Current Concepts in Dermatology

Karthik Krishnamurthy, D.O., FAOCD
Program Chair

Faculty

Karthik Krishnamurthy, DO

Dr. Karthik Krishnamurthy, Assistant Professor of Dermatology at Albert Einstein College of Medicine, received dual B.S. degrees in Biochemistry and Chemistry from the University of Missouri before earning his medical degree at Nova Southeastern University in Fort Lauderdale, where he was the recipient of the prestigious Kenneth Burnell Research Award for his work on the hunger cycle. Following an Internal Medicine Internship at the Stroger-Cook County Hospital in Chicago where he was name Best Teaching Intern, Dr. Krishnamurthy completed his dermatology residency at Saint Barnabas Hospital in the Bronx, serving as Chief resident.

Dr. Krishnamurthy has a special interest in academic dermatology and research, and received the Allergan Research Award for his review of bleomycin in dermatology, the A.P. Ublrich Research Grant for the study of a novel intralesional, inorganic material for the treatment of warts, and the Intendis Reseach Award for his study of transcutaneous aborption. His publications appear in various dermatology journals and is frequently invited to contribute to dermatology textbooks, serving as cover co-editor of the upcoming *Dermatologic Emergencies* textbook (Springer 2012). He will be transitioning to Editor-in-Chief of the *Journal of the American Osteopathic Journal of Dermatology* this year. In addition, he is often sought for expert interview by various media sources and is an invited lecturer both locally and nationally, having received the Daniel Koprince Award and a New York Academy of Medicine Award for his presentations.

Dr. Krishnamurthy is committed to medical education, and teaches residents and medical students daily in clinical settings, as the Director of Dermatology at Jacobi Medical Center, the largest NY public hospital. Paralleling his academic pursuits, Dr. Krishnamurthy is the recipient of the 2011 Academic Dermatology Leadership Program and the 2012 Editorial Mentorship program, both granted by the American Academy of Dermatology.

Dr. Krishnamurthy additionally serves as the Director of the Cosmetic Clinic at the Dermatology Center, located at Montefiore Medical Center. A founding member of multidisciplinary pigmented lesion/melanoma clinic at the Montefiore Einstein Center for Cancer Care - Melanoma Program, Dr. Krishnamurthy delivers care and researches skin cancer in the indigent Bronx population, and runs the widely popular Free Skin Cancer Screenings every May during National Melanoma Month.

Also dedicated to Einstein's continued growth, Dr. Krishnamurthy serves on the Emerging Einstein Leaders (EEL) Board as Executive Secretary. The EEL focuses on increasing awareness and fundraising for Einstein's various, unique projects and services ranging from cancer research to breakthroughs in human development.

Faith McNicholas, MD

Faith 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, JDNA Annual meetings and AAD monthly webinars and regional symposia.

She is a member of AAPC and is a Certified Professional Coder (CPC) with specialization in dermatology coding and the American Health Information Management Association (AHIMA). She has certification in Medical Billing, medical coding, management of medical office and healthcare practice and a degree Health Information and Management Technology.

John Coppola, DO, FAOCD

John C. Coppola, D.O. 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".

Disclosure: Progressive Medical Research

Jennifer Cather, MD

Dr. Cather is medical director at Modern Dermatology in Dallas, Texas and co-director of Cutaneous Lymphoma and Graft vs Host Clinics at Baylor University Medical Center in Dallas. Dr. Cather received her medical degree from the University of Texas Southwestern Medical School at Dallas and served her internship in internal medicine at Parkland Memorial Hospital in Dallas. She then completed a clinical research fellowship at M.D. Anderson Cancer Center in Houston, followed by a residency in dermatology at The University of Texas-Houston Medical School in Houston.

Actively involved in clinical research, Dr. Cather has been principal or sub-investigator of more than 40 clinical trials. She has lectured extensively and has published widely. Articles under Dr. Cather's authorship or co-authorship have appeared in Journal of the American Academy of Dermatology, American Journal of Hematology, Cutis, Dermatologic Therapy, Dermatologic Clinics, and other journals. Her articles cover a broad range of topics including investigational therapies for psoriasis, cutaneous T-cell lymphoma, and melanoma. Dr. Cather belongs to the American Academy of Dermatology, the American Medical Association, the Texas Medical Association, the Women's Dermatologic Society, the American Society for Laser Medicine and Surgery, and the National Psoriasis Foundation.

Disclosures: AbbVie, Celgene, Janssen, Leo, Merck, Novartis, Pfizer

Aaron Bruce, DO, FAOCD

Dr. Bruce is a board certified dermatologist who joined Rogers Dermatology Clinic in March of 2013. Prior to arriving in Bozeman, Dr. Aaron Bruce worked as a skin cancer specialist in a large dermatology practice in Northern Colorado. In 2010 he completed a one year Mohs Fellowship Training Program accredited by the American College of Mohs Surgery specifically focused on the diagnosis and treatment of skin cancer. Under the direction of Ronald Siegle, MD, Brian Biernat, MD, and Peter Seline, MD, Dr. Bruce performed over 1,000 cases of Mohs micrographic surgery and advanced reconstructions.

Dr. Bruce is only one of five dermatologic surgeons to have completed this type of fellowship in the entire state of Montana, and the only Mohs surgeon in Southwestern Montana.

In addition to publishing several articles in a variety of medical journals, Dr. Bruce has lectured locally and at national meetings. A magna cum laude graduate of Arizona State University, Dr. Bruce was an Arizona State Regent Merit Scholar, and a recipient of a National Science Foundation research grant focusing on evolutionary biology.

Dr. Bruce is married with three young children and enjoys spending time with his family particularly in the mountains. Whether cycling, hiking, or skiing, Dr. Bruce is a passionate outdoorsman. He is ecstatic to fulfill his life-long dream of living in the Rocky Mountains.

Steven Grekin, DO, FAOCD

Dr. Steven Grekin has made it his personal and professional mission to help his patients put their best face forward. Years of research at the International Skin Rejuvenation Institute in Paris, France, and Quebec, Canada, have led Dr. Grekin to understand the secrets to younger, smoother, more radiant skin. He now brings these secrets to his patients in America.

Respected here and abroad as an expert in cosmetic dermatology, Dr. Grekin comes from a long line of physicians-six are dermatologists. He has participated in international teaching and training courses, and is an internationally recognized lecturer in his field.

Guided by cutting-edge principles of modern dermatology, natural medicine, and the highest quality medical care, Dr. Grekin offers his patients an elegant, intelligent program distinguished by its unique flexibility to restore every skin type to its youthful, natural best!

His family has been providing health care in the United States for almost 100 years. Dr. Grekin is committed to helping patients from all over the world. He now offers his programs on-line, so that he may reach out and help as many people as he can put their best face forward.

Disclosures: Medicis/Valeant, Aqua Pharmaceuticals, Merz

Stuart M. Brown, MD

Dr. Stuart M. Brown is a native of Maryland, having matriculated both as an undergraduate and in the School of Medicine at the University of Maryland. Following a rotating internship, he entered the U.S. Army, where he did his Dermatology Residency Training while in San Antonio. After several years in the Southwest, he realized that type of climate welcomed him and his family, so he settled in Dallas, which offered a chance for private practice along with the opportunity to teach clinical dermatology at the local branch of the University of Texas. Over these many years, he has continued to be involved in Dermatologic Organizations, rising to be President of several; furthermore, he has been extremely active in the teaching program of the AAD and his voice is readily recognized by his involvement in Dialogues in Dermatology.

Disclosures: Johnson & Johnson, Pfizer

Ronald Rapini, MD

Dr. Rapini received his M.D. degree from The Ohio State University in 1978. He then completed a transitional internship at Marshfield Clinic in Marshfield, WI, in 1979; a residency in Dermatology at the University of Iowa Hospitals and Clinics in 1982; and a fellowship in Dermatopathology at the University of Colorado Health Sciences Center in 1983.

Dr. Rapini then came to Houston when he was named Assistant Professor in the Department of Dermatology at UTMS in 1983. He was promoted to

Associate Professor in 1988 and held that position until 1993, when he went to Texas Tech University as Chair and Professor in the Department of Dermatology. In 2002, Dr. Rapini returned to Houston when he was named to his current positions as Chair and Professor in the Department of Dermatology at MD Anderson and Chair and Josey Professor in the Department of Dermatology at UTMS.

Dr. Rapini has been the Clinical Medical Director for the UTMS Dermatology Clinic since 2002 and has directed office-based laboratory testing for UTMS since 2005. He also served as the Director of the Mohs Clinic at MD Anderson in 2009 and Associate Medical Director of the MD Anderson Melanoma and Skin Center from 2003 to 2008.

Dr. Rapini currently serves on the editorial board for Skin & Allergy News. He also was an editor for Texas Dermatologist and served on the board for The American Journal of Dermatopathology. Furthermore, he has been a reviewer for numerous publications. Since 1981, Dr. Rapini has authored more than 120 articles published in peer-reviewed journals, 23 invited articles, and 33 book chapters and edited or authored 7 books.

Adam Friedman, MD

Adam Friedman, MD is Director of Dermatologic Research at the Unified Division of Dermatology of Albert Einstein College of Medicine. 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. He holds several patents derived from these investigations, and has published over 90 papers/chapters and two textbooks on both his research as well as a variety of clinical areas in dermatology with an emphasis on emerging medical therapies. Dr. Friedman has presented his research in both national and international forums, and has received awards from multiple organizations such as the American Academy of Dermatology and American Society for Dermatologic Surgery. Recently, he was featured on the online forums Dermtube, DermMatters, Nanotechnology Thought Leaders, and Dermquest.

Dr. Friedman is also committed to resident and medical education. He chaired of 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, publishes a column on Everyday healthy entitled The Skin You're In and inline with his research interests, as the 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 co-founder of the newly formed Einstein Emerging Leaders, a group of young professionals who host events through which they can introduce Einstein to like-minded young professionals and who have an interest in making the world a better place through the support of healthcare and research.

Dr. Friedman has appeared on television news programs such as Good Morning America, and has been quoted in numerous leading publications, including WebMD, In Style, Reuters, Good Housekeeping, and Women's Day.

Disclosures: Amgen, Onset, Liquidia, Salvona, Microcures, Valeant, La Roche Posay

James Q. Del Rosso, DO, FAOCD

James Q. Del Rosso, D.O., is a Clinical Assistant Professor of Dermatology at the University of Nevada School of Medicine. Dr. Del Rosso also served as Assistant Professor of Dermatology and head of the Section of Dermatology at the Ohio University College of Osteopathic Medicine in Athens. In addition, he was a Clinical Assistant Professor of Internal Medicine, Section of Dermatology, at Ohio State University in Columbus. Dr. Del Rosso has lectured extensively on an international level on many issues related to dermatology and is well-published.

Dr. Del Rosso received his D.O. degree from the Ohio University College of Osteopathic Medicine. He completed a rotating internship at Doctors Hospital in Columbus, a residency in dermatology at Atlantic Skin Disease and Skin Surgery Associates in Fort Lauderdale, Florida and a fellowship in Mohs micrographic surgery and cutaneous oncology at Ohio State University. Most recently, Dr. Del Rosso was appointed to the Board of Directors of the Council for Nail Disorders, the American Society for Mohs Surgery, and to the American Osteopathic Board of Dermatology. He is board certified in both dermatology and Mohs micrographic surgery.

Disclosures: Allergan, Bayer Dermatology, Dermira, Eisai, Ferndale, Galderma, LeoPharma, Medicis/Valeant, Merz Pharmaceuticals, Onset Dermatologics, Pharmaderm/Fougera, Promius, Promus, Ranbaxy, Taro, Unilever, Warner Chilcott

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, Florida. 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.

Disclosure: Skin Medica

David Fivenson, MD

David Fivenson is board certified in dermatology and immunodermatology. From 1989-2002 he was in full time academic practice at Henry Ford Hospital, prior to starting this practice. He is a nationally recognized specialist in autoimmune skin disease, wound care, clinical research and cutaneous T cell lymphoma.

He has published more than100 peer reviewed articles, has lectured extensively at national and international medical conferences and has been repeatedly listed with Who's Who in America, Best Doctors in America and Castle Connelly's Top Docs.

Amy Spizuoco, DO, FAOCD

Dr. Amy Spizuoco is a board certified dermatologist and dermatopathologist. She received her Bachelor of Arts at SUNY Binghamton with a double major in Italian and Biology. And earned her medical degree at New York College of Osteopathic Medicine. She completed a medical internship at Lutheran Medical Center. She then went on to Alta Dermatology Residency Program in Mesa, Arizona where she spent a year researching Reflectance Confocal Microscopy, and subsequently completed her dermatology residency.

During residency she received training at the Mayo Clinic Scottsdale as well as Phoenix Children's Hospital. She was named Chief Resident in her last year of residency. After residency, Dr. Spizuoco completed a fellowship in dermatopathology.

Currently Dr. Spizuoco is a member of the American Academy of Dermatology, the American Osteopathic College of Dermatology, the American Society for Dermatopatholgy, the American Society of Mohs Surgery, the American Society for Dermatologic Surgery, the New York State Osteopathic Medical Society, the Women's Dermatologic Society, and the Dermatologic Society of Greater New York.

Alan Menter, MD

Dr. Alan Menter was born in England and received his dermatology residency training in South Africa. He subsequently undertook further postgraduate training and research at Guy's Hospital and St. John's Hospital for Diseases of the Skin in London, England. After moving to the United States, he completed a fellowship in Dermatology at Southwestern Medical School in Dallas. He was Board Certified in dermatology in 1977.

Dr. Menter has written over 200 articles, 2 books, and 10 book chapters in peer reviewed medical publications, and has an international reputation as a clinician/researcher. In 2004, he spearheaded the formation of the International Psoriasis Council, for which he currently serves as President.

His recent international lectures include Brasilia, Buenos Aires, Copenhagen, Florence, Istanbul, London, Madrid, and Tokyo, as well as national lectures in Houston, Las Vegas, Los Angeles, New York City, Phoenix, San Antonio, and St. Louis. He has presented at various American Academy of Dermatology conferences and at the World Congress of Dermatology in Buenos Aries in 2007.

Disclosures: Amgen, Janssen, AbbVie

Lloyd J. Cleaver, DO, FAOCD

Dr. Lloyd Cleaver, D.O. founded the Cleaver Dermatology Clinic in 1986. Dr. Cleaver completed his internship and residency at the Navy Regional Medical Center in San Diego, California.

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 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.

Cliff Lober, MD, JD

Dr. Lober received his M.D. degree from Duke University School of Medicine in 1974. He then completed his internship at Mayo Clinic in 1977 and his residency at University of Tennessee in 1982.

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

Dr. Lober has received four Presidential Citations from the American Academy of Dermatology and was named "Surgeon of the Year" in 1992 by the Florida Society of Dermatology and Dermatologic Surgeons. He was awarded the first ever "Distinguished Service Award" by the Florida Society of Dermatology and Dermatologic Surgery. Dr. Lober has served on the Board of Directors of the AAD and chaired its section on Health Practice, Policy, and Research. He is currently Chairman of the Carrier Policy and Medical Liability Task Force.

Kelly Nelson, MD

Medical School: MD, University of North Carolina–Chapel Hill School of Medicine, 2004

Residency: Internal Medicine, UNC Hospitals, 2004-2005
Dermatology, UNC Hospitals, 2005-2008

Clinical Interests: Management of patients with history of melanoma; patients at high risk of developing melanoma.

Rene Bermudez, DO, FAOCD

Medical School: Philadelphia College of Osteopathic Medicine, 1999

Internship: Doctors Hospital of Stark County Massillon, Ohio, 2000

Residency: Internal Medicine, Summa Health System Akron, Ohio, 2002

Residency: Dermatology, Summa Health System Cuyahoga Falls, Ohio, 2005

Fellowship: Mohs Micrographic Surgery, Kirksville College of Osteopathic Medicine/Dermatology Associates of Tulsa Tulsa, Oklahoma, 2010

Board Certification: American Osteopathic Board of Dermatology

Scott Wickless, DO, FAOCD

Scott received his undergraduate degree from the University of Michigan-Ann Arbor, and subsequently received his medical degree from A.T. Still University Kirksville College of Osteopathic Medicine. Dr. Wickless completed his internship at Henry Ford Hospital and his Dermatology residency at Michigan State University. Dr. Wickless then completed fellowship training in Dermatopathology and Cutaneous Oncology at Northwestern University Feinberg School of Medicine.

Dr. Scott C. Wickless is board-certified in both Dermatology and Dermatopathology. He specializes in medical dermatology, skin cancer, and interpretation of skin biopsies. His dual certification allows better integration of clinical information with microscopic observations for the treating physician. He is a member of the American Society of Dermatopathology, International Society of Dermatopathology, American Osteopathic

College of Dermatology and the American Academy of Dermatology. He has formerly served on peer-review teams for *The Lancet*, *Archives of Dermatology* and the *Journal of the American Academy of Dermatology*.

Scott has served as clinical faculty at both Northwestern University and Loyola University in Chicago, IL, where he also functioned as Director of the Dermatopathology Unit at the Edward Hines, Jr. VA Hospital. Dr. Wickless has authored multiple abstracts, textbooks and peer reviewed journal articles, including the *New England Journal of Medicine*, *Journal of the American Academy of Dermatology*, the *Journal of Cutaneous Pathology* and *Archives of Dermatology*.

James M. Dahle, MD

James M. Dahle, MD, is a practicing board-certified emergency physician and editor of the website www.whitecoatinvestor.com, created to help those that wear the white coat get a "fair shake" on Wall Street.

He provides investing and personal finance information to physicians, dentists, residents, students, and other highly-educated, busy professionals.

Disclosure: The White Coat Investor, LLC.

DERMATOLOGY RESIDENT FACULTY

Holly Kanavy, DO
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Trey Haunson, DO
Lewis Gale Hospital – Montgomery/VCOM

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Teresa Ishak, DO
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Christina Feser, DO
Oakwood Southshore Medical Center

Jesse Jensen, DO
Bosford Hospital/McLaren Oakland

Raymond Knisley, DO
Advanced Desert Dermatology

Ryan Pham, DO
UNTHSC/TCOM

Tang Le, DO
South Texas Osteopathic Dermatology

AOCD 2014 Midyear Meeting
Current Concepts in Dermatology
Dallas, Texas
February 20-23, 2014
American Osteopathic College of Dermatology
Continuing Medical Education Needs Assessment Statement

ACCREDITATION:
The AOCD is accredited by the American Osteopathic Association.

MEETING OBJECTIVES:
The 2014 Midyear Meeting will provide a diversified CME program focusing on the art and science of Dermatology. Information will be presented through lectures and scientific paper presentations. Attendees will be updated on a broad range of new developments in dermatology and acquire a better understanding of advances in medical and surgical therapies. They will also gain greater insight into current trends in dermatopathology. Therapeutic updates will include discussions on Psoriasis, 2014 Dermatology Coding & Regulatory Updates – ICD10 CM, 2013 NCCN Melanoma Guidelines, Managing Psoriasis Patients, Prevention, Diagnosis, and Treatment of Skin Disease, Cosmetic Dermatology, Dermatopathology Update, Osteopathic Continuous Certification Update, Legal Dilemmas in Dermatology, Mohs Micrographic Surgery, and Update on Cutaneous Lymphomas

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

NEEDS ASSESMENTS
The program was developed based upon the needs of physicians within the association identified through:

- A program evaluation/survey provided to meeting participants at both our annual and midyear meeting
- Requests submitted on participants' activity evaluation forms
- Informal comments
- Patient problem inventories compiled by potential participants
- Consensus of faculty members within a department or service area
- Recommendations from previous program chairmen and presenters
- 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
- Input from experts regarding advances in medical knowledge

- Acquisition of new facilities or equipment
- Legislative, regulatory, or organizational changes effecting patient care
- Epidemiological data
- Quality assurance/audit data
- Re-credential review
- Morbidity/Mortality
- Statistics infection control data
- Surgical procedures statistics
- Professional society requirements
- Journal articles/literature citations

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 the AOCD are:

- To maintain the highest possible standards in the practice of dermatology
- To stimulate study and to extend knowledge in the field of dermatology
- 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.
- To contribute to the best interests of the osteopathic profession by functioning as an affiliated organization of the American Osteopathic Association

The objectives of the AOCD Continuing Medical Education Committee are:

- To insure from time to time, an in-depth postgraduate course in dermatology, other than the annual convention, and to insure continuing medical education to the membership of this College.
- To develop and maintain on going Needs Assessments as required by the AOA.
- To develop postgraduate outcome evaluation forms for program attendees.
- To review postgraduate outcome evaluation forms received from program attendees.
- To develop long range CME course curricula.
- To assist the Education Evaluation Committee of the College in incorporating the inclusion of Osteopathic principles and practices in dermatology residency training.
- To assure the inclusion of appropriate Osteopathic content in the Continuing Medical Education programs presented by AOCD.
- 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.

Purpose

The purpose of the AOCD/CME program is to provide AOA-accredited continuing medical education activities to inform the Osteopathic 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 of the AOCD will monitor the quality of all programs conducted.

Content Areas
The content of CME activities produced by the AOCD is initiated and determined by its members. The CME program approves the 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:

State-of-the-art clinical information
Public health issues
Educational methodology
Professionalism and success in medicine
Cultural proficiency
Bioterrorism Education

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 program will also actively seek to broaden its audience through developing affiliations with CME providers on the national level.

Types of Activities
The core activities presented by the AOCD/CME program are live conferences. The program 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.

Expected Results
As a result of participation in the AOCD/CME program, practicing clinicians will:
Improve competency; Maintain specialty board certification; and Cultivate lifelong learning.

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.

This program anticipates being approved for 26.5 hours of AOA Category 1-A credit pending approval by the AOA CCME, the American Academy of Dermatology (Program #698100).

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.
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.

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

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

Unresolved issues regarding compliance with the AOA "Uniform Guidelines" can be brought to the attention of the AOA Division of CME by calling:

800-621-1773, extension 8262
or by writing:

AOA CME Office
142 East Ontario Street
Chicago, IL 60611

Tentative Schedule* We reserve the right to withdraw the program or to make changes in the published itinerary whenever conditions warrant or if it is deemed necessary.

What's Under the Ulcer David Fivenson, MD	Objectives: 1. Recognize typical vs. atypical skin ulcers. 2. Identify autoimmune diseases that present as skin ulcers. 3. Appreciate that ulcers of skin can be key to many diverse skin disorders and not just snelly things to "turf" to some wound care clinic. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis or treatment. 3. Advances in medical knowledge. ***References: Chourcair, MM and Fivenson, DP: Leg Ulcer Diagnosis and Management. Derm clin 2001;19:659-78.*** ***Callen, JP: Vasculitis, in Dermatological Signs of Internal Disease, Third Edition; Callen, JP, Jorizzo JC, Bologia JL, Piette WV and Zone JJ Editors, Saunders 2003;25-31.*** **Core Competencies: 2,6,7**
Thoughts that Make Dermatology Practice (and Life) Easier Stuart Brown, MD	Objectives: Following this lecture the attendee should be able to: 1. List innovative ways to manage patients via new or old therapies. 2. Make diagnoses easier with new or old information. 3. Recognize and use available medications for "off lab usage". 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:*** ***http://www.ama-assn.org/ama*** ***http://www.skinandallergynews.com/specialty-focus/medical-dermatology/medical-dermatology-landing.html*** **Core Competencies: 2,3,4,6**

2014 Dermatology Coding and Regulatory Updates – ICD-10-CM Coding Education Faith C.M. McNicholas, RHIT, CPC, CPCD, PCS, CDC	Objectives: 1. Understand new and revised regulatory and coding updates pertaining to Dermatology in 2014. 2. Learn chapter specific coding guidelines and concepts in dermatology specific ICD-10-Cm and the correlation to Current Procedural Terminology (CPT) coding. 3. Easily identify correct and appropriate use of dermatology specific ICD-10-CM using easy step-by-step code crosswalk leading to accurate ICD-10-CM code selection Needs: 1. Legislative, regulatory or organization changes effecting patient care. ***References: CDC/NCVHS ICD-10-CM Code reference*** ***AMA ICD-10-CM Coding Manual*** ***AMA Current Procedural Terminology (CPT) Manual*** **Core Competencies: 6,7**
Update on the Appropriate Use Criteria or MOHS Micrographic Surgery Rene Bermudez, DO, FAOCD	Objectives: 1. Update and review the appropriate use criteria for MOHS micrographic surgery. 2. Review indications for MOHS micrographic surgery. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis or treatment. 3. Availability of new medication(s) or indication(s) ***References: Dermatologic Surgery, Vol38:10. Oct 2012; p.1582-1603.*** ***JAAD 2012; 67; 551.*** **Core Competencies: 2,3,4,6**

Safety and Continued Improvement in Dermatology Kelly Nelson, MD	Objectives: 1. Understand the differences between latent and active errors. 2. Consider the concept of operating "above the line" when involved in patient safety events. Needs: 1. New methods of diagnosis or treatment. 2. Advances in medical knowledge. 3. Legislative, regulatory, or organizational changes effecting patient care. ***References: Kim JK et al. Standardized patient identification; specimen handling; a retrospective analysis on improving patient safety. JAAD 2013; 68(1):53-56.*** **Core Competencies: 2,3,5,6**
2013 NCCN Melanoma Guidelines – Are You Following the Standard of Care? John Coppola, DO, FAOCD	Objectives: 1. Familiarize colleagues and residents with the updated 2013 NCCN Clinical Practice Guidelines for Melanoma. 2. Discuss the application of the guidelines in the community setting. 3. Discuss the role of both the dermatology and the oncologist in the treatment of various melanoma stages. Needs: 1. New methods of diagnosis or treatment. 2. Availability of new medication(s) or indication(s). 3. Advances in medical knowledge. ***References: www.nccn.com. Bichakjian et al, Guidelines of Care for the Management of Primary Cutaneous Melanoma, JAAD V65N5; 1032-1047.*** **Core Competencies:2,3,6,7**

Cosmetic Dermatology – It's a Marathon Not a Sprint Michelle W. Foley, DO, FAOCD	Objectives: 1. Discuss the ethical implications of cosmetics in dermatology. 2. Discuss how the growth of cosmetic demands will affect dermatology practices now and in the future. 3. Discuss new and novel cosmetic treatments, maintaining patient's satisfaction and physician fulfillment. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis and treatment. 3. Development of new technology. 4. Advances in medical knowledge. ***References: Baumann, L., Ethics in cosmetic dermatology, Clinics in Dermatology(2012)30,522-527. Imadojemu,S. and Fiester, A. Are there moral obligations to cosmetic dermatology patients beyond informed consent? JAAD 2012;67:136-8. Sadick, N. et al. Cosmetic dermatology of the aging face, Clinics in Dermatology (2009) 27, S3-S12.*** **Core Competencies: 2,3,4,6**
Managing Psoriasis Patients Across the Life Course Jennifer Cather, MD	Objectives: 1. Identify comorbidities and other factors that inform treatment decisions in patients with moderate-to-severe plaque psoriasis. 2. Discuss rationale for choosing systemic agents in specific patients with moderate-to-severe plaque psoriasis. 3. Select the most appropriate treatment for psoriasis patients at different stages in their life. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis or treatment. 3. Advances in medical knowledge. ***References: Menter, et at. JAAD, 2008 May;58(5):826-50. American Academy of Dermatology Work Group. JAAD. 2011 Jul;65(1):137-74.*** **Core Competencies: 2,3,6**

Legal Dilemmas in Dermatology Clifford W. Lober, MD, JD	Objectives: 1. Analyze legal dilemmas to facilitate appropriate patient care. 2. Recognize legal implications of treatment alternatives. 3. Understand legal consequences of alternative treatment options. Needs: 1. Legislative, regulatory, or organizational changes effecting patient care. ***References: Legal Medicine, 7h ed, by Mosby Elsevier, 2007, pgs. 253-265.*** ***"Legally Speaking", Dermatology World – AAD website, 2 – 12/2013 issues.*** **Core Competencies: 3,4,5,7**
Reconstruction of the Upper Lip Aaron M. Bruce, DO, FAOCD	Objectives: 1. Review anatomy of the upper lip. 2. Review common defects and repair options. 3. Review complications with reconstruction of the upper lip. Needs: 1. Advances in medical knowledge. ***References: Baumann D and Robb G. "Lip Reconstruction". Semin Plast Surg. 2008 November;22(4):269-280.*** **Core Competencies: 2,3,6**

Update on Cutaneous Lymphomas Scott Wickless, DO, FAOCD	Objectives: 1. Review the EORTC-WHO classification of cutaneous lymphomas. 2. Provide insight into the clinical pathologic features of cutaneous lymphoma. 3. Discuss evaluation, prognosis and treatment options including emerging therapies. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis or treatment. 3. Availability of new medication(s) or indications(s). 4. Development of new technology. 5. Advances in medical knowledge. 6. Legislative, regulatory, or organizational changes effecting patient care. ***References: Gerami P, Wickless SC, Querfeld C, Rosen ST, Kuzel TM, Guitart J. "Cutaneous involvement with marginal zone lymphoma". JAAD. 2010 Jul; 63(1):142-5. Gerami P, Wickless SC, Rosen S, Kuzel TM, Ciurea A, Havey J, Guitart J. "Applying the new TNM classification system for primary cutaneous lymphomas other than mycosis fungoides and Sezary syndrome in primary cutaneous marginal zone lymphoma". JAAD. 2008 Aug;59(2):245-54.*** ***Guitart J, Wickless SC, Oyama Y, Kuzel TM, Rosen ST, Traynor A, Burt R. "Long-term remission after allogeneic hematopoietic stem cell transplantation for refractory cutaneous T-cell lymphoma". Arch Dermatol. 2002 Oct; 138(10):1359-65.*** **Core competencies:1,2,3,4,5,6,7.**

Osteopathic Continuing Certification Update Lloyd Cleaver, DO, FAOCD	Objectives: 1. Understanding of the OCC process that ensures osteopathic physicians are current in their specialty. 2. Understanding of the five components of OCC which include: 1. Unrestricted License 2. Lifelong Learning 3. Cognitive Assessment 4. Practice Performance 5. Continuous AOA Membership Needs: 1. Ensuring college membership understands new requirements for accreditation and maintenance of our board certification. ***References: http://www.osteopathic.org/inside-aoa/development/aoa-board-certification/Pages/osteopathic-continuous-certification.aspx*** **Core competencies: 1,3,5,6**

Dermatology Q & A: Common Encountered Challenges Related to Dermatologic Diagnosis and Therapy James Q. Del Rosso, DO, FAOCD	Objectives: Discussion of commonly encountered challenges in practice, pitfalls to avoid in clinical evaluation and treatment, and methods to develop practical checklists to provide consistent comprehensive follow up. 1. List potentially significant drug interactions that are likely to be encountered in dermatology practice. 2. Develop follow up and monitoring approaches that are helpful in management patients treated with frequently used systemic therapies in dermatology practice such as antibiotics and antifungal agents. 3. Explain pathophysiologic mechanisms associated with epidermal barrier dysfunction, acne, rosacea, and atopic dermatitis with clinical correlations to therapies used. 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. ***Reference:*** ***Del Rosso JQ, Cash K. "Topical corticosteroid application and the structural and functional integrity of the epidermal barrier." J Clin Aesthet Dermatol. 2013 Nov;6(11):20-7.*** ***Del Rosso JQ, Kircik LH. "The sequence of inflammation, relevant biomarkers, and the pathogenesis or acne vulgaris: what does recent research show and what does it mean to the clinician?" J Drugs Dermatol. 2013 Aug;12(8 Suppl):s109-15.*** ***Del Rosso JQ, Gallo RL, Tanghetti E, Webster G, Thiboutot D. "An evaluation of potential correlations between pathophysiologic mechanisms, clinical manifestations, and management of rosacea. Curtis. 2013 Mar;91(3 Suppl):1-8.*** **Core comp – 2,3,4,6**

Pitfalls in Personal Finance and Investing James Dahle, MD	Objectives: 1. Assist dermatologists in managing their personal and practice finances in a manner that promotes good patient care and career longevity. 2. Assist dermatologists in developing, implementing, and maintaining a sensible investing plan for retirement. 3. Assist dermatologists in interactions with financial professionals. Needs: 1. Legislative, regulatory, or organizational changes effecting patient care. 2. Legislative changes affecting physician and practice financial stability. 3. Availability of new investing, incurrence, and retirement products. 4. New advances in portfolio design. ***References: Cooley et al, "Portfolio Success Rates: Where to Draw the Lines". Journal of Financial Planning, April 2011.*** ***Neufeld, "The Tyranny of Compounding Fees". Journal of Financial Planning, December 2011.*** **Core Competencies:6**
Melanocytic Conundrums Ronald Rapini, MD	Objectives: 1. Learn to manage dysplastic nevi. 2. Understand new melanocytic neoplasm terminology. 3. Understand the problem of borderline "grey zone" melanocytic neoplasms. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis or treatment. 3. Advances in medical knowledge. ***References: "The Dysplastic Nevus". JAAD 67: issue 1, e1-e16, July 2012.*** ***Ko CJ et al. "Spark's Nevi". J Cutan Pathol 36:1063-1068, 2009.*** **Core Competencies: 2,3,6,7**

The Spectrum of Comorbidities in Psoriasis with Special Reference to Cardiovascular Issues Alan Menter, MD	Objectives: 1. Understanding of Psoriasis Comorbidities. 2. Understanding of systemic inflammation, Psoriasis & Cardiovascular disease. 3. Understanding of Psoriatic arthritis for the Dermatologist. Needs: 1. New methods of diagnosis or treatment. 2. Advances in medical knowledge. ***References: Definition of Severe PsO: Treatment with PUVA, UVB, MTX, Azathioprine, Cyclosporine, Acitretin, Hydroxyurea, or Mycophenolate Neimann AL, et al. JAAD Nov 2006;55:829-835. VE Friedewald Jr, et al. AJC editor's consensus: Psoriasis and Coronary Artery Disease. Dec 15;102(12):1631-1643,2008.*** **Core Competencies: 1,2,3,4,5,6,7**

Nanotechnology for the Prevention, Diagnosis, and Treatment of Skin Disease Adam Friedman, MD	Objectives: 1. Describe the role of nanotechnology in dermatology. 2. Discuss the important areas of research in nanotechnology for the diagnosis and treatment of skin disease. 3. Recognize the risks and benefits of nanotechnology for consumers and patients. Needs: 1. New advances in dermatologic treatment. 2. New methods of diagnosis or treatment. 3. Development of new technology. 4. Advances in medical knowledge. ***References: "Nanotechnology in Dermatology". Ed. Nasir, Friedman, Wang. Springer Publishing LLC. 2013, XVII, 291p.*** ***Nasir A, Wang S, and Friedman A. "The Emerging Role of Nanotechnology in Sunprotection: An Update". Expert Review Dermtol. 2011;6(5):437-439.*** ***Belcher-Paz K and Friedman A. "Nanotechnology and the Diagnosis of Dermatological Infectious Diseases". J Drugs Dermatol. 2012;11(7):846-851.*** ***Pelgrift R, and Friedman A. "Nanotechnology as a Therapeutic Tool to Combat Microbial Resistance". Adv Drug Deliv Rev. 2013 Jul 24. Doi:pii:S0169-409X(13)00165-8.*** ***"Nanomedicine in Drug Delivery". Ed. Kumar, Mansour, Friedman and Blough. CRC Publishing LLC. 2013, 450p.*** **Core Competencies:2,3,6**
The Future of Dermatology Practice Steven Grekin, DO, FAOCD	Objectives: 1. Discuss recent and anticipated changes made to healthcare policy. 2. Discuss the effects that these changes may have on the dermatology practice. 3. Discuss methods for which these changes can be accommodated in the dermatology practice. Needs: 1. Legislative, regulatory, or organizational changes effecting patient care ***References:*** http://www.ama-assn.org/ama/pub/physician-resources/solutions-managing-your-practice.page? **Core Competencies:3,4,5**

Dermatology Update Amy Spizuoco, DO, FAOCD	Dermatopathology is a fundamental aspect of the practice of dermatology and this review will help to ensure practitioners understand and review current diagnostic guidelines and protocols ultimately to improve diagnostic skills of the physician. Objective: 1. Increase clinician's awareness of subtle findings in common lesions. 2. Recognize and identify certain patterns that can assist in formulating a diagnosis. 3. Improve the ability to combine histological and clinical information to render a diagnosis. Needs: 1. New methods of diagnosis or treatment. 2. Development of new technology. 3. Advances in medical knowledge. ***Reference:*** ***Rapini Practical Dermatopathology; 1st Edition*** **Core Competencies:2,3**
Resident Lectures	Dermatology often is an anecdotal specialty when it comes to rare diseases and rare manifestations of common disease states. Communication between colleagues often helps even with the most challenging cases. Having seen types of these reviews sometimes help isolated dermatologists who otherwise do not have access to seeing such cases. 1. Understand critical aspects of unusual cases and how to distinguish them from routine disease process. 2. Recognize situations where unusual testing modalities such as electron microscopy are of utility. 3. Communicate effectively with other disciplines in complex cases so as to facilitate patient care. www.aocd-grandrounds.org **Core comp - 2,4,5,6,7** During the resident's third year of training, one of the above manuscripts or papers must be presented as a 20 minute lecture at the AOCD annual or midyear meetings. This presentation is considered a major presentation and should be referenced and of professional quality. Basic Standards for Residency Training in Dermatology Revised, BOT 8/2012

The American Osteopathic College of Dermatology's Current Concepts in Dermatology

(Program #698100)

is recognized by the American Academy of Dermatology

for 26.5 AAD Recognized Credits and may be used toward the AAD CME Award.

American Osteopathic Association

142 East Ontario Street

Chicago, IL 60611

CME Guide for Osteopathic Physicians – 2013-2015

CME Requirements

All members of the American Osteopathic Association (AOA), other than those exempted, are required to participate in the Continuing Medical Education (CME) program and to meet specified CME credit hour requirements for the **2013-2015 CME cycle.**

One hundred and twenty credits of CME are required for membership in the American Osteopathic Association within this three-year cycle. Of this total, thirty CME credits must be obtained in Category 1-A- and the remaining ninety credit hours of the CME requirement may be satisfied with either Category 1-A, 1-B, 2-A, or 2-B credits. Physicians entering the program in mid cycle will have their credit requirements prorated. Your individual CME Activity Report outlines your total CME requirement and the amount of credits required in categories 1 and 2.

Members who obtain one hundred and fifty credits or more of AOA approved applicable CME credit in a three-year CME cycle will be given a certificate of excellence in CME. These hours must be earned by December 31ST, but reported no later than May 31st of the current CME cycle.

In recognition that members of the AOA who hold specialty or subspecialty certificates in those specialties with less than three hundred certificate holders, may have difficulty accruing the necessary AOA 1-A credits required for membership, such members may apply AMA or AAFP category 1 credits to their AOA 1-A credit requirement up to the maximum of 15 CME credits per cycle to meet the Category 1-A credit requirement for membership. To qualify for AOA Category 1-A CME credit under this policy the following criteria must be met:

1. Osteopathic physicians must be a member of the AOA
2. Physicians' must be AOA and/or ABMS certified
3. The specialty/subspecialty must be listed as a qualifying specialty

Lists of specialties and subspecialties with less than 300 certified members are available on the Website at www.osteopathic.org. This policy does not apply to Certificate of Added Qualification (CAQ's) or ABMS subspecialty which is equivalent to the AOA CAQ.

For eligibility in this program, contact your certifying board. Specialty colleges may petition the CCME to have members exempted from the current policy of allowing DOs with less than 300 DOs boarded in that specialty, to use 15 AMA credits as AOA 1-A credit. If the specialty college feels that they are offering sufficient quality programs to meet the physicians needs each CME cycle, specialty colleges can request an exemption from this policy with a detailed report of identified courses.

Note this only applies to the AOA thirty Category 1-A membership requirement. For credits required for certification see section IX, CME requirement for certified physicians, or contact your specialty certifying board.

The acceptance of AMA, AAFP, or credits from any other certifying body by the CCME in order to fulfill AOA CME requirement does not convert said credits to AOA credits.

The AOA assigns CME credit to four categories: 1-A, 1-B, 2-A, and 2-B.

I. Category 1-A Credit

AOA Category 1-A credits will be granted to attendees for formal educational programs designed to enhance clinical competence and improve patient care. These programs must be sponsored by an AOA accredited Category 1 CME sponsor and are limited to:

A. Formal Osteopathic CME

- Consisting of formal face-to-face programs that meet the Category 1 quality guidelines, faculty requirements, and which are sponsored by AOA-accredited Category 1 CME sponsors.

- Topics must be related to any of the seven (7) Core Competencies listed below, as the core competencies have been recognized throughout the continuum of osteopathic education as essential and critical to the development and maintenance of osteopathic physicians overall education.

- Seven (7) Core Competencies:
    1. Osteopathic Philosophy/Osteopathic Manipulative Medicine – Demonstrate and apply knowledge of accepted standards in osteopathic manipulative treatment appropriate to the specialty. Remain dedicated to life-long learning and to practice habits in osteopathic philosophy and OMM.

    2. Medical Knowledge - Demonstrate and apply knowledge of accepted standards of clinical medicine in the respective area; remain current with new developments in medicine and participate in life-long activities.

    3. Patient Care - Demonstrate the ability to effectively treat patients and provide medical care that incorporates the osteopathic philosophy, patient empathy, awareness of behavioral issues, the incorporation of preventive medicine and health promotion.

    4. Interpersonal and Communication Skills - Demonstrate interpersonal and communication skills that enable a physician to establish and maintain professional relationships with patients, families, and other members of health care teams.

    5. Professionalism – Uphold the Osteopathic Oath in the conduct of one's professional activities that promotes advocacy of patient welfare, adherence to ethical principles, and collaboration with health professionals, life-long learning, and sensitivity to a diverse patient population; be cognizant of physical and mental health in order to effectively care for patients.

    6. Practice-Based Learning and Improvement - Demonstrate the ability to critically evaluate methods of clinical practice, integrate evidence based medicine into patient care; show an understanding of research methods; improve patient care practices.

7. Systems-Based Practice – Demonstrate an understanding of health care delivery systems; provide effective and qualitative patient care with the system; and practice cost effective medicine.

B. Osteopathic Medical Teaching

Physicians who deliver formal osteopathic medical education in a didactic format are eligible to receive Category 1-A credit on an hour-for-hour basis. Methods of such education are limited to:

1. Formal delivery of osteopathic medical education lectures in colleges of osteopathic medicine.

2. Formal delivery of osteopathic medical education to students, interns, residents, and staff of AOA approved healthcare facilities. Teaching credit must be submitted by the CME Department of an AOA-accredited Category 1 CME college of osteopathic medicine or Category 1 CME sponsoring hospital.

C. Standardized Federal Aviation Courses

The Federal Aviation Administration "Aviation Medicine" course and the United States Armed Services, "Flight Surgeon Primary Course", are eligible for Category 1-A credit.

D. Federal Programs

AOA Category 1-A credit will be awarded for formal CME programs to participants who are on active duty or employed by a uniformed service. Category 1-B will be awarded to all other federal CME activities.

E. Grand Rounds

Grand rounds will be considered for AOA Category 1-A credit when submitted as, a series of at least three programs, as opposed to being submitted on a lecture-by-lecture basis. The Category 1 CME Sponsor must meet the Accreditation Requirements to award AOA Category 1-A credit.

F. Judging Osteopathic Clinical Case Presentations and Research Poster Presentations

Osteopathic physicians serving as formal judges for osteopathic clinical case presentations and research poster presentations at a formal CME function will be awarded AOA Category 1-A credits on an hour-for-hour basis up to a maximum of ten credits per AOA 3-year CME cycle.

II. Category 1-B Credit

Category 1-B credit will be awarded for the following:

A. Publications, Inspections, Examinations, and Committee Meetings

Development and publication of scientific papers and electronically communicated osteopathic educational programs; serving as an osteopathic healthcare facility, college accreditation, internship, residency or OPTI surveyor or consultant; conducting, and developing certifying board examinations; participating on an osteopathic state licensing professional review board; and for healthcare committee and departmental meetings which review and evaluate patient care whether the committee work is in an osteopathic or allopathic institution.

B. Osteopathic Preceptoring

Osteopathic physicians serving as preceptors in any AOA approved osteopathic medical education program may be granted Category 1-B credit**.**

A maximum of sixty AOA Category 1-B credits for preceptoring may be applied to the 120-hour requirement.

Osteopathic Physicians that teach/preceptor osteopathic residents regardless of the institution residency affiliation may be granted Category 1-B credit. To obtain credit in non AOA accredited institution/hospitals the Program Director or DME must send a signed evaluation to the Division of CME verifying the teaching activity.

No credit is available for preceptoring physician assistants, nurse practitioners, or allopathic medical students.

C. Certification Examination Credit

Fifteen Category 1-B credits will be awarded to AOA members who pass an AOA recertification examination or obtain a certification of added qualification.

D. Activities in Non-AOA Accredited Institutions

Category 1-B will be granted to osteopathic physicians who participate in non-AOA accredited institution/hospital activities such as: hospital staff activities, educational lectures, and lecturing when the institution/hospital is an AOA recognized associate institution/hospital that trains osteopathic students, interns and/or residents. Under this rule, a non-AOA accredited institution/hospital is defined as an institution/hospital that is directly associated with an OPTI for purposes of training osteopathic students, interns and/or residents. Accreditation of the hospital/institution by the Healthcare Facility Accreditation Program, HFAP, of the AOA is not required.

E. Non-Osteopathic CME Programs

The Council on Continuing Medical Education may recognize allopathic specialty or subspecialty programs for Category 1-B credit, when there is essentially no equivalent course content available within the osteopathic profession and that such recognition will apply to all physicians in that specialty or subspecialty. These courses must be provided by an AMA accredited provider, be AAFP approved, or provided by an internationally known sponsor acceptable to the CCME.–A program is defined as a program of 3 credits or more. Home study activities/courses do not qualify under this policy.

To request consideration of a non-osteopathic course for Category 1-B credit, write to the Division of CME at AOA Headquarters in Chicago and provide a copy of the Non-osteopathic programs - Category 1B form, available at www.osteopathic.org, along with the printed program (or syllabus) and documentation of attendance. Recommendations for accepting Category 2-A as Category 1-B will be sent to the Category 1 sponsor (Specialty College) designated staff, from the AOA Division of CME. The designated staff must provide documented evidence that the specialty was covered in their program agenda. The designated staff must sign their verification and submit the documentation to the CCME for review in its deliberations.

The AOA performs reviews of such courses as a member service. Whereas, non-members who request AOA Category 1-B credit for allopathic sponsored CME

programs must submit an application fee of $25.00 and a $10.00 processing fee for each program submitted for review.

F. Journal Reading

Osteopathic physicians can earn two credit hours of AOA Category 1-B credit for reading the Journal of the American Osteopathic Association (JAOA) and other osteopathic journals approved by the CCME and passing the respective CME quiz with a minimum grade of 70%.

The reading of medical journals qualifies for AOA Category 2-B credit and is awarded a ½ credit for each journal article read and quiz successfully completed. Non-members who forward hard copies of completed quizzes to the AOA Division of CME will be charged a fee of $25.00 per *JAOA* quiz for staff time to grade, record and provide a letter to the DO as documentation.

G. Test Construction, Committee Work

1. Formal
   a. Test construction committee work will be awarded Category 1-B credit for meeting of a seminar, meeting of an AOA official certifying board, or an AOA practice affiliate's postgraduate in-service examination committee, or at a meeting of the National Board of Osteopathic Medical Examiners.

   b. Ten Category 1-B credits will be awarded for administering the oral and practical examinations. Also, these credits may be awarded for specialty continuing medical education (CME) up to the maximum of ten credits per CME cycle.

2. Informal
   a. One Category 1-B credit will be awarded for each test item written, with a maximum of ten credits per cycle, when submitted to an AOA official certifying board and/or The National Board of Osteopathic Medical Examiners.

   b. Two Category 1-B credits will be awarded, with a maximum of twenty credits per cycle, for clinical cases developed and submitted to the National Board of Osteopathic Medical Examiners and osteopathic board examinations.

Credit will not be awarded for meetings that are primarily administrative in nature.

III. Category 2-A Credit

A. Category 2-A includes formal educational programs that are AMA accredited, AAFP approved, an internationally known sponsor acceptable to the CCME, or sponsored by AOA-accredited Category 1 CME Sponsors that do not meet the 1-A faculty/hours requirement for Category 1-A credit.

Category 2-B Credits

B. Category 2-B credit also shall be awarded for: the preparation and presentation of scientific exhibits at a county, regional, state, or national professional meeting (ten credits per scientific exhibit); home study; reading medical journals; viewing non-osteopathic medical video and audio tapes and cassettes; journal type CME on the Internet; faculty development; physician administrative training; quality assessment

programs; observations at medical centers; courses in medical economics; CME programs on the Internet; risk management programs that are administrative in nature; programs dealing with experimental and investigative areas of medical practice, and ABMS recertification examination or a certificate of added certification (fifteen credits). Five credits may be granted for reading medical textbooks. A copy of the home study form may be found at www.osteopahtic.org.

IV. CME on the Internet

Osteopathic physicians may earn up to a maximum of 9 credits of their Category 1-A requirement from interactive Internet CME (i.e., up to nine Category 1-A CME credits for members with a requirement of thirty Category 1-A credits). Category 1-A interactive Internet CME credits earned in excess of nine will be applied to the Category 1-B and Category 2-A or category 2-B CME requirements.

A. Interactive CME

Category 1-A credit will be awarded for real-time, interactive conferencing CME on the Internet or case presentations, which includes both an online pre and post test and allows the participant to ask questions of the presenter in real-time during or within 48 hours after the presentation. The CME event must meet AOA quality guidelines, the 1-A faculty/hours requirement, and must be sponsored by an AOA-accredited Category 1 CME sponsor. These courses would be considered live on the Internet.

Category 2-A credit will be awarded to real-time, interactive CME programs on the Internet that are produced by CME providers accredited by AMA or approved by the AAFP. These courses must be real-time, interactive simultaneous conferencing.

To receive credit for interactive Internet CME, osteopathic physicians must complete a CME quiz with a passing grade of 70% which includes a post-test, and the sponsor of the program must provide this information to the AOA, along with the category and number of CME credits requested. A quiz may be taken a maximum of three times to achieve a passing grade of 70%, this includes two retakes if the quiz is failed initially.

B. Non-Interactive CME

Category 1-B credit will be awarded to audio and video programs on the Internet sponsored by AOA-accredited Category 1 CME sponsors. These courses are typically programs that are available on an on demand schedule and are not a real-time, interactive simultaneous conference.

Category 2-B credit will also be awarded to journal-type CME on the Internet that is produced by an AOA-accredited sponsor, AMA sponsor, or approved by the AAFP. These courses are essentially static, textbook type programs. They may have hypertext jumps to help the reader pursue specific information.

The AOA Council on CME reserves the right to evaluate each interactive CME Internet program and activity and to deny CME credit at its discretion.

V. Specific Course Credits and Limitations

Risk management and managed care programs will be awarded Category 1-A, 1-B, 2-A, or 2-B credit based on the standard CME classifications with the following exceptions:

A. Risk Management Programs

1. Risk management programs will be granted Category 1-A credit if they are clinical in nature, sponsored by an AOA-accredited Category 1 CME sponsor, and meet the 1-A faculty/hours requirement for AOA Category 1-A credit.

2. Risk management programs will be granted Category 2-A credit if they are clinical in nature sponsored by an AOA-accredited Category 1 CME sponsor but do not meet the 1-A faculty/hours requirement; are sponsored by an AMA-accredited organization; or an AAFP-approved program.

3. Risk management programs will be granted Category 1-B credit if they are administrative in nature and sponsored by an AOA-accredited Category 1 CME sponsor.

4. Risk management programs will be granted Category 2-B credit if they are administrative in nature and are provided by an AMA-sponsor or AAFP-approved.

5. A maximum of five CME credits may be earned for risk management courses per year.

B. Managed Care Programs

1. Managed care programs will be granted Category 1-A if they are sponsored by an AOA-accredited Category 1 CME sponsor and meet the 1-A faculty/hours requirement for AOA Category 1-A credit.

2. Managed care programs will be granted Category 1-B credit, if they are sponsored by an AOA-accredited Category 1 CME sponsor and the program does not meet the AOA Category 1-A faculty/hours requirement.

3. Managed care programs will be granted Category 2-A credit if they are sponsored by an AMA-sponsor or AAFP-approved.

4. A maximum of five CME credits may be earned for managed care courses per year.

VI. CME Credit for Standardized Life Support Courses

The following standardized life support courses including provider, refresher and instructor will be awarded AOA Category 1-A CME credit up to a maximum of 8 credits per three year cycle. The remainder of the credits for the standardized courses will be awarded Category 1-B CME credit up to the limits as indicated in the table below.

Course Name	Provider Course	Refresher Course	Instructor Course
Advanced Trauma Life Support	17	8	11
Advanced Cardiac Life Support	12	6	8
Basic Life Support (health care provider)	4	2	8
Pediatric Advanced Life Support (AHA)	14	8	9
Advanced Pediatric Life Support (AAP)	14	8	9
Neonatal Advanced Life Support	8	4	6
Advanced Life Support in Obstetrics	17	8	9
Fundamentals of Critical Care Support (FCCS)	14.5	14.5	14.5
Advanced HAZMAT Life Support (AHLS)	24	24	31
Advanced Burn Life Support (ABLS)	7	7	4.5
Basic Disaster Life Support (BDLS)	7.5	7.5	7.5
Advanced Disaster Life Support (ADLS)	15.5	15.5	4

Credit will be awarded for successful completion of an eligible standardized life support course as per the above table. Online standardized courses will be awarded CME credit for the practical part only.

VII. Bioterrorism Courses

Bioterrorism courses are eligible for Category 1-A credit up to a maximum of 8 credits per three year CME cycle. The remainder of the credits will be awarded Category 1-B CME credit. Self-Study or Home Study courses are not eligible for 1-A or 1-B credit.

VIII. Non-Qualified Activities

A. Volunteer Work

The AOA applauds volunteer work, but such work does not qualify for CME credit.

B. Post Graduate Studies

Studies undertaken in the quest for advanced degrees, whether master of science, master of public health, master of business administration, or doctorate, does not qualify for CME credit.

C. Medical Facility Tours

Such tours do not qualify for CME credit.

IX. CME Requirements for Certified Physicians

A. AOA Board Certified Physicians

1. Physicians who are board certified are required to earn a minimum of 50 CME credits within their specialty in each three-year CME cycle. These credits may be earned in Category 1 or Category 2. (Please see Specialty Board for clarification.)

2. Certifications of Added Qualification (CAQs). For osteopathic physicians holding certification(s) of added qualification (CAQs), a minimum of 25% of the credits (13 credits) must be earned at the level of the CAQ. At least 30% of the specialty CME credits (15 credits) must be earned in the primary certification.

3. CME sponsored by osteopathic specialty affiliates in the individual's declared specialty, will be applied to this requirement on an unlimited hour-by-hour basis.

4. CME sponsored by AOA CME Sponsors other than the individual's declared specialty affiliate may be awarded by the certifying board with jurisdiction up to a maximum of 25 credits per cycle.

B. ABMS Board Certified Physicians

1. Physicians who are both AOA and ABMS board certified are required to earn the same specialty CME credit hours as DOs who are AOA board certified only in order to meet AOA specialty requirements.

2. Physicians who are solely certified in an ABMS specialty are required to obtain a minimum of 10 Category 1-A credits in AOA sponsored CME programs during each three year CME cycle in order to meet AOA specialty requirements.

3. Physicians who are solely certified through the ABMS must meet the 120 hour AOA membership requirement.

Please contact the certifying board for information regarding the use of preceptoring or other credits towards this requirement. Osteopathic Physicians may refer to www.osteopathic.org for additional information regarding the "AOA Specialty Continuing Education (CME) Policy" regarding specialty CME program requirements.

Note: Under current AOA policy, failure to meet the AOA specialty CME requirement is interpreted as a failure to meet the individual physician's CME requirement. This could result in the loss of AOA membership and in turn result in the possible loss of certification.

X. Exemptions/Reductions

A. General

AOA members exempted from the CME program requirements include: retired members who do not hold an active license to practice medicine; AOA members outside the geographic boundaries of the United States and Canada; student members; interns, and residents; fellows; members participating in AOA recognized postgraduate programs; military members assigned positions other than in his/her specialty or who are involved in significant military operations; and disabled members. AOA Life Members in active practice have a CME requirement.

B. Osteopathic Physicians in the Military Reductions/Waivers

The council is aware of the difficulty that osteopathic physicians in the military, Veterans Administration, and U.S. Public Health Service may have in acquiring osteopathic continuing medical education. The Uniformed Services encourages

osteopathic physicians to meet his/her full obligation to CME and the AOA also believes it is essential that, as an osteopathic physician, a portion of this education should be osteopathic in nature. The AOA policy related to osteopathic physicians in the military is that five credits per year or up to fifteen of the thirty AOA Category 1A credit requirements per three-year cycle will be reduced. This reduction is available only to those physicians on active duty who have accumulated a total of one hundred and twenty credits of CME and who request said reduction from the Council on CME. The total CME requirement will be proportionally adjusted for time spent out of the United States.

Osteopathic physicians serving in the uniformed services, who are engaged in active military operations, may be granted a waiver of his/her AOA CME requirement for membership if that physician is CME deficient at the end of the current CME cycle.

Any osteopathic physician, other than career military personnel, who is called to active duty, emergency need duty, military operation, or placed on stand-by, and is CME deficient at the end of a CME cycle, may request to have his/her CME requirement waived or reduced.

C. Extenuating Circumstances

If there are extenuating circumstances that prevents a physician from obtaining sufficient credit, such as serious illness, financial, or family problems, he/she is urged to report this to the AOA Council on Continuing Medical Education and the Membership Department, as he/she may qualify for a reduction in requirements. Changes in a physician's practice status since the beginning of the CME cycle may reduce his/her AOA CME requirement. For additional information on extenuating circumstances, please contact the Director of CME at 800-621-1773, extension 8262.

AOA exemptions or reductions in the number of required credits, for membership or certification, do not pertain to individual state CME licensing requirements. The Council on CME will grant no reductions without due cause unless policy advises otherwise.

XI. Failure to meet the AOA CME Requirement – End of CME Cycle

Beginning with the current CME cycle ending Dec. 31, 2012, AOA members will have five months following the close of a cycle to fulfill his/her CME requirements. Previously, members were allowed 17 months following the close of a cycle to fulfill the CME requirement and maintain his/her AOA membership and AOA board certification. If there are any questions about the change, contact the CME Service Center at cme@osteopathic.org

Note: Under current AOA policy, failure to meet the AOA specialty CME requirement is interpreted as a failure to meet the individual physician's CME requirement. This could result in the loss of AOA membership and in turn result in the possible loss of certification.

XII. Reporting CME Activities

To report AMA or AAFP CME programs, a certificate of attendance must be provided to the AOA Division of CME indicating the total number of hours attended. Reporting of AOA CME credit is the responsibility of the approved AOA sponsor.

Other Questions

If there are any questions concerning the CME program or ways in which to receive, credit or questions regarding a physician's status, please contact the AOA Division of CME at 800-621-1773 Ext. 8262. In addition, the Frequently Asked Questions (FAQs) are available online at www.osteopathic.org.

The following CME Reporting forms are available at www.osteopathic.org.

1. Healthcare Facility Education Activities
2. Individual Certification
3. Home Study
4. Non-Osteopathic Programs – Category 1-B
5. Exemption/Reduction Form
6. 1-A AMA Specialty/Subspecialty

"AOA Coming Events," a listing of upcoming CME programs, are available in the Continuing Medical Education section at www.osteopathic.org.

Members may view his/her CME Activity Report (CAR) by visiting www.osteopathic.org. Additionally, CME online courses are available at this site.

The Council on CME maintains the right to update this guide as needed. The Council reserves the right to evaluate all programs and activities on an individual basis and to deny or accept CME credits at its discretion. Osteopathic physicians are responsible for remaining abreast of the rules and regulations of CME.

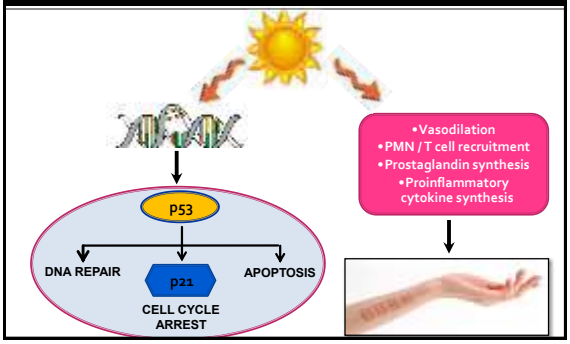
Thursday, February 20, 2014
(6.5 CME)

8:00 a.m. to 12:00 p.m.	Board of Trustees Meeting
10:00 a.m. to 12:00 p.m.	Registration
12:00 p.m. to 12:20 p.m.	*Enhancing DNA Repair in the Skin: A Pilot Study of Low-Dose Chloroquine and Ultraviolet Light* **Holly Kanavy, DO** St. Barnabas Hospital
12:20 p.m. to 12:40 p.m.	*Henoch-Schonlein Purpura in an Adult Patient* **Trey Haunson, DO** Lewis Gale Hospital – Montgomery/VCOM
12:40 p.m. to 1:00 p.m.	*A Case of Telangiectasia Macularis Eruptiva Perstans (TMEP)* **Samuel Wilson, DO** Lewis Gale Hospital – Montgomery/VCOM
1:00 p.m. to 2:30 p.m.	*2014 Dermatology Coding & Regulatory Updates – ICD10 CM Coding Education* **Faith McNicholas, CPC, CPCD, PCS, CDC, RHIT**
2:30 p.m. to 3:30 p.m.	*2013 NCCN Melanoma Guidelines – Are You Following the Standard of Care?* **John Coppola, DO, FAOCD**
3:30 p.m. to 4:30 p.m.	*Managing Psoriasis Patients across the Life Course* **Jennifer Cather, MD**
4:30 p.m. to 4:50 p.m.	*Cutaneous Polyarteritis Nodosa (CPAN) versus Macular Lymphocytic Arteritis (MLA)* **Teresa Ishak, DO** OPTI-West/College Medical Center
4:50 p.m. to 5:10 p.m.	*PSEK: Management of an Extraordinary Syndrome with Ordinary Therapy* **Michael Kassardjian, DO** OPTI-West/College Medical Center
5:10 p.m. to 5:30 p.m.	*Multisystemic Langerhans Cell Histiocytosis* **Emily Matthews, DO** West Palm Hospital
5:30 p.m. to 6:30 p.m.	*Observations and Ommisions: Pearls and Pitfalls of Facial Reconstruction* **Aaron Bruce, DO, FAOCD**

Enhancing DNA repair in the skin - a pilot study of low-dose chloroquine and ultraviolet light.

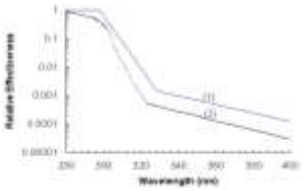
Holly Kanavy, DO
St. Barnabas Hospital

Effects of acute UV exposure in the skin



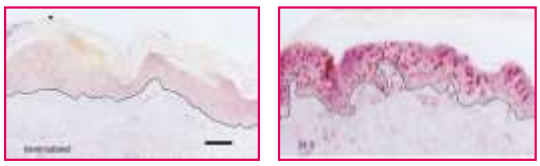
Erythema correlates with DNA Damage

- DNA is a chromophore for UV light in erythema response
- Action spectra for erythema and thymine dimer formation are nearly identical



(1)Human erythema action spectrum and (2) actinic action spectrum.
JAAD 2008; 58:S139-48

Thymine Dimers increase after UV exposure



Arch Dermatol 2002;138:1480-1485.

Chloroquine

- **clinical utility in photodermatoses**
- **Several mechanisms of action proposed**
  - **Anti-inflammatory**
    - Targets monocytes and macrophages
      - Inhibit lysosomal degradation of antigen
      - inhibit antigen presentation to and activation of CD_4+ T cells
    - Inhibits transcription of proinflammatory cytokines
      - IL-1, IL-6, and TNF-α
    - Inhibition of prostaglandin synthesis (via PLA-2)
    - Inhibit Toll-like receptors (TLR) stimulation

Lupus 2006; 15:268-275

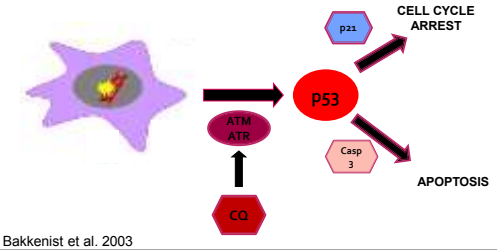
Chloroquine

- **Chloroquine may make a more effective Melanin**
  - Chloroquine has a high affinity for melanin
    - Accumulates in melanin-containing tissue (retina, skin)
    - CQ and melanin pigment colocalization in mouse studies
- **Intercalation into DNA**
  - prevent thymine dimer formation
  - lead to induction of apoptosis
    - (perceived as DNA damage)

Mol Pharmacol 1988;33:470-476
Arch Dermatol 1980;116:587-591
Zhou et al. 2002

p53 Pathway Activation

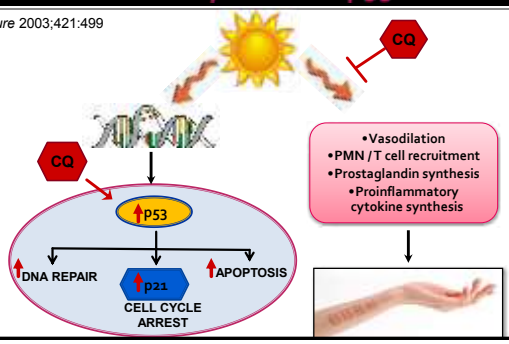
- CQ activates the DNA damage response pathway through ATM



Bakkenist et al. 2003

Chloroquine can reduce erythema and may activate p53

Nature 2003;421:499



Objectives

- Does chloroquine treatment prior to UVB irradiation result in:
  - Photoprotection (↑ Minimal Erythema Dose)
  - Upregulation of the p53 pathway
  - Decreased DNA damage
- *Is the photoprotective effect of chloroquine related to activation of p53, or are these independent effects?*

Clinical Relevance

- Incorrect repair of UVB-induced DNA damage
  → Mutations in epidermal cells
  → Skin Cancer
- Xeroderma Pigmentosum
  - rare inherited disorder characterized by an inability to repair DNA damage caused by ultraviolet light
  - 5000-fold increased risk for NMSC
  - 1000-fold increased risk for MM

Kramer, et al 2008.

Methods

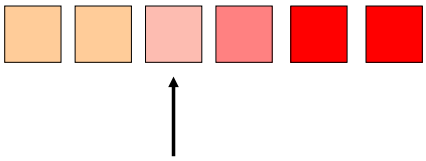
- Open label, single arm study
- 30 subjects, aged 23-60 years, Fitzpatrick skin types I and II
- Chloroquine 500 mg per week for 4 weeks
- The minimal erythema dose (MED) was determined for each subject, and skin biopsies of MED sites were obtained before and after chloroquine therapy.
- DNA damage was assessed using immunohistochemical detection of thymine dimers.
- Activation of the p53 pathway was assessed by detection of phosphorylated p53 and its downstream target p21.

Study Criteria

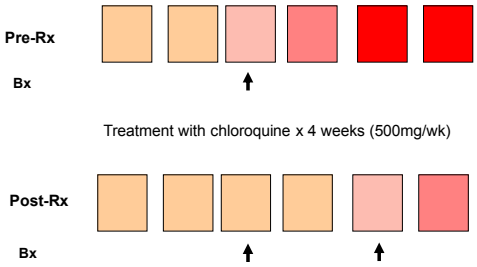
- Inclusion Criteria
  1. Skin Types I-II: skin that burns easily and tans rarely or never
  2. Age range 22-60 years
  3. Normal pre-treatment laboratory values
  4. Not pregnant and not planning a pregnancy for the duration of the study and up to 3 months after the study is completed.
  5. Willingness and ability to complete the entire study
  6. Able to understand and give written consent to participate in the study
- Exclusion Criteria
  1. Inappropriate skin type, age range, lab values
  2. Contraindication to take chloroquine:
     a) Chronic Liver Disease
     b) Renal disease
     c) Retinopathy
     d) Hypersensitivity to chloroquine
     e) G6PD deficiency
     f) Poor auditory function
     g) Drug interactions
  3. Pregnancy

Minimal Erythema Dose

- The minimal amount of UVB light that produces redness in the skin after 24 hours



Phototesting



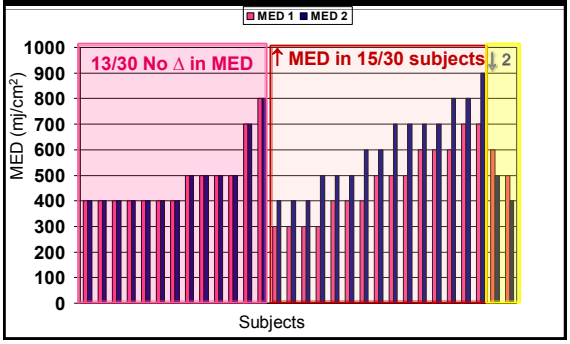
Study Endpoints

- Change in MED
- Biologic Correlates measured using IHC
  - Evidence of DNA damage
    - Thymine Dimers
  - Evidence of p53 pathway activation
    - Phospho-p53
    - p21

Results

- 30 patients
- 13 F, 17 M
- Median age 45 yrs (range 23 – 60 yrs)
- No adverse side effects reported from chloroquine treatment

MED Results

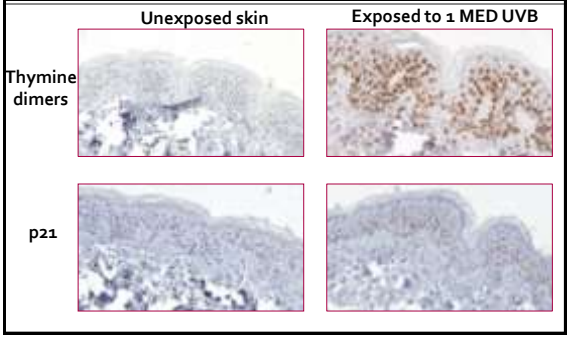


Biologic correlates

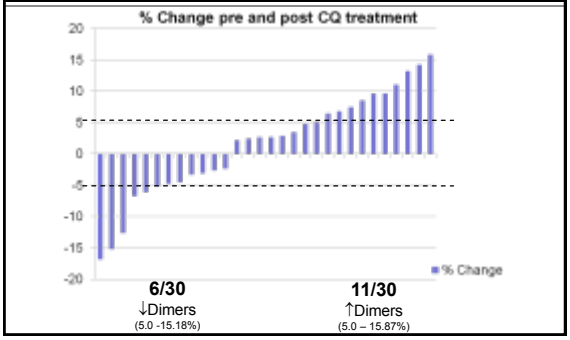
Expected Results

- If the photoprotective effect of chloroquine is related to the activation of p53, then we would expect to see more evidence of p53 pathway activation among patients exhibiting photoprotection from chloroquine (i.e. increased MED) compared to patients with no increase in MED

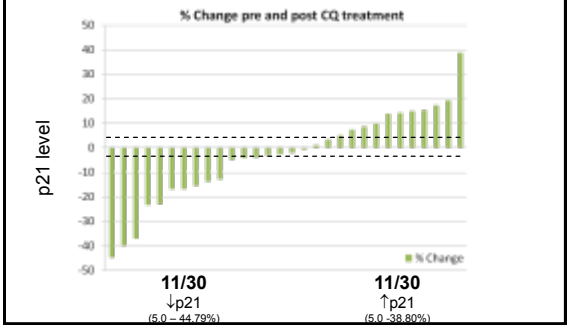
Immunohistochemistry



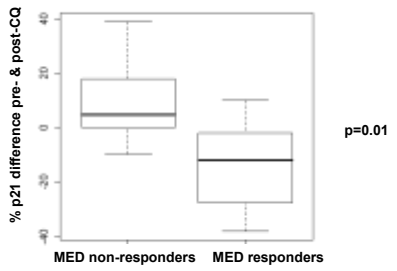
Thymine Dimers



p21



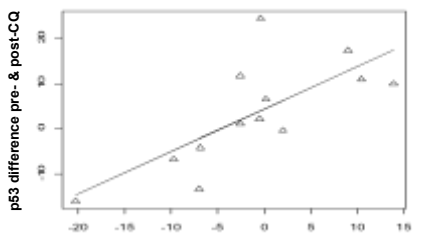
MED-responders and non-responders differ in their p21 response to chloroquine



MED non-responders exhibited greater evidence of p53 pathway activation than MED responders

- Change in p53 expression showed a positive correlation with change in p21 expression that trended toward statistical significance (r=0.48, p=0.09).
- Change in level of Thymine dimers was significantly correlated with the change in the p21 expression (r=0.6, p= 0.03)
- No correlations were seen among MED responders

Change in thymine dimers and change in p53 levels is correlated only among MED non-responders



r=0.73, p=0.005

Summary

- 50% of subjects had a positive MED response to CQ treatment (increased MED post-CQ)
- MED response to CQ appears to separate patients into 2 groups with respect to activation of the p53 pathway by CQ
- MED non-responders showed correlations between markers of p53 pathway activation
- MED responders did not show evidence of p53 pathway activation among the biologic correlates studied

Conclusions & Implications

- CQ appears to augment p53 pathway activation in the skin in response to UVB
- The effect appears to be independent of the photoprotective effect from CQ
- Additional investigation into the mechanism of action of CQ in the skin will be needed to better identify the basis of an individual patient's response to CQ.
- Oral pharmacologic agents that produce photoprotection may not necessarily improve p53-mediated DNA repair

Acknowledgements

- David Polsky, MD, PhD, NYU
- Cindy Hoffman, DO, St. Barnabas Hospital

Henoch-Schönlein Purpura in an Adult Patient

Trey Haunson, DO, PGY-4

Program Director: Daniel S. Hurd, DO, FAOCD

No financial disclosures

Objectives

- Present a case report of an adult male diagnosed with HSP
- Discuss the following, particularly as they pertain to the adult patient with HSP
  - Epidemiology
  - Pathogenesis
  - Clinical, histologic and laboratory findings
  - Differential diagnosis
  - Diagnostic criteria
  - Management
  - Prognosis

Case Presentation

- 41yo Caucasian male
  - Admitted with chief complaint of "a rash" on his legs
    - Began 1-2 weeks prior to admission
    - Lower legs → thighs, groin, buttocks, lower abdomen
  - Associated itching, burning and new-onset lower extremity swelling

Case Presentation

- Past medical history
  - Chronic lumbar arthritis
- Medications
  - Nabumetone (NSAID)
  - Prednisone
  - Amoxicillin

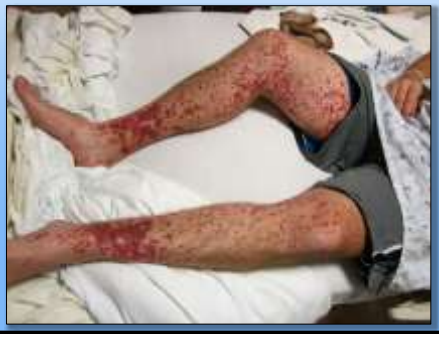
Case Presentation

- Review of systems
  - Flu-like symptoms 3-4 weeks prior to admission
  - Otherwise non-contributory
    - Denied GI symptoms
    - Stable chronic low back pain
    - No new arthralgias

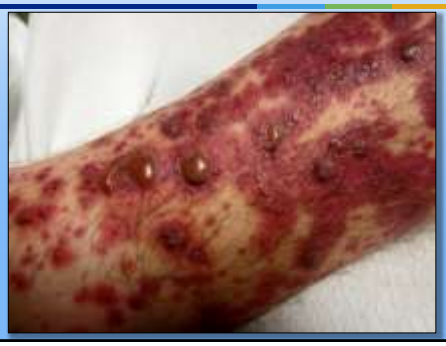
Case Presentation

- Past dermatologic history
  - None
- Past surgical history
  - None
- Family history
  - Non-contributory
- NKDA

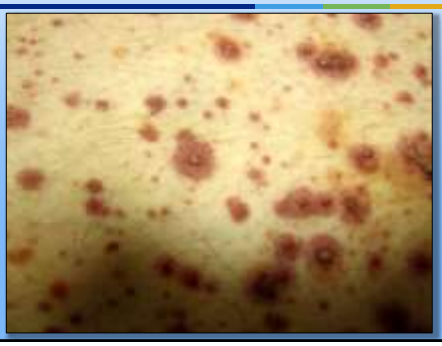
Physical Exam



Physical Exam



Physical Exam



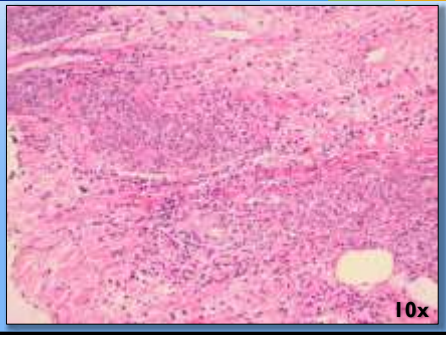
Differential Diagnosis

- Henoch-Schönlein purpura
- Leukocytoclastic vasculitis
- Erythema multiforme

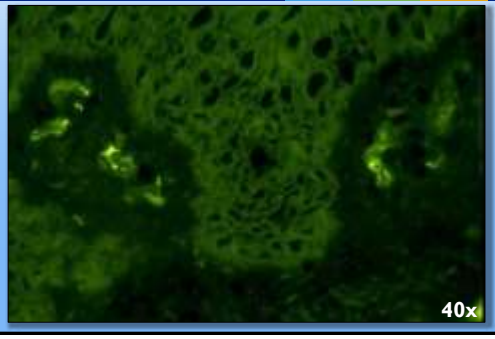
Labs

- Unremarkable
  - CBC with differential
  - PT, PTT, INR
  - CMP
  - Urinalysis
  - ASO and anti-DNase B antibody titers

Biopsy (H&E)



Biopsy (DIF)



Diagnosis

Henoch-Schönlein purpura (HSP)

Follow-up

- Completed course of amoxicillin
- Increased prednisone to 100mg/daily with a slow taper over an additional 6 weeks
- Experienced cutaneous flares 1-2 times weekly
- Dapsone initiated at 25mg daily
- Recommended follow-up with primary care for monthly BUN, creatinine and urinalysis for the next 12 months
- Continues to lack renal involvement

Discussion

A vasculitis of childhood?

