeks
- Manual debridement with No. 15 scalpel blade
- IL Candida
- Topical 5-Fluorouracil nightly
- Salicylic Acid 17% home treatment
- Topical immunotherapies
- Squaric Acid dibutylester (SADBE)
- Dinitrofluorobenzene (DNFB)
- Measure serum zinc level and treat if low
- FG correlations
- Laser (IFL, utilizing hemoglobin as the chromophore)
- Bleomycin
- Podophyllin or trichloroacetic acid for genital warts
- Duct tape
- Cidofovir
- Imiquimod
- Adapalene
- Laser (PDL, utilizing hemoglobin as the chromophore)
- IL Candida Q 3 weeks until clear, max of 3 sessions
- Cryo Q 1 wk until clear, max of 10 sessions
- IL Candida statistically significant better response than cryo

“Donut” use cantharidin…

- …or you could end up with this ringlike arrangement of warts

Human Herpesviruses

Natalie Edgar, DO
Human Herpesviruses (HHV)

- Double-stranded DNA viruses
- Pathogenesis sequence
  - 1° infection → latency → reactivation

<table>
<thead>
<tr>
<th>HHV</th>
<th>Virus Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>HHV-1</td>
<td>Herpes simplex virus type 1 (HSV-1)</td>
</tr>
<tr>
<td>HHV-2</td>
<td>Herpes simplex virus type 2 (HSV-2)</td>
</tr>
<tr>
<td>HHV-3</td>
<td>Varicella-zoster virus (VZV)</td>
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<tr>
<td>HHV-4</td>
<td>Epstein-Barr virus (EBV)</td>
</tr>
<tr>
<td>HHV-5</td>
<td>Cytomegalovirus (CMV)</td>
</tr>
<tr>
<td>HHV-6</td>
<td>Human herpes virus 6 (HHV-6)</td>
</tr>
<tr>
<td>HHV-7</td>
<td>Human herpes virus 7 (HHV-7)</td>
</tr>
<tr>
<td>HHV-8</td>
<td>Human herpes virus 8 (HHV-8)</td>
</tr>
</tbody>
</table>

Epstein-Barr Virus (HHV-4)

- One of the most ubiquitous viruses, infecting 90-95% of adults worldwide
- Utilizes the CD21 cell surface receptor to infect B lymphocytes
- Virus remains latent in B-cells and periodic reactivation may occur
- Variety of clinical diseases

- **Mononucleosis ampicillin eruption**
  - Generalized, pruritic, erythematous to copper-colored macules
  - 7-10 days after starting aminopenicillin abx for presumed strep pharyngitis
  - 80-100% of pts
  - Not a true hypersensitivity
  - Also in CMV infection

- **Hydroa vacciniforme**
  - Childhood-onset photodermatosis that resolves by adulthood
  - Photodistributed, hemorrhagic crusted papulovesicles that heal w/ scarring
  - Study found 94% of children with typical disease, had lesional T-cells positive for EBV

- **Gianotti-Crosti Syndrome**
  - Acute, symmetric papular eruption on the face, extremities, & buttocks
    - Spares the trunk
  - EBV > Hepatitis B
  - Likely represents a virus-induced delayed hypersensitivity
Epstein-Barr Virus (HHV-4)

**Drug Reaction with Eosinophilia and Systemic Symptoms**
- CMV, HHV-6, HHV-7 have also been implicated in conjunction with medication and genetics
- Morbilliform eruption with follicular accentuation and facial edema 2-6 weeks after initiating drug
- Peripheral eosinophilia and systemic symptoms

Epstein-Barr Virus (HHV-4)
- Other clinical presentations include
  - Genital ulcers (aka Lipschutz ulcers)
  - Hypersensitivity to mosquito bites
  - Oral hairy leukoplakia
  - Lymphoproliferative disease
  - Nasopharyngeal carcinoma
  - Smooth muscle tumors

Other Viral Exanthems

Dawnielle Endly, DO

Enteroviruses

- ssRNA
- Most common exanthem:
  - Hand-foot-and-mouth disease (HFMD)

HFMD Enteroviruses

- Most common: Coxsackie A16
- Cardiopulmonary and neurological complications: Enterovirus 71
- Superinfection in those with atopic dermatitis: Coxsackie A6
  - “Eczema coxsackium” is a Kaposi’s varicelliform-like eruption

HFMD

- Vesicles on palms and soles
- Erosive stomatitis
- Onychomadesis
Measles (Rubeola)

- RNA virus in the *Paramyxovirus family*
- Incidence greatly decreased with vaccination
- Prodrome: fever with 3 C’s
  - Cough, conjunctivitis, coryza (nasal congestion)

Measles

- Late complication: **Subacute sclerosing panencephalitis**
- Treatment: **Vitamin A**
  - Low Vit A is associated with increased measles related morbidity and mortality

Erythema Infectiosum (EI)

- **Fifth Disease**
- **Parvovirus B19 infection**
  - ssDNA
- Most common in school aged children

**EI**

- Lacy extremity-predominant exanthem
- Slapped cheeks

Erythema Infectiosum (EI)

- **Arthritis** occurs in 10%
  - Most commonly small joints (hands, wrists)
  - 30-60% of adult women
- Greatest susceptibility of fetal infection: <20 weeks gestation
  - Risk of fetal anemia resulting in *hydrops fetalis* and possible miscarriage
Another manifestation of Parvovirus B19...

Papular-purpuric glove and sock syndrome

Which HPV derived protein degrades p53 and is implicated in carcinogenesis?

A) E1
B) E3
C) E6
D) E7

A child with atopic dermatitis suffers from HFMD and suddenly develops a Kaposi’s varicelliform-like eruption. What virus is associated with this occurrence?

A) Coxsackie virus A16
B) Coxsackie virus A6
C) Enterovirus 71
D) Chikungunya

Summary

- Certain subtypes of human papillomavirus may cause squamous cell carcinoma when E6 degrades p53 and E7 inactivates RB
- Epstein-Barr virus is a herpes virus that is associated with a wide range of dermatologic conditions, including hydroa vacciniforme, Gianotti-Crosti syndrome, and DRESS syndrome
- Coxsackie A6 is an enterovirus that may cause a wide-spread eruption termed “eczema coxsackium” in atopic patients

References

1. Bolognia Ch 78, 79, 80, 81, 87
5. Hurwitz Ch 15, 16

Thank you!
Granulomatous, Metabolic and Depositional Disease

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Non-Infectious Granulomas

- Sarcoidosis
- Granuloma annulare
- Necrobiosis lipoidica
- Necrobiosis xanthogranuloma

Sarcoidosis

- Multisystem granulomatous disease characterized by non-caseating granulomas involving lungs and lymph nodes, heart, skin, eyes, liver, kidneys, muscles, joints, and brain
- Unclear etiology, but related to increased activity of cell-mediated immune system

Epidemiology

- Bimodal age distribution in women (25-35 and 45-65)
- Increased incidence in African Americans

Clinical Findings

- In 1/3 of pts; may be presenting symptom
- Non-scaly, skin colored to red-brown papules and plaque, may develop within pre-existing scar or within site of previous trauma, usually annular
- Distribution: symmetric face, lips, upper trunk, extremities
- Destructive presentation: hyperpigmentation, subcutaneous nodules, acquired ichthyosis
- Nail changes
- Clubbing, subungual hyperkeratosis, onycholysis

Variants of Sarcoidosis

- Darier-Roussy disease
- Papular, firm, multiple subcutaneous nodules without erythematous changes. Also known as sarcoid panniculitis
- Lupus pernio
- Papular nodules and plaques in nose most affected by cold stimuli, nose, cheek. Associated with lung involvement (50%) and upper respiratory involvement (20%)
- Ludger's panniculitis
- Acute sarcoidosis, erythema nodosum, hilar adenopathy, fever, migrating polyarthritis, and acne inaz
Histology of Sarcoid

- Superficial and deep dermal epithelioid cell granulomas devoid of prominent infiltrates of lymphocytes or plasma cells
- 10% have fibroblastic deposition
- Multinucleated histiocytes (giant cells) may contain eponymous stellate inclusions (asteroid bodies) or rounded laminated basophilic inclusions (Schaumann bodies)
- Non-caseating granulomas

Diagnosis of Sarcoidosis

- Diagnosis of exclusion
- Supporting clinical history and histologic evidence of non-caseating granulomas
- Radiologic findings
  - Bulbar paratracheal LAD, pulmonary infiltrates
- PFTs
  - Restrictive pattern
- Laboratory
  - ANA elevated in 30%
  - ACE elevated in 60%
- Anemia, eosinophilia, lymphopenia, elevated ESR, hypercalcemia

Treatment of Sarcoidosis

- Topical or intralesional corticosteroids
- Systemic manifestations
  - Oral prednisone for 4-6 weeks at 1mg/kg/day
- Cutaneous manifestations
  - Hydroxychloroquine or chloroquine, MTX