- 75% are <10 years of age
- 25% are adults
  - May present atypically
  - More likely to have long-term complications

Epidemiology

- Most common vasculitis in children
  - Peak onset at age 4-7 years
- Incidence
  - Children: 135-180 per million
  - Adults: 3-14 per million
- Peak incidence in winter and spring
- Slight male predominance

Possible triggers associated with HSP*

Bacterial infections:	Viral infections:	Parasites:	Vaccinations:	Medications:	Malignancies:	Inherited:
• Group A beta hemolytic streptococci • *Staphylococcus aureus* • *Helicobacter pylori* • *Mycoplasma*	• Hepatitis A, B, E • Herpes simplex • Parvovirus B19 • Coxsackievirus • Varicella • Adenovirus • Cytomegalovirus • HIV	• *Toxocara canis*	• MMR (Measles, Mumps, Rubella) • Pneumococcal • Influenza • Meningococcal • Hepatitis B	• NSAIDs • ACE inhibitors • Angiotensin II receptor antagonists • Vancomycin • Cefuroxime • Quinolones • Clarithromycin • Acetaminophen • Codeine • Etanercept • Ranitidine • Streptokinase	• Non-small cell lung cancer • Prostate cancer • Lymphoma • Multiple myeloma	• α1-antitrypsin deficiency • Familial Mediterranean fever • HLA-DRB1*01 • HLA-B35 • ICAM-1 469 K/E

* not a comprehensive list

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* not a comprehensive list

Pathogenesis

- Often preceded by upper respiratory tract infection

Antigen-antibody complexes deposit in vessel walls

↓

Activation of alternative complement pathway

↓

Inflammatory cell activation and recruitment

↓

Vascular damage

Clinical Features

- Classic tetrad:

Palpable purpura	Abdominal pain
Arthralgias	Nephritis

Lesion Morphology

- **Non-blanching petechial macules and purpuric papules**
  - "Palpable purpura" (100%)
  - Larger ecchymotic areas
  - Hemorrhagic vesicles/bullae
  - Necrotic foci
    - 60% of adults
    - <5% of children

Lesion Distribution

- Symmetric buttocks and lower extremities
- Lesions rarely occur on the face and upper extremities
- Sparing of the trunk is typical
- Livedo reticularis or widespread lesions may indicate an underlying IgA paraproteinemia

Clinical Course

- Lesions regress within 10-14 days
  - **May relapse intermittently**
  - **Fade more quickly with bed rest**
  - **Recur more frequently and severely with ambulation**
- Complete resolution takes weeks to months

Systemic Features

- GI (50-75%)
  - Colicky abdominal pain (65%)
    - **Significant predictor of nephritis**
  - Nausea / Vomiting
  - GI bleeding (30%)
- **GI symptoms may appear prior to cutaneous lesions (25%)**

Systemic Features

- Rare GI manifestations
  - Intestinal perforation
  - Pancreatitis
  - Pseudomembranous colitis
  - Acute acalculous cholecystitis
  - Hemorrhagic ascites with serositis
  - Biliary cirrhosis

Systemic Features

- Arthralgias (>80%)
  - **More common in adults**
  - Due to periarticular edema
  - Dorsal hands, knees, ankles, feet
  - May precede skin lesions
  - Can be incapacitating
  - Non-destructive
  - Responds to NSAIDs

Systemic Features

- Nephritis
  - Common, but usually mild and self-limited
    - 40-50% of children
  - More frequent and severe in adults
    - Progression to nephritic syndrome and chronic renal failure is possible
      - 10-30% of adults
      - 1% of children

Systemic Features

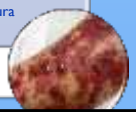
- Acute-onset dependent edema
- Fever
  - 20% of adults
  - 40% of children

Systemic Features

- Rare systemic involvement
  - Acute scrotal swelling (15% of boys)
  - Central nervous system
  - Peripheral nervous system
  - Pulmonary
  - Genitourinary tract

- Arthropod bites
- Morbilliform drug eruptions with hemorrhage in dependent sites
- Erythema multiforme
- Pityriasis lichenoides et varioliformis acuta
- Infectious emboli (septic vasculitis)
  - Infective endocarditis
  - Acute meningococcemia
  - Rickettsial infections
  - Fungi (e.g. *Rhizopus*)
- Lichenoid capillaritis (pigmented purpura)
- Papular urticaria
- Systemic lupus erythematosus
- Dermatitis herpetiformis
- Acute hemorrhagic edema of infancy
- Idiopathic thrombocytopenic purpura
- Thrombotic thrombocytopenic purpura
- Atypical cellulitis

Differential diagnosis of palpable purpura

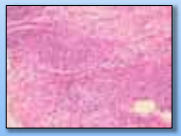


Diagnostic criteria for HSP

- **Required**
  - Palpable purpuric eruption with normal platelet levels
- **Additional (at least 1 required)**
  - Diffuse abdominal pain
  - Arthralgia
  - Nephritis (hematuria/proteinuria)
  - Histologic evidence of IgA deposits in small vessels of kidneys or GI tract

Diagnosis

- Histology
  - H&E (lesional)
    - Leukocytoclastic vasculitis of small vessels
  - DIF (perilesional)
    - Perivascular IgA, C3 and fibrin
  - Not specific for HSP
    - Clinical correlation required



Diagnosis

- Required Labs
  - Platelet count
  - Coagulation studies
  - Urinalysis
  - BUN, creatinine

Diagnosis

- Elective Labs
  - Lipase
  - ESR
  - Serum IgA
  - C3 and C4 levels
  - ANA
  - Serum immunoelectrophoresis
  - ANCA
- CBCs are typically within normal limits

Diagnosis

- Studies not routinely ordered
  - Abdominal ultrasound
  - Abdominal radiographs
  - Stool guaiac
  - Upper GI endoscopy
  - Renal biopsies

Management

- Mainly supportive
  - Acetaminophen
  - NSAIDs
- Depending on severity of renal involvement
  - Systemic corticosteroids
  - Cytotoxic agents
    - Cyclophosphamide
    - Cyclosporine
    - Azathioprine

Management

- Systemic corticosteroids
  - Effective in treating nephritis, arthralgias, abdominal pain, and reducing the duration of cutaneous lesions
    - Does not prevent latent nephritis
    - Does not prevent recurrence of new skin lesions
  - 1-2 mg/kg prednisone or methylprednisolone daily for 2 weeks with a slow taper

Management

- Less-commonly employed
  - Dapsone
  - Colchicine
  - Factor XIII
  - Plasmapheresis
  - Aminocaproic acid
  - Intravenous immunoglobulin

Prognosis

- Complete recovery is typical
  - 94% of children
  - 89% of adults
- Cutaneous recurrences in 5-10%
- Long-term prognosis largely defined by extent of renal involvement
  - **2% experience chronic renal impairment**

Risk factors for chronic renal impairment

- Adult patients
- Presenting with renal failure, nephritic or nephrotic syndrome
- Fever
- Arterial hypertension
- Elevated ESR
- Persistent purpura
- Progressively increasing proteinuria during follow-up

Criteria for nephritic syndrome

- **Required**
  - Hematuria
  - Urinary sediment with RBC casts
- **Additional Features**
  - Mild to moderate proteinuria (<3g in 24 hours)
  - Edema
  - Hypertension
  - Elevated serum creatinine
  - Oliguria (<400 mL in 24 hours)

Criteria for nephrotic syndrome

- Proteinuria (>3.5 g in 24 hours)
- Hypoalbuminemia
- Edema
- Hyperlipidemia
- Lipiduria
- Hypercoagulability

Prognosis

- **Renal involvement is unpredictable**
  - Development of latent nephritis may be delayed for weeks to months following symptom onset
  - A third of patients experience relapses for several months
  - Urinary abnormalities may persist for 2-5 years following acute nephritis (30-50%)
  - Nephritis may reappear after apparent complete recovery

Prognosis

- Long-term follow-up is necessary
  - **Monthly BUN, creatinine, and urinalysis for at least 12 months**
  - **Referral to nephrology if evidence of renal involvement**
- Girls and young women with a history of HSP are at increased risk of developing pregnancy-induced hypertension and/or proteinuria

HSP in summary

- A vasculitis of childhood
- Typically excellent prognosis
- Adult patients
  - Present atypically
  - Greater risk of long-term renal impairment
- Prognosis depends on renal involvement
  - May be delayed in onset and recurring
  - Discussed factors predictive of poorer prognosis
- Long-term follow-up necessary

HSP in summary

- Our patient
  - Adult male
  - Possible antecedent infection
  - Chronic NSAID therapy
  - Typical cutaneous features present
  - Typical systemic features absent
  - Diagnosis confirmed with biopsy
  - Currently lacks detectable renal involvement
  - Monitored for delayed-onset nephritis

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External Images

1. http://dermimages.med.jhmi.edu/images/hsp_2_070201.jpg
2. http://www.hdcn.com/symp/lund/jtimg30.jpg
3. http://upload.wikimedia.org/wikipedia/commons/2/2f/Henoch-schonlein-purpura.jpg
4. http://uvahealth.com/Plone/ebsco_images/2506.jpg

Thank you!

A CASE OF TELANGIECTASIA MACULARIS ERUPTIVA PERSTANS (TMEP)

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3RD YEAR DERMATOLOGY RESIDENT
LEWISGALE HOSPITAL MONTGOMERY
BLACKSBURG, VIRGINIA

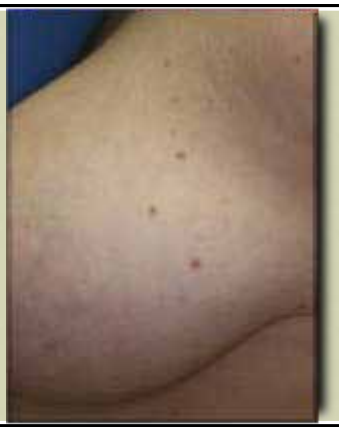
NO FINANCIAL DISCLOSURES

OBJECTIVES

- Present a case of telangiectasia macularis eruptiva perstans (TMEP)
- Discuss the etiology, pathogenesis, and clinical presentation, diagnosis, differential diagnosis, evaluation, and management of TMEP
- Examine when a bone marrow biopsy may be appropriate
- Review the serum tryptase level as it relates to systemic disease
- Recognize potential triggers and activators of disease

CASE PRESENTATION

- 20-year-old Caucasian female
- Chief complaint
  - Persistent "tan spots" on her thighs, abdomen, and chest
  - 1 year duration



CASE PRESENTATION

- Past medical history
  - Generalized anxiety
  - Rare headaches
- Dermatologic history
  - Linear scleroderma at the age of 8

CASE PRESENTATION

- Family history
  - Unremarkable
- Family dermatologic history
  - Unremarkable
- Medications
  - Xanax (alprazolam) as needed
  - Adderall (dextroamphetamine and amphetamine) as needed

PHYSICAL EXAM

- General
  - Well-developed and nourished
- Integumentary system
  - Multiple 2-3mm tan-pink, blanchable, telangiectatic macules on her breasts, abdomen, and thighs
- Physical rubbing resulted in a mild urticarial wheal (positive Darier's sign)
- Lymphatic system
  - No lymphadenopathy

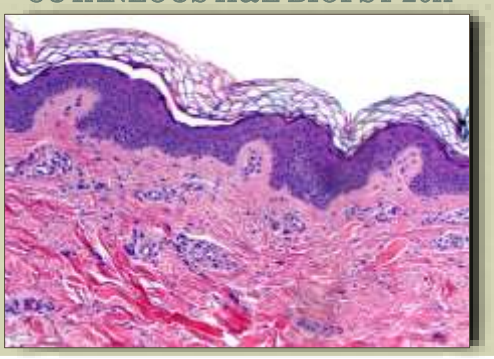
DIFFERENTIAL DIAGNOSIS?

- Post-inflammatory hyperpigmentation
- Ephilides/Lentigines
- Cutaneous mastocytosis
  - Urticaria pigmentosa
  - Telangiectasia macularis eruptiva perstans

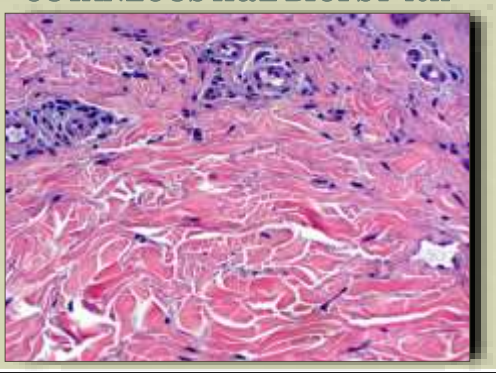
EVALUATION AND WORK UP

- Cutaneous Biopsy H&E
- CBC with differential
  - Within normal limits
- Serum tryptase
  - Withheld due to patients asymptomatic presentation

CUTANEOUS H&E BIOPSY 20X



CUTANEOUS H&E BIOPSY 40X



MANAGEMENT/COURSE

- Patient education
  - Activators and triggers of disease
- RX: Epinephrine injector (Epipen)
- Regular follow-up
  - Dermatologist
  - Primary care physician
  - Yearly CBC with differential

INTRODUCTION

- Mastocytosis
  - Rare collection of clinical disorders: both cutaneous and systemic
  - Cutaneous involvement: most prevalent
  - Increased number of mast cells in any organ system

WHO CLASSIFICATION OF CUTANEOUS MASTOCYTOSIS (CM)

Telangiectasia Macularis Eruptiva Perstans (TMEP)
Solitary Mastocytoma
Urticaria Pigmentosa • Typical • Nodular • Plaque
Diffuse Cutaneous Mastocytosis

TMEP: BACKGROUND

- Originally describe by Parkes-Weber more than 80 years ago as a variant of UP
- Rare form of cutaneous mastocytosis
- Indolent in nature
- Most common in adulthood
  - Rare cases in childhood
- May be associated with systemic involvement

PATHOGENESIS

Mutation: Codon 816V

c-KIT proto-oncogene encodes KIT (CD117) a receptor for mast cell growth factor

KIT + Mast cell growth factor

Normal mast cell development and differentiation

Pediatric mastocytosis is a clonal disease associated with D816V and other activating c-KIT mutations.

Author information

- Results
  - The entire c-Kit sequence was analyzed from cutaneous biopsies of 50 children
  - Mutation of Codon 816 (exon 17) was found in 42% of cases
  - Mutations outside of exon 17 were observed in 44%
  - All somatic and caused constitutive activation of c-kit

N Engl J Med. 1993 May 6;328(18):1302-7.

Altered metabolism of mast-cell growth factor (c-kit ligand) in cutaneous mastocytosis.

Longley BJ Jr, Morganroth GS, Tyrrell L, Ding TG, Anderson DM, Williams DE, Halaban R.

Author information

- Results
  - Patients with cutaneous mastocytosis
    - Altered distribution and production of mast-cell growth factor
    - Findings suggest that some forms of cutaneous mastocytosis represent a mast cell hyperplasia not neoplasia

TMEP: CUTANEOUS MANIFESTATIONS

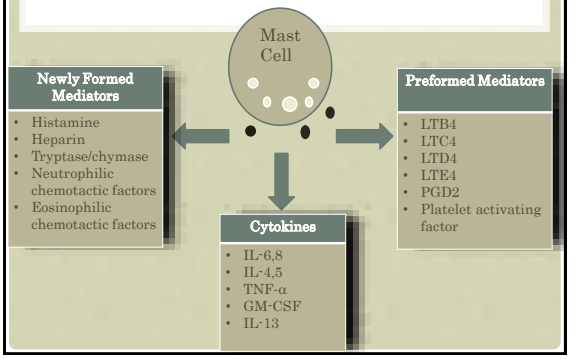
- Morphology
  - Ill-defined, erythematous telangiectatic macules with an underlying tannish-brown color
  - Size: 2-6mm
- Distribution
  - Often symmetric distribution of trunk and extremities
- Negative or subtle Darier's sign

CLINICAL PRESENTATION

- Asymptomatic/localized symptoms

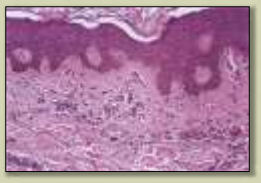
- Systemic symptoms
  - Fever
  - Unintentional weight loss
  - Flushing
  - Palpitations
  - Pruritus
  - Gastrointestinal complaints
  - Anaphylaxis
  - Bone pain
  - Dyspnea
  - Headaches

MAST CELL MEDIATORS



DIAGNOSIS

- History and physical exam
- Cutaneous biopsy
  - Giemsa, Toluidine blue, and Leder stain
  - Immunohistochemical stains: tryptase, KIT (CD117)



DIFFERENTIAL DIAGNOSIS

Cutaneous Disease Asymptomatic

- Post-inflammatory Hyperpigmentation
- Nevi
- Telangiectasia
- Ephilides/lentigines
- Pseudolymphoma
- Poikiloderma vasculare atrophicans

Systemic Symptoms

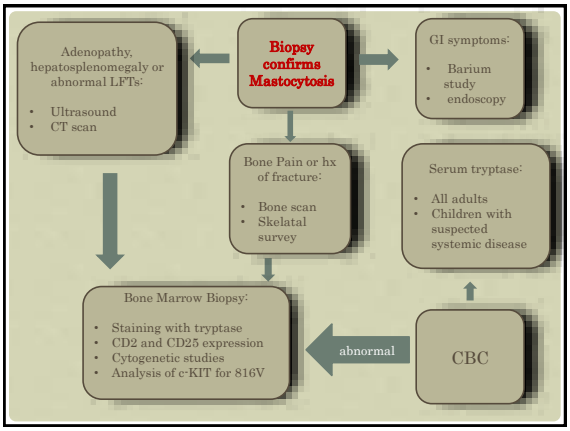
- Systemic mastocytosis
- Mast cell activation syndrome (MCAS)
- Pheochromocytoma
- Carcinoid syndrome

EVALUATION

- Complete blood count (CBC)
- Serum tryptase
- 24-Hour urinary N-methylhistamine
- Additional testing
  - Bone marrow biopsy
    - c-Kit for codon 816 mutation
    - Mast cell expression of CD2 and 25
  - GI endoscopy
  - CT imaging
  - DEXA

EVALUATION: CONTINUED

- SCORMA (SCORing MAstocytosis) Index
  (A) Percent of skin involvement
  (B) Intensity of disease
  (C) Five subjective symptoms
  Flushing, diarrhea, pruritus, bone pain, and having specific triggers
- A/4 + 5B + 2C/5
- Thought to be comparable to serum tryptase




Guidelines and diagnostic algorithm for patients with suspected systemic mastocytosis: a proposal of the Austrian competence network (AUCNM).

Author information

ADULT PATIENTS WITH CUTANEOUS MASTOCYTOSIS

- A bone marrow biopsy is recommended independent of the clinical course, symptoms, and serum tryptase level
- Even if no *KIT* mutation in the skin and/or peripheral blood is detectable
- Even if the serum tryptase level is normal: bone marrow biopsy is usually recommended.
- Increasing serum tryptase level or elevated tryptase (> 100 ng/mL) or other clinical or laboratory signs of a systemic neoplastic process (e.g. organomegaly), a bone marrow biopsy is required, even in children

SERUM TRYPTASE

- Main Component of the mast cell secretory granules
- Most patients that develop systemic disease have levels > 20ng/ml
- Tryptase level of 75 ng/ml: 100% positivity for systemic disease
- Tryptase levels 20-75 ng/ml: 50% positivity
- May be used as a marker for mast cell burden
- One of the minor criteria for the diagnosis of systemic mastocytosis

WHO CRITERIA SYSTEMIC MASTOCYTOSIS

ONE MAJOR AND 1 MINOR **OR** 3 MINOR

Major

- Multifocal dense infilrates of mast cells (aggregates of ≥ 15 mast cells)
- Bone Marrow or extracutaneous tissue

Minor

- > 25% of mast cells in BM or extracutaneous tissues are spindled or atypical
- Mast Cells (CD117+) express CD2, CD25 or both
- Presence of c-Kit codon 816 mutation in blood, BM, or extracutaneous tissues
- **Serum tryptase persists >20ng/ml**

MANAGEMENT

- Symptomatic relief
  - H1 antagonists
  - Oral Disodium Cromoglycate
  - Leukotriene antagonists (montelukast)
  - Topical corticosteroids
  - 585-nm flashlamp-pumped pulse dye
  - Epinephrine injector (epipen)
  - Medical alert bracelet
- Avoidance of triggers

POTENTIAL TRIGGERS AND ACTIVATORS OF MASTOCYTOSIS

Known Mast Cell Releasing Triggers

Ethanol
Psychological/Emotional stress
Physical exercise
Bacterial toxins
Food allergens (e.g., shellfish, peanuts)
Immunologic stimuli (e.g., IgE)
Solar radiation
Hot/cold temperature extremes
Venoms (e.g., hymenoptera)
Pharmaceutical agents:

- Acetylsalicylic acid
- d-Tubocurarine
- Dextromethorphan
- Gallium
- Iodine-based contrast dyes
- Narcotics (e.g., morphine, meperidine, codeine)
- Nonsteroidal anti-inflammatory drugs
- Polymyxin B

Adapted from Watkins CE, Bokor WB, Leicht S, Youngberg G, Krishnaswamy G. Telangiectasia macularis eruptive perstans: more than skin deep. Dermatology Reports. 2011; 3(1)

MANAGEMENT

- Aggressive or severe systemic mastocytosis
  - Radiation
  - Interferon-α-2β Chemotherapeutics
  - Imatinib (Gleevac)

SUMMARY: TMEP

- Rare form of cutaneous mastocytosis
- Indolent in nature
- Management
  - Controlling symptoms
  - Avoidance of triggers
- Identifying patients with underlying systemic involvement is key
  - Serum tryptase
  - Bone marrow biopsy?
- Frequent follow-up, and yearly monitoring of CBC, serum tryptase, and 24-hour histamine has been advised

SUMMARY: OUR PATIENT

- Remains asymptomatic
- Advised to follow up with her PCP and dermatologist on a frequent Basis
- Yearly CBC with differential
- If symptoms develop, further evaluation will be completed

ACKNOWLEDGMENTS

- Daniel S. Hurd, DO, FAOCD
- Allison K. Divers, MD, FAAD
- Colleagues
- The Patient

THANK YOU

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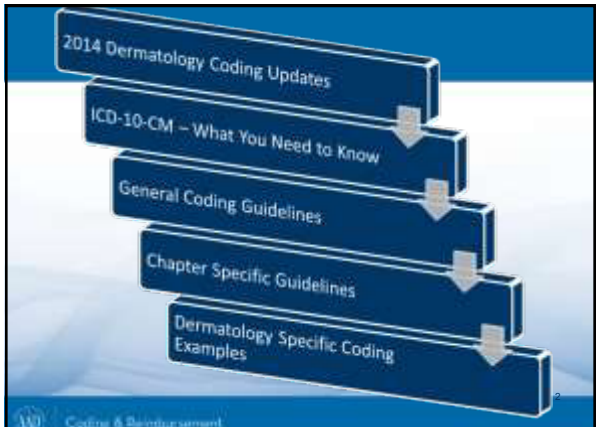
2014 Dermatology Coding Updates

ICD-10-CM
Conventions and Guidelines

Faith C. M. McNicholas, RHIT, CPC, CPCD, PCS, CDC
Manager – Coding & Reimbursement
ICD-10-CM/PCS Expert

American Osteopathic College of Dermatology (AOCD)
Mid-Year Meeting
Dallas, TX

February 20-23, 2014



The News!

- ✓Incident to according to state laws?
- ✓Tele health changes in the wind
- ✓2014 Fee Schedule with SGR fix
  - ➢Practice Expense (PE) decrease by 5% or more
- ✓ Conversion factor increased **5.2%**
  - ➢ 34.0230 to 35.8228

2014 MPFS News

The Good News:

- ➢ 21% MPFS reduction averted until 03/21/14
- ➢ Conversion factor increased by 4.8% from **2013** - $34.0232 to **2014** - $35.8228

Now the Bad News:

- ➢ Practice Expense (PE) decrease by 5% or more

2014 Fee Schedule
http://cms.gov/Medicare/Medicare-Fee-for-Service-Payment/FeeScheduleGenInfo/index.html

2014 Coding Changes

CPT Changes effective January 1, 2014

Revision: Soft tissue

- ➢ 21015 though 26047 - Radical resection of tumor (e.g., ~~malignant neoplasm~~ sarcoma), soft tissue…

New code:

- ➢ **+ 15777** - Implantation biologic implant (e.g., acellular dermal matrix) for soft tissue reinforcement (ie breast, trunk) (list separate in addition to code for primary procedure

ICD 9 & ICD10 Diagnostic Changes effective Oct 1, 2013

- ➢ None – All Diagnoses codes are frozen until 2015

2014 CPT Musculoskeletal Revisions:

- Excision of Subcutaneous soft connective tissue tumors (including repair)
- Originally revised in 2010
- **Now – emphasis**: Codes intended for use for connective tissue tumors and not melanoma
  - Revised guidelines to emphasize that such codes are reserved '***for simple or marginal resection of tumors confined to subcutaneous tissue below the skin but above the deep fascia……' For excision of benign lesions of cutaneous origin (eg, sebaceous cyst), see 11400 - 11406***

AMA CPT Changes to Complex Repair

Effective January 1, 2014 AMA CPT Changes:

► **(~~13150~~ has been deleted)** ◄

► (For 1.0 cm or less, see simple or intermediate repairs) ◄

▲ **13151** Repair, complex, eyelids, nose, ears and/or lips;1.1 cm to 2.5 cm

▲ **13152** 2.6 cm to 7.5 cm

+▲13153 each additional 5 cm or less (List separately in addition to code for primary procedure)

(Use 13153 in conjunction with 13152)

To avoid Duplicate Claim Denials

➢ **Modifier –76** should be appended to procedure(s) or surgical service(s) to indicate a repeat procedure/surgery was performed on the same day for patient management purposes.

Example: 11401, 11401-76

➢ **Modifier –91** should be appended to laboratory procedure(s) or service(s) to indicate a repeat test or procedure performed on the same day for patient management purposes.

Example: 88305, 88305-91

Mohs Surgery LCD changes

- **CGS** (J15) L31877
  When billing for MOHS on the trunk or extremities, please insert one or more of the qualifying terms in the notepad of the electronic claim.
- **Noridian** (JE & JF) L 24331 & L33475
  That description should include depth of invasion, pathological pattern, cell morphology, and, if present, perineural invasion or presence of scar tissue. (MLN SE1318)
  - Includes clarification on reporting 2nd day MMS
- **Novitas** (JL) L27503
  MMS for the trunk, arms and legs is not medically necessary except in the lesions and clinical conditions noted below…

Reporting Tip: MMS second day

- If Mohs surgery on a single site cannot be completed on the same day, report 17311 as primary code for the following day

http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE1318.pdf

MMS LCD 31877

➢ **Associated Information:** patients medical record must contain documentation that fully supports the medical necessity for services included within LCD.

➢ (See "Indications and Limitations of Coverage.")

✓ When billing for MOHS on the trunk or extremities, please insert one or more of the qualifying terms in the notepad of the electronic claim.

✓ Documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Undated CMS MLN: SE1318

MMS Documentation Requirements (Noridian: JE & JK)

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

http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/downloads/SE1318.pdf

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Coding & Reimbursement

2014 Pathology Coding Updates

▲ **88342** Immunohistochemistry or immunocytochemistry, each separately identifiable antibody per block, cytologic preparation or hematologic smear; first separately identifiable antibody per slide

● **+ 88343** each additional separately identifiable antibody per slide (list separately in addition to code for primary procedure

(Use 88343 in conjunction with 88342)
(When multiple antibodies are applied to the same slide, use one unit of 88342 for the first separately identifiable antibody and one unit of 88343 for each additional separately identifiable antibody)

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Coding & Reimbursement

2014 New G Codes!

CPT code	Medicare G Code	National Allowable
88342	G0461	88.04
88342/TC	G0461/TC	57.39
88342/26	G0461/26	30.65
+ 88343	G0462	68.08
+ 88343/TC	G0462	55.61
+ 88343/26	G0462	12.48

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Coding & Reimbursement

Interprofessional Telephone/Internet Consultation Codes 99446 - 99449

Check directly with your payer for coverage guidelines

- **What is it:** Non-face-to-face assessment and mgt service by physician/QHP with specialty expertise
- Typically provided in complex and/or urgent situations that do not allow for timely face-to-face service e.g. geographical distance
- **Who can report**: physician/QHP with specific specialty expertise who
  - Has had no face-to-face encounter in the last 14 days with patient
  - Cannot accept transfer of care until after the telephone/internet consultation
- **Who is the patient**: New and/or established patients to consultant
  - If established (must not have had encounter with physician/QHP within the last 14 days)

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Coding & Reimbursement

Interprofessional Telephone/Internet Consultation Codes 99446 - 99449

- **What is included**: Review of pertinent records, lab and imaging studies, medication profile as well as pathology specimen
- <50 percent of the time devoted to medical consultation (verbal/internet)
- Do not report if consultation less than 5 mins or sole purpose is to transfer care
- **Documentation requirements**: Written/verbal request by treating physician/QHP
- Reason for request
- Verbal opinion
- Written report from the consultant to the treating physician/QHP

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Coding & Reimbursement

CMS Revalidation: Again!

What is the Revalidation Project - how will it affect you?

✓ The revalidation project is an effort by CMS, mandated by Section 6401(a) of the Affordable Care Act, to verify all information on file for existing Medicare Providers, and to ensure they meet all standards associated with the new screening criteria

✓ Approximately 1.5 Million Providers & Suppliers must be revalidated by **March 25, 2015**

✓ Sometime in the next 24 months you will receive a request to revalidate the information on your Medicare enrollment(s)

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Coding & Reimbursement

Any practice changes, check if CMS needs an update

Medicare Enrollment Policy updates relate to:

- Correspondence addresses;
- Out-of-state practice locations;
- Submission of Change of Ownership (CHOW) applications after an initial or CHOW application has been submitted;
- Scope of revocations & re-enrollment bars

MLN Matters® Number: MM8019

http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/MM8019.pdf

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Coding & Reimbursement

'Incident-to'

- Per Medicare – provider must be in office suite, immediately available
- Supervision continuous but physical presence of physician not required at all times
- Medicare: Check with state law or commercial carrier for specific direction
- Check with commercial carrier for direction

http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c15.pdf

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Coding & Reimbursement

OIG Makes Case for E/M Audits

Office of Inspector General's ***Coding Trends of Medicare Evaluation and Management Services***

- ✓ "E/M services have been vulnerable to fraud and abuse."
- ✓ CMS payments increased 48% from 2001 to 2010 to $33 billion
- ✓ Providers are required to **report the overpayment within 60 days of identification and refund the overpayment within the same 60 day period.**

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Coding & Reimbursement

2014 Diagnosis Changes

October 2013 to 2014

- NO ICD-9 or ICD-10 Diagnostic Changes
  - **All diagnoses codes are frozen**

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Coding & Reimbursement

AAD 2014 Coding Tools

- New and revised AMA CPT® procedure, ICD-9-CM diagnosis, and HCPCS codes
- Coding tips to ensure accurate code utilization
- PQRS, e-prescribing, and EHR incentive updates
- ICD-10-CM implementation overview with code crosswalks and examples
- Recovery Audit Contractor (RAC) Audit tools

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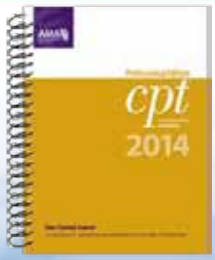
Coding & Reimbursement

2014 Coding Tools



Effective 01/01 every year

Effective 10/01 every year

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Coding & Reimbursement

CMS CONFIRMED

➢ **Go Live Date:**

Tuesday, October 1, 2014

➢ In the meantime:

✓ **CMS to host 'End to End' ICD10 Testing**

❖ **March 3 – 7, 2014**

http://www.cms.gov/Regulations-and-Guidance/HIPAA-Administrative-Simplification/Affordable-Care-Act/End-to-End-Testing.html

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Coding & Reimbursement

ICD10: What to Do Now!

- Transition education needed NOW on ICD10 guidelines & code sets
- Dual coding system after April 1, 2014 will enhance proficiency
  - ➢ Code one batch per week prior to "go live" date
- Network with peers to seek answers to coding scenarios using ICD-10-CM codes
- CMS to update all LCDs with ICD10 diagnoses by Mid April

MedLearn MM8348

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Coding & Reimbursement

ICD-10 Info Web Sites

NCHS Classification of Diseases, ICD-9 & ICD-10-CM
http://www.cdc.gov/nchs/icd.htm

Centers for Medicare and Medicaid Services, ICD-10-CM
https://www.cms.gov/ICD10/

American Academy of Professional Coders
https://www.aapc.com/ICD10

American Academy of Dermatology
http://www.aad.org/ICD10/

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Coding & Reimbursement

Why replace ICD-9?

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Coding & Reimbursement

ICD-9-CM Lacking…..

- Sufficient specificity and detail
- Ability to support U.S. transition to an interoperable health data exchange
- **Need for a uniform language is paramount**
- Currently, use of different slang, abbreviations, terms for the same diagnosis or treatment
- Standardization through use of SNOMED Clinical Terms (SNOMED CT) critical

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Coding & Reimbursement

What has changed?

Seven characters long

Used to translate patient condition from words to alpha-numeric codes

Makes for easy storage, retrieval, standardization

Makes healthcare data interoperable

Improved code granularity

HIPAA Requirement

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Coding & Reimbursement

Why all the fuss?

ICD-10	Is a more mature ICD-9
ICD-10	Is inevitable
ICD-10	In comparison to institutions and facilities, work for physician preparation is minimal
ICD-10	Preparation and Implementation - Embrace it; Don't postpone it!

October 1, 2014

- ✓ ICD-9-CM codes will not be accepted for services provided on or after this date
- ✓Claims for dermatological services provided on or after this date **must use ICD-10 codes** for medical diagnosis
- ✓CPT codes **will continue** to be used for outpatient services

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ICD-10-CM will replace ICD-9-CM

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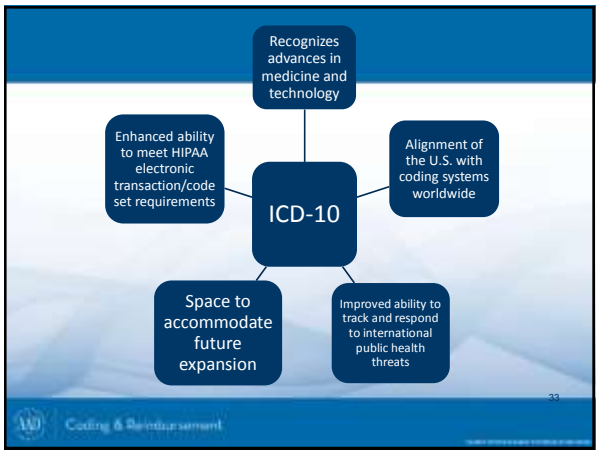

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ICD-10-CM Composition

- Alphanumeric codes (A00-Z99)
- Addition of sixth and seventh character extensions (e.g., injuries, external causes)
- Addition of detail (e.g., laterality)
- Expanded codes (e.g., injury)
- Revised codes (e.g., skin & Subcutaneous)
- Combining certain codes: Underlying cause & clinical manifestation codes

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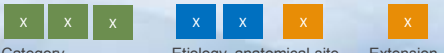
ICD-9 Format vs. ICD-10 Format

➢ **ICD-9 Format**

Category — Etiology, anatomical site, manifestation

➢ **ICD-10 Format**



Category — Etiology, anatomical site & Severity — Extension

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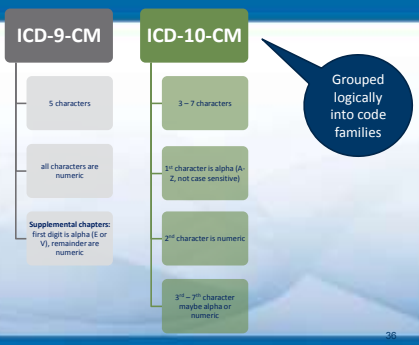
Structural Differences



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ICD-10-CM Code Structure

All categories contain three characters

- First character of category is always a letter
- Second and third characters can either be a number or alpha character

Subcategories contain four or five characters

- Characters can either be numbers or letters

Complete code can be three, four, five or six characters

- Final character in code can either be a number or letter

Some categories contain seventh character extensions

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Coding & Reimbursement

Three Character Categories

Chapter 2: Neoplasms
(C00 – D49)

Chapter 12:
Dis. Of the Skin & Subcutaneous Tissue
(L00 – L99)

Chapter 18: Symptoms, Signs & Abnormal Clinical Lab. Findings
(R00 – R99)

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Coding & Reimbursement

Note the…

Four Character Categories	Five-Six Character Classification
D03 Melanoma in situ	**C44.70** Basal cell carcinoma of skin, lower limb
D03.0 Melanoma in situ of lip	**C44.712** Basal cell carcinoma of skin, right lower limb

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Coding & Reimbursement

Dummy Placeholders or Are They?

A placeholder is represented by character "X"

- Can be used as a 5th character placeholder, at certain six character codes to allow for future expansion.

T81.4XXA

- Infection following a procedure e.g. wound abscess following a procedure

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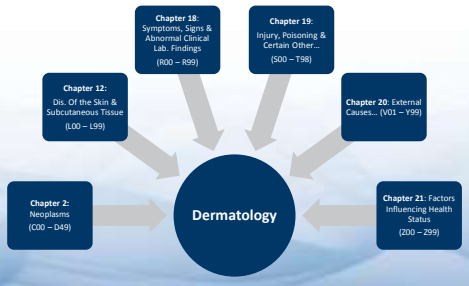
Coding & Reimbursement

ICD-10-CM for Dermatology



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Coding & Reimbursement

Where Do I Start?

Educate yourself

Attend seminars, online webinars	sign up for newsletters

Check periodically for updates

www.aad.org/ICD-10	http://www.cms.gov/ICD10/

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Coding & Reimbursement

Take Charge!

Become an expert

Practice applying ICD-10-CM codes

Practice, Practice, Practice

Network with peers

Seek answers to cases and confirm application of ICD-10-CM codes

Take advantage of state society/associations

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Coding & Reimbursement

First things first….

- Inventory processes and systems that will be impacted
- Plan for staff training
- Conduct staff gap analysis of coding knowledge
- Develop a budget

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Coding & Reimbursement

Implementation Phases

Planning

- Establish project management structure, governance, risk management
- Plan to communicate with external partners

Communication & Awareness

- Create a communication plan
- Assess training needs and develop a training plan
- Meet with staff to discuss effect of ICD-10-CM and identify responsibilities

Assessment

- Assess business and policy impacts
- Assess technological impacts
- Evaluate vendors

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Coding & Reimbursement

Implementation Phases

Operational Implementation

- Identify system migration strategies
- Implement business and technical modifications
- Prepare and deliver training

Testing

- Complete Level I internal testing
- Complete Level II external testing

Transition

- Prepare and establish the production and go-live environments
- Deliver ongoing support

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Coding & Reimbursement

To Understand ICD-10-CM Coding System

Review code structure and coding conventions for ICD-10-CM

Learn the fundamentals of the ICD-10-CM system

Analyze and practice applying the ICD-10-CM coding guidelines

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Coding & Reimbursement

Knowledge differences

Clinicians

- New concepts in ICD-10
- Require clinical documentation adherence

Coders

- Brush up on A&P
- In-depth understanding of medical terminology required
- Work in collaboration with clinical staff

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Coding & Reimbursement

Default Codes

- Code listed next to a main term in the Index are referred to as 'default code'
- Usually unspecified
- NEVER code directly from the default code

Vignette

- Vignette: • Thickened, red, scaly patches under armpits, groin area
- Assessment: • Psoriasis
- ICD-10-CM Code: • L40.x

Psoriasis ICD-9-CM: 696.1

- Rationale: Look up Psoriasis in Alpha Index
- Go to Tabular: Multiple code match; Locate Root code L40
- Then: Identify code for specific Psoriasis; Assign appropriate code

Psoriasis: L40

Index	Tabular
Psoriasis: L40.9 *(Remember not to code from the index! This code is defaulted to Psoriasis, unspecified)*	**Psoriasis L40** **requires 4th & 5th characters to determine type of psoriasis (e.g. vulgaris, generalized pustular, flexular etc)*

Conventions

- NEC: Use 'other specified' code in tabular list
- NOS: Equivalent to 'unspecified'

Vignette

- Vignette: • Thickened, red, scaly patches under armpits, groin area •
- Assessment: • Flexural Psoriasis
- ICD-10-CM Code: • L40.8

Rationale NEC

Rationale	Go to Tabular	Then
Look up Psoriasis in Alpha Index Then Flexular	Locate Root code L40	Identify code for Flexular Psoriasis Assign appropriate code

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Vignette

- Vignette: • Red, prominent, flat and pale scar tissue •
- Assessment: • Scar NOS
- ICD-10-CM Code: • L90.5

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Rationale NOS

Rationale	Go to Cicatrix	Then
Look up Scar in Alpha Index Instruction: See also *Cicatrix*	Look up skin – L90.5	Go to Tabular section Look up L90.5 Identify Scar NOS Code appropriately

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Scar NOS: L90

Index	Tabular
Scar, scarring L90.5 *(See also cicatrix): Proceed and look up Cicatrix, skin*	**Atrophic disorders of skin L90** **See** Scar condition and fibrosis of skin L90.5 *(Note: Excludes Note 2)*

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Old and New Concepts

- Combination Codes
- Granularity
- Laterality
- Principal/first Listed Diagnosis

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General Coding Guidelines

Principal or First Listed Diagnosis

- Where no sequencing rules apply
- No findings

Sequence patient chief complaint first

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Code First/Use Additional Code

- Codes that have both an underlying etiology,
- multiple body system manifestations due to the underlying etiology require sequencing
- Code the underlying condition first followed by the manifestation.

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Vignette 'Code first'/ 'Use additional Code'

Toxic erythema
- Code first poisoning due to drug or toxin, if applicable
- (T36 – T50 with fifth or sixth character 1-4 or 6)

Then
- Use additional code for adverse effect, if applicable to identify drug
- (T36 – T50 with fifth or sixth character 5)

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Toxic Erythema ICD-9-CM: 695.0

Rationale
Look up Erythema in Alpha Index
Then toxic – L53.0

Go to Tabular Section
Identify Root code L53
Identify Toxic erythema – L53.0
Instruction: Code first poisoning due to drug or toxin, if applicable (T36-T65 with 5th or 6th character 1-4 or 6)
Use additional code for adverse effect, if applicable , to identify drug (T36-T50 with 5th or 6th character 5)

Then
Choose appropriate code

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Conventions

Use of 'and' represents 'and/or'
- **With/without**
  - Final character of code set can be either
  - Insufficient documentation, default to 'without'

Laterality
- final character of the bilateral codes indicates laterality

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Guidelines

- Code also → Report two codes to fully describe condition
- 'see' and 'See also' → Reference another term in the index
- Brackets, colons, parenthesis, etc. → Work exactly the same as in ICD-9-CM

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Example

Dysplastic nevi

↓

See

↓

Neoplasm, skin, benign

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Vignette

- **Vignette**
  - 5 mm diameter ill-defined, funny looking mole with irregular margins on right lower arm.
  - varying shades of color, though mostly pink with flat and bumpy components
- **Assessment:**
  - Dysplastic Nevi
- **ICD-10-CM Code:**
  - D23.61

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Rationale Dysplastic Nevi ICD-9-CM: 238.2

Rationale
Look up Nevus in Alpha
Then Dysplastic
Instruction: see Neoplasm, skin, benign

Go to Neoplasm Table
Locate Neoplasm, skin, benign
Consider lesion symptoms before choosing code

Go to Tabular section
Identify code
Choose appropriate **location** and **laterality**

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Signs and Symptoms

Similar to ICD-9-CM coding

Use with confirmed diagnosis only if not associated with confirmed diagnosis

Do not report if there is a confirmed diagnosis

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Coding guidelines

Integral to disease process
- Signs & Symptoms routinely associated with disease
- Do not assign as additional code – unless specifically instructed in classification

Not integral disease process
- Signs & Symptoms routinely associated with disease
- Report when present

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Example

Rash and other nonspecific eruption

- R21 – Rash NOS

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Documentation Guidelines

Acute & Chronic Conditions

When documented as both Acute and Chronic — And separate codes available

Code both

Sequence Acute or Sub-acute first

Then code chronic

Follow instructions & guidelines

Etiology/Manifestation

Conditions with underlying etiology

Look for "*Use additional code*" | Or "*code first*' instruction

Code underlying condition first

Then code the manifestation

General Coding Guidelines

- Complication of surgery & other medical care:
- Treatment resulting from surgery or other medical care
- Complication code is listed first

Radiation-related disorders of the skin and subcutaneous tissue (L55-L59)

- 3 character codes, specify type
- L55.x Sunburn
- L56.x Other acute skin changes due to ultraviolet radiation
- Multiple matches – pick most specific for accurate coding
- L57.x Actinic Keratosis
- L59.x Other disorders of the skin & subcutaneous tissue related to radiation

Other disorders of the skin and subcutaneous tissue (L80-L99)

702.xx - Seborrheic Keratosis

- **L82.x** Seborrheic Keratosis
  Incls: dermatosis papulosa nigra Leser-Trélat disease
- **L82.0** Inflamed seborrheic keratosis
- **L82.1 Other seborrheic keratosis**
  Seborrheic keratosis NOS

Multiple Codes, Single Condition

L57.x

- Skin changes due to chronic exposure to nonionizing radiation
- Use additional code to identify the source of the ultraviolet radiation (W89, X32)

Radiation-related disorders of the skin and subcutaneous tissue (L55-L59)

692.xx Contact dermatitis and other eczema

- **3 character codes, specify type**
- **L55.x Sunburn**
- **L56.x Other acute skin changes due to ultraviolet radiation**

702.x Other dermatoses

- **Multiple matches – pick most specific for accurate coding**
- **L57.x Actinic Keratosis**
- **L58.x Radiodermatitis**
- **L59.x Other disorders of the skin & subcutaneous tissue related to radiation**

Other disorders of the skin and subcutaneous tissue (L80-L99)

702.xx - Seborrheic Keratosis

- **L82.x** Seborrheic Keratosis
  Incls: dermatosis papulosa nigra
  Leser-Trélat disease
- **L82.0** Inflamed seborrheic keratosis
- **L82.1 Other seborrheic keratosis**
  Seborrheic keratosis NOS

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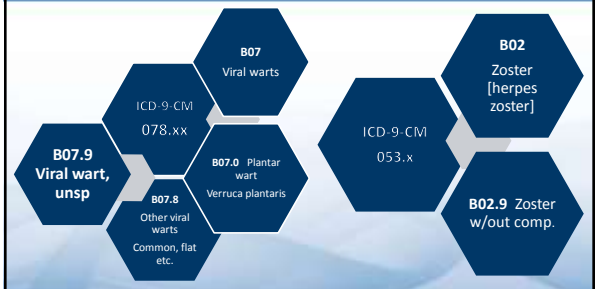
Coding & Reimbursement

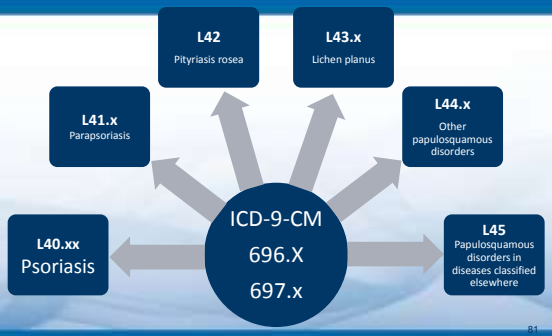
Certain skin infections included in the infectious disease chapter



80

Coding & Reimbursement

Papulosquamous disorders (L40-L45)



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Coding & Reimbursement

Intraoperative and post-procedural complications … (L76)

L76.xx
Intraoperative and post-procedural complications of skin and subcutaneous tissue

e.g., **L76.21**

Post-procedural hemorrhage and hematoma of skin and subcutaneous tissue following a dermatologic procedure

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Coding & Reimbursement

ICD-9-CM ⟶ Acne NOS – 706.1

ICD-10-CM

- 8 codes
- need enough information as to what type of Acne pt presents
- L70 Acne (Root code)
  Excludes2 acne keloid (L73.0)
- Include appropriate 4th digit

ICD-10-CM

- L70.0 Acne Vulgaris
- L70.1 Acne conglobata
- L70.4 Infantile Acne
- L70.8 Other Acne
- L70.9 Acne, Unspecified

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Coding & Reimbursement

Vignette

- **Vignette:** Painful, inflamed papules, pustules on face, back, upper chest,
- **Assessment:** Acne Vulgaris
- **ICD-10-CM Code:** L70.0

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Coding & Reimbursement

Rationale Acne

Rationale Look up Acne in Alpha Index

Then Vulgaris

Go to Tabular Locate Root code L70

Then Identify code for Acne Vulgaris

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Vignette
multiple codes, single condition

Vignette
- Small bumps, pustules on face after several weeks of applying a topical steroid

Assessment:
- Rosacea-like condition caused by potent topical steroid use

ICD-10-CM Code:
- L71.8

86

Rationale Rosacea

Rationale
- Look up Rosacea in Alpha Index
- Then specified NEC – L71.8

Go to Tabular section
- Locate Root code L71
- Instruction: Use additional code for adverse effect, if applicable, to identify drug (T36-T50 with 5th or 6th character 5)
- Identify Other Rosacea code L71.8

Then
- Use additional code to identify drug
- Choose appropriate code to identify drug – T36-T50
- Choose appropriate code

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Guidelines

Conditions that are an integral part of a disease process

Signs and symptoms that are associated routinely with a disease process should not be assigned as additional codes, unless otherwise instructed by the classification.

Conditions that are not an integral part of a disease process

Additional signs and symptoms that may not be associated routinely with a disease process should be coded when present

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Combination codes

A single code used to classify:

Two diagnoses, or

A diagnosis with an associated secondary process (manifestation)

A diagnosis with an associated complication

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Generally requires 2 codes

1st code – condition of nature of sequale

2nd code - sequela

Sequela/Late Effects

Not restricted to time limits

Exception:

sequela is sequenced before manifestation

Unless code includes manifestation description

Never use Acute code with late effect condition

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To Include

Includes Notes

- Note appears immediately under a three character code title
- further defines; give examples of the content of the category
- two conditions cannot occur together e.g., congenital form versus an acquired form of the same condition

Inclusion terms

- List of terms is included under some codes
- conditions for which that code is to be used
- ***Not necessarily exhaustive. Additional terms found in the Alphabetic Index which may also be assigned to a code***

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Coding & Reimbursement

Vignette *'Includes'*

- **Vignette:**
  - 3 mm diameter ill-defined, funny looking mole with irregular margins on trunk.
  - varying shades of color, though mostly pink with flat and bumpy components
- **Assessment:**
  - Melanocytic Nevi
- **ICD-10-CM Code:**
  - D22.5

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Coding & Reimbursement

Rationale

- **Rationale:** Look up Nevus in Alpha; Then skin; Then trunk – D22.5
- **Go to Tabular Section:** Identify Root code D22; Includes: Atypical nevus, Nevus NOS
- **Then:** Identify code for trunk; Choose appropriate code

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Coding & Reimbursement

To Exclude: two types

Excludes Notes: *Each type of note has a different definition for use; though similar, they both indicate that codes excluded from each other are independent of each other*

Excludes1: pure excludes note Means "**NOT CODED HERE**!"

- Indicates **code excluded; should never be used at the same time as the code above** the Excludes1 note
- two conditions cannot occur together e.g., congenital form versus an acquired form of the same condition

Excludes2: Means "**NOT INCLUDED HERE**"

- indicates that the condition excluded is not part of the condition represented by the code, but a patient may have both conditions at the same time
- **Acceptable** to use both the code and the excluded code together, when appropriate.

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Coding & Reimbursement

Allergic contact dermatitis (L23.x)

Excludes1

- allergy NOS (T78.40)
- Contact dermatitis NOS (L25.9)
- Dermatitis NOS (L30.9)

Excludes2

- Dermatitis due to substances taken internally (L27.x)
- Irritant contact dermatitis (L22)

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Coding & Reimbursement

Vignette *'Excludes'*

- **Vignette:**
  - Reddish, itchy right wrist underlying watch strap location. Strap buckle contains nickel
- **Assessment:**
  - Allergic contact dermatitis
- **ICD-10-CM Code:**
  - D23.0

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Coding & Reimbursement

Allergic contact dermatitis ICD-9-CM: 692.9

Rationale
Look up Dermatitis in Alpha Index
Then allergic
Then due to
Then nickel – L23.0

Go to Tabular Section
Identify Root code L23
Excludes1: Contact dermatitis NOS, allergy NOS,…….
Excludes2: dermatitis taken internally,…….

Then
Identify code for allergic contact dermatitis due to metals
Choose appropriate code

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Chapter 2 (C00-D49): Malignant Neoplasms

Neoplasms of the skin are classified first by malignant, in situ, benign, uncertain behavior, and unspecified behavior; and within this, by site.

C43.xx
Malignant melanoma of skin

C44.xxx
Other and unspecified neoplasm of skin

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Malignant Neoplasms Documentation Guidelines

Chapter 2 Neoplasms (C00-D49)

Location

Morphology

Documentation must state whether lesion is:
- Benign
- In-situ
- Malignant

Uncertain histologic behavior

Laterality (where applicable)

99

Diagnosis for Malignancy

Reason for the encounter is to diagnose presence of malignancy

Reoprt sign & symptom code; unless confirmation of diagnosis is made

Confirmation of malignancy should be assigned when there is confirmation from pathology report

100

Code selection for malignancies

Confirmed but not treated
- Report malignant diagnosis code

Excised, destroyed etc.
- Report malignant diagnosis code

Follow-up after treatment
- Report history of….

101

Why document Laterality

C44.0 Malignant neoplasm of skin of lip
Malignant neoplasm of basal cell carcinoma of lip
Excls1. malignant neoplasm of lip (C00.x)

C44.1 Malignant neoplasm of eyelid, incl. canthus Excls1. connective tissue of eyelid (C49.x)

C44.10 Malignant neoplasm of skin of eyelid, incl. canthus, **unspecified** side

C44.11 Malignant neoplasm of skin of **right** eyelid, incl. canthus

C44.12 Malignant neoplasm of skin of **left** eyelid, incl. canthus

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Malignant Melanoma

ICD-9-CM

- **172 Malignant neoplasm of skin** **Incls:**
  melanocarcinoma
  melanoma in situ off skin
  melanoma (skin) NOS

  Excls:
  skin of genial organs (184.0-184.9, 187.1-187.9)
  sites other than skin – code to malignant neoplasm of site of skin

ICD-10-CM

- **C43 Malignant melanoma of skin**
  Excls1: Melanoma in situ (D03.x) **Excls2:** malignant melanoma of skin of genital organs (C51-C52, C60.x, C6.x) Merkel cell ca (C4a.x) sites other than skin – code to malignant neoplasm of the site

  e.g., **C43.30 malignant melanoma of other and unspecified parts of face**

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Coding & Reimbursement

Malignant Neoplasms

ICD-9-CM

- **173 Other malignant neoplasm of skin** **Incls:** malignant neoplasm of: sebaceous glands sudoriferous.. **Excls:** Kaposi's sarcoma (176.0 – 176.9)
  Malignant melanoma of skin (172.0 – 172.9)
  Skin of genital organs (184.0–184.9, 187.1–187.9)

ICD-10-CM

- **C44 Other Malignant neoplasm of skin** **Incls:**
  malignant neoplasm of: sebaceous glands
  malignant neoplasm of sweat glands

  Excls.
  Kaposi's sarcoma of skin (C46.0)
  malignant melanoma of skin (C43.x)
  malignant neoplasm of skin of genital organ (C51–C52, C60.x, C63.2)

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Coding & Reimbursement

Malignant Neoplasms

ICD-9-CM

- **173.0 Skin of Lip**
  Excls: Vermilion border of lip (140.0-140.1, 140.)
- **173.1x Eyelid, incl. canthus**
  Excls: cartilage of eyelid (171.0)

ICD-10-CM

- **C44.0 Malignant neoplasm of skin of lip**
  Malignant neoplasm of basal cell carcinoma of lip
  Excls1. malignant neoplasm of lip (C00.x)
- **C44.1 Malignant neoplasm of eyelid, incl. canthus**
  Excls1. connective tissue of eyelid (C49.x)
- **C44.10 Malignant neoplasm of skin of eyelid, incl. canthus, unspecified side**
- **C44.11 Malignant neoplasm of skin of right eyelid, incl. canthus**
- **C44.12 Malignant neoplasm of skin of left eyelid, incl. canthus**

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Coding & Reimbursement

Malignant Neoplasms

ICD-9-CM

- **173.01 Basal cell carcinoma of skin of Lip**
- **173.51 Basal cell carcinoma of skin of trunk, except scrotum**

ICD-10-CM

- **C44.01 Basal cell carcinoma of skin of Lip**
- **C44.02 Squamous cell carcinoma of skin of Lip**
- **C44.519 Basal cell carcinoma of skin of other part of trunk**
- **C44.129 Squamous cell carcinoma of skin of other part of trunk**

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Coding & Reimbursement

Malignant Melanoma

- **C43.60 Malignant melanoma of unspecified upper limb, incl. shoulder**
- **C43.61 Malignant melanoma of right upper limb, incl. shoulder**
- **C43.62 Malignant melanoma of left upper limb, incl. shoulder**

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Coding & Reimbursement

Neoplasms

Malignant Neoplasms

- **C44 Other Malignant neoplasm of skin**
  Incls: malignant neoplasm of:
  sebaceous glands
  malignant neoplasm of sweat glands

  Excls. Kaposi's sarcoma of skin (C46.0)
  malignant melanoma of skin (C43.x)
  malignant neoplasm of skin of genital organ (C51–C52, C60.x, C63.2)

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Coding & Reimbursement

Basal Cell Carcinoma

- C44.711 Basal cell carcinoma of unspecified lower limb, incl. hip
- C44.712 Basal cell carcinoma of right lower limb, incl. hip
- C44.719 Basal cell carcinoma of left lower limb, incl. hip

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Squamous Cell Carcinoma

- C44.721 Squamous cell carcinoma of unspecified lower limb, incl. hip
- C44.722 Squamous cell carcinoma of right lower limb, incl. hip
- C44.729 Squamous cell carcinoma of left lower limb, incl. hip

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Other malignant neoplasms

C44.0
- Malignant neoplasm of skin of lip
- Malignant neoplasm of basal cell carcinoma of lip
  Excls1: malignant neoplasm of lip (C00.x)

C44.1
- Malignant neoplasm of eyelid, incl. canthus Excls1. connective tissue of eyelid (C49.x)

C44.10
- Malignant neoplasm of skin of eyelid, incl. canthus unspecified side

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Other malignant neoplasms - eye

C44.11
- Malignant neoplasm of skin of right eyelid, incl. canthus

C44.12
- Malignant neoplasm of skin of left eyelid, incl. canthus

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B9 Neoplasm of skin of lower limb, incl. hip

- Multiple codes – pick most specific for accurate coding
- D23.70 Other benign neoplasm of skin of unspecified lower limb, incl. hip
- D23.71 Other benign neoplasm of skin of right lower limb, incl. hip
- D23.72 Other benign neoplasm of skin of left lower limb, incl. hip
- D23.9 Other benign neoplasm of skin, unspecified

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ICD-9-CM → ICD-10-CM

238.2
Neoplasm Uncertain behavior, Skin

- One-to-one match
- D48.5 Neoplasm of uncertain behavior of skin
- Excludes: skin of genital organs (D39.8, D40.7), vermilion border of lip (D37.0)

216.7
B9 Neoplasm of skin of lower limb, incl. hip

- Multiple matches – pick most specific for accurate coding
- D23.70 Other benign neoplasm of skin of unspecified lower limb, incl. hip
- D23.71 Other benign neoplasm of skin of right lower limb, incl. hip
- D23.72 Other benign neoplasm of skin of left lower limb, incl. hip
- D23.9 Other benign neoplasm of skin, unspecified

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Uncertain and Unspecified Codes

D48.5
Neoplasm of Uncertain behavior, skin

D49.2
Neoplasm of unspecified behavior of bone, soft tissue and skin

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History of….

There are two types of history Z codes

Personal – C85.x

Family – C80.x

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Screening

NOTE:
Check with your payer for coverage guidelines

Testing/checking for diseases in well patients to provide early detection and/or treat

Can be listed as primary diagnosis if that is the only reason for the encounter

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Z-Code as Primary DX

Principle/First Listed
- Only certain Z codes may be used as PDx/first listed

Look for
- PDx next to the code
- e.g. Z01.82 Encounter for allergy testing

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Abnormal Test Findings

laboratory, pathologic, and other diagnostic results

Do not code
unless the physician indicates their clinical significance.

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Coding Rule

Each diagnosis code can only be reported **once** for an encounter

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ICD-10 Testing will be available!

CMS: on/or before 03/18/14, your local Medicare contractor will report to CMS:

- Number of trading partners conducting testing during the testing week(s);
- Percentage of trading partners that conducted testing during the testing week (versus number of trading partners supported) by contract;
- Percentage of test claims accepted versus rejected;
- Report of any significant issues found during testing.

Note: Check with all your payers for ***testing opportunities***

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CMS: ICD-9 to ICD-10

Translation
- National Coverage Determination (NCD);
- Local Coverage Determination (LCD) policies

Look out for
- Periodic updates

Visit often
- http://www.cms.gov/Medicare/Coverage/CoverageGenInfo/ICD10.html

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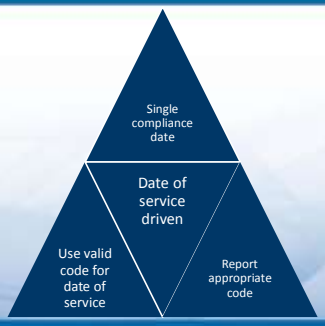
October 1, 2014



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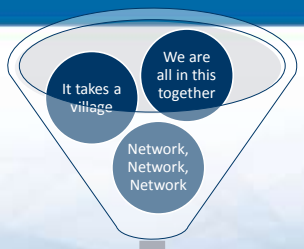

Successful ICD-10 Implementation

⇩

Quality in Healthcare

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In Summation

- Clinical detail of ICD-10-CM has potential to:
- Improve reimbursement fairness
- Enable more accurate and detailed statistics
- Improve the ability to asses quality
- Support improved data retrieval and analysis

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Need help? Got a Question?

ppm1@aad.org

fmcnicholas@aad.org

peiden@aad.org

www.aad.org/icd-10-faqs

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CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

ICD-10

Official CMS Industry Resources for the ICD-10 Transition

www.cms.gov/ICD10

Talking to Your Vendors About ICD-10: Tips for Medical Practices

An important step in preparing for the change to ICD-10 is to talk with any software vendors, clearinghouses, or billing services you use to be sure they are ready to provide the support you need. Your vendors will need to have products and services on a schedule that allows adequate time for you to conduct testing.

ICD-10 DEADLINE
OCT 1, 2014

Start the Conversation with Your Vendors

Talk with your vendors now to be sure that you can count on them to:

- Have fully functional, compliant products and services ready in plenty of time to allow for thorough ICD-10 testing
- Help you avoid potential reimbursement issues and interruptions to workflow

Ask your vendors to establish a comprehensive approach that will deliver compatible products when you need them. Points to consider discussing with your vendors include:

- System upgrades/replacements needed to accommodate ICD-10
- Costs involved and whether upgrades will be covered by existing contracts
- When upgrades or new systems will be available for testing and implementation
- Customer support and training that they will provide
- How their products and services will accommodate both ICD-9 and ICD-10 as you work with claims for services provided both before and after the transition deadline for code sets

Talking to your vendors now about ICD-10 will help ensure that your transition goes smoothly.

ICD-10 Resources

There are many professional, clinical, and trade associations offering a wide variety of ICD-10 information, educational resources, and checklists. Call or check the websites of your associations and other industry groups to see what resources are available.

The CMS website also has official resources to help you prepare for ICD-10. CMS will continue to add new tools and information to the site throughout the course of the transition. Visit **www.cms.gov/ICD10.**

JUNE 2013

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES ICD-10

Official CMS Industry Resources for the ICD-10 Transition
www.cms.gov/ICD10

ICD-10 Basics for Medical Practices

The ICD-10 transition takes planning, preparation, and time, so medical practices should continue working toward compliance. The following quick checklist will assist you with preliminary planning steps.

- ❒ **Identify your current systems and work processes that use ICD-9 codes.** This could include your clinical documentation, encounter forms/superbills, practice management system, electronic health record system, contracts, and public health and quality reporting protocols. It is likely that wherever ICD-9 codes now appear, ICD-10 codes will take their place.
- ❒ **Talk with your practice management system vendor about accommodations for ICD-10 codes.**
  - Confirm with your vendor that your system has been upgraded to Version 5010 standards, which have been required since January 1, 2012. Unlike the older Version 4010/4010A standards, Version 5010 accommodates ICD-10 codes.
  - Contact your vendor and ask what updates they are planning to make to your practice management system for ICD-10, and when they expect to have it ready to install.
  - Check your contract to see if upgrades are included as part of your agreement.
  - If you are in the process of making a practice management or related system purchase, ask if it is ICD-10 ready.
- ❒ **Discuss implementation plans with all your clearinghouses, billing services, and payers to ensure a smooth transition.** Be proactive, don't wait. Contact organizations you conduct business with such as your payers, clearinghouse, or billing service. Ask about their plans for ICD-10 compliance and when they will be ready to test their systems for the transition.
- ❒ **Talk with your payers about how ICD-10 implementation might affect your contracts.** Because ICD-10 codes are much more specific than ICD-9 codes, payers may modify terms of contracts, payment schedules, or reimbursement.
- ❒ **Identify potential changes to work flow and business processes.** Consider changes to existing processes including clinical documentation, encounter forms, and quality and public health reporting.

Background

ICD-10 DEADLINE
OCT 1, 2014

About ICD-10

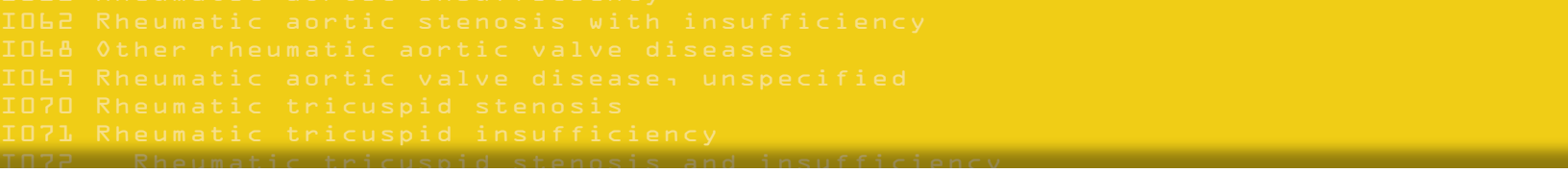
ICD-10 CM/PCS (International Classification of Diseases, 10th Edition, Clinical Modification/ Procedure Coding System) consists of two parts:

ICD-10-CM (diagnosis coding) was developed by the Centers for Disease Control and Prevention for use in all U.S. health care settings. Diagnosis coding under ICD-10-CM uses 3 to 7 digits instead of the 3 to 5 digits used with ICD-9-CM, but the format of the code sets is similar.

ICD-10-PCS (inpatient procedure coding) was developed by the Centers for Medicare & Medicaid Services (CMS) for use in U.S. inpatient hospital settings only. ICD-10-PCS uses 7 alphanumeric digits instead of the 3 or 4 numeric digits used under ICD-9-CM procedure coding. Coding under ICD-10-PCS is much more specific and substantially different from ICD-9-CM procedure coding.

The transition to ICD-10-CM/PCS does not affect Current Procedural Terminology (CPT) codes, which will continue to be used for outpatient services.

Visit **www.cms.gov/ICD10** for ICD-10 and Version 5010 resources from CMS.



- **Assess staff training needs.** Identify the staff in your office who code, or have a need to know the new codes. There are a wide variety of training opportunities and materials available through professional associations, online courses, webinars, and onsite training. If you have a small practice, think about teaming up with other local providers. For example, you might be able to provide training for a staff person from one practice, who can in turn train staff members in other practices. Coding professionals recommend that training take place approximately six months prior to the ICD-10 compliance deadline.
- **Budget for time and costs related to ICD-10 implementation, including expenses for system changes, resource materials, and training.** Assess the costs of any necessary software updates, reprinting of superbills, trainings, and related expenses.
- **Conduct test transactions using ICD-10 codes with your payers and clearinghouses.** Testing is critical. You will need to test claims containing ICD-10 codes to make sure they are being successfully transmitted and received by your payers and billing service or clearinghouse. Check to see when they will begin testing, and the test days they have scheduled.

This fact sheet was prepared as a service to the health care industry and is not intended to grant rights or impose obligations. The information provided is only intended to be a general summary. It is not intended to take the place of either the written law or regulations. We encourage readers to review the specific statutes, regulations, and other interpretive materials for a full and accurate statement of their contents.

CMS CENTERS FOR MEDICARE & MEDICAID SERVICES

ICD-10

Official CMS Industry Resources for the ICD-10 Transition

www.cms.gov/ICD10

ICD-10 Basics for Small and Rural Practices

On **October 1, 2014**, the health care industry will transition from ICD-9 to ICD-10 codes for diagnoses and hospital inpatient procedures. This means everyone covered by HIPAA must use ICD-10 codes for health care services provided on or after October 1, 2014.

The following is a list of important questions to address now to help you prepare your practice for ICD-10.

- **Will you be able to submit claims?** If you use an electronic system for any or all payers, you need to know if it will be able to accommodate the ICD-10 version of diagnoses and hospital inpatient procedures codes. If your billing system has not been upgraded for the current version of HIPAA claims standards—Version 5010—you will **not** be able to submit claims. Check with your practice management system or software vendor to make sure your claims are in the HIPAA Version 5010 format and that your system or software can include the ICD-10 version of diagnoses and hospital inpatient procedures codes.
- **Will you be able to complete medical records?** If you use any type of electronic health record (EHR) system in your office, you need to know if it will capture ICD-10 codes. Look at how you enter ICD-9 codes (e.g., do you type them in or select from a drop down menu) and talk to your EHR vendor about your system's capabilities for ICD-10.
- **How will you code your claims under ICD-10?** If you currently code by look up in ICD-9 books, purchase the ICD-10 code books in early 2014. Take a look at the codes most commonly used in your office and begin developing a list of comparable ICD-10 codes. Alternatively, check your software for an ICD-10 look up functionality. Also, you may want to explore ICD-10 training options and determine if formal training is necessary.
- **Where do you use ICD-9 codes?** Talk to your colleagues and keep a log of everywhere you see and use an ICD-9 code as you do your job. If the code is on paper, you will need new forms (e.g., patient encounter form, superbill). If you see the code on your computer, check with your EHR or practice management system vendor to see when your system will be ready for ICD-10 codes.
- **Are there ways to make coding more efficient?** For example, develop a list of your most commonly used ICD-9 codes and become familiar with the ICD-10 codes you will use in the future for that case; invest in an inexpensive software program that helps small practices with coding. Also, think about ways to make sure the new coding does not delay payments. Look at your most common non-visit services—do any sometimes trigger reviews or denials related to medical necessity? It is important to understand how to code these services correctly under ICD-10.

Background

ICD-10 DEADLINE
OCT 1, 2014

About ICD-10

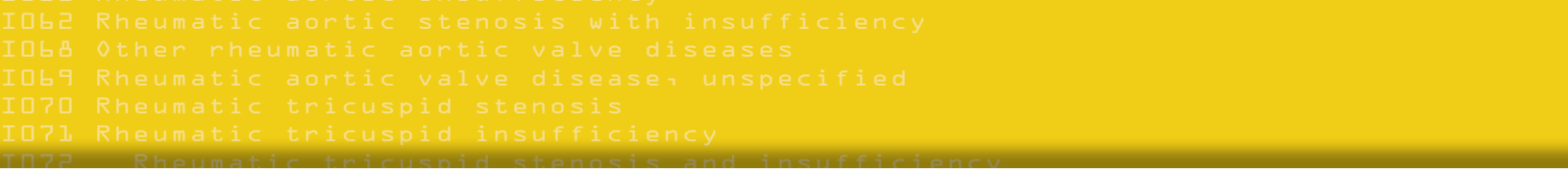
ICD-10 CM/PCS (International Classification of Diseases, 10th Edition, Clinical Modification/ Procedure Coding System) consists of two parts:

ICD-10-CM (diagnosis coding) was developed by the Centers for Disease Control and Prevention for use in all U.S. health care settings. Diagnosis coding under ICD-10-CM uses 3 to 7 digits instead of the 3 to 5 digits used with ICD-9-CM, but the format of the code sets is similar.

ICD-10-PCS (inpatient procedure coding) was developed by the Centers for Medicare & Medicaid Services (CMS) for use in U.S. inpatient hospital settings only. ICD-10-PCS uses 7 alphanumeric digits instead of the 3 or 4 numeric digits used under ICD-9-CM procedure coding. Coding under ICD-10-PCS is much more specific and substantially different from ICD-9-CM procedure coding.

The transition to ICD-10-CM/PCS does not affect Current Procedural Terminology (CPT) codes, which will continue to be used for outpatient services.

Visit **www.cms.gov/ICD10** for ICD-10 resources from CMS.



ICD-10 Resources

Visit the CMS ICD-10 website for information and resources on ICD-10. The Provider Resources section of the website has helpful fact sheets, checklists, timelines, and other resources to help practices transition to ICD-10.

Also, be sure to check out ICD-10 resources and trainings available from your payers, vendors, and professional associations such as the American Academy of Professional Coders and the American Health Information Management Association.

This fact sheet was prepared as a service to the health care industry and is not intended to grant rights or impose obligations. The information provided is only intended to be a general summary. It is not intended to take the place of either the written law or regulations. We encourage readers to review the specific statutes, regulations, and other interpretive materials for a full and accurate statement of their contents.

Managing Psoriasis across the Life Course

Jennifer Cather, MD
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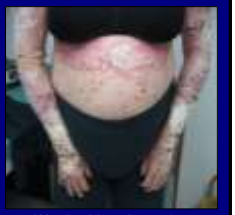
Modern Research Associates
Dallas, TX

Disclosure

- Consultant: AbbVie, Janssen, Leo, Novartis
- Speaker's bureau: AbbVie, Janssen
- Research: Amgen, Celgene, Merck, Novartis, Pfizer

Psoriasis in adults

- May have additional health problems
  - Obesity, diabetes, CVD
  - Depression
- May have lifestyle issues
  - Alcohol, smoking
- Often heavily pre-treated
- Compliance is an issue
- May not see PCP
- Life issues (financial, time, competing priorities)

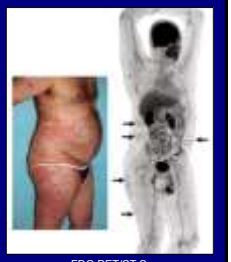


We should not be seeing patients like this in the clinic!

Neimann *et al*. J Am Acad Dermatol. 2006 Nov;55(5):829-35.
Davidovici *et al*. Invest Dermatol. 2010 Jul;130(7):1785-96.

There are complications of NOT treating psoriasis

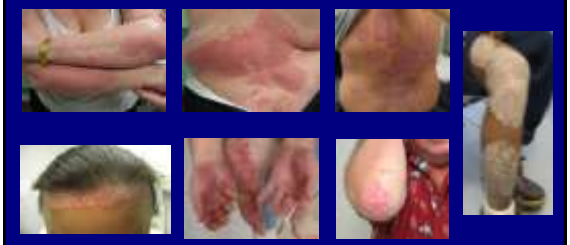
- Many are not in treatment
- Elevated inflammatory burden and co-morbidities
- Impact on quality of life
  - Physical functioning and psychosocial impact
- Economic impact
  - Time lost from work, reduced productivity at work, not promoted/ in leadership roles



FDG-PET/CT Scan

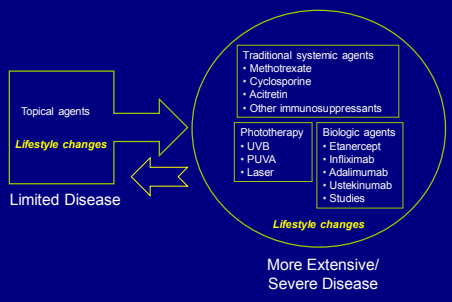
Mehta *et al*. JAMA Dermatol. 2011 Sep;147(9):1031-1039.

Topicals or systemic therapy?



Photos from Modern Dermatology Associates, Dallas TX

Many treatment options exist



*Choice of therapy depends on individual patient

Systemic therapy is effective

Treatment	Target	Approval Psoriasis	Approval Psoriatic Arthritis
Traditional Systemics			
Acitretin	Retinoic acid receptor	1996	NA
Cyclosporine	T-cells	1997	NA
Methotrexate	Folate metabolism	1972	RA 1988
Biologics			
Adalimumab	TNF-alpha	2008	2005
Certolizumab Pegol	TNF-alpha	Not applicable	2013
Etanercept	TNF-alpha	2004	2002
Golimumab	TNF-alpha	Not applicable	2009
Infliximab	TNF-alpha	2006	2005
Ustekinumab	IL12/IL23 p40	2009	2013

•New biologics on the horizon include IL-17 inhibitors, JAK-inhibitors, and IL-23 inhibitors among others.

Controlling psoriasis

- More treatment options today than ever
- Treatment is individualized – not one size fits all
- Know multiple options - one agent won't work on all patients
- Consultations with colleagues about difficult cases work!
- Important to manage comorbidities, especially if patients don't have a PCP
- Skin cancer screenings are necessary (especially for those with a history of immunosuppressive therapies)
- Promote overall health and well-being

Systemic medication workup

- Physical examination and medical history
  - Age appropriate cancer screening: pap, mam, colon
  - Cancer & infection history
  - Vaccination history
  - TBSE
- Social history
  - Weight
  - Alcohol
  - Tobacco
- Family planning
- Labs
  - CBC & CMP
  - hs-CRP
  - Hepatitis (B and C) +/- HIV screen
  - TB Test (yearly)

Concerns with immunosuppressive therapy

- Infection
- Malignancies
- Demyelinating diseases
- Hepatotoxicity
- New onset psoriasis with anti-TNFs
- Injection site reactions (biologics)

Neti Pots and infections

- Neti Pot use is increasing
- Linked to at least 2 deaths from *Naegleria fowleri* (a brain-eating amoeba) when using tap water to flush sinuses
- Use distilled, sterile, or previously boiled water to make the irrigation solution
- Clean and dry Neti Pot between uses

http://abcnews.go.com/Health/Wellness/fatal-infections-linked-neti-pots/story?id=15170230#.Twdq-hyROyw
http://www.cdc.gov/parasites/naegleria/faqs.html

Psoriasis Across the Life Course

Artemas Ward, 1835, Library of Congress

Psoriasis and children

- Psoriasis runs in families
- Children with psoriasis (71%) often have a first degree relative with psoriasis
- Onset often preceded by upper respiratory infection or skin injury
- Chronic disease that will last a lifetime
- No treatment guidelines and limited data in kids
- Childhood spans 0-18 years
- Comorbidities unknown

Busch *et al*. Skin Therapy Lett. 2012 Jan;17(1):5-7.

Treating children with psoriasis is based on experience (not evidence)

Treatment of childhood psoriasis

- Safety concerns for a lifetime of treatment
- Parents who have psoriasis often want to treat more aggressively
- Long courses of UVB, methotrexate, and etanercept are frequently used

Rescue Phase → Transition Phase → Maintenance Phase

Busch *et al*. Skin Therapy Lett. 2012 Jan;17(1):5-7.

Biologic therapy in children

- No guidelines for dosing and monitoring
- Off-label use in children
  - Etanercept (2 and older) approved JIA
  - Adalimumab (4 and older) approved JIA
  - Infliximab (6 and older) approved pediatric Crohn's
- Limited data in psoriasis
  - 1 randomized double-blind trial (etanercept)
  - Case series and case reports

Recommendations for dosing & monitoring in pediatric psoriasis

Luu and Cordora. Skin Therapy Lett. 2013 Feb;18(2):1-4.

Case 1 – Young boy who failed topicals

- 10 yo, thin
- Dad has plaque psoriasis and is on adalimumab
- Tried all topicals without success
- Psychosocial issues
- *Current Tx*: etanercept

Case 2: Teenage psoriasis

- Post-strep onset
- Duration > 6 -12 mos


Before


After

- Interim analysis of 264 week open-label extension in pediatric patients (n=182, weight-based dosing
  - 76.9% completed week 96; 61% PASI75
  - Intermittent use, 80% maintained/ regained PASI 75

Paller *et al*. J Am Acad Dermatol. 2010 Nov;63(5):762-8.
Seigfried *et al*. J Am Acad Dermatol. 2010 Nov;63(5):769-74.

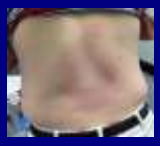
Teenagers and psoriasis

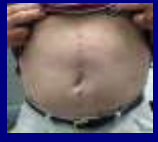
Psoriasis in teenagers

- Teenagers experiment with things they can control (lifestyle and behavior)
- Some are sexually active
- They may not be honest about sexual activity
- Teenagers can get pregnant
- Methotrexate can be difficult due to pregnancy risk and alcohol consumption

Case 3 – Man with metastatic prostate cancer

- 60 yo
- Metastatic prostate cancer
- Quality of life issues with psoriasis (sleep, household)
- Pain (arthritis? mets?)
- Comanagement with oncologist
- Failed acitretin, MTX
- *Current Tx*: etanercept since June
- Prostate cancer stable





MTX = Methotrexate

Case 4 – Woman with psoriatic arthritis and comorbidities

- 53 yo, obese
- Doctor's wife; in wheel chair, now uses walker
- PsO and PsA for lifetime
- Multiple comorbidities:
  - Hypertension
  - Diabetes
  - Depression
- *Current Tx*: infliximab + MTX
- Challenges with:
  - Inverse psoriasis
  - Stasis dermatitis
  - Lifestyle issues

PsO = Psoriasis ; PsA = Psoriatic arthritis; MTX = Methotrexate

Case 5 – Heavily pre-treated adult

- 52 yo, 110 kg
- 15-20% BSA; No PsA
- Past Tx: acitretin, MTX, etanercept, alefacept, studies!
- *Current Tx*: adalimumab for 8 years

BSA = Body surface area; PsA = Psoriatic arthritis

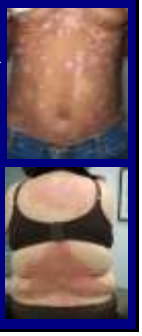
Case 6 – Woman with multiple comorbidities

- 55 yo woman, 93.4kg
- Gastric bypass, hypertension, diabetes, depression, hypothyroid
- >15% BSA
- Past Tx:
  - MTX (early fibrosis)
  - Etanercept (126 kg)
- *Current Tx*: Adalimumab since 2003

MTX = Methotrexate

My clinical experience with TNF-antagonists

- Worldwide experience
- Up to 8 indications depending on agent
- Treatment of choice for PsO + PsA
- Monotherapy or combination therapy (e.g. MTX, topicals)
- Synergy with MTX
- Higher BMI patients do better on monoclonals
- Rotation within the class possible but diminishing returns after 2; consider ustekinumab after 2



PsO = Psoriasis ; PsA = Psoriatic arthritis; MTX = Methotrexate

Treating patients with new-onset psoriasis

- Label update (2009) for all α-TNFs
- Typical patient has Crohn's or RA and develops treatment emergent rash
- Limited information in literature/ guidelines
- Some recommend abandoning TNF-inhibitors, while others are treating through
- Consider risk–benefit to decide if you should try to treat through

http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm174474.htm

Cases 7-8 – Women of childbearing potential

Young adult in college

45 mg Ustekinumab

30 yr old - noncompliant

90 mg Ustekinumab

My clinical experience with ustekinumab

- ~225 active patients on ustekinumab
- Significant improvement in skin disease
- Compliance is high
- Interval adjustments happen
- Psoriatic arthritis
  - Improvement in ACR20 scores (Phase III results: 42% 45 mg, 50% 90 mg, 23% placebo at wk 24)
  - FDA approved 9/23/13
- Pregnancy category B but no data to support decision making in pregnancy or lactation

McInnes *et al*. Lancet. 2013 Aug 31;382(9894):780-9.

Psoriasis in Women of Childbearing Potential

Psoriasis in Women

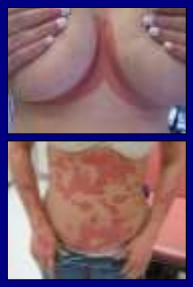
Women

- Often prioritize the health of other family members above their own
- Many have been to 5-6 dermatologists
- Greater psychosocial impact from psoriasis
- Interested in natural treatments, dietary modifications (gluten free), and supplements
  - Natural = Safe?

Stern *et al.* J Investig Dermatol Symp Proc. 2004 Mar;9(2):136-9.
Gelfand *et al.* J Am Acad Dermatol. 2004 Nov;51(5):704-8.
National Psoriasis Foundation Survey Panels.

Women's issues

- May experience sexual impacts from their psoriasis
  - Nearly one-third of respondents (29%) report their disease interfered with their sexual activities in the past month
- May become pregnant
- May be breastfeeding



National Psoriasis Foundation 2005 Spring Survey n=426

Lower rates of pregnancy

- Claims database study comparing 30,733 matched pairs (1:1 women w PsO vs women w/o)
- Women with PsO had lower rates of pregnancy (3.1% vs. 3.6%) and live births (1.4% vs. 2.1%)
- Women < 35 years of age (7,374 matched pairs)
  - 22% lower likelihood for pregnancy
  - 39% lower likelihood for live births

Cather *et al.* Winter AAD Meeting, 2012. PsO = Psoriasis

Why aren't women with psoriasis having children?

- Sexual impact has been underappreciated
- Infertility/ lower rates of pregnancy?
- Increased risk of pregnancy loss?
- Voluntary childlessness?
  - Concerns about heredity of disease
  - Active disease decreasing sexual activity
  - Psychosocial issues limiting relationships

Why we discuss family planning

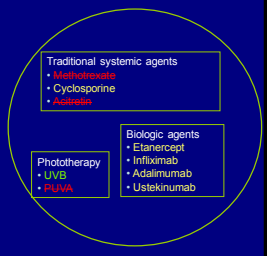
- Active disease can affect outcomes
- Not all medications are safe during pregnancy
- ~50% of pregnancies in US are unplanned
- Important to discuss before pregnancy
- Times when psoriasis is better than others
- Most women will have uncomplicated pregnancies
- Skin should be in good shape for delivery

When a psoriasis patient in my clinic becomes pregnant

- Patient calls when she becomes pregnant
- Ob/gyn recommends stopping all systemic therapies; Usually comfortable with topicals / UV) unless joint disease
- Because psoriasis often gets better during pregnancy, she isn't seen until psoriasis worsens and needs to restart drug (post-partum flare)
- Cycle is repeated with multiple pregnancies
- Special considerations for joint disease

Fewer options for women trying to get pregnant

- Pregnancy category X: acitretin and methotrexate
- Pregnancy category C: cyclosporine
- Pregnancy category B: Anti-TNF agents and ustekinumab
- Topical corticosteroids and calcipotriene are widely used and pregnancy category C



More extensive/ severe disease

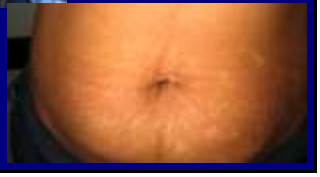
Menter *et al.* J Am Acad Dermatol. 2008 May;58(5):826-50.
Stelera Prescribing Information, Dec 30, 2009.
Strober *et al.* J Am Acad Dermatol. 2009 Jul;61(1 Suppl 1):S1-S46.

Half-life of biologic agents – Pregnancy category B

- Adalimumab - ~2 weeks (10-20 days across studies)
- Etanercept - 102 ± 30 hours (4.25 days)
- Infliximab - 7.7 - 9.5 days
- Ustekinumab - 15 - 46 days (across studies)

[1]From prescribing information.

Etanercept "Peri-Pregnancy"

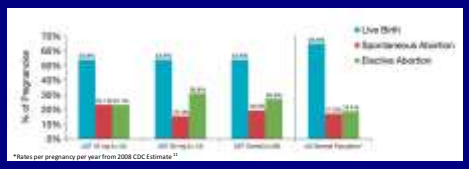


For women who become pregnant on biologics

- OTIS - Organization of Teratology Information Specialists
- Phone: 1-877-311-8972 (toll-free)
- www.otispregnancy.org
- Pregnancy registries for Enbrel and Humira; No signal to date

Ustekinumab pregnancy outcomes

- 29 cases of pregnancy reported in clinical development program (981 women, 473 18-44 yrs)
  - 14 live births, 7 elective abortions, 5 spontaneous abortions, 3 with unknown outcomes
  - Treatment discontinued per protocol upon report of pregnancy
- 14 live births were generally healthy
  - 2 babies had neonatal jaundice that resolved w phototherapy

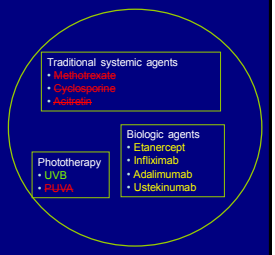


*Rates per pregnancy per year from 2008 CDC Estimate [11]

Cather et al. Fall Clinical Dermatology Meeting 2013.

Fewer options during lactation

- Lactating mothers receiving acitretin, cyclosporine, or methotrexate should not breast feed
- Anti-TNF agents are not usually used during lactation, although the risk of toxicity is probably negligible
- La Leche League
  - www.llli.org



More extensive/ severe disease

Menter *et al*. J Am Acad Dermatol. 2009 Sep;61(3):451-85.
Skomsvall *et al*. Nat Clin Pract Rheumatol. 2007 Mar;3(3):156-64.
Strober *et al*. J Am Acad Dermatol. 2009 Jul;61(1 Suppl 1):S1-S46.

Psoriasis in older adults

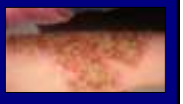
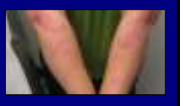
- Many have Medicare as their primary insurance
- Most are on methotrexate, and there are side effects (e.g. kidney and liver function)
- Physical limitations may influence treatment
- Steadiness is an issue with UVB
- Topicals challenging with thin skin
- Many on studies
  - www.clinicaltrials.gov

Polypharmacy – a growing problem

- Many see multiple providers
- Concomitant medications
- Drug interactions are a challenge
- Coordination of care is essential

Helping patients cope

- Help patients control their disease
- Educate patient AND family
- Identify social problems and compliance issues
- Understand school/work challenges
- Psychosocial counseling and support groups as needed
- Family/parents must be included in treatment plan

Managing psoriasis across the lifespan

- Chronic disease that lasts a lifetime
- Treatment is individualized – not one size fits all
- Resources to help patients cope may be needed, especially for younger patients
- Discuss family planning with your female patients
- Promote overall health and well-being

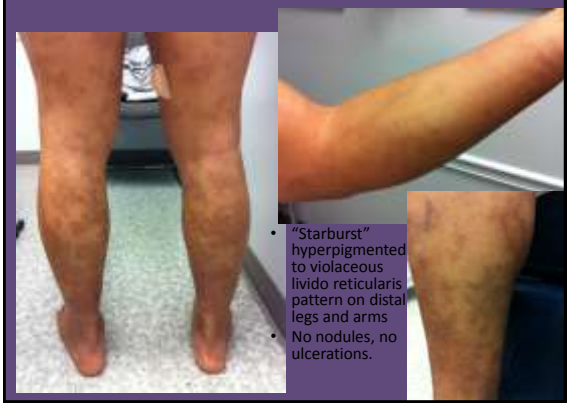
Cutaneous Polyarteritis Nodosa (CPAN) versus Macular Lymphocytic Arteritis (MLA)

Teresa Ishak, DO
PGYIV – Dermatology Resident
Western University/ Pacific Hospital of Long Beach

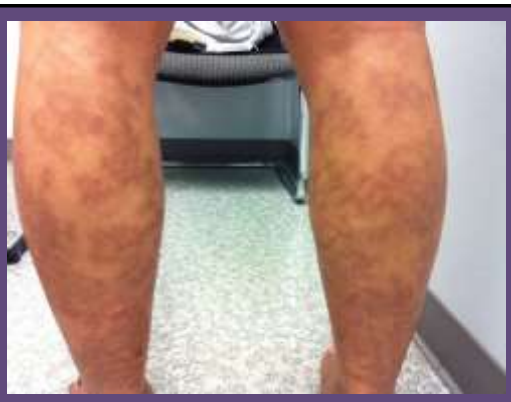
Case presentation

- 23 year-old African American male with history of rash on arms and legs for 2 ½ years
  - Started on the lower extremities
  - Slowly spreading to upper extremities
  - Asymptomatic

- **Past medical history**: acne vulgaris, treated on minocycline. No history of HTN, or any other autoimmune conditions
- **Past surgical history:** none
- **Family History**: no history of SLE or other autoimmune conditions
- **Social History:** denies smoking, etoh, IVDA
- **Allergies**: none
- **Current Medications:** naproxen and plaquenil
- **ROS:** Essentially negative.
  - No fevers, myalgias, arthralgias, weight loss, fatigue, abdominal pain, or preceding URI or infection.



- "Starburst" hyperpigmented to violaceous livido reticularis pattern on distal legs and arms
- No nodules, no ulcerations.

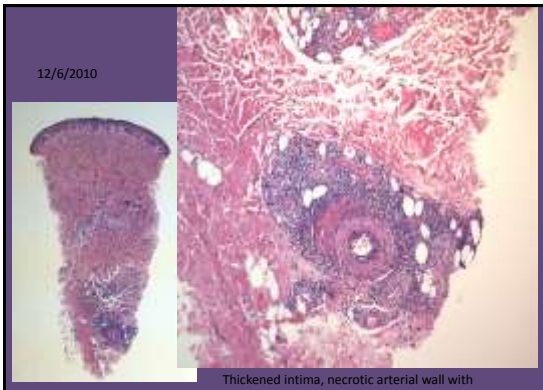


Lab work up

- CMP: WNL
- Sed rate: 1
- CBC: WNL
- pANCA: negative
- cANCA: negative
- ANA: negative
- C3: 119 (normal)
- C4: 29 (normal)
- RF: 4 (normal)
- CRP: WNL
- Hepatitis screen: negative
- UA: WN

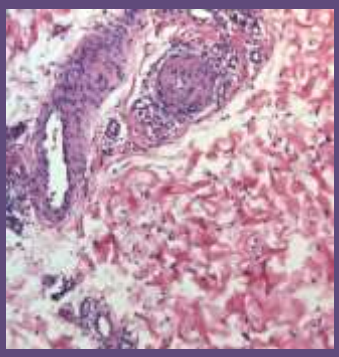
Essentially a normal lab work up

12/6/2010



Thickened intima, necrotic arterial wall with extensive fibrin deposition and mixed inflammatory infiltrate

8/22/2011



Dermatopathologist report: Biopsy consistent with polyarteritis nodosa.

Previous Treatments

- Ultravate ointment
- Dapsone 3/4/10- 12/15/2010
- Naproxen 500mg BID: 11/2011 - ?
- Plaquenil 200mg BID: 2/2012 - ?

Note: Rheumatology is considering starting systemic steroids if there is no significant improvement

Cutaneous Polyarteritis Nodosa

Brief overview of Systemic Polyarteritis Nodosa (PAN)

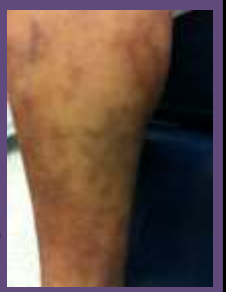
- Multi systemic vasculitis → predominantly medium-sized arterial vessel disease
- Any age, but typically 40-60
- Associated with HBV, inflammatory bowel disease, SLE, Familial Mediterranean fever, Hairy cell leukemia
- Clinical:
  - Cutaneous findings: **50%** with systemic PAN
    - Livedo reticularis, "punched-out" ulcers, painful subcutaneous nodules and digital infarcts, Raynaud phenomenon
  - Extra cutaneous symptoms: weight loss, fever, abdominal pain, arthralgias, myalgias, mononeuritis multiplex, congestive heart failure, kidney involvement, orchitis, CVA are rare

Cutaneous Polyarteritis Nodosa (CPAN)

- First described in 1931 by Lindberg
- Represents 10% of PAN cases
- Reported average age: 43 (6-72)
- Mild systemic symptoms: fever, myalgias, arthralgias, peripheral neuropathy
- Clinical:
  - livedo reticularis
  - tender subcutaneous nodules
  - cutaneous ulcerations
  - Other findings: petechiae, purpura, cutaneous necrosis
  - Most commonly on legs
    - 97% legs
    - 33% arms
    - 8% trunk
  - Chronic, relapsing and remitting benign course; months to years
    - with spontaneous remission or induced by steroid therapy

Diagnosis

- No specific testing for CPAN
- After histological confirmation of presence of vasculitis, CPAN diagnosis can only be made following **exclusion of systemic PAN**
  - Check arterial BP, CBC, ESR, liver and renal function tests, cryoglobulins, ANA, ANCA, RF and complement levels
  - Then evaluate based on symptoms:
    - electromyogram and muscle enzymes for myalgias or muscle weakness
    - nerve conduction studies for paresthesias
    - guaiac stool +/- colonoscopy for abdominal pain
    - renal angiogram for pts with renal dysfunction and/or HTN
  - Also consider ASO titer if pt reports recent illness
  - Evaluation of IBD, infection, medication history



- Lab Studies
  - Mild Anemia
  - Moderate leukocytosis
  - ESR elevated (60%)
  - ASO titers (especially in kids)
  - pANCA (usually minocylcine induced CPAN)
- Histology
  - Fibrin deposition in arterial walls of medium-sized vessels in the deep dermis and subcutis
  - Neutrophilic debris
  - Mixed inflammatory infiltrate

CPAN - Etiology

Unknown

- Viewed as an immune complex-mediated disease
  1) DIF shows IgM and C3 deposition in vessel walls in 9/10 pts *(Diaz-Perez et al, 1980)*
  2) 16 pts – 78% IgM anti-phosphatidylserine-prothrombin complex antibodies → ? Activate classical complement pathway to cause CPAN *(Kawakami et al, 2007)*
- Group A- beta hemolytic streptococcal infection
  - URI *(Fathalla et al, 2005)*
  - One case after necrotizing faciitis *(Stein et al, 2001)*
- Associated w/ Hep B infection *(Trepo et al, 2001)*
  - Treatment options are distinct for Hep B related PAN
- Associated with IBD
  - 5/79 pts with CPAN had IBD *(Daoud et al, 1997)*
- Case reports of CPAN associated with Hep C, Parvo B-19, mycobaterium tuberculosis
- Minocycline induced CPAN

Minocycline induced CPAN

- Proposed diagnostic criteria for minocycline induced CPAN *(Culver et al, 2005)*
  - Consider this condition if pt has 6 of the 7 criteria
    - 1) minocycline use >12 months **
    - 2) skin manifestations including livedo reticularis and/or subcutaneous nodules **
    - 3) arthritis and/or myalgias and/or neuropathy in the distribution of the rash
    - 4) lack of systemic involvement **
    - 5) skin biopsy with necrotizing vasculitis of medium sized vessels **
    - 6) pANCA positivity
    - 7) improvement after discontinuation of minocycline

Progression to systemic PAN??

- *Daoud et al, 1997:*
  - 79 patients followed an average of 7 years had no progression to systemic PAN
- *Chen, 1989:*
  - 2 of 20 patients progressed to systemic PAN in 18 years
- *Fathalla et al, 2005:*
  - 4 children followed average of 5 years – no organ involvement
- *Minkowitz et al, 1991:*
  - 7 of 9 patients in a retrospective study involved at least one organ other than the skin

FOLLOW UP:

- Follow up Q 6months to Q year with full evaluation for systemic PAN
- History, physical, vitals, ESR, CBC, complement levels, liver and renal function studies

Treatment options

- A number of treatment options have been used in the treatment of this skin disorder
- NSAIDS or colchicine
- Pts more refractory to conservative treatment and have extra-cutaneous symptoms → systemic steroids
  - Then steroid sparing agents: NSAIDs, colchicine, hydroxychloroquine, dapsone, azothioprine, cyclophosphamide, methotrexate
- Penicillin for antecedent streptococcal infection

Newly described vasculitic syndromes

1) MACULAR ARTERITIS (MA)
2) LYMPHOCYTIC THROMBOPHILIC ARTERITIS (LTA)
3) MACULAR LYMPHOCYTIC ARTERITIS (MLA)

Macular arteritis (MA)

Cutaneous arteritis presenting with hyperpigmented macules: Macular arteritis

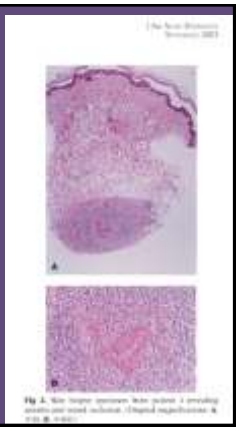
- First described in 2003 by Fein et al. – "Macular Arteritis"
  - 3 African American patients with persistent hyperpigmented patches on the lower extremities
  - Otherwise asymptomatic, no systemic disease

Macular arteritis (MA)

Histology-

Lymphoplasmacytic inflammatory infiltrate around small arteries → Reticular dermis and subcutaneous fat

marked intimal thickening and narrowing of vessel lumen



Lymphocytic Thrombophilic Arteritis (LTA)

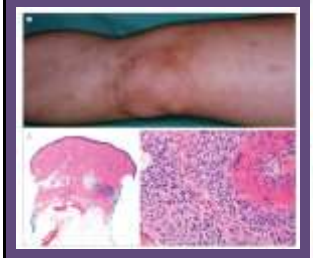
Lymphocytic Thrombophilic Arteritis

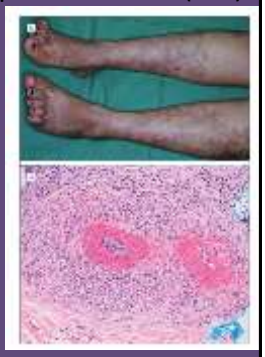
A Newly Described Medium-Sized Vessel Arteritis of the Skin

- Described by Lee et al in 2008
- 5 patients (young women) with slowly progressing patchy reticulated hyperpigmentation of the lower limbs and extensor extremities.
  - No purpura, no ulcer
  - No symptoms, no systemic involvement
- Distinct entity from CPAN

Arch Dermatol. 2008;144(9):1173-1182

Lymphocytic Thrombophilic Arteritis (LTA)





Arch Dermatol. 2008;144(9):1173-1182

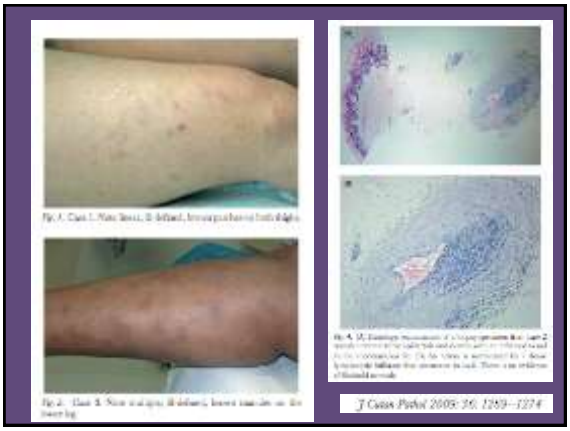
Cutaneous Lymphocytic Thrombophilic (Macular) Arteritis: A Distinct Entity or An Indolent (Reparative) Stage of Cutaneous Polyarteritis Nodosa? Report of 2 Cases of Cutaneous Arteritis and Review of the Literature

- Macarenco et al in 2012
- Suggests that MA and LTA is latent, non nodule forming form of CPAN
- Chronic tissue destruction (due to unknown antigen) propels the vasculitic process

Macular Lymphocytic Arteritis (MLA)

Macular lymphocytic arteritis: a unique benign cutaneous arteritis, mediated by lymphocytes and appearing as macules

- Saleh et al described a new term in 2009.
- Review of literature and three new cases
- Primary cutaneous condition, no systemic disease
- "Macular lymphocytic arteritis" – emphasized the macular and lymphocytic nature of the disease
- Several cases needed **<u>serial sectioning</u>** to reveal the arteritis



J Cutan Pathol 2009: 36: 1269–1274

Macular Lymphocytic Arteritis: Three Cases Questioning Its Classification as Primary Lymphocytic Vasculitis

Caroline Garcia[a] Michel Clanet-Lorand[b] Pascal Roger[c] Jean-Marie Joujoux[a] Laurent Mounier[a,b] Pierre-Emmanuel Stoebner[a,b]

- Garcia et al – December 2013
- Three cases of MLA – hyperpigmented reticulated macules on the legs and arms
- Conclude this is a indolent form of CPAN
- Suggest monitoring patients for progression

Take home points

- Minocycline induced cutaneous polyarteritis nodosa should be considered – thorough medication history important
- Macular lymphocytic arteritis (MLA)
  - is it a spectrum of CPAN ??
  - Important to recognize this under diagnosed entity
  - Do **serial sections** if MLA is suspected
  - Monitor for progression of disease – unlikely, but recommend monitoring

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PSEK: Management of an Extraordinary Syndrome with Ordinary Therapy

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Disclosure

- No financial relationships with commercial interests

Objectives

- Case presentation
- Review Progressive Symmetric Erythrokeratoderma
- Review the various differential diagnosis
- Review management options for PSEK and other palmoplantar keratodermas

Clinical Presentation: HPI

- 5 year old female presented with dry, scaly, thickened palmoplantar plaques.
- Lesions began at birth, progressed over a period of time, then became stationary.
- Repeat infections due to recurrent fissures in hyperkeratotic areas.
- Periodic exfoliation of lesions, particularly on the dorsal aspects of the hands and feet.

Clinical Presentation: PMH

- Born without complication
- Noted exfoliation inguinal region, followed by fluid-filled vesicles on the trunk and axilla in the neonatal period.
- 3 months of age, thickening and peeling palmoplantar surfaces, patches on extensor surfaces of the extremities, trunk and inguinal regions
- Overall health and development unaffected

Clinical Presentation PMH

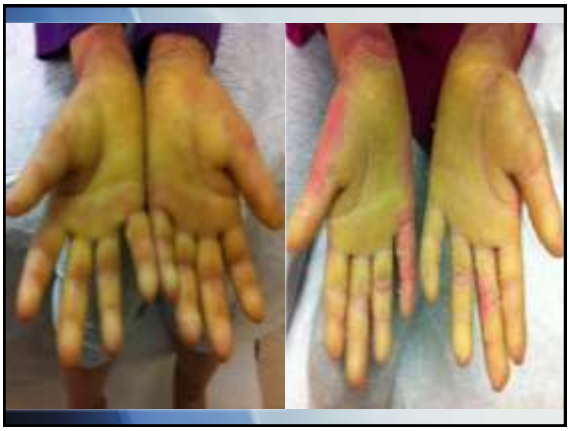
- No seasonal variation
- No associative cutaneous or systemic abnormalities noted.
- No mucocutaneous lesions noted.
- Lesions had a progressive and relapsing course

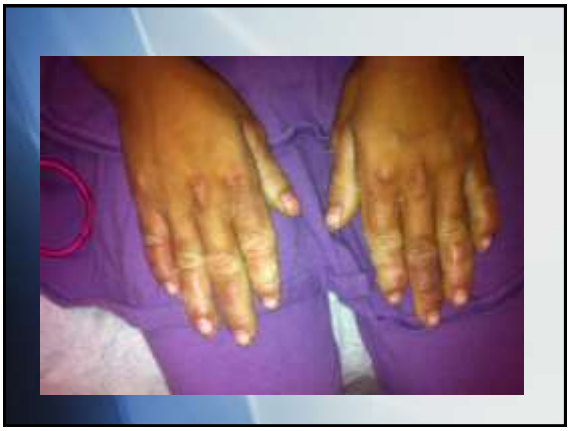
Clinical Presentation

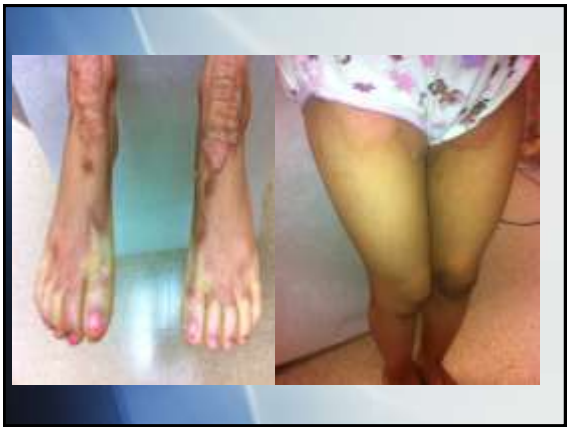
- Medications:
  - Occasional use of mid-potency topical corticosteroids
  - Repeated use of systemic and topical antibiotics
- Family Hx: No history of similar condition

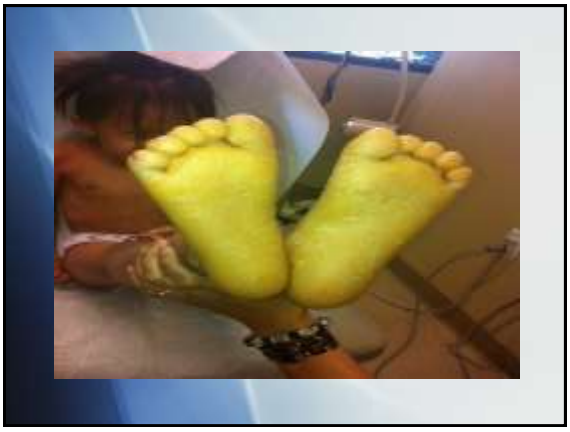
Clinical Presentation: Physical Exam

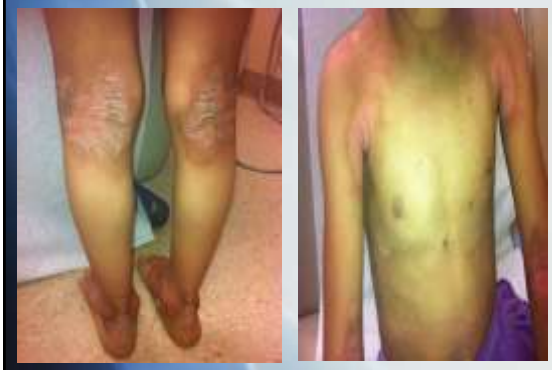
- Symmetric well defined thickened hyperkertotic scaly plaques bilaterally on the ankles and dorsal aspects of the feet with exfoliations
- Palmar and plantar surfaces thickened hyperkeratotitic plaques consistent with an extreme palmoplantar keratoderma
- Hyperkeratotic erythematous psoriasiform plaques on chest, popliteal and antecubital fossas.









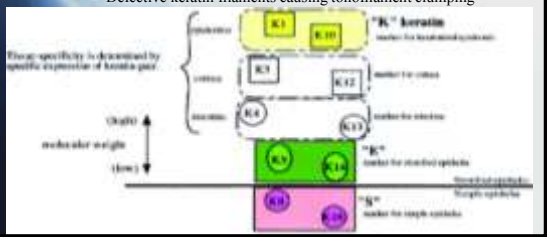


Differential Diagnosis

- Erythrokeratoderma Variabilis
- Bullous Congenital Icthyosiform Erythroderma
- Psoriasis
- Pityriasis Rubra Pilaris
- Vohwinkel Syndrome
- Keratitis Ichthyosis Deafness Syndrome

Differential Diagnosis

- Epidermolytic Hypkeratosis (Bullous Congenital Ichthyosiform Erythroderma)
  - Autosomal Dominant, 50% spontaneous mutation
    - Mutation in Keratin 1 and Keratin 10 genes
      - Defective keratin filaments causing tonofilament clumping



Epidermolytic Hyperkeratosis

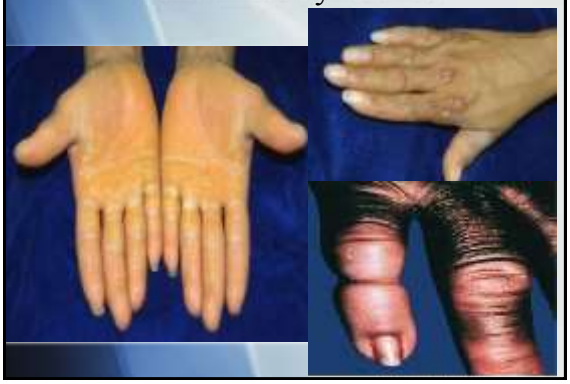
- Neonates: erythroderma, diffuse superficial bullae, rupture leaving denuded areas

- 3 months: Localized to generalized hyperkeratosis
  - Ichthyosis typically generalized, more prominent flexures and overlying joints
  - May have prominent palmoplantar keratoderma
  - Pungent body odor

Differential Diagnosis

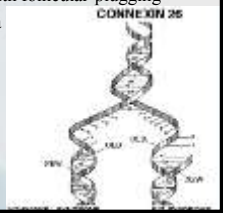
- Vohwinkel Syndrome
  - Autosomal Dominant (sporadic cases also reported)
  - Two mutations reported
    - GJB2 gene encoding Connexin-26
      - Hearing loss associated
    - Loricrin gene on 1q21
      - Major function in formation of cornified cell envelope
        - Ichthyosis associated not deafness
  - Diffuse palmoplantar keratoderma (honeycomb)
  - Constrictive bands of digits (pseudoainhum)
  - Starfish-shaped hyperkeratotic plaques dorsal hands, extensor surfaces
  - Scarring alopecia
  - Hearing loss in classic variant

Vohwinkel Syndrome

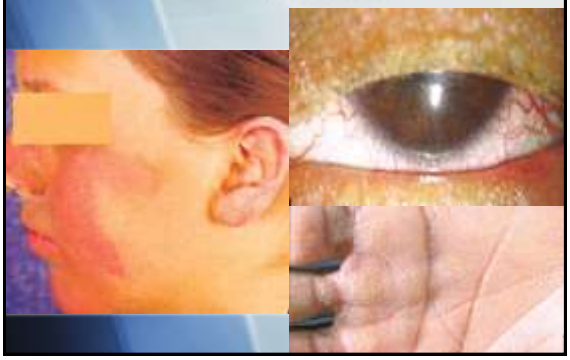


Differential Diagnosis

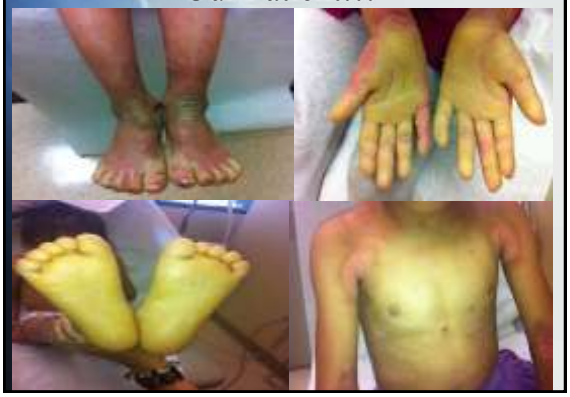
- Keratitis Ichthyosis Deafness Syndrome
  - Autosomal dominant and recessive reported
    - GJB2 gene encoding Connexin 26 on 13q11-12
      - At birth may present with transient erythroderma
      - Later develop well demarcated keratotic plaques
    - Generalized mild hyperkeratosis with follicular plugging
    - Stippled Palmoplantar keratoderma
    - Alopecia
    - Sensorineural deafness
    - Progressive keratitis
      - May progress to secondary blindness



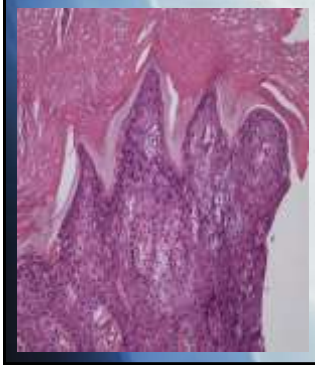
KID Syndrome



Our Patient…



Histopathology



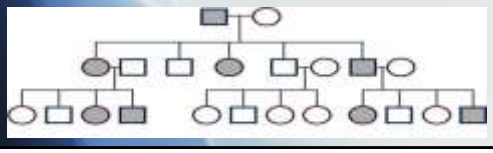
- Papillated epidermal hyperplasia, hypergranulosis, parakeratosis and compact orthokeratosis.
- Lipid vacuoles in the stratum corneum
- Some foci of parakeratosis between the granular layer and the overlying orthokeratotic cornified layer.

Final Diagnosis

- Progressive Symmetric Erythrokeratoderma (PSEK)

Discussion

- PSEK (Gottron's Syndrome)
- 30 cases reported in the literature
- Rare autosomal dominant genodermatosis
  - 40 – 50% sporadic due to new genetic mutations
- First described by Darier in 1886, presented by Gottron in 1922

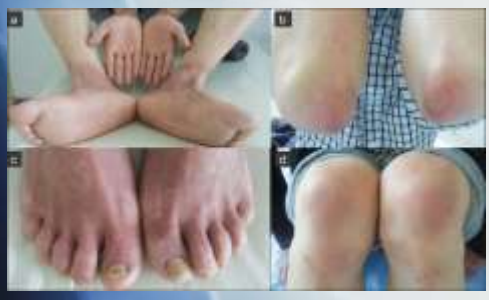


Discussion

- Presents as large fixed non-migratory geographic and symmetrical plaques typically on the knees, elbows, palms and feet during infancy or early childhood
- Lesions commonly are progressive over a few years and then become stable

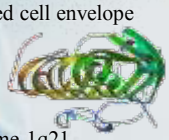
Discussion

Discussion



Discussion

- Family history in 50% of patients
- Spontaneous mutation in the Loricrin gene
  - Loricrin is the major structural component of the cornified cell envelope



- Chromosome 1q21
  - Loricrin same gene mutation associated with Vohwinkel Syndrome

Discussion

- Associated features of PSEK:
  - Keratoderma
  - Ataxia
  - Syndactyly

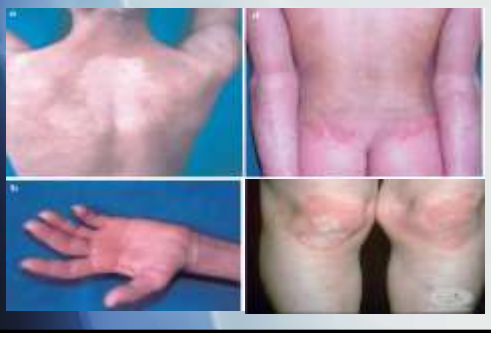
Discussion

- Comparison to EKV
  - Described by Mendes da Costa in 1925
  - Seasonal variations
  - Migratory and change shapes
    - Temperature, wind, emotional conditions
  - Typically involve the abdomen, thorax and extremities
    - Not as symmetric as PSEK
    - Palms and soles not as commonly affected

Discussion

- Comparison to EKV
  - Missense mutation of connexin genes
    - GJB3 or GJB4
    - Chromosome 1p35.1
  - Histopathology:
    - Psoriasiform hyperplasia with focal parakeratosis, well preserved granular layer with no munro's microabscesses

Erythrokeratoderma Variabilis



Comparison PSEK and EKV

	PSEK	EKV
Location	**Spares trunk**	Thorax and abdomen
Cutaneous plaques	**Stationary**, hyperkeratotic erythematous	Erythematous irregularly shaped, variable (solid, annular, polycyclcic) and **migratory** hours to days
Palmoplantar keratoderma	50% of patients	Less common
Histopathology	Nonspecific: Hyperkeratosis with areas of focal parakeratosis, well preserved granular layer, acanthosis and a scant perivascular infiltrate in papillary dermis	Nonspecific: Hyperkeratosis with areas of focal parakeratosis, well preserved granular layer, acanthosis and a scant perivascular infiltrate in papillary dermis
Electron Microscopy	1) **Lipid vacuoles** in stratum corneum 2) Swollen mitochondria coalescing in perinuclear location specific for PSEK	Increase numbers of unmyelinated nerve fibers in papillary dermis
Genetics	**Loricrin gene** Chromosome 1q21	**Connexin GJB3/GJB4** Chromosome 1p34-35.1

Discussion

- Management PSEK:
  - Topical retinoids
  - Keratolytics / Humectants
  - Glucocorticoids
  - Calcipotriene
  - Systemic Isotretinoin

Discussion

- Tazarotene
  - Active metabolite Tazarotenic acid
    - Binds RAR-β and RAR-γ
    - Normalizes epidermal differentiation
      - Decreases cell-cell adhesion between corneocytes
    - Exhibits antiproliferative effect
    - Inhibits ornithine decarboxylase
      - Marker for proliferative activity expressed by basal cells
  - Reported therapeutic effects:
    - Psoriasis
    - Keratoderma

Discussion

- Urea
  - Keratolytic / Humectant
    - Disperses keratin in stratum corneum
    - Dissolves intracellular matrix of cells of stratum corneum
      - Promotes desquamation
      - Resultant softening of hyperkeratotic areas
    - Reduces thickness of keratoderma
    - Therapeutic response reported to 10 – 40% Urea
- Lactic Acid
  - Keratolytic / Humectant
  - α-hydoxy acid
    - Increases hydration of stratum corneum
      - Improved pliability and softening effect

Discussion

- Salicylic Acid
  - β-hydroxy acid
    - Lipid soluble
    - Facilitates desquamation by solubilizing intracellular cement that binds scales in stratum corneum
      - Loosens keratin
    - In Children should not exceed 30g of 6% salicylic acid per day: Salicylism
      - Fever
      - Confusion/delirium/psychosis
      - Tinnitus
      - Metabolic acidosis

Discussion

- Calcipotriene
  - Synthetic vitamin D3 analog
    - Affinity for vitamin D receptor
      - Binding modulates T cell gene transcription
        - Decrease cell differentiation and basal cell layer proliferation
        - Normalizes keratinocyte differentiation
          - Immunomodulatory effect keratinocytes
    - Reported therapeutic effects:
      - Psoriasis
      - Inflammatory linear verrucous epidermal nevus
      - Confluent and Reticulated Papillomatosis (CARP)

Discussion

- Dremel
  - Rotating diamond-edged wheel
  - Mechanical debridement

Discussion

- Oral Retinoids
  - Isotretinoin/Acitretin/Etretinate
    - Affinity to retinoic acid receptors (RAR) and retinoid X receptors (RXR)
    - Directly inhibit ornithine decarboxylase
      - Reducing inflammatory proliferative phase
    - Inhibit collagenase activity
    - Reduce epithelial cell-cell adhesion
      - Arrest cornification
      - Decrease stratum corneum thickness
      - Reduce inflammation in the epidermis
    - Normalize epithelial growth and differentiation
      - Improvement of disorders of keratinization

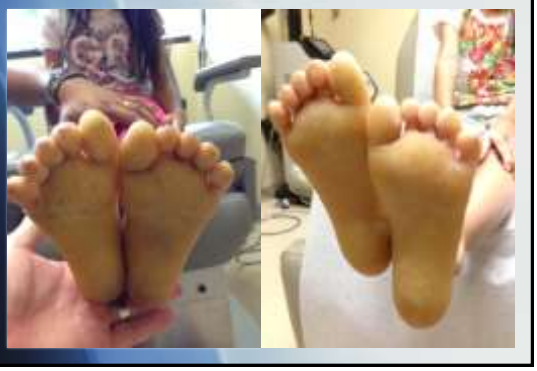
Discussion

- Oral Retinoids
  - Reported therapeutic effects in keratodermas
    - Inhibition of keratinization
      - Erythrokeratoderma Variabilis
      - Vohwinkel's Syndrome
        - Improvement of palmoplantar keratoderma and pseudoainhum
        - Some evidence suppression of expression of defective loricrin protein.
      - Pityriasis rubra pilaris
      - Epidermolytic hyperkeratosis
      - Keratitis Ichthyosis Deafness (KID) Syndrome
      - Psoriasis

Discussion

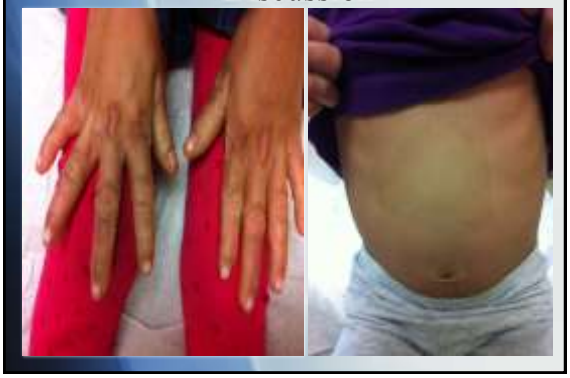
- Our Management:
  - Trunk/Extremities
    - Betamethasone valerate ointment mixed with emollient trunk
  - Palmoplantar surfaces
    - Tazarotene under occlusion every other night, then reduced to twice a week
    - 2 weeks later added 40% urea q day
    - Dremel once a month
  - After 8 weeks…

Discussion



Discussion

Discussion



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Multisystemic Langerhans Cell Histiocytosis

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West Palm Hospital

No relevant financial disclosures

Objectives

- Discuss clinical presentation of pediatric LCH
- Examine the new classification scheme and its relationship to therapy
- Discuss the intricate role of the RAS-RAF-MEK-ERK (MAPK) and PI_3K-AKT signaling pathways in LCH
- Explore the future of personalized molecular treatment with less toxic therapeutic options

Clinical Presentation

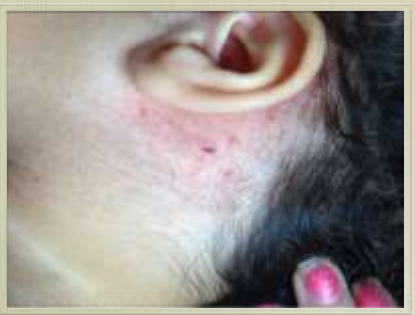
- 22 month old female presented with 2 month history of poor PO intake, diarrhea, anasarca and a non-resolving scalp dermatitis. She had previously failed treatment for seborrheic dermatitis.
- Past medical and surgical history-negative
- Birth history- uncomplicated term vaginal delivery

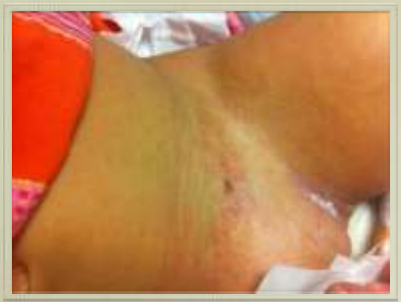
Physical exam

- Vitals: T: 98 HR :140 RR: 14 SPO2: 100% RA
- General: no acute distress
- HEENT: normal
- Heart: Tachycardia with regular rhythm, no murmurs
- Lungs: clear to auscultation
- Abdomen: distended with palpable liver and spleen 1 cm below costal margin. Non-tender to palpation. Positive bowel sounds x4
- Extremities: 2+ pitting edema bilateral upper and lower extremities
- Neuro: no focal deficits

Dermatologic exam

- Skin: Erythematous to brown hemorrhagic crusted papules with yellow scale and background petechiae (face, scalp, flexural folds)





Admission Labs/Imaging

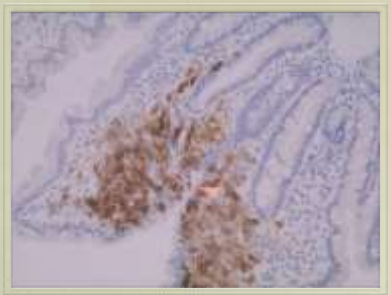
- BASIC METABOLIC PROFILE: WNL
- ALBUMIN: 1.6 g/dl
- LIVER FUNCTION TESTS: WNL
- PLATELETS: normal
- CBC: HBG 6.6 g/dl HCT 22.0%,
- MCV: 70.1 fl
- RETIC COUNT: 6.05% (H)
- PT/PTT/INR: normal
- ABD U.S.: MILD HEPATOSPLENOMEGALY, MILD ASCITES AND DIFFUSE INCREASED ECHOGENICITY OF THE LIVER. KIDNEYS- NORMAL

Differential

Acrodermatitis enteropathica
Seborrheic dermatitis
Immunodeficiency
Hematologic malignancy
Scabies
Cystic Fibrosis
Celiac disease
Psoriasis

Hospital Course

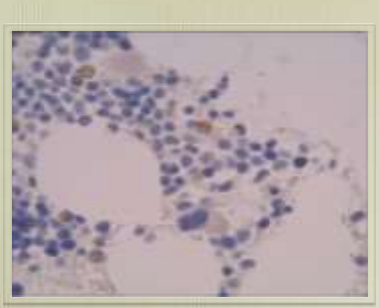
- Persistent diarrhea with positive occult stool and anemia.
- GI consulted.
  - EGD and flexible sigmoidoscopy:
    - Duodenal biopsy- infiltration of Langerhans cells
    - Normal flexible sigmoidoscopy and normal gastric biopsy
    - Negative celiac panel, normal fecal fat, normal stool , alpha-1 anti-trypsin, negative hepatitis panel, normal zinc level



Duodenum (+) CD1a

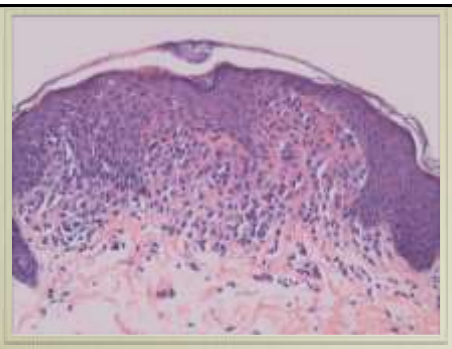
Hospital Course

- Hematology/Oncology consult
  - Bone Marrow biopsy- easy infiltration of Langerhans cells
  - CT brain, chest, abdomen/pelvis- mild mesenteric LAD
  - Negative bone survey
  - Persistent anemia requiring court order for transfusion
  - Flow cytometry- normal, with a normocellular bone marrow
  - Negative hemoglobin electrophoresis, normal immunoglobulins, normal G6PD



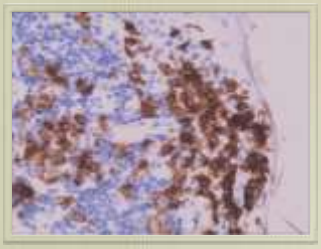
Bone Marrow (+) CD1a

Dermatology consulted!



Left groin

Left groin (+) Langerin



Left Temple (+) Langerin

Diagnosis/Treatment

- Multisystem Langerhans Cell Histiocytosis (MS-LCH)
- (Skin, Small bowel, bone marrow, (+/-) liver/spleen)
- Induction chemotherapy initiated
  - Vinblastine + prednisone + 6 mercaptopurine
  - Followed by vinblastine + prednisone weekly for 6 weeks

Follow-up

- Following initial therapy, cutaneous manifestations of LCH had markedly improved. Repeat bone marrow biopsy performed- persistent Langerhans cells.
- Salvage therapy started:
  - Clofarabine 12.5mg/m2 x 5 days
  - Pentamidine for PCP prophylaxis

Follow-up

- -->Following first course of Clofarabine, patient developed severe pancytopenia with subsequent bacteremia
  - ANC: 30
  - Blood cultures: coagulase negative staph
  - Hospitalized and treated with appropriate antibiotics
- -->Clofarabine dose was decreased by half due to above complications. Patient has since tolerated medication well, currently on 3rd course of treatment.

Background

- Originally described by Lichtenstein
- Histiocytosis "X" (reflecting the unknown)
- To some degree, this still accurately reflects the state of our knowledge
- Histiocyte means "cell of the tissue"

Langerhans cells

- -Bone marrow derived dendritic cell, reside in the skin and lymph nodes
- -Functions as an antigen presenting cell
- -Immunophenotypically positive for S100, CD1a, and Langerin (CD207)
- -Positive Langerin expression indicates the presence of Birbeck granules
- *Dermatologic and Systemic disease caused by clonal proliferation of Langerhans cells

Etiology

- Reactive? EBV has been associated with increased incidence of LCH
- Genetic? Higher occurrence in monozygotic twins and t (7,12) translocation suggests inherited genetic defect
- Neoplastic? Langerhans cells have been shown to harbor specific mutations in their clonal state as well as stain positively for various components of the MAPK pathway. LCH cells also have a strong immunoreactivity for p53 and Ki-67 markers.

- Considered a pediatric disease, but can present at any age, even well into adulthood
- Can affect any organ with the most common sites being skin, lymph nodes, bone, ears, pituitary, and lungs
- Clinical course varies: spontaneously regressing to rapidly progressive and deadly multisystemic disease
- Characteristic clinical manifestations include anemia, thrombocytopenia, fever, lymphadenopathy, and hepatosplenomegaly
- Despite the initial presentation, all patients should be closely monitored for the progression to advanced systemic disease

Dermatology. Bolognia JL, et al. 2012, third edition, 1529-1536. Elsevier Saunders

Discussion

- Classification:
- 1. Letterer-Siwe: acute form, <1 year, aggressive fulminant course, multisystem
- 2. Hashimoto-Pritzker (congenital self-healing): red brown papulo-nodules at time of birth
- 3. Hand-Schuller-Christian: age 2-6 years, diabetes insipidus, cranial bone lesions, exophthalmos
- 4. Eosinophilic granuloma of bone: localized variant

Discussion

- Single system LCH (SS-LCH): defined as one organ or system involved (bone, skin, lymph node, lungs, CNS)

- Multisystem LCH (MS-LCH): two or more organs/ systems involved (with or without "risk organs")
risk organs defined as hematopoietic, spleen, liver, lung

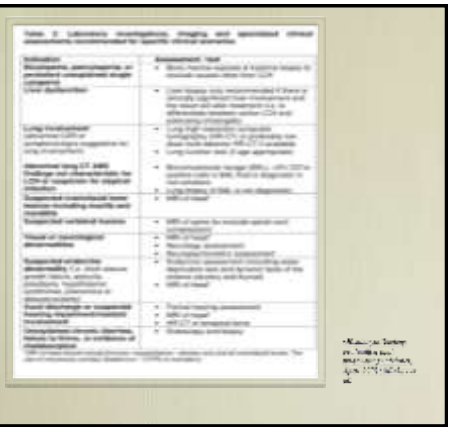
Histiocyte Society Evaluation and Treatment Guidelines, Minkov Milen, et al. April 2009

3. LABORATORY AND RADIOGRAPHIC EVALUATION:

Table 1: Recommended baseline evaluation upon diagnosis and reactivation

Full blood count:
• hemoglobin, white blood cell and differential count, platelet count
Blood chemistry:
• total protein, albumin, bilirubin, ALT(SGPT), AST(SGOT), alkaline phosphatase, GT
• BUN, creatinine, electrolytes
• Ferritin
Coagulation studies:
• INR/PT, APTT/PTT, fibrinogen
Early morning urine sample:
• Specific gravity and osmolality
Abdominal ultrasound:
• Size and structure of liver and spleen
Chest radiograph (CXR)
Skeletal radiograph survey*:
* Functional imaging such as bone scan is optional and can be performed in addition to skeletal survey. PET scan has proven to be the most sensitive functional test used in the identification of LCH lesions and in evaluating patient response to therapy.

Histiocyte Society Evaluation and Treatment Guidelines, Minkov Milen, et al. April 2009



Treatment

- Revolves around degree of clinical involvement
- Mild skin-limited disease: Topical mid potency steroids, NBUVB, topical nitrogen mustard, oral thalidomide
- Bony lesions respond well to curettage or localized radiation therapy
- Severe multisystemic disease: chemotherapy
- Hematopoietic stem cell, liver, or lung transplant may be required for patients with the most severe disease unresponsive to systemic chemotherapy

Dermatology, Bolognia JL., et al. 2012, third edition, 1509-1535, Elsevier Saunders

Indications for systemic therapy

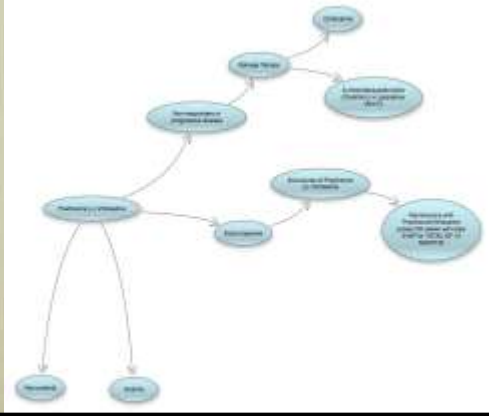
- SS-LCH with CNS lesions
- SS-LCH with multifocal bone lesions
- SS-LCH with "special site lesions"
* defined as craniofacial bony lesions, ocular, ear, oral, or CNS*
- MS-LCH with/without involvement of "high risk organs"
*high risk defined as liver, lungs, spleen, hematopoietic)

Histiocyte Society Evaluation and Treatment Guidelines, April 2009, Minkov, et al.

Traditional Systemic Therapy

- *Initial induction therapy: 6 week course with vinblastine (+) prednisone (+) 6-MP
- *Salvage therapy: Traditionally Cytarabine and Cladribine, but significant toxicity

Histiocyte Society Evaluation and Treatment Guidelines, Medico Mitos, et al. April 2005



On the Horizon: Clofarabine

- Need significant results with limited toxicity
- Clofarabine: purine nucleoside antimetabolite used in treatment of ALL as second line
- Multiple studies have shown rapid response to single agent Clofarabine with limited toxicity

Clofarabine salvage therapy for refractory multifocal osteolytic disorders, including Langerhans cell histiocytosis, JMS, and Erdheim-Chester disease. Klein, D. et al. Pediatric Blood Cancer 2013 Sept.

Clofarabine salvage therapy for refractory high-risk pediatric cell histiocytosis. Alvarado, G. et al. Pediatric Blood Cancer 2013 June; 60, 9, 1529-32.

Clofarabine in refractory Langerhans cell Histiocytosis. Rodriguez-Galindo, C. et al. Pediatric Blood Cancer 2008 Nov; 51 (5): 703-708.

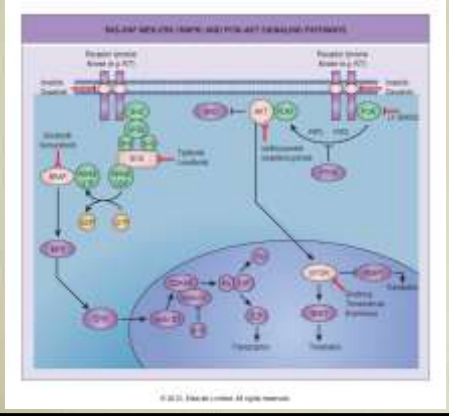
Mitogen activated protein kinase pathway

- MAPK: coordinates a large variety of cellular responses including cell cycle regulation, cell survival and apoptosis, cell proliferation and differentiation by transmitting signals to nuclear targets

Immunology, Kindt, T. et al. 2013. 8th edition. Elsevier Saunders

BRAF

- Most common mutation is caused by a single amino acid substitution of valine for glutamine at codon 600
- Mutation results in activation of MEK-ERK signaling with increased proliferation and protection from apoptosis.



Bolognia 3rd edition, 2012

On the Horizon: Imatinib(TKIs)

- Several cases of Langerhans cell histiocytosis have been reported to express PDGFR alpha/ beta as well as c-KIT by immunohistochemistry

Immunohistochemical and molecular cytogenetic evaluation of potential targets for tyrosine kinase inhibitors in Langerhans cell histiocytosis. *Caponetti GC et al. Human pathology. 2012 Dec; 43 (12): 2223-8.*

- Goal was to evaluate a series of cases of LCH for expression of immunohistochemical and molecular markers that would identify patients who might benefit from TKIs
- PDGFR alpha, PDGFR beta, cKIT
- 14 cases of LCH
- 4/14 were positive for PDGFR alpha by fluorescence in situ hybridization (no positivity for beta or cKIT, but this has been demonstrated in other studies)
- A subset of cases of LCH may harbor gene rearrangements and thus clinical trials are warranted to evaluate therapy with tyrosine kinase inhibitors such as Imatinib

LCH and BRAF

Recurrent BRAF mutations in Langerhans cell histiocytosis. Blood. 2010 September 16; 116 (11): 1919-1923

- This study identified the oncogenic BRAF V600E mutation in 35/61 specimens (mutation frequency of 57%)
- The langerhans cells also stained for phospho-MEK and phospho-extracellular signal-regulated kinase (ERK) independently of the BRAF mutation status.
- Since all of the LC stained for the MAPK and ERK pathway with the same intensity as the BRAF mutated cells, this strongly suggests that the MAPK pathway may generally be activated in LCH, but BRAF mutations are not the ONLY cause.
- Further research is needed.
- This study did not make any definitive conclusions regarding the effect of mutation status on clinical outcomes

On the horizon: Vemurafenib

BRAF V600E mutant protein is expressed in cells of variable maturation in Langerhans cell histiocytosis. *Blood. 2012 Sept; 120 (12): e28-34*

-89 patients with LCH

-34/89 lesions had (+) mutations

Saving orphans: BRAF targeting of histiocytosis. *Blood. 2013 Feb 28; 121(9):1487-8.*

-Significant therapeutic activity of Vemurafenib in 3 patients with rare histiocytic disorders including LCH and Erdheim-Chester disease

In conclusion

What's already known about this topic?

- LCH is a clonal proliferation of langerhans cells that may have single system or multisystem involvement.
- Systemic chemotherapy has provided minimal therapeutic benefit and significant toxicity.

What does this case presentation add?

- Initial evaluation by dermatologists can provide rapid diagnosis by skin biopsy.
- Future classification of LCH will likely shift to molecular classification which will have profound implications for systemic drug therapy and thus "personalized" molecular treatment.
- Focus on the MAPK and PI3K-AKT signaling pathways will likely continue to provide new successful treatment options without associated significant toxicity.

References

- **BRAF V600E mutant protein is expressed in cells of variable maturation in Langerhans cell histiocytosis.** *Blood. 2012 Sept; 120 (12): e28-34*
- **Saving orphans: BRAF targeting of histiocytosis.** *Blood. 2013 Feb 28; 121(9): 1487-8.*
- **Recurrent BRAF mutations in Langerhans cell histiocytosis.** *Blood. 2010 September 16; 116 (11): 1919-1923*
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OBSERVATIONS AND OMMISIONS:

PEARLS AND PITFALLS OF FACIAL RECONSTRUCTION

Aaron Bruce, DO, FAOCD
Board Certified Dermatology
Fellowship Trained Skin Cancer and Reconstructive Surgeon
Montana Skin Cancer and Dermatology Center, PC
Bozeman, MT

SURGICAL DEFECT MANAGEMENT

- Granulation?
  - Small, superficial, concavities
  - Wound care, contraction, variable scar
- Primary?
  - Fast Healing, minimal care
  - Long linear scar can be hard to "hide"
- Graft?
  - FTSG vs STSG
  - Delayed vs immediate
  - Donor Site, contraction, Bolster Dressing
  - Less the optimal cosmetic outcome
- Flap or some combination of the above?