Granuloma Annulare

- Etiology
  - Trauma, insect bite reactions, tuberculin skin testing, sun exposure, PUVA therapy and viral infections
- Clinical presentation
  - Pink, violaceous, or flesh colored plaques composed of small papules forming arciform to annular plaques
  - Usually symmetric and acral distribution

Types of Granuloma Annulare

- Localized Ga
  - Pink to red nontender papules and plaques in annular formation
  - Located on the extremities
- Generalized
  - Small, skin-colored or pink-violaceous papules symmetrically distributed on trunk and extremities
  - Usually involves trunk and at least 1 extremity
- Subcutaneous Ga
  - “Pseudorheumatoid nodules”
  - Painless, firm, subcutaneous nodules
  - Most common in lower extremities
- Perforating Ga
  - Small, umbilicated papules with a central crust or hyperkeratotic core
  - May become pustular or ulcerated
- Patch Ga
  - Patch of erythema on extremities and trunk
  - Usually symmetric and macular
- Annular elastolytic giant cell granuloma (AEGCG)
  - Photoinduced subtype of Ga vs Ga appearing on sun-damaged skin
Diseases Associated with Granuloma Annulare

- DM
- Hyperlipidemia
- Thyroid disease
- Infectious agent
- Possible connections with Borrelia burgdorferi
- Tb related immune response that mimics GA
- Chronic Hep B
- Chronic Hep C
- HIV
- Paraneoplastic syndrome
- seen in solid-organ tumors, Hodgkin and non-Hodgkin lymphoma, leukemias
- Presentation atypical; painful lesions on palms and soles

Histology of Granuloma Annulare

- Focal degradation of fibrin and elastin fibers with deposition of mucin
- Two patterns of granulomatous inflammation
  - palisading
  - interstitial

Treatment of Granuloma Annulare

- Spontaneous resolution occurs within 2 years in 50% of pts, but 40% recur
- Intralesional or topical corticosteroids
- PUVA
- Cryotherapy
- CO2 Laser treatment
- Systemic agents may be used in severe cases
  - Oral Niacinamide
  - Immunosuppressants
  - Biologics
  - Malarials: hydroxychloroquine, chloroquine
  - TNF-alpha inhibitors: infliximab and adalimumab

Necrobiosis Lipoidica

- Clinical presentation
  - Yellow-brown, atrophic, telangiectatic plaques with an elevated violaceous rim, typically located in the pretibial region
  - Start as small, firm, red-brown papules, 9 central epidermal atrophy
  - Multiple and bilateral
  - Rarely, SCC develops in lesions of NLD
- Diabetes association
  - 30-40% of NLD have DM

Histology of Necrobiosis Lipoidica

- Layers of granulomatous inflammation in the dermis parallel to normal/atrophic epidermis, extending into subcutaneous fat without mucin deposition
- Palisaded and interstitial dermatitis with superficial or deep perivascular infiltrate

Treatment of Necrobiosis Lipoidica

- Treatment
  - High potency topical corticosteroid or intralesional injection into active border
  - ASA in combination with dipyridamole
  - Niacinamide
Metabolic and Depositional Diseases

- Amyloidosis
  - Systemic
  - Cutaneous
  - Mucinoses
    - Sclerosing and edema
    - Scleroderma
    - Reticular erythematosus mucinosis
- Porphyrias
- Familial hyperlipidemias
- Gout
- Pseudogout

Amyloidosis

- Several diseases sharing common feature of abnormal deposition of eosinophilic amyloid protein in various tissues
- Amyloid properties: insoluble fibril protein aggregates with β-pleated sheet configuration

2 Categories
- Cutaneous
- Systemic
  - Associated with increased morbidity and mortality

Types of Cutaneous Amyloidosis

- Macular
- Lichen
- Nodular
- Secondary

Macular Amyloidosis

- Keratinocyte derived
- Presents with hyperpigmented small firm papules in rippled appearance coalescing into thin plaques
  - Located on interscapular region of the back
  - Asymptomatic or moderately pruritic
  - +/- notalgia paresthetica
  - Treatment → Reduce friction, high potency topical corticosteroid, topical capsaicin
  - Seen in MEN type 2A syndrome

Lichen amyloidosis

- Keratinocyte derived
- Small flat-topped shiny papules, highly pruritic
- Located over shins
- Treatment → Reduce friction, high potency topical corticosteroid, phototherapy

Nodular amyloidosis

- AL (immunoglobulin light chains, typically λ)
- Single or multiple waxy nodules ± purpura on limbs/trunk
- May progress to systemic involvement (7% of cases)
- Treatment → Excision or laser ablation
Secondary amyloidosis

- Keratinocyte derived
- Amyloid deposits seen both in benign and malignant cutaneous tumors

Histology of Amyloidosis

- Lichen/Macular amyloidosis → deposits of eosinophilic, homogenous and amorphous material in papillary dermis with melanin incontinence
- Nodular amyloidosis → waxy eosinophilic fissured nodules involving dermis
- Characteristic staining pattern → Apple-Green Birefringence under Polarized Light with Congo Red stain
- Other stains → Methyl violet, Crystal violet, Periodic acid-Schiff (PAS) positive (diastase resistant), Sirius red, Pagoda red 9, Scarlet red, and Thioflavin T

Types of Systemic Amyloidosis

- Primary systemic amyloidosis
- Secondary systemic amyloidosis
- Hemodialysis-associated amyloidosis
- Familial amyloidosis
- Senile systemic amyloidosis

Primary Systemic Amyloidosis

- Amyloid immunoglobulin light chain (AL)
- Associated with underlying plasma cell dyscrasia
- Cutaneous clinical presentation:
  - Up to 50% with macroglossia
  - Ecchymosis and ‘pinch’ purpura
  - Waxy nodules and plaques
  - Bullae lesions (especially hemorrhagic)
- Non-cutaneous clinical presentation:
  - Hoarseness, carpal tunnel syndrome, RA-like arthropathy, shoulder pad sign, cardiac arrhythmia, heart failure, restrictive cardiomyopathy
- Abdominal fat pad aspiration to confirm amyloid deposits and establish diagnosis in absence of cutaneous findings

Secondary Systemic Amyloidosis

- Amyloid deposition in organs due to underlying chronic inflammatory or infectious process
  - Rheumatoid arthritis, tuberculosis, chronic abscess, and periodic fever syndromes, etc.
  - Non-immunoglobulin protein: amyloid associated (AA)

Hemodialysis-associated Amyloidosis

- Due to increased secretion of β2-microglobulin in patients with long-term hemodialysis
- Deposition of amyloid in synovial membranes
  - Results in carpal tunnel syndrome and spondyloarthropathy
Familial Amyloidosis

- Deposition of transthyretin-derived amyloid (ATTR) in peripheral and autonomic nervous system
- Transthyretin transports thyroid hormones and retinol
- Produced by the liver
- Slowly progressive disorder resulting in peripheral and autonomic neuropathy
- Treatment → Orthotopic liver transplantation

Senile Systemic Amyloidosis

- Late-onset disease seen in elderly patients
- Due to deposition of Transthyretin-derived amyloid (ATTR) fibrils in the heart
- Causes CHF and cardiomyopathy

Mucinoses

- Heterogenous group of skin disorders involving abnormal accumulation of mucin
- Mucin
  - Mixture of acid glycosaminoglycans normally produced in small amounts by fibroblasts
  - Special stains for mucin include alcian blue, colloidal iron, and toluidine blue
- 4 Types
  - Scleromyxedema, Lichen myxedematosus, Scleredema, Reticular erythematous mucinoses

Scleromyxedema

- Generalized symmetric eruption of several firm waxy papules accompanied by induration and thickening of the skin
- Located on hands, forearms, face ("leonine facies"), neck, thighs, and upper trunk
- Associated with IgG λ (lambda light chain) monoclonal gammopathy
- Poor prognosis
- Treatment → stem cell transplant, oral immunosuppressants (including thalidomide); monthly melphalan associated with increased mortality

Scleromyxedema

- 3 Forms:
  - Infection-related → Streptococcal
    - Self limited induration of cervicofacial area with extension to proximal extremities and trunk in women and children
  - Gammopathy-related
    - Insidious onset and similar presentation to above due to monoclonal gammopathy
  - Diabetes-related
    - Progressive erythema and induration of neck and back in obese men with IDDM
- Treatment (for latter 2 types) → UV therapy, ciclosporin, oral glucocorticoid, or cyclosporine

Lichen Myxedematosus

- AKA: Popular mucinosis
- Localized form of scleromyxedema with small shiny papules on extensor extremities
- Does NOT progress to scleromyxedema
- Shows little tendency for spontaneous resolution
- Treatment → Observation or topical corticosteroids

Scleredema

- 3 Forms:
  - Infection-related → Streptococcal
  - Self limited induration of cervicofacial area with extension to proximal extremities and trunk in women and children
  - Gammopathy-related
  - Insidious onset and similar presentation to above due to monoclonal gammopathy
  - Diabetes-related
  - Progressive erythema and induration of neck and back in obese men with IDDM
- Treatment (for latter 2 types) → UV therapy, ciclosporin, oral glucocorticoid, or cyclosporine
Reticular erythematous mucinosis

- Erythematous macules and papules in a reticulated pattern on midline chest and back
- Possibly induced by UV light
- Treatment → oral antimalarials and sun protection

Porphyria

- Inherited or acquired disorders due to enzyme deficiency causing increased production of porphyrins during heme synthesis
- Porphyrins absorb light intensely in the Soret band (400-410nm)
- Forms reactive oxygen species with subsequent damage to skin, liver, and/or erythrocytes

Porphyria Cutanea Tarda (PCT)

- Triggers:
  - Alcohol, Hepatitis C, Estrogen, Polychlorinated hydrocarbons, iron overload, HIV

Types of Porphyria

<table>
<thead>
<tr>
<th>Type</th>
<th>Defect</th>
<th>Description</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porphyrin Cutanea Tarda (PCT)</td>
<td>Uroporphyrinogen decarboxylase</td>
<td>Tense bullae, erosions, milia, scarring on sun-exposed skin; hypertrichosis, scleroderma-like changes, facial hyperpigmentation</td>
<td>Phlebotomy every 2 weeks, low-dose hydroxychloroquine</td>
</tr>
<tr>
<td>Congenital Erythropoietic Procaryotic Porphyria (CEP)</td>
<td>Uroporphyrinogen III cosynthase</td>
<td>Extreme photo-sensitivity, erythrodontia, red urine, hemolysis</td>
<td>Avoid light, transfusions for anemia, bone marrow transplant and splenectomy</td>
</tr>
<tr>
<td>Acute Intermittent Porphyria (AIP)</td>
<td>Porphobilinogen Deaminase</td>
<td>No skin findings: Neurologic and psychiatric findings</td>
<td>Remove trigger (barbiturates, alcohol, etc.), glucose loading, hematin infusion</td>
</tr>
<tr>
<td>Variegate Porphyria (VP)</td>
<td>Protoporphyrinogen oxidase</td>
<td>Overlap between AIP and PCT</td>
<td>Same as AIP</td>
</tr>
<tr>
<td>Hereditary Coproporphyria</td>
<td>Coproporphyrinogen oxidase</td>
<td>Mild version of AIP, may have PCT-like skin findings</td>
<td>Same as AIP</td>
</tr>
<tr>
<td>Hepatoerythropoietic Porphyria</td>
<td>Uroporphyrinogen decarboxylase</td>
<td>Overlap between PCT and CEP</td>
<td>Photoprotective only</td>
</tr>
</tbody>
</table>

Familial Hyperlipidemias

<table>
<thead>
<tr>
<th>Type</th>
<th>Defect</th>
<th>Lipid Abnormalities</th>
<th>Clinical Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>I- Familial Lipoprotein Lipase Deficiency</td>
<td>Lipoprotein lipase (LPL) or apoprotein CII defect</td>
<td>↓ LPL activity</td>
<td>Eruptive xanthomas, acute pancreatitis, lipemia retinalis</td>
</tr>
<tr>
<td>IIa- Familial Hypercholesterolemia</td>
<td>LDL receptor defect</td>
<td>↑ Cholesterol (LDL)</td>
<td>Tendinous and tuberosus xanthomas, xanthelasma</td>
</tr>
<tr>
<td>IIb- Familial Combined Hypercholesterolemia</td>
<td>LDL receptor defect</td>
<td>↑ Cholesterol, ↑ TG</td>
<td>Tendinous and tuberosus xanthomas, xanthelasma</td>
</tr>
<tr>
<td>III- Familial Dysbetalipoproteinemia</td>
<td>Apoprotein E defect</td>
<td>↑ Cholesterol, ↑ TG</td>
<td>Xanthoma Striatum Palmare, tuberous xanthomas</td>
</tr>
<tr>
<td>IV- Familial Hypertriglyceridemia</td>
<td>↑ Production of VLDL</td>
<td>↑ TG</td>
<td>Eruptive xanthomas, acne, xanthelasmas, lipemia retinalis</td>
</tr>
<tr>
<td>V- Familial Hypertriglyceridemia</td>
<td>Apoprotein C-2 defect</td>
<td>↑ TG, ↑ Cholesterol</td>
<td>Eruptive xanthomas, xanthelasmas, lipemia retinalis</td>
</tr>
</tbody>
</table>

Types of Xanthomas

- Eruptive Xanthomas
- Xanthelasmas
- Xanthoma Striatum Palmare

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I, IV, V</td>
<td>Type II, III</td>
</tr>
</tbody>
</table>
Gout

- Recurrent attacks of acute inflammatory arthritis
- Due to hyperuricemia leading to deposition of needle-like monosodium urate crystals in skin and joints
- Presents with firm, skin-colored white-yellow papules or nodules (tophi) that may ulcerate and drain chalky material
- Negative birefringence under polarized light

Treatment
- Acute attacks: Indomethacin, Colchicine

Pseudogout

- Deposits of calcium pyrophosphate dihydrate crystals in joints
- Crystals appear shorter than urate crystals and are rhomboidal in shape
- Weakly positive birefringence under polarized light

References


7. Photos courtesy of Dr. Gary White and Regional Dermatology; Jere Mammino DO; DermNet New Zealand. http://creativecommons.org/licenses/by-nc-nd/3.0/nz/; Mayo Foundation for Medical Education and Research; Dr. Jan R. Mekkes. DermatoloogAMC Amsterdam, JAMA. Plastic Surgery Key: Disorders of the Subcutis; Atlas of Pathology
Objectives

1. Tumors of Fat
2. Tumors of Smooth Muscle
3. Tumors of Skeletal muscle
4. Histiocytic Neoplasms
5. Tumors of Bone
6. Appendageal tumors
7. Neural tumors
8. Fibrohistiocytic Tumors

Benign Tumors of Fat: Lipoma

- Epidemiology
  - Most common benign tumor of fat
  - Any age, more common during or after puberty
- Clinical Presentation
  - Asymptomatic, soft, subcutaneous nodule
- Associated with
  - Bannayan-Riley-Ruvalcaba
  - Gardner’s syndrome
  - Proteus syndrome
  - MEN1
  - Familial multiple lipomatosis
  - Deiters’ disease
  - Madelung’s disease
  - CLOVE syndrome
- Treatment
  - Observation or Excision

Angiolipoma

- Epidemiology
  - Lipoma variant
  - Clinically indistinguishable except they tend to be painful, greater tendency to be multiple
  - Primarily in teenagers and young adults
- Clinical Presentation
  - Commonly present on upper extremities and trunk
- Treatment
  - Excision
Angiolipoma

Epidemiology
• Majority found in middle-aged to older men

Clinical Presentation
• Usually presents as a solitary, slow growing, mobile, painless subcutaneous nodule without epidermal change
• Upper back and posterior neck

Treatment
• Excision

Spindle Cell Lipoma

Spindle cell lipoma
Spindle cell lipoma, Myxoid lipoma, Pleomorphic lipoma - Floret cells

- Spindle cell, myxoid & pleomorphic lipoma - exist as a morphologic continuum

Hibernoma

- Epidemiology
  - Rare, benign tumor that is derived from brown fat
  - Young adults in their twenties and thirties
- Clinical Presentation
  - Interscapular area, thighs, shoulder, neck, chest, arm and abdominal cavity, retroperitoneum
  - Hibernomas are slow-growing tumors located in the subcutis or, occasionally, within skeletal muscle
- Treatment
  - Surgical resection is curative
  - May be difficult to excise as they often are in close proximity to neurovascular structures

- Monosomy or partial loss of chromosomes 13 and 16 are the most common alterations seen in spindle cell, pleomorphic and myxoid lipoma
Nevus Lipomatosus Superficialis

Epidemiology
- Rare hamartoma develops shortly after birth or during the first two decades of life

• Treatment
- Excision

Clinical Presentation
- Grouped, soft papulonodules
- Most commonly located on the buttocks or upper thighs

Malignant Tumors of Fat

- Well differentiated Liposarcoma/Atypical Lipomatous tumor
- Myxoid Liposarcoma
- Round cell Liposarcoma
- Dedifferentiated Liposarcoma

• They are very rare in kids and very rare in the skin
• They are mostly deep seated tumors in the subcutaneous locations (the most common location being in the retro peritoneum)
• Very rarely encountered in a dermatology
• For boards need to remember the translocation encountered in Myxoid Liposarcoma \( t(12;16)(EWSR1;DDIT3) \)

Leiomyomas

Epidemiology
- Benign tumors derived from cutaneous smooth muscle
- Majority of these lesions arise from arrector pili muscles, the media of blood vessels

• Clinical Presentation
  - Solitary or multiple
  - Pink, red, or dusky brown, firm dermal nodules of varying size
  - Subject to episodes of paroxysmal spontaneous pain
  - Common locations include back, face, extensor surfaces of the extremities and usually arranged in groups