FLAPS

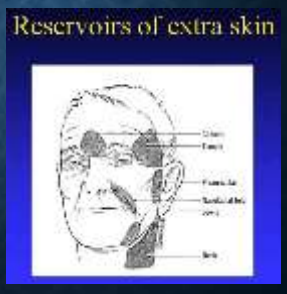
- Better cosmetic outcome
  - Adjacent tissue provides "best match"
- More options to hide scar
- More control of tension vectors
- Replace loss of tissue volume for deeper defects
- Avoid having a second surgical site (donor site)

DECISION MAKING

- Defect
  - Simplest
  - Function
  - Cosmesis
  - Tumor surveillance
- Patient
  - Cosmetic concerns
  - Smoking or overall "bad protoplasm"
  - Wound care
- Discuss options
  - Be direct, firm, cautiously optimistic
    - Managing expectations is the key to patient happiness
      - Review Hypertrophic scars, flap/graft failure, contraction etc…
    - Having some "buy-in" from younger patients

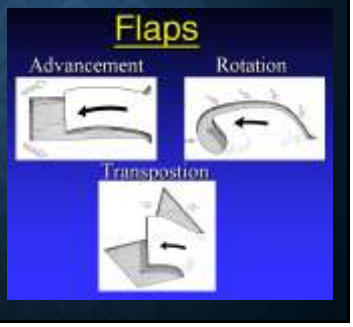
TISSUE RESERVOIRS

- Source
- Mechanism of movement
- Final scar location
- Cosmetic Units



TISSUE MOVEMENT

- Primary
  - Movement into surgical defect
  - Advancement, rotation, and transposition
- Secondary
  - Movement into secondary defect



SCAR PLACEMENT

- Favorable incision lines
  - Junction lines between cosmetic units
  - Skin tension lines
- Optimizing the scar
  - Deep suspension sutures
  - Wound edge eversion
    - Exaggerate nose, forehead, chin
  - Suture selection of duration
  - Revision/ILK/sanding if necessary

THE CHEEK

- Anatomic Considerations:
  - Danger zones (MM, Temporal branch, Stenson's)
  - Undermine below follicles in men
- Aesthetic Considerations:
  - Curvilinear along tension lines
  - Capitalize on cosmetic junctions if possible
  - Free margins: eyelid, lip
    - Sit the pt up to eval, upward gaze/contraction

THE FOREHEAD

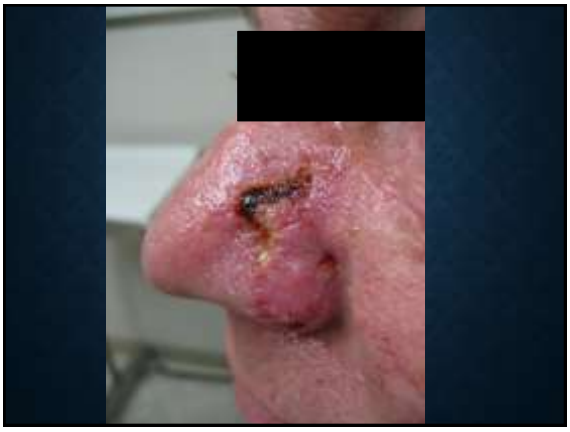
- Anatomic Considerations:
  - Warn patients of distal sensory loss
  - Have suture/stats ready if working near superficial Temporal A.
    - Trace it out with marker using the pulse if not obvious
- Aesthetic Considerations:
  - Eyebrow symmetry (1cm elevation)
  - Utilize hairline if possible

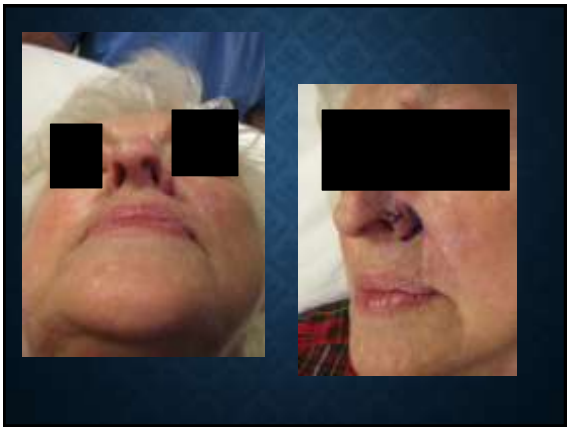
THE TEMPLE

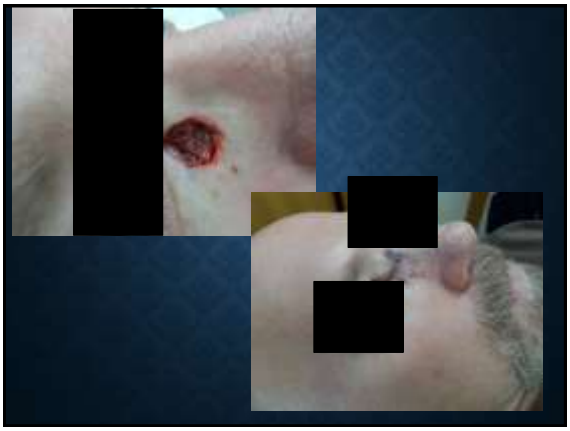
- Anatomic Considerations:
  - Temporal branch of Facial Nerve
- Aesthetic Considerations:
  - Many options to hide scars
  - Secondary intention/grafts usually do well
  - M-plasty in the crows feet. (not a flap)

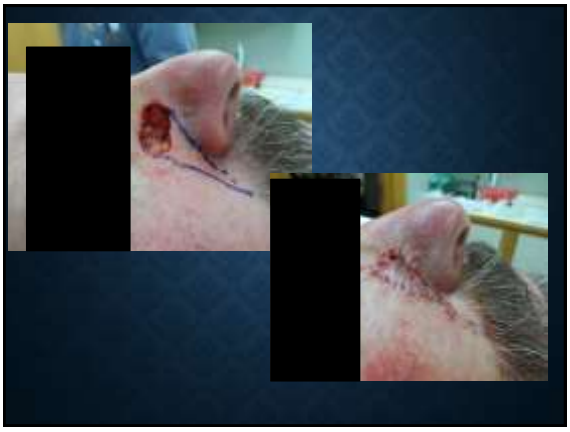
THE NOSE

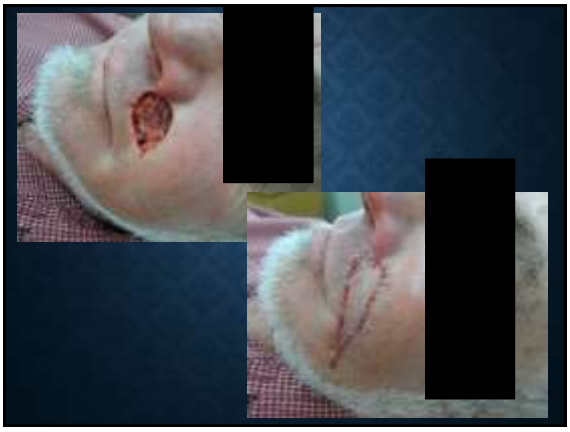
- Anatomic Considerations:
  - Lower 1/3 vs Upper 2/3
  - Prefer Flaps if possible if can't be closed primarily
  - Int/Ext valves
- Aesthetic Considerations:
  - Capitalize on subunits/junctions
  - Alar Rim
  - Soft Triangle

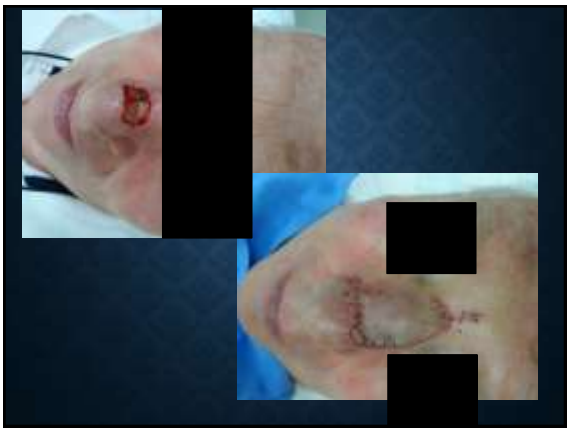


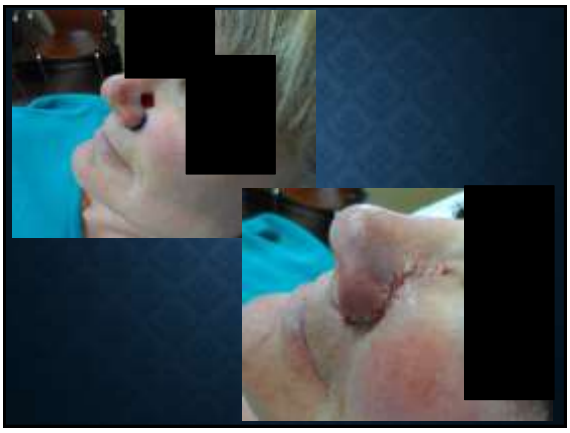


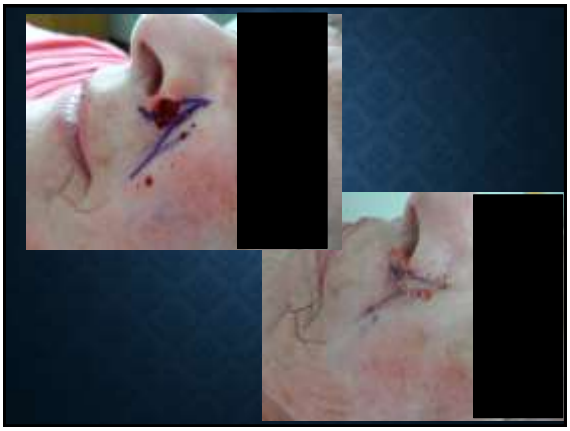


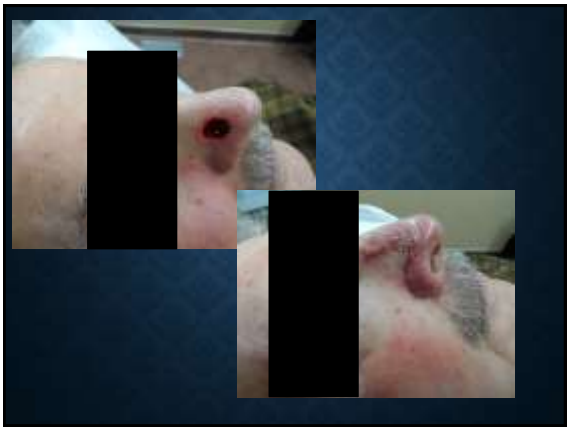


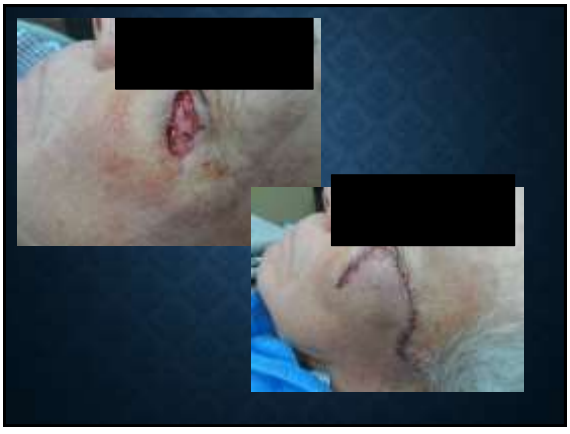


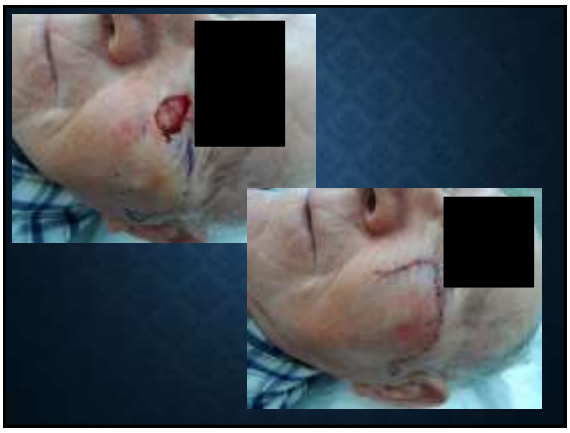


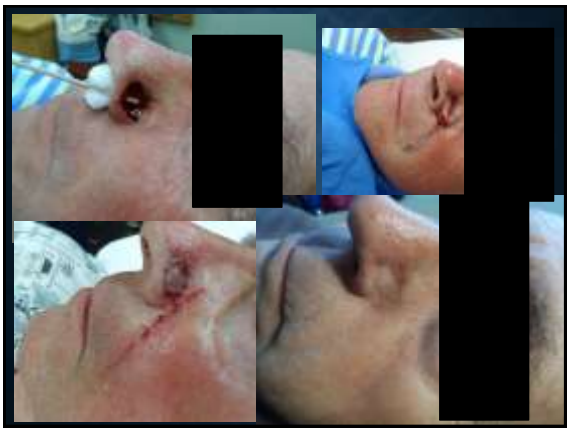


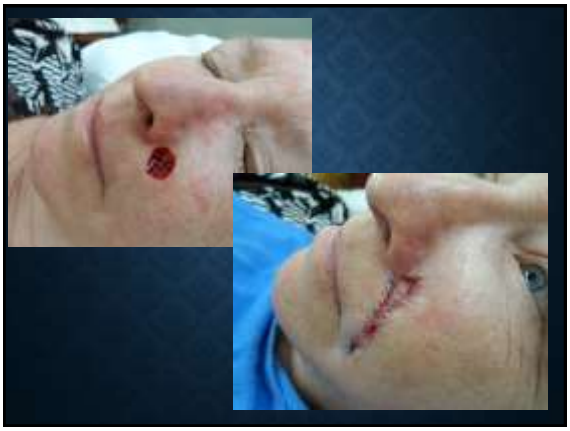


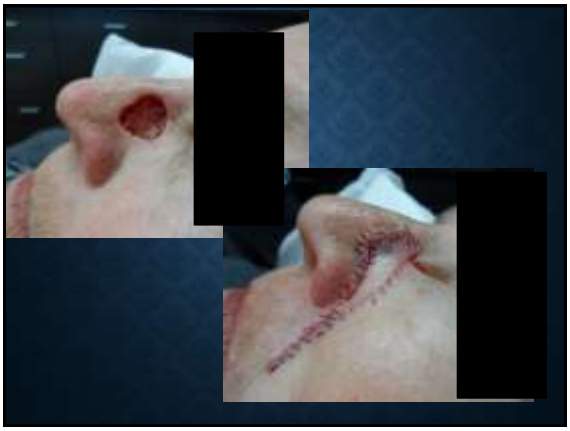


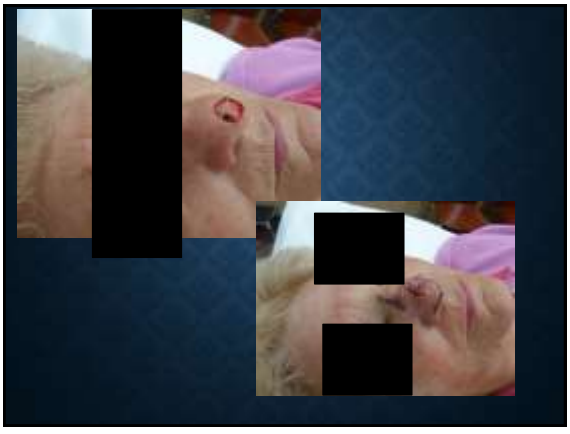


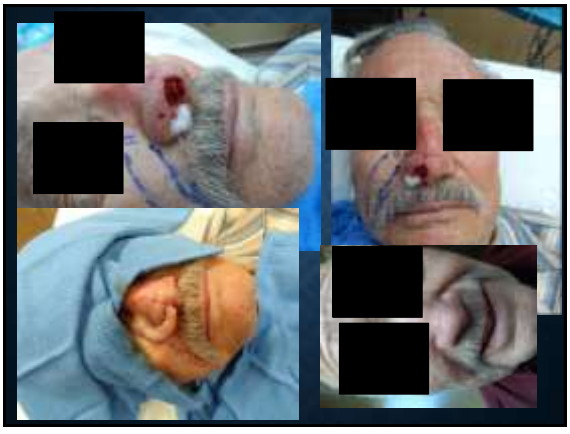


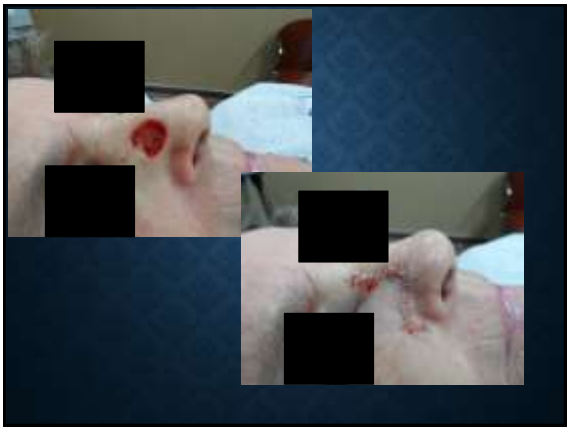


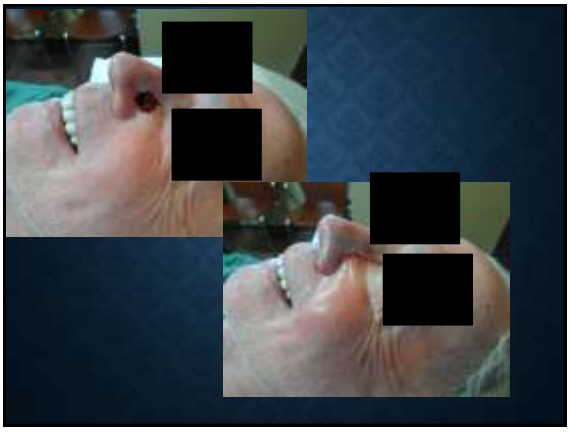


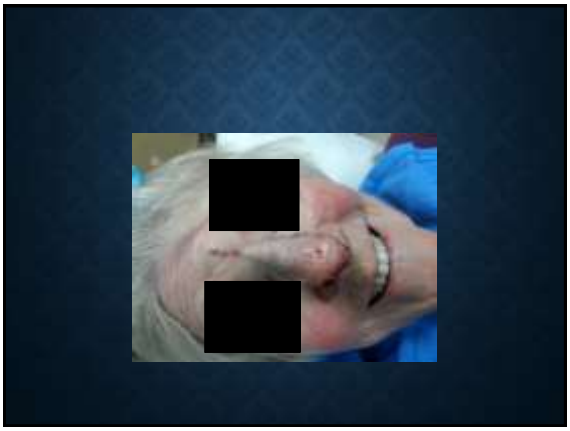


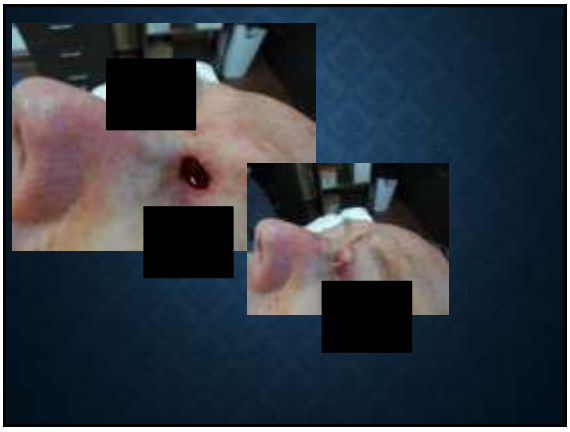


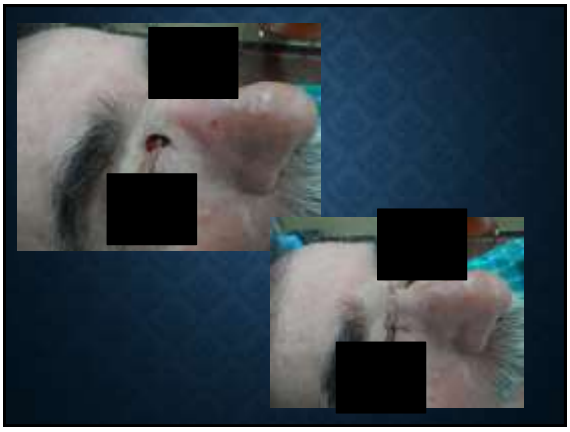


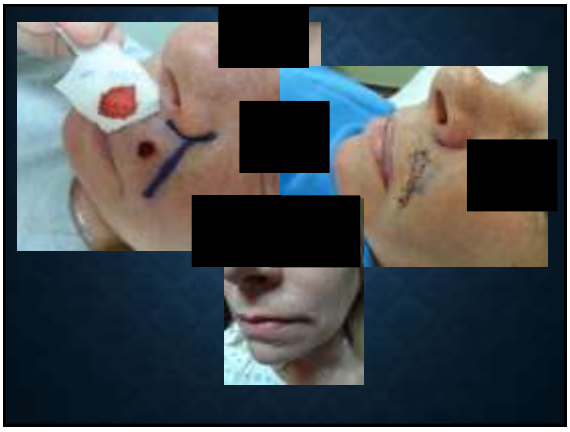


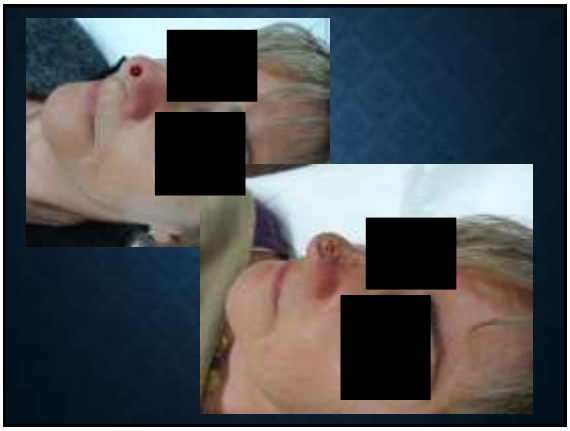


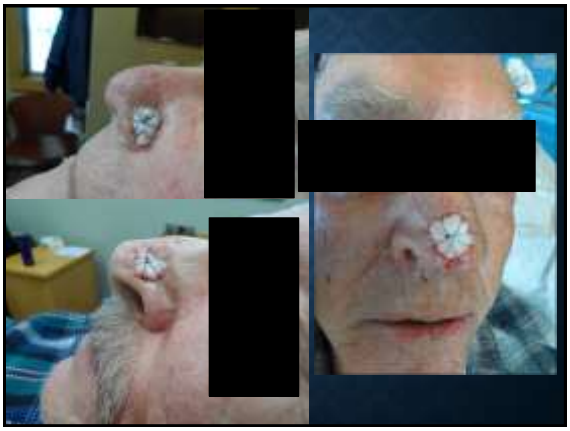


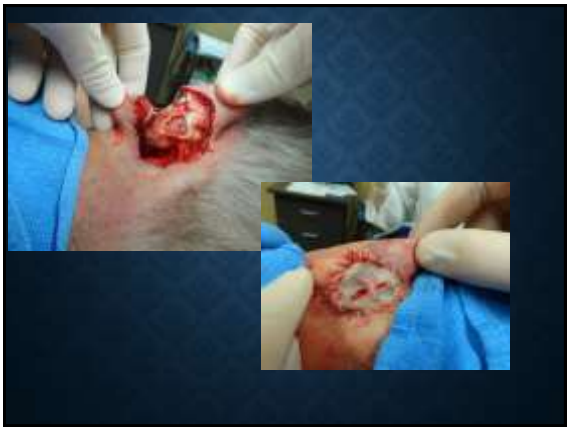


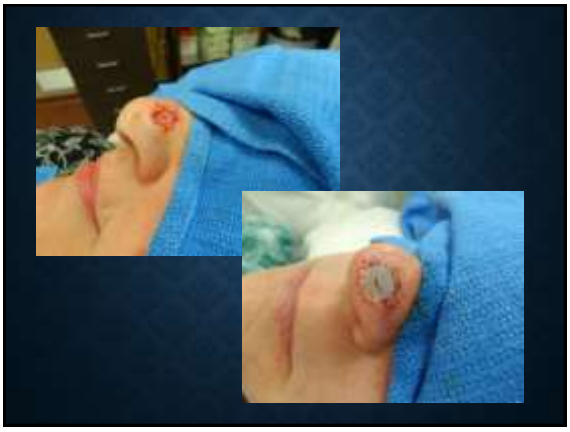




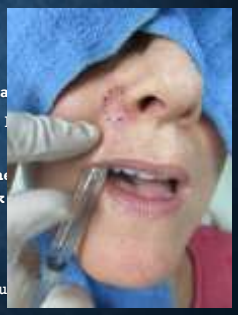






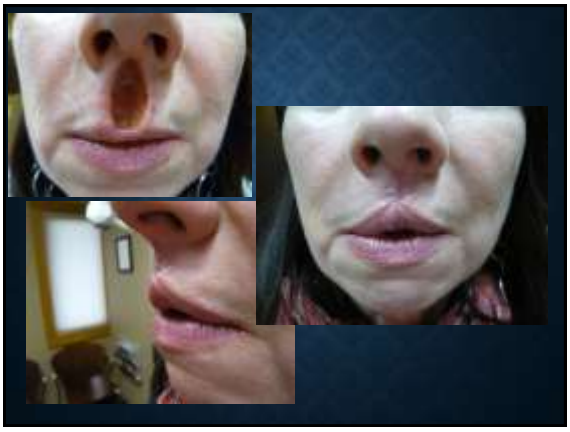


- **See 1 citation found by title ma**
- Dermatol Surg. 2013 Aug 5. doi: ahead of print]
- **Make Your Patients Happy: An Using an Intraoral Field Block**
- Perry B, Bruce A, Biernat B.
- **Author information**
- PMID: 23915138 [PubMed - as su

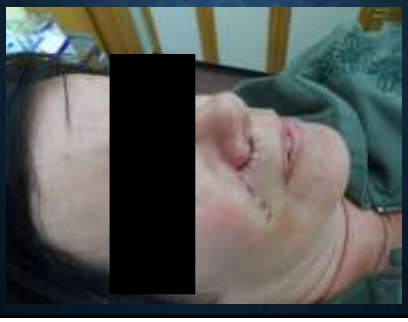


THE LIP UPPER/LOWER

- Anatomic Considerations:
  - Natural plane for undermining above the muscle
- Aesthetic Considerations:
  - Numerous junctions
  - Free margin
  - Mark and respect the vermillion border (before anesthesia)
  - Minimal distortions translate into disfigurement

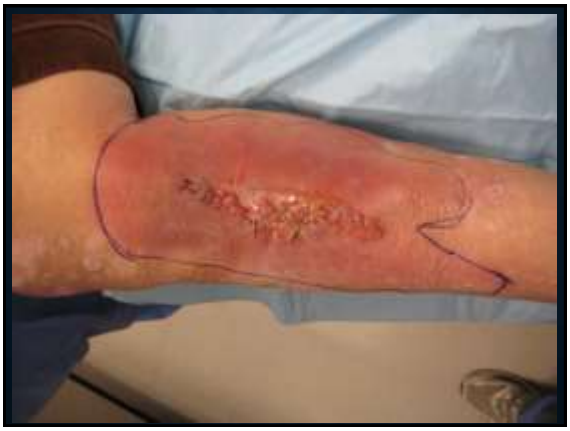


PRESERVE THE APICAL TRIANGLE (ISTHMUS) AT ALL COSTS.



LOWER EXTREMETIES

- Preop
  - Hx of infections?
  - Extensive scrub from the knee down
- Compression 4-6 weeks



RAISE YOUR GAME

- Call every surgical patient the night after surgery
- Bolster (tie-over)dressings for virtually all grafts
- Intraoral anesthesia when applicable
- Fast dissolving gut suture if possible

Friday, February 21, 2014
(8 CME)

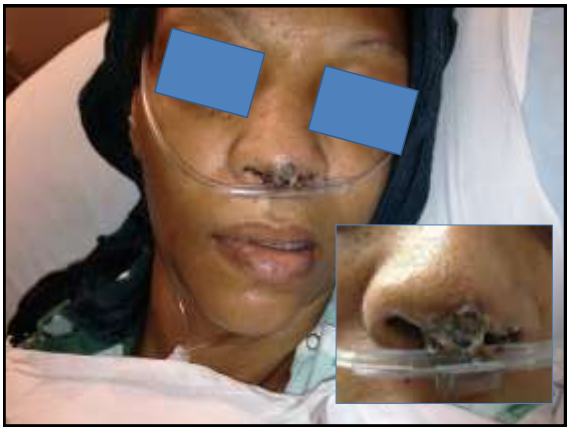
7:00 a.m. to 8:00 a.m.	Breakfast with Exhibitors
7:30 a.m. to 7:50 a.m.	*A 50 year old Woman with a Scaling Nose and Ischemic Stroke* **Lise Brown, DO** NSUCOM/Broward General Medical Center
7:50 a.m. to 8:10 a.m.	*Oral Ulcerations: How to Deal With It "Derm-Style"* **Panagiotis Mitropoulos, DO** NSUCOM/Broward General Medical Center
8:10 a.m. to 8:30 a.m.	*Multicentric Reticulohistiocytosis: Case Report and Treatment Review* **Justin Rubin, DO** NSUCOM/Broward General Medical Center
8:30 a.m. to 9:30 a.m.	*The Future of Dermatology Practice* **Steven Grekin, DO, FAOCD**
9:30 a.m. to 10:30 a.m.	*Thoughts That Make Dermatology Practice (and Life) Easier* **Stuart Brown, MD**
10:30 a.m. to 11:30 a.m.	*Melanocytic Conundrums* **Ronald Rapini, MD**
11:30 a.m. to 12:00 p.m.	Break with Exhibitors
12:00 p.m. to 1:00 p.m.	Product Theater Lunch (No AOA CME credit)
1:00 p.m. to 1:20 p.m.	*Amyloidosis: A Review of Cutaneous Disease* **Jared Heaton, DO** NSUCOM/Largo Medical Center
1:20 p.m. to 1:40 p.m.	*Diet and Dermatoses: What You Should Know* **Julian Ngo, DO** NSUCOM/Largo Medical Center
1:40 p.m. to 2:00 p.m.	*Dueling a Grueling Case of Granuloma Annulare* **Clayton Schiltz, DO** Genesys Regional Medical Center
2:00 p.m. to 2:30 p.m.	Break with Exhibitors
2:30 p.m. to 3:30 p.m.	*Nanotechnology for the Prevention, Diagnosis, and Treatment of Skin Disease* **Adam Friedman, MD**
3:30 p.m. to 4:30 p.m.	*Dermatology Q&A* **James Q. Del Rosso, DO, FAOCD**
4:30 p.m. to 5:30 p.m.	*Cosmetic Dermatology: It's a Marathon, Not a Sprint* **Michelle Foley, DO, FAOCD**
5:30 p.m. to 6:30 p.m.	Product Theater Dinner (No AOA CME credit)

A 50 year old Woman with a Scaling Nose and Ischemic Stroke

Lise D. Brown DO, PGY3
Broward Health Medical Center
Nova Southeastern University
AOCD Midyear Meeting, Dallas, TX
2.20.14

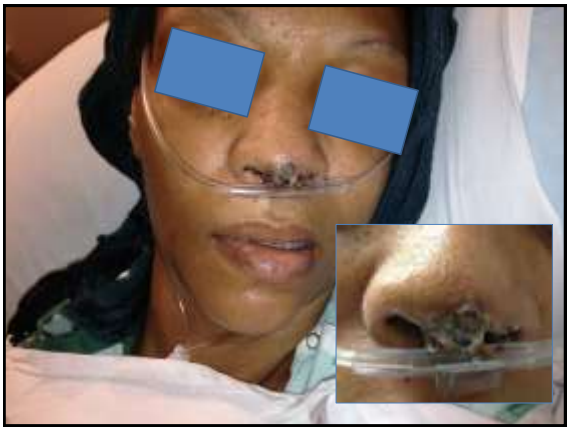
History of Present Illness

- 50 yr old AA female with a prior history of ischemic CVAs admitted for HA, LBP, and BLE pain and weakness.
- Vitals: Tc 96.5, BP 151/113, PR 70's, RR-18
- Accu-check: 174
- Initial labs: CBC with diff, CMP, PT, aPTT
  - All WNR
- Brain CT without contrast: negative



Medical History

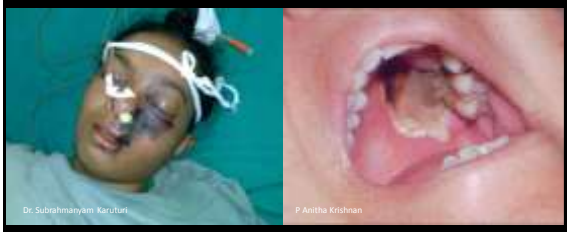
- PMHx:
  - IDDM – controlled
  - labile HTN
  - 2 previous ischemic strokes within the past year
  - difficulty ambulating
  - depression with psychosis
- SHx:
  - tubal ligation
- All: demerol, iodine
- Home meds: clonodine, insulin, folic acid, Valtrex, protonix, pravastatin, Plavix, Aricept
- SocHx: denies tobacco products or IDA
- FamHx: brother, MS



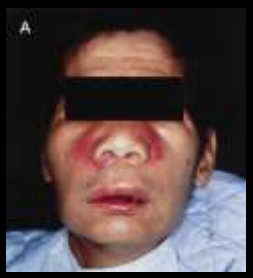
Face tent mask (face shovel) with humidified air

Differential Diagnosis of Sinonasal Lesions

Infectious	Neoplastic	Inflammatory	Other
Mucormycosis	SCC	Churg Strauss	Intranasal cocaine use
Deep fungal infections Invasive aspergillosis	BCC	Wegener's granulomatosis	Foreign body rxn
Tuberculosis (lupus vulgaris, orificial TB)	NK-T cell lymphoma, nasal type	Sarcoidosis (lupus pernio)	Chronic ACD/ICD
NTM (leprosy)		Polyarteritis Nodosa	Mechanical trauma (nose picking)
Primary syphilis Gummata			
Rhinosporidiosis			
Leishmaniasis			
Rhinoscleroma			



Mucormycosis



DIAGNOSIS IN ONCOLOGY Arthur Skarin, MD, Consultant Editor
Lethal Midline Granuloma Revisited: NK/T-cell lymphoma, nasal type.

Extranodal NK-T cell lymphoma, nasal type (WHO classification)

- PTCL < 15% of all NHL
- Synonymous terms:
  - Lethal midline granuloma
  - Polymorphic reticulosis
  - Angiocentric lymphoma (REAL classification)
- Asia, Peru and Mexico
- Epstein-Barr virus
- Localized disease to nose, sinus, palate
- Angiocentric/angiodestructive
- NK cells: small lymphocytes with azurophilic granules and express CD56
- Immunophenotype: CD2, CD56, cytoplasmic CD3
- T-cell gene rearrangement studies are usually negative
- Not to be confused with LYMPHOMATOID GRANULOMATOSIS

Work-Up and Plan

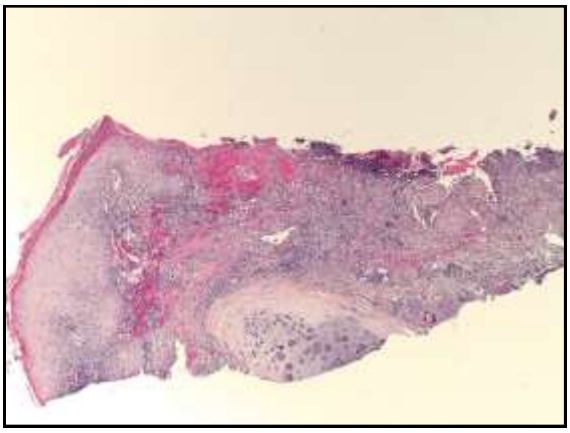
- CT paranasal sinuses (mild mucosal thickening of ethmoid sinuses)
- ENT consulted
- Cutaneous biopsy nasal columella
  - Punch biopsy – H & E
  - Punch biopsy – tissue culture (bacterial, fungal, atypical mycobacterium, M. tuberculosis)
- Serologies/Labs
  - ESR, ANA assay, ANCA, RPR, UA with urinary sediment
- Discontinue Mupirocin
- Topical steroids

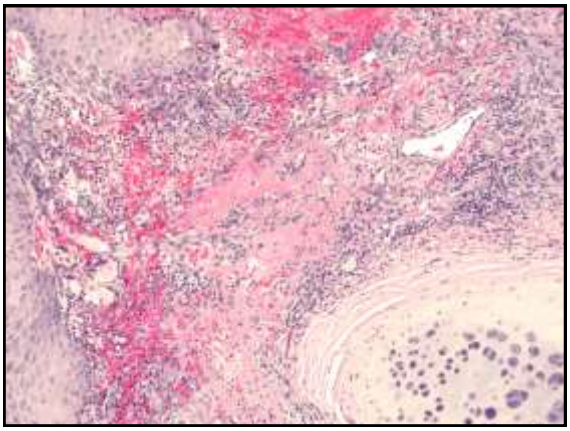
Hospital day 3

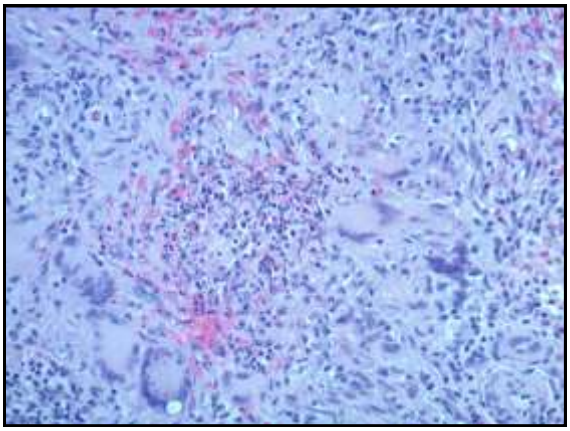
- Profound bradycardia, respiratory failure, and loss of consciousness
- Brain MRI: acute to subacute pontine infarcts.
  - *"Mild to moderate foci T2 hyperintensity in the white matter most likely small vessel ischemic disease, but given the location of some of these lesions, demyelinating process is also possible"*
  - mastoiditis – IV Rocephin
- Persistent vegetative state

Biopsy Results

- H & E:
  - "focal necrotizing granulomatous inflammation"
- PAS, GMS, AFB (ZN) – negative
- Tissue cultures negative

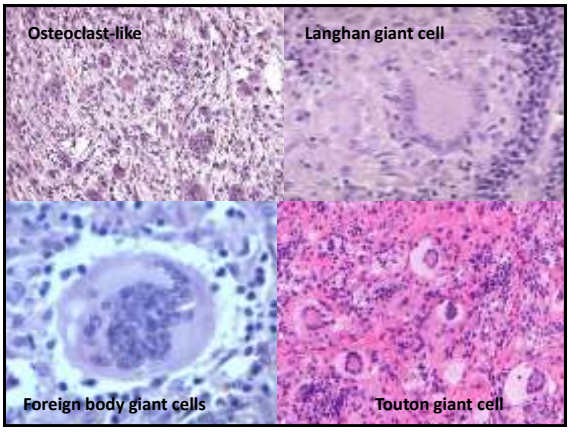






Granulomata

- Compact collections where histiocytes preponderant inflammatory cells
- Tissue macrophages
- Non-specific inflammatory response to antigens
- APC and are phagocytic
- May or may not contain MNG



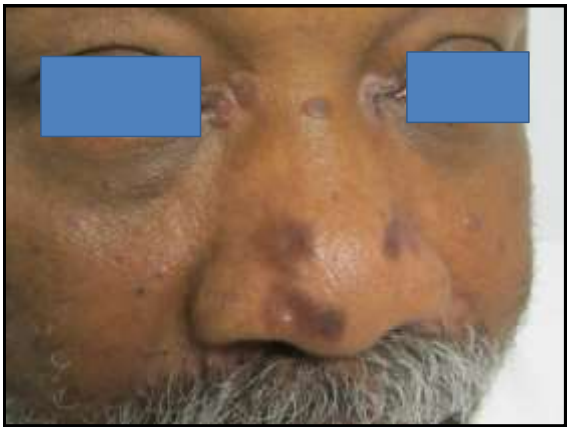
Granuloma morphology: what does it really mean?

- Necrotizing granulomas
  - "caseating"
  - areas of cellular necrosis
- Non-necrotizing granulomas
  - "non-caseating"
- Necrobiotic granulomas
  - degenerated collagen

Elk lung and lymph node. Infection by *Corynebacterium pseudotuberculosis*.

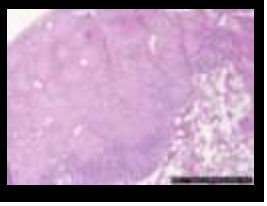
Granulomatous Reaction Patterns

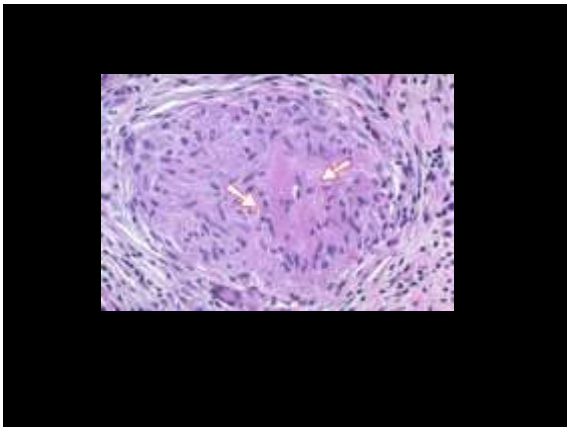
- Sarcoidal granulomas
- Palisading granulomas
  - Granuloma annulare (GA)
  - Necrobiosis lipoidica
  - Rheumatoid nodules
  - Infections
- Tuberculoid granulomas
- Suppurative granulomas
- Foreign body granulomas



Non-caseating granulomas: sarcoidal granulomas

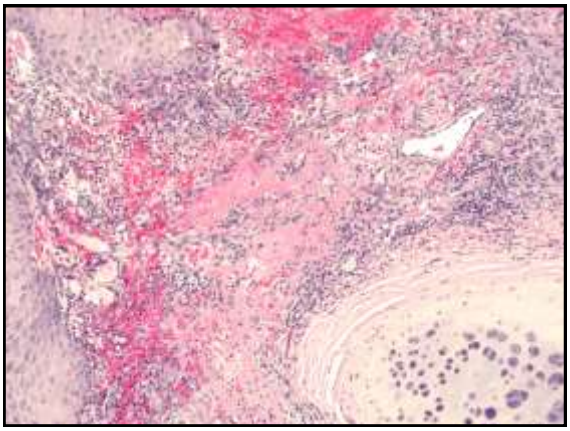
- Discrete, compact collections of epithelioid histiocytes
- Prototype: sarcoidosis
- Sarcoid-type allergic contact granulomatous inflammation
- Foreign body granulomas
  - Silica
  - Zirconium
  - Beryllium





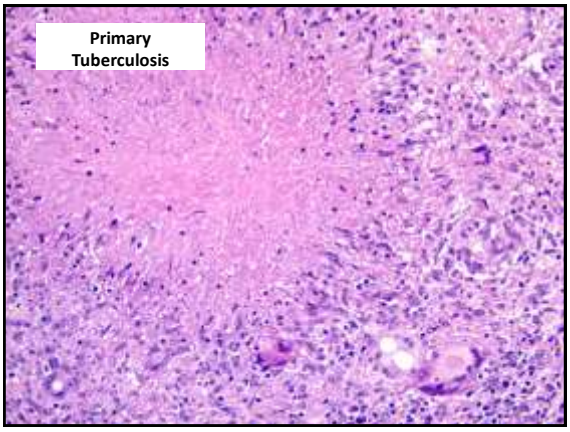
Sarcoidosis?

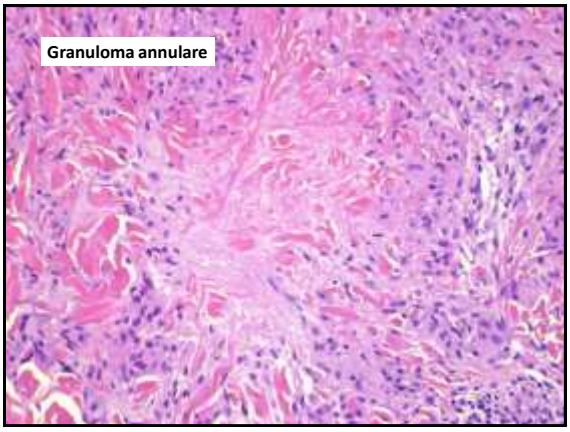
- CXR: negative for bilateral mediastinal LAD
- ACE 19 (9-67)
- 2D Doppler echocardiogram - unremarkable
- EKG – unremarkable
- Serum calcium – 10mg/dL



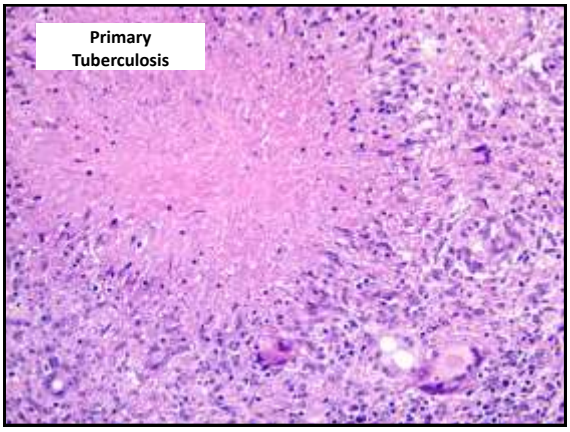
Palisading Granulomas

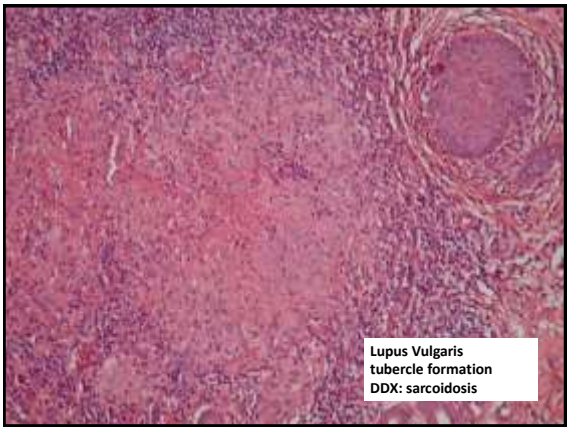
- Infectious:
  - Deep mycoses
  - NTM
  - TB
  - Cat scratch disease
- Inflammatory:
  - Wegener's granulomatosis
  - Churg Strauss dx
  - Necrobiosis
    - » Granuloma annulare
    - » Rheumatoid nodules
- Reactions to foreign material





CUTANEOUS TB	Tuberculous chancre	Lupus vulgaris
SYNONYM	Primary inoculation TB	Tuberculosis luposa
INCIDENCE	RARE	Women >> men
TRANSMISSION	Inoculation of previously uninfected person	Face: lymphatic or hematogenous spread Extremities: inoculation
IMMUNE STATUS	No specific immunity	Previously sensitized with strong DTH
TST	Early: negative Late: positive	Positive
	Multibacillary	Paucibacillary (AFB negative)
HISTOPATH	Granulomatous inflammation with central caseation, epitheliod and Langhan giant cells (M. marinum)	Well-developed tubercles with scant caseation, neutrophilic inflammatory infiltrate
OTHER	LAD, spontaneously resolves 3-12 weeks	"apple-jelly" nodules on diascopy, annular granulomatous plaque, destruction





Infectious Disease work-up

- RPR, HIV – non reactive
- Blood cultures – negative
- Quantiferon Gold – positive
- PPD – negative
- Imaging of the spine was not performed

Interferon-gamma release assays (IGRAs)

- Latent pulmonary disease
- Not affected by Bacille-Calmette-Guerin (BCG) vaccination status
- QuantiFERON-TB Gold In-Tube (3rd gen):
- False positive
  - False positive results can occur with *M. szulgai, M. kansasii, and M. marinum.*
  - Improper storage

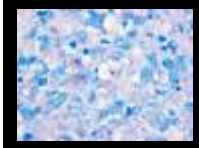
Atypical mycobacterial cutaneous infections

- 125+ NTM species
- NTM: abundant in nature, soil, potable water, food, milk
- Multiuse vials (steroid, local anesthetics)
- Variable clinical presentation
- Preceded by trauma or procedure
- Increase incidence in US
  - RGM >> SGM

Non-tuberculous Mycobacteria

- Atypical mycobacterial infections of the nose or paranasal sinuses are exceedingly rare
  - *M. kansasii* – granulomatous infection and perforation of nasal septum
  - *M. marinum* – adalimumab tx for RA

Ziehl-Neelsen (classic): bacteria stain bright red due to retention of carbol-fuchsin dye; background is methylene blue counterstain. MT and NTM.



Fite: to detect *M. leprae* (leprosy) ; combines peanut and vegetable oil with xylene to minimize exposure of bacteria cell wall to organic solvents and protect precarious acid-fastness of organism.

Auramine-rhodamine: auramine binds to mycolic acid in cell wall; detection requires a fluorescence microscope. 100 fold increase in sensitivity.

Mycobacterium CULTURE

Solid media

1. Egg based: Lowenstein-Jensen
2. Middlebrook 7H11 agar
2. Blood based

Liquid systems

1. Middlebrook 7H9
2. BACTEC MGIT 960 system

Identification of mycobacteria species

- Culture isolates:
  - Biochemical analysis (e.g., nitrate reductase activity)
  - Nucleic acid hybridization probes

Diagnosing mycobacterial cutaneous infections

- Gold standard
  - AFB smears
  - Culture
- 5000-10,000 bacilli/ml of specimen to detect AFB on smears
  - AFB seen in only 13% to 31% of cases
- 10-100 live bacilli on cultures

Statement of the Council of the Infectious Disease Society of America. Am J Respir Crit Care Med 161:1376-1395, 2000

MYCO **Mycobacteria DNA by PCR - Qualitative**

Description
Real-Time PCR is used to amplify the 16S rRNA gene to detect all known species of mycobacteria, and the 196110 gene, which is specific to the *M. tuberculosis* complex. The *Mycobacterium tuberculosis* complex consists of *M. tuberculosis, M. bovis, M. bovis BCG, M. africanum, M. microti,* and *M. canetti*. This assay detects as few as 10 cells/sample for species in the *M. tuberculosis* complex and 50 cells/sample for atypical mycobacteria. The sensitivity of this assay compared to culture is 95% for the *M. tuberculosis* complex and 85% for atypical mycobacteria.

Clinical Utility
According to the CDC, nucleic acid amplification testing should be performed on at least one respiratory specimen from each patient with symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not been established, and for whom the test result would alter case management of TB control activities. Compared with AFB smear microscopy, an added value of DNA testing lies in its ability to confirm rapidly the presence of *M. tuberculosis* in AFB smear-negative, culture-positive specimens.

CDC. Updated Guidelines for the Use of Nucleic Acid Amplification Tests in the Diagnosis of Tuberculosis. MMWR 2009; 58(01); 7-10.

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Can Foreign Material induce Necrotizing Granulomas?

NON-birefringent (FBG)

- Zirconium (underarm deodorant)**
- Beryllium (fluorescent bulbs)**
- Aluminum
- Tattoo (most commonly, red ink, mercury sulfide/cinnabar)
- Keratin (ruptured cyst) and hair

**sarcoidal granulomas (as well as silica)

Histopathology 2010, 56, 183–193. DOI: 10.1111/j.1365-2559.2009.03453.x

Persistent nodules at injection sites (aluminium granuloma)—clinicopathological study of 14 cases with a diverse range of histological reaction patterns

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[1]Department of Cellular Pathology, St George's Hospital, London, UK, [2]Centre for Ultrastructural Imaging, Guy's Campus, King's College London, London, UK, [3]Universitätsklinikum Münster, Klinik und Poliklinik für Dermatologie, Münster, Germany, and [3]Department of Dermatopathology, St John's Institute of Dermatology, St Thomas' Hospital, London, UK

Date of submission: 11 March 2009
Accepted for publication: 29 April 2009

Table 1. Clinical features of patients

Case	Age, years	Sex	Site	History of injection	Time interval between initial injection and presentation with swelling	Clinical features	Histological pattern
1	19	F	Upper arm	Hepatitis B vaccination	Not known	Asymptomatic nodule	Perinodular
2	25	F	Upper arm	Desensitization (3 months)	8 years	Asymptomatic nodule	Perinodular
3	19	F	Upper arm	Tetanus booster	Not known	Asymptomatic nodule	Perinodular
4	48	F	Upper arm	Desensitization	3 years	Erythematous swelling	Perinodular
5	50	F	Upper arm	No history	–	Asymptomatic nodule + plaque	Perinodular with foreign body-type giant cells
6	57	F	Upper arm	No history	–	Itchy nodule	Perinodular
7	28	F	Upper arm	Desensitization (2 courses)	3 years	Itchy nodules and plaque	Pseudolymphoma
8	27	F	Upper arm	Tetanus booster	7 months	Asymptomatic nodule	Pseudolymphoma
9	48	M	Upper arm	No history	–	2-year history of itchy nodules	Pseudolymphoma
10	39	F	Upper arm	Numerous vaccinations at this site	–	Asymptomatic nodule	Lupus vulgaris-like
11	28	F	Upper arm	No history	–	Asymptomatic nodule	Perinodular
12	3	M	Thigh	Vaccination (no precise details available)	Not known	Asymptomatic nodule	Necrotizing granuloma (tennis)
13	28	F	Upper arm	No history	–	Asymptomatic nodule	Necrotizing granuloma
14	57	F	Upper arm	No history	–	Asymptomatic nodule	Necrotizing granuloma (tennis)

Histiocytic Reaction Associated with Topical Aluminum Chloride (Drysol Reaction)

RONALD J. BARR, MD
KENNETH S. ALPERN, MD
SHIRLENE JAY, MD

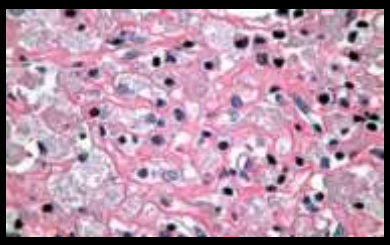
toxicosis. In the past few years, dermatologists have begun to use aluminum chloride (Drysol) as a hemostatic agent for minor surgical procedures. An unusual histiocytic reaction was noted on biopsies of skin previously treated with aluminum chloride. This reaction consisted of a proliferation of histiocytic cells that contained prominent basophilic cytoplasmic granules.

To determine the cause of this reaction and the nature of the basophilic granular material within the histiocytic cells,

sections. Four cases are presented in which re-excised tissue previously treated with aluminum chloride were examined with special histochemistry staining and energy diffraction studies.

RESULTS. The granules of these histiocytes stained positively with the aluminum stain, a stain specific for aluminum, although no aluminum was found using the less sensitive energy diffraction studies.

CONCLUSIONS. These studies support the concept that aluminum chloride can cause a proliferative histiocytic reaction when used as a topical coagulating agent. (J Dermatol Surg Oncol 1993;19:1017–1021.



"DRYSOL cells"

Giemsa stain, diastase PAS positive
characteristic histiocytes with violaceous granular cytoplasm

Wegener's granulomatosis

- Granulomatosis with polyangiitis (GPA)
- Systemic vasculitis of the small and medium vessels
- ANCA-associated vasculitides
- Prevalence: 3 cases per 100,000
- Mean age at diagnosis is 55 years
- Men and women are similarly affected
- > 90% of pts are Caucasian (1% to 4% of patients are African-Americans, Hispanics, and Asians)
- ~ 82 to 94% classic WG are PR3-ANCA positive

Wegener's Granulomatosis

- Classic triad:
  - Necrotizing granulomatous inflammation of the URT and LRT
  - Glomerulonephritis
  - Systemic vasculitis (skin and oral mucosa)
  - Classic triad: granulomas, necrosis and vasculitis only present in 16%
- Pathogenesis
  - Environmental and genetic factors
  - HLA-DRB1-15 markedly increases the risk of PR3-associated ANCA vasculitis among African Americans

Upper Respiratory Tract

- 75% initial symptoms:
  - nasal, sinus, tracheal, and hearing loss
- More than 90% eventually develop upper airway/ear abnormalities.
- Kiesselbacch locus, mucosa, turbinates
- nasal pain and stuffiness, rhinitis, epistaxis, and crusts
- prolonged inflammation → mucosal erosions, septal perforation, and nasal bridge collapse—the "saddle-nose" deformity
- the most common findings on sinus CT were mucosal thickening in the nasal cavity and paranasal sinuses

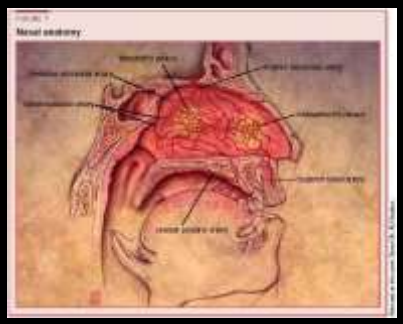
Devany KO et al. Interpretation of head and neck biopsies in Wegener's granulomatosis. A pathologic study of 126 biopsies in 70 patients. *Am J Surg Pathol* 1990; 14:555-64.

Histopath: nasal and sinus tissue

- extensive tissue necrosis
  - mixed population of inflammatory cells
- necrotizing granulomas
- direct evidence of vasculitis is rarely seen

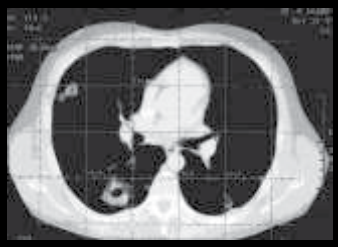
Wegener's granulomatosis. Yi ES, Colby TV. Semin Diagn Pathol. 2001;18(1):34. Department of Pathology, University of California San Diego School of Medicine, USA.

Kiesselbacch locus/area

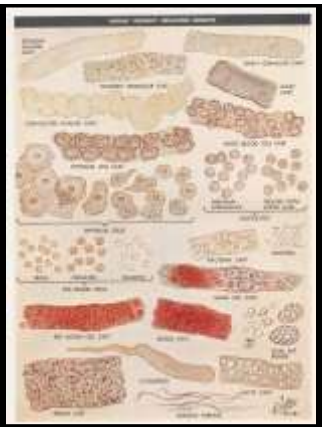


Incidental vasculitis

- Not uncommon to find changes of neutrophilic small vessel vasculitis underlying an ulcer formed by another process (trauma)
- Should be obtained from non-ulcerated sites



Rheumatology , Fifth Edition Marc C. Hochberg, Alan J Silman, Josef S Smolen, Michael E Weinblatt, and Michael H Weisman



Urinary sediment

– CXR: no nodules or infiltrates
– ANA, ANCA, dsDNA – negative
– UA proteinuria 30mgdL
– Urinary sediment negative for RBC casts

Limited Wegener's Granulomatosis

- "initial phase"
- "nonrenal"
- "indolent"
- "localized"

"limited disease, in contrast to severe disease, includes manifestations of WG that pose no immediate threat to either the patient's life or the function of vital organs"

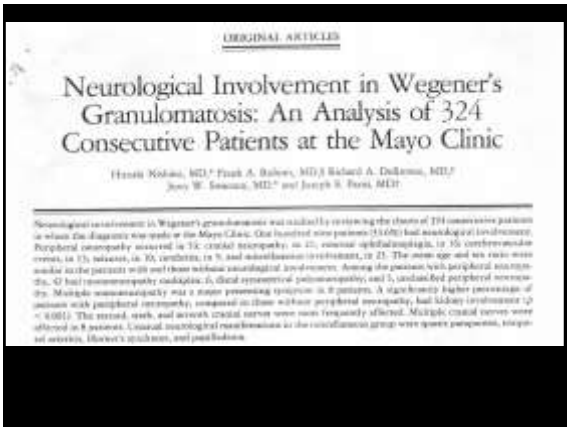
Limited versus severe Wegener's granulomatosis: baseline data on patients in the Wegener's granulomatosis etanercept trial.

Author Information

Abstract

OBJECTIVE: To report baseline data on 158 patients with Wegener's granulomatosis (WG) enrolled in the WG Etanercept Trial (WGET), and to examine demographic and clinical differences between patients with limited disease and those with severe disease.

- Younger
- Women
- Caucasian
- 67% ANCA positive (90% in the severe group)
- Chronic, recurring URT dx
- Indolent

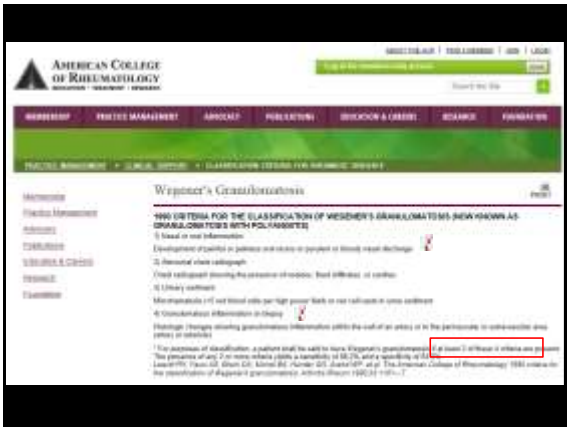


ORIGINAL ARTICLES

Neurological Involvement in Wegener's Granulomatosis: An Analysis of 324 Consecutive Patients at the Mayo Clinic

Neurologic Sequela/Vasculitic Neuropathy

- Peripheral neuropathy
  - Mononeuritis multiplex
- CNS
  - Almost all forms of vasculitis can involve the vessels feeding the brain parenchyma and cause stroke-like episodes
  - CVA is a rare event
  - Direct invasion of granulomas from paranasal sinuses
  - Remote granulomas in meninges or cerebrum
  - Vasculitis
  - Normal angiogram does not exclude vasculitis
  - No pathognomonic MRI findings in vasculitis



In Summary

- Necrotizing granulomas of the nose/paransasal sinuses
- Always examine the soft/hard palate, orophyaryx
- Look and palpate for facial swelling and CN palsy
- Image the paranasal sinuses
- Columella as ideal site for biopsy
- Consider “zebra” diagnoses in patients from endemic regions (lymphoma, TB)
- Serial histochemical stains
- Real-time PCR on FFPE blocks

Oral Ulcerations

How to deal with it "derm-style"

Panagiotis Mitropoulos D.O.
NSU/BG Dermatology Residency Program

OBJECTIVES

- Review basic anatomy and physical examination of the mouth
- Discuss diagnostic approach of oral ulcerations
- Outline the "do's and don'ts" in performing oral mucosa biopsy

Physical exam

- Posterior mid dorsal tongue with well defined ulceration, with mild peripheral erythema

Physical exam

- multiple small irregular, fibrin-covered erosions and areas of moderate erythema involving particularly the gingivae
- conjunctival, nasal, genital mucosae were uninvolved

Differential Dx

- Pemphigus vulgaris
- Mucous membrane pemphigoid
- Erosive lichen planus
- Lupus erythematosus
- Erythema multiforme
- Trauma
- Aphthous stomatitis
- Malignancy
- Fungal infection
- Viral infection
- Bacterial infection

The Oral Cavity

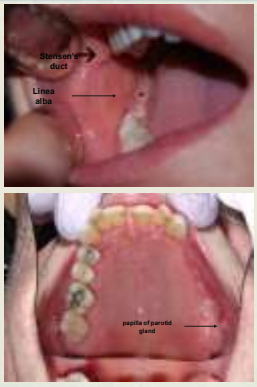
- Lips
- Teeth
- Gingiva
- Oral mucous membranes
- Palate
- Tongue
- Oral lymphoid tissue

Gross Anatomy
Oral vestibule

- The oral vestibule is a slit-like space bounded externally by the lips and the cheek mucosa and internally by the alveolar mucosa

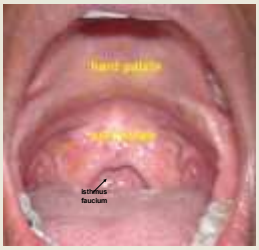
Gross Anatomy
Stensen's duct and Linea alba

- The retrocommissural region is situated between the labial commissure and the opening of **Stensen's duct** (the drainage duct of the parotid gland), located **opposite the second upper molar**
- Stensen's duct runs through the buccinator muscle
- A horizontal slightly elevated streak (called the **linea alba** or occlusal line) traverses this region. Coincides with **level of the biting plane**



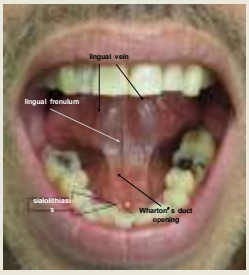
Gross Anatomy
Oral Cavity proper

- The oral cavity proper is bounded laterally and in front by the alveolar arches with their contained teeth; behind, it communicates with the pharynx by a constricted aperture termed the isthmus faucium.
- It is roofed in by the **hard and soft palates**, while the greater part of the **floor is formed by the tongue**, the remainder by the reflection of the mucous membrane from the sides and under surface of the tongue to the gum lining the inner aspect of the mandible. It receives the secretion from the submaxillary and sublingual salivary glands.



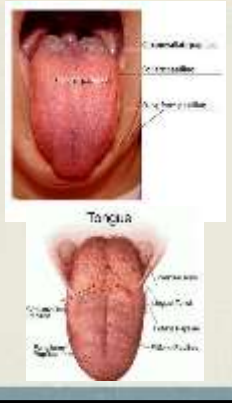
Gross Anatomy
Floor of mouth

- The floor of mouth forms the **inferior limit of the oral cavity**
- The **sublingual papillae (also referred to as caruncles or folds)** can be identified on both sides of the frenulum in the anterior part of the floor of mouth when the tip of the tongue is raised
- The excretory duct of the **submandibular gland (Wharton's duct)** runs in the floor of the mouth along the medial border of the sublingual gland to pierce the surface of the mouth at the paramedian sublingual caruncle. The sublingual glands have multiple small ducts that drain directly into the floor of the mouth



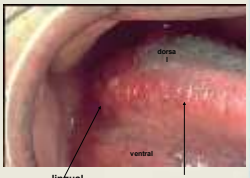
Gross Anatomy
Tongue

- The **anterior part** is the visible part situated at the front, and roughly **two-thirds** the length of the tongue.
- The ***posterior part*** is the part closest to the throat, and roughly ***one-third*** of length.
- The two parts (**anterior and posterior**) of the tongue are divided by the **terminal sulcus** (shallow groove)
- The **left and right sides** of the tongue are separated by the **lingual septum**.



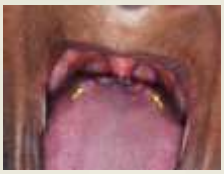
Gross Anatomy
Tongue

- The **lateral borders of the tongue** are pink and shiny, with occasional vertical superficial fissures **(foliate papillae)**, particularly in the posterior regions
- Each groove can contain more than 100 taste buds, housing more than **one-third of total taste buds in the mouth**.
- **Lingual tonsils** are located at the **posterior lateral base of the tongue** and may enlarge because of local inflammation, infection, or neoplasia
- Saliva tends to pool against the lateral borders of the tongue; exogenous agents (EtOH, tobacco) may accumulate and result in **higher incidence of tongue cancer at the lateral border**



Gross Anatomy
Tongue

- The **circumvallate papillae** (vallate papillae) are the **largest papillae** on the tongue. Most people have **about 6 to 12** of on the posterior tongue, arranged in an **inverted v-shape**, pointing towards the throat
- The **taste buds** on the circumvallate papillae respond primarily to **sour** and **bitter flavors**. Because of their location on the very back of the tongue, these buds can make you gag in response to bad food and thereby serve as a natural defense against poisoning
- They can be quite prominent and are **often mistaken by patients** for cancerous growths



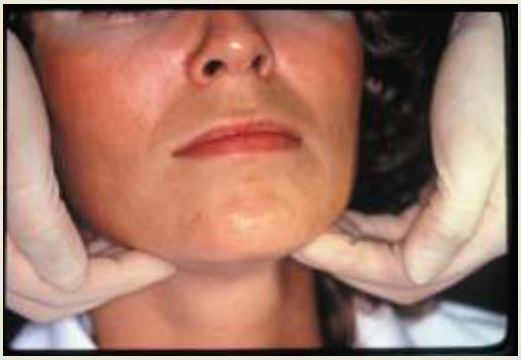
circumvallate papillae

The Extraoral examination

- Begins as soon as the physician meets the patient
- **Overall assessment** of the head and neck
- Inspect for asymmetry, erythema, masses, and overlying skin changes

The Extraoral examination

- Sit the patient in an upright (appr. 45 degrees) position
- PALPATE SYSTEMATICALLY
- **Supraclavicular lymphadenopathy** may be facilitated when patient performs **valsalva maneuver**
- **Anterior cervical chain** lymphadenopathy is most commonly associated with **inflammation or metastatic processes**
- Always **palpate the parotid and submandibular glands** for masses

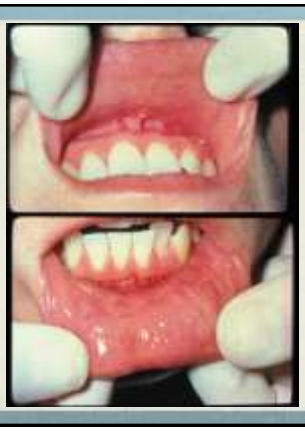


The Intraoral examination

- Remove all dentures, retainers, or mouth guards
- However, **inspect appliances in place first** to assess any associated trauma
- Use a small **piece of gauze** (2x2) to **dry the mucosa**, as moisture often alters the appearance of intramural lesions
- Gauze can also be used to maneuver the tongue and lips for better visualization
- If available you may also use cheek retractors or dental mirrors to further facilitate visualization of the oral cavity

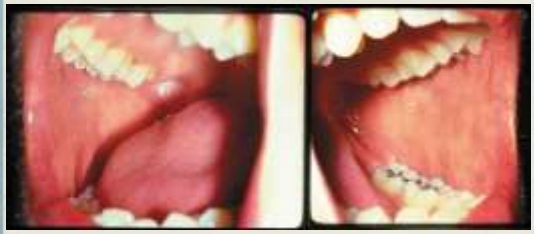
The Intraoral examination

- Examine the mucosal aspect of the lips by everting
- Healthy intramural mucosa appears pink and moist
- This can be a time where you can diagnose a number of common conditions
  - Labial melanotic macules
  - Actinic, irritant, allergic, or angular cheilitis
  - Herpes labialis
  - Melkersson-Rosenthal syndrome
  - Cheilitis granulomatosa
  - SCC
  - Trichilemmomas



The Intraoral examination

- Visualize the buccal mucosa by gently stretching the cheek
- Place one index finger inside the cheek at each of the maxillary and mandibular alveolar sulci with **patient's mouth partially open**

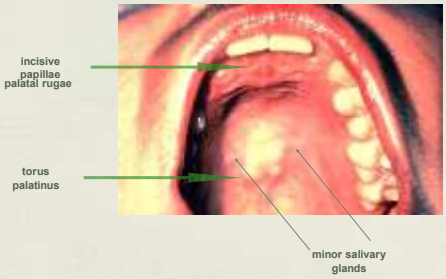


NONPATHOLOGICAL VARIANTS

The Intraoral examination

- To **evaluate the palate**, ask patient to tilt head upwards and **point the chin towards the ceiling**
- **Palatal rugae** (horizontal fibrous connective tissue), are located on the **anterior aspect** of the hard palate
- The **anterior hard palate is often traumatized** by ingestion of **hot foods** (i.e. pizza burn)
- The hard palate may rarely be the site of neoplastic (i.e. minor salivary gland neoplasms) and infectious processes (i.e. herpes simplex infection)

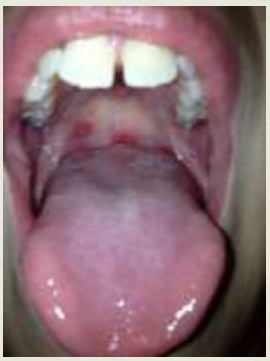
Hard Palate



The Intraoral examination

- The mucosa is orange-pink in color and non-keratinized
- the soft palate is a common site for **Coxsackie virus infection** (herpangina, hand-foot mouth disease)
- **bifid uvula** may indicate a **sub-mucosal bony cleft** of the hard palate, so **palpate the midline**

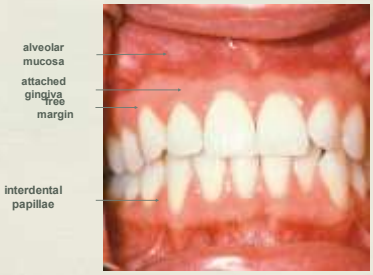
Coxsackie infection
Herpangina



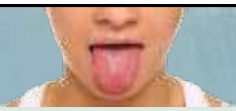
The Intraoral examination

- Teeth loss should prompt evaluation of underlying pathology
- **Most common** causes:
  - Trauma
  - Periodontal disease
  - Dental carries
- **Pathological causes** of teeth loss
  - Langerhans cell histiocytosis
  - Nutritional deficiency
  - Rheumatoid arthritis
  - Dementia
  - Neuropathy
- **Loss of tooth enamel** without loss of teeth, think **bulimia** or severe **GERD**

Normal gingiva

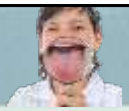


The Intraoral examination
Tongue



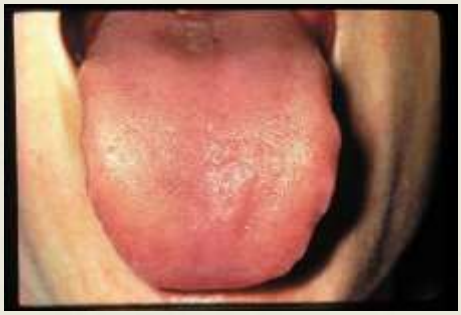
- The **lateral tongue** and **floor of the mouth** are the **most common sites for oral cancer**
- Ask patient to extend tongue, and gently but firmly grip the anterior tongue between your index finger and thumb utilizing a **2x2 gauze**
- **Inspect** dorsal, ventral, lateral aspects of the tongue **carefully**
- **Only the anterior 2/3 of the tongue is visible clinically**
- The posterior 1/3 of the tongue is visible using a laryngoscope

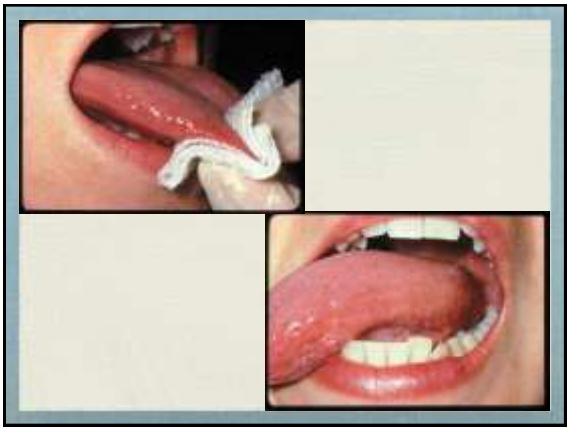
The Intraoral examination
Tongue



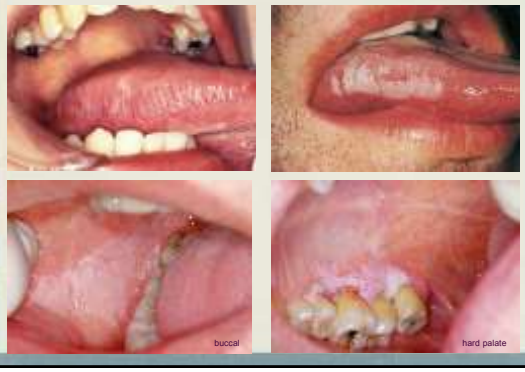
- **Vascular dilatation** is commonly seen on the **lateral aspects of the tongue**
- **Oral hairy leukoplakia** presents with *corrugated, white, vertical ridges* on the **lateral border** of the tongue
- Remember that it is associated with **Epstein-Barr** virus and is seen in patients with **HIV** or other **immunosuppressed** states

Normal tongue



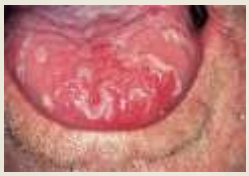


Oral Hairy Leukoplakia

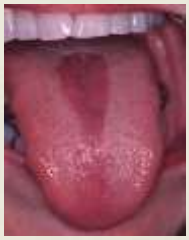


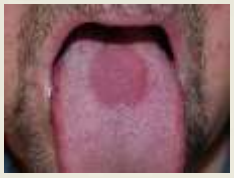
Fissured tongue

Geographic tongue
(benign migratory glossitis)



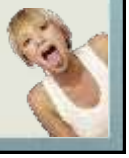
Median Rhomboid Tongue
(central papillary atrophy)



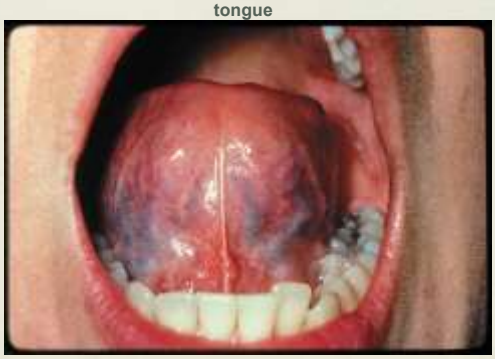


The Intraoral examination
Tongue

- The mucosa on the **ventral tongue** is thin, non-keratinized, and lacks papillae
- The sublingual **veins** are easily **visualized**
- Inspect for physiological variants (varices, and fimbriae)



Normal ventral tongue



Fimbriae on ventral tongue

Fimbriae on ventral tongue

Caviar tongue

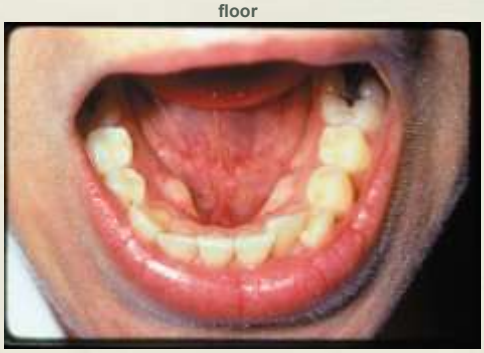
Caviar tongue

Normal caviar

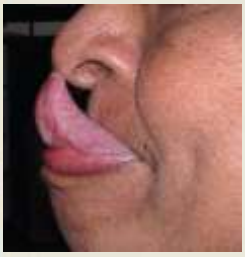
The Intraoral examination
Ventral Tongue

- The tongue is attached to the floor of the mouth via the **lingual frenulum**
- Patients with **Ehlers-Danlos lack a lingual frenulum**. That is why they are able to touch the tip of their nose with their tongue **(Gorlin sign)**
- When the frenulum is **foreshortened** or overattached, "**tie tongue**" (ankyloglossia) results
- Do not forget the **floor** of the mouth is a **common** site of of **oral cancer**

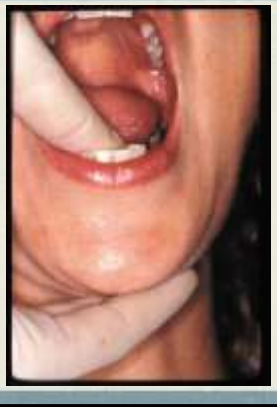
Normal mouth floor



Gorlin sign

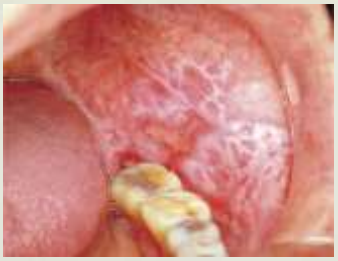


Ankyloglossia
"Tie tongue"



So one day a patient presents with the following. What could this be?

A. Leukoedema
B. Candidiasis
C. White sponge nevus
D. Leukoplakia
E. Lichen planus



Oral Ulcerations Algorithm

Nutritional
- B12 deficiency
- Iron deficiency
- Niacin deficiency
- Thiamin deficiency
- B2 deficiency
- B6 deficiency
- Vitamin C deficiency
- Vitamin A deficiency
- Potassium deficiency

Trauma
- Thermal injury
- Mechanical injury
- Radiotherapy
- Electrical injury

Infectious

Viral
- HSV
- Varicella
- Coxsackie
- EBV
- CMV
- Measles
- HIV

Bacterial
- Syphilis
- Gonorrhea

Fungal
- Blastomycosis
- Cryptococcosis
- Histoplasmosis
- Paracoccidiodomycosis

Parasitic
- Leishmaniasis

Neoplastic
- SCC
- Lymphoma
- Leukemia
- Multiple myeloma
- Sarcoma

Drugs
- Biphosphonates
- NSAIDS
- Methotrexate
- Nicorandil
- Propylthiouracil
- Beta-blockers
- Cocaine

Autoimmune / Systemic
- Pemphigus vulgaris
- Paraneoplastic pemphigus
- Cicatricial pemphigoid
- Bullous pemphigoid
- Systemic lupus erythematosus
- Lichen planus
- Erythema multiforme
- Bechet's disease
- Linear IgA dermatosis
- IgA pemphigus
- Drug induced pemphigus
- Dermatitis herpetiformis
- Epidermolysis bullosa acquisita
- Inflammatory bowel disease
- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Familial benign pemphigus

Allergic

Adjuvant Oral Ulcerations Algorithm

Acute

Abrupt onset, short duration
- Traumatic ulcer
- Recurrent aphthous stomatitis
- Behcet's disease
- Viral infections
- Bacterial infections
- Necrotizing sialometaplasia
- Allergic reactions
- Erythema multiforme

Chronic

slow onset, insidious progression
- Drug-induced ulcers
- Erosive lichen planus
- Pemphigus vulgaris
- Mucous membrane pemphigus
- Lupus erythematosus
- Reiter's syndrome
- Tuberculosis
- Mycosis
- Eosinophilic ulcer
- Malignancy
- Bacterial & Parasitic diseases
- Nutritional deficiency

The Oral Biopsy

Indications

- Any lesion that **persists for more than 2 weeks** with no apparent etiologic basis
- Any inflammatory lesion that **does not respond to local treatment after 10 to** 14 days
- Persistent hyperkeratotic changes of surface tissues
- Any **persistent tumescence**, either visible or palpable beneath relatively normal tissue
- Inflammatory **changes of unknown cause** that persist for long periods
- Lesion that **interfere with local function**
- Any lesion that has the **characteristics of malignancy**

The Oral Biopsy

Know when to defer to ENT or Oral Surgery

- For **sites that are deep or in proximity to important structures**
  - Stensen's duct
  - Posterior soft palate
  - Floor of mouth
- Avoid biopsy of **vascular lesions** (given the risk of excessive bleeding)
- Multiple **neurofibromas** (risk of possible transformation to neurosarcoma)
- Tumors of the **greater salivary glands**

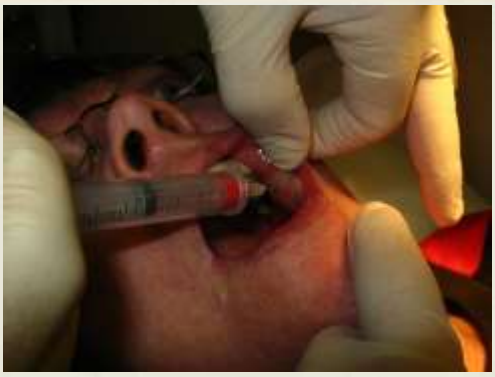
The Biopsy Procedure

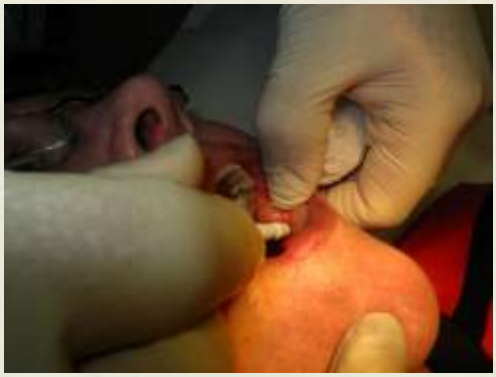
- Patient positioned the same as for the oral exam
- Local **anesthesia by direct infiltration** of the biopsy site
- Technique and tools are similar to that of non-mucosal skin
- *One Exception*: Chalazion clamp

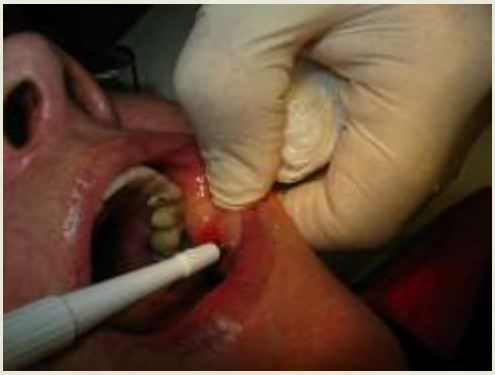
The Biopsy Specimen

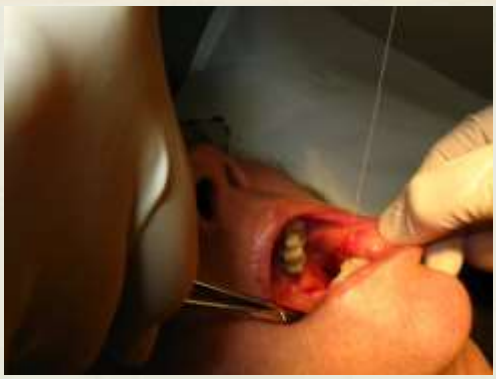
H&E	Formaldehyde 
DIF	Michel's medium (or normal saline) 
Tissue culture	Sterile saline without preservatives 
Viral studies	Hank's medium 

PUNCH BIOPSY TECHNIQUE
Buccal Mucosa









After the Biopsy

- Hemostasis can be readily achieved with **resorbable sutures**, **electrocautery**, or application of **silver nitrate** or **aluminum chloride**

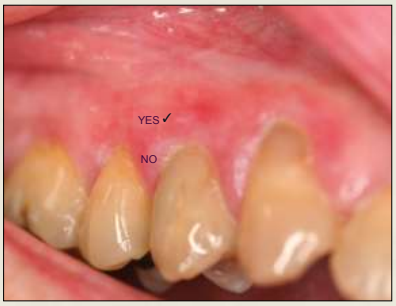
- Discomfort following a simple biopsy is **typically mild**, similar to an acute bite injury, lasting for 2–3 days, and rarely requires more than **over-the-counter analgesics for pain management**

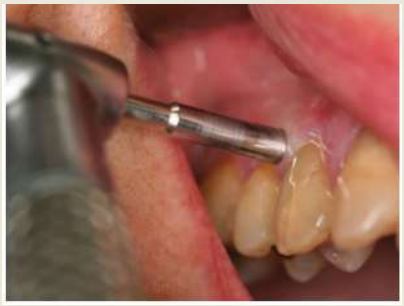
PUNCH BIOPSY TECHNIQUE
Tongue

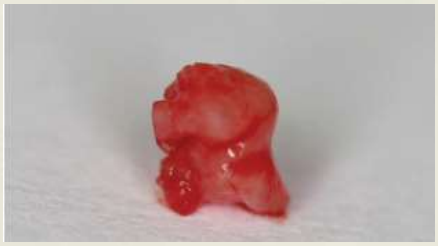
A B C

PUNCH BIOPSY TECHNIQUE
Gingiva

SO, WHERE TO BIOPSY ?