• Multiple leiomyomas may be associated with Birt-Hogg-Dube syndrome and hereditary leiomyomatosis and renal cell cancer syndrome
- Autosomal dominant mutation in fumarate hydratase

• Treatment
- Excision

Pilar leiomyoma

Cross sections with nodular, nodular and verrucous

Longitudinal section with "papillomatous" growth pattern
HLRCC (Hereditary leiomyomatosis renal cell carcinoma syndrome)

- Multiple cutaneous & uterine leiomyomas
- Renal cell carcinoma (papillary or collecting duct renal cell carcinoma)
- Autosomal dominant disorder
- Loss of function of tumor suppressor gene - Fumarate hydratase (FH)(1q42.3~q43), resulting in fumarate hydratase deficiency

Leiomyosarcoma

Epidemiology
- Rare soft-tissue sarcoma, occurs primarily in adults, more common in females
- Soft-tissue (Cutaneous) leiomyosarcomas are limited to the dermis
  - Solitary, usually not metastasize
  - Subcutaneous leiomyosarcoma that primarily arise in or extensively involve the subcutis
  - Metastasize in approximately 25-40% of cases, with a mortality rate of between 30%-50%

Clinical Presentation
- Solitary, deeply seated, firm nodules, with variable associated erythema and hyperpigmentation
- Can arise anywhere on the body, more common on the extensor surfaces of the extremities

Prognostic Factors in Leiomyosarcoma

- Treatment
  - Wide excision with meticulous examination of all surgical margins
- Tumor size >5 cm
- Are associated with aggressiveness

Rhabdomyosarcoma

Epidemiology
- Rhabdomyosarcoma is the most common soft-tissue sarcoma in children and adolescents
- Usually arise from the deep soft tissues, dermal origin is rare
- Multiple soft-tissue neoplasm of skeletal muscle origin
- 3 histological types: Alveolar, Embryonal and Pleomorphic
- Alveolar most common type in the skin
- Tends to display aggressive behavior in both adults and children

Clinical Presentation
- Presents as an asymptomatic mass on the head and neck, especially the nasal cavity and paranasal sinuses
- As the tumor grows, pain and swelling become the most common symptoms

Treatment
- Surgery, radiotherapy, and chemotherapy

Alveolar Rhabdomyosarcoma

T (2;13) resulting in PAX3-FKHR fusion is see in Alveolar Rhabdomyosarcoma
Benign Bone Tumors: Bone-forming tumors

Osteoid Osteoma and Osteoblastoma

- **Osteoid Osteoma**
  - **Clinical Presentation**
    - Smaller lesions that occur in the cortex of long bones
    - Presents with nocturnal pain
    - Multiple seen in **Gardner Syndrome**
  - **Treatment**
    - NSAIDs for pain relief
    - Excision; do not tend to recur

- **Osteoblastoma**
  - **Clinical Presentation**
    - Bigger lesions; most frequently in the axial skeleton
    - Pain but not worse at night
  - **Treatment**
    - Higher rate of recurrence

- **Epidemiology**
  - Both tumors are typically seen in the second decade of life
  - More common in males
  - Pathology
    - Resemble each other, with increased osteoid tissue formation surrounded by vascular fibrous stroma and periosteal sclerosis

Malignant Tumors of Bone

Osteosarcoma

- **Epidemiology**
  - Most common malignant tumors of bone in pediatric population
  - Second most common is Ewing’s sarcoma
  - Associated dermatologic disorders
    - Rothmund-Thomson syndrome (AR, RECQL4, photosensitive genodermatosis, poikiloderma, hypohidrotic erythroderma)
    - Li-Fraumeni syndrome (AR, TP53 mutation, multiple malignancies)
    - Bloom syndrome (AR, RECQL2, RECQL3, photosensitive, decreased IgG)
  - Neurophilic eccrine hidradenitis

Histiocytic Neoplasms

Langerhans Cell- Derived

- Langerhans Cell Histiocytosis/Histiocytosis X
- Congenital Self Healing Retiformhistiocytosis/CSHR (Hashimoto Pritzker disease)

Non-Langerhans Cell Histiocytosis/ Histocytic Neoplasms

- JXG/Xanthogranuloma
- Clinical & Histologic variants of JXG.

Langerhans Cell Histiocytosis

- **Epidemiology**
  - Can occur at any age
  - Peak incidence between 1 and 4 years of age
- **Clinical Presentation**
  - Eosinophilic granuloma (Localized bone disease)
  - Hand-Schuller-Christian disease (Skull lesions, exophthalmos, diabetes insipidus)
  - Letterer-Siwe disease (Acute or subacute disseminated form)
- **Treatment**
  - Depends on the extent of the disease
  - Topical treatments for localized disease
  - Systemic treatment uncommon
  - Chemotherapy (Vincristine or topotecan)
IHC

- Langerhans histiocytes are:
  - CD1a++
  - S100+
  - Langerin+ (CD 207)

**Epidemiology**
- Common form of non-LCH
- Benign, self-limited disease of infants, children, and sometimes adults
- Systemic involvement is very rare

**Clinical Presentation**
- Firm, round papule or nodule of varying size
- Early lesions are erythematous to orange or tan
- Mature lesions are yellow in color
- Most often solitary, can be multiple
- Head, neck, and trunk are the most common location
- Eye is the most common extracutaneous organ involved (iris is the site most often involved)
- Potential complications: hyphema, glaucoma, blindness
- Need ophthalmology referral

**Treatment**
- No treatment necessary for solitary lesions
- Systemic disease treated with chemotherapy similar to LCH

---

**Juvenile Xanthogranuloma**

- Important association
  - Juvenile chronic myelogenous leukemia (JCML)
  - Neurofibromatosis type 1

- New ophthalmology referral

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**Juvenile Xanthogranuloma**
Other “Non-Langerhans Cell” Histiocytic Neoplasms (Clinical & Histologic Variants Of JXG/XG)

- Spindle cell Xanthogranuloma
- Progressive Nodular Histiocytosis
- Generalized Eruptive Histiocytoma
- Benign Cephalic Histiocytosis
- Papular Xanthoma
- Xanthoma Disseminatum
- Scalloped Cell Xanthogranuloma

Epidermal Nevus

- Epidemiology
  - Benign congenital lesions characterized by hyperplasia of epidermal structures
  - Usually present at birth
  - Affects both sexes equally
- Clinical Presentation
  - Often favor the extremities, but may occur anywhere
  - Blanche's distribution: linear on extremities, arcuate on trunk
- Treatment
  - Challenging; Superficial destructive therapies lead to high recurrence rate
  - Cryotherapy, dermabrasion, electrodesiccation, CO2 laser ablation
  - Topical therapies have variable results
  - Retinoids, 5-FU, steroids
  - Full-thickness surgical excision are effective for smaller, localized lesions

Epidermal Nevus Syndromes

- 5 well-defined epidermal nevus syndromes:
  - Schimmpenning syndrome
  - Nevus comedonicus syndrome
  - Pigmented hairy epidermal nevus syndrome
  - Proteus Syndrome
  - CHILD
- Biopsy should be performed to check for Epidermolytic Hyperkeratosis (EHK)
  - These patients can transmit these mutations to offspring
- Extracutaneous abnormalities seen in patients with ENS include:
  - Seizures, Mental retardation, Hemiparesis
  - Cranial nerve palsies, Developmental Delay
  - Kyphosis/Scoliosis, Limp hypertrophy
  - Macrocephaly, Colobomas
  - Corneal/Retinal changes, Cataracts
  - Cardiac and GU defects
Epidermolytic Hyperkeratosis

- Epidemiology:
  - Unique variant of epidermal nevus
  - Often present at birth or appear during early childhood
- Clinical Presentation:
  - Most often on an extremity
  - Presents as erythematous, pruritic, scaly, verrucous papules that coalesce into linear plaques

Inflammatory Linear Verrucous Epidermal Nevus

- Epidemiology:
  - Unique variant of epidermal nevus
  - Often present at birth or appear during early childhood
- Clinical Presentation:
  - Most often on an extremity
  - Presents as erythematous, pruritic, scaly, verrucous papules that coalesce into linear plaques
- Treatment:
  - Topical or intralesional steroids may help with pruritus and reduce inflammation
  - Similar to epidermal nevus treatments

Nevus Sebaceous of Jadasson

- Epidemiology:
  - Common congenital lesion accruing mainly on face and scalp
  - Generally present at birth, but may be noted during early childhood or rarely adult life
- Clinical Presentation:
  - Well-circumscribed, hairless, yellow-orange to tan plaque
  - Multiple nevi sebaceous may occur in association with Schimmelpenning syndrome
- Treatment:
  - Surgical excision has been recommended traditionally out of concern for development of secondary neoplasms
  - Most common secondary benign neoplasm is SPAP
  - The most common secondary malignant neoplasm is BCC
  - Most of them are probably trichoblastomas
  - Apocrine glands are not normally found in the scalp; but occur in a “nevus sebaceous” as the lesion matures.
Tumors of the Epidermal Appendages