After the Gingival Biopsy

- Hemostasis can be readily achieved with **electrocautery**, or application of **silver nitrate,** or **aluminum chloride**

- A **non-eugenol** containing periodontal dressing (*Coe-PakTM, GC America Inc.*) can be used for covering **gingival biopsy sites**

INTRAORAL BIOPSY
Things to Know

- Do not use topical anesthesia, antiseptics, or iodine-based preparations that may contaminate the lesion
- Infiltrative anesthesia preferred **BUT** administer it **deep** or **in a field around the proposed biopsy site**
- If available, sample may be placed onto filter paper with the **mucosal surface upwards** so to avoid twisted artifacts and curling of specimen
- If you close with sutures any small **dog ears** formed are **not an issue**; leave them alone

INTRAORAL BIOPSY
General Comments

- **Obtain consent** forms with the indication and possible risks
- Risks are mostly site related:
  - PARESTHESIA: lips, tongue
  - SWELLING, BRUISING: tongue, lips, buccal mucosa
- Most patient do not experience significant pain post-operatively; typically pain reduced in **3 days**
- Give standard post-biopsy site care instructions

IN SUMMARY

- Understanding oral anatomy is a must
- Be systematic
- Have a positive approach to oral biopsies
- Be confident in your knowledge and skills

Multicentric Reticulohistiocytosis: Case Report and Treatment Review

By: Justin Rubin, D.O. PGY-4 NSU/Broward Health

OBJECTIVES

- Introduce a case report of Multicentric Reticulohistiocytosis (MRH).
- Discuss the history, pathogenesis, exam findings, diagnosis, and work-up of MRH.
- Discuss treatment options.
- Review the literature on treatment options, specifically biologic therapy.

HPI

- A 69-year-old caucasian female presented with a 2 month history of "multiple itchy red bumps around fingers, arms, chest, ears, and back of the neck."
- Four months prior to the rash, the patient was having joint pains in her bilateral hands and was diagnosed with rheumatoid arthritis by a rheumatologist and was empirically started on methotrexate 15mg qwk.

PMHx

- The patient's past medical history was significant for glaucoma and hypothyroidism.
- The patient reported no allergies.
- Review of systems was positive for swelling of fingers, decreased range of motion in all her fingers in all planes.
  - ROS- negative for fevers, night sweats, chills, weight loss.

PHYSICAL EXAM

- Physical examination revealed a well-developed, well-nourished female.
- Examination of the patient's hands revealed synovitis, and decreased range of motion in her metacarpophalangeal (MCP), proximal (PIP) and distal interphalangeal (DIP) joints.

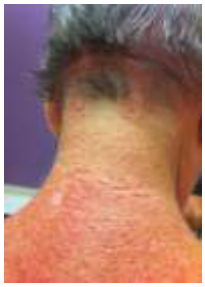
PE cont.

- Joint examination further revealed 2+ generalized swelling of the MCP, PIP and DIP joints with pain on motion and tenderness to palpation.
- Muscle strength was 5/5 in upper extremities.

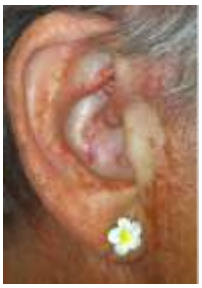
PE cont.

- Skin exam revealed multiple beaded red papules around her posterior neck and ears in a cobblestone pattern.
- Multiple red beaded papules also were present periunugally, resembling coral beads.
- Upon her presentation, two 4mm punch biopsies were performed one on the left hand third digit DIP and one on the posterior neck.

POSTERIOR NECK INITIAL VISIT

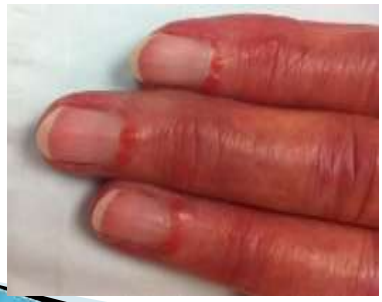


RIGHT EAR INITIAL VISIT



LEFT HAND INITIAL VISIT

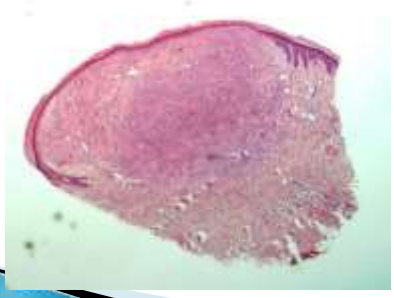
RIGHT HAND INITIAL VISIT



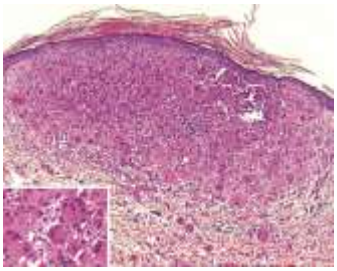
HISTOPAHTOLOGY

- The punch biopsy revealed numerous multinucleated giant cells and macrophages showing abundant eosinophilic, finely granular cytoplasm coined “ground glass” appearance.
- In keeping with the patient’s clinical presentation and histopathology, Multicentric Reticulohistiocytosis (MRH) was given as a final diagnosis.

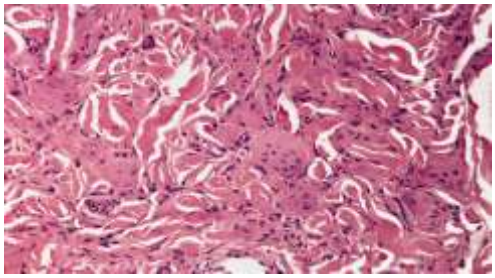
MRH Histopathology Low power



MRH Histopathology Medium Power



MRH Histopathology High Power



Dermal infiltrate with histiocytes and multinucleated giant cells and abundant "ground glass" cytoplasm

LABS

- The following laboratory studies were ordered:
  - Complete blood count (CBC)
  - Complete Metabolic Panel (CMP)
  - Fasting lipid panel
  - Erythrocyte sedimentation rate (ESR)
  - C reactive protein (CRP)
  - Thyroid Panel

LABS cont.

- Antinuclear antibodies (ANA) with reflex
- Rheumatoid factor (RF)
- Anti-cyclic citrullinated peptide (Anti-CCP)
- Random spot urine protein fixation
- Serum protein electrophoresis (SPEP) with immunofixation

LABS cont.

- Serum IgG, IgA, IgM levels
- B2 microglobulin
- Human immunodeficiency virus Ab
- Quantiferon gold
- Computed Tomography of Chest/Abdomen/Pelvis
- Thyroid ultrasound
- Transvaginal ultrasound

LABS cont.

- Mammogram
- Pap smear
- Colonoscopy
- EGD
- PET scan
  - All laboratory studies and imaging were found to be within normal limits.

TREATMENT

- Pharmacological therapy for this patient included continuing the methotrexate 15mg qwk, Prednisone 60mg daily for 1 month, decreased to 50mg for the second month, then tapered by 5 mg each month thereafter.
- Pt was referred to ophthalmology for visual field testing and plaquenil clearance.
- Pt was started on plaquenil 200mg twice daily 1 wk after initial visit.

Tx cont.

- Calcium 1000mg daily, Vitamin D 800 IU daily, Fosamax 75mg qwk.
- The patient was also written a prescription for infliximab but secondary to insurance issues, this was not started until 1 month after her 2 month follow-up appointment.

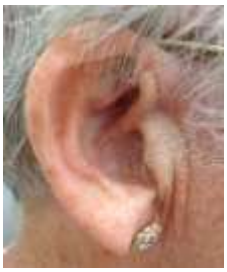
FOLLOW-UP 2 months

- At follow-up, approximately two months after initiation of plaquenil and prednisone, the patient had significant clinical improvement of her red beaded papules around her hairline, ears and periungually.
- The patient stated that her arthritic pains and range of motion remained relatively the same and made her activities of daily living challenging.

LEFT HAND 2 MONTH F/U

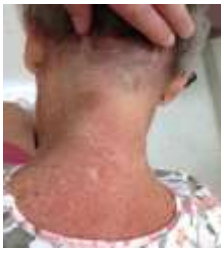
RIGHT HAND 2 MONTH F/U

RIGHT EAR 2 MONTH F/U



LEFT EAR 2 MONTH F/U

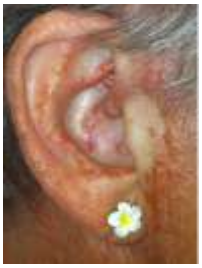
POSTERIOR NECK 2 MONTH F/U



FOLLOW-UP cont. 4 months

- Four months after initial visit and one month after starting infliximab, the patient's arthralgia's and synovitis of joints had significantly improved.
- Pt received infliximab dosed at 3mg/kg IV infusion q2wks for the first 2 doses, then changed to q6wks for the remaining doses.

RIGHT EAR 4 MONTH F/U

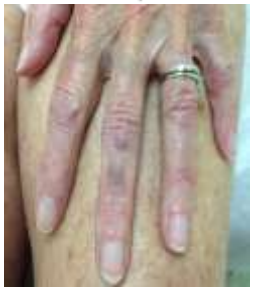


Week 0

Week 16

LEFT HAND 4 MONTH F/U

Week 0

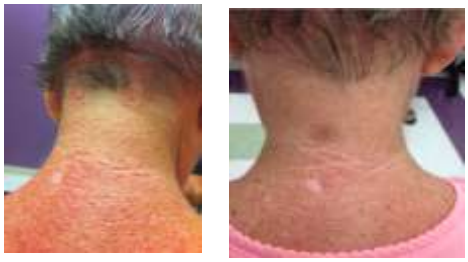


Week 16

RIGHT HAND 4 MONTH F/U

Week 0 Week 16

POSTERIOR NECK 4 MONTH F/U



Week 0 Week 16

FOLLOW-UP 8 months

- Current dose of prednisone is 20mg/day following the schedule of tapering by 5mg qmonth.
- The patient has been on this treatment regimen for 8 months and is currently in remission.

DISCUSSION

- Up until recently, biologics were rarely used in the treatment of MRH.
- There is limited literature available about biologic therapy in MRH.
- This case serves to review the literature in order emphasize the necessity and benefits of using biologics when treating MRH.


Proceedings of the Royal Society of Medicine

Nodular Non-diabetic Cutaneous Xanthomatosis with Hypercholesterolæmia and Atypical Histological Features

- The first case report of multicentric reticulohistiocytosis (MRH) was in 1937 by Weber and Freudentha (50).


JAMA Dermatology

MULTICENTRIC RETICULOHISTIOCYTOSIS OF THE SKIN AND SYNOVIA

Reticulohistiocytoma or Ganglioneuroma

- The term multicentric reticulohistiocytosis was first introduced by Goltz and Laymon in 1954(4).

HISTORY OF MRH

- MRH is a rare multisystem disorder with roughly 250 cases reported(1).
- The condition is classified as one of the non-Langerhans cell histiocytosis (48) and most commonly affects the skin, mucous membranes, joints and can progress to widespread systemic involvement(1).
- Disease onset is typically fourth decade of life with a mean age of 43(2,3).
- The disease may also affect children and elderly (52,53).
- Females are affected two to three times more than males(2,3,41).

HISTORY cont.

- When patients present, 40% present only with joint symptoms, 30% present only with skin symptoms, and 30% present with both(41).
- Skin involvement occurs most commonly within 6 months to 3 years after the onset of arthritis but may also occur simultaneously or prior to joint disease making it a challenging diagnosis(49).
- The skin lesions in our patient presented 4 months after the onset of the arthritis.

HISTORY cont.

- Cutaneously, MRH presents as a bilateral symmetric eruption of several pruritic, 2 to 20mm firm, round, red papules that most frequently occur on acral areas of the body, most commonly hands, specifically digits and nails, head and the juxta-articular regions of extremities(1,49).
- The papules can present as discrete, scattered, or grouped which creates a "cobblestone appearance" (42).

EXAM FINDINGS

- When lesions present in the vermicular area adjoining the nostrils, this is pathognomonic(41).
- The lesions may undergo Kőebner's phenomenon by sun induced light(58,3).
- The cutaneous eruption may also present with systemic symptoms including fever, fatigue and weight loss(41).
- 33-50% of patients will have mucous membrane involvement which presents as multiple erythematous papules and nodules affecting nasopharyngeal and oral mucosa(14,41).

EXAM FINDINGS cont.

- Other associated cutaneous findings include leonine facies(3), xanthelasma(49), nail dystrophy including brittleness, longitudinal ridging and atrophy(3,54).
- When papules present periungually, this is known as "coral beads"(64).

- Patients may also present with a dermatomyositis like eruption with multiple erythematous macules and patches(9,56,57, 58, 59).

EXAM FINDINGS cont.

- The joint disease in MRH can significantly affect patients daily routine.
- Once diagnosed, patients should be referred to a rheumatologist as the arthritis is destructive and can result in permanent deformities.
- 50% of patients will progress to arthritis mutilans(1,42).
- The DIP joint is most commonly affected (75%) and is a clinically distinguishing feature(27).

EXAM FINDINGS cont.

- PIP is the next most commonly affected.
- Other joints affected include MCP, wrists, shoulders, knees, hips, ankles, feet, elbows, temporo-mandibular and atlanto-axial spine(3,41,42,49).
- The maximal destruction of the interphalangeal joints is known as "opera glass" or accordion hands which is shortening and telescoping of the involved fingers (3,27).
- The destruction of joints typically lasts for 2 to 10 years or more(49).

EXAM FINDINGS cont.

- Other organs and systems that can be involved include cardiac, respiratory, neurological, ophthalmological, gastrointestinal, salivary glands and thyroid gland(49).
- The most common cardiac complication is constrictive pericarditis (60).

PATHOGENESIS

- The pathogenesis of MRH is not certain but literature indicates that it may be secondary to elevated levels of tumor necrosis factor alpha (TNF)- α(5,6,67,68,69).
- It may also be due to overexpression of monocyte chemoattractant protein-1 (MCP-1), which is stimulated by TNF-α.
- This was evidenced by decreasing levels in a patient undergoing treatment(7).

PATHOGENESIS cont.

- More recently, the literature suggests that MRH may be considered a systemic osteoclastic disease as patients with MRH have increased osteoclastic activity.
- Some authors have proposed that macrophages in the synovial fluid in MRH patients may have the ability to differentiate into osteoclasts(48, 8,35).

DIFFERENTIAL DX

- Rheumatoid Arthritis
- Psoriatic Arthritis
- Reactive Arthritis
- Gout
- Dermatomyositis
- Erosive Osteoarthritis
- Leprosy
- Sarcoidosis
- Papular Mucinosis
- Juvenile Xanthogranuloma
- Generalized Eruptive Histiocytosis
- Progressive Nodular Histiocytosis
- Xanthoma Disseminatum
- Rosai-Dorfman

DIAGNOSIS

- Diagnosis of MRH requires a skin or synovial tissue biopsy(49).
- Periodic acid-Schiff stain results are positive and are diastase-resistant.
- Synovial biopsy may demonstrate lipid-laden giant cells and histiocytes(3).
- H& E will reveal an infiltrate consisting of mononuclear histiocytes and multinucleated foreign body-type giant cells approximately 50 to 100 um in diameter with eosinophilic finely granulated cytoplasm that has a ground glass appearance(4,24,46) .

DX cont.

- The histiocytic infiltrate may consist of proinflammatory cytokines including tumor necrosis factor-a (TNF-a)(67,68,69), interleukin (IL)-1, IL-6, IL-12, and prostaglandin E2(43-45).
- Positive for CD45, CD68, and vimentin.
- Negative for S100, factor XIIIa and CD1a(49).

WORK-UP

- Any patient with the diagnosis of MRH should have a thorough workup to rule out malignancy (49) as MRH can be associated with malignancy up to 30% of the time including lung, stomach, breast, ovary, cervix, colon.
- Breast and ovarian appear to be the most common(49).
- There have also been reports of lymphoma, leukemia, sarcoma, malignant mesothelioma, malignant melanoma, liver, and renal cancer (10,11, 12, 49,3,33,34,31,62).

WORK-UP cont.

- MRH has been associated with autoimmune disease including:
  - Rheumatoid arthritis
  - Sjögren syndrome(28)
  - Primary biliary cirrhosis(29)
  - Systemic lupus erythematosus(19)
  - Systemic vasculitis (30)
  - Endocrinopathies including diabetes mellitus and hypothyroidism(49)

WORK-UP cont.

- Laboratory tests that should be obtained include a CBC to look for anemia, ESR as this may be elevated(49), fasting lipid profile to look for dyslipidemia(3).
- 50% of patients present with anemia
- 30-58% of patients are affected by dyslipidemia(1,54).

WORK-UP cont.

- There are reports of MRH being associated with IgG hypergammaglobuinemia and cryoglobulinemia and so a SPEP and cryoglobulin levels should be tested for.
- To rule out rheumatoid arthritis RF, and anti-cyclic citrullinated peptide (anti-CCP) levels should be tested for.
- To rule out malignancy, a CT scan of abdomen, pelvis, chest should be ordered.
- Tuberculosis should be investigated with a purified protein derivative, or quantiferon (3,42).

WORK-UP cont.

- To help further obtain a diagnosis, affected joints should have imaging with X-rays which can reveal well-circumscribed marginal erosions.
- Other findings include marked resorption of subchondral bone(1,33,327).
- There is one report that demonstrates that scintigraphy with Gallium-67 citrate may also be used as way to assess the recovery and extent of disease(27).

TREATMENT

- MRH has been reported to spontaneously remit within 5-10 years of diagnosis but early aggressive treatment is recommended to prevent any irreversible sequelae(1).
- Joint replacement may be an option in patients who have deformity and burned out disease.
- Systemic therapy is the mainstay treatment with first line therapy being immunosuppressive and cytotoxic agents.
- Symptomatic therapy for relief of arthritis can be treated with non-steroidal anti inflammatory drugs (NSAIDS) (49).

TREATMENT OPTIONS

- Prednisone
- Hydroxychloroquine
- Cyclophosphamide (14)
- Methotrexate (14,15, 16,17)
- Chlorambucil(13)
- Azathioprine (18,37)
- Leflunomide (38)
- Cyclosporine (19)
- Mycophenolate mofetil (66)
- Bisphosphonates including alendronate(40) and zoledronic acid (35).

TREATMENT cont.

- NSAIDS, hydroxychloroquine and corticosteroids are more conducive for symptomatic treatment as case reports do not show remission(49) where as methotrexate, chlorambucil or cyclophosphamide have(13,14,49,23).
- Recently biological agents have become popular including infliximab (21,22), etanercept (5, 64) and adalimumab.

- The first report of MRH induced remission with a biologic was by Matejicka et al. The patient was initially on methotrexate 25mg weekly, 15 mg prednisone daily and hydroxychloroquine 200 mg twice daily.
- After failing to improve with cyclophosphamide 75mg daily, cyclosporine was substituted to the regimen which gave transient symptomatic improvement but eventually "pencil in cup" deformities and Dupuytren's contractures formed.

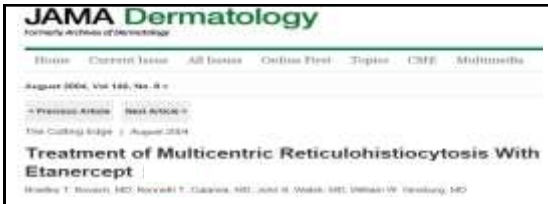
Matejicka 2003

- Cyclosporine was discontinued and the patient was started on etanercept 25mg subcutaneously twice weekly.
- Improvement of joint and cutaneous findings were seen in 6 weeks which was evidenced by follow up radiographs.
- This subsequently allowed for tapering of methotrexate and prednisone.
- The patient continued on etanercept and hydroxychloroquine with no flares (64).

- Yeter KC and Arkfeld present a case report of a patient treated with methotrexate 15mg weekly with etanercept 50 mg/week, subcutaneous for 12 weeks

Yeter 2012

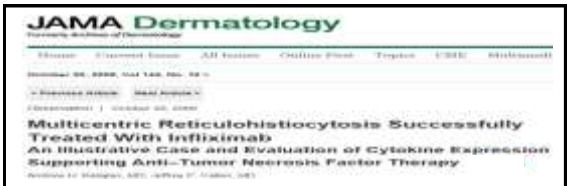
- The patients skin lesions, pruritus significantly improved but the patient still had morning stiffness.
- Prednisone 5mg daily was added which did not help.
- 6 weeks later, etanercept was replaced with adalimumab 40 mg subcutaneous q2wks with continuation of the same dose of methotrexate and prednisone.
- The patients arthralgias still did not improve.
- Minocycline 50 mg orally two times a day was thus added to the regimen which improved the patients arthralgias and the patients disease remitted(24).



- Kovach et al report a patient who did not have adequate response on prednisone, methotrexate, hydroxychloroquine.
- The patient was also refractory to chlorambucil.

Kovach 2004

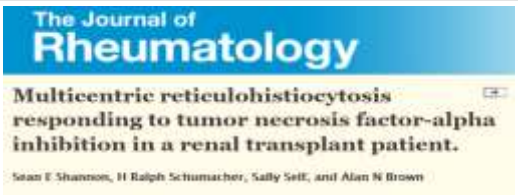
- The patient was also started on cyclophosphamide and had slight improvement of cutaneous manifestations but the drug was discontinued secondary to gross hematuria.
- The patients skin lesions and joint symptoms completely resolved with the combination of etanercept 25mg biweekly, prednisone 10mg daily and leflunomide 20mg daily.



- Kalajian report a case of 63 year old gentleman who was refractory to combination treatment of prednisone, methotrexate and etanercept.
- The patients etanercept was replaced with infliximab, 5mg/kg infusion at weeks 0,2,6 and then every 8 weeks while continuing methotrexate and prednisone.

Kalajian 2008

- The patients constitutional symptoms, articular and cutaneous manifestations started to improve after 3 infusions.
- His cutaneous symptoms improved over 12 months with near complete resolution except for larger nodules.
- No new cutaneous lesions formed while on infliximab.



- Shannon et al presented a 37 year old renal transplant patient who was on prednisone 10mg every day, mycophenolate mofetil 250mg twice daily and cyclosporine 125 mg twice daily who developed articular symptoms of MRH (66)

Shannon 2005

- The patients symptoms rapidly resolved on 40mg adalimumab therapy every other week, prednisone 10mg every day, cyclosporine 125mg orally twice daily and mycophenolate mofetil 250mg by mouth twice daily(66).
- Patient had joint improvement in 8 weeks and CRP levels returned to normal.
- Patients adalimumab was discontinued and the patients synovitis recurred which resolved with restarting adalimumab therapy.

Successful treatment of multicentric reticulohistiocytosis with a combination of infliximab, prednisolone and methotrexate.

- Lee at al also described a case of a 53 year old female who had skin and articular disease who was started on infliximab 5mg/kg, methotrexate 7.5 every week and prednisolone 30mg orally every other day.
- Patients skin lesions improved significantly, prednisolone dose was tapered to 5mg over 2 weeks, with joint improvement over 3 months.

ANTI-TNF THERAPY

- TNF blocking agents should be carefully used as there is an increased risk of malignancy reported with their use(70).
- Infection and malignancy should be ruled out prior to initiation of treatment.
- There is a growing body of evidence supporting treatment of MRH with TNF inhibition.
- The high proportion of histiocytes and presence of TNF-alpha in the inflammatory infiltrate of MRH makes biologics have an important role in the treatment of MRH and present as a promising therapeutic option.

CONCLUSION

- I presented a case report of MRH
- I discussed the history of MRH, pathogenesis, exam findings, diagnosis, and work-up
- I discussed my treatment plan and other treatment options
- I reviewed the literature of biologic treatments for MRH

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The Future of Dermatology Practice

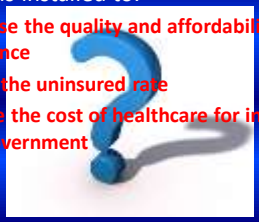
Steven Grekin, D.O., F.A.O.C.D.

Objectives

- To discuss:
  - recent and anticipated changes made to healthcare policy
  - the effects that these changes may have on the dermatology practice
  - methods by which we can overcome the obstacles created by these changes in every day practice

What is the "Affordable Care Act?"

- Signed into law March 23, 2010
- Programs installed to:
  - increase the quality and affordability of health insurance
  - lower the uninsured rate
  - reduce the cost of healthcare for individuals and the government



Centers for Medicare & Medicaid Services. The Center for Consumer Information & Insurance Oversight. Health Insurance Market Reforms Accessed December 10, 2013.

Are these goals actually being accomplished?

- Studies demonstrate only a *modest* benefit in patient outcomes
- No actual decrease in healthcare spending
- More regulation and paperwork
- Less patient care and decreased reimbursement

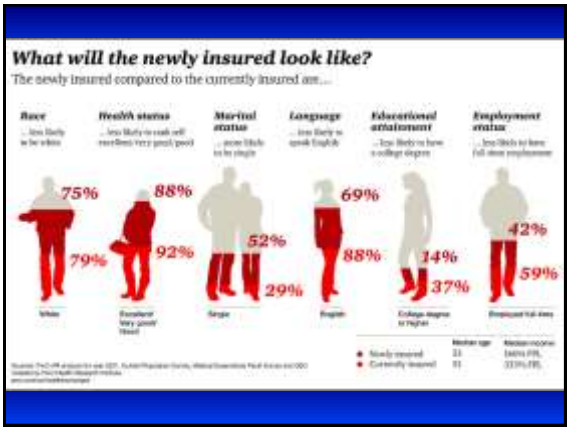
Manchikanti, L., et al. "Patient Protection and Affordable Care Act of 2010: reforming the health care reform for the new decade." *Pain Physician*, v. 14 issue 1, 2011, p. E35-67.

What Can We Expect?

Increased Coverage

- Millions of newly insured Americans looking for physicians- including specialists
- Projected to add 12 million people to Medicaid by 2015
- "Marketplace" insurance to offer similar reimbursement?
  - **Likely 10%-20% cut**
- Can you survive financially on these new plans?

Manchikanti, L., et al. "Patient Protection and Affordable Care Act of 2010: reforming the health care reform for the new decade." *Pain Physician*, v. 14 issue 1, 2011, p. E35-67.



Marketplace Exchange

- Provides a set of *government-regulated* and *standardized* health care plans from which individuals may purchase health insurance eligible for federal subsidies.
  - All exchanges must be fully certified and operational by January 1, 2014, under federal law.
  - **What if patient fails to pay their bill?**

What is the Health Insurance Marketplace? [illegible] Accessed December 17, 2013.

Higher Deductibles

May largely impact specialists with expensive services

- This will force more communication between physician and patient about costs of procedures
- Will patients opt out of services because of cost?

8 Ways That the ACA is Affecting Doctors' Incomes. *Medscape*. Aug 15, 2013.

Increasing Rules and Regulations

- Higher practice costs
- New payment methodologies
- EMR
- Increasing penalties

8 Ways That the ACA is Affecting Doctors' Incomes. *Medscape*. Aug 15, 2013.

Payment adjustments for Medicare providers based on 2013 reporting year

Program	Incentive	Penalty	Reporting year	Penalty year
PQRS	[illegible]	-1.5%	2013	2015
eRx	[illegible]	-2%	2013	2014
Meaningful Use*	$8,000 - $15,000	-1%	2013	2015

*Meaningful Use penalties based on the 2013 reporting year may not apply to all providers eligible for that program. For more information, see the Meaningful Use information below.

Avoid Medicare Penalties by Reporting Quality Data This Year. Posted March 19, 2013 by Naushad Godrej. [illegible] Accessed December 17, 2013.

Decreasing Reimbursement

- Independent Payment Advisory Board
  - 15 members appointed by President
  - Aim is to reduce per capita growth rate in Medicare spending
  - Physicians will be primary targets
  - A healthcare rationing body…?

Manchikanti, L., et al. "Patient Protection and Affordable Care Act of 2010: reforming the health care reform for the new decade." *Pain Physician*, v. 14 issue 1, 2011, p. E35-67.

Decreasing Reimbursement

- "Non-profit" Patient-Centered Outcomes Research Institute (http://www.pcori.org/)
  - Will examine clinical effectiveness of medical treatment, procedures, drugs, and medical devices.
  - Possible detriment to clinical innovation in the delivery of care..?

Manchikanti, L., et al. "Patient Protection and Affordable Care Act of 2010: reforming the health care reform for the new decade." *Pain Physician*, v. 14 issue 1, 2011, p. E35-67.

New Payment Methods

- Bundled payments
- Patient-centered medical homes
- **Accountable Care Organizations (ACOs)**
- **Pay-for-Performance (P4P)**

What are ACOs?

- Network of hospitals and physicians
- Coordinate care for group of patients
- Incentivized to cooperate and save $$
- Penalties incurred for not meeting benchmarks
- Requires sophisticated IT systems, data-reporting, and shared networks

Bennett, DD. "Accountable Care Organizations: what are they and how will they impact dermatology?." *Cutis (New York)*, v. 92 issue 4, 2013, p. 171-3.

ACO Management. http://www.acomanagement.org Accessed December 17, 2013.

ACOs: The Negatives

- Incentivizes physicians to not treat appropriately
- Responsibility of health lies solely in *physician's* hands, not patient's
- Mergers and consolidation may lead to greater market share and provide leverage for driving up prices.
  - FTC recent order unwinding of St. Lukes purchase of large physician network in Boise ID
    - http://www.nytimes.com/2014/02/05/business/economy/health-law-goals-face-antitrust-hurdles.html?_r=0

Pay-for-Performance (P4P)

- Reimbursement reflects provider performance based on:
  - Certain care processes
  - Scores on patient satisfaction surveys
  - Patient outcomes

"Medicare and Medicaid programs: Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Hospital Value-Based Purchasing Program; organ procurement organizations; quality improvement organizations; Electronic Health Records (EHR) Incentive Program; provider reimbursement determinations and appeals. Final rule with comment period and final rule." Federal Register. v. 78 issue 237. 2013. p. 74825-5209.

Pay-for-Performance (P4P)

- Rewarded for meeting pre-established targets
- Disincentives include eliminating payments for negative consequences of care or increased costs
  - Will this force physicians to deselect for patients?

"Medicare and Medicaid programs: Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Hospital Value-Based Purchasing Program; organ procurement organizations; quality improvement organizations; Electronic Health Records (EHR) Incentive Program; provider reimbursement determinations and appeals. Final rule with comment period and final rule." Federal Register. v. 78 issue 237. 2013. p. 74825-5209.

Physician Quality Reporting System

- Will be applied to Medicare in 2015
- Pay will be adjusted to reflect PQRS and cost data from Medicare fee-for-service claims
- Provides incentives for quality of care delivered to Medicare patients

"Medicare and Medicaid programs: Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Hospital Value-Based Purchasing Program; organ procurement organizations; quality improvement organizations; Electronic Health Records (EHR) Incentive Program; provider reimbursement determinations and appeals. Final rule with comment period and final rule." Federal Register. v. 78 issue 237. 2013. p. 74825-5209.

Physician Quality Reporting System

- Burdened with time-consuming compliance and reporting requirements
- 2% payment reduction in Part B claims if fail to report during 2014
  - Is the penalty significant enough to make up for workload and resources required?

"Medicare and Medicaid programs: Hospital Outpatient Prospective Payment and Ambulatory Surgical Center Payment Systems and Quality Reporting Programs; Hospital Value-Based Purchasing Program; organ procurement organizations; quality improvement organizations; Electronic Health Records (EHR) Incentive Program; provider reimbursement determinations and appeals. Final rule with comment period and final rule." Federal Register. v. 78 issue 237. 2013. p. 74825-5209.

Physician Quality Reporting System

- AAD is trying to develop meaningful quality measures, as there are currently few for dermatologists.

Physician Compare Website

- Created by Centers for Medicare and Medicaid Services
- Patients can search for and pick their physician
- PQRS data to be uploaded to this site
- 30-day period for physician review before data posted
- Criticized by AMA

American Medical Association. AMA letter to CMS on Physician Compare. July 17, 2013. Accessed July 19, 2013 .

Increasing Penalties

- Penalty imposed on physicians who do not meet e-prescribe levels
  - Increasing from 1% to 2% in 2014
- 2015: Penalties for not having electronic health records (EHRs)
  - Purpose is to reduce paperwork and administrative costs, but for whom?
  - Expensive
  - Requires MORE administration
  - Slows practices down

Centers for Medicare & Medicaid Services. Electronic prescribing (eRx) incentive program. Accessed August 1, 2013.

Payment Cuts

- Centers for Medicare and Medicaid Services released 2014 Medicare Physician Fee Schedule
  - Dermatologists face a 2% reduction in Medicare payments
- Impact will vary depending on practice's mix of services

"Breaking news: Dermatology to see overall 2 percent cut in payments in 2014. AAD Member Alert. December 2, 2013.

From an Employer's Perspective

- Employers with <50 employees are not required to provide health insurance
- Tax credits for providing insurance:
- 35% if < 25 full-time employees with average wages <$50,000
- Full credit: <10 employees with average wages <$25,000

"Small Business Health Care Tax Credit for Small Employers." IRS. http://www.irs.gov/uac/Small-Business-Health-Care-Tax-Credit-for-Small-Employers. Visited Dec 2013.

How can we overcome the challenge of increased practice costs in the face of decreased reimbursement?

Consolidate

- Independent physician practices declined from 57% in 2009 to 39% in 2012:
  - Declining reimbursement
  - Lowered contract negotiating power of smaller providers
  - Shifted referral patterns
- Consider joining groups to spread out overhead and strengthen reimbursement negotiations

Carruthers, J. Higher co-pays, higher stakes. Dermatology World. Aug 2013.

Stay Informed

- Become familiar with practice realities in your respective marketplace
- Learn about the different payment models
- Policymakers predict the currently primary care-centered ACO payment model will spread to specialty care

See More Patients

- What is the impact of a 2% cut on your bottom line?
- If average collection for office visit is $150, reimbursement then becomes $147
- 50 pts x $150 = **$7500** vs 50 pts x $147 = **$7350**
- Add one more patient per day to fill gap

Establish a Dashboard

- Measure, measure, measure!
- Determine where you can improve revenues and increase efficiency
- Invest in resources that compare yourself to similar practices
- Assess practice patterns that may trigger an audit

Calculate

- What is the procedure value per hour?
- Utilize non-physician clinicians and other ancillary personnel to the full extent
- Free up the physician to see more pts and generate more revenue
- Cut wasteful spending. Analyze expenditures quarterly

Collect

- Collect co-pays upfront
- Keep credit cards on file
- A practice utilizing technology-driven solutions has increased patient collections from 42% to 50%
  - Patients check-in with tablets
  - Credit cards swiped and kept on file, automatically charging co-pays at every subsequent check-in
  - Prompted to pay outstanding balances

Carruthers, J. Higher co-pays, higher stakes. Dermatology World. Aug 2013.

Improve Patient Satisfaction

- Prior experience is the most important antecedent of satisfaction
- Heed advice from business colleagues: **The customer is always right!**
- Use your patient's name and details about personal life
- Give them realistic expectations of treatment outcomes

Improve Patient Satisfaction

Plug and Play

- Airlines provide satisfaction by demonstrating efficiency
  - Concept of line-up
  - Cohesiveness
  - Communication

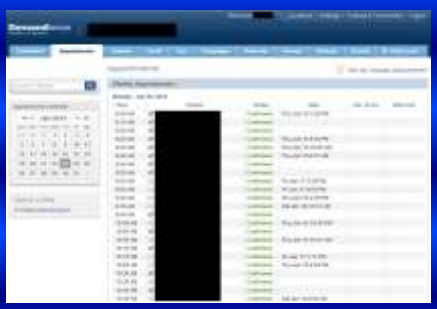
Grekin Skin Institute Line Up

Plug and Play

- Car dealerships know when lease is up
  - Reach out to patients
  - Is winter coming? Send reminder to atopic derm patients

Send reminder e-mails, texts or postcards about appointments, full body exams, etc

Text and Email reminders



Social Media

- Keep up with the times
- Facebook, Instagram and Twitter are all FREE outlets for advertising

Create a Website

- Create a website that sells you and your practice
  - Provide educational material
  - Provide a link for "feedback" for continued improvement

Alter Perception

- AAD researched the perceptions of dermatology practice by other physicians
- Dermatologists are perceived as *valuable* colleagues

Bowers, J. A Matter of Perception. Dermatology World. Oct 2013.

Alter Perception

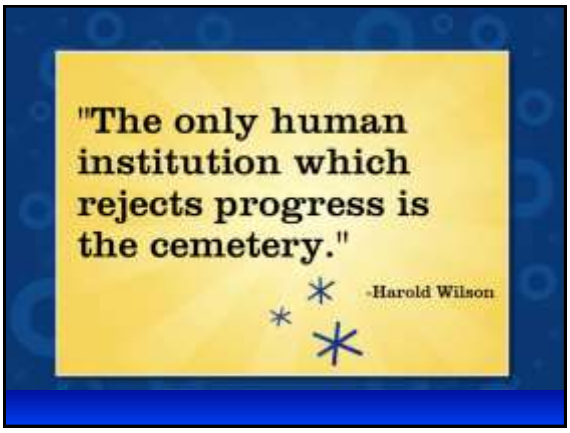
- Negative perceptions:
  - Access to dermatologists is limited, both for inpatient and outpatient
  - Favor surgical cases over routine problems
  - Unwilling to accept insurance
  - Shifting focus to cosmetic-related services
  - Not visible or engaged in local communities

Get Involved

- Word-of-mouth is the most important method for referrals
- Accept consults at a hospital
- Stay in contact with your referring physicians
- Offer free services, such as skin cancer screenings

Bottom Line

- Do not ignore the business aspect of medicine
- Constantly measure for constant improvement
- Cut wasteful spending
- See more patients
- Communicate to increase efficiency and reduce errors
- Continue improving patient satisfaction
- Utilize all staff and mid-level providers



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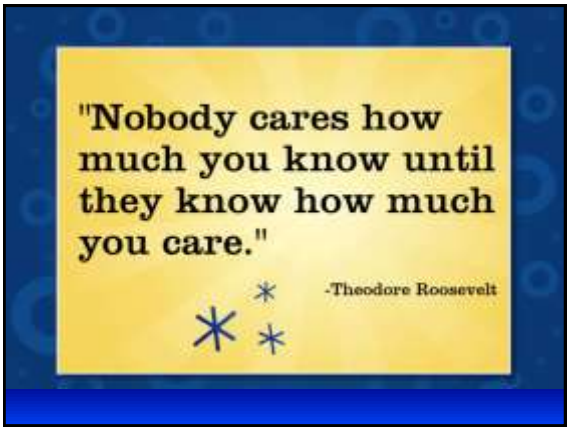

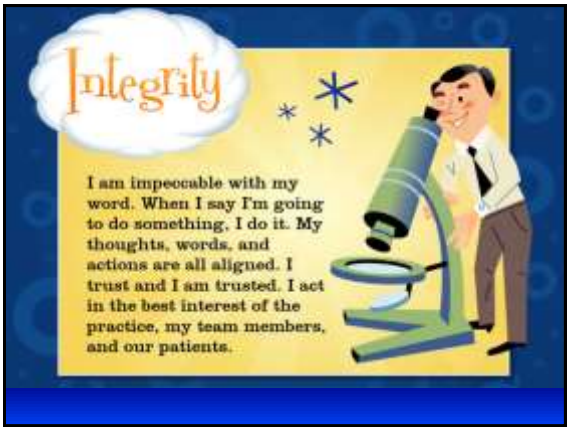


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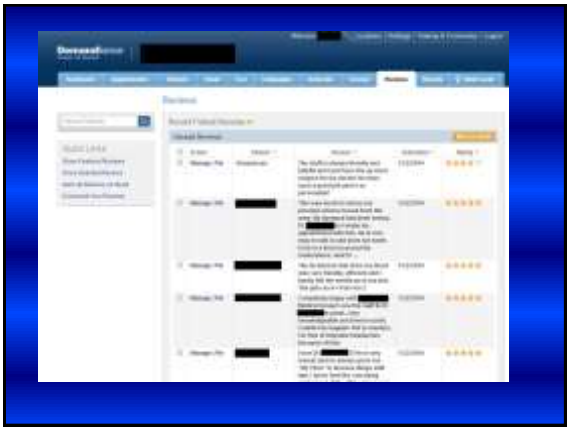



4,116

Melanocytic conundrums

Ron Rapini MD, Josey Chair, Dept Derm
Professor of Pathology
Univ Texas Medical School at Houston
MD Anderson Cancer Center

By now you're probably sick of the relentless attack of the alien melanocytes DAILY in your practice

Melanocytes come from the neural crest – born to wander – "wunderlust"

If you think about it, there are not too many tumors 1 mm in size which regularly metastasize

Main goal of the dermatopathologist should be to be helpful; even though often we don't know for sure what all these melanocytic neoplasms are…

Plastic surgeon:

"I am sorry; I just need a definitive diagnosis so I can know what to do. . ."

(complaining about report "atypical melanocytic proliferation – atypical nevus favored over melanoma")

"Morphological diagnosis, whether of birds, fish, plants, or pathological processes in human beings, is 100% subjective"

Ackerman AB. Discordance among expert pathologists in diagnosis of melanocytic neoplasms. Hum. Pathol. 1996; 27; 1115-1116.

Really, H&E stain is primitive approach of using pink and blue dyes to predict complex biological behavior

- Future probably lies with more sophisticated methods like FISH, CGH, etc, but many feel that they are not quite ready for prime time due to limited availability, cost, and unresolved issues

We, the H&E Olympians attempt to predict biologic behavior from pink and blue splotches

What is the predicated biologic behavior of this person?

Predictive clues?

1. Texas shirt
2. Orange color
3. Shorts
4. Weird hat
5. Beer in hand
6. Socks pulled up
7. Long hair

Homerun hitters vs Base hitters

- Homerun hitter dermpaths (one diagnosis – melanoma - most of the time) are either really really right or really really wrong
- Base hitter dermpaths (differential all the time) are almost always right, but often not much help
- The ART of pathology is to be a homerun hitter as much as possible but to go for the base hit when necessary

Five dermatopathologists have seen this slide…

- Three think that it is benign and two favor malignancy
- They can have their opinion, but definitive answer may be unknown

Vague terms ("The favorite plant of radiologists and pathologists is the hedge")

- Consistent with
- Suggestive of
- Near the margin
- Narrow margin
- Approximates the margin

Clues – Ackerman published several books on various clues in dermpath

- Our diagnoses and predictions are based upon various clues or other findings
- Not all clues are valid: I prefer not to use algorithms for that reason (blind alley if rely too heavily on just one finding)
- I prefer to look at multiple findings in tandem

"Our criteria may be wrong, but at least we have criteria"

- Better than using "feeling in your gut"
- Not all criteria have equal sensitivity and specificity
- Use multiple criteria

DOGMA

- Do not believe everything
- Healthy but not excessive skepticism
- "Rules" of diagnosis frequently broken
- Criteria for both clinical and histologic diagnosis vary according to the authority

Healthy skepticism

- "An attitude of skepticism is the greatest gift of science to mankind"

NEJM 322:235, 1990

By the way, it takes a lot of chutzpah to talk about dysplastic nevus

First rule is to talk about things you know a lot about, and preferably things your audience knows less about than you do

OK, with that introduction (and with the knowledge that lawyers are lurking, we are ready to discuss:

DYSPLASTIC NEVI!

First of all – we cannot agree on what to call it

Dysplastic nevus (DN)

Nevus with architectural disorder (NAD, NWAD)

Clark's nevus

Active nevus

Atypical nevus

Atypical mole

And we have invented many other terms for the grey zone lesions

- MELTUMP –mel tumor uncertain malig potential
- SAMPUS – superficial atyp mel prolif uncertain signif
- SIMP – sun-induced mel prolif
- AMP – Atyp mel prolif
- AST – Atyp Spitz tumor

The concept of dysplastic nevus is very controversial: induces spasms in many dermatopathologists

Ackerman AB. Histopathology. 1988 Sep;13(3):241-256. **What naevus is dysplastic, a syndrome and the commonest precursor of malignant melanoma? A riddle and an answer.**

Dysplastic nevus

= Clark's nevus = "active nevus"

- 5% or 50% of population – criteria vary!
- More significant if +FH melanoma, multiple atypical nevi
- "Most common nevus in man" - Ackerman
- "Growth industry for derm" - Clark

Dysplastic nevus

- NIH consensus conference (JAMA 1992): Clinician should call them "atypical moles", pathologist should call them "nevus with architectural disorder" and should grade the cytology "mild, moderate, severe"

My 3 favorite things to distinguish melanoma from dysplastic nevus (but exceptions to all of this)

1. More pagetoid
2. More atypia
3. More lymphocytes ("smart bombs")

(Ackerman's favorite was asymmetry, I think, but flat dysplastic nevi don't have enough dermal component to evaluate that)

Pagetoid melanocytes (Ackerman calls "scatter")

- Melanoma
- Spitz nevus, pigmented spindle cell nevus
- Congenital nevi in neonates
- Acral nevi
- Irritated nevi (especially centrally)
- Keratinocyte processing artifact

Lymphocytes in benign nevi

- Halo nevus
- Spitz nevus
- Traumatized nevus
- Demodex mites and other stimuli

Lots of things in pathology have plenty of cytologic atypia and are still benign

It has been said that you MUST have cytologic atypia to call something dysplastic nevus

Ackeman complained that most of them have NO cytologic atypia, hence the term nevus with architectural disorder

Grading dysplasia in dysplastic nevi

- NIH consensus conference 1992 recommended grading cytology despite lack of concordance
- I grade only cytology as mild, moderate, severe
- Cockerell in Dallas does not grade at all, but points out which ones need re-excision
- MDACC grades both cytology and architecture
- Barrett: Only mild or severe, never moderate

Lack of concordance on grading "dysplasia"

- Piepkorn (J Cutan Pathol 6:542, 1992) found only 38% agreement
- Important to know threshold of your particular dermatopathologist

Dysplastic nevus grading is a mess

- Need to know <u>who is reading the biopsy</u> and their habits to know what it all means.

- Lab A: won't grade them at all, but will let you know which ones they are worried about and should be excised.
- Lab B grades them only as SEVERE or MILD, but never MODERATE because that is too vague.
- Lab C will grade both the CYTOLOGY and the ARCHITECTURE into 3 grades, double-grading them

Duke, Univ Chicago, MD Anderson

Grade BOTH cytology AND architecture because the authors of paper on that migrated to those places

Shea CR, Vollmer RT, Prieto VG. Hum Pathol. 1999;30:500-5. **Correlating architectural disorder and cytologic atypia in Clark (dysplastic) melanocytic nevi.**

"may provide additional information for clinical management"

Shea et al – grading architectural disorder

- Circumscription
- Asymmetry
- Nest cohesiveness
- Suprabasal melanocytes
- Confluence
- Single cell proliferation

Immunostains for problem: melanoma versus nevus?

- K-67: Less than 5% = nevus, more than 10% = melanoma (problem that lymphocytes will often stain – so some use a double labelling technique with panMel)
- HMB-45: Stratified staining (nevus is negative deeper in dermis)

Dyplastic nevus photography

- Dysplastic nevi grow and change, so change alone is not a concern, but usually we don't know for sure and tend to biopsy
- Normal constant change in nevi and DN limits value of photography

Debate at AAD meeting regarding whether all these patients with multiple dysplastic nevi need photography

Probably the answer is that "some do," but not all

Rapini RP: Photographs for Clark's "dysplastic" nevi? J Am Acad Dermatol 19(6):1130-1132, 1988.

Dermoscopy

- Very important for clinician to be familiar with dermoscopy (the dermatologist's high-tech device – adds to the clout)
- But beginners sometimes become worse with dermoscopy; most studies show about 15% improvement in diagnosis overall with experience

Shaving OK in dysplastic nevi?

- Cosmetic result can be superior
- Take 2 mm superficial margin and make sure you get under the lesion
- Check for pigment at base after shave
- Better to have shave of 11 mm macule than 6 mm punch biopsy

Clear margins in dysplastic nevi?

Controversial

Probably those with mild atypia do not need clear margins, but some docs re-excise anyway

Duffy et al: Arch Derm survey of derms, 148:259, 2012

If margins CLEAR on dysplastic nevus, would you just observe?

Mild: 91%

Moderate: 80%

Severe: 35%

Duffy et al: Arch Derm survey of derms, 148:259, 2012

If margins INVOLVED on dysplastic nevus, would you just observe?

Mild: 69%

Moderate: 15%

Severe: 1%

Rates of clinical recurrence after biopsy of DN and benign nevi were extremely low. Re-excision of nevi, including mildly to moderately DN with a positive margin, may not be necessary.

J Am Acad Dermatol 2010;62:591-6

My recommendation:

Mild atypia – don't re-excise
Severe atypia – always re-excise
Moderate atypia – "jump ball"

Tallon B, Snow J (New Zealand). Am J Dermatopathol. 2012
Epub ahead of print. **Low Clinically Significant Rate of Recurrence in Benign Nevi.**

- The rate of recurrence requiring re-excision is very low at 0.3%. This suggests that few cases of clinical recurrence are re-excised. Re-excision of benign nevi including mild and moderately dysplastic nevi may not be necessary.

Dysplastic nevus?

- No, lentigo maligna (melanoma in situ!)

Four lessons with this case, with general rules

Lessons from this case

1. If lesion recurs beyond scar, consider more worrisome, and less likely just "recurrence" – recurrent nevi mostly IN the scar, arising from deeper component

Lessons from this case

2. If you think it is dysplastic nevus, but it is present on sundamaged skin of older individual, consider an upgrade to LM

Lessons from this case

3. If it is growing or changing, pay attention

Listen to the patient; if they are worried then maybe you should be worried (though SKs, lots of B9 things grow)

Lawyers are all around

The light brown unimpressive melanoma

- Not to cause paranoia, but…..Incidence of melanoma increasing dramatically along with increased liability concerns
- "If the patient is worried, consider being worried yourself"
- "When in doubt, cut it out"
- "If the patient says it is growing or changing, pay attention"

Lessons from this case

4. Mostly OK to shave dark macules even though some say everything should be punched and shaved to adipose

Better to shave entire large macule than to just punch part of it

AAD guidelines of care say it is sometimes ok and advantageous to shave suspected melanomas

Lentigo maligna –
NO 2 mm punch

Lentigo maligna

= melanoma in situ of sundamaged skin

- We think it is a different subset because it stays in situ for centuries
- If you miss it, chances are next year it will still be in situ
- Only 5% become invasive? – unlike melanoma in situ of covered sites?

Melanoma

- ABCDE criteria
- Asymmetrical
- Border irregular (notched)
- Color variegated: BLACK, brown, blue, red, white
- Diameter greater than 6 mm
- Evolution (changing, growing)

Lentigo maligna

= melanoma in situ of sundamaged skin

- Atrophic epidermis
- Severe solar elastosis
- Older age
- Can be subtle!! – MART-1 helps?

Lentigo maligna is defined as (1) subset of melanoma in situ (2) on sundamaged skin

- Problem is: what is sundamaged?
- Worthwhile to subclassify?
- Atrophy of epidermis NOT necessary!
- Lentigo maligna melanoma means invasive but LM is a melanoma too (in situ) – terminology problem

Mostly I accept some architectural disorder in congenital nevi without calling them "dysplastic"

"My skin-colored mole regrew after it was shaved"

Recurrent melanocytic nevus

- Kornberg & Ackerman: "Pseudomelanoma" Arch Dermatol 111:1588, 1975
- 60% have pagetoid cells
- Heavily pigmented junctional melanocytes usually directly overlying a scar
- 10-30% of shaved nevi recur or persist

Do you think some recurrent nevi can be called recurrent (persistent) DYSPLASTIC nevi?
For me, mostly "no"

Jentigo? Lentiginous junctional nevus?

Tiny "speck" nevi – do you require DNs to be at least 6 mm?

Do you think MOST halo nevi are DYSPLASTIC nevi?

- Most halo nevi are on the trunk where many dysplastic nevi occur
- They do tend to have the architectural features of DN

Nevi of "special sites" or "site-specific nevi" (groin, genitals, breast, etc)

I just call most of them "dysplastic nevus" and don't use "site-specific" or "special site"

Jean Bolognia thinks of nevus spilus (speckled lentiginous nevus) as a "garden" and within the garden you can have lots of things beside just background lentigo with benign nevi

- Within the garden you can have dysplastic nevus, Spitz nevus, blue nevus, anything
- VERY rare for nevus spilus to become malignant

SPARK NEVUS

- Features of Spitz + Clark = Spark
- I find the term useful sometimes

Ko CJ, McNiff JM, Glusac EJ. J Cutan Pathol. 2009 36:1063-8. **Melanocytic nevi with features of Spitz nevi and Clark's/dysplastic nevi ("Spark's" nevi).**

Pigmented lichenoid keratosis

- COMMON cause of consultation
- When pigment not prominent, clinically thought to be BCC
- Probably mostly are lentigo, seborrheic keratosis or pigmented actinic keratosis that becomes inflamed
- Are these regressed melanomas?

What to call it

- BLK – benign lichenoid keratosis, but they are not all benign, some are precancer
- LK – I like
- PigLK – If lots of pigment – just vacuolar degen made melanin incontinence, vs regressed melanocytic neoplasm?
- LAK – if precancer, atypia

Pigmented AK

- Mistaken for lentigo, LM, SK clinically and pathologically
- BUT, has atypical budding keratinocytes, parakeratosis
- May extend down follicle, but so can LM
- Melanocytes tend to have dusky or vacuolated cytoplasm

Pigmented AK

- Parakeratosis helpful in my opinion – but some of my colleagues say "PigAK does not require parakeratosis"
- MART-1 helpful or does it cause overdiagnosis of lentigo maligna?

Journal of the American Academy of Dermatology (review)
Volume 67, Issue 1 , 1.e1-1.e16, July 2012
The dysplastic nevus: From historical perspective to management in the modern era (review)

Amyloidosis

A Review of Cutaneous Disease

Jared R. Heaton, DO PGY-4
Program Director: Dr. Richard Miller

I have no relevant financial relationships with industry to disclose

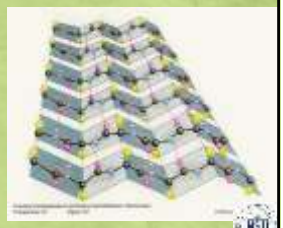
NOVA SOUTHEASTERN UNIVERSITY
LARGO MEDICAL CENTER
GRADUATE MEDICAL EDUCATION
Medical Education in the Sun Coast Tradition

Objectives

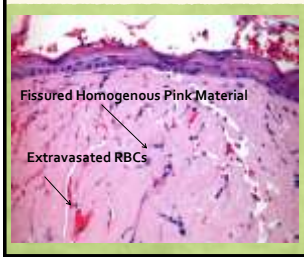
- Review the **amyloid protein**
- Discuss the **classification** of amyloidosis
- Review both the **clinical and histological presentation** of the different forms of amyloidosis
- Discuss the **work up, diagnosis and treatment** of cutaneous, systemic and familial amyloidosis
- Highlight important **board relevant features** of amyloidosis

What is Amyloid

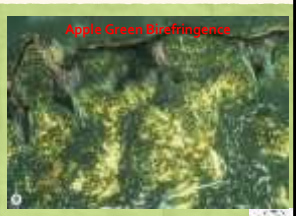
- Term introduced by Virchow in 1854
- Extracellular deposition of an **insoluble fibrilar protein** in a **beta pleated sheet** configuration
- 4 Distinct components:
  - Amyloid **fibril** (major)
    - Determines subtype
  - Amyloid **P component** (minor)
  - **Ground substance** (minor)
  - **ApoE lipoprotein** (minor)



Histological Features of Amyloid



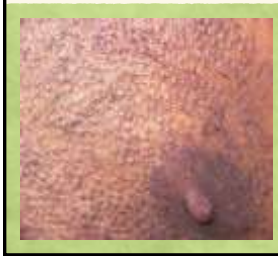
Histological Features of Amyloid



Classification

- Cutaneous
- Systemic
- Familial

Classification: Cutaneous



- ***Primary Cutaneous***
  - **Macular** (K-cyte derived)
  - **Lichenoid** (K-cyte derived)
  - **Nodular** (AL) – (Plasma cell derived)
- ***Secondary Cutaneous***
  - Associated with **skin tumors**
  - Reported with PUVA Therapy
  - K-cyte derived

Classification: Systemic

- ***Primary Systemic***
  - **Plasma cell dyscrasia**
  - **Amyloid light chain (AL)** produced by plasma cells
- ***Secondary Systemic***
  - **Chronic illness** (TB, RA, DM, SLE, Scleroderma)
  - **Amyloid associated (AA)** produced by the liver
- ***Dialysis-Related***
  - **Beta 2 Microglobulin**

Classification: Familial

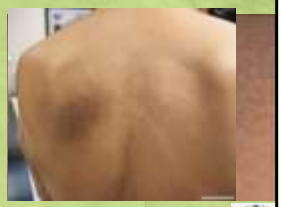
- ***Heredofamilial***
  - Familial Amyloidodic Polyneuropathy
  - Senile systemic Amyloidosis
- ***Syndrome Associated***
  - Sipple Syndrome (MEN 2A)
  - Muckle-Wells
  - Familial Mediterranean Fever
  - TNF Receptor Associated Periodic Syndrome

Primary Cutaneous: Macular Amyloid

- ***Epidemiology***
  - Asian, South American Populations
  - Females 3 : 1
  - Early Adulthood
  - Tends to be chronic

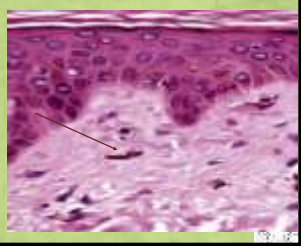
Primary Cutaneous: Macular Amyloid

- ***Clinical Features***
  - Common in the interscapular area (associated with notalgia paresthetica), but also thighs, breasts, shins and buttocks
  - 2-3mm subtle brown rippled macules
  - Mild to moderately pruritic



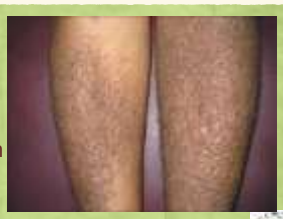
Primary Cutaneous: Macular Amyloid

- ***Pathogenesis***
  - Chronic trauma / scratching in predisposed individuals
  - Apoptosis of K-cytes leading to amyloid deposition
- ***Histology***
  - Amyloid deposition high in the papillary dermis
  - Pigment incontinence is common



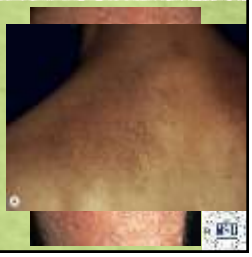
Primary Cutaneous: Lichen (Papular Amyloid)

- ***Epidemiology***
  - Most common form of primary cutaneous amyloidosis
  - Asian Chinese Population
  - Males = Female
  - Young Adulthood



Primary Cutaneous: Lichen (Papular Amyloid)

- ***Clinical Features***
  - Common on the front of the shins and extensor aspect of the forearms
  - Firm skin colored or hyperpigmented scaly papules and plaques
  - Very pruritic
  - "Biphasic Amyloidosis" – Features of Macular and Lichenoid



Primary Cutaneous: Lichen (Papular Amyloid)

- ***Pathogenesis***
  - Chronic trauma / scratching in predisposed individuals
  - Apoptosis of K-cytes leading to amyloid deposition
- ***Histology***
  - Amyloid deposition high in the papillary dermis
  - Pigment incontinence is common
  - **Acanthosis, hypergranulosis, hyperkeratosis**

Treatment of Macular and Lichen Amyloidosis

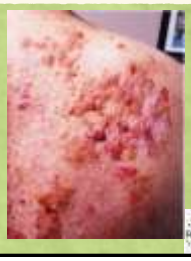
- ***Treatment***
  - Reducing friction to the skin
  - Identify cause if possible
  - High potency topical steroids under occlusion
  - Intralesional corticosteroids
  - Topical calcinuerin inhibitors
  - UVB, PUVA, Dermabrasion, Oral Retinoids, CO_2 Laser

Primary Cutaneous: Nodular Amyloidosis

- ***Epidemiology***
  - Rare
  - More common in Females
  - Onset 6^{th} to 7^{th} decade
  - Associated with **Sjögren's Syndrome in 25%** of cases
  - Associated with various other autoimmune conditions: Systemic Sclerosis, RA

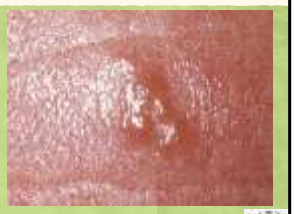
Primary Cutaneous: Nodular Amyloidosis

- ***Clinical Features***
  - Multiple waxy yellow / red papules and nodules
  - Face, trunk and extremities
  - Lesions typically asymptomatic
  - Variable size millimeters to centimeters



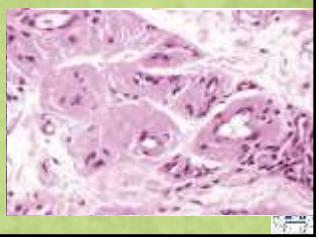
Primary Cutaneous: Nodular Amyloidosis

- ***Pathogenesis***
  - A deposition of amyloid from a localized group of **plasma cells** in the skin
  - **Amyloid light chain (AL)**
  - Indistinguishable from cutaneous lesions of systemic amyloid



Primary Cutaneous: Nodular Amyloidosis

- ***Histology***
  - Extensive collection of amyloid extending down into the dermis
  - Amyloid deposition within **blood vessels and nerve sheaths**
  - Perivascular **plasma cells**
  - AL chain staining +



Primary Cutaneous: Nodular Amyloidosis

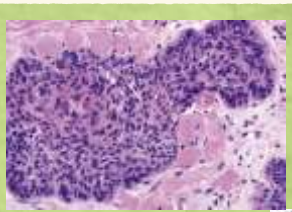
- ***Systemic Evaluation is Essential***
  - 40% of patients with primary systemic amyloidosis present with identical cutaneous findings
- ***Initial tests***
  - CBC
  - CMP
  - Chest X-ray
  - ECG E
  - Echocardiogram
  - UA
  - **SPEP and UPEP**
- ***Additional tests***
  - BMB
  - **Abdominal fat pad biopsy**
  - **Oral or rectal mucosa biopsy**
  - Transverse carpel ligament biopsy,
  - Iodine-123 amyloid p scintigraphy

Primary Cutaneous: Nodular Amyloidosis

- ***Progression to Systemic Involvement***
  - Originally thought to be up to **50%**
  - Observed in approximately **7%**
- ***Monitoring for progression***
  - Cutaneous exam
    - **Periorbital purpura, macroglossia and shoulder pad sign**
  - *Others signs*
    - Nephrotic syndrome, lytic bone lesions, restrictive cardiomyopathy

Secondary Cutaneous Amyloidosis

- **Cutaneous Neoplasms**
  - BCC
  - Trichoeps / Trichoblasts
  - SKs
  - SPAP
  - Pilomatricomas
- **Others**
  - PUVA therapy
  - Chronic actinic damage
  - Repeated insulin injections



Primary Systemic Amyloidosis

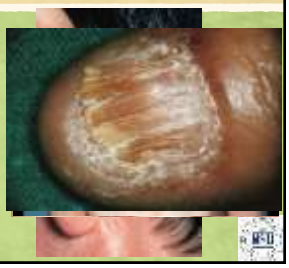
- ***Epidemiology***
  - Onset is around 65
  - Slightly more common in males
  - Involves many organ systems: GI, kidney, liver, heart and skin
  - Cutaneous manifestations in approximately 40%

Primary Systemic Amyloidosis

- ***Clinical features***
  - Non Cutaneous
    - Weight loss, hoarseness, dyspnea, paresthesias
    - Edema from cardiac and or renal involvement
    - GI bleeding,
    - **Macroglossia**
    - **Bilateral carpal tunnel syndrome (may be first sign)**

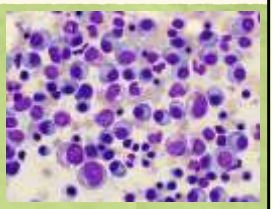
Primary Systemic Amyloidosis

- ***Clinical features***
  - Cutaneous
    - Purpura / Ecchymosis
    - Shiny, hemorrhagic and waxy translucent papules
    - Alopecia and nail dystrophy
    - **Raccoon sign**
    - **Shoulder pad sign**



Primary Systemic Amyloidosis

- ***Pathogenesis***
  - Due to a systemic plasma cell dyscrasia (Multiple Myeloma)
  - Amyloid light chain (AL) λ
  - Indistinguishable histologically from cutaneous amyloid



Primary Systemic Amyloidosis

- ***Initial tests***
  - CBC
  - CMP
  - Chest X-ray
  - ECG
  - Echocardiogram
  - UA
  - **SPEP and UPEP**
- ***Additional tests***
  - BMB
  - **Abdominal fat pad biopsy**
  - **Oral or rectal mucosa biopsy**
  - Transverse carpel ligament biopsy
  - Iodine-123 amyloid p scintigraphy

Primary Systemic Amyloidosis

- ***Treatment***
  - No truly effective treatment
  - Poor prognosis – median survival 43 months
    - Much less with cardiac involvement
  - Treatment
    - High dose **Melphalan** and peripheral blood **stem cell transplant** in younger pts
    - Thalidomide, Lenalidomide, Bortezomib in combination with Melphalan and corticosteroids

Secondary Systemic Amyloidosis

- ***Secondary Systemic***
  - **Chronic Illness** (TB, RA, DM, SLE, Scleroderma)
  - **Amyloid Associated (AA)** produced by the liver
  - Cutaneous lesions are very rare
  - Treat the Inflammatory condition to halt progression

Hemodialysis-Associated Amyloidosis

- ***Dialysis-Related***
  - **Beta 2 Microglobulin** (Aβ2M)
  - Deposits in synovial membranes
  - Results in **carpal tunnel syndrome and sponyloarthropathies**
  - Cutaneous involvement is rare
  - Treatment is high flux dialysis or kidney transplant

Heredofamilial

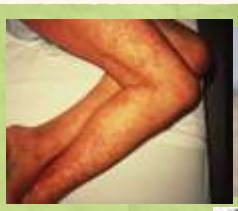
- ***Heredofamilial***
  - **Familial Amyloidotic Polyneuropathy**
    - AD
    - Mutation in **transthyretin gene**
    - **ATTR** (produced by the liver)
      - TTR transport protein for **thyroxine and retinol**
    - **Peripheral and autonomic neuropathy**
    - Treatment is **orthotopic liver transplant**
- ***Senile systemic Amyloidosis***
  - Late onset acquired
  - **ATTR**
  - Heart is predominantly involved **causing CHF, cardiomyopathy and conduction disorders**

Syndrome Associated: Men2A

- ***Sipple Syndrome (Multiple Endocrine Neoplasia 2a)***
  - AD Disorder
  - **RET protooncogene**
  - **Triad**
    - **Thyroid Carcinoma**
    - **Pheochromocytoma**
    - **Hyperparathyroidism**
  - **Lichen or Macular Amyloidosis** (K-cyte derived)

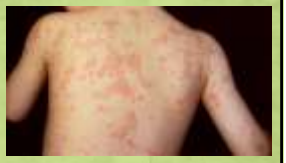
Syndrome Associated: FMF

- ***Familial Mediterranian Fever***
  - AR
  - Mutation in a gene that **encodes pyrin (AKA marenostrin),** an inflamasome
  - Recurrent epidosdes of **polyserositis, fever, erysipelas-like erythema (legs) and small vessel vasculitis**
  - Treatment is **Colchicine** for polyserositis and AA deposition
  - No cutaneous amyloidosis



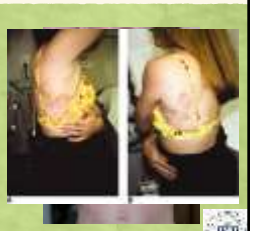
Syndrome Associated: Muckle Wells

- ***Muckle-Wells Syndrome***
  - AD
  - Mutation in gene **CIAS1** that encodes **pyrin-like protein** that plays a role in inflammation
  - **Urticaria, deafness, systemic amyloidosis and acute attacks of fever**
  - Treatment is glucocorticoids or **Anakinra** (recombinant human IL-1 receptor antagonist)



TNF receptor associated periodic syndrome (TRAPS)

- ***TRAPS***
  - AD
  - Mutation in **TNFR 1**
  - Periodic high fevers, **erythematous annular or serpiginous patches**, abdominal pain, arthalgias, myalgias and renal amyloidosis
  - Treatment is **TNF inhibitors** or glucocorticoids



Summary

- Review the **amyloid protein**
- Discuss the **classification** of amyloidosis
- Review both the **clinical and histological presentation** of the different forms of amyloidosis
- Discuss **work up, diagnosis and treatment** of cutaneous, systemic and familial amyloidosis
- Highlight important **board relevant features** of amyloidosis

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DIET AND DERMATOSES: WHAT YOU SHOULD KNOW

Julian M. Ngo, D.O., PGY4
NSUCOM/Largo Medical Center
February 21, 2014

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DISCLOSURES

- No Relevant Conflicts of Interest Exist

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DIET AND DERMATOSES: WHAT YOU SHOULD KNOW

- Objectives
  - Provide an overview of common dermatoses in which diet and nutrition may play a role
  - Review relevant associations of reported dietary effects on these diseases
  - Review current literature regarding some of the controversies and facts about diet and dermatologic diseases

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WHY BE AWARE...?

- Dietary modification is an extremely popular treatment modality for patients with dermatologic conditions
- To be able to educate patients regarding facts and myths about diet and skin disease
- Dietary manipulation has the potential to reduce healthcare cost while improving pt outcomes with safe alternatives

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DERMATOLOGIC DISORDERS WITH POSSIBLE DIETARY CORRELATION

- Psoriasis
- Atopic Dermatitis
- Acne
- Urticaria
- Dermatitis Herpetiformis
- Allergic Contact Dermatitis
- Deficiency dermatoses
- Epidermolysis Bullosa
- Porphyrias
- Pruritus
- Bullous Pemphigoid
- Linear IgA
- Pemphigus
- Genetic and metabolic disorders
- Alopecia

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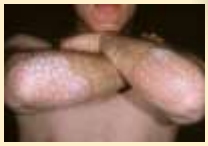
Psoriasis

- Affects 2% of the world's population
- Pathogenesis is multifactorial (genetics, immunologic, environmental factors)
- Treatment ranges from topical medications to biologics



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Psoriasis

- Associated Dietary Factors
  - Gluten-free Diet
  - Low-Calorie Diet
  - Vegetarian Diet
  - Fish oil
  - Alcohol

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J.R. Ricketts et al: "Nutrition and psoriasis",Clin Dermatol. 2010 Nov-Dec;28(6):615-26. doi: 10.1016/j.clindermatol.2010.03.027. Review.

Gluten-free Diet

"Gluten is a vague term - .....to categorize things that are bad."
-Seth Rogen

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This Is the End. Dir. Seth Rogen and Evan Goldberg. Perf. Seth Rogen, Jay Baruchel, James Franco. Mandate Pictures, Point Grey Pictures/Columbia Pictures, 2013. Film.

Gluten-free Diet

- Some studies have suggested increased incidence of IgG/IgA anti-gliadin antibodies in psoriatic patients?[18,19]
- Gluten-free diet in patients with psoriasis and elevated anti-gliadin antibodies may result in improvement in psoriasis[20]
- May be beneficial to screen psoriatic patients for celiac disease

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J.R. Ricketts et al: "Nutrition and psoriasis",Clin Dermatol. 2010 Nov-Dec;28(6):615-26. doi:

Gluten-free Diet

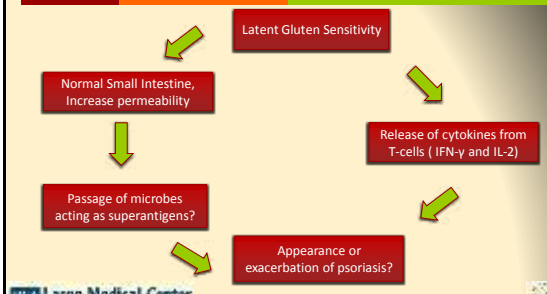

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Chart adapted from Wolters M. Diet and Psoriasis: experimental data and clinical evidence. Br J Dermatol 2005; 153:706-714

Gluten-free Diet

www.glutenfreesociety.org

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Low Caloric Diet and Vegetarian Diet

- Several studies have shown
  - Clinical improvement in signs and symptoms[15,25]
  - Improvement in therapeutic response to Medications[14,16]
- Weight reductions may improve co-morbidities leading to decreased mortality[8,9]

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N.Lakdawala et al. "The role of nutrition in dermatologic diseases: Facts and controversies"Clin Dermatol. 2013 Nov-Dec;31(6):693-700. doi: 10.1016/j.clindermatol.2013.05.004.

Polyunsaturated Fatty Acids

- Mostly negative results from randomized controlled oral intake studies
- Improvement shown with parental infusion of n-3 fatty acid emulsion[31]
- Beneficial in cyclosporine-induced nephrotoxicity[3]
- Reduced isotretinoin, etretinate[4], and acitretin-induced hypertriglyceremia[5]

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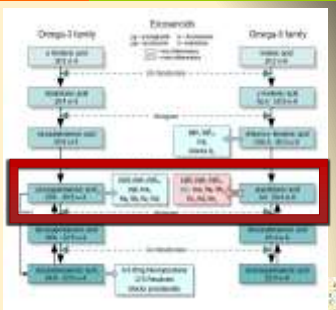
J.R. Ricketts et al: "Nutrition and psoriasis",Clin Dermatol. 2010 Nov-Dec;28(6):615-26. doi:

Polyunsaturated Fatty Acids

AA = PGE_2 and LTB_4
(potent inflammatory mediators)
vs.
EPA = **PGE_3 and LTB_5**
(less potent inflammatory mediators)



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Alcohol

- Alcohol consumption may predispose individuals with a family history of psoriasis to develop it (esp. men)[13,15]
  - Alcohol consumption higher in psoriatic patients
- Poorer prognosis associated with alcohol intake[16]
  - Increased severity with alcohol consumption
    - Women => increased BSA involvement
    - Men => resistance to treatment

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J.R. Ricketts et al: "Nutrition and psoriasis",Clin Dermatol. 2010 Nov-Dec;28(6):615-26. doi: 10.1016/j.clindermatol.2010.03.027.

Atopic Dermatitis

- Chronic inflammatory disorder with relapsing and remitting course
- Affects 10-20% of US children
- 2% of adult population
- Combination of immunologic, genetic, and environmental factors
- Erythematous papules/plaques with excoriations commonly involving antecubital/popliteal fossa, neck, wrist/hands
- Treatment can be difficult

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What should you consider...?

- Maternal diet during pregnancy and lactation
- Breastfeeding vs. formula
- Hydrolyzed formula vs. CMF
- Delayed introduction of solids foods
- Dietary exclusion diets
- Probiotics and prebiotics

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N.Lakdawala et al., "The role of nutrition in dermatologic diseases: Facts and controversies"Clin Dermatol. 2013 Nov-Dec;31(6):677-700. doi: 10.1016/j.clindermatol.2013.05.004.

Maternal Diet

- Maternal dietary antigens cross placental barrier and are found in in breast milk[26]
- Studies focus on restriction of highly allergic foods
  - Eggs, cow's milk, and peanuts (no longer recommended)
  - 2011 Cochrane review of trials involving egg and cow's milk restriction => **no significant difference in incidence of AD during first 18 months[27]**

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Lakdawala N, Babalola O 3rd, Fedeles F, McCusker M, Ricketts J, Whitaker-Worth D, Grant-Kels JM. The role of nutrition in dermatologic diseases: facts and controversies. Clin Dermatol. 2013 Nov-Dec;31(6):677-700

Maternal Diet

- **No convincing evidence to support maternal dietary restriction**
- Risk of maternal dietary restriction on health of fetus
  - Low mean gestational weight, increased risk for preterm birth, lower mean birth weight
- Vitamin and mineral supplementation **not recommended**

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Lakdawala N, Babalola O 3rd, Fedeles F, McCusker M, Ricketts J, Whitaker-Worth D, Grant-Kels JM. The role of nutrition in dermatologic diseases: facts and controversies. Clin Dermatol. 2013 Nov-Dec;31(6):677-700

Breast Feeding vs. Formula

- 1936 Grulee et al – first described protective effect of breastfeeding on infant eczema
- 2001 meta-analysis showed breastfeeding for **3 months** led to significant decrease in incidence of AD in pt with + FH
- 2003- von Berg et al - The German Infant Nutritional Intervention trial
  - **4 months breast feeding was protective against AD**

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Lakdawala N, Babalola O 3rd, Fedeles F, McCusker M, Ricketts J, Whitaker-Worth D, Grant-Kels JM. The role of nutrition in dermatologic diseases: facts and controversies. Clin Dermatol. 2013 Nov-Dec;31(6):677-700

Hydrolyzed formula vs. CMF

- Cow's milk formula allergy hypothesized to underlie allergic manifestations
- 2009 Cochrane review, meta-analysis of 3 trials showed **significantly reduced incidence of AD with hydrolyzed formula** use at 1 year with 3 and 6 year follow up[28]

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Lakdawala N, Babalola O 3rd, Fedeles F, McCusker M, Ricketts J, Whitaker-Worth D, Grant-Kels JM. The role of nutrition in dermatologic diseases: facts and controversies. Clin Dermatol. 2013 Nov-Dec;31(6):677-700

Delay Introduction of Solid Foods

- 1989 – Zeiger et al – Landmark study
  - Suggested association between solid food introduction before 6 months and allergy-associated foods (eggs, milk, fish) before 2 years
  - 2000 AAP – recommended at risk infants avoid eggs until 2 years of age and peanuts, tree nuts, and fish until 3 years of age

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Greer et at, Effects of early nutritional intervention on the development of atopic disease in infants and children: the role of maternal Dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. Pediatrics 2008;121:183-91

Delay Introduction of Solid Foods

- Newer studies show mixed results and little evidence to support delay of solid foods beyond 6 months
  - One study showed increase AD with delay of solid foods after 6 months, citing lack of exposure during this time => sensitization
- 2004 AAP recommendations for solid foods to be introduced **4-6 months and whole cow milk at 12 months**

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Greer et at, Effects of early nutritional intervention on the development of atopic disease in infants and children: the role of maternal Dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. Pediatrics 2008;121:183-91

Dietary Exclusion

- 2008 Cochrane review of 3 main elimination diets[29]
  - Milk and egg exclusion, "few foods diet", amino acid based elemental diet
  - Showed **little evidence in reducing severity of AD**, except in patients with IgE specific to diet
- **Not recommend**, except in cases of specific allergies

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Greer et at, Effects of early nutritional intervention on the development of atopic disease in infants and children: the role of maternal Dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. Pediatrics 2008;121:183-91

Probiotics/Prebiotics

- Studies show conflicting results
- **Not enough evidence to substantiate use in standard practice**
- Case reports of sepsis in infants using probiotics

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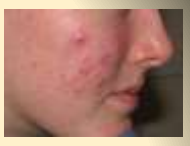
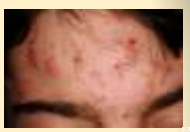
N Lakdawala et al. "The role of nutrition in dermatologic diseases: Facts and controversies"Clin Dermatol. 2013 Nov-Dec;31(6):677-700. doi: 10.1016/j.clindermatol.2013.05.004.

Acne

- Multifactorial disorder of pilosebaceous unit
- Affects 40-50 million people in US
- Estimated annual cost $2.5 billion in US
- Pathogenesis: genetics, sebum production, comedone formation, hormonal, inflammation, *P. acnes*
- Erythematous comedones, papules, pustules, cystic lesions on face and trunk
- Dietary associations still controversial





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History

- 1930's-60' dietary advice was standard part of acne treatment
  - Cambell et al – suggested impaired glucose tolerance existed in patients with acne
    - Avoidance of excessive carbohydrates and high-sugar foods
      - No chocolate, fats, sweets and carbonated beverages

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History

- 1969 – Fulton et al – investigated chocolate on acne and found chocolate did not affect course of acne vs. placebo
- 1971 – Anderson et al – studied acne triggers involving chocolate, milk, roasted peanuts, or cola found no flares of acne produced
- Previous studies flawed

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Dairy Products

- Adebamowo et al – examined connection between dairy products and acne
  - Positive association noted
  - Study flaws precludes definitive link, however weak association still possible
- **Insufficient evidence to recommend dairy restriction as treatment[30]**

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Bowe et al, Diet and Acne; J Am Acad Dermatol. 2010 Jul;63(1):124-41

Glycemic Index/Load

- Glycemic index (GI) – developed in 1981
  - **Potential to increase blood sugar** based on carbohydrate content
- Glycemic Load = Based on **GI x carbohydrate content/serving size**

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Burris et al; Acne: The Role of Medical Nutrition Therapy J Acad Nutr Diet. 2013 Mar;113(3):416-30

Glycemic Index/Load

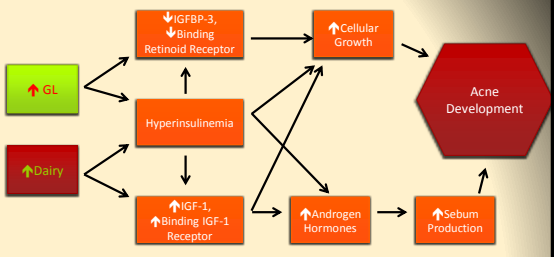

Chart Adapted from Burris et al; Acne: The Role of Medical Nutrition Therapy J Acad Nutr Diet. 2013 Mar;113(3):416-30

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Glycemic Index/Load

J Am Acad Dermatol. 2007; 57(2): 247-256

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Glycemic Index/Load

www.glycemicindex.com

Low GI - < 55
Low GL = <10

High GI - >70
High GL - >20

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Glycemic Index/Load

www.glycemicindex.com

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Omega-3 Fatty Acids

- Western diets have a higher ratio of omega-6 to omega-3 fatty acid vs. non-westernized diets
- Its been postulated that Omega-3 fatty acids suppresses inflammatory cytokines (LB4) leading to improvement of acne
- Limited studies performed
  - One study reported decreased acneiform lesions on exam

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Bowe et al, Diet and Acne; J Am Acad Dermatol. 2010 Jul;63(1):124-41

Vitamin A

- 1981 – Kligman et at – reported oral vitamin A is effective in acne treatment when used in high doses
- Most dermatologist reluctant to recommend oral Vitamin A for fear of hypervitaminosis
  - Hypervitaminosis => hepatotoxicity, teratogenicity, alopecia, decreased bone density, xerosis and pseudotumor cerebri

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Bowe et al, Diet and Acne; J Am Acad Dermatol. 2010 Jul;63(1):124-41

Iodine

- Iodine long implicated as cause of acne
- Eruptions typically monomorphic, consisting predominately of pustules
  - Type of eruptions associated with iodine containing drugs
- Possible reason for positive association btw milk and acne

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Bowe et al, Diet and Acne; J Am Acad Dermatol. 2010 Jul;63(1):124-41

SUMMARY

- **Psoriasis**
  - 3 month trial of Gluten-free diet may improve psoriasis in patients with positive IgG/IgA anti-gliadin antibodies
  - Low-calorie or Vegetarian may lead to clinical improvement and enhance therapeutic response to treatment
  - Fish oil may help treatment induced hypertriglyceremia and cyclosporine-induced nephrotoxicity
  - Alcohol should be avoided

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SUMMARY

- **Atopic Dermatitis**
  - Maternal restriction diet not recommended
  - Exclusion diets not recommended, esp. with specific allergies
  - Breast milk and hydrolyzed milk is best
  - Solid foods should be introduced btw 4-6 months of age
  - Not enough evidence for pre/probiotic recommendation

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SUMMARY

- **Acne**
  - Possible weak association with dairy products, elimination may help
  - Stronger evidence for + association with high glycemic index/load foods – recommend low glycemic diet
  - No recommendation for Fish oil or Vitamin A

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SUMMARY

- Overview of some common dermatoses in which diet and nutrition play a role
- Review relevant association of dietary effects on common dermatoses
- Review current literature regarding some of the controversies and facts about diet and dermatologic disease

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Thank you!

- Dr. Miller
- All of our wonderful attendings
- Fellow Residents
- My fantastic wife, mom, and kids

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My Crew!!

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Dueling a grueling case of Granuloma Annulare

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Agenda

- Presentation of Patient Case
- Discussion of disease
- Discussion of treatments
  - Future and Potential Treatments

Case Presentation

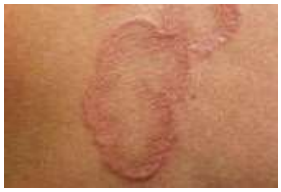
- A 42 year old female patient with no significant dermatologic medical history presented for the evaluation of an enlarging, circular rash on her right posterior shoulder.
- The patient stated the "rash" started approximately one and a half years prior with no history of injury, bite or other irritation to the area and had been intermittently growing and spreading since then. The rash was described as non-painful, slightly swollen, and mildly itchy.

Patient Presentation

- She had been seen several times over the prior year by a different dermatologist. The lesions had not improved with multiple injections and intermittent topical steroid use. Prior biopsies had been performed.
- The patient was otherwise well, with no other associated symptoms and was taking only one medication, Elestrin, for the treatment of chronic, stable depression.

Clinical Exam

- On physical exam, the patient had several erythematous annular lesions, up to 3cm in diameter with palpable raised borders, central clearing and no associated scale, located on her right shoulder and arm.



Ddx

Higher Suspicion

- Granuloma Annulare
- Tinea Corporis
- Erythema Annulare Centrifigum
- Annular Elastolytic Giant Cell Granuloma (Actinic Granuloma)

Ddx

Low Suspicion

- Arthropod Bite
- NLD
- Rheumatoid Nodule
- Crohn's related granuloma
- Perforating disorder (EPS)
- Leprosy
- Cutaneous Sarcoidosis
- Sub Acute Cutaneous and /or Discoid Lupus.

Treatment and Disease Course

- **A working diagnosis of Localized Granuloma Annulare** was made and the patient was started on a high potency topical steroid cream twice daily.
- A fungal culture was performed (neg.)
- Records obtained from the previous dermatologist, including recent bloodwork and biopsy results confirmed the suspected dx.

Treatment: Oral Steroid

- On follow up a few months later, the patient had a significant and "distressing" flare.
- She was treated with a 4 wk tapering dose of oral prednisone and was instructed to continue with the topical steroids.
- **Oral steroid tx was helpful.** The lesions improved, with flattening, decreased erythema and no enlargement of existing lesions, as well as no development of new lesions.
- Unfortunately, once the oral steroids were discontinued the lesions returned and new lesions began to develop.

Treatment: Steroid/ILK

- Over the next several months, the patient was treated with Intralesional injections of Triamcinolone at doses of 2.5-5mg/ml and given topical steroids.
- The ILK helped somewhat, but the lesions eventually continued to enlarge and new lesions on the shoulder, back and right arm developed.
- Add'l prednisone tapers were given for flares, with similar beneficial results. But after cessation, the condition worsened once again.

Treatment: Dapsone

- Due to concerns from both patient and provider, of being on long term oral steroids, a new treatment was started.
- After checking appropriate bloodwork, including CBC, Chemistry Panel and G6PD, the patient was started on dapsone 25mg P.O. daily, eventually reaching a dose of 50mg twice daily.
- Dapsone helped to partially control and slow the progression of her GA, for a period of almost 6 months.

Dapsone

- A sulfone drug that is highly absorbed in the gut and **inhibits neutrophils** and myeloperoxidase in the respiratory burst mechanism (in neuts, eos and **monocyte/histiocytes**)
- Inhibits dihydropteroate synthetase in the folic acid pathway.
- Metabolized by two pathways- Acetylation & Hydroxylation
  - G6PD deficiency, in the dapsone hydroxylase pathway, leads to an increase in Dapsone hydroxylamine metabolites which are damaging to red blood cells, increasing hemolysis.

Dapsone SE's

- Commonly causes dose related hemolytic anemia and methhemoglobinuria as well as GI upset and peripheral neuropathies, all of which resolve with D/C
- Rarely may cause Liver toxicity/hepatitis, agranulocytosis and hypersensitivity syndrome
- Must evaluate baseline CBC, Chemistry w/LFT's and G6PD, then follow CBC and Chem/LFT's for 1st three months
- Avoid concomitant use with MTX or Sulfa drugs(↑hemolysis)
- Allergic cross reactivity w/other Sulfa drugs (tmp/smx) is rare

Treatment: TCI / Imiquimod

- Eventually, the GA began to progress again. While continuing dapsone, other changes were made.
- The patient was switched from topical steroid to topical tacrolimus[6] for several months, with little change and then to topical Imiquimod cream.
- Unfortunately, the condition continued to worsen despite all of the new treatments. **Dapsone was discontinued.**

Treatment: LN2 and UVB

- The patient was treated with a combo of ILK, Liquid Nitrogen(LN_2), topical steroids
- Lesions treated with **LN_2 showed temp. improvement** in elevation of the border and intensity of color, but displayed noticeable **hypopigmentation** and eventually progressed once tx's were stopped.
- Pt. was also started on Narrow Band UVB-3x/wk
  - Case reports have shown effectiveness for the treatment of GA[4].
  - Not effective in our patient

Treatment: Further Investigation

- At this point, the patient has had GA for over (2) years and has been treated with:
  - Topical Steroid (Med – to Ultra High Potency)
  - Topical Tacrolimus / Imiquimod
  - Intralesional Steroid Injections, LN_2
  - Oral Steroids
  - Oral Dapsone
  - NUVB – 2 mos of tx 3x/wk
- None of which have been satisfactory or effective long term
  - So it was decided to check bloodwork again, including CBC, Chemistry, LFT's, Lipid Panel, ANA, TSH and thyroid antibodies, as well as to perform a new biopsy.

Re-Biopsy and Labs

- Repeat biopsy sections stained with H&E and special fungal stain, showed no signs of fungal infection.
- The results were again classic for Granuloma Annulare.
- Blood work showed no significant abnormalities. However, her lipids were slightly elevated. (Chol./Triglyc)

Discussion of GA

- A generally benign and self limited granulomatous dermatitis of unknown etiology, with degeneration of collagen and elastic fibers in the dermis.
- Clinically it commonly presents as erythematous papules and annular erythematous plaques, with a firm raised border and central clearing.
- Most commonly affects the dorsal hands, but may be widespread and rarely affects the face

Etiology

- The etiology of GA is unknown, however many potential causes have been proposed, including: trauma, infection, insect bites, sun exposure and malignancy. Familial cases have been reported[1]
- Based on studies of T-cell populations present in GA, a delayed type hypersensitivity reaction to an unknown antigen/s has been proposed[1].
- Similarities to tuberculosis as well as studies showing an increase in IL-2 production in GA biopsies, suggest a Th-1 mediated process[4].
- A study by Fayazzi in 2000 concluded that expression of TNF-α along with MMP2 /9 was responsible for the matrix degradation seen in GA, giving credibility to the use of TNF-α inhibitors a potential tx

Etiology

- A 2005 study by Macaron and Cohen showed an increase in production of Glioma-associated oncogene homologue-1 (Gli-1) in granulomatous tissue reactions, including Keloids, Sarcoidosis, NLD and GA.
- Gli-1 has also been proven to be elevated in BCC. Patched gene normally inhibits Gli-1. Studies in mice have proven that increased Gli-1 production leads to diffuse BCC.
- This study also proposes the possible efficacy of TCI's (tacrolimus) which inhibit Gli-1, as a possible treatment option for these conditions[6]

Associations

- May be associated with many potential underlying disorders as well as medications, however definitive studies are lacking[2]
- There are reported associations of GA with:
  - **Autoimmune Thyroiditis**
  - **Diabetes Mellitus**
  - **Lipid Abnormalities**
  - HIV, Hepatitis B/C
  - Herpes Zoster /zoster scars
  - RA as well as proposed associations with:
  - **Malignancies** including both lymphoma and solid tumors[4]

Associations: Malignancy

- **Association with malignancy is rare** and tends to occur in an older subset of patients
- The **malignancy commonly precedes diagnosis** of GA, however cases have been observed with the GA being the presenting sign[2]
- Cases associated with malignancy may occur more commonly **with atypical presentations**, including both distribution and lesional characteristics including associated vasculopathy[5]

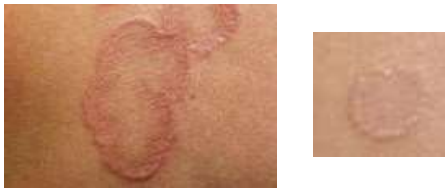
Overview: Types

- Localized GA
- Generalized GA
- Deep or Subcutaneous GA
- Perforating GA
- Patch GA
- Atypical GA

Localized GA

- Annular groups of skin-colored to erythematous papules most commonly occurring on the dorsal hands and/or feet
- Occurs most commonly in the young, with two thirds of patients under the age of 30[1].
- 2:1 female to male predominance and no racial predilection.
- Generally self limited, lasting months up to several years
- This form accounts for about 75 % of GA[4]

Localized GA- Annular

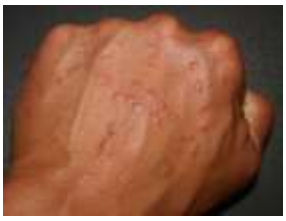


Generalized GA

- Defined by the simultaneous presence of **at least ten skin lesions or by widespread** small annular plaques and papules
- Occurs in approx. 8–15 % of patients with GA
- Lesions are generally small pink/red/violaceous papules or small groups of coalesced papules
- The average **age of onset is older,** in adulthood
- Outbreaks more **persistent** up to several years or more and often **resistant to therapy**
- **May be assoc. w/ lipid abnormalities**

Generalized/Disseminated GA

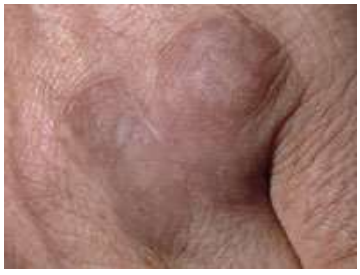
- Disseminated GA consists of multiple widespread skin-colored to erythematous papules
- Some consider disseminated a unique subset of GA, while most use disseminated and generalized interchangeably



Deep / Subcutaneous GA

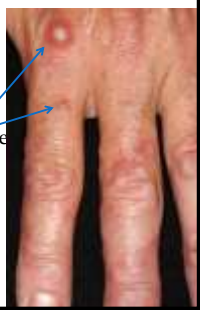
- Subcutaneous GA, also known as pseudo rheumatoid nodules, is more common **in children <(6yrs)** and consists of firm subcutaneous nodules, often on the hands or **lower extremities**
- Lesions are often larger, deep dermal or subQ nodules that are less red to skin colored and typically painless
- Up to 50% may also have classic type lesions
- Histopathology is similar/indistinguishable from rheumatoid nodules
- Patients have no other symptoms of RA

Deep GA (Pseudo Rheumatoid)



Perforating GA

- Small red, crusty papules
- Primarily on dorsal hands and fingers
- Clinically distinct from other forms because of **central umbilication** of the lesions secondary to the **transdermal elimination** of degenerated collagen
- Rare < 5% of GA cases



Atypical GA

- **Widespread** granulomatous lesions that do not fit the classic description of annular , generalized or other forms of GA
- Unusually widespread annular/localized appearing lesions
- Unusually aggressive or **persistent** variants
- **Mixed** presentations or unusual distributions:
  - Localized w/disseminated papular or patch
  - Patch w/perforating or deep etc.

Ddx

- Granuloma Annulare
- Tinea Corporis
- Erythema Annulare Centrifigum
- Annular Elastolytic Giant Cell Granuloma (Actinic Granuloma)
- Arthropod Bite
- NLD
- Rheumatoid Nodule,
- Crohn's related granuloma
- Perforating disorder (EPS)
- Leprosy
- Cutaneous Sarcoidosis
- Sub Acute Cutaneous and /or Discoid Lupus.

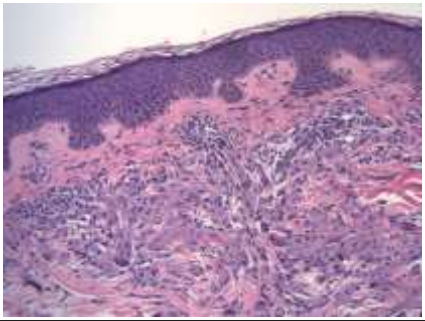
Diagnosis

- GA is diagnosed most commonly based on its clinical and histological characteristics.
- **Biopsy is the standard**
- There are no definitive laboratory tests to confirm the condition.

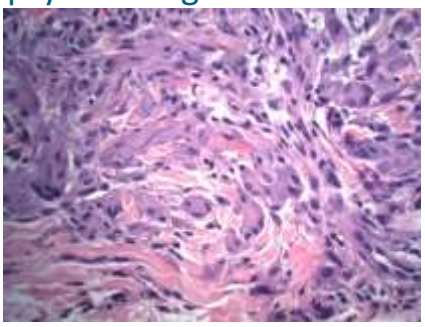
HistoPathology

- Granuloma Annulare generally displays one of two common histological presentations.
  - In the **pallisaded pattern**, a peripheral palisade of histiocytes surrounds altered collagen and mucin known as necrobiosis. There may be scattered multinucleate giants cells as well as sparse eosinophils and lymphocytes surrounding the necrobiotic areas.
  - In the **interstitial pattern** there is a busy appearing dermis with a patchy interstitial infiltrate of predominantly histiocytes intermixed with lymphocytes and mucin.

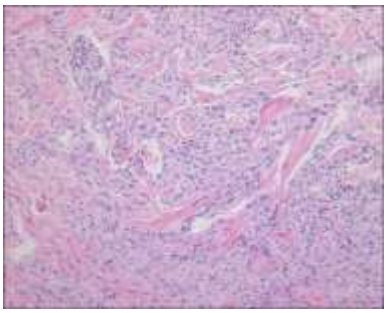
Histo: Pallisaded



Biopsy H&E High Power



Histo: Interstitial



Discussion of Treatments

- GA is typically a non-scarring, relatively asymptomatic, self limited condition and therefore may not require any treatment.
- However, due to cosmetic concerns, progression or associated pruritis, treatment may often be necessary.
- **Common treatments include**: topical and intralesional steroids, oral steroids, UVB, Liquid nitrogen and biopsy[1]

Treatments

- GA may occasionally be persistent and resistant to std. treatment. In these case a myriad of potential treatments have been documented[4].
- However, to date no large randomized trials have been performed to support or compare the use of these treatments. Most regimens are based off of published small case reports[4].

Treatments

- Other Tx's include:
  - Surgical removal – for isolated lesions
  - Dapsone
  - Antimalarials
  - K+ iodide, Fumaric Esters
  - Pentoxifylline,Nicotinamide
  - MTX,Cyclosporine
  - Isotretinoin
  - Biologics(adalimumab, etanercept, others)
  - PDT, PUVA, Laser tx
  - ROM therapy

Now Back to the Patient

Malignancy Screening

- Due to the pt's age and unusually persistent, multi-therapy resistant, atypical nature of our patients GA-
- **Malignancy is a concern**
  - To this point, most of the malignancy screening has been performed by her primary care physician and OB/GYN, including reg. phys. exams, CXR, labs.
  - However, we have discussed additional potential screening with the patient, including CT's and EGD, Colonoscopy

Treatment: Adalimumab

- With what we now know about the potential mechanisms at work in GA, a **TNF-α inhib.** is a good theoretical option
- Add'l workup including hepatitis panel, CXR and PPD was performed.
- With results negative, the patient was **started on Adalimumab 40mg subQ every two weeks.**
- After several months of treatment, the patient **began to show promising improvement**.

Biologics / Adalimumab

- Fully Human Monoclonal Ab
- Inhibition of TNF-alpha →immunosuppression
- Case reports show efficacy for treating GA[12,13]
- Must evaluate for active infection (fungal/bacterial) as well TB (PPD or QG)
- May lead to increase risk of malignancy/lymphoma
- Recommended to evaluate baseline CXR, labs (CBC, LFT's) and TB screen, then follow up every labs every 3-6 months and yearly for CXR/PPD[3]
- Contraindicated for h/o demyelinating dz
- Caution with h/o severe CHF

Treatment: Adalimumab

- Although her lesions never resolved, they did show **improvement in elevation, erythema and especially progression.**
- She had only one flare of her GA, (early on) that required a short course of oral steroid, otherwise the patient was:
  - **Controlled on Adalimumab** and ILK with **fair results** over the next **eight months.**

Treatment: Adalimumab

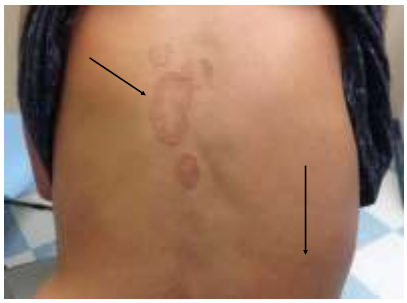
- Once again, the GA began to breakthrough and then worsen.

- The loss of effectiveness led to the discontinuation of the once promising Adalimumab.

Treatment: Hydroxychloroquine

- After several months of tx with steroids, new bloodwork and an eye exam were performed and
  - **Hydroxychloroquine was started**
- **After only two months, the patient was distressed** that the GA was not responding to the treatment.
- It was also noted that the patients ANA had risen from 1:40 previously to 1:160 and she had an elevated Total Complement(CH50) level.
- The patient did not however, have any significant arthritic pain or other physically concerning signs.

Further Spread



Antimalarials

- Hydroxychloroquine, Quinacrine, Chloroquine
- May cause ocular toxicity
  - Worse with Chloroquine
  - Need Ophthalmic exam prior to starting
- May stack Hydroxychloroquine with Quinacrine
- Often take several months to fully take effect.
- Reported to be effective in controlling generalized GA[9,10]

Treatment: Hydroxychloroquine

- Despite being advised that the antimalarial treatment commonly needs > 2 months to fully take effect,
  - **the patient requested the hydroxychloroquine be dc'd and asked to see a rheumatologist.**
- The patient was referred to Rheumatology for evaluation of the elevated values as well as for any possible systemic association with her unusually persistent GA.
- At this point she had been living with her GA for **over 4 years.**

Treatment: Electrodessication

- After a negative workup from Rheumatology, the patient was again temporarily treated with oral steroids and ILK.
- Knowing that LN2 lead to some improvement, low power Electrodessication(2 watts) was tried, hoping for regression with less hypo-pigmentation than LN2.
- The borders of one lesion were lightly desiccated.

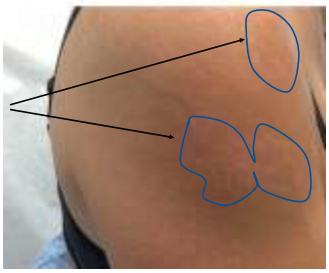
Treatment: Electrodessication

- At follow up the desiccated lesion showed noticeable improvement
- Several more lesions were treated, over several visits., with similar improvement.

Cautiously optimistic?

Treatment: Electrodessication

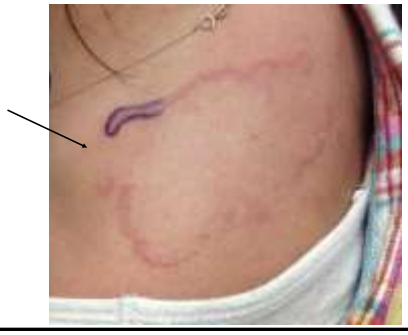
Areas improved after ED



Treatment: Electrodessication

- Again, after initially promising improvement the desiccated lesions began to show recurrence with a new expanding border, just outside of the previously treated border, as well as development of new lesions.

Further Spread



Treatment: Cyclosporine

- Having run through a multitude of unsuccessful treatments at this point, Cyclosporine was considered.
- After ruling out any active infection, CBC, Chemistry, Renal and Liver function as well as Mg levels and blood pressure were checked- **all within normal limits**
- **Cyclosporine** therapy was initiated **at 100mg BID** (3mg/kg)

Cyclosporine

- An immunosuppressive agent that inhibits calcineurin, thereby inhibiting NFAT and IL2 production, ultimately decreasing the proliferation and activation of CD_4/CD8 cells.
- Not cytotoxic and does not suppress bone marrow.
- Pregnancy category C, but
- Safe in children age >2

Cyclosporine

- Commonly causes **reversible** HTN, nephrotoxicity, headache and paresthesias, which **resolve with d/c**
- May cause ↑K+, ↓Mg, hypertrichosis (eyelashes) and gingival hyperplasia
- Prolonged use leads to an increase risk of NMSC, ↑risk of other forms of malignancy is rare at dermatologic doses <5mg/kg/dy and duration < 2yrs3
- Off label for GA

Treatment / ROM

- After further discussion, it was suggested and mutually agreed, that the pt. be referred to **University of Michigan Dermatology**, for add'l evaluation.
- The next month after evaluation by UofM, it was decided to discontinue the cyclosporine and try the patient on ROM therapy.
- ROM therapy is a combination antibiotic therapy, short for Rifampin, Ofloxacin and Minocycline.

ROM Therapy

- ROM is a newer regimen that has been successfully used worldwide to treat patients with paucibacillary leprosy and is being investigated for use in multibacillary leprosy.
- Published case reports(Marcus/Hamzavi) have shown efficacy for ROM in the treatment of GA resistant to multiple traditional therapies[7,8]
- The typical dosage and regimen consists of: Rifampin 600mg, Ofloxacin 400mg and Minocycline 100mg
- All antibiotics are administered orally once per month for a duration of typically 3-6 months

ROM Therapy

- ROM therapy has a long track record of safety due to its worldwide usage for paucibacillary leprosy.
- Common adverse reactions include:
  - GI discomfort, NVD- common with tetracyclines
  - Orange/red discoloration of urine and tears- secondary to Rifampin
- However most patients tolerate the short term, once monthly regimen very well.

Back to the Patient

- As of the creation of this PowerPoint, the patient has completed two doses (2 months) of the monthly ROM treatment
- So far there has been little to no improvement, with worsening of some lesions, as well as, development of new lesions noted.
- Typical ROM therapy is 6 months, so we will continue to observe on a monthly basis.

Summary of treatment

- At this point the patient has now had **GA for <u>over 5 yrs</u>**
- She has been treated with:
  - Topical Steroid (Med – to Ultra High Potency)
  - Topical Tacrolimus / Imiquimod
  - Intralesional Steroid Injections, LN_2, ED, NUVB
  - Oral Steroids
  - Dapsone
  - Adalimumab
  - Hydroxychloroquine
  - Cyclosporine
  - ROM

Interesting possibilities??

- Shortly before her GA began to develop, the patient had a vaginal mesh surgically implanted for a bladder prolapse.
- She subsequently found that the particular mesh implanted has been recalled. She has so far, opted not to have it removed.
- Could this be the trigger for her GA? A literature search of pub med, did not discover any reported cases of mesh related GA. However, we know from OB/Gyn literature that they can cause a variety of problems.

Future Possibilities

- Photodynamic Therapy[11]
  - ALA-PDT[14]
- Laser Therapy
  - Excimer Laser[15]
  - Pulse Dye[13]
- Statin
  - Reports have documented an association between increased Cholesterol/Triglycerides and generalized GA[4]
  - Knowing that our pt. has had mildly, but persistently elevated lipids, perhaps a statin is worth a try?

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Thank You!

Suggestions??

Science at the heart of medicine

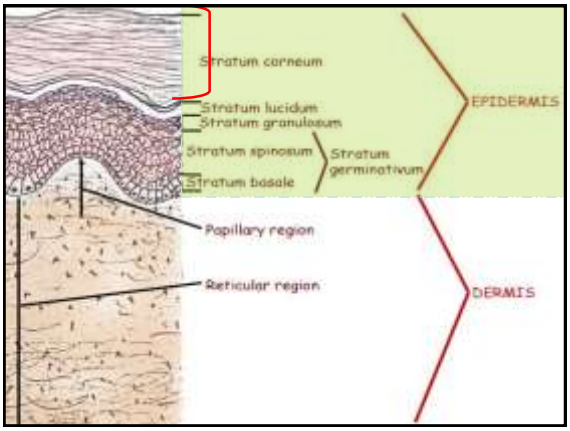
The Emerging Role of Nanotechnology in the Diagnosis, Prevention, and Treatment of Skin Disease

Adam Friedman, MD, FAAD
Assistant Professor of Dermatology
Assistant Professor of Physiology and Biophysics
Director of Dermatologic Research

EINSTEIN
Albert Einstein College of Medicine

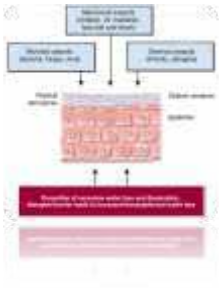
COI

- Co-inventor of technologies TBD
- Consulting/Ad board: Sanova works, Prodigy, Oakstone institute, Liquidia, Loreal, Amgen, Onset, Aveeno, GSK
- Textbook: Nanotechnology and Dermatology



Stratum Corneum and Topical Therapy

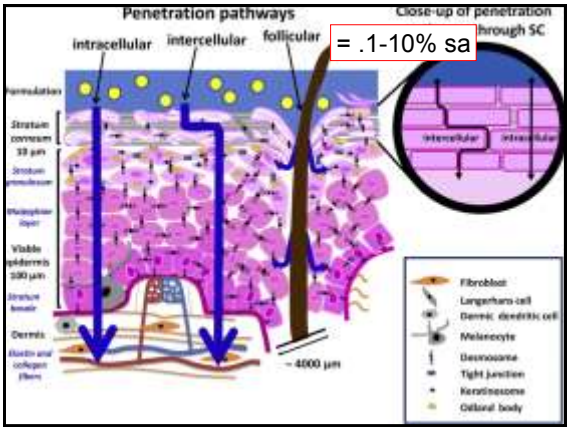
- Low permeability to water soluble drugs due to lipid enriched bilayer and convoluted extracellular pathway
- What lipid species provide this?
  - Ceramides
  - Cholesterol
  - Free fatty acids

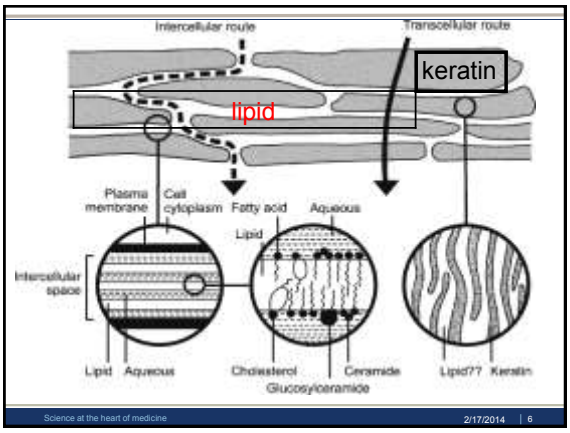


All skin not equal: Different sites = Different absorption

CUTANEOUS ABSORPTION BY ANATOMIC SITE

Site of application	Absorption
Forearm (flexor)	1*
Forearm (extensor)	1.1
Plantar surface	0.14
Ankles	0.42
Palms	0.83
Back	1.7
Scalp	3.5
Axillae	3.6
Chest and abdomen	6
Cheeks, lower aspect	13
Scrotum	42





Tricks to enhance penetration

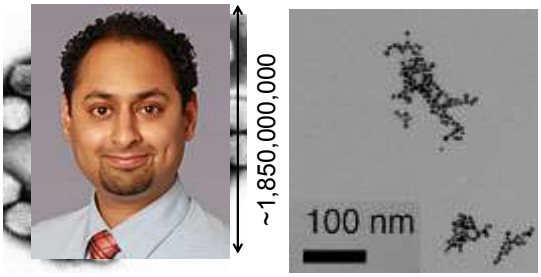
- Solvents and surfactants
  - Ethanol, acetone, detergents
  - Defects in keratinocytes and rearranges bilayer
- Stripping
  - Adhesive tape, cyanoacrylate glue-> increases transepidermal water loss and reduces lipid adhesion
- Electroporation
  - Ultrashort pulses with large voltages
  - Induces structural rearrangement and leads to pore formation

What is nanotechnology?

- Nanotechnology:
  - "The understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications."[1]

[1] The National Nanotechnology Initiative, Strategic Plan 2007

Head to Head

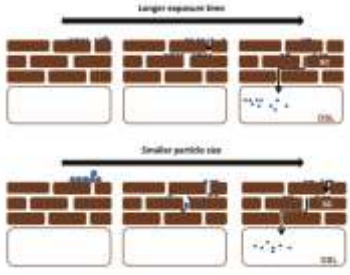


What's the big (or little) deal?

- At this size, matter behaves *differently*
  - As size ↓, surface area relative to volume grows exponentially
    - **Chemical properties** are altered or even magnified: hydrophobic, hydrophilic, or electrically charged
    - The **optical qualities** of matter can also be manipulated at the nano-scale.
    - **Physical properties** change at the nano-level

Three properties of matter--chemical, optical, and physical--can be manipulated and exploited

Simple benefits of nanomaterals: The Derm Perspective



04 SEPTEMBER 2012
Cleantech & Nano

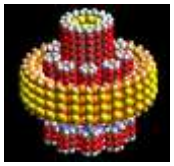
Press Release

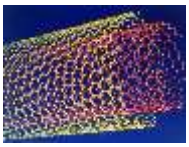
Nanomedicine Market Expected to Grow at a CAGR of 12.57% by 2016 in New Research Report at RnRMarketResearch.com

1990 2000 2005 2010 2020

Types of Nanotechnology

- **Nanomaterials**
  - > Nanostructured fluids
  - > Nanocomposites
  - > Nanostructured solids
- Nanocomputers
- Nanomachines





Nanomaterials: Overview

- Plenty already out there
  - > Nanoparticles
  - > Nanoemulsions
  - > Nanopigments
  - > Nanomagnets
  - > Quantum dots
  - > Zeolites
  - > Nanotennis balls
  - > Nanofibers
  - > Nanoceramics
  - > Fullerenes

Current Nanotechnology Products

Skin care	Sunscreens, antibacterial cleansers, makeup, toothpaste, shampoo, lipstick, face powder, blush, anti-wrinkle cream, eye shadow, perfume, aftershave lotion, appliances, self-cleaning surfaces
Food	Nano-nutraceuticals
Household	Antibacterial cleansers, pet litter
Clothing	Sporting goods, shoe inserts
Automotive	Tires, engines, steppers
Military	Armor, camouflague, radioprotection
Electronics	LED screens on digital cameras

Nanoparticles: A Generic Term

- Small (*obviously*) object that behaves as a whole unit in terms of its transport and properties
  - > Can mix and match different physical, chemical, and optical properties at the nanoscale
    - Disperse vs aggregate
    - Polymerize vs deconstruct
    - Solid vs hollow
    - Increase or decrease cell uptake
    - Immediate vs controlled release
    - Targeting
  - > Possible to develop infinite variety of applications

Nanoparticles in OTC Dermatology

- Nanoparticles already have a role in cosmetics based on current marketplace
- 54 np products 2005, 1015 in 2009, ?? 2013
  - > L'oreal has over 200 patents in nanotechnology!
    - Facial foundations: Create illusion of smooth skin surface
    - Pigmented cosmetics: Eye shadow, blush
      - – Pigment blending with smaller size np allow better complexion color matching
      - – Can create "invisible" layer, no powder particles seen on skin surface
    - Moisturizers: Enhance skin barrier

US Patent 6335022; Simonnet; J._T., Sonneville; O., Legret; S.; L'Oreal, **1999**.
www.nanoinstitute.com

Simple Benefits of Nanoparticles

Cosmetics design.com • USA

Breaking News on Cosmetics Formulation & Packaging in North America

Moisturizing the number one product claim for nanotechnology in cosmetics

By Andrew McDougall+, 05-Jun-2012

Nanoemulsions

- Classic: Oil is dispersed in water
  - > Lipophilic interior + Hydrophilic exterior
    - Transport hydrophobic materials into the skin
      - Lipids, anti-oxidants, retinoids, steroids
- As emulsified particle size ↓, the "nano" favorable properties emerge:
  - > Good sensory texture
  - > Invisible
  - > Hydrophilic exterior allows for rapid penetration into the outer layers of the skin and hair
  - > Do not undergo phase separation

A Picture is Worth….

*http://www.nanotechproject.org/inventories/

Consumer Product	Manufacturer	Nanotechnology Contents
Cosmetics		
Bionova Nano Skin Tech Range	Barney's New York	"Nano complexes"
Serge Lutens Blusher	Barney's New York	"Nano dispersion technology"
Coco Mademoiselle Fresh Moisturizer Mist	Chanel	Nanoemulsion
Defy: Age Management Exfoliator	Bellapelle Skin Studio	Fullerenes
After Glow Brush	ColoreScience	Nanovitamins A and E
Blush colores	ColoreScience	Nanovitamins A and E
Sunforgettable Corrector Colores	ColoreScience	Titanium Dioxide and Zinc Oxide
Moisturizing Dermatone Lips 'n Face Protection Crème	Dermatone	Zinc Oxide
Dr Brandt New lineless Cream	Dr Brandt	Fullerences
Renutriv range	Este'e Lauder	Novasomes
Revitalift Double Lifting	L'Oreal Paris USA	Nanosomes
Hydra Flash Bronzer	Lancome	Nanocapsules
Renergie Microlift Eye	Lancome	Nanoparticles made of silicon and protein
Revlon Colorstay Stay Natural Powder	Revlon	Aluminum

New Database

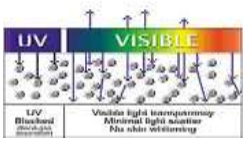
- http://nano.taenk.dk/

Nano for Medical Dermatology

Nanotechnology for the Prevention, Diagnosis and Treatment of Skin Cancer

Nanopigments

- Rely on the property of particle size rather than photochemical interaction to scatter/absorb light
  - > Can be used to generate brilliant colors
    - Samsung TVs
      - *The Official TV of the NFL!*
  - > **Can be used to hide color**



Nanopigments

- Sunblocks
  - > SunVex Dailywear Lotions
  - > D-Fense Antioxidant Moisturizer with SPF 17
  - > Cotz SPF 58
  - > Daily Sun Defense SPF 20
  - > Solar Rx SPF 30+ Nano-Zinc Oxide Sunblock
  - > Sport UV Defense SPF 45
  - > ZinClear Nano Zinc Oxide

www.koboproducts.com

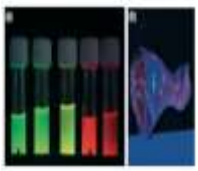
Molecular Diagnosis of Melanoma

- Melanoma is a heterogeneous disease
  - > Different mechanisms with different gene mutations
  - > GREAT NEED to identify the molecular signatures for each melanoma patient
    - **Personalized medicine**
      - BRAF inhibitor for for those with a BRAF mutation
  - > Nanotechnology?
    - Microcantilever arrays using a BRAF-specific oligonucleotide probe.
      - Detect mutated BRAF at the concentration of 500 pM but normal BRAF at a 50-fold higher concentration.
      - No PCR needed

Nat Nanotechnol. 2013;8(2):125-129.

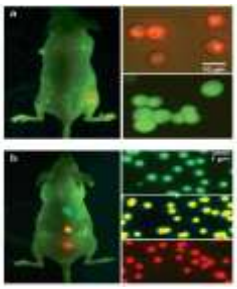
Quantum Dots

- Semiconductor nanocrystals
  - > Semiconductor core encapsulated by another shell
    - 3rd silica shell for water solubility
- Unique optical and electronic properties such as:
  - > Tunable fluorescence emission from visible to infrared wavelengths
  - > Range and very high levels of brightness



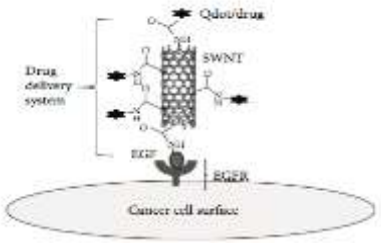
QD for the Diagnosis of Melanoma

- PEG-COOH capped highly fluorescent CdSe/ZnS core/shell QDs conjugated with antibody against CD146
  - > + cells = high brightness, photostability, and specificity.
- Coculture system to test QDs conjugated with antibodies (ab732 or Ab733) against melanoma.
  - > Distinguished between melanoma and melanocytes



Analyst. 2012;137(6):1440-1445
Photochem Photobiol Sci. 2011;10(5):842-851

Nano-Theranostics

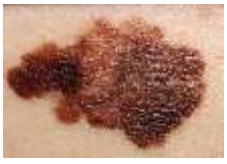


Journal of Chromatography B

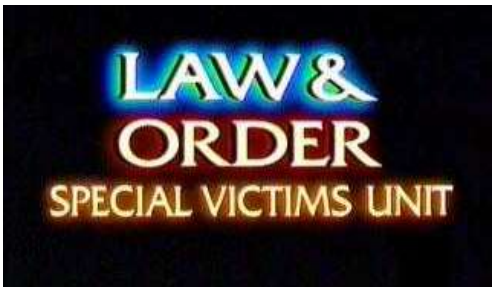
Volatile biomarkers from human melanoma cells

Jae Kwak[a], Michelle Gallagher[a], Mehmet Hakan Ozdener[a], Charles J. Wysocki[a,b], Brett R. Goldsmith[c], Amaka Isamah[a], Adam Faranda[a], Steven S. Fakharzadeh[a], Meenhard Herlyn[a], A.T. Charlie Johnson[a], George Preti[a,d,*]

- Volatile organic compounds (VOC) distinct in cancer
- Attempts to distinguish melanoma from nevi using chromatography/mass spectrometry and gas sensor array
- Nanotechnology-enabled e-nose system - 100s of sensors
  - > Functionalized DNA-coated carbon nanotube sensors
- Qualitative and quantitative differences in volatile sulfur compounds such as dimethylsulfone, dimethyldi- and trisulfide
  - > Owing to altered metabolism
- Differences in VOCs from normal and melanoma cells, as well as different types of melanoma cells by their total expressed VOCs.



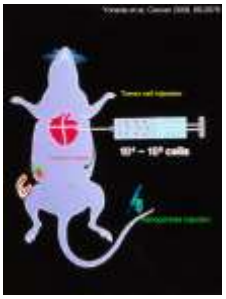
Going Mainstream?



"loophole" 8.13

Nanomagnets

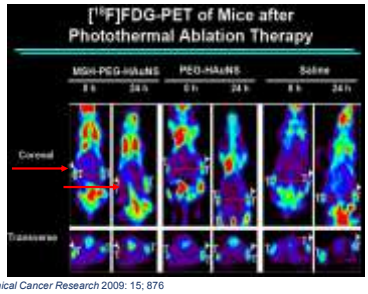
- Nano sized magnetic materials no longer exhibit a net magnetic force
  - > *Paramagnetic*
- Allows for magnetic field directed imaging/therapy



Gold Nanoparticles

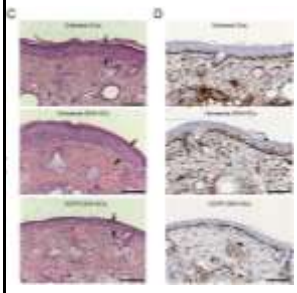
- Coupled with antibody
- Binds to cancer cells
- The gold absorbs laser emission
  - > Near- infrared
- Allows for selective photothermolysis of tumor

Targeted Photothermal Ablation of Murine Melanomas with Melanocyte-Stimulating Hormone Analog–Conjugated Hollow Gold Nanospheres



Lui W et al *Clinical Cancer Research* 2009: 15; 876

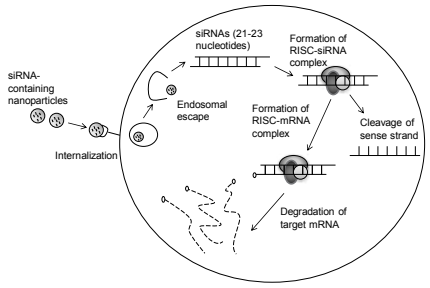
EGFR knockdown by spherical nucleic acid nanoparticle conjugates



Suppresses downstream ERK phosphorylation, and reduces epidermal thickness by ~40%.

Zeng, D et al. Proc Natl Acad Sci U S A. 2012 Jul 24;109(30):11975-80.

The mechanism of RNA interference via exogenous siRNA

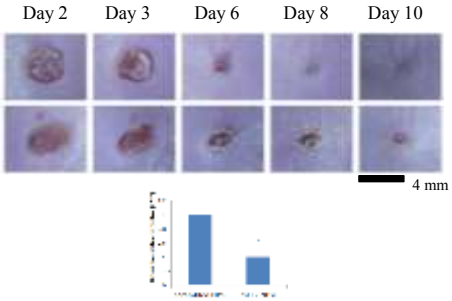


Barriers to siRNA utility

- Degradation
- Uptake
- Immunogenicity

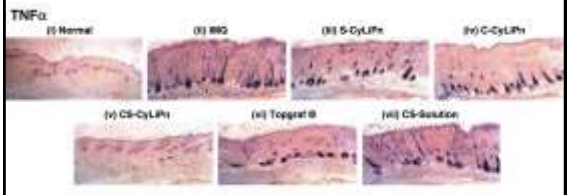
siRNA and wound healing

siRNA nanoparticles targeting FL2 mediated microtubule cleavage accelerates wound healing



Topical delivery of anti-TNFα siRNA and capsaicin *via* novel lipid-polymer hybrid nanoparticles efficiently inhibits skin inflammation *in vivo*

Pinaki R. Desai [a,1], Srujan Marepally [a,c,1], Apurva R. Patel [a], Chandrashekhar Voshavar [b,c], Arabinda Chaudhuri [c], Mandip Singh [a,*]



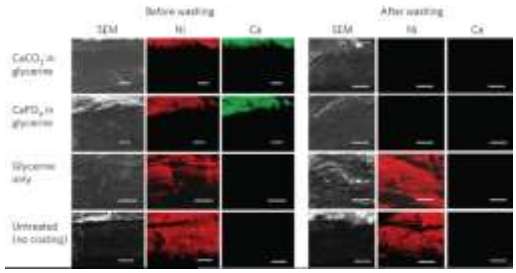
Nanoparticles for the Prevention of Contact Dermatitis

Nanoparticles reduce nickel allergy by capturing metal ions

- Calcium carbonate or calcium phosphate nanoparticles
- The nanoparticles captured nickel ions by cation exchange
  - > Remained on the surface of the skin
  - > Removed by simple washing with water

Vemula P et al .Nat Nanotechnol. 2011;6(5):291-5.

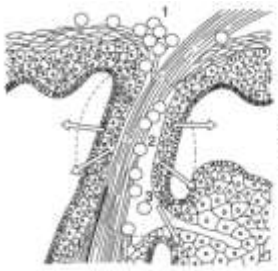
Nanoparticles reduce nickel allergy by capturing metal ions



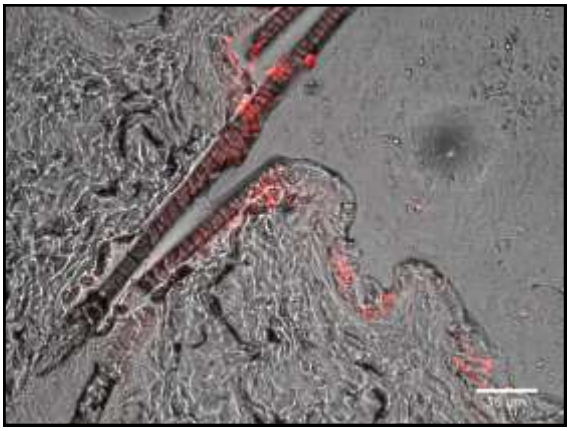
Acne Vulgaris: An Ideal Nano Target?

	Erythema	Scaling	Burning	Flare	Resistance	Other
Tretinoin*	+++	+++	++	++	-	-
Isotretinoin	++	++	+	+	-	-
Adapalene	+	+	+	+	-	-
Tazarotene	++	+	+	+	-	-
Azelaic acid	+	+	++	-	-	-
Benzoyl peroxide	++	++	+	+	-	Bleaches hair/clothes
Topical antibiotic	(+)	(+)	(+)	(+)	+++	

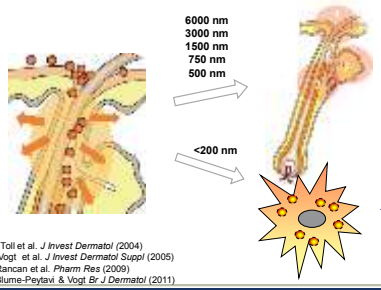
Follicular targeting



1. Selective entry into the infundibulum
2. High local concentration
3. Controlled releases = controlled onset of action

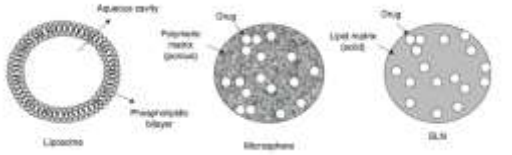


Particle-Based Hair Follicle Targeting



Toll et al. *J Invest Dermatol* (2004)
Vogt et al. *J Invest Dermatol Suppl* (2005)
Rancan et al. *Pharm Res* (2009)
Blume-Peytavi & Vogt *Br J Dermatol* (2011)

Nanotechnology as a vehicle of improved delivery



Clindamycin
Tea tree oil
Salicylic acid
Cyproterone acetate
Finasteride
Benzoyl peroxide
All-trans retinoic acid

Benzoyl peroxide
All-trans retinoic acid

Cyproterone acetate
Isotretinoin
All-trans retinoic acid

Castro GA. Expert Opin. Drug Deliv. (2008) 5(6)

Microsc. Microanal. 19 (Suppl 4), 2013
© Microscopy Society of America 2013
doi:10.1017/S1431927613008913

Evaluation of a New Topical Treatment for Acne with Azelaic Acid-Loaded Nanoparticles

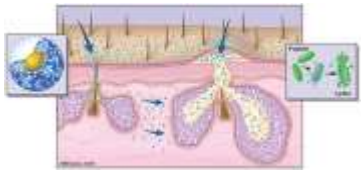
A. Gomes*, L. Azevedo**, P. Rijo***, M. Baptista***, S. Candeias*, N. Martinho*, A. Fernandes***, A. Roberts*** and C. Reis*

Almost there…

What's *New:* RU-58841 and Cyproterone acetate Nanoparticles

- Big Idea: Topical Anti-androgens
  - Decrease epithelial turnover and sebum production
  - Concentrate drugs in pilosebaceous unit
  - Avoid SE in systemic administration
- Neither ingredients approved in US
- Studies limited - *in vitro* and *ex vivo*

What's New: Soybean Nanoemulsions

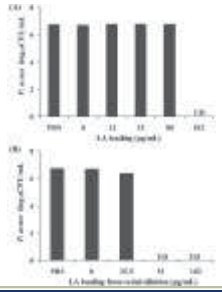


Disrupts outer lipid membrane

www.nanobio.com

What's *New*: Lauric Acid Liposomes

- LA is an amphiphilic molecule consisting of a hydrophobic hydrocarbon chain + hydrophilic carboxylic acid headgroup.
- >BPO against P. acnes
- But!
  - > Poor water solubility
- Good candidate for bilayered wall of liposomes



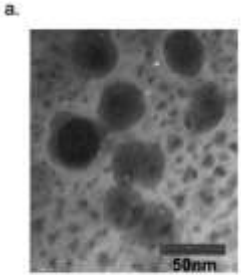
Yang D. *Biomaterials* 2009; 30(30): 6035-6040

What's New: Chitosan Nanoparticles

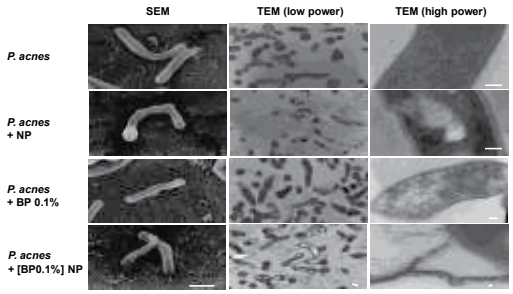
- Natural polysaccharide biopolymer
- Antimicrobial properties
  - > Polycationic character at weakly acidic pH

Higher surface to volume ratio = higher surface charge density = increased microbial affinity

membranes/walls
  - – Decreased osmotic stability
  - – Membrane disruption
    - » Eventual leakage of intracellular elements
- Enter the nuclei
  - – Bind to microbial DNA
- > Chelator : Metals, Lipids



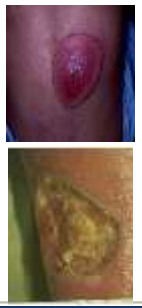
Friedman, AJ et al. J Invest Dermatol. 2013;133(5):1231-9.



Friedman, AJ et al. J Invest Dermatol. 2013;133(5):1231-9.

Can We "ESKAPE" This Crisis: Nanotechnology for SSTIs?

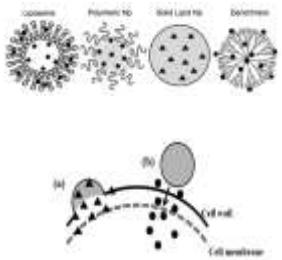
- Multidrug-resistant (MDR) pathogens are rising at an alarming rate
- 'ESKAPE' pathogens
  - > *Enterococcus faecalis, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp.*
  - > Emphasize the fact that they 'escape' the effects of many antibacterial agents.
- Public health threat of epidemic proportions!!



Boucher HW et al. *Clinical Infectious Diseases.* 2009;48(1):1-12.

Nano-cillin: Approach 1

1. Drug loaded nanoparticles (Nps)
   1. Physical encapsulation, adsorption, or chemical conjugation
   - Benefits
     - Improve serum solubility
     - Prolong systemic circulation lifetime
     - Sustained and controlled release
       - Tissues and cells specific deliver
     - Concurrent therapy
     - Deliver previously *undeliverable* actives

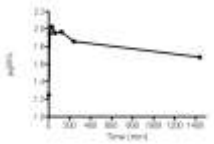


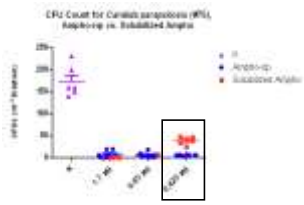
Nano-encapsulated drugs galore…

- Enhanced antimicrobial action *topically*
  - Tobramycin
  - Silver Sulfadiazine
  - Doxycycline
  - Azole antifungals
  - Terbinafine
  - Penciclovir

Amphotericin Nanoparticles

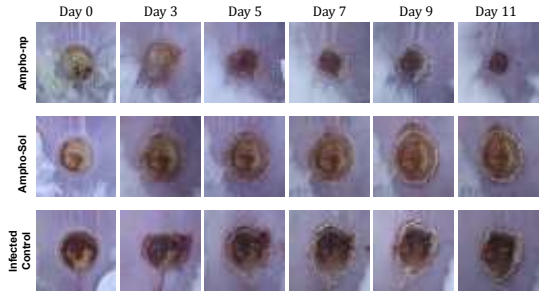
Content Release Profile of Ampho-nps





Nanomedicine. Published online 6/14/13.

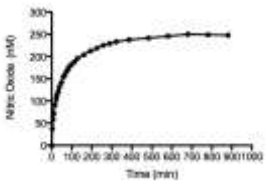
Amphotericin-np effectively treat *C. albicans* infected burn model



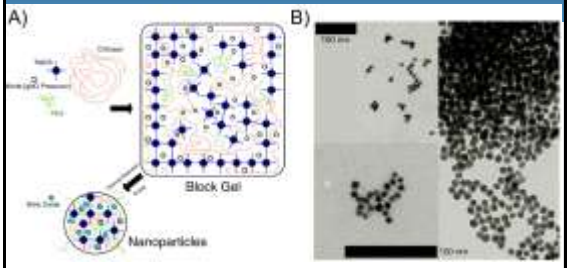
Nanomedicine. Published online 6/14/13.

Nitric Oxide Nanoparticles: A Hybrid Technology

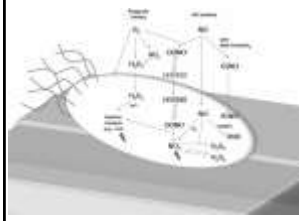
- "Deliver the undeliverable"
- Novel composite material
  - Combines the robust, malleable, and porous properties of silane-based sol-gel matrices with the thermal reduction potential of sugar glasses[1,2]

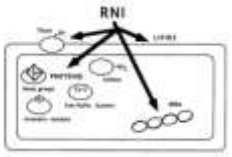


[1]Ray et al. *J Am Chem Soc* 200 124: 7270-1
[2]Friedman et al. *Nitric Oxide* 2008 19(1): 12-20.



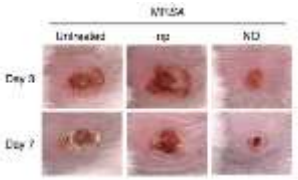
Mechanisms of Direct Antimicrobial Action: Cytostatic and Cytotoxic

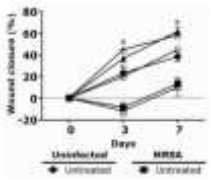




Jones ML, et al. *Appl Microbiol Biotechnol* 2010 Aug 3. [Epub ahead of print]
Fang FC. J Clin Invest. 1997 Jun 15;99(12):2818-25

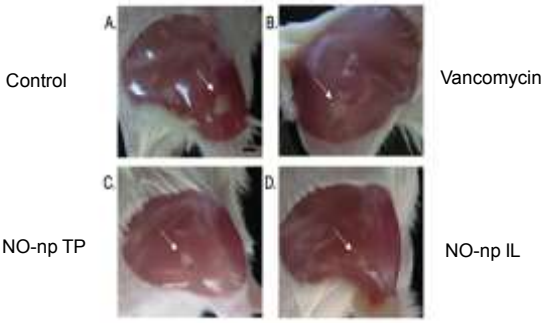
NO-np Accelerate Wound Closure in MRSA Infected Excisional Wound



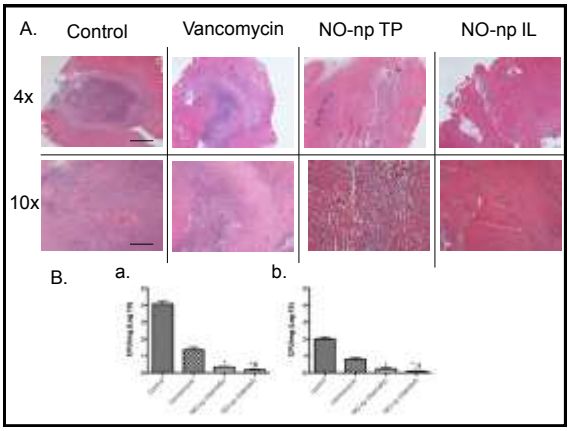


Martinez et al. *J Invest Dermatol.* 2009: 129; 2463–2469

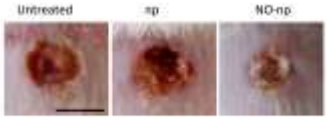
NO-np Accelerate Intramuscular Abscess Clearance

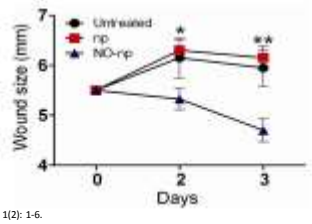


Schairer D. *Virulence* 2012; 3(1):1-6.

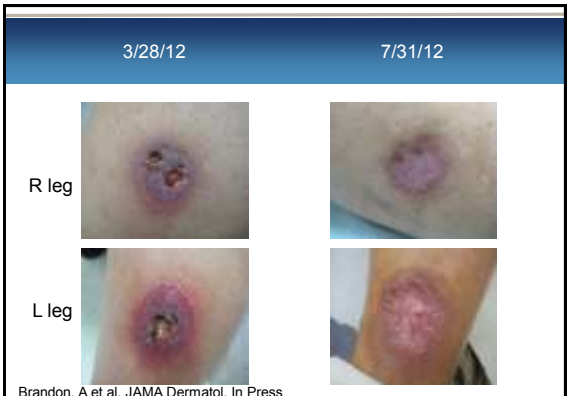


NO-np Accelerate Wound Closure in *A. baumanii* Infected Excisional Wound





Mihu et al, *Virulence*. 2010; 1(2): 1-6.

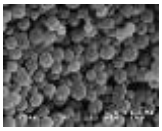


Brandon, A et al. JAMA Dermatol. In Press

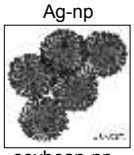
Antimicrobial Nanomaterials: Approach #2

- Rely on innate nano-scaled antimicrobial activity
  - > Minerals/metals
    - **Silver**
    - Copper
    - Magnesium
    - Zinc
  - > Carbohydrates/lipids
    - **Chitosan**
    - **Soybean oil**

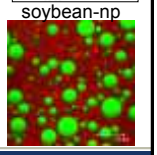
Chitosan-np



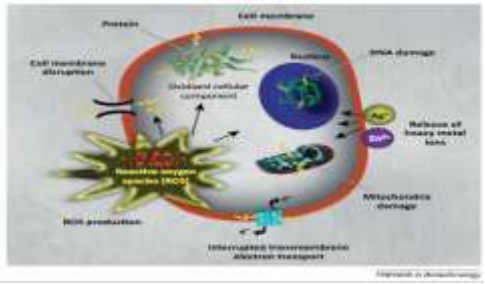
Ag-np



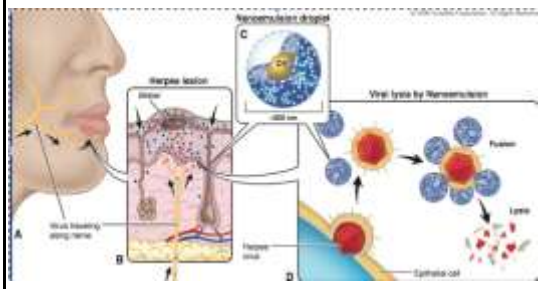
soybean-np



MOA of Nanosilver



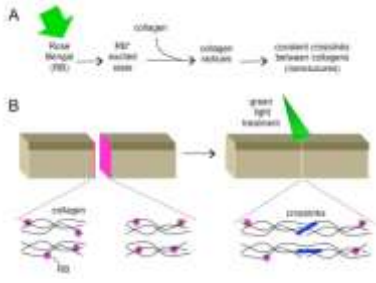
Soybean Oil Nanoemulsion for Herpes Labialis



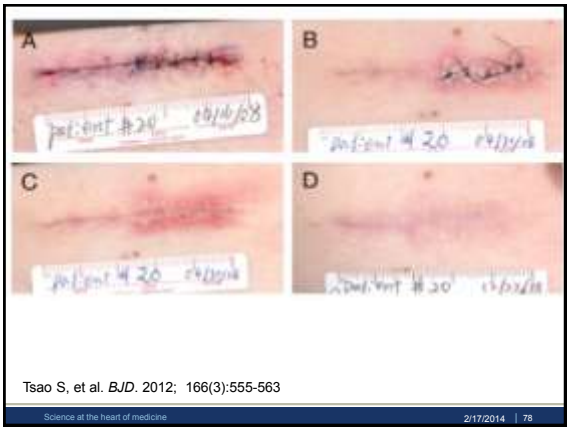
Jones T et al. P1801. AAD Annual Meeting. San Antonio, Texas, 2008.

Nanotechnology for Procedural Dermatology

Nanosutures



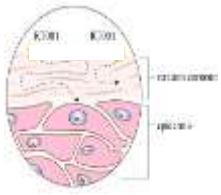
Tsao S, et al. *BJD*. 2012; 166(3):555-563



Tsao S, et al. *BJD*. 2012; 166(3):555-563

Nano-BoNTA

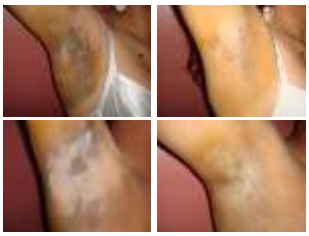
- ***Big idea: Needle-less Botox***
- At least two companies
  - Transdermal Corp., Birmingham, Michigan
    - Ionic nanoparticle technology
      - Mixed micelles + penetration enhancers
  - Revance Therapeutics, Newark, California
    - Combination 150kD BoNTA + peptidyl macromolecule transport system.
      - Bound to BoNTA through electrostatic interactions
- FDA trials underway
  - So far so good



Revance Therapeutics. http://www.revance.com/385-t0010ci?side.
Trasdermal Corp. http://www.transdermalcorp.com/

Hyperhidrosis; Before and After (at week 16)

Botulinum toxin type A gel BID x 1 week;
6 units per day (42 units at the end of the study).



www.transdermalcorp.com

Skin & Allergy News | digital network

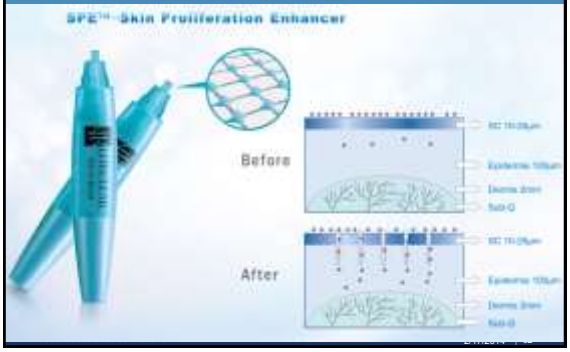
News and Views that Matter to Dermatology

Nanotechnology Vehicle Speeds Numbing of Topical Lidocaine

By: DAMIAN McNAMARA, Skin & Allergy News Digital Network

06/14/11

Nanotechnology for Preventive Health



Nanoproducts in Development

- Topical g-amino butyric acid (GABA)
- Topical hyaluronic acid
- Topical siRNA
- Topical vaccines
- Topical botulinum toxin
- Topical sirolimus
- Topical minoxidil
- Topical anesthetics
- Topical chemoagents
- Topical melanin
- Topical antioxidants
- Topical pro-erectogenic agents
- Topical enzyme replacement
- Scarless sutures

Nanotechnology Safety

Nano-scare??

New Products Bring Side Effect: Nanophobia
By NATASHA SINGER December 4, 2008

Safety

- Theoretically harmful
- As size ↓, the surface to volume ratio exponentially ↑ , making nanosized materials that are potentially/predicted to be toxic and highly reactive even more dangerous.
  - As size ↓, its ability to penetrate most if not all, human tissues, also exponentially ↑

Attention: Game Changer!

What's the deal with nanosunscreens?

Cosmetics design.com | USA

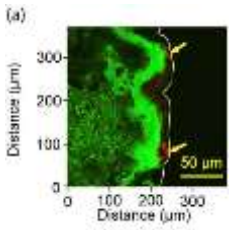
Nanoparticles in sunscreen may prove toxic if accidentally eaten

Nano-Sunscreens: The theoretical danger

- Formation of free radicals?
  - > TiO2 and ZnO are known photocatalysts
    - Exposed to UV light, they emit electrons.
    - Induce the formation of peroxides, free radicals, and other ROS.
    - ? potential to damage proteins, lipids, and DNA
- Mineral sunscreens used under UV exposure for years
  - No studies demonstrating the production of free radicals
- Capable of fully penetrating the epidermis and entering cells?
  - > No evidence to date in vivo

Characterization of optical properties of ZnO nanoparticles for quantitative imaging of transdermal transport

- International team of scientists from Australia and Switzerland
- Optically tested for concentration of ZnO nanoparticles (zinclear) at different skin depths
  - > Nonlinear optical microscopy
- Rubbed for 5 minutes, left on for 8 hours, then washed
  - > **Nanoparticles did not penetrate beneath the stratum corneum**



Song Z et al. Biomedical Optics Express. 2011; 2 (12) 3321-3333

Commericial vs Experimental

- Large particle size safer
- Anionic coating decreases penetration into SC due to charge
- Polymer coating increases size, transforms to smooth spheres, decreases penetration
- Commercial np formulation 15% 50nm ZnO and 5% 30nm TiO_2

Oversight: FDA Draft Guidance 4/2012

- Safety assessment of nanomaterials when used in cosmetic products:
  - > The legal requirements for cosmetics manufactured using nanomaterials
    - Cosmetics not subject to premarket approval
      - – Legally responsible for the safety of their products
  - > Modification of standard safety tests
  - > Companies are encouraged to consult the FDA

The Nanodermatology Society Responds

nano werk

Nanodematology Society responds to FDA's new draft guidelines on the use of nanotechnology in food and cosmetics

The AAD Responds

- "While widespread use of nanotechnology in medicine is currently under evaluation, one of the main benefits of nanoparticles in sunscreens is that the small molecules can provide more protection and more even coverage on the skin surface than larger particles," said Dr. Siegel. "Considerable research on the use of nanoparticles on healthy, undamaged skin has shown that the stratum corneum, the outermost layer of the skin, is an effective barrier to preventing the entry of nanoparticles into the deeper layers of the skin."
- 5.16.2012

Prog

8.2012

And now what?

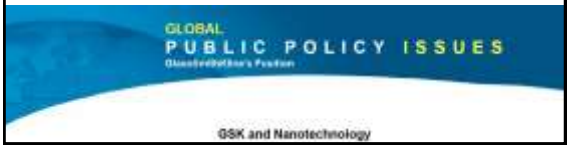
- 5/8/2013
  - > Open forum - public invite
- 6/ 2013
  - > Cosmetic Good Manufacturing Practices
    - Draft Guidance – no nano?
- 8/26/2013
  - > EPA has issued its final significant new use rules (SNURs) for 17 substances, mostly constituting substances at the nanoscale.
  - > If intend to manufacture, or process any of these 17 chemical substances for significant new use --> notify EPA at least 90 days before commencing that activity.

As nanotechnology is being used to develop new drugs, FDA is working to ensure quality, safety, and effectiveness

Posted on October 24, 2013 by FDA Voice

By: Celia N. Cruz, Ph.D.

Johnson & Johnson
Guidelines: Responsible Use of Nanotechnology
March 2013



GSK and Nanotechnology

Worldwide directions for the future

- Europe
  - > 7/ 11/2013: European Cosmetics Regulation EC No. 1223/2009 fully enforced across EU.
  - > **Definition: Nanomaterial' means an insoluble or biopersistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.**
  - > 3 requirements for industry
    - Notification to the EC 6 months prior to market
    - Safety assessment
    - Labeling of ingredients that are nanomaterials
- Australia - Government rejected mandatory labeling of nanomaterials in sunscreens - postponed to re-discuss in 2013
  - > Isnt it almost 2014???

1. H.R. 5786,
2. Regulation (EC) No. 1223/2009, November 30, 2009

digital network

Skin & Allergy News

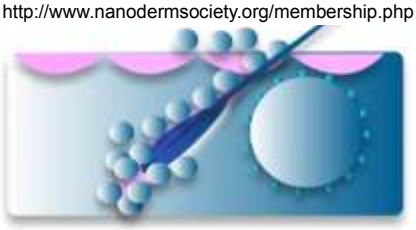
News and Views that Matter to Dermatology

Blog: More Nanodermatology, Please!

09/13/11

The Nanodermatology Society

http://www.nanodermsociety.org/membership.php



The Dermatology Foundation

has supported & advanced my career.