Trichofolliculoma

- **Epidemiology**
  - Benign appendageal neoplasm of hair follicle derivation
  - Usually occurs as a solitary lesion on head and neck of adults, but may occur during childhood
- **Clinical Presentation**
  - 2-10mm, slow-growing, flesh-colored papule or nodule with a smooth surface
  - Often a central pore with a protruding tuft of hair
- **Treatment**
  - Surgical excision

Pilomatricoma

- **Epidemiology**
  - Benign tumor derived from hair matrix
  - Usually present as a solitary lesion on the face, neck, upper trunk, or upper extremities
  - Usually develops within first two decades of life

- **Clinical Presentation**
  - Flesh-colored to white, firm papules or papulonodules
  - May have overlying pink to blue hue
  - Generally very hard, due to calcifications

- **Multiple pilomatricomas** have been noted in patients
  - Myotonic Dystrophy
  - Gardner syndrome
  - Rubinstein-Taybi syndrome
  - Trisomy 9

Trichoepithelioma

- **Epidemiology**
  - Occur as solitary non-hereditary tumor seen in early adult life or occasionally during childhood
  - Multiple small lesions occurring primarily on the face inherited in an autosomal dominant fashion
  - Begin during early childhood or several pterygium as small, firm, flesh-colored papules
  - Other associations include
    - Rombo- (Trichoeps + BCCs, milia, neuroepithelioma, hypotrichosis)
    - Rambam- (Trichoeps + cylindromas + milia)
- **Clinical Presentation**
  - Distributed mainly on the face, nose, nasolabial folds, forehead, upper lip, syphain and occasionally scalp
- **Treatment**
  - Can be difficult when multiple lesions are present
  - Single lesions can be treated with surgical excision, EMD, or laser therapy
Trichoepithelioma

Epidemiology
- Benign appendageal neoplasm derived from hair follicle
- Predominantly occur in adults, can be seen in kids
- Equally common in males and females

Clinical Presentation
- Can be solitary or multiple flesh-colored papules, occasionally with verrucous surface
- Most common on head and neck
- Multiple trichoepitheliomas may be seen in the setting of Multiple Hamartoma syndrome or Cowden disease

Treatment
- Can be difficult when multiple
- Single lesions can be surgically excised

Trichilemmoma / Trichilemmal verruca

Epidemiology
- Benign appendageal neoplasm derived from hair follicle
- Predominantly occur in adults, can be seen in kids
- Equally common in males and females

Clinical Presentation
- Can be solitary or multiple flesh-colored papules, occasionally with verrucous surface
- Most common on head and neck
- Multiple trichilemmomas may be seen in the setting of Multiple Hamartoma syndrome or Cowden disease

Treatment
- Can be difficult when multiple
- Single lesions can be surgically excised

Multiple Hamartoma Syndrome (Cowden disease)

- AD
- Characterized by hamartomas of multiple organ systems
- Mucocutaneous lesions include trichilemmomas, palmoplantar keratoses, oral papillomatosis, sclerotic fibromas
- Extracutaneous manifestations include fibrocystic breast disease, breast fibroadenomas, thyroid adenomas, meningiomas, and intestinal polyposis
- Increased risk of breast cancer, endometrial cancer, cancer of GI tract and thyroid gland

Syringoma

Epidemiology
- Can occur at any age, but frequently present initially during puberty
- Seen in increased frequency in patients with Down Syndrome

Clinical Presentation
- Benign tumors of eccrine glands
- May occur as isolated or multiple lesions
- Small, firm, flesh-colored to yellow, translucent papules
- Most common location is the eyelids, but can be seen on neck, torso, extremities and genitalia

Treatment
- Can be difficult for multiple lesion
- Cryosurgery, desiccation, CO2 lasers have all been used
Cylindroma

- **Clinical Presentation**
  - Also known as turban tumors
  - Benign tumor of either eccrine or apocrine glands
  - Firm, rubbery, pink to bluish plaques or nodules
  - Locally priornly on the scalp, occasionally on the face, trunk, or extremities
  - Multiple lesions may occur as part of Broek-Spiegler Syndrome (CYLD gene mutation, 16q12-13)

- **Treatment**
  - Surgical excision, although CO2 laser surgery been used with some success

Angiofibroma

- **Epidemiology**
  - May occur as isolated or multiple lesions
  - Multiple facial angiofibromas are commonly seen in patients with tuberous sclerosis, MEN type 1, and Birt-Hogg-Dube syndrome

- **Clinical Presentation**
  - Clinical subtypes include fibrous papules, pearly penile papules and periungual fibromas
  - Angiofibromas present as flesh-colored papules
  - Periungual fibromas present as flesh-colored filiform growths of proximal nail fold - multiple lesions are pathognomonic for tuberous sclerosis

- **Treatment**
  - Solitary lesions can be treated with shave excision or electrocautery
  - Pearly penile papules do not require treatment
  - Multiple lesions of Tuberous Sclerosis can be treated with Rapamycin (Sirolimus)-an mTOR inhibitor

Neurofibroma

- **Epidemiology**
  - Sporadic in healthy individuals
  - Common marker of Neurofibromatosis type 1
  - Neurofibromas are benign tumors composed of neurogenous tissue, including Schwann cells, endothelial and perineurial cells
  - Often present during young adulthood or childhood

- **Clinical Presentation**
  - Soft, flesh-colored papules or papulonodule
  - Exhibit a positive "buttonhole" sign

- **Treatment**
  - Excision can be used
  - Electrocautery for smaller lesions
  - Can be difficult when multiple

When multiple neurofibromas are present, the diagnosis of NF1 must be considered
- Plexiform neurofibroma present as a large, lobulated nodular plaque, may have a "bag of worms" consistency on palpation
- Pathognomonic for NF1

- **Treatment**
  - Excision can be used
  - Electrocautery for smaller lesions
  - Can be difficult when multiple
Malignant Peripheral Nerve Sheath Tumor

- Malignant counterpart of neurofibroma
- Rare cutaneous tumor
- Mostly seen in patients with Neurofibromatosis type 1, developing in a preexisting Neurofibroma

Dermatofibroma (fibrous histiocytoma)

- Epidemiology
  - Benign neoplasm of connective tissue
  - Only occasionally seen in children
- Clinical Presentation
  - Small, well-defined dermal nodule
  - Tan to brown color
  - Can be found anywhere
  - Most common on extremities
  - "Dimple sign" useful diagnostic feature
- Treatment
  - No treatment is necessary
  - Can be excised

Dermatofibroma

Inclusion Body Fibromatosis/Infantile digital fibroma

- Epidemiology
  - Infants under 1 year of age
  - Boys and girls are equally affected
- Clinical Presentation
  - Firm, smooth, skin-colored, dome-shaped nodules on the dorsolateral aspects of the fingers and toes
- Treatment
  - Spontaneous regression within 2–3 years is the usual natural history
  - Conservative observation, if small, to wide local excision if large or compromises function
  - High local recurrence rates
Fibrous Hemartoma of Infancy

- Epidemiology
  - Rare, benign soft tissue tumor
  - Usually presents before 2 years of age
  - More common in boys
- Clinical Presentation
  - Most common locations are upper trunk, axillae, upper extremities
  - Painless, flesh-colored subcutaneous nodule or plaque
  - Most cases are solitary
  - Slow growing
- Treatment
  - Full surgical excision

Dermatofibrosarcoma Protubersans

- Epidemiology
  - Seen mostly in adults (second and fifth decade)
  - Pediatric and even congenital cases are rarely seen
- Clinical Presentation
  - Erythematous to blue papules and nodules
  - Increase in size and become multinodular and protuberant
  - Some lesions present as atrophic plaques
  - Trunk and proximal extremities are most common locations
- Pathology
  - Chromosomal translocation t(17;22) COL1A1 and PDGFB genes
- Treatment
  - Complete excision
  - MMS has been used in both pediatric and adult cases
  - Radiation and Imatinib have been used if clear margins could not be abstained
References