DF

Thank you for your attention

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Saturday, February 22, 2014
(8 CME)

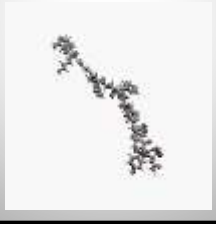
7:00 a.m. to 8:00 a.m.	Breakfast with Exhibitors
7:30 a.m. to 7:50 a.m.	*A Review and Update on Melanocyte Stimulating Hormone Therapy* **Jordan Fabrikant, DO** NSUCOM/Larkin Community Hospital
7:50 a.m. to 8:10 a.m.	*Filler Up: Not Always a Smooth Ride* **Matthew Zarraga, DO** Wellington Regional Medical Center
8:10 a.m. to 8:30 a.m.	*Hair Keratin: Fabulous or Frightening?* **Suzanne Micciantuono, DO** Wellington Regional Medical Center
8:30 a.m. to 9:30 a.m.	*What's Under the Ulcer* **David Fivenson, MD**
9:30 a.m. to 10:30 am	*Dermatopathology Update* **Amy Spizuoco, DO, FAOCD**
10:30 a.m. to 10:50 a.m.	*Dihydroxyacetone: A Safe Alternative to Ultraviolet Tanning?* **Mariel Bird, DO** Oakwood Southshore Medical Center
10:50 a.m. to 11:10 a.m.	*Androgenetic Alopecia and the Role of Low Level Laser Therapy* **Christina Feser, DO** Oakwood Southshore Medical Center
11:10 a.m. to 11:30 a.m.	*Current Methods of Treatment for Facial Acne Scarring* **Jesse Jensen, DO** Bosford Hospital/McLaren Oakland
11:30 a.m. to 12:00 p.m.	Break with Exhibitors
12:00 p.m. to 1:00 p.m.	Product Theater Lunch (No AOA CME credit)
1:00 p.m. to 2:00 p.m.	*The Spectrum of Comorbidities in Psoriasis with Special Reference to Cardiovascular Issues* **Alan Menter, MD**
2:00 p.m. to 2:30 p.m.	Break with Exhibitors
2:30 p.m. to 3:30 p.m.	*Osteopathic Continuous Certification Update* **Lloyd Cleaver, DO, FAOCD**
3:30 p.m. to 3:50 p.m.	*A Case Report of a Patient with Lichen Planus Pemphigoides Treated with Ustekinumab* **Raymond Knisley, DO** Advanced Desert Dermatology
3:50 p.m. to 4:10 p.m.	*Androgenic Alopecia* **Ryan Pham, DO** UNTHSC/TCOM
4:10 p.m. to 4:30 p.m.	*Oral Lesions: The Good, the Bad, and the Ugly* **Tang Le, DO** South Texas Osteopathic Dermatology
4:30 p.m. to 5:30 p.m.	*Legal Dilemmas in Dermatology* **Cliff Lober, MD, JD**
5:30 p.m. to 6:00 p.m.	Break with Exhibitors/Prize Drawing
6:00 p.m. to 7:30 p.m.	Welcome Reception **Aboretum Cedar/Oak/Maple**

Jordan Fabrikant DO

Program Director: Stanley Skopit DO MSE FAOCD

Melanocyte Stimulating Hormone Therapy:

By Jordan Fabrikant, D.O.

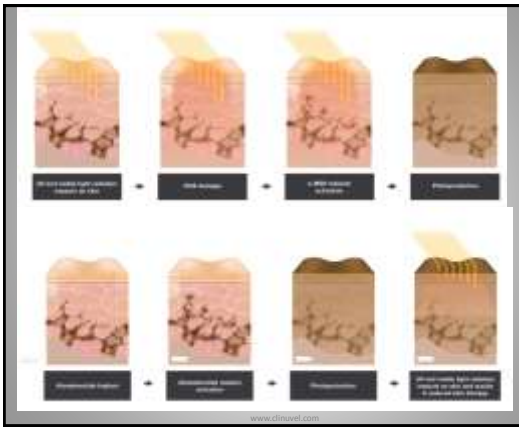


What is it?

- Afamelanotide is a synthetic analog of the naturally occurring melanocortin peptide hormone alpha melanocyte stimulating hormone(α-MSH) that has been shown to **induce skin pigmentation through melanogenesis**.
- Subsequently it **increases photoprotection** to UV exposed skin.
- α-MSH was first synthesized at the University of Arizona. Researchers there knew that one of the best defenses against skin cancer was melanin activated in the skin.
- They hypothesized that an effective way to reduce skin cancer rates in people would be to induce the body's natural pigmentary system to produce a photoprotective barrier prior to UV exposure.

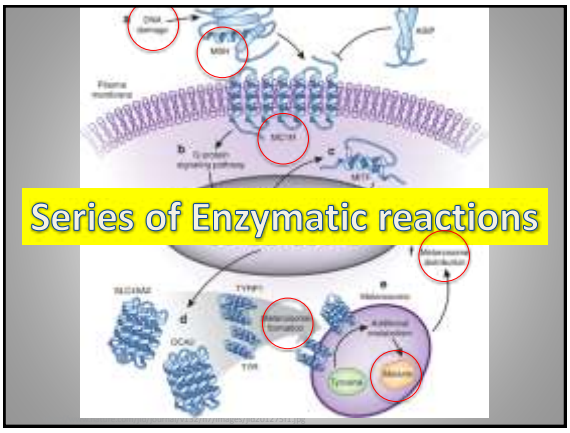
What is it?

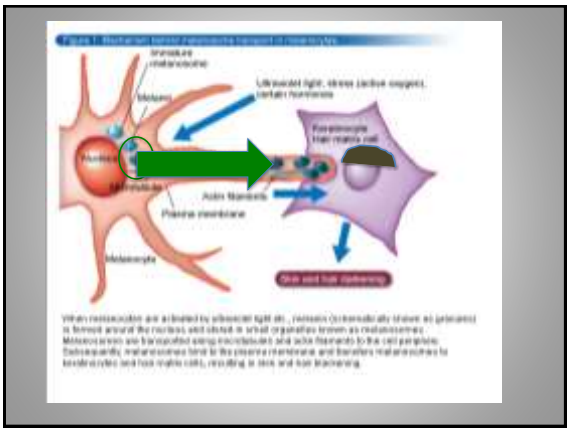
- **Natural α-MSH has too short a half life** in the body to be practical as a therapeutic drug. So they decided to find a more potent and stable alternative.
- The researchers headed by Victor J. Hruby and Mac E. Hadley, found a peptide, **[Nle^4, D-Phe^7]-α-MSH, that was approximately 1,000 times more potent than natural α-MSH**.

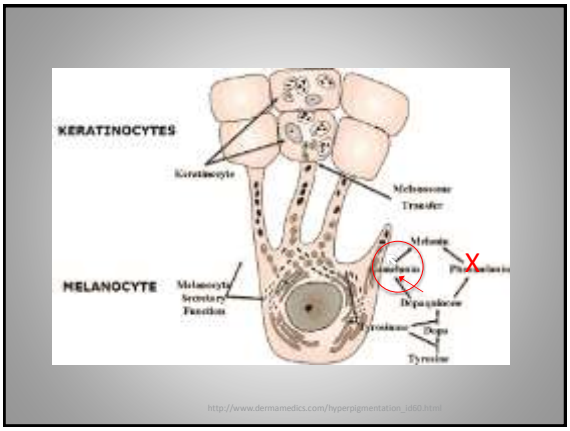


Mechanism of action

- SCENESSE® (afamelanotide) is a selective **agonist of the MC1R** (melanocortin 1 receptor) As an analogue of the naturally occurring melanocortin alpha-MSH, it's part of the **natural human tanning response.**
- Results in the melanocyte favoring the production of eumelanin (black/brown) over pheomelanin (red/yellow).

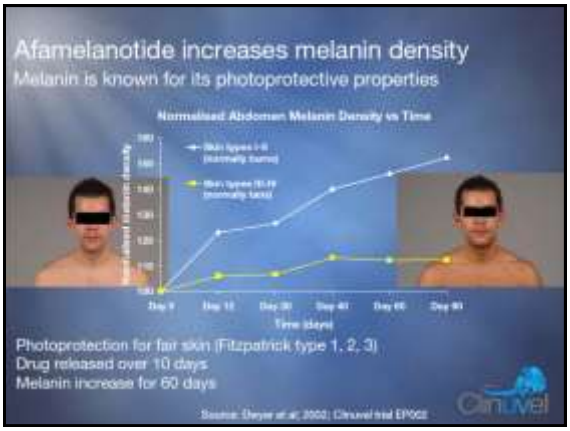

Series of Enzymatic reactions




KERATINOCYTES
MELANOCYTE
X


The result


Afamelanotide
Skin pigmentation: before and 30 d after 1 dose
Melanin density at different body sites 30 d after one dose


Afamelanotide increases melanin density
Melanin is known for its photoprotective properties
Photoprotection for fair skin (Fitzpatrick type 1, 2, 3)
Drug released over 10 days
Melanin increase for 60 days

Before I go any further, you may be wondering about carcinogenicity

- Concerns were present in the minds of the original researchers as to it possibly having the potential to cause melanocytes to turn malignant or to enhance the proliferation of pre-existing melanomas and possibly other skin cancer types.
- These concerns led the researchers to conduct a series of preclinical studies to examine the carcinogenic potential that α-MSH had in both in vivo and in vitro skin models.
- According to the researchers these studies established a, "lack of carcinogenic potential"[1].
- Further studies reported that α-MSH did not enhance anchorage-independent clonogenic cell growth, a hallmark of malignancy, and it had no effect on tumor incidence, size or on metastatic spread in *in vitro* and animal models[2].
- Instead, one study reported that α-MSH actually inhibited melanoma cell proliferation in vitro[3].

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DNA Damage and Cellular Stress Responses

Molecular Cancer Research

Alpha-Melanocyte–Stimulating Hormone Suppresses Oxidative Stress through a p53-Mediated Signaling Pathway in Human Melanocytes

Ana Luisa Kadekaro[1], Juping Chen[1,2], Jennifer Yang[1], Shuma Chen[1], Joshua Jameson[1], Vivi B. Swope[1], Tan Cheng[1,2], Matthew Kadekaro[1], and Zalfa Abdel-Malek[1]

"We propose that activation of the p53 pathway could potentially be used as a **melanoma preventative strategy**. The fact that melanoma tumors express wild type p53 offers the unique opportunity of using alternative strategies based on targeting p53 for the treatment of advanced stage disease." -May 2012-

University of Cincinnati — UC College of Medicine **Department of Dermatology**

- Research/Clinical Interests:
- Sunlight is the most important environmental factor for melanoma development. Regardless of which spectrum of UVR is important in the genesis of melanoma, there is strong evidence in support of oxidative stress as the main cause of the malignant transformation of human melanocytes (MCs). A large percentage of individuals from Caucasian populations are carriers of disabling mutations on the melanocortin 1 receptor (MC1R) gene, the receptor of a-melanocyte stimulating hormone (a-MSH) and major regulator of the tanning responses of the skin. My research focuses in investigating the molecular pathways induced by UVR in human MCs, with emphasis on the antioxidant mechanisms that protect the cells against reactive oxygen species (ROS) and carcinogenesis. Our major contribution to the field of photobiology and skin carcinogenesis was to identify a new physiological role for a-MSH in the skin. **We demonstrated that a-MSH elicits early responses in MCs that are independent of melanin synthesis (tanning) and protect against the damaging effects of UVR, by reducing oxidative stress and increasing the repair of damaged DNA.** Our studies also revealed that this protection was absent in MCs derived from individuals with the clinical phenotype of red hair, fair and freckled skin and inability to tan. Our reports evidenced that MCs carrying variants of the MC1R sustained high levels of oxidative stress and DNA damage. The goal of my studies is to identify molecular targets to be tested in new strategies for prevention and development of melanoma. We anticipate that directly targeting key molecules of antioxidant pathways in MCs will be especially beneficial to individuals that are genetically susceptible to oxidative stress and melanoma.
- - See more at: http://med.uc.edu/dermatology/contact/directory/profile.aspx?epersonID=kadekaal#sthash.yXxZJBXa.dpuf

- When case reports happen…

A Suspicious Lesion Arising in a 28-Year-Old Female After Administration of Melanotan II

Daniel Child, Paul Aanderud, and Steven Grekin JAOCD Volume 24

- Patient had a superficial spreading malignant melanoma, Clark's level II.
- "The patient also reported a long history of visiting tanning salons with an estimation of biweekly visits over a 10-year period."

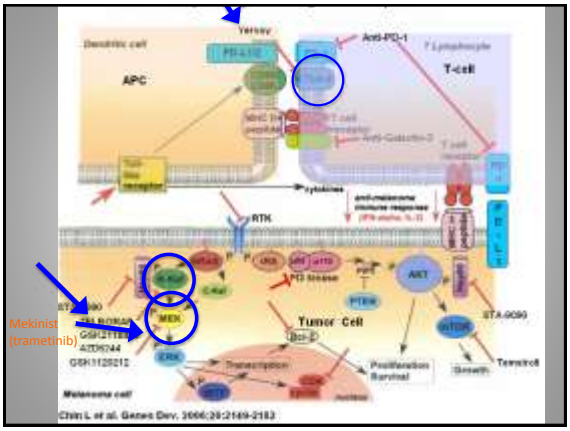
A Suspicious Lesion Arising in a 28-Year-Old Female After Administration of Melanotan II

Daniel Child, Paul Aanderud, and Steven Grekin JAOCD Volume 24

- "…α-MSH not only has been shown to have direct stimulatory effects on melanoma cells by inducing change in cell shape and increased dendricity, but it also down regulates adhesion molecules that would normally allow interaction of the immune cells with melanoma.[1]"
- "This interaction may allow melanoma to escape immune detection and increase its survival.[2]"

1.Thody AJ. A-MSH and the regulation of melanocyte function. Ann NY Acad Sci. 1999; 885: 217-229.
2. Hedly SJ, Murry A, Sisley K, et al. Alpha-Melanocyte stimulating hormone can reduce T-cell interaction with melanoma cells in vitro. Melanoma Res 2000; 10(4):323-330.

- So what causes melanoma?
- Until recently…..



- A new study suggests….

So what causes melanoma?

Dr. Levi A. Garraway

- Changes are in regions that control genes, not in the genes themselves. **The mutations are exactly the type caused by exposure to ultraviolet light**, indicating they might be among the first DNA changes in a cell's path to melanoma.
- Two independent mutations within the core promoter of TERT, the gene coding for the catalytic subunit of telomerase, which occur in 50 of 70 (71%) of melanomas examined.

Lei Huang, Eran Hodis, Mary Jue Xu, Gregory V. Kryukov, Linda Chin, Levi A. Garraway. Highly Recurrent TERT Promoter Mutations in Human Melanoma. Science DOI: 10.1126/science.1229259.
Nikhil Figl, P. Sivaramakrishna Rachakonda, Christine Fischer, Antje Sucker, Andreas Gast, Stephanie Kadel, Ina Moll, Elke Nagore, Jürgen Hemminki, Dirk Schadendorf, Rajiv KumarTERT Promoter Mutations in Familial and Sporadic Melanoma. Science

- "The brakes or the gas that control the genes that cause cancer are as important as gene mutations."
- -Elaine Mardis of Washington University

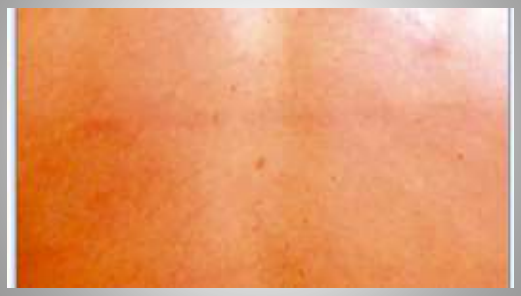
- What about Dysplastic Nevi?

The dysplastic nevus: From historical perspective to management in the modern era.
Keith Duffy, Douglas Grossman (JAAD CME, July 2012)

- Cardones and Grichnik reported a 40 year old man developed several new DN's after self administration of α-MSH[1].
- Langan et al reported 2 patients with rapidly changing DN's after self administration of Melanotan I and II[2].

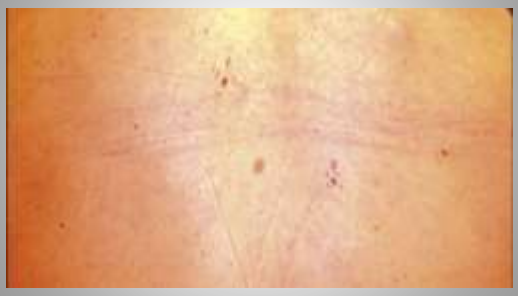
1. Cardones AR, Grichnik JM. Alpha-melanocyte-stimulating-hormone-induced eruptive nevi. Arch Dermatol 2009;145:441-4.
2. Langan EA, Ravnilogan D, Jamieson LA, Rhodes LE. Changes in moles linked to use of unlicensed "sun tan jab". BMJ 2009;338:b277.

1 year before using α-melanocyte-stimulating hormone



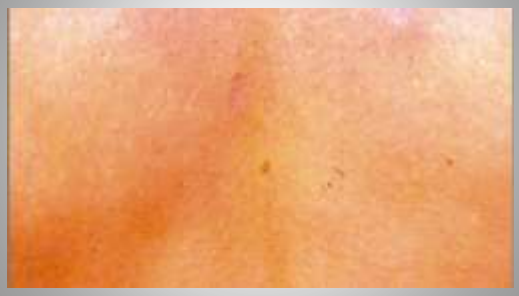
Cardones AR, Grichnik JM. Alpha-melanocyte-stimulating-hormone-induced eruptive nevi. Arch Dermatol 2009;145:441-4.

increased pigmentation and growth of preexisting nevi on α-MSH



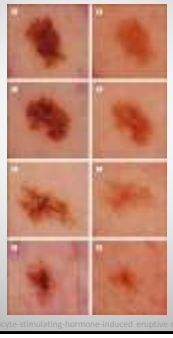
Cardones AR, Grichnik JM. Alpha-melanocyte-stimulating-hormone-induced eruptive nevi. Arch Dermatol 2009;145:441-4.

α-MSH use was discontinued, and at 6 month follow up, the nevi progressively lightened and lost their growth features.



Cardones AR, Grichnik JM. Alpha-melanocyte-stimulating-hormone-induced eruptive nevi. Arch Dermatol 2009;145:441-4.

Dark brown pigmentation with peripheral pigment extensions (pseudopods) and peripheral dots. Fading of these features 6 months later.



Cardones AR, Grichnik JM. Alpha-melanocyte-stimulating-hormone-induced eruptive nevi. Arch Dermatol 2009;145:441-4.

They admit it

- "We propose that administration of a superpotent α-MSH analogue in our patient, who **had a background of melanoma and atypical nevi**, may have driven his already genetically mutated melanocytic stem cells to produce several new, atypical nevi."

Cardones AR, Grichnik JM. Alpha-melanocyte-stimulating-hormone-induced eruptive nevi. Arch Dermatol 2009;145:441-4.

A nice conclusion by Keith Duffy, Douglas Grossman (JAAD CME, July 2012)

- Presence of Dysplastic Nevi are associated with increased melanoma risk in individuals, but there is no increased risk of a Dysplastic Nevus turning into a melanoma compared to a common nevus turning into a melanoma.

They hit it on the head!

- "Our cases highlight a further area of concern: change in appearance of pre-existing melanocytic nevi.
- Unregulated use of Melanotan I and II may confuse clinical presentation by promoting nevus pigmentation."

These are NOT the same!

- Patented injectable 16mg resorbable formulation
  - Size grain of rice
  - Controlled-release over 7-10 days
  - Physician administered
  - Protection for 60 days

-Controlled studies under FDA regulations

-Does not cross Blood Brain Barrier
*Linear
*2 amino acids were changed

VS

Twice weekly injections but doses are variable depending on the website

-Counterfeit

-Crosses BBB
*circular molecule

Polylactide resorbable implant formulation

biocompatible polymer √
- biodegradable/safety known

unique dissolution rate √

stability √
- intended shelf-life >2 yrs

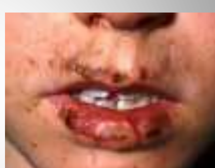
ease s.c. administration √

- Medical Uses of Afamelanotide

- 1) Erythropoietic protoporphyria
- 2) Polymorphous light eruption
- 3) Phototoxicity associated with systemic photodynamic therapy
- 4) Solar urticaria
- 5) AK and SCC in skin cancer in patients who have received an organ transplant
- 6) Vitiligo
- 7)Acne?
- 8) Hailey Hailey?

Erythropoietic Protoporphyria (EPP)

- Autosomal Dominant
- Deficiency of the enzyme ferrochelatase in heme synthesis
- Eosinophilic deposits in cutaneous lesions
- Symptoms begin in early childhood and include photosensitivity, pruritis, burning, erythema, and edema.
- Increased protoporphyrins may be found in the blood or feces.

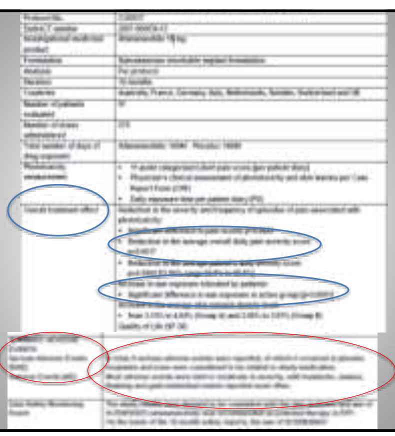


Erythropoietic Protoporphyria (EPP)

On May 5, 2010 the Italian Medicines Agency (AIFA - Agenzia Italiana del Farmaco) became the first governmental health organization ever (even before the drug received approval in Europe) to authorize afamelanotide as a medicine for therapeutic treatment of Italian citizens to reduce painful photosensitivity stemming from the orphan disease erythropoietic protoporphyria(EPP). In April 2012 it was approved in Switzerland.

Chronic skin lesions of EPP

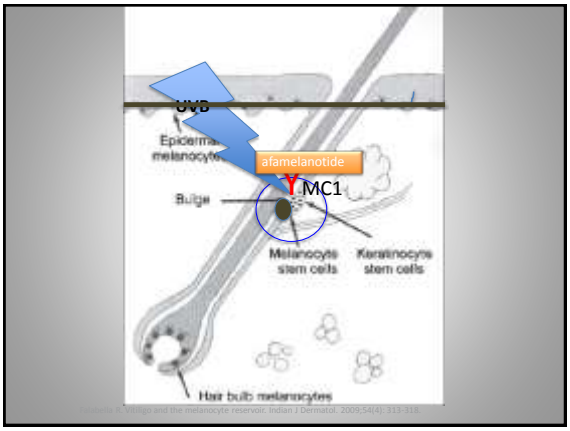
Acute photosensitivity reaction in EPP



Mechanism of action in Vitiligo

- Recent data suggest that a key source of immature pigment cells capable of full differentiation reside in the bulge region of the hair follicle[1]. Basically, a "melanocyte reservoir."
- These hair follicle melanoblasts in the bulge, are devoid of a melanocortin receptor system.
- NB–UVB phototherapy stimulates the expression of MC1R receptors on these melanoblasts for binding of afamelanotide[2].
- Combination of afamelanotide and NB–UVB act synergistically to promote migration of follicular melanocytes to the epidermis as well as eumelanogenesis.

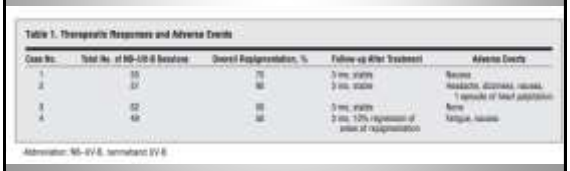
1. Falabella R. Vitiligo and the melanocyte reservoir. Indian J Dermatol. 2009;54(4): 313-318.
2. Osawa M, Egawa G, Mak SS, et al. Molecular characterization of melanocyte stem cells in their niche. Development. 2005;132(24):5589-

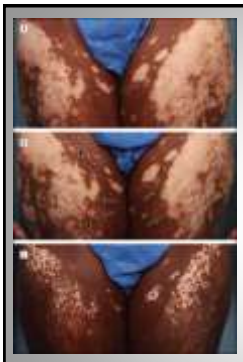


The Efficacy of Afamelanotide and Narrowband UV-B Phototherapy for Repigmentation of Vitiligo

Pearl E. Grimes, MD; Iltefat Hamzavi, MD; Mark Lebwohl, MD; Jean Paul Ortonne, MD; Henry W. Lim, MD (January 2013 *Archives in Dermatology*)

- 3 cases showed excellent repigmentation.
- 1 month of NB-UVB alone, followed by monthly SQ injections of 16mg afamelanotide.





Before initiation of treatment.

After 11 narrowband UV-B (NB–UV-B) treatments and 14 days after the first 16-mg afamelanotide implant, improvement is seen in the follicular areas of pigment loss. Arrows indicate areas of repigmentation.

After 55 NB–UV-B treatments and the fourth implant, marked improvement of the thigh area is seen.

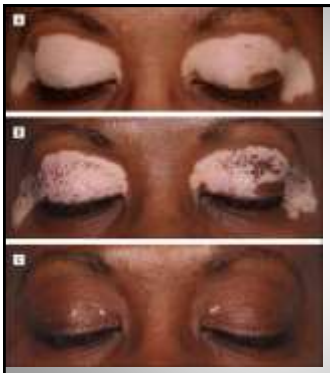
A, Before initiation of treatment.

B, After 11 narrowband UV-B (NB–UV-B) treatments and before first implant, minimal improvement is seen compared with baseline.

C, After 13 NB–UV-B treatments and 4 days after the first implant, follicular and confluent areas of repigmentation are seen predominantly on the right hand.

D, After 28 NB–UV-B treatments and second afamelanotide implant, near-complete repigmentation of the hands is seen.

E, After no NB–UV-B treatments for 3 months and no implant for 5 months, persistence of repigmentation is seen.

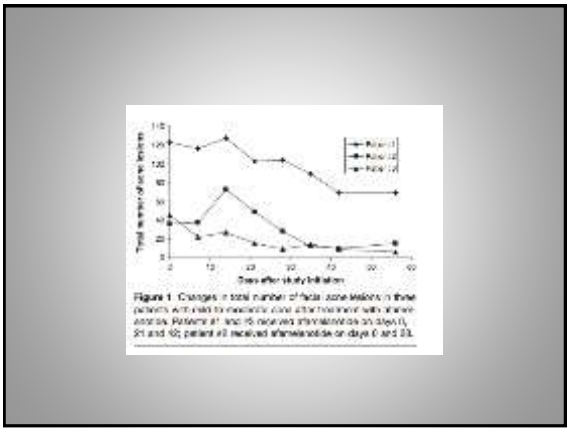


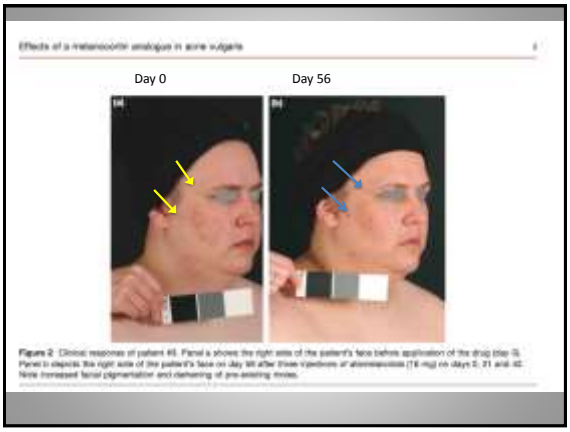
A, Near-complete periorbital depigmentation and no change after 12 narrowband UV-B (NB–UV-B) sessions.

B, After 15 NB–UV-B treatments and 2 days after the first implant.

C, After 62 NB–UV-B treatments and fourth implant, near-complete repigmentation is seen.

ACNE??





Results

	Day 0	Day 56
The number of *inflammatory* acne lesions (papules, pustules, nodes)	46 ± 30.3	23.7 ± 15.6
The *total* number of facial acne lesions (inflammatory and non-inflammatory lesions)	68 ± 27.6	30 ± 19.7
Dermatology Life Quality Index (DLQI) and Cardiff Acne Disability Index.	7.7±4.7	4.3±2.8

Laboratory parameters included differential blood counts, electrolytes, urine analysis, and liver and kidney function tests. All results were WNL.

Hypotheses for MOA in ACNE

- In mice, targeted disruption of the melanocortin 5 receptor **(MC-5R) led to decreased sebum production**.[1]
- **anti-inflammatory** and indirect antioxidative effects may also account for the beneficial effects of afamelanotide in these patients.[2]
- α-MSH and related peptides have direct **anti- bacterial** effects against gram-positive bacteria. However, it is unknown whether Nle4-D-Phe7-a- MSH has direct antimicrobial activity against P. acnes.[3]
-

Hailey Hailey?

Efficacy of the melanocortin analogue Nle4-D-Phe7-α-melanocyte-stimulating hormone in the treatment of patients with Hailey–Hailey disease

G. Biolcati,[1] C. Aurisi,[1] L. Barbieri,[1] S. Ciaffi,[2] L. Screpanti[2] and C. Talora[2]

Clinical and Experimental Dermatology doi:10.1111/ced.12203

Clinical and Experimental Dermatology doi:10.1111/ced.12203

- "Real-time RT-PCR analysis showed that **Nrf2 mRNA was significantly downregulated in keratinocytes derived from cutaneous lesions of patients with HHD"**
- "Treatment of HHD-derived keratinocytes with afamelanotide contributed to **upregulation of Nrf2 [nuclear factor (erythroid-derived 2)-like 2]**, a redox-sensitive transcription factor that plays a pivotal role in **redox homeostasis during oxidative stress**."
- **"Nrf2 is an important target of the afamelanotide signalling that reduces oxidative stress"**

Clinical and Experimental Dermatology doi:10.1111/ced.12203

To Date (August 5, 2013)

- Administered in over 800 patients
- More than 2500 injections

How can we change tanning habits?

Scientists find some whales sun tan to protect themselves from sunburns

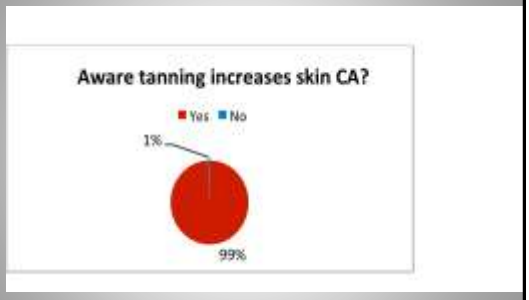
VANCOUVER - Some pale whales appear to tan in order to protect themselves from sunburn, says a new study.

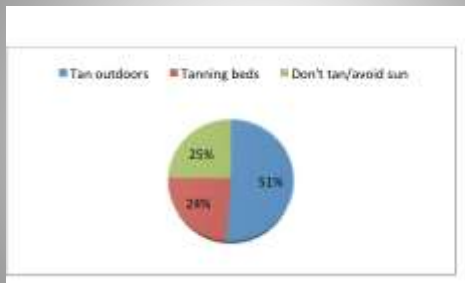
Even whales want to tan!

Our Tanning Study Methods

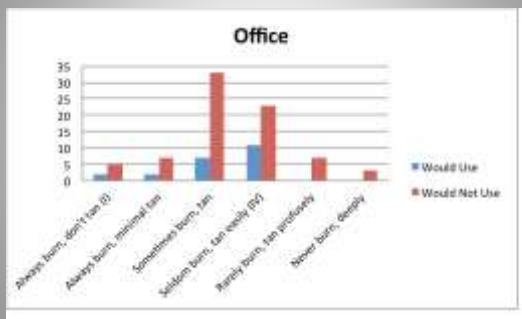
- Surveyed 300 volunteers with a tanning questionnaire.
- 100 in a dental office (in Newton, PA)
- 100 at the beach (Clearwater Beach, FL)
- 100 outside of tanning salons (Dallas, Texas)

- **Tanning Questionnaire:**
- Are you male or female? _____
- How old are you? _____
- Do you tan outdoors or at tanning beds? If so, which one? _____
- Is the primary reason you tan to look darker (cosmetic)? Is there another reason you tan? If so, what is the other reason? _____
- Are you aware that tanning both outdoors and in tanning beds can increase the risk of developing skin cancer? _____
- Have you used tanning lotions or sprays? _____
- If you do not prefer using tanning lotions or sprays, what is your main complaint in using them? _____
- If there was an FDA approved injectable medication that gave you a natural tan without subjecting your skin to UV radiation (e.g.: the sun), would you use it? _____
- If such a medication were available and if it were affordable, would you make use of it and additionally stop tanning? _____

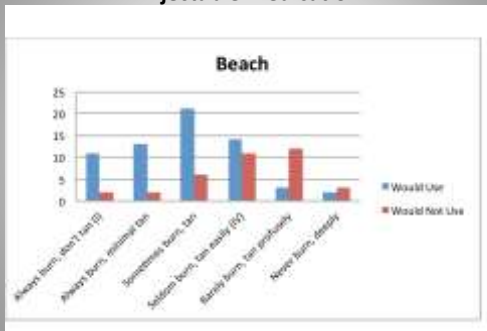




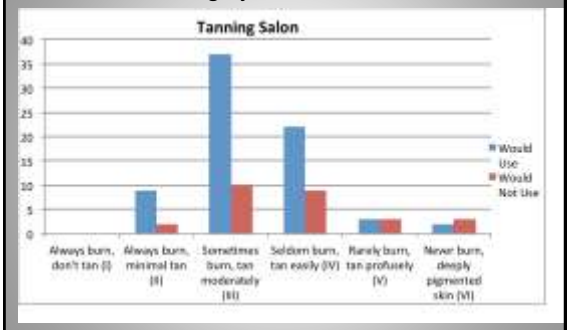
Office Participants Response Regarding Tanning Injectable Medication

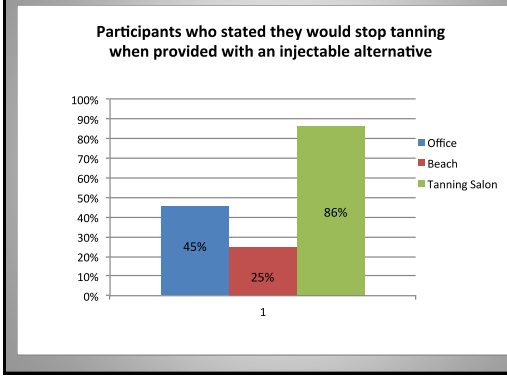


Beach Participants Response Regarding Tanning Injectable Medication



Tanning Salon Participants Response Regarding Tanning Injectable Medication





What have we learned?

Until the dermatology community understands the psychology of those who tan, changes in tanning behavior will not likely be altered. We must accept the fact that societal pressure to be tan is far stronger than the fear of being diagnosed with skin cancer in a significant proportion of the population. If offered by dermatologists, a tanning alternative, such as afamelanotide, may assist in diminishing patients' risks for acquiring skin cancer by significantly decreasing tanning behavior because it can provide patients with the tan they so strongly desire without UVR exposure. Unregulated MSH products are currently available and frequently purchased over the internet, in gyms, and tanning salons demonstrating the market potential and patient need. This necessitates the urgent need for clinical trials to evaluate the safety and efficacy of medicinal tanning agents.

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- Clinical and Experimental Dermatology doi:10.1111/ced.12203

Questions?

Thank you

FILLER UP: NOT ALWAYS A SMOOTH RIDE

Matthew Zarraga, DO
PGY-4
Wellington Regional Medical Center/LECOM

Disclosure Statement

- None

Introduction

- ~2 million soft tissue filler soft tissue filler procedures in 2012
- ↑ 5% from 2011
- 2nd to botulinum toxin injections

Properties of Fillers – Cross-Linking

- Naturally occurring HA
  - Excellent biocompatibility and affinity for water
  - Soluble polymer that is cleared rapidly when injected into normal skin
- Cross-Linking – improve biocompatibility and biological activity
- Degree of cross-linking
  - ↑ Cross-link density = ↓ Distance between cross linked segments = ↑ Hardness of gel = ↓ Rate of degradation

Properties of Fillers - Elastic Modulus (G')

- Relates to its stiffness or ability to resist deformation while it is being injected
- High G' better resistance to skin tension forces therefore used for volumization and lifting of facial zones that have high levels of muscle activity
- Low G' better for filling fine rhytides

Properties of Fillers - Swelling

- Varies from product to product
- Swelling is dependent on:
  - Its equilibrium for bound water
  - Concentration
  - Cross-link density
  - Process used to hydrate gel

Properties of Fillers – Particle Size and Viscosity

- Cross-linked gels must be sufficient particle size that they can be injected easily through an appropriately sized needle
- Relates to how it flows from the needle
- Larger gel particles are more difficult to push through a small-bore needle

Know What You're Injecting: Types of Fillers

- Hyaluronic Acid
- Calcium Hydroxylapatite (CaHa)
- Poly-L-Lactic Acid (PLLA)
- Collagen
- Polymethylmethacrylate (PMMA)
- Silicone
- Fat
- Cultured Autologous Fibroblasts

Types of Fillers

Hyaluronic Acid (HA)

- Glycosaminoglycan disaccharide composed of alternately repeating units of D-glucuronic acid and N-acetyl-D-glucosamine
- HA is naturally occurring in the ECM
- Found in many human tissues including skin, synovial fluid of joints, vitreous fluid of the eye and scaffolding within cartilage

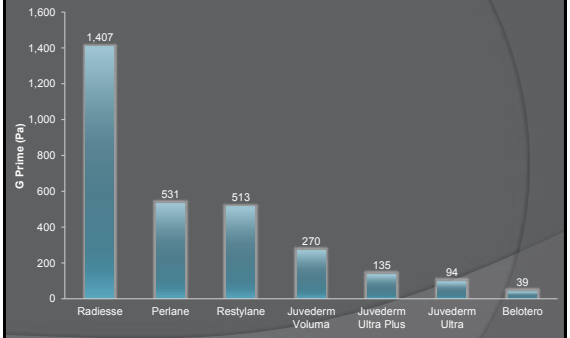
Hyaluronic Acid (HA)

Calcium Hydroxylapatite (CaHa)

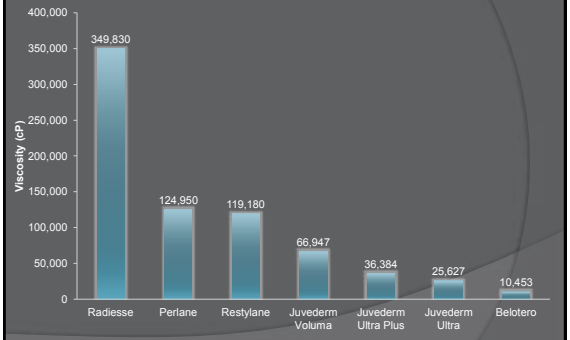
- Normally found in bone and teeth
- Synthetically produced smooth, uniform CaHa microspheres in a gel carrier
- Gel carrier suspends the particles and allows them to be readily delivered by injection
- CaHa microspheres induce long-term collagenesis

Calcium Hydroxylapatite (CaHa)

Elasticity



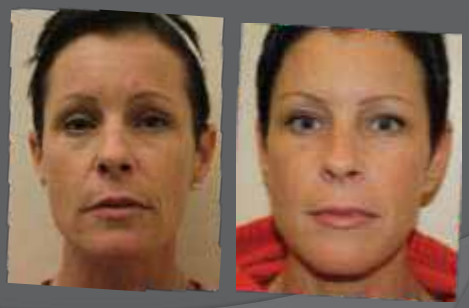
Viscosity



Poly-L-Lactic Acid

- Biostimulatory agent
- PLLA is a biodegradable, biocompatible synthetic polymer derived from the alpha-hydroxy-acid family
- When injected, leads to the production of a fibrous tissue response that is hypothesized to result in the formation of collagen
- By stimulating the host's own collagen, PLLA acts to volumize tissue in a gradual, progressive and predictable manner

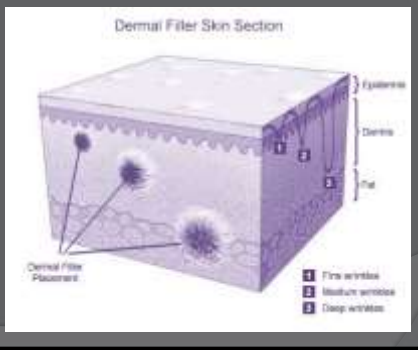
PLLA



Filler Treatment Areas

Filler Treatment Areas

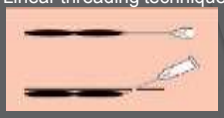
Know Your Injection Depth of Fillers



Know Your Injection Techniques

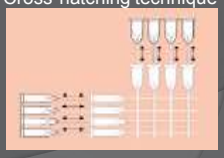
Serial puncture technique

Linear threading technique



Fan technique

Cross-hatching technique



Injection Site Reactions

- Most common adverse effect with filler treatment
- Swelling
- Redness
- Tenderness
- Pain
- Bruising
- Itching

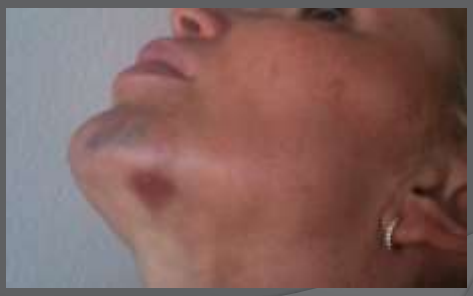
Swelling From Filler Injections

Swelling From Filler Injections

Swelling From Filler Injections

Bruising from Filler Injections

Bruising from Filler Injections



Know Your Products Associated with Bruising and Swelling

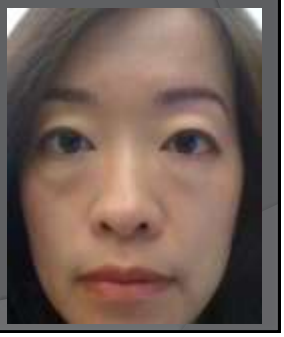
- Aspirin
- NSAIDs
- Vitamin E
- Herbal Supplements – *"F the 4G's"*
  - *F*ish oil
  - *G*arlic
  - *G*inger
  - *G*ingko biloba
  - *G*inseng

Intra-Injection Procedures to Decrease Bruising and Swelling

- Injection speed (<0.3ml/min)
- Injection technique (fan-like needle use)
- Use of blunt tipped cannulas
- Mix epinephrine into filler
- Meticulous hemostasis (pressure)
- Ice/Cooling

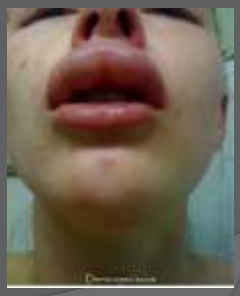
Rayleigh Effect

- Scattering of light by particles small enough to make the effect selective so that different colors are deflected through different angles
- Restylane – blue color
- Juvederm – green-grey color
- Belotero – NONE
- Prevent with proper injection
- Treat with hyaluronidase



Product Sensitivity

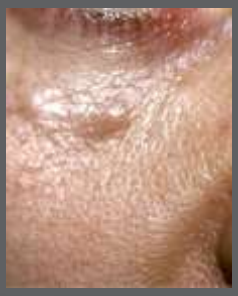
- Very rare side effect with HAs
- Angioedema occurred with HA injected into lips
- No respiratory compromise
- Treated with 8mg dexamethasone then 6 day prednisone taper
- Edema resolved 5 days post-procedure

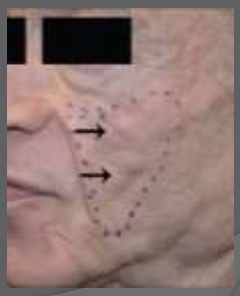


Nodules and Papules

- May be caused by inappropriate (superficial) placement
- Facial zones most susceptible to superficial nodules:
  - Periorbital region
  - Nasal dorsum
  - Lips

Nodules and Papules

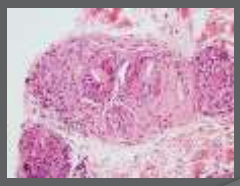




True Granuloma

- Rare; 0.1% of patient population
- Usually occurs with semi-permanent or permanent filler injections
- Appear within 6 months do treatment usually
- Dermal nodules with mild erythema
- Present singly or in small clusters
- May or May not be tender
- Not fluctuant like an infection
- Persistent nodules resulting from a granulomatous foreign-body reaction

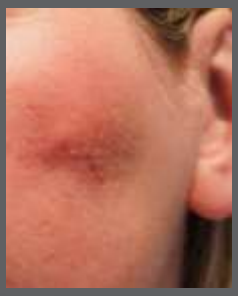
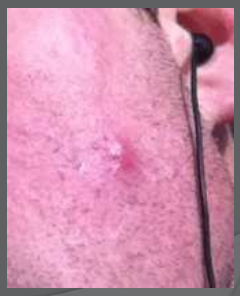
True Granuloma



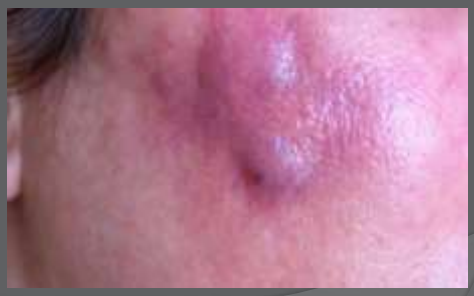
Infection

- Can occur as an early or late complication
  - Early onset infections may occur within hours and present with acute induration and erythema, soreness or itching
  - Late onset infections can present with fluctuant papules, nodules or systemic symptoms
- Multiple inflammatory nodules corresponding to injection sites may be due to contaminated product
- Sterile abscesses
- Biofilms

Infections

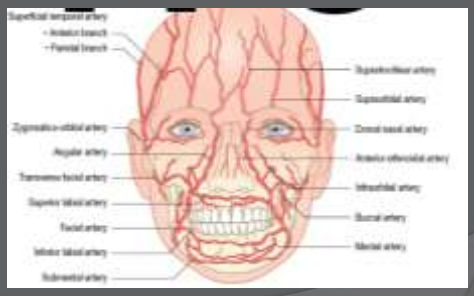
Sterile Abscess



Infection

- Infections must be cultured
- Most caused by resident flora (Staph and Strep)
- Atypical Mycobacterial infections must be considered if unresponsive to antibiotics and infections lasting >2 weeks
- Multiple inflammatory nodules corresponding to injection sites may be due to contaminated product
- May trigger recurrent herpetic lesions

Know Your Facial Vasculature Anatomy



Vascular Compromise

- Impending necrosis can be identified by an immediate local blanching upon injection of a specific region or a delayed retiform duskiness of the skin after injection

Necrosis


Necrosis

- May be caused by:
  - Direct injection of a filler into a vessel
  - Compression of a vessel secondary to the pressure of the volume of the injected filler
- Glabella and nasal ala are the 2 most commonly affected areas

Necrosis Prevention

- Prevent glabellar necrosis by:
  - Aspirating before injecting
  - Inject superficially and medially
  - Avoid over correction by using low volumes in 2+ treatment sessions (rather than one high volume session)

Necrosis Treatment

- Warm compresses
- Nitroglycerin paste
  - ½-1" of ointment within 3cm of injection site/proximal to ischemia
  - Occlude with plastic wrap for 12 hours, then 12 hours off
  - Repeat cycle until resolution
- Aspirin 325mg
- Hyaluronidase (for hyaluronidase acid filler injections)
  - Combine 75U of hyaluronidase and 1.5cc of 0.5% lidocaine and inject into HA filler excess. Should see improvement within 24 hours but may take several days for 100% resolution
- Low molecular weight heparin 30mg SC q12 hours until clinical improvement noted (max 14 days)

Blindness

- Due to filler embolization into ophthalmic vasculature
- When injecting the glabella, blindness results from retrograde spread of intravascularly injected material into the ophthalmic artery

Conclusion

- Fillers are the 2nd most common sought after cosmetic procedure
- Know your fillers and their properties
- Know possible complications, prevention and treatment
- Master your technique
- Do NOT overdo it

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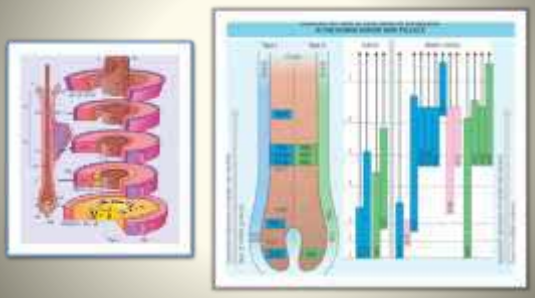
Last of the Mohicans

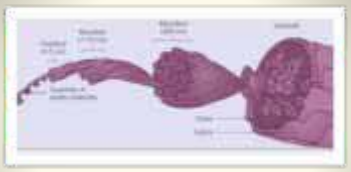
Hair Keratin: Fabulous or Frightening??

Suzanne Micciantuono, DO
Wellington Regional Medical Center

Biology of the Hair Follicle



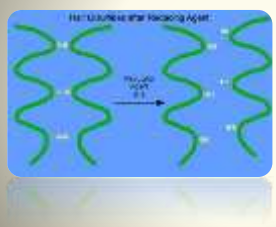
Hair Shaft Structure



The cortex is covered by the cuticle, which is rich in high-sulfur proteins and arranged like roof tiles

The cuticle is responsible for maintaining the shaft within the follicle and protecting the shaft from weathering. Cuticular damage causes hair shafts to fracture, split, and break off.

How does processing affect hair structure?



Hair keratin contains disulfide bonds which join cysteine amino acids

Traditional semi- or permanent hair relaxers, like ammounium thioglycolate, break these disulfide bonds

Formalin (methylene glycol) is a cross-linking agent and binds keratin to the hair

So what is Brazilian Keratin Hair Treatment?

- Started in Brazil over 10 years ago
- Certain preservative chemicals bind keratin to the hair, smoothing and straightening curl for months
- The treatment is thought to work by linking keratin to the cuticle with formalin - a cross-linking agent which binds keratin to the hair
- Brazilian keratin treatment does not alter the structure of the hair and thus likely does not penetrate beyond the cuticle

What does BKT claim to do??

- Reduce curls
- Reduce frizz
- Improve strength
- Improve overall texture of hair

Hair Keratin Project

- Objective
  - To determine the effect Brazilian Hair Keratin treatment has on the hair cuticle

Hair Keratin Treatment Project

- 20 hair samples taken
- 18 successfully treated and analyzed
- 10 treated with non-formalin-based product; 8 treated with formalin-based product
- Samples analyzed by scanning electron microscopy

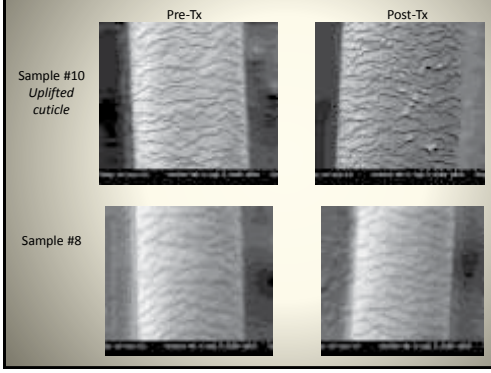
Demographics

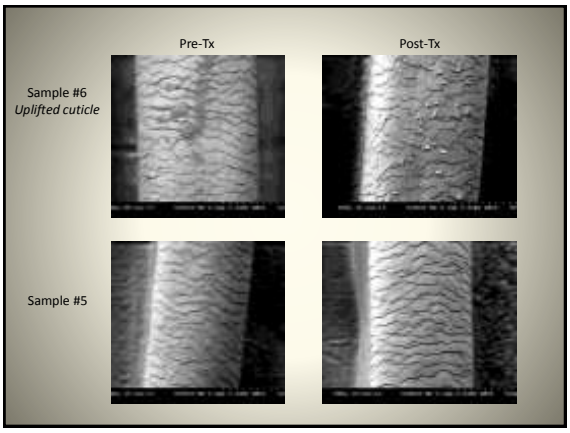
	Non-formalin tx (n=10)	Formalin-based tx (n=8)
Male	2	2
Female	8	6
Age < /=50 yo	7	5
Age > 50 yo	3	3
H/o color processing (dye or highlights)	7	5

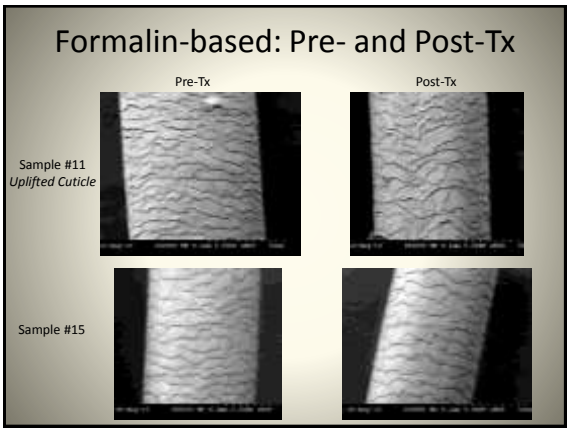
Methods

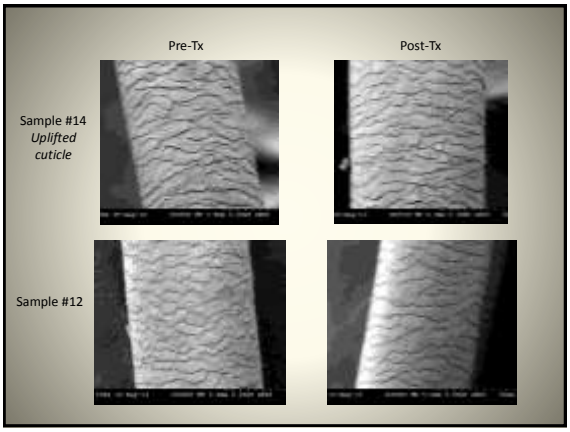
- Hair samples treated to the root according to standard 72-hour procedure
  - Hair washed with tea tree shampoo, dried until slightly damp, keratin treatment applied, dried, flat-ironed at 450° F, allowed to set for 72 hours, samples washed with sulfur-free shampoo, dried
- Samples mounted and sent for analysis
- Mid-shaft examined with scanning electron microscopy
- Statistical analysis performed and images logged

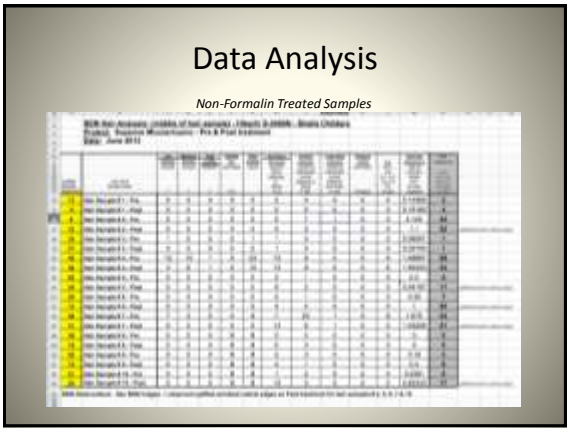
Non-Formalin: Pre- and Post-Tx

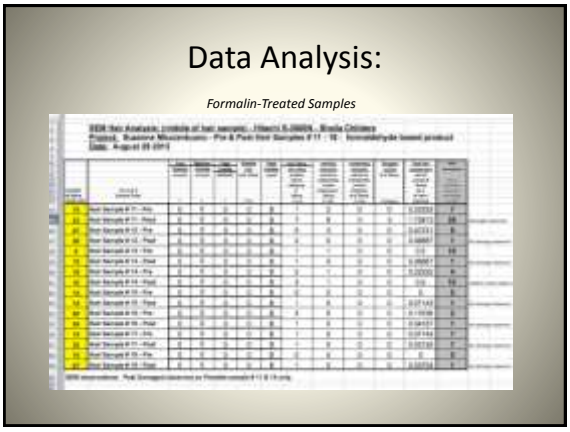












Conclusions

- 50% non-formalin treated samples had statistically more damage; 50% developed uplifted cuticle
- 25% formalin-treated samples had statistically more damage; 25% developed uplifted cuticle

Additional Considerations

- Perhaps keratin treatment prevents further hair damage by eliminating the need for frequent flat-ironing
  - Studies have shown that above 140°C, structural hair damage is profound[1]

[1] *Int J Cosmet Sci*. 1984 Oct;6(5):201-11

BKT Concerns

- Heat-requiring process
- Use of formaldehyde as a preservative

Formaldehyde Concentrations

- Different formula strengths exist
  - Preparations of BKT typically have between 1-4% formalin concentration
- An increased concentration of formalin does not correlate with better or longer lasting results
- Study brand contains 1.8% formaldehyde

What about formaldehyde-free treatments?

- May be misleading
- There has to be some derivative of formalin (methylene glycol) or preservative to bind the keratin to the hair cuticle
- Products claiming to be "formaldehyde free" often contain glutaraldhyde

FDA Regulation

- The Occupational Safety and Health Administration (OSHA) requires manufacturers of products that contain or release formaldehyde to include information about formaldehyde and its hazards on the label and in the Material Safety Data Sheet (MSDS)
- Formaldehyde must be listed if it is in the product at 0.1% or more (as a gas or in solution) or if the product releases formaldehyde above 0.1 parts of formaldehyde per million parts (ppm) of air

Other Side Effects

- Contact dermatitis secondary to formaldehyde exposure
- Telogen effluvium
- Hair breakage following coloring and BKT

Stylist/Client Safety Precautions

- Adequate ventilation
  - "Source-capture" ventilation system
- A passive air-monitoring badge can also be worn and will measure formaldehyde in the air
- At the minimum, gloves and masks should be worn by both the client and stylist

Study Limitations

- Small sample size
- Standardized technique
- More information needed on hair effects (tensile strength)

Thank you!!!!

Dihydroxyacetone: A Safe Alternative to Ultraviolet Tanning?

Mariel Bird, DO, PGY-IV
Oakwood Southshore Medical Center

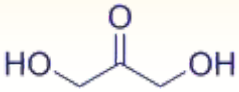
1

http://www.yourdictionary.com/images/definitions/lg/tanning-bed.jpg

2

Dihydroxyacetone (DHA)

- The most common ingredient in sunless tanners
- Three carbon sugar first introduced in the 1920s as a substitute for glocose in the treatment of diabetics.
- Its identification as a tanning agent occurred in the 1950s when it was used in tolerance testing for glycogen storage disease.[1]



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3

- Currently, DHA is the only additive currently approved by the Food and Drug Administration (FDA) for use as a tanning agent.[1]

1. Fu, J., et al. Sunless Tanning. J Am Acad Dermatol 2004;50:706-13.

4

http://www.wingwire.com/app/webroot/files/3_534_1341449484.png

5

Unlike bronzers, which immediately dye the skin and may be removed by washing, DHA works by a non-enzymatic reaction with amino acids in the stratum corneum.[2]

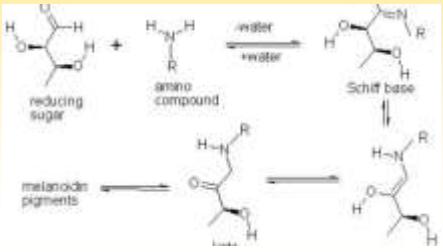
http://3.bp.blogspot.com/_o8/x9oCzsxs7O8/s1600/bronzer_face_apply.gif

2. Levy, S. Dihydroxyacetone-containing sunless or self-tanning lotions. J Am Acad Dermatol 1992;27:989-93.

6

Maillard Reaction

End products are polymers collectively known as MELANOIDINS that impart pigment to the skin.[3]



3. Lloyd, Fong, Sayre. In vivo formation of Maillard Reaction Free Radicals in Mouse Skin. J Invest Dermatol 117:740-2.2001.

7

http://blog.khymos.org/wp-content/2012/05/mff_yeast_bun.jpg

8

DHA – The Basics

- After application, color change can be seen in as little as one hour, with maximal darkening between 8 and 24 hours and disappearance of color over 5 to 7 days.[1,2]
- Desired level of pigmentation can be achieved using successive applications separated by several hours and can be maintained by continued applications every 2 to 4 days.
- Depth of color correlates with thickness of SC and concentration of DHA applied; therefore inability to induce tanning in areas that lack a stratum corneum (mucous membranes).[2]

1. Fu, J., et al. Sunless Tanning. J Am Acad Dermatol 2004;50:706-13.
2.Levy, S. Dihydroxyacetone-containing sunless or self-tanning lotions. J Am Acad Dermatol. 1992;27:989-93

9

Sunless Tanners

- Formulated in self-application lotions and creams; may be aerosolized for professional use.
- Concentration of DHA in professional products is typically 8-14% (>330mM), opposed to over-the-counter agents that range 3-5%.[4]

4. Mogensen, B., et al. Assessment of DHA in self-tanning creams applied in spray booths. National Environmental Research Institute of Denmark. Survey of Chemical substances in consumer products. 72; 2006

10

"Spray Tan"

- Self-tanning spray was introduced to the market in 1999.
- DHA is automatically sprayed onto the customer's body to achieve a more even covering of product than through manual application.
- When DHA is formulated to aerosolize, exposure occurs through skin, eye, and mucous membrane contact, as well as inhalation.[4]

4. Mogensen, B., et al. Assessment of DHA in self-tanning creams applied in spray booths. National Environmental Research Institute of Denmark. Survey of Chemical substances in consumer products. 72; 2006.

11

Manual Turbine Spray

In an open booth, DHA is sprayed onto the customer by an operator.

Disadvantages

- ✧ Total of 2 – 3 minutes to apply to an entire body with a 13 cm spray width.
- ✧ Lotion consumption ≈ 25 mL per trtmt

Advantages:

- ✧ Aerosol/DHA "cloud" is minimal so that the customer and operator have minimal exposure
- ✧ "Hand-crafted" even application

http://www.millenniumtrainingacademy.com/images/ent.JPG

4. Mogensen, B., et al. Assessment of DHA in self-tanning creams applied in spray booths. National Environmental Research Institute of Denmark. Survey of Chemical substances in consumer products. 72; 2006.

12

"Closed" Spray Tan Booth

The customer stands on a metal plate in the booth. The tanning product is electrically charged and sprayed out through nozzles.

Advantages:
- ✧ Privacy
- ✧ Treatment time is seconds
- ✧ Charged aerosol more accuracy and less product used
  - ▪ ≈ 15 mL per treatment

Disadvantages:
- ✧ Thick wet, aerosol mist in the booth
- ✧ Customer comes out wet and must towel off, which can lead to streaking

http://aranthasgourmetbeauty.files.wordpress.com/2012/06/mystic-tan.jpg

4. Mogensen, B., et al. Assessment of DHA in self-tanning creams applied in spray booths. National Environmental Research Institute of Denmark. Survey of Chemical substances in consumer products. 72; 2006.

13

"Open" Spray Tan Booth

- The customer stands in an open booth, and the DHA is sprayed out by moving nozzles.

Advantages:
- ✧ Privacy
- ✧ Treatment time is seconds
- ✧ Even application as if hand-brushed
- ✧ Allows for pre – and post-treatment "add-ons" and a moving heated dryer

Disadvantages:
- ✧ Lotion consumption ≈ 25 mL per treatment.
- ✧ Higher cost to customer.

http://sites.securemgr.com/folder14225/site_images_system/user/versa-spa-graphic-over-islands-two.jpg

4. Mogensen, B., et al. Assessment of DHA in self-tanning creams applied in spray booths. National Environmental Research Institute of Denmark. Survey of Chemical substances in consumer products. 72; 2006.

14

FDA Advisory

- No formal federal or state guidelines have been issued regarding the regulation of commercial establishments that offer sunless tanning booth services.
- FDA approval of the use of DHA is restricted to external application and does not include the eyes, lips or any body surface covered by mucous membranes.
- Special protection for eyes, lips, mucous membranes (including nose filters) are recommended.
- Long term effects of DHA from repeated inhalation have never been examined.[5]

5. http://www.fda.gov/cosmetics/productandingredientsafety/productinformation/ucm134064.htm. Accessed07-09-2012

15

16

17

Factors influencing sunless tanning with dihydroxyacetone

B.-C. NGUYEN AND I.E. KOCHEVAR

I. Occlusion
- Inhibits the development of pigment
- Pigment will appear after removal of occlusion (DHA is not lost or destroyed) and at a higher level of pigmentation.
- High hydration, rather than the absence of oxygen, inhibited color development.[6]

6. Nguyen, BC and Kochevar, IE. Factors influencing sunless tanning with dihydroxyacetone. Br J Dermatol. 2003 Aug; 149(2):332-40.

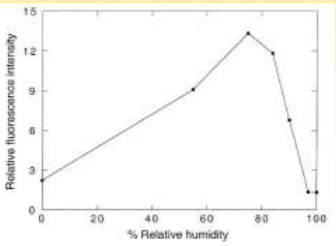
18

Factors influencing sunless tanning with dihydroxyacetone

B.-C.NGUYEN AND I.E.KOCHEVAR

II. Relative Humidity

- At RH < 75%, increased hydration favors pigment formation
- At RH > 75%, hydration decreases pigmentation



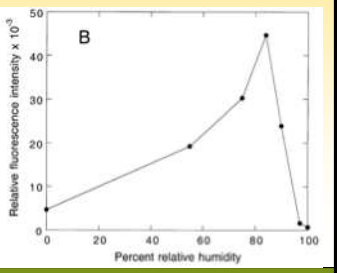
6. Nguyen, BC and Kochevar, IE. Factors influencing sunless tanning with dihydroxyacetone. Br J Dermatol 2003 Aug; 149(2):332-40.

19

Influence of Hydration on Dihydroxyacetone-Induced Pigmentation of Stratum Corneum

Bich-Cac Nguyen and Irene E. Kochevar

- 5% DHA murine epidermis
- Relative Humidity of 0-100%
- Pigment formation assessed by fluorescence
- Similar results found but max RH at 84%



6. Nguyen, B. and Kochevar, I. Influence of Hydration on Dihydroxyacetone-Induced Pigmentation of the Stratum Corneum. J Invest Dermatol 120:655-61, 2003.

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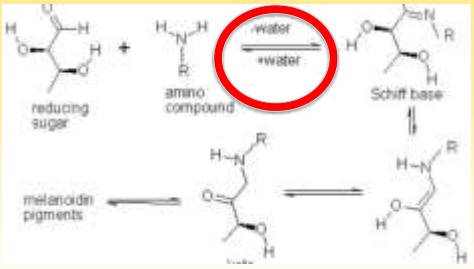


- Water is required to pull a proton off of the amino group to initiate DHA combining with amino acids.
- Optimal is at 75% RH corresponding to 11% water content.

6. Nguyen, BC and Kochevar, IE. Factors influencing sunless tanning with dihydroxyacetone. Br J Dermatol 2003 Aug; 149(2):332-40.

21

- The spray tanning industry takes advantage of this property and uses "post" spray tan hydrating sprays.

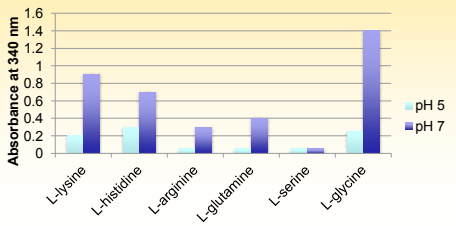
http://www.flawlessbydiane.com/wp-content/uploads/2013/04/hydrating.jpg

22

Factors influencing sunless tanning with dihydroxyacetone

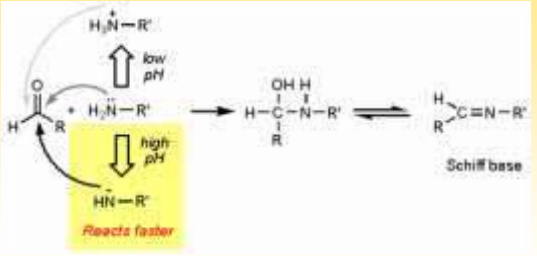
B.-C.NGUYEN AND I.E.KOCHEVAR

III. pH



Adapted from: Factors influencing sunless tanning with dihydroxyacetone. Nguyen, BC and Kochevar, IE. Br J Dermatol 2003 Aug; 149(2):332-40.

23



http://blog.khymos.org/wp-content/2008/09/maillard-first-step.png

24

- The spray tanning industry takes advantage of this property and uses "prep" sprays to prime the skin for DHA application.

http://cdn3.volusion.com/kqck4.kwqw7/v/vspfiles/photos/5010-1.jpg%3F1337252063

25

Photoprotectivity

26

DHA and the Light Spectrum

- DHA has an absorption peak of 270 nm.
- DHA-induced colored compounds absorb light in UVA and visible spectrum, 350-500 nm.
- Visible spectrum is responsible for skin coloration we see.[7]

http://cdn.ldgi.com/wp-content/uploads/ultra-visible.jpg

7. Faurschou, A., et al. Sun protection effect of dihydroxyacetone. Arch Dermatol. 2004; 140:886-7

27

The Use of Dihydroxyacetone for Skin Tanning

- Part I: Sunscreen properties
  - 10 white males; 3 test areas on forearm
    1. 2% DHA lotion
    2. 10% PABA sunscreen
    3. Control

    After 24 hours a 4+ erythema dose UV
- Results
  - Test area #1 develops 2+ - 4+ erythema
  - Test area #2 develops no erythema
  - Control develops no erythema
- Authors conclude DHA is not effective against sunburn.[8]

8. Shaffer, B. et al. The Use of Dihydroxyacetone for Skin Tanning. Arch Dermatol. 1961(83):437-8.

28

- Part II: Effect on melanogenesis
  - 2 white males; 4 test areas on back
  - Daily DHA for 7 days, then daily 4+ MED for 7 days

I: 2% DHA, no UV Brown discoloration No erythema	II: 2% DHA, UV Brown discoloration 4+ erythema
III: No DHA, no UV Normal skin color No erythema	IV: No DHA, UV 4+ erythema

Histologic examination:
Sections I and III found to be normal epidermis.
Sections II and IV consistent with sunburn.

8. Shaffer, B. et al. The Use of Dihydroxyacetone for Skin Tanning. Arch Dermatol. 1961(83):437-8.

29

The Use of Dihydroxyacetone for Skin Tanning

- Authors deem DHA "relatively safe under most circumstances" provided patients are warned that DHA does not offer protection against UV exposure.[8]

8. Shaffer, B. et al. The Use of Dihydroxyacetone for Skin Tanning. Arch Dermatol. 1961(83):437-8.

30

Photoprotectivity

Once daily application of 20% DHA cream for two days provides a SPF of 3 on Day 1.

Durability of SPF decreases linearly over time (loss of 0.2 SPF units/day), for the 5-7 days following application, despite the appearance of tanned skin.[9]

SPF can be increased by multiple applications of higher concentrations of DHA as more UV absorbing products are formed in the skin.

9. Faurschou, A. and Wulf, H.C. Durability of the sun protection factor provided by dihydroxyacetone. Photodermatol Photoimmunol Photomed 2004; 20:239-42.

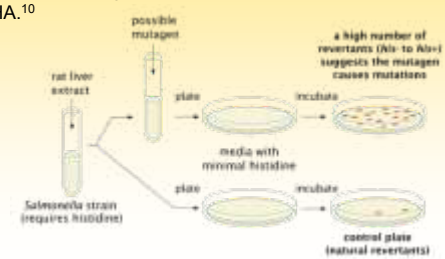
31

Is DHA Carcinogenic?

32

Mutagenesis in bacteria

Pham, et al. first reports Ames test (+) in two OTC tanning lotions containing 3.5% and 7.5% DHA, as well as pure 8% DHA.[10]



http://en.wikipedia.org/wiki/File:Ames_test.svg

10. Pham, H., et al. Mutagenicity of skin tanning lotions. J Environ Pathol Toxicol. 1979 Dec;3(1-2):227-31.

33

Sunless tanning with dihydroxyacetone delays broad-spectrum ultraviolet photocarcinogenesis in hairless mice.
A.B. Petersen et al. Mutation Research 542 (2003);129-38.

- n = 143, female hairless mice divided into 8 groups
- Application of DHA lotion 5% and 20% twice weekly
- 0, 4, or 8 standard erythema dose (SED) broad spectrum radiation
- Endpoints were development of 1st and 3rd skin tumor (>1.0 mm)

34

Group	DHA (%) *Applied 2mg/cm^3 twice weekly	UV dose (SED) *exposed 4 times weekly	UV induced melanin production	1st tumor (weeks)	3rd tumor (weeks)
1	0	0	none	No tumors	No tumors
2	0	4	control	28	30
3	0	8	control	32	32
4	20	0	none	No tumors	No tumors
5	5	4	↔	28	30
6	20		↓↓ (63%)	30	40+
7	5	8	↔	27	37
8	20	8	↓ (28%)	28	32

- 5% DHA at 4 SED and 8 SED was not sufficient to significantly modify UV-induced pigmentation or development of tumors.[11]

11. Petersen, A. et al. Sunless tanning with dihydroxyacetone delays broad-spectrum ultraviolet photocarcinogenesis in hairless mice. Mutation Research 542 (2003);129-38.

35

Group	DHA (%) *Applied 2mg/cm^3 twice weekly	UV dose (SED) *exposed 4 times weekly	UV induced melanin production	1st tumor (weeks)	3rd tumor (weeks)
1	0	0	none	No tumors	No tumors
2	0	4	control	28	30
3	0	8	control	32	32
4	20	0	none	No tumors	No tumors
5	5	4	↔	28	30
6	20	4	↓↓ (63%)	30	40+
7	5	8	↔	27	37
8	20	8	↓ (28%)	28	32

20% DHA at 4 and 8 SED significantly decreased UV induced pigmentation, but only 20% DHA at 4 SED significantly protected against tumor development.

11. Petersen, A. et al. Sunless tanning with dihydroxyacetone delays broad-spectrum ultraviolet photocarcinogenesis in hairless mice. Mutation Research 542 (2003);129-38.

36

- Author's conclude that frequent (twice weekly) topical application of DHA in high concentrations (20%) may delay skin cancer development in hairless mice at moderate UV exposure (4 SED).[Petersen]
- No *in vivo* human studies to date have been done to show effects on photocarcinogenesis.

11. Petersen, A. et al. Sunless tanning with dihydroxyacetone delays broad-spectrum ultraviolet photocarcinogenesis in hairless mice. Mutation Research 542 (2003):129-38.

Any free amino group can be a target for reducing sugars, including nucleic acids found in DNA:

1. Direct DNA Glycation
   - Glycated DNA easily undergoes depurination resulting in the production of potentially mutagenic sites
2. Reactive Oxygen Species (ROS)
   - Directly damage DNA

http://cdn.zmescience.com/wp-content/uploads/2012/04/dna.jpg

Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes

- Influence of DHA on proliferation, survival, and DNA damage in cultured human epidermal keratinocytes.
- Protocol:
  I. Keratinocytes cultured for 3-4 days
  II. Treated with DHA for 1,3 or 24 hours at concentrations ranging 5-100mM
  III. With or without antioxidants
     Tocopherol (vitamin E)
     Desferal (iron chelator)
     Catalase (converts H_2O_2 into H_2O)

12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes

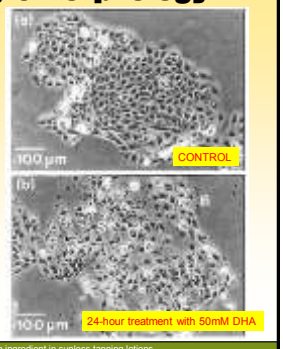
- Measurements of
  - Morphology
  - Keratinocyte viability and colony formation
  - DNA damage
  - Cell cycle arrest

12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

Results: Keratinocyte Morphology

Changes to morphology were dose and time dependent and included:

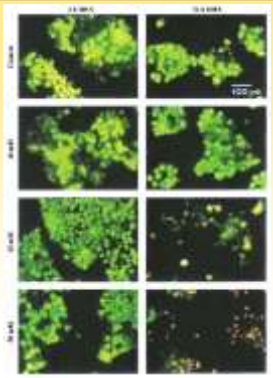
- Chromatin condensation
- Cytoplasmic budding
- Cell detachment from colonies



12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

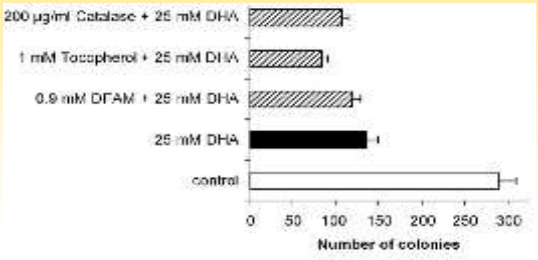
Results: Keratinocyte Viability

- 25 mM and higher DHA diminished the number and size of colonies at 24 hour incubation periods
- Cells did not recover after 2 days



12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

Results: Influence of Antioxidants on Colony Formation

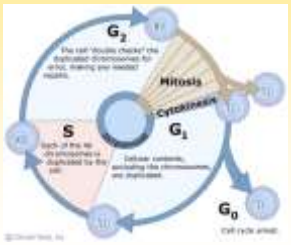


12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions. Induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

Results: DNA Damage & Cell Cycle Arrest

- Cyclin B_1 – indicates the proportion of cells in the G_2/M cycle = measures whether cell block has occurred
- Ki67 – present in proliferating cells = determines survival

- DHA caused a rapid, dose-dependent cell-cycle block in S phase, with a subsequent block in G_2/M phase 1 day after treatment.
  - 50% ↑ of cells in G_2/M
- These effects reversible after a 3 hour DHA treatment, but not after a 24 hour treatment.



http://zebrafish.umdnj.edu/Pre-Enrollment/Resources/Biology/Eukaryotic%20Cell/images/cellcycle.png

12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions. Induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes

- Author's Conclusions:

1. DHA induces DNA damage >> cell-cycle block >> apoptosis if damage is beyond repair capacity of the cells
2. Likely direct redox toxicity of DHA via formation of ROS, as pretreatment with antioxidants did not prevent DNA breaks
3. No direct evidence that DHA induces the same biological effect *in* vivo.

12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, Induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.

CONCISE COMMUNICATION — British Journal of Dermatology

Does it look like melanoma? A pilot study of the effect of sunless tanning on dermoscopy of pigmented skin lesions

J. Dahlén Gyllencreutz,* K. Bergqvist Bastrup† and K. Terstappen‡

- 38 dermoscopic images of pigmented skin lesions (PSLs).
- No lesions considered to be malignant before DHA application were recruited.
- Pictures taken before, one week after daily application of DHA for 4 days, and then 1-2 months after DHA application.
- Evaluation performed by 2 dermatologists experienced in dermoscopy diagnosis.[13]

13. Gyllencreutz, J. et al. Does it look like melanoma? A pilot study of the effect of sunless tanning on dermoscopy of pigmented skin lesions. British J Dermatol. (2013)168:867-70.