<table>
<thead>
<tr>
<th>Time</th>
<th>Primary Pathway (Salon I/II)</th>
<th>Resident Pathway (Plaza Ballroom)</th>
</tr>
</thead>
</table>
| 7:00 a.m. - 8:00 a.m. | Valeant Product Theater: *Contemporary Insights into the Treatment of Female Acne*  
*James Del Rosso, DO, FAOCD*  
*Held in Plaza Ballroom*  
(No CME Awarded) |                                                                                       |
| 8:00 a.m. - 9:00 a.m. | *Contemporary Ethical Controversies in Dermatology*  
*Ben Stoff, MD* |                                                                                       |
| 9:00 a.m. - 10:00 a.m. | *Look-Alikes, Controversies and What's New in Pediatric Dermatology*  
*Leslie Potter Lawley, MD* | *Resident Dermatopathology Lecture*  
*David Barron, MD* |
| 10:00 a.m. - 10:30 a.m. | Break with Exhibitors |                                                                                       |
| 10:30 a.m. - 11:30 a.m. | *International Volunteerism in Dermatology: Short-Term Travel, Long-Term Impact*  
*Ben Stoff, MD* |                                                                                       |
| 11:30 a.m. - 12:30 p.m. | *Clues in Contact Dermatitis*  
*Salma Faghri de la Feld, MD* |                                                                                       |
| 12:30 p.m. - 1:30 p.m. | Pfizer Product Theater: *Introducing a New Nonsteroidal Topical Prescription Treatment Option for Mild-to-Moderate Atopic Dermatitis*  
*G. Scott Drew, DO, FAOCD*  
*Held in Plaza Ballroom*  
(No CME Awarded) |                                                                                       |
| 1:30 p.m. - 2:00 p.m. | Break with Exhibitors |                                                                                       |
| 2:00 p.m. - 3:00 p.m. | *Bullous Disease as a Window Into the Body*  
*Ron Feldman, MD* |                                                                                       |
| 3:00 p.m. - 4:00 p.m. | *Don't Sweat It: Treatments for Hyperhidrosis*  
*Zakiya Rice, MD* |                                                                                       |
| 4:00 p.m. - 5:00 p.m. | *So Many Drugs, So Little Time*  
*James Q. Del Rosso, DO, FAOCD* |                                                                                       |
Saturday, April 1, 2017
Primary Pathway
AUTOIMMUNE BLISTERING DISEASES; WINDOW TO SYSTEMIC DISEASE

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Emory University
ron.j.feldman@emory.edu

Disclosures
- I have no conflict of interest to declare
- I will be talking about off-label use of medications

Learning Objectives
- To define mechanisms of autoimmune blistering diseases (AIBD)
- To understand that bullous diseases can provide insight into systemic disease
- To review treatments for both bullous diseases and related systemic diseases

Autoimmune Blistering Diseases

**Epidermal**
- Pemphigus foliaceus
  - Endemic
  - P. Erythematosus
  - IgA Pemphigus
  - P. Herpetiformis
- Pemphigus vulgaris
  - P. Vegetans
- Paraneoplastic Pemphigus

**Subepidermal**
- Bullous pemphigoid
- Mucous membrane pemphigoid
- Epidermolysis bullosa acquisita
- Bullous systemic lupus
- Linear IgA disease
- Pemphigoid gestationis
- Dermatitis herpetiformis
- Lichen planus pemphigoides
- p200/Laminin γ1-pemphigoid

Adhesion Molecules in the Skin

Schmidt E and Zillikens D, Dtsch Arztebl Int, 2011

Epidermal Blistering Disease
- Epidermis
- Dermis

Subepidermal Blistering Disease
- Epidermis
- Dermis
Indirect Immunofluorescence/ELISA

Schmidt and Zillikens, The Diagnosis and Treatment of Autoimmune Blistering Diseases, Dtsch Arztebl Int 2011; 108(23): 399–405.

Pemphigus

Hertl M, Journal of Clinical Investigation, 2006

Pemphigus Foliaceus

Pemphigus Vulgaris

Direct Immunofluorescence—Intercellular IgG (IgA), C3

Pemphigus Vulgaris

Pemphigus

Pemphigus Foliaceus

Pemphigus Vulgaris

Tissue Bound Antibodies Loss of Cellular Adhesion
Efficacy of Rituximab Therapy in Pemphigus

- Meta-analysis from 30 studies; 578 patients
- Complete Remission (CR) rates after one cycle: 76%
- Mean time to CR 5.8 months
- CR duration 14.5 months
- Relapse rate 40%
- Major adverse events: 3.3%

Wang HH et al, Acta Derm Venereol 2015

Bullous Pemphigoid

Role of IgE in Bullous Pemphigoid?

Role for IgE Directed Therapies- Omalizumab?

Ujle H. J of Dermatological Science. 2015

Schmidt E, Zillikens D. Lancet 2013

Mucous Membrane Pemphigoid
Mucous Membrane Pemphigoid +/- Ocular Cicatricial Pemphigoid

Linear IgG (IgA/IgM)/C3 at Basement Membrane Zone

Subepidermal Blistering Diseases

Development of Autoimmunity

Genetic Susceptibility

Biologic Therapies

Tomaselli E et al, Front Immunology, 2014

Pathways to Peripheral Tolerance

Activated T Cell
Indifferent T Cell
Dead T Cell
Sleeping T Cell
Suppressed T Cell

Genetic Susceptibility for Autoimmune Diseases

Survey based registry: 61/393 (15.5%)
Patients with Pemphigus

<table>
<thead>
<tr>
<th>Disease</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid Disease</td>
<td>55</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>24.6%</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>13.1</td>
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<tr>
<td>Diabetes Type 1</td>
<td>8.2</td>
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<tr>
<td>Ulcerative colitis</td>
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<tr>
<td>Vitiligo</td>
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<tr>
<td>Alopecia areata</td>
<td>1.6</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>1.6</td>
</tr>
</tbody>
</table>


Prevalence of Autoimmunity

- 295 pemphigus patients
- Comparing to age-standardized prevalence ratios (SPRs) in Canadian general population
  - Higher prevalence in pemphigus group
    - Thyroid disease: 1.53 (1.08-2.10)
    - Diabetes: 2.20 (1.64-2.87)
    - Inflammatory Bowel Disease: 1.48 (0.4-3.80)
  - Lower prevalence in pemphigus group
    - Rheumatoid arthritis: 0.74 (0.36-1.36)

Heelan K et al, Clin, Exp Dermatology 2015
Coexistence of AIBD and Psoriasis

- Retrospective cohort of 145 cases in Japan
- BP Laminin γ1
- Psoriasis vulgaris 122 80 43
- Pustular psoriasis 13 5 8
- Psoriatic erythroderma 7 4 3
- Psoriatic arthritis 3 3 0

Ohata C et al, JAAD 2015

Bullous Pemphigoid

- Data from National Inpatient Sample, 2002-2012 (~72 million adults)
- Commonly associated autoimmune diseases (Odds ratios/OR)
  - Cushing syndrome: 10.72 (1.5-76.73)
  - Hidradenitis suppurativa: 6.76 (1.68-27.17)
  - Systemic lupus erythematosus: 8.68 (4.77-15.79)
  - Multiple sclerosis: 4.07 (3.22-5.14)
  - Rheumatoid arthritis: 1.26 (1.12-1.42)
  - Hypothyroid: 1.21 (1.13-1.30)

Ren Z et al, British Journal of Dermatology, 2017

Autoimmune Phenomenon

Targeted Biologic Therapies:
- Checkpoint Inhibitors Targeting PD-1 and PD-L1
  - Bullous pemphigoid
  - Following Rituximab Therapy for Pemphigus
  - Psoriasis
  - Sarcoid
  - Multiple Sclerosis*

Guidelli G, Rheumatol Int 2013
Nadoo J et al, Cancer Immunology Research 2016
*Unpublished observations

Skin Windows

“Bullous Window to Systemic Disease”


Case History

- 66 year old male presented with worsening skin rash and oral erosions
  - History of chronic lymphocytic leukemia in 2008
  - Treated with fludarabine, cyclophosphamide and rituximab
  - Remission until Spring 2013
  - Developed axillary lymphadenopathy along with diffuse erythematous rash with areas of blistering
  - Retreated with rituximab in June 2013
  - Oral erosions with severe lip involvement; admitted for possible Steven’s Johnson syndrome
  - Skin biopsies inconclusive
  - Treated with tapering courses of systemic corticosteroids

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Paraneoplastic Pemphigus (PNP)
- Pemphigus in setting of malignancy:
  - NHL, CLL, Castleman disease, Thymoma, Retroperitoneal sarcomas
  - Painful mucosal erosions with refractive mucositis
  - Polymorphous skin eruptions
    - Blistering
    - Urticaria
    - Erythema multiforme
    - Lichen planus
  - Cicatrizng conjunctivitis
  - “Paraneoplastic autoimmune multiorgan syndrome”
- Confirm by histology—immunofluorescence


Can Look like both pemphigus and pemphigoid!

Paraneoplastic Pemphigus
- Pulmonary involvement later in course of disease in ~30% of patients
  - Respiratory failure
  - Features of bronchiolitis obliterans
  - Functional obstructive or restrictive bronchiolitis
  - Mostly irreversible
- Link with Pemphigus??


Respiratory Epithelium in PNP
- Loss of Cellular Adhesion, Similar to pemphigus
- Autoantibodies Deposited by immunofluorescence

Nousari HC, et al, NEJM, 1999

Increased Desmoglein 3 in areas of Squamous Metaplasia!

Nousari HC, et al, NEJM, 1999

Hata T, et al, J Immunology, 2013
Bullous Window to Systemic Disease

- Increased skin injury from autoantibodies
- Induction of various cytokines—Interleukin-22?
- Downstream effects on respiratory epithelium—Squamous metaplasia?
- Induction of ectopic expression of Desmoglein 3 in respiratory epithelium
- Humoral attack—similar to classic pemphigus
- Respiratory failure

Case History

- 44 year old African American male
- Referred for worsening blisters mostly on extremities
- Diagnosed with Crohn’s disease shortly before blistering began
- Previously treated with courses of prednisone and sulfasalazine

Linear IgG/C3 at Basement Membrane

Subepidermal Blistering Diseases

Epidermolysis bullosa acquisita

- Autoantibodies bind to collagen VII in the dermis
- Potential for scarring
- Link with Inflammatory Bowel Disease?

Kim JH, JEADV 2012
Type VII Collagen is Present in Skin and Colon

Serum autoantibodies to type VII collagen

Bullous Window to Systemic Disease

- Tissue injury, inflammation in skin or gastrointestinal tract, exposing epitopes on collagen VII
- Development of cross reactive antibodies?
- Exposure of other antigens during inflammation, development of other AIBD
- Bullous pemphigoid—CD/UC
- Linear IgA disease—UC
- Dermatitis herpetiformis—Celiac disease
- EBA most commonly associated with CD
- Inflammatory bowel disease tends to precede AIBD

Case History

- 40 year old female
- 5 years post kidney/pancreas transplant for diabetes
- On prednisone and mycophenolate
- Attempted to wean down mycophenolate
- Creatinine levels increased to 3.3
- Developed widespread pruritic rash
- Subsequently developed tense blisters

Linear IgG/C3 at Basement Membrane Zone

Serum ELISA
Elevated anti-BP180 antibodies (BPAG2/Collagen XVII)
Bullous Window to Systemic Disease

- Bullous pemphigoid in the setting of renal allograft failure?
- Usually with reduction in dose of immunsuppression
- Injury to glomerular basement membrane, epitope spreading?
- Common antigen between glomerular basement membrane zone and cutaneous? Collagen XVII, IV?

Cavaliere G et al, Eur J Dermatol 2014

Antibodies against Type IV Collagen: Skin and Renal Glomerulus

Case History

- 74 year old Caucasian female
- Diagnosed with Lewy Body Dementia in 2011
- Developed worsening pruritus in 2013
- Treated with antihistamines and topical steroids
- Developed gingival erosions and blisters on lower extremities
- Biopsied by oral surgery— inconclusive
- Seen by dermatology in 2014— widespread erosions on gingiva and across her abdomen and back

Skin Kidney

Ghohestani RF, et al, Lab Invest 2003

Linear IgG/C3 at Basement Membrane Zone

Tissue Bound Antibodies Loss of Cellular Adhesion

- Bullous pemphigoid
- Bullous pemphigoid disease area index (BPDAI)
  - Cutaneous: 34/120
  - Oral: 16/120
- Age of onset >70 years
- Disease relationship with underlying dementia??

Case History
Bullous Pemphigoid

- Data from National Inpatient Sample, 2002-2012 (~72 million adults, cont)
  - Neuropsychiatric disorders!
    - Demyelinating disorders: 3.57 (1.48-8.61)
    - Presenile Dementias: 2.63 (1.34-5.18)
    - Parkinson’s disease: 1.86 (1.65-2.10)
    - Epilepsy: 1.67 (1.41-1.98)
    - Other neurological disorders: 1.98 (1.86-2.11)

Ren Z et al, British Journal of Dermatology, 2017

Neuropsychiatric disorders!

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Ren Z et al, British Journal of Dermatology, 2017

Bullous Pemphigoid

- Significant increase in odds of developing BP in people with neurological diseases diagnosed more than 12 months previously
  - Dementia and Parkinson’s—3 fold increase
  - Stroke and Epilepsy—2 fold increase
  - Neurological disease precedes the BP
  - Patients with Parkinson’s have circulating autoantibodies to collagen XVII and localize to neurons

Laffitte E, et al, Br Journal of Dermatology, 2004

BPAG1 in the Central Nervous System?

- Knockout mice for BPAG1/BP230
  - Develop skin fragility as expected
  - Dystonia, ataxia?
  - Severe neurodegeneration and myelin abnormalities in CNS and peripheral nervous system?

Guo L et al, Cell 1995

Expression of BPAG1 (BP230)

- Brain, Spinal Cord
- Striated muscle, bone cartilage
- Epidermis

"Dystonin" peripheral sensory neurons, motor neurons, oligodendrocytes, Schwann cells

*BPAG2/Collagen XVII is also expressed in the Brain

Bousquet O and Coulombe P, Current Biology 1996

BP patients with neurological diseases recognize BPAG 1 protein in the brain

- Serum samples from BP and neurological diseases (BPND) compared with serum from BP without neurologic disease (BP)
  - Recognized BPAG1—epidermal extracts:
    - 72% BP/ND vs 50% BP
  - Recognized BPAG1—brain extracts:
    - 55% BP/ND vs 9% BP

Chen J et al, Gerontology, 2011

Bullous Window to Systemic Disease

- Neurological disorders cause damage to blood brain barrier?
- Loss of immune privilege—inappropriate exposure of brain antigens—BPAG1 or BPAG2?
- Develop cross reactive autoantibodies to skin??

BP and Venous Thromboembolism

- **INVENTEP**
  - Incidence of VENous ThromboEmbolism in bullous Pemphigoid study
  - Cohort of 432 patients
  - BP patients have four-fold increased risk of VTE compared to age, sex matched controls
  - Increased during acute phase of disease up to 15-fold

  Cugno M et al, Thrombosis and Haemostasis, 2015

- **Mechanism**?
  - Related to increased expression of tissue factor by proinflammatory cytokines and eosinophils
  - Elevation of prothrombin fragments—coagulation activation
  - Anticoagulate patients with active disease?

  Zebrowska Z et al, Mediators Inflammation, 2015

- **AIBD can be window into systemic inflammation/injury of multiple organ systems**

Conclusion

- Bullous diseases fascinating group of autoimmune diseases
- Diagnostic and therapeutic decisions potentially affected

THANKS FOR THE INVITE!

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Don’t sweat it: treatments for hyperhidrosis

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Director Dermatology Clinical Trials Unit
Emory University School of Medicine
April 1, 2017

Objectives
1) Review the quality of life (QoL) impact of hyperhidrosis (HH)
2) Review the known pathophysiology of HH
3) Review the treatment options for HH

Outline
Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
Treatment of HH

Outline
ID: A 21 year old female
HPI: 8 year history of excess sweating of her palms bilaterally
MEDS: NONE
ROS: Negative
**Question #1**
Her diagnosis is most consistent with:
A) Generalized HH
B) Regional HH
C) Primary focal HH
D) Aquagenic palmar keratoderma
E) None of the above (this is degree of sweating is normal)

---

**What is Hyperhidrosis?**

_Sweating that is more than required to maintain normal thermal regulation_

Hornberger et al. JAAD. 2004.

---

**Diagnosis of Primary Focal Hyperhidrosis**

- Focal, visible, excessive sweating of at least **6 months** duration, **without apparent cause**, with at least **2** of the following characteristics:
  - Bilateral and relatively symmetric
  - Impairs daily activities
  - Frequency of at least one episode per week
  - Age of onset less than 25 years
  - Positive family history
  - Cessation of focal sweating during sleep

Hornberger et al. JAAD. 2004.

---

**Primary vs. Regional vs. Generalized**

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical presentation</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Focal HH</td>
<td>Focal, bilateral, symmetric sweating</td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Secondary Focal HH</td>
<td>Focal sweating, asymmetrical</td>
<td>Neurological disorders (i.e. Frey syndrome), Neoplasms, Trauma</td>
</tr>
<tr>
<td>Generalized HH</td>
<td>Generalized sweating</td>
<td>Endocrine disorders (i.e. Pheochromocytoma, Thyrotoxicosis etc.), Drugs, Tumors, Filariasis, Spinal cords injury, Cutaneous diseases</td>
</tr>
</tbody>
</table>


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**Aquagenic palmar keratoderma**
Outline

Defining HH (reviewing classification)
**Epidemiology of HH**
QoL in HH
Pathophysiology of HH
Treatment of HH

---

**Prevalence of HH**

- 2.8% of the United States Population (7.8 million)
  - Comparable to psoriasis
  - Underestimate (widely undiagnosed and untreated)

Strutton et al. JAAD. 2004.

---

Question #2

What is the prevalence of HH?

A) 0.03%
B) 1%
(C) 2.8%
D) 10%
E) 28%

---

Prevalence of HH (Cont.)

- 2/3rd of HH patients do not consult their physician
- HH patients wait for a mean of 8.9 years before seeking treatment
  - Not knowing treatment options
  - Not able to find a provider familiar with HH treatment options
  - Not knowing insurance coverage options
  - Embarrassment

Walling et al. JAAD. 2009.

---

Outline

Defining HH (reviewing classification)
**Epidemiology of HH**
QoL in HH
Pathophysiology of HH
Treatment of HH
“Never let them see you sweat!”