CONCISE COMMUNICATION — British Journal of Dermatology

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J. Dahlén Gyllencreutz,* K. Bergqvist Bastrup† and K. Terstappen‡

Results:

- In body nevi, the dermoscopic features included dots and/or globules, but these changes did not change dermoscopic diagnosis and both evaluators recommended follow-up.[13]

13. Gyllencreutz, J. et al. Does it look like melanoma? A pilot study of the effect of sunless tanning on dermoscopy of pigmented skin lesions. British J Dermatol. (2013)168:867-70.

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- However, in facial solar lentigo, equivocal lesions were registered by both evaluators significantly more often after DHA use than before, resulting in recommendation of biopsy.[13]
- (42% vs 12%, P = 0.0210)
- (69% vs 19%, P = 0.001)

13. Gyllencreutz, J. et al. Does it look like melanoma? A pilot study of the effect of sunless tanning on dermoscopy of pigmented skin lesions. British J Dermatol. (2013)168:867-70.

- Asymmetrical follicular pigmentation, mimicking Lentigo Maligna Melanoma
- Fine circles, double circles, and signet-ring-like circles

49 13. Gyllencreutz, J. et al. Does it look like melanoma? A pilot study of the effect of sunless tanning on dermoscopy of pigmented skin lesions. British J Dermatol. (2013)168:867-70.

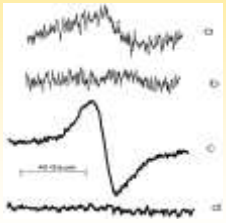
Effects of DHA on Skin Aging

50

In Vivo Formation of Maillard Reaction Free Radicals in Mouse Skin

Roger V. Lloyd, Anna J. Fong, and Robert M. Sayre*

- DHA applied to hairless mouse skin both *in vivo* and *ex* vivo
- Electron spin resonance showed that free radicals are produced only in the treated skin when compared to normal skin controls.[3]



A. Skin treated with DHA in vivo
B. Untreated control skin in vivo
C. Skin treated with DHA ex vivo
D. Untreated control skin ex vivo

51 3. Lloyd, Fong, Sayre. In vivo formation of Maillard Reaction Free Radicals in Mouse Skin. J Invest Dermatol 117:740-2,2001.

UV-generated free radicals (FR) in skin: Their prevention by sunscreens and their induction by self-tanning agents

K. Jung[a,*], M. Seifert[a], Th. Herrling[b], J. Fuchs[c]

- 5%, 10%, 20% DHA or 1%, 3%, 5% Sunscreen applied (contained two UVB, one UVA, and one broadband filter) to porcine skin samples
- UVA and UVB irradiation
- ESR measured after each irradiation
- Radical Sun-protection Factor (RSF)

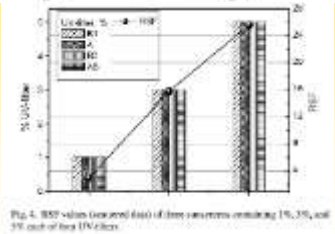
$$= \frac{N(\text{free radicals})_{\text{unprotected}}}{N(\text{free radicals})_{\text{protected}}}$$

RSF > 1 = Diminished UV-induced free radical production
RSF < 1 = Enhanced UV-induced free radical production[14]

52 14. Jung, K., et al. UV-generated free radicals in skin: Their prevention by sunscreens and their induction by self-tanning agents. Spectrochimica. 69;(2008):1423-28.

UV-generated free radicals (FR) in skin: Their prevention by sunscreens and their induction by self-tanning agents

K. Jung[a,*], M. Seifert[a], Th. Herrling[b], J. Fuchs[c]

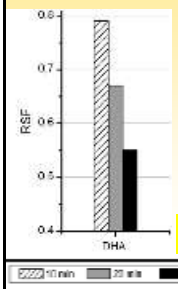


- Direct linear relationship between the % [ ] of sunscreen and RSF
- RSF was always > 1 = Diminished free radical production

53 14. Jung, K., et al. UV-generated free radicals in skin: Their prevention by sunscreens and their induction by self-tanning agents. Spectrochimica. 69;(2008):1423-28.

UV-generated free radicals (FR) in skin: Their prevention by sunscreens and their induction by self-tanning agents

K. Jung[a,*], M. Seifert[a], Th. Herrling[b], J. Fuchs[c]



Concentration (%)	RSF		
	DHA		
	10'	20'	40'
5	0.93	0.95	1.00
10	0.81	0.74	0.64
20	0.79	0.67	0.55

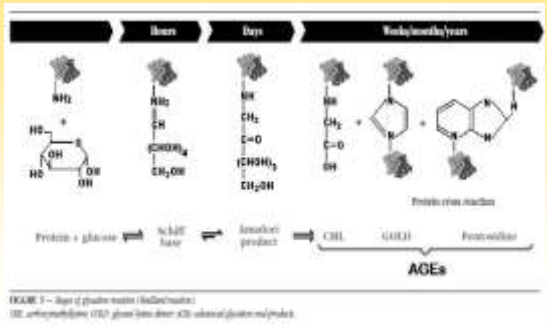
[1] Penetration time (min)

RSF was always < 1 = Enhanced free radical production

54 14. Jung, K., et al. UV-generated free radicals in skin: Their prevention by sunscreens and their induction by self-tanning agents. Spectrochimica. 69;(2008):1423-28.

- After 40 min of penetration time of 20% DHA on the skin, more than 180% of additional free radicals are generated during UV irradiation with respect to untreated skin.[14]
- After application of DHA, one can stay less time in the sun to reach the amount of UV-induced free radicals that are formed in untreated skin.[14]
- In order to avoid a pronounced photoaging process, sun exposure should be avoided during the first 24 hours after the application of DHA.[14,15]

14. Jung, K., et al. UV-generated free radicals in skin: Their prevention by sunscreens and their induction by self-tanning agents. Spectrochimica. 69;(2008):1423-28.
15. Sivamani, R., et al. The benefits and risks of UV tanning and its alternatives: the role of prudent sun exposure. Dermatol Clin. 2009 April;27(2):149-51.



http://www.scielo.br/img/revistas/jbpml/v49n2/a04fig03.jpg

- DHA is a potent glycation and cross linking agent.[16]
- AGE formation is enhanced by higher temperatures (41ºC), pH (8), and DHA concentration.[17]

16. Tessier, F., et al. Triosidines: novel Maillard reaction products and cross-links from the reaction of triose sugars with lysine and arginine residues. Biochem J. (2003) 369, 705-19.
17. Seneviratane, C., et al. In vitro glycation of human serum albumin by dihydroxyacetone and dihydroxyacetone phosphate. Biochem Biophys Research Com. 417(2012):817-23.

http://www.dermalinstitute.com/assets/userfiles/what-causes-skin-aging-page-8.jpg

18. Dyer, D. et al. Accumulation of Maillard Reaction Products in Skin Collagen in Diabetes and Aging. J Invest. 91(june 1993):2463-69.

Prevalence studies on sunless use and behaviors

- What is the prevalence and demographics of sunless tanning users?
- Does the use of sunless tanning products change the amount of sun exposure, sunscreen use, or the frequency of indoor UV tanning use?

- Majority of individuals who use spray-on sunless tanning do NOT alter their sun exposure or sunscreen use; however they decrease their usage of tanning beds.[19]
- 11% of adults in the United States have used some form of sunless tanning agent in the past year; 25% used them >10 times.[20,21]
- Sunless tanning users are more likely to be higher educated females, but have a history of sunburn and tanning bed use.[20,22]

19. Sheehan, D.,Lesher, J. The Effect of Sunless Tanning on Behavior in the Sun: A Pilot Study. South Med J. 2005 Dec;98(12):1192-5
20. Brooks, K., et al. Use of artificial tanning products among young adults. J Am Acad Dermatol 2006;54:1060-6.
21. Buller, D. et al. Prevalence of sunburn, sun protection, and indoor tanning behaviors among Americans: Review from national surveys and case studies of 3 states. J Am Acad Dermatol 2011;65:S114.e1-11.
22. Stryker, J. et al. Prevalence of sunless tanning product use and related behaviors among adults in the United States: Results from a national survey. J Am Acad Dermatol 2007;56:387-90.

- Sunless tanning lotion users may be more likely to ACCENTUATE the tans they receive from the sun or from tanning beds.[20]

20. Brooks, K., et al. Use of artificial tanning products among young adults. J Am Acad Dermatol 2006;54:1060-6.

"Double Dip" Tanning

- Enhancement of UV tan by offering combination package of UV session and then Sunless Spray Tan session successively.

"Cocktail Tanning"

Parting Thoughts

- Sunless tanning products may not have the desired effect of decreasing adverse UV light exposure when attitudes and beliefs about tanning are not addressed.
- Are we sending the wrong message if we encourage sunless tanning???

References

1. Fu, J., et al. Sunless Tanning. J Am Acad Dermatol 2004;50:706-13.
2. Levy, S. Dihydroxyacetone-containing sunless or self-tanning lotions. J Am Acad Dermatol 1992;27:989-93.
3. Lloyd, Fong, Sayre. In vivo formation of Maillard Reaction Free Radicals in Mouse Skin. J Invest Dermatol 117:740-2,2001.
4. Mogensen, B., et al. Assessment of DHA in self-tanning creams applied in spray booths. National Environmental Research Institute of Denmark. Survey of Chemical substances in consumer products. 72; 2006
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12. Petersen, A., et al. Dihydroxyacetone, the active browning ingredient in sunless tanning lotions, Induces DNA damage, cell-cycle block and apoptosis in cultured HaCaT keratinocytes. Mutation Research 560(2004):173-8.
13. Gyllencreutz, J. et al. Does it look like melanoma? A pilot study of the effect of sunless tanning on dermoscopy of pigmented skin lesions. British J Dermatol. (2013)168:867-70.
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15. Sivamani, R., et al. The benefits and risks of UV tanning and its alternatives: the role of prudent sun exposure. Dermatol Clin. 2009 April;27(2):149-51.
16. Tessier, F., et al. Triosidines: novel Maillard reaction products and cross-links from the reaction of triose sugars with lysine and arginine residues. Biochem J. (2003) 369, 705-19.
17. Seneviratane, C., et al. In vitro glycation of human serum albumin by dihydroxyacetone and dihydroxyacetone phosphate. Biochem Biophys Research Com. 417(2012):817-23.
18. Dyer, D. et al. Accumulation of Maillard Reaction Products in Skin Collagen in Diabetes and Aging. J Clin Invest. 91(june 1993):2463-69.
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22. Stryker, J. et al. Prevalence of sunless tanning product use and related behaviors among adults in the United States: Results from a national survey. J Am Acad Dermatol 2007;56:387-90.

Androgenetic Alopecia and the Role of Low Level Laser Therapy

Christina Feser, D.O., PGY-4
Oakwood Southshore Medical Center
Trenton, Michigan

Objectives

1. To discuss the nature, classification, and pathogenesis of androgenetic alopecia (AGA)
2. To discuss the current and prospective treatment modalities for AGA
3. To explain the proposed mechanisms behind the utilization of low level laser therapy (LLLT) in the treatment of AGA
4. To evaluate currently existing LLLT devices
5. To discuss clinical results from a single site, investigator initiated study evaluating the safety and efficacy of the LaserCap® used in the treatment of AGA

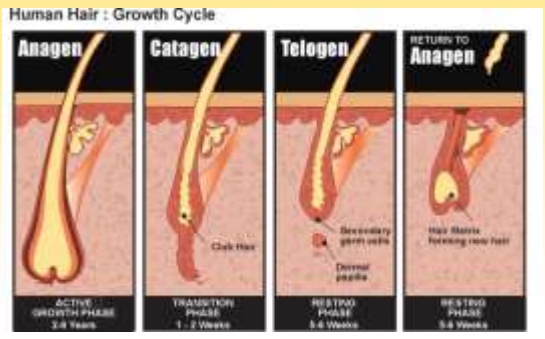
Disclosures

- Clinical research associate in a single site, investigator initiated study to determine the safety and efficacy of the LaserCap® used for the treatment of androgenetic alopecia
- I have no financial interests in the devices to be discussed

Androgenetic Alopecia

- Androgenetic alopecia (AGA) is also known as male or female pattern hair loss
- Characterized by a step-wise miniaturization of the hair follicles from terminal to vellus hairs
- Features dysregulation of the human hair cycle dynamics with progressive shortening of the anagen phase and lengthening of the telogen phase

Paus R, Cotsarelis G. The biology of hair follicles. *N Engl J Med* 1999;341:491-7.



http://www.pacifichairinstitute.com/the-growth-cycle-of-a-human-hair/

Prevalence

Males

- Affects 16% of men between the ages of18 and 29 years
- Affects 54% of men 30 years and older
- In Caucasians estimated to effect:
  - 30% of males in 3rd decade of life
  - 40% of males in 4th decade of life
  - 50% of males in 5th decade of life

Females

- Affects 6-12% of women between the ages of 20 and 30 years
- Affects greater than 55% of women older than 70 years of age

1. Gan DC, Sinclair RD. Prevalence of male and female pattern loss in Maryborough. *J Investig Dermatol Symp Proc* 2005;10(3):184-9.
2. Wang TL, Zhou C, Shen YW, Wang XY, Ding XL, Tian S, *et al.* Prevalence of androgenetic alopecia in China: A community-based study in six cities. *Br J Dermatol* 2010;162:843-7.

Pathogenesis

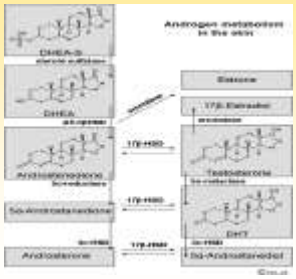
- Genetic Predisposition
  - AD? Polygenic?
  - AR/EDA2R, PAX1/FOXA2 loci
  - *Stu1 polymorphism*
  - HADC9 locus
  - Aromatase, estrogen receptors growth factors, insulin, 5-α reductase
- Hormonal Triggers
- Infectious Agents
  - *Propionibacterium, Staph, Malassezia, Demodex*
- Environmental Factors
  - Chemical irritants
  - Pollutants
  - UVR

Ellis JA, Harrap ST. The genetics of androgenetic alopecia. *Clin Dermatol* 2001;19:149
Brockschmidt FF, Heilmann S, Ellis JA, Eigelshoven S, Hanneken S, Herold C, et al. Susceptibility variants on chromosome 7p21.1 suggest HDAC9 as new candidate gene for male-pattern baldness. *Br J Dermatol* 2011;165:1293-302

Pathogenesis

Sperling, L. Dermatology. 3rd Ed. Alopecias. Spain. Elsevier;2012:987-989

Pathogenesis



Otberg N, Finner AM, Shapiro J. Androgenetic Alopecia. *Endocrinol Metab Clin N Am.* 2007;(36):379-98.

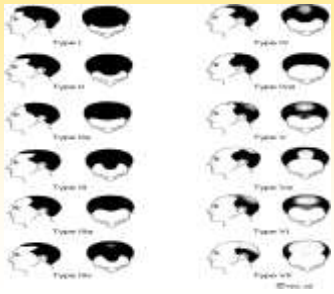
Pathogenesis

Sperling, L. Dermatology. 3rd Ed. Alopecias. Spain. Elsevier;2012:987-989

Diagnosis

- History and Physical Examination
  - Acute or chronic?
  - Systemic illnesses?
  - New medications?
  - Family history?
  - Lifestyle?
  - Hormonal dysfunction?

Norwood-Hamilton Classification



Otberg N, Finner AM, Shapiro J. Androgenetic Alopecia. *Endocrinol Metab Clin N Am.* 2007;(36):379-98.

Ludwig Classification

13 Sperling, L. Dermatology. 3rd Ed. Alopecias. Spain. Elsevier;2012:987-989

Diagnosis

Non-Invasive:
- Hair Pull Tests
- Trichoscopy
- Global Photography
- Trichoscan

Invasive:
- Laboratory evaluations
- Scalp Biopsy
- Trichogram

14 Kaliyadan F, Nambiar A, Vijayaraghavan S. Androgenetic alopecia: An update. *Indian J Dermatol Venereol Leprol* 2013;79:613-25.

Histology

15 Sperling, L. Dermatology. 3rd Ed. Alopecias. Spain. Elsevier;2012:987-989

Disease Associations

- Early-onset coronary artery disease
- Insulin resistance
- Obesity
- Hypertension
- Dyslipidemia
- Prostate cancer

16 Matilainen V, Koskela P, Keinanen-Kiukaanniemi S. Early androgenetic alopecia as a marker of insulin resistance. *Lancet* 2000;356(9236):1165-66.

Treatment Modalities

- Non-Medical
  - Camouflage
  - Hair extensions, wigs, prostheses
- Medical
  - Minoxidil
  - Finasteride
- Surgical
  - Transplantation

17 Camacho FM, Garcia-Hernandez M. Psychological features of androgenetic alopecia. *J Eur Acad Dermatol Venereol. 2002;16(5):476-80.*

Prospective Treatment Modalities

- Supplements
- Prostaglandin analogues
- Antiandrogens
- Corticosteroids
- Botulinum toxin
- Lasers
- Lights

18 Lewy Lauren, Emer, Jason. Female pattern alopecia: current prospectives. *Int J Wom Health*; 2013;5: 541-556.
Bergfeld W, Mesinkovska NA. Hair: What is new in the diagnosis and management? female pattern hair loss update: diagnosis and treatment. *Dermatol Clin* 31(2013):119-127.

Tissue Response to Laser

- High Energy
  - Ablation
  - Fully destructive
  - CO_2 resurfacing laser
- Medium Energy
  - Thermal Effect
  - Direct tissue effect
  - Pulsed dye laser
- Low Energy
  - Photochemical reaction
  - Indirect tissue effect

19

What is Low Level Laser Therapy?

- Red light therapy, cold laser, soft laser, biostimulation, and photobiomodulation
- Therapeutic modality relying upon tissue response to wavelengths in the red and near IR spectrum (650-900nm)
- Potential applications discovered in 1967
- Uses:
  - Reduce neurological disorders and nerve pain
  - Reduce inflammation, edema, and chronic joint pain
  - Promote wound healing

20 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.

Mechanism of Action

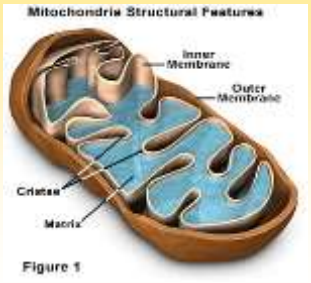
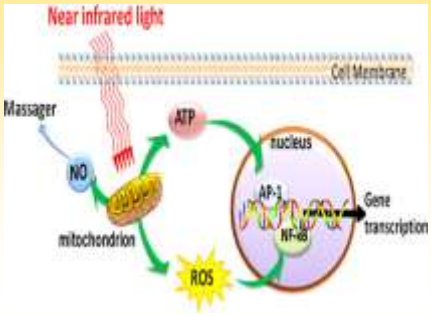


Figure 1

21 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.

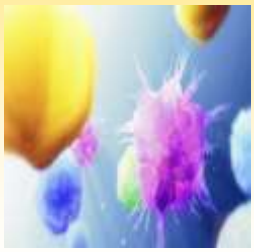
Mechanism of Action



22 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.

LLLT and the Immune System

- Mast cells
- Fibroblasts
- Lymphocytes
- Macrophages



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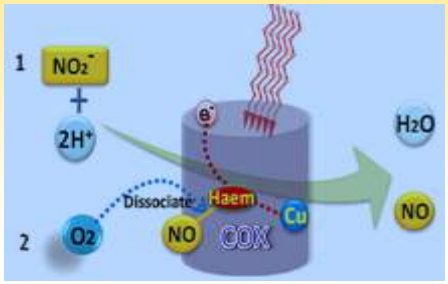
23 Hawkins, D., and H Abrahamse. Biological effects of helium-neon laser irradiation on normal and wounded human skin fibroblasts. *Photomed. Laser Surg. 23:251-259, 2005.*

Mechanism of Action

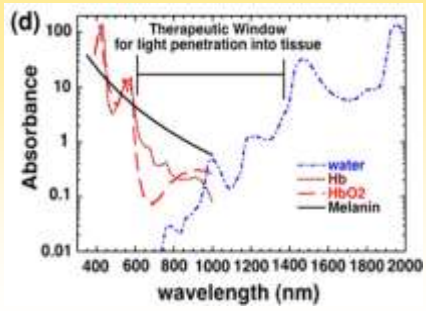


24 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.

Light Sources

- Lasers
  - Coherent light
  - Monochromaticity
  - Helium-neon (HeNe) laser 632.8 nm
  - Gallium arsenide (GaAs) laser
- LEDs
  - Non-coherent light
  - Wide range of wavelengths

25 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.



26 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.

Dosing

- **"The Medicine"**
  - Wavelength
  - Irradiance
  - Pulse structure
  - Coherence
  - Polarization
- **"The Dose"**
  - Energy
  - Energy Density
  - Irradiation Time
  - Treatment Interval

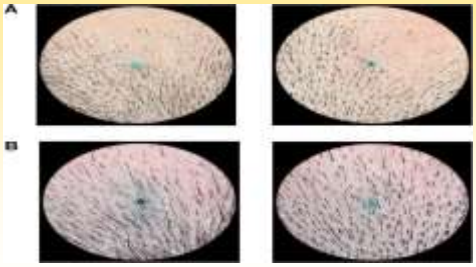
27 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.


The Growth of Human Scalp Hair Mediated by Visible Red Light Laser and LED Sources in Males

"TOPHAT655"

28

Results



29 Lanzafame, RJ, Blanche RR, Bodian AB *et al.* The growth of human scalp hair mediated by visible red light laser and LED source in males. *Lasers in Surg and Med 45:487–495 (2013).*

HairMax LaserComb®

2007

- FDA approved as the first medical laser device marketed for the treatment of MPHL
- Handheld home device
- 655nm
- 9 beams
- Used 3 times weekly
- 15 minutes per use
- Cost: $295-545

30 Hairmax.com. [homepage on the Internet] Boca Raton: Lexington International LLC;2001-2014. Available from http://www.hairmax.com. Accessed January 6, 2014.

ORIGINAL RESEARCH ARTICLE

HairMax LaserComb® Laser Phototherapy Device in the Treatment of Male Androgenetic Alopecia

A Randomized, Double-Blind, Sham Device-Controlled, Multicentre Trial

Matt Leavitt,[1] Glenn Charles,[2] Eugene Heymann[3] and David Michaels[4]

1 Private Dermatology Practice, Midland, Florida, USA
2 Private Hair Transplantation and Restoration Practice, Boca Raton, Florida, USA
3 Biostatistician, Montgomery Village, Maryland, USA
4 Lexington International, LLC, Boca Raton, Florida, USA

 Leavitt M, Charles G, Heymann E, Michaels D. Hairmax LaserComb laser phototherapy device in the treatment of male androgenetic alopecia: a randomized, double-blind, sham device-controlled, multi-centre trial. *Clin Drug Investig.* 2009;29(5):283-292.

No improvement in male-pattern hair loss using laser hair-comb therapy: a 6-month, half-head, assessor-blinded investigation in two men

- Single-site, Investigator initiated 26 week study
- Two male Subjects (aged 32 and 58)
- Split scalp study
- Device used three times weekly
- 7.5 minutes per use
- Unit area and phototrichograms obtained
- No significant difference between treated versus untreated scalp

 Rushton, DH, Gilkes HH, Van Neste DJJ.. No improvement in male pattern hair loss using laser hair-comb therapy: a 6-month, half-head, ass3ssor-blinded investigation in two men. Clin and Exp Derm. *2011 (37) 300-315*

Low-Level Light Therapy for Androgenetic Alopecia: A 24-Week, Randomized, Double-Blind, Sham Device–Controlled Multicenter Trial

Hyeon Kim, MD,[1*] Jae Woong Choi, MD,[2*] Jin Young Kim, MD,[1] Jong Won Shin, MD,[3] Sun-young Lee, MD, PhD,[1] and Chang-Hun Huh, MD, PhD[1]

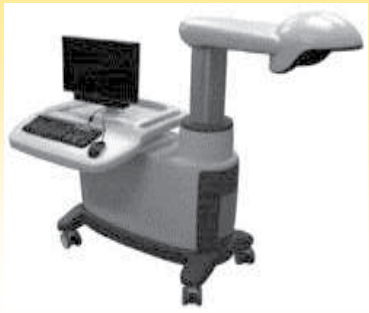
 Kim H, Choi JW, Kim JY, Shin JW, Lee SJ, Huh CH. Low-level light therapy for androgenetic alopecia: a 24-week randomized, double-blind, sham device controlled multicenter trial. *Dermatol Surg.* Epub April 3 2013.

The Oaze®

- 3R Home Device
- 18 minute treatment time
- Total Energy density 92.15 mW/cm^2
- Laser diodes: 650 nm, 27 units, 4.0mW
- LEDs
  - 630 nm, 24 units, 3.5mW
  - 660 nm, 18 units, 2.5mW

Cost: $1000+ online

 Kim H, Choi JW, Kim JY, Shin JW, Lee SJ, Huh CH. Low-level light therapy for androgenetic alopecia: a 24-week randomized, double-blind, sham device controlled multicenter trial. *Dermatol Surg.* Epub April 3 2013.



 Symphonylaser.com. Accessed January 3, 2014.

LaserCap®

2013

- FDA 510k clearance
- 224 LEDs, 5mW
- 650 nm
- 575cm^2 treatment area
- Use two times weekly
- 30 minutes per use
- Cost: $2999.00

 http//:lasercap.us. [homepage on the Internet] Accessed January 3 2014

Study Design

- Single Site, investigator initiated, open-label trial to evaluate the safety and efficacy of the LaserCap® used for the treatment of alopecia
- IRB approved
- Written informed consent obtained from all subjects prior to enrollment
- 8 female subjects enrolled
- Patient population from 19-59 years of age, mean 37 years

37

Protocol

- 26 week trial
- Subjects to use device three times weekly, 30 minutes per use
- Global photography and trichograms obtained on a monthly basis
- Subjective assessment of patient obtained each visit
- **Inclusion:**
  - Male or female 18 years or older
  - Diagnosis of alopecia including pattern hair loss and telogen effluvium
- **Exclusion:**
  - Use of minoxidil, finasteride, anti-androgens, topical estrogens, progesterone, tamoxifen, anabolic steroids, cyclosporine, diazoxide, phenytoin, psoralens, lithium, phenothiazines within six months of enrollment
  - Scarring alopecia
  - Hair transplantation
  - Certain underlying medical conditions which could affect hair growth

38

Results

Patient Details:
- 41 year-old female
- Caucasian
- Long slow history of slow progressive hair loss
- No therapies prior to enrollment

Treatment Protocol:
- LaserCap ® 30 mins every other day
- No topical or oral treatments

Comments:
- Significantly increased density of central part width

39

40

Results

Patient Details:
- 58 year-old female
- Caucasian
- Long slow history of slow progressive hair loss
- No therpaies prior to enrollment

Treatment Protocol:
- Lasercap® every other day
- No topical or oral treatments

Comments:
- Dramatic increase in central scalp density

41

42

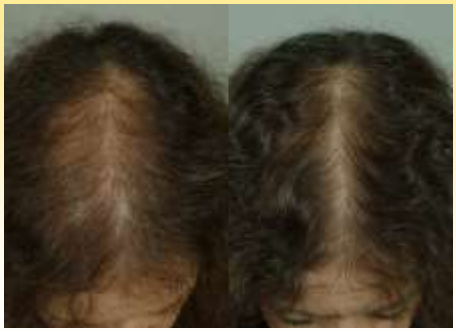
Results

Patient Details:
- 57 year-old female
- Caucasian
- Long slow history of slow progressive hair loss
- Six months post-hair transplantation experienced episode of significant shedding

Treatment Protocol:
- Lasercap ® every other day
- No topical or oral treatments

Comments:
- Dramatic reversal of hair loss
- Increased central scalp density

43



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Results

Patient Details:
- 34 year-old female
- Caucasian
- Long slow history of slow progressive hair loss
- Significant daily shedding
- No therpaies prior to enrollment

Treatment Protocol:
- Lasercap ® every other day
- No topical or oral treatments

Comments:
- Dramatic reversal of daily shedding
- Increased overall density

45

46

The Controversy

- Use is empirical as underlying mechanisms are not fully understood
- Large number of parameters must be chosen for each treatment including the wavelength, fluence, power density, pulse structure, and timing of application

47 Chung H, Dai T, Sharma SK, et al. The nuts and bolts of low-level laser (light) therapy. *Annals of Biomed Engin.* 2012;40(2):516-33.

Conclusion

- Androgenetic alopecia is a common, distressing condition affecting both males and females
- Currently few FDA approved therapies exist
- Low level laser therapy can be considered a safe and effective approach to treatment
- Further studies necessary to determine optimization of wavelength, energy density, and treatment duration

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http://goguiltypleasures.files.wordpress.com/2012/10/bag-o-back-hair.jpg

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Thank You

- Steven Grekin, DO
  - Program Director, Dermatology
  - Oakwood Southshore Medical Center
- Robert Haber, MD
  - Associate Professor of Dermatology,
  - Case Western Reserve University

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Questions?

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Current Methods of Treatment for Facial Acne Scarring

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McLaren/Botsford Hospitals
Pontiac, MI

Objectives

- Define different types of acne scarring
- Provide literature review on medical, surgical, and laser treatment for acne scarring
- Determine the type of treatment best suited for addressing acne scars

Conflicts of Interest

- I have no conflicts of interest to declare.

Scarring

- Scar (n.)
  Fibrous tissue that replaces normal tissue caused by increased tissue formation or loss of tissue.
- Macular scar
  Follicular inflammation limited to the superficial dermis and epidermis resulting in discoloration without loss or gain of tissue.

Classification of Acne Scarring

- Dystrophic
- Macular
- Depressed

Grading of Acne Scarring

- Goodman's Global Scarring Rating

Goodman's Global Scarring System		
Grade	Level	Features
1	Macular	Hyper, hypopigmented
2	Mild	Mild atrophy or hypertrophy, noticeable from 2' distance
3	Moderate	Not easily concealed, noticeable at > 2' distance
4	Severe	Very noticeable and no flattening with stretching of the skin

Pathophysiology

- P. acnes
  - Slowly degraded
- Extent and depth
  - Sloughing may be significant with necrosis of the follicle
  - Rupture of the follicle with complement pathway activation
  - Ongoing inflammation persistently degrades supporting structure
- Post-inflammatory hyperpigmentation
  - Biopsies of comedonal acne exhibit marked inflammation versus acne lesions in whites(ref)

Pathophysiology

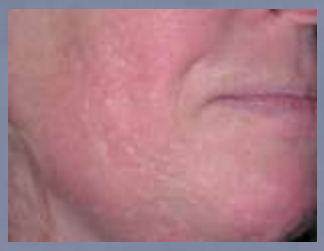
- Transcription factors
  - NFKB and Activator Protein -1 (AP-1) are activated
    - Upregulation of several MMPs
  - Degradation of mature collagen and specific cleavage of type I collagen

Acne Scar Types—Macular Scarring

- Macular
  - Hyperpigmentation in Skin Types IV-VI due to melanin deposition into the papillary dermis
- Post Inflammatory Erythema
  - Skin Types I-III
- Post Inflammatory Hyperpigmentation

Macular Scarring-Post inflammatory erythema

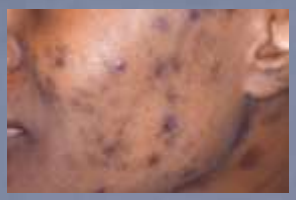
Macular Scarring (Hypopigmentation)



Roxo RF, Sarmento DF, Kawalek AZ, Spencer JM. Successful treatment of a hypochromic scar with manual dermabrasion: case report. Dermatol Surg 2003;29:189–91.

Camirand A, Doucet J. Needle dermabrasion. Aesthetic Plast Surg 1997;21:48–51.

Macular Scarring-Post inflammatory hyperpigmentation



Acne Scar Types—Tissue Loss

- *Icepick (≤ 2mm)*
  - *These have a deep, V-shaped appearance that tend to be < 2 mm in size, and extend into the deep dermis.*
- *Boxcar (2-4 mm)*
  - *Have a uniformly U-shaped appearance with a superficial diameter from 2-4 mm*
- *Rolling (≥ 5mm)*
  - *Large, poorly demarcated depressions*

Treatments of Acne Scarring

- Macular Scarring
- Tissue Loss

Topical Treatments for Macular Scarring

Topical Treatments for Macular Scarring

- Retinoids
  - Tretinoin, Adapalene, Tazarotene
    - May address erythema through downregulation of TLR-2 and AP-1
    - Inhibit tyrosinase and tyrosinase related protein-1 to decrease melanin deposition and increase turnover of melanin-laden keratinocytes
      - Thus may lighten pigmentary changes and ameliorate the appearance, or illusion, of scars.

Topical Treatments for Macular Scarring

- Retinoids
  - Blocking transcription factor AP-1, which activates matrix metalloproteinases, would otherwise degrade collagen. Procollagen I is thus increased in the skin.
  - Increase epidermal thickness
  - Histology confirms collagen I, II, VII deposition

Topical Treatments for Macular Scarring

- Other topicals
  - Azelaic Acid
  - Glycolic Acid Lotion

Stratigos AJ, Katsambas AD. Optimal management of recalcitrant disorders of hyperpigmentation in dark-skinned patients. Am J Clin Dermatol 2004;5:161-8.

Goldman MP. The use of hydroquinone with facial laser resurfacing. J Cutan Laser Ther 2000;2:73-7.

How are we using retinoids in acne scarring?

- #1. We should be addressing the acne *first*.
- #2. In skin types IV-VI, add hydroquinone for 6-12 weeks.
- #3. Reassess.

Chemical Peeling

Chemical Peeling

- What kinds of chemical peels are effective in acne scarring?
  - Salicylic Acid 20-30%
  - Trichloroacetic Acid 25-35%
  - Jessner's Solution 14/14/14%
  - Kojic Acid
  - Glycolic Acid
  - Pyruvic Acid

Chemical Peeling

- Superficial to medium-depth chemical peels
- May be used for *diffuse* or *focal* scarring

Cuce LC, Bertino MC, Scattone L, Birkenhauer MC. Tretinoin peeling. Dermatol Surg 2001;27:12–4.
Wang CM, Huang CL, Hu CT, Chan HL. The effect of glycolic acid on the treatment of acne in Asian skin. Dermatol Surg 1997;23:23–9.

Trichloroacetic Acid

- White inorganic crystalline substance
  - Causes coagulation of epidermal proteins
  - Self-neutralizing

Salicyclic Acid

- Lipophilic B-hydroxy acid
- Causes desquamation without inflammation
- Safe for use on ALL skin types
  - Keratolytic and comedolytic

Studies on Salicylic Acid

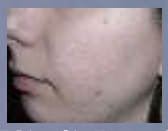
- Salicylic acid peels range in concentration from 20–30%,
  - Performed every 3–4 weeks, total of three to five treatments.

- Kligman D, Kligman AM (1997) Salicylic acid as a peeling agent for the treatment of acne. Cosmetic Dermatol 10 : 44–47
- Grimes PE (1999) The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups. Dermatol Surg 25 : 18–22
- Kligman D and Kligman AM (1988) Salicylic acid peels for the treatment of photoaging. Dermatol Surg 24 : 325–328

Jessner's Solution

- Stratum corneum separation and dermal edema
- Complications are rare due to limited penetration
  - Self-neutralizing

Chemical Peeling

- Salicylic acid 25% followed by TCA 30%. Five peeling sessions were used.

Chemical Peeling

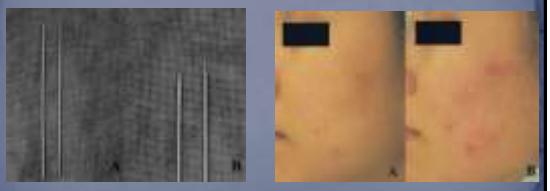

- Before and after four sessions of TCA 30%


- Before and after six salicylic acid 30% peels

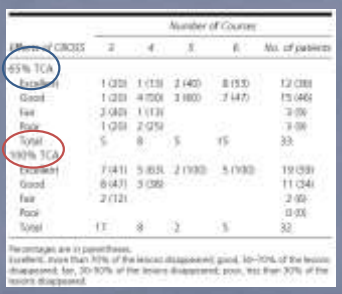
Chemical Peeling for Focal Scarring

C.R.O.S.S. Technique

- Published in 2002.
- Use of highly potent trichloroacetic acid placed within the scar

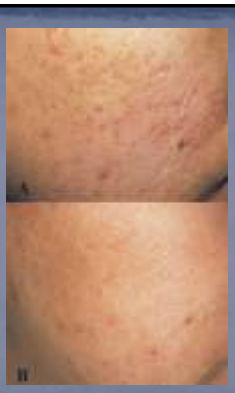


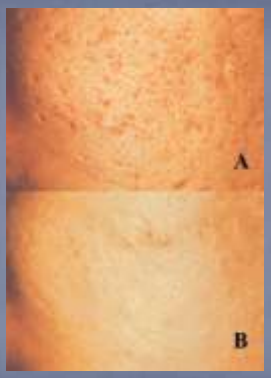
C.R.O.S.S. Technique

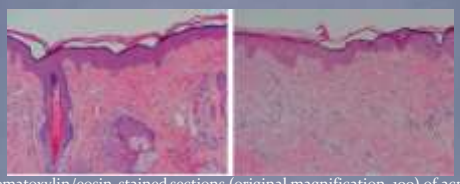


Number of Courses					
Effect of CROSS	2	4	5	6	No. of patients
65% TCA					
Excellent	1 (20)	1 (13)	2 (40)	8 (53)	12 (38)
Good	1 (20)	4 (50)	3 (60)	7 (47)	15 (46)
Fair	2 (40)	1 (13)			3 (9)
Poor	1 (20)	2 (25)			3 (9)
Total	5	8	5	15	33
100% TCA					
Excellent	7 (41)	5 (83)	2 (100)	5 (100)	19 (59)
Good	8 (47)	3 (50)			11 (34)
Fair	2 (12)				2 (6)
Poor					0 (0)
Total	17	8	2	5	32

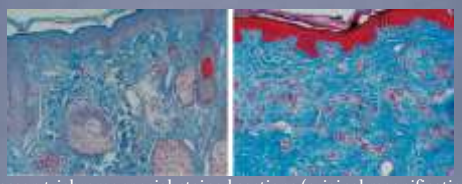
Percentages are in parentheses.
Excellent, more than 90% of the lesions disappeared; good, 50–70% of the lesions disappeared; fair, 30–50% of the lesions disappeared; poor, less than 30% of the lesions disappeared.







Hematoxylin/eosin-stained sections (original magnification, 100) of acne scars before (left) and at 1-year follow-up (right) after therapy with 95% trichloroacetic acid. Note overall increased hyalinization of dermal collagenous tissue, with focal knobby collagen fibers visible in bottom left corner.



Masson trichrome special-stained sections (original magnification, 100) of acne scars before (left) and at 1-year follow-up (right) after therapy with 95% trichloroacetic acid. Note overall increased hyalinization of dermal collagenous tissue (blue).

Surgical Treatments

Surgical Treatment of Focal Acne Scarring

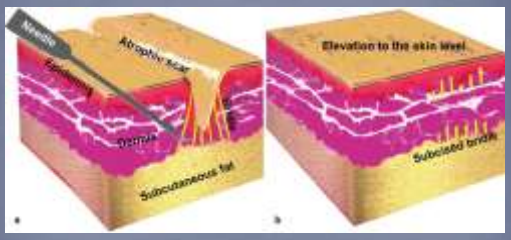
- Icepick Scars
- Boxcar Scars

Subcision

Orentreich DS. Subcutaneous incisionless (subcision) surgery for the correction of depressed scars and wrinkles. Dermatol Surg 1995;21:543–9.

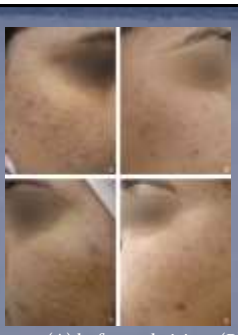
Branson DF. Dermal undermining (scarification) of active rhytids and scars. Enhancing the results of CO_2 laser skin resurfacing. Aesthetic Surg 1998;18:36–7.

Subcision

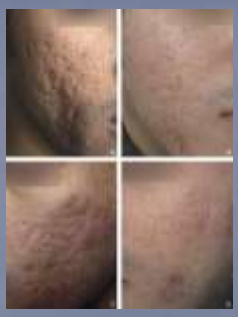


TCA verus Subcision

- Ramadan et al
  - Twenty patients with skin types III-IV
  - 100% TCA versus subcision
  - Results:
    - The mean decrease in size and depth of scars was significantly greater for the subcision side than the 100% TCA CROSS ($p<0.001$). More side effects in the form of pigmentary alteration were observed with the 100% TCA CROSS method.



Rolling acne scars (A) before subcision, (B) 10 months after subcision, (C) before chemical reconstruction of skin scars (CROSS), and (D) 10 months after CROSS.

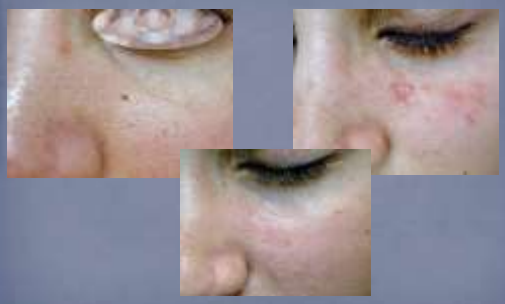


Surgical Techniques

Punch Excision (Icepick Scars)

- Ideally suited for acne scars < 2 mm in diameter
  - 1 mm scars are simply punched, and left to heal by secondary intention
  - 1-2 mm scars may be punched and sutured with 5-0 or 6-0 nylon

Gravelink JM, White VR. Concurrent use of laser skin resurfacing and punch excision in the treatment of facial acne scarring. Dermatol Surg. 1998;24:527–30.
JohnsonW. Treatment of pitted scars: punch transplant technique. J Dermatol Surg Oncol 1986;12:260.

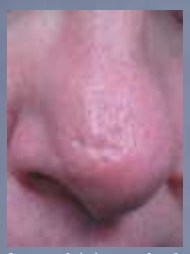
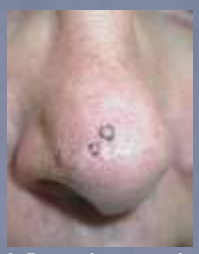


Punch Grafting (Ice Pick Scars)

- Ideally suited for scars < 2mm in diameter
  - Obtained from postauricular skin
  - Donor graft should be 0.5 mm larger than the excision
  - May simply be held in place utilizing Steri-Strips (3M, St. Paul, MN)
  - Six weeks later area may be treated with dermabrasion

Punch Elevation (Boxcar Scars)

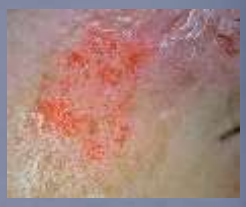
- Optimal scars should have a smooth base and vertical edges
  - A trephine or punch may be used to excise tissue equal in size to the inside diameter of the scar
  - Elevate the tissue slightly higher than the surrounding skin to overcome tissue retraction with healing
  - Place Steri-Strips

Before and (B) 1 week after punch float technique to the nose

Dermabrasion

- One of the original best treatments for acne scarring
- Mechanically removing the epidermis and papillary dermis
  - TGF-B upregulation results in myofibroblastic deposition of Type I and III collagen
  - Altered, thick bundles of parallel collagen

Zisser M, Kaplan B, Moy RL. Surgical pearl: manual dermabrasion. J Am Acad Dermatol 1995;33:105–6.
Harris DR, Noodleman FR. Combining manual dermasanding with low strength trichloroacetic acid to improve actinically injured skin. J Dermatol Surg Oncol 1994;20:436–42.


Needling (Collagen Induction Therapy)

- Mechanism of Action
  - Alteration of the resting potential of the cell from normal -70 mV to -100 mV induces fibroblast migration to injury site
  - Wounding results in the inflammatory phase of wound healing
    - Recruiting PMNs and platelets with FGF, PDGF, TGF-a, TGF-b, connective tissue activating peptide III, and neutrophil activating peptide 2
  - Day 5 after needling, phase 2 begins
    - PMNs are replaced by monocytes which become macrophages and release these growth factors

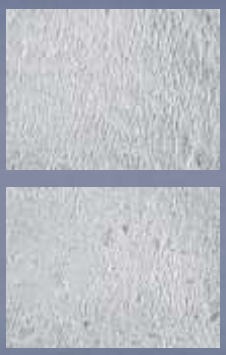
Needling

- Low oxygen tension due to disruption of blood vessels
- Collagen Type I and III are produced
- Collagen III is gradually replaced by Collagen I during remodeling over the next year

Needling

- Study from U. of Naples reported needling 250-300 pricks/cm2
  - Afterwards, wiping with sterile saline

Needling, 1.5 years apart, two procedures



Average reduction of 25% in textural irregularity

Needling versus CROSS

- Leheta et al
- Thirty participants were randomly equally divided into two groups; group 1 underwent four sessions (4 weeks apart) of PCI, and group 2 underwent four sessions (4 weeks apart) of 100% TCA CROSS.
- Results
  - Acne scarring improved in 100% of patients. Scar severity scores improved by a mean of 68.3% (p0.001) in group 1 and a mean of 75.3% (p0.001) in group 2. The difference in the degree of improvement was not statistically significant between the groups (p = .47).

Laser Therapy

Laser Therapy

- CO_2 10,600, Erbium:YAG 2940
  - Collagen heating, remodeling, and increased production
  - Water as the chromophore

CO_2 Laser Therapy

- Anatomic variation
  - Lateral cheek and temple responded less favorably than medial cheek, perioral, and forehead.

Trimas SJ, Boudreaux CE, Metz RD. Carbon dioxide laser abrasion. Is it appropriate for all regions of the face? Arch Facial Plast Surg. 2000 Apr-Jun; 2(2):137-140.

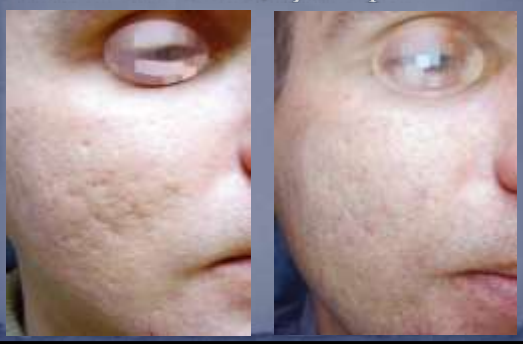
CO_2 Laser Therapy

- Fractional Photothermolysis
  - Noncontiguous microscopic columns of dermal thermal injury
  - Microscopic injury zones contribute to rapid healing
  - Stimulation of normal collagen

CO_2 Laser Therapy

- Geronemus et al reported 17 patients with deep acne scars
  - 25-50% improvement using digital photography
- Alster et al reported 53 patients
  - 51-75% clinical improvement in 90% of patients
- Both studies showed transient erythema and edema

Erbium YAG Laser, 1 year apart



CO_2 Laser Therapy

- Cho et al.
  - 20 patients
    - 76-100% (1)
    - 51-75% (9)
    - 26-50% (7)
    - 0-25% (3)
- Cho et al.
  - 1550-nm non-ablative erbium-glass NAFL with an ablative 10,600nm CO_2 fractional device in southeast Asian patients

CO2 Laser Therapy

- At 3 months after the treatment, the mean grade of improvement based on clinical assessment was 2.070.5 for NAFL and 2.570.8 for AFL.
- On each side treated by NAFL and AFL the mean duration of posttherapy crusting and scaling was 2.3 and 7.4 days respectively and that of post-therapy erythema was 7.5 and 11.5 days respectively.
- The mean VAS pain score was 3.972.0 with NAFL and 7.072.0 with AFL

CO_2 Fractionated Laser Therapy

- Ortiz et al
  - 3 months after treatment, 87% of subjects sustained significant improvement in the appearance of acne scarring
- Chapas et al
  - After 2–3 treatments, patients had 26–50% improvement in texture, atrophy, and overall improvement. Topographic analysis of depths of scar: 43–79.9% (66.8% mean improvement)

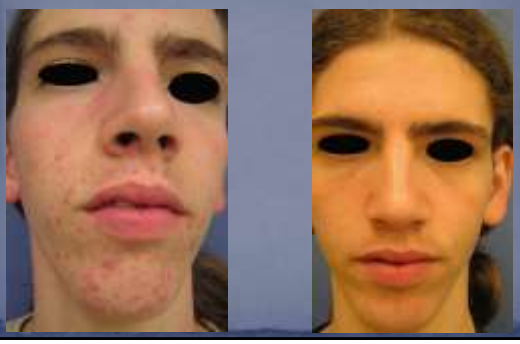
Laser Therapy

- PDL or IPL
- Q-Switched Nd:YAG

Intense Pulsed Light

- 500 to 1200 nm in the visible spectrum
- Red scars, and hypertrophic or keloid scars which often contain telangiectasias may benefit from IPL treatment.
  - The concept is to reduce the number of containing blood vessels (neocapillaries) which can stop the growing process and improve the color.

Intense Pulsed Light



Intense Pulsed Light

- Bellew (Bellew et al. 2005) compared in a side-by-side manner the effect of PDL and IPL on hypertrophic scars after breast reduction and mastopexy.
- After two treatments, improvement was obtained in both groups with no significant differences between them. Erol (Erol et al. 2008) treated with IPL 109 patients with hypertrophic scars after surgeries, trauma, acne and burns. Five patients had keloids. The average number of treatments was eight and they were performed at 2–4 week intervals. Overall clinical improvement was found in 92.5% of the patients, while 65% had good to excellent results.

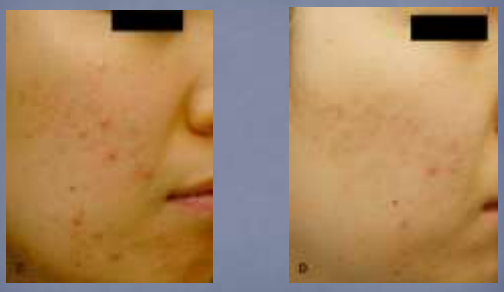
Laser Therapy

- Q-Switched Nd:YAG
  - Penetrates deeply without affecting epidermal pigment

Laser Therapy

- Jung JY et al. JAAD 2012; 66(4):626-633
  - Dual-pulsed Q-switched Nd:YAG
    - Prospective, split-face study in 22 patients
    - Application of a carbon suspension to the face
    - 7 mm spot, 10 Hz, Fluence 1.8-2.0 J/cm2
  - 58% and 52% reduction in inflammatory and non-inflammatory lesions at 4 weeks

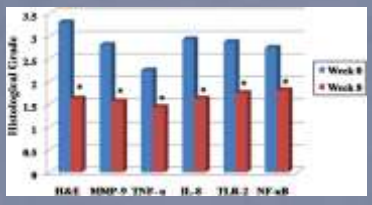
Laser Therapy



Laser Therapy

- Histology studies revealed down-regulation of IL-8, MMP-9, TLR-2, NF-KB, and TNFa (NF-kB is a critical transcription factor for up-regulation of many proinflammatory cytokine genes, and it is activated in inflammatory acne lesions in vivo.20-22) TNF-a and IL-1, which also stimulate the production of secondary cytokines, such as IL-8.
- Increased IL-8 expression, in the skin, has been reported to be significantly associated with epidermal hyperplasia, follicular hyperkeratosis, and acne inflammation.7 AP-1, another important transcription factor associated with inflammation and activation, induces MMP-1, -8, -9,13,23-25 which degrade dermal matrix. P acnes triggers inflammatory cytokine responses in acne by activation of TLR-2.26

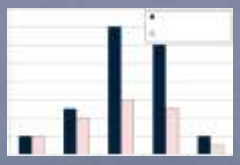
Laser Therapy

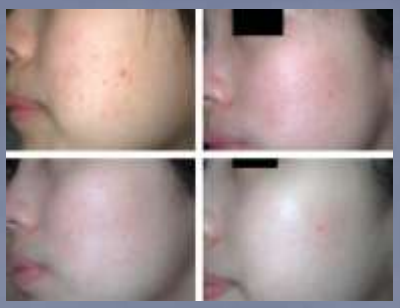


Histopathologic inflammation severity and immunohistochemical staining intensities for nontreated and laser-treated sides at baseline versus 4 weeks after 3 laser treatments. *P<.05 versus baseline.

Laser Therapy with Isotretinoin

- Yoon JH, Eun JP, Kwon IH et al. Journal of Dermatologic Treatment 2014; 25: 142-146
  - Low-dose oral isotretinoin
  - 1550 nm Erbium fractional laser
  - No hypertrophic scarring or keloids





Before, after first, second, and third sessions.

Laser-Assisted Lipolysis

- Liposuction in conjunction with 1064 nm Nd:YAG laser has resulted in improvements in skin tightening.

Soft Tissue Augmentation

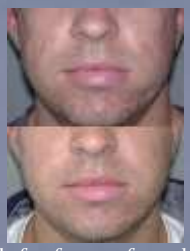
- Hyaluronic acid fillers
- Autologous Fat
- Poly-L-Lactic Acid

Coleman SR. Long-term survival of fat transplants: controlled demonstrations. Aesthetic Plast Surg 1995;19:421–5.

Eppley BL, Snyders RV Jr, Winkelmann T, Delfino JJ. Autologous facial fat transplantation: improved graft maintenance by microbead bioactivation. J Oral Maxillofac Surg 1992;50:477–82.

Pinski KS, Roenigk HH Jr. Autologous fat transplantation: long term follow-up. J Dermatol Surg Oncol 1992;18:179–82.

Coleman SR. The technique of periorbital lipoinfiltration. Oper Tech Plast Reconstr Surg 1994;1:120.



Before and after fat transfer and subcision.

Minimal Incision Facelift

- May be considered an option in addition to other surgical modalities.

Conclusion

- Prevention of acne scarring is always first line therapy.
- Classification of acne scarring simplifies potential possibilities for therapy.
- Many techniques make treatment of acne scarring a viable option for the practitioner.
- Though studies are not robust in some areas, clinical improvement is evident.

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AMERICAN OSTEOPATHIC COLLEGE OF DERMATOLOGY
AOCD
FOUNDED 1958

MID YEAR MEETING
DALLAS, TX
FEBRUARY 23RD, 2014

UNT | HEALTH SCIENCE CENTER

ANDROGENIC ALOPECIA

Ryan Pham, D.O
UNTHSC/TCOM
PGY-4

Epidemiology:

- MOST COMMON CAUSE OF HAIR LOSS.
- Males>Females
  - Usually more severe and earlier onset in males than females
- Up to 70% of men and 40% of women are affected at some point in their lives.
  - Up to 50% of men will have some degree of hair loss by age 50.
  - Up to 65% of women > 65y/o
  - Up to 80% of men > 70 y/o
- Chinese less common than whites, even though Koreans were just as common

Pathophysiology:

- **HORMONAL**: Androgens are among driving force with dihydrotesterone (DHT) being the major player affecting the dermal papillae.
  - Type 1 and 2 5-alpha reductase enzyme (Testosterone→DHT) is present at hair follicles , and is increased in AGA. (H)
  - Decreased levels of sex hormone binding globulin (SHBG), follicle stimulating hormone (FSH), testosterone. (G)
  - "Androgen Paradox" – with age, androgen shift to stimulate hair on the face, but suppress hair growth on temples and vertex. Due to stimulation of IGF-1 on face→growth, while stimlating TFG B1, TGF B2, IL-6 and inhibiting IGF-1 on scalp →catagenic miniurization. (F)
- Decrease functional vitamin D receptors in mice have lead to lack of regeneration of hair follicles. (B)
- Few have lymphocytic microfolliculitis targeting the bulge epithelium along with immunoreactants of basement membrane zone. (C)
- More information has to be elucidated as it has been speculated that prostaglandin D2 and prolactin levels also plays a role in AGA.

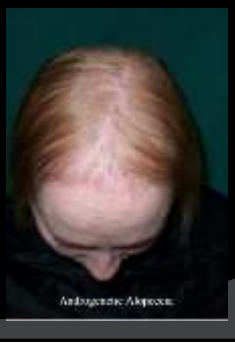
Pathophysiology:

- **GENETICS**: predetermined and is progressive showing conversion from terminal hairs(large thick pigmented) to vellus hairs (short wispy non-pigmented).
  - Normal terminal to vellus ratio is 4:1
  - Physiologic shortening of the anagen phase with telogen phase remaining constant
  - Men with father with androgenetic alopecia (AGA) is 2.5X more likely to have it. (E) Goes back to paternal grandfather as well. One study showed 10x increase if mother is afflicted
  - Major genetic foci, *EDA2R* on x-chromosome close to the androgen receptor gene *(AR)*, *PAX1/FOXA2* on chromosome 20 and *HDAC9* on chromosome 7. (A) *P2RY5* gene on chromosome 3, variants can cause early alopecia or wooly hair

Presentation:

- Patterned Hair Loss
- Areas of involvement will vary between individuals
- Males
  - 1. Gradual recession of the frontal hairline
  - 2. Thinning of temporal areas
  - 3. Vertex balding
- Females
  - 1. Frontal hairline tend the be spared
  - 2. Bitemporal recession but less severe than males
  - 3. Generallized thinning over the crown

Female Patterned Alopecia

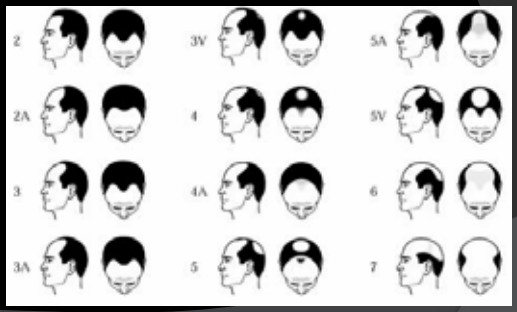


Male Patterned Alopecia

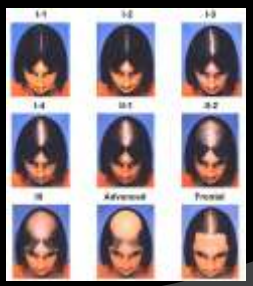
Progression of both Types

- Male
- Female

Norwood/Hamilton Classification Scale



Ludwig /Savin Classification Scale



Diagnosis/Work Up:

- Usually unnecessary as history and physical exam are highly specific and sensitive
- Laboratory Studies: more commonly performed on woman
  - 1. Thyroid studies
  - 2. CBC
  - 3. Testosterone/DHEA-S
  - 4. Fe levels
  - 5. ANA/Anti-Smith
- Trichoscopy – to differentiate among common scalp diseases (alopecia areata, tinea captitis, cicatricial alopecia).
- Biopsy: usually punch biopsy x 2, one vertically sectioned and one horizontally sectioned for pathological examination
- Histology:
  - 1. Miniaturization of hair follicles
  - 2. Increased ratio of telogen to anagen ratio
  - 3. Rarely a superficial, perifollicular infiltrate
  - 4. Perifollicular fibrosis (D)

Psychological Effects:

- Can cause mental distress with lowered self image satisfaction
- Some relates hair for women to represent femininity and attractiveness while in men it represents youth and vitality.

Non-medical Treatments:

- Styling, wigs, hair pieces

Treatments: Topical

- Minoxidil 2 – 5% (Rogaine, Regaine, Avogain, Avacor, Tugain, Mintop, Amexidil, Spectral DNC, Vanarex, Ioniten - oral)
  - Mechanism:
    - contains nitric oxide (NO), also a potassium channel agonist → vasodilation → increased oxygen, blood, growth factors, and nuitrients to hair follicules.
    - Increase telogen phase hairs to shed leading to newer anagen phase hairs
  - Advantages:
    - Mainly topically used
    - is over the counter (OTC)
    - relatively inexpensive
    - Various strengths for men and women.
  - Disadvantages:
    - Must be used indefinitely to maintain hair regrowth. Loss of gain within 30-60 days of discontinuing medicadtion.
    - Not good for large areas of hair loss.
  - Side effects: generally well tolerated. Most commonly irritation to area of applied possibly from the other ingredients (alcohol, propylene glycol). Unwanted hair growth of other areas. As stated before patient could experience further hair loss from increased shedding of telogen phases hairs.

A study has shown that it is safe for women to use men's strength minoxidil 5%. (I)

Treatments: Topical

- Ketoconazole 2% (Nizoral)
  - Mechanism:
    - anti-fungal → reduced scalp microflora → possibly decrease follicular inflammation
    - Androgen receptor blocker → Blocks local synthesis of DHT
- Finasteride Topical
  - Research to create a liposomal system to be able to work topically
  - Such as microemulsions, liquid crystalline

Treatments: Oral

- Finasteride (Propecia, Proscar)
  - Mechanism: 5 alpha-reductase inhibitor (mainly type II) → dec DHT, inc testosterone, estradiol
  - Side Effects: Gynecomastia, erectile dysfunction, and depression.
    - Resolves with discontinuation of medication

Treatments: Oral

- Cimetidine (Tagemet)
- Cyproterone Acetate
  - Synthetic steroidal Anti-androgen and progestin
  - Shown to be effect as 2% minoxidil
  - Risk of thromboembolism similar to oral contraceptaives (OCP's)
- Estrogen
  - Indirect anti-androgen by increasing SHBG → binds more DHT, testosterone
  - Overseas there is topical formulation
- Spironolactone (Aldactone)
  - Selective androgen receptor modulator
  - Increase SHBG that binds DHT→ decrease active androgen
- Flutamide
  - High anti-androgenic properties →chemical castration
    - SE: gynecomastia, lipid profile changes, emotional lability
- Dutasteride (Avodart)
  - Competitive inhibitors of 5-alpha reductase (both types)
  - Side effect mostly sexual dysfunction

Treatment: Procedural

- Hair Transplantation – grafts are harvested from follicular units in area of the scalp that is not influence by hormone such as the occipital and posterior temporal scalp.
  - Follicular Unit Transplantation – strip of skin is excised from the patient's scalp then using a stereoscopic microscope, follicular units are dissected individually. The wound is repaired with primary closure.
  - Follicular Unit Extraction – Individual follicular units are extracted straight from the donor scalp using small (0.8-1mm) punches to harvest.
- Scalp Reduction

Follicular Unit Extraction: Pearls

- Occipital scalp hairs are considered permanent and unaffected in AA that will last a lifetime. (L)
- The donor site has to be delineated carefully, as it should only include only permanent hairs that will not be prone to influences of androgenic hormones. (J) The reason for this is to not deplete an area that is at risk of further hair loss and transplant donor hairs that will eventually miniaturize over time. (K)
  - Boundaries of the occipital zone include the vertex superiorly, the neck line inferiorly, and the temporal scalp anteriorly.
- The posterior temporal scalp may also display the same permanent behavior that is not subject to hormonal influence as well.
- Once the donor area is marked, it is of utmost importance to not extract more than 50% of the density of the donor area, causing over thinning of the area (iatrogenic alopecia).

Follicular Unit Extraction: Pearls

- There are a few independent factors that can produce variable results from person to person even with identical area and number of donor grafts and recipient sites.
  - Patients with curly hair will have a fuller appearance than straight hair; as curly hairs intrinsically cover more visual areas horizontally.
  - Contrasting colors of the scalp and hair plays a role as well. Balding patients with blonde hair and fair complexion or black hair and dark complexion will not be visibly noticeable as compared to any individual with different shades.
  - Certain ethnicities, such as Middle Eastern, South Asians, and Hispanics, naturally have thicker hairs and more hairs per follicular unit on average than others; while the average hair density for a Caucasian person is anywhere from 80 -120 follicular units per cm2, which is significantly higher than Asians and African Americans.

FUT vs. FUE

Technique	Advantages	Disadvantages
Follicular Unit Transplantation	- Optimal extraction of grafts from central portion of hormone independent follicular units.	-A large linear scar from donor area → harder for patient to wear hair short. - More down town to recover from procedure - Scalp tightness
Follicular Unit Extraction	- No linear incision → less scarring, quicker recovery. - Patient can wear hair shorter to minimally noticeable scarring. -Can be used to treat previous occipital scarring from FUT -Less invasive, less nerve damage, less bleeding, from reduced damage to occipital and temporal blood vessels	- Increase risk of follicular transection. - Possibly require multiple sessions.

Follicular Unit Transplantation

Follicular Unit Extraction

Follicular Unit Recipient Sites

Follicular Unit Extraction

NEOGRAFT

Proposed Algorithm for FUE

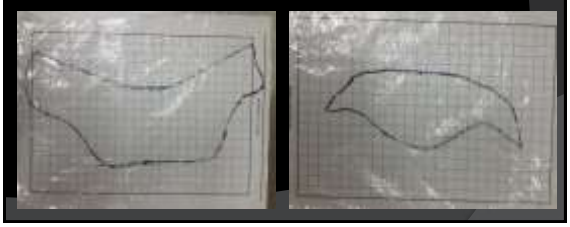
- *Available donor grafts = (patient's donor hair density x 0.5) x total donor area*
- *Ideal recipient grafts needed = [(Patient's donor hair density x 0.5) - patient's recipient hair density] x total recipient area*
- Then comparing these two values, will yield these possible outcomes:
  - *If available donor grafts > ideal recipient total → Most likely the procedure will achieve cosmetic result in both the density and area desired.*
  - *If available donor grafts = ideal recipient total → Likely the procedure will achieve ideal results or slightly less then what was planned.*
  - *If available donor grafts < ideal recipient total → Most likely will not be able to achieve cosmetic result. To mitigate this either the entire total alopecia area will have thinner density than desired, or the density can be achieved in only a limited area than the total alopecia area.*

Calculating Donor Avaliablity for FUE

Densisometer

Donor site

Recipient site



Other Experimental Treatments:

- HIF-1 – helps prevents apoptosis in hypoxic conditions. Transfected fibroblast cells when administered to hair follicles → inc VEGF → inc blood vessel growth → inc nutrients and other growth factors → inc hair growth
  - Topical ciclopirox – typically used for anti-fungal properties but have been shown to increase HIF-1
- IGF-1 – topically used in experimental mice showing thicker and more rapid hair growth.
- Prostaglandin D2 – found to be higher concentration in balding scalp.
- WNT protein – research is being done to use this signaling pathway to regenerate hair follicles by reawakening genes from embryonic development.
- Laser Therapy – some evidence that light certain wavelengths can stimulate hair growth

Treatment advantages and disadvantages

Treament Type:	Advantages	Disadvantages
Non Medical (wigs, hair pieces)	Low to no side effects	Appears noticeably unnatural
Topical	Relatively safe side effect profile	Needs to have constant maintenance therapy for continued results. Often requires multiple topicals at once.
Oral	Easier application so possibly higher compliance with therapy.	Higher side effect profile versus other modalities. Cost of medication. Often have to be used in conjunction with topical medications.
Procedural	Permanent effects. Rebuild hair line with naturally appearing follicular units	High initial cost. Possibly require multiple sessions. Is most invasive of options.

Oral Lesions: The Good, The Bad & The Ugly

Tang D. Le, D.O.
South Texas Dermatology Residency
February 2014

Disclaimer

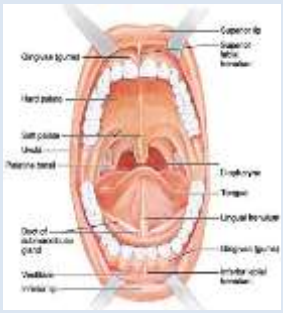
- No conflict with any financial groups regarding the material discussed in the presentation

Objectives

- Review the common oral lesions: clinical finding, etiology, prognosis and treatment option

The Good	The Bad	The Ugly
Foliate Papillae	Aphthous stomatitis	Squamous cell carcinoma
Fordyce granules	Lichen Planus	Verrucous carcinoma
Torus palatinus/Mandibularis	Candidiasis	Pyostomatitis vegetans
Irritation fibroma	Pyogenic granuloma	Melanoma
Mucocele	Nicotinic stomatitis	AIDS Hairy Leukoplakia

Normal Oral Anatomy

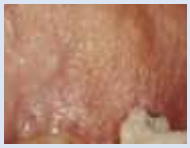


Foliate Papillae

- An area of vertical folds and grooves located on the extreme posterior-lateral surface of tongue
- The long axis is "up and down" at the right angle to the long axis of the tongue
- Usually bilaterally symmetrical
- Etiology:
  - Normal anatomical variant
- Prognosis:
  - Good
- Treatment:
  - None required
  - Reassurance

Fordyce Granules

- Flat or elevated yellow plaques just beneath the mucosal surface
- Eighty percent of the population are affected
- Reaching maximum numbers at puberty
- Etiology:
  - Ectopic sebaceous glands
  - Normal anatomical variant
- Prognosis:
  - Good
- Treatment:
  - None required
  - Reassurance



Torus Palatinus/Mandibularis

- Bony exostoses in the midline of the hard palate and on the lingual aspect of the mandible
- Start in childhood and reach peak incidence in young adults, eventually stop growing
- Torus palatinus occur in 20-35% of the population; and torus mandibularis occur in 10% of population
- Etiology:
  - Developmental over-growths of normal bone
- Prognosis:
  - Good
- Treatment:
  - Reassurance
  - Excision if symptomatic

Irritation Fibroma

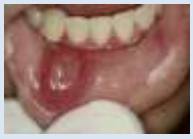
- Dome-shaped soft tissue mass usually found on buccal mucosa along the line of occlusion
- Same color as the surrounding mucosa
- Patients are generally aware of the lesion being present from months to years with little change
- Etiology:
  - Trauma to the affected mucosa
- Prognosis:
  - Good
- Treatment:
  - Reassurance
  - Excision if symptomatic

Mucocele

- Collection of saliva in the oral mucosa
- Soft elevations whose color ranges from normal mucosa to light blue or even white
- The lesion gets "larger, then smaller, then larger"
- The mucosa of the lower lip and buccal mucosa are the most common sites
- Etiology:
  - Traumatic severance of salivary ducts permitting saliva escape into mucosa
- Prognosis:
  - Good
- Treatment:
  - Surgical excision deep enough to include the underlying gland that feeds it

Aphthous Stomatitis

- Painful ulcers ranging in size from less than 1 mm to 2 cm, single or multiple
- Begins as a red macular, ulcerates and then covered by a pyogenic membrane producing the characteristic yellow-white center with surrounding erythematous flare
- Occurs on freely movable mucosa
- Common sites: lips, cheeks, soft palate, floor of mouth, ventral and lateral tongue
- Affect all age groups but more common in young adults and females



Aphthous Stomatitis

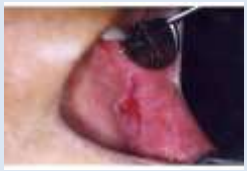
- Etiology:
  - Too many theories: bacterial, viral, immunopathology, hormone
- Prognosis:
  - Healing time varies from 4 days to months
  - Major aphthae may also cause scarring
- Treatment:
  - Reduce pain: Orobase with benzocaine, Zilactin
  - Anti-inflammatory agents: topical steroids or Aphthasol
  - Systemic prednisone for severe or widespread disease

Lichen Planus

- Reticular pattern:
  - Lacy, white lines
- Erosive pattern:
  - Most common form of mucosal lichen planus
  - Small risk of SCC within long standing lesions
  - Associated with liver disease (HCV)
- Early lesions appear as purple, maculopapular pruritic lesions then ulcerate

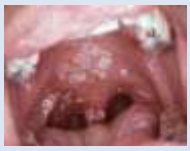
Lichen Planus

- Etiology:
  - Immune mediated disease but target antigen is yet to be identified
  - Iatrogenic: amalgam, semiprecious metals, gold, drugs
- Prognosis:
  - May last for years but few spontaneous remission
  - Predispose the patient to oral cancer at about 1%
- Treatment:
  - Topical steroid for symptom relief
  - Systemic prednisone for widespread, severe disease
  - Topical tretinoin, cyclosporin, and tacrolimus



Candidiasis

- Loosely adherent white patches or plaques on the mucosal surfaces
- Severity of infection varies from small localized areas to generalized stomatitis
- Candida may also presents as red lesions as erythematous candidiasis
- Etiology:
  - Candida organism
  - Common in:
    - Very young population
    - Very old population
    - Population with xerostomia
    - Long term antibiotic therapy
    - Immunosuppressed patients
    - Undergoing systemic chemotherapy or radiation to neck and head



Candidiasis

- Prognosis:
  - Good
- Treatment:
  - Mouthwash of nystatin oral suspension 400000 to 600000 units four times daily for at least one week
  - Fluconazole tablet is often used

Pyogenic Granuloma

- Red, nodular overgrowth of granulation tissue that arises from the mucosal or skin surface
- Two third of oral lesions are found on the gingival > lips > tongue > buccal mucosa
- Females are more often affected, especially during pregnancy
- Bleed easily and some cause mild pain
- Etiology:
  - Mild trauma and infections are prominently mentioned

Pyogenic Granuloma

- Prognosis:
  - Good
  - May reccur
- Treatment:
  - Conservative excision

Nicotine Stomatitis

- Numerous, slightly raised, white, papular lesions of the posterior hard palate and soft palate
- Central portion of the papules are red and represent inflamed orifices of minor salivary gland ducts
- In more severe cases, the palatal mucosa is white and criss-crossed by fissures
- Etiology:
  - Smoking, chiefly pipe and cigar
  - Scalding hot tea and soup

Nicotine Stomatitis

- Prognosis:
  - Usually disappears after discontinuance of the causative factor
- Treatment:
  - Biopsy is needed if persistent or symptomatic

Squamous Cell Carcinoma

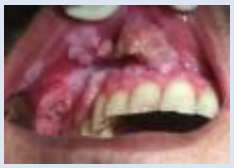
- Early carcinoma may clinically appear as leukoplakia or erythroplakia or both
- 90% of all oral cancers are squamous cell type
- Incidence rate of approximately 8 cases per 100000 persons
- It is about three times as common in men as in women
- The tongue and floor of the mouth are the most common areas
- Etiology:
  - Smoking and alcohol are risk factors
  - Human papilloma virus
  - Mutations that control the cell cycle, protooncogenes and tumor suppressor genes

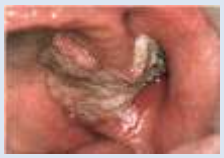
Squamous Cell Carcinoma

- Prognosis:
  - Overall five year survival rate is about 50%
  - Early diagnosis increases the chance of survival
  - Biopsy is needed for all oral ulceration lasting more than 2-3 weeks
- Treatment:
  - Surgical excision and possible radiation
  - Chemotherapy is adjunctive at this time

Verrucous Carcinoma

- White, fungating, cauliflower-like mass, generally several centimeters in size
- Commonly in older patients in seventh decade of life
- High destruction of underlying bone and other structures on a broad advancing front
- Etiology:
  - HPV type 16 and 18
  - Strongly associated with the use of smokeless tobacco or cigarettes



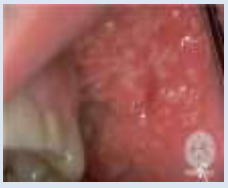


Verrucous Carcinoma

- Prognosis:
  - High recurrence rate up to 30%
- Treatment:
  - Surgical excision
  - Chemotherapy
  - Some controversy exists regarding the use of radiotherapy as primary treatment because of the risk of anaplastic transformation and metastasis
    - Ferlito A, Rinaldo A, Mannara (1998) reported that this modality of treatment controls disease in only 43% of cases and leads to anaplastic transformation in about 7% of cases with 100% mortality

Pyostomatitis Vegetans

- Shallow ulcers and erosions, miliary abscess and pustules that coalesce to form "snail track lesions"
- These develop within an erythematous mucosa in which vegetations may be a feature
- Men are twice as commonly affected as women
- Etiology:
  - Ulcerative colitis – 70%
  - Crohn's disease – 10 – 15%
  - Liver disease – 25%



Pyostomatitis Vegetans

- Prognosis:
  - Improve with treatment of underlying cause
- Treatment:
  - Symptomatic treatment
  - Treating underlying cause

Melanoma

- Primary mucosal melanoma is rare disease but is a biologically aggressive neoplasm
- Accounts for 1.3% of cutaneous melanoma and 0.03% of all new cancer diagnosis
- Peak age is between 70 – 79 years, slightly male predominant
- Hard palate and maxillary alveolus are common site of involvement
- Ill-defined pigmented lesion but 1/3 of oral melanomas are amelanotic
- Vast majority of patients lack early symptoms => delayed in diagnosis

Melanoma

- Etiology:
  - Oral mucosal melanoma is not yet fully elucidated
- Prognosis:
  - Most mucosal melanoma are diagnosed at advanced stage with a Breslow depth greater than 4 mm
  - 5-year survivors are less than 5%
- Treatment:
  - Surgical excision with sentinel lymph node dissection
  - Multitude of adjuvant treatments