QoL in HH

“I usually wear black and try not to lift my arms.”
“My feet are always infected with fungus and are sore.”
“My pen slips out of my hands and my paper is always wet.”
“I am not able to play baseball (my favorite sport) because the bat flies out of my hands”
“I have not taken a job outside my house.”
“I would do anything to improve my sweating!”

QoL in HH (Cont.)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dermatology Quality Life Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperhidrosis</td>
<td>10.1</td>
</tr>
<tr>
<td>Severe acne</td>
<td>9.2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>9.2</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>8.9</td>
</tr>
<tr>
<td>Atopic Dermatitis</td>
<td>7.8</td>
</tr>
<tr>
<td>Hailey-Halley</td>
<td>6.1</td>
</tr>
<tr>
<td>Darier’s Disease</td>
<td>5.9</td>
</tr>
<tr>
<td>Vitiligo</td>
<td>4.8</td>
</tr>
</tbody>
</table>


Outline

- Defining HH (reviewing classification)
- Epidemiology of HH
- QoL in HH
- Pathophysiology of HH
- Treatment of HH
**Question #3**
The underlying pathophysiology of HH is due to an:

A) Increased density of eccrine glands
B) Increased size of eccrine glands
C) Increased activity of the eccrine glands
D) Increased release of the acetylcholine (ACh)
E) Increased uptake of the ACh

**Pathophysiology of HH**

- Poorly understood
- Normal density and size of eccrine glands
- **Overstimulation of the eccrine glands innervated by postganglionic cholinergic sympathetic fibers**


**Pathophysiology of HH (Cont.)**

- Probably genetic
  - Gene unknown
  - AD, variable penetrance
  - 30-50% have a known family history of HH

Haider et al. CMA. 2005.

**Outline**

Defining HH (reviewing classification)
Epidemiology of HH
QoL in HH
Pathophysiology of HH
**Treatment of HH**

**Question #4**
Topical anti-perspirants mechanism of action (MOA) is:

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells
**Treatment of HH**

<table>
<thead>
<tr>
<th>Non-invasive</th>
<th>Minimally invasive</th>
<th>Moderately invasive</th>
<th>Surgical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical medications</td>
<td>Intermittent</td>
<td>Microwave Thermolysis</td>
<td>Excision</td>
</tr>
<tr>
<td>Systemic medications</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Topical
  - Aluminum/Zirconium salts
  - Used all locations, **most effective axillae**

**Question #5**

The most common side effect after use of topical anti-perspirant is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis

---

**Treatment of HH**

\[ M^{n+} \text{Cl} + n \text{ moles Base} \rightarrow M(\text{base})_3 \text{ ppt } + n\text{HCl} \]

Base may be OH from water, lactate, or protein

*Best applied to dry area in the evening before bed.*

**Question #6**

**Glycopyrrolate’s MOA:**

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells
Treatment of HH

- Systemic medications
  - **Anticholinergics** (glycopyrrolate >> oxybutynin)
  - Beta-blockers
  - Calcium Channel Blockers
  - Alpha andrenergics
  - Benzodiazepines

Question #7
The most common side effect after the use of a systemic anticholinergic is:

A) Irritation
B) **Dry eyes and mouth**
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis

Treatment of HH

- Systemic anticholinergics are best to use:
  - Generalized HH
  - Multiple areas of involvement
  - Large areas of involvement
  - Craniofacial
  - Multi-therapy approach with other agents

Treatment of HH

- Anticholinergic side effects
  - Ocular: **Dry eyes**, mydriasis, cycloplegia
  - GI: **Dry mouth**, reduced gastric secretions
  - RESP: **Bronchodilation**, reduced secretions
  - GU: Urinary retention (relaxes smooth muscle ureters a bladder wall)
  - CARD: Cardiac arrhythmias (bradycardia at low doses and tachycardia at high doses)

Treatment of HH

- Anticholinergic Contraindications
  - **Absolute**
    - Glaucoma
    - Impaired gastric emptying
    - Urinary retention

Paller et al. JAAD. 2012.
Treatment of HH

• Anticholinergic caution
  – Outdoor occupation/athlete
  – Pediatric patients
  – Age >65 years old
    • Systemic anticholinergics associated with dementia

Gray et al. JAMA Internal Med. 2015.

Question #8
The MOA of iontophoresis is:

A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells

Treatment of HH

• Iontophoresis
  – Passing of ionized substance through intact skin by use of electrical current
  – For primary focal palmar/plantar HH
    • One of the best options


Question #9
The most common side effect after the use of iontophoresis is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis

Treatment of HH

- Adverse events from iontophoresis
  - Stinging/tingling/ “pins and needles” during treatment
  - Erythema along the waterline of the hand
  - Dermatitis, vesiculation

Question #10
The MOA of botulinum toxin (BTX) is:
A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells

Treatment of HH
- BTX A
  - Onabotulinumtoxin A (Botox®)
    - FDA approved July 19, 2004 for severe primary axillary HH
  - Abobotulinumtoxin A (Dysport®)
    - Not FDA approved for HH
  - Incobotulinumtoxin A (Xeomin®)
    - Not FDA approved for HH
    - May be stored at room temperature

Lowe et al. JAAD. 2007

Treatment of HH

- 100 units of Botox®
- Dilute 4ml sterile NS
- 2.5 units per 0.1ml

- 30 gauge, 1ml syringe
- 1.5-2cm apart
- 2.5 units to each site

Videos

http://www.sweathelp.org/education-and-resources/online-learning.html

Question #11
A worrisome side effect after the use of BTX for palmar HH is:

A) Irritation
B) Dry eyes and mouth
C) Muscle paralysis
D) Dysesthesia
E) Compensatory hyperhidrosis

Treatment of HH

- BTX side effects
  - Injection site pain
  - Injection site bleeding
  - Compensatory HH
  - Muscle weakness (craniofacial and palmar)
Question #12
The MOA of miraDry is:
A) Physical blockade of eccrine ducts
B) Decreased release of ACh
C) Increased destruction of ACh
D) Decreased uptake of ACh
E) Thermolysis of eccrine cells

Treatment of HH
• miraDry System
  – Manufactured by Miramar
• Axillary HH (and hair removal)
• FDA approved January 2011
• Uses microwave energy (580MHz) resulting in the thermolysis of eccrine glands

Treatment of HH
• miraDry side effects
  – Dysethesia (transient altered sensation in treatment arm)
  – Local swelling
  – Compensatory hyperhidrosis (rare)
  – $3K

Investigational Anticholinergic Topical Gel May Be Safe, Effective For Treatment Of Axillary Hyperhidrosis, Study Suggests
• Medscape (3/9, Tucker) reports that research presented at the American Academy of Dermatology meeting suggested “an investigational anticholinergic topical gel is safe and effective for the treatment of axillary hyperhidrosis.” The gel, Sofpironium bromide (BBI-4000), “is a specially formulated ‘soft’ topical anticholinergic designed to block sweat production, and its rapid metabolic deactivation and excretion reduces the adverse effects associated with anticholinergic agents.”

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1) Review the quality of life impact of hyperhidrosis (HH)
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www.clinicaltrials.gov
*Available Canada
Patients with hyperhidrosis are a JOY to care for!

http://www.sweathelp.org/

- Diagnosis and treatment algorithms
- Informed consents
- Videos
- Brochures and posters
- Clinical research postings
- CPT and ICD-10 codes (insurance letters)
- Literature references
- And MUCH MORE...

*Ms. Lisa Peretti

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**Questions:**
zaressL@emory.edu

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**Treatment of HH**

- **Glycopyrrolate (PO)**
  - **Adults**
    - 1 and 2mg tablets
    - Start 1mg PO BID
    - Increase 1mg every 2 weeks, depending on clinical side effects
    - Max 8mg/day
  - **Children**
    - Oral suspension 0.5mg/mL
    - Start 0.02mg/kg PO TID
    - Increase 0.02mg/kg every 1-4 weeks, depending on clinical side effects
    - Max 3mg/day

---

**Billing and Coding**

- **E&M 99212-99213**
- **ICD-10 Primary Focal Hyperhidrosis**
- **L74.512 axilla**
- **L74.513 palms**
- **L74.514 soles**
- **R61 Craniofacial**
- **CPT**
  - 97033, iontophoresis, each 15min
    - Typically bill for 2-4 units, depending on how many areas are treated
  - 64650 chemodenervation of eccrine glands, axillae
  - 64653 chemodenervation of eccrine glands, other areas (i.e. scalp, face, neck),
    - 64999 unlisted procedure, nervous system (i.e. hands and feet)
  - J0585, per unit of onabotulinumtoxinA

---

**HDSS**

<table>
<thead>
<tr>
<th>How would you rate your HH</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweating noticeable, never interferes</td>
<td>1</td>
</tr>
<tr>
<td>Sweating tolerable, sometimes interferes</td>
<td>2</td>
</tr>
<tr>
<td>Sweating barely tolerable, frequently interferes</td>
<td>3</td>
</tr>
<tr>
<td>Sweating intolerable, always interferes</td>
<td>4</td>
</tr>
</tbody>
</table>
Upcoming Meetings:

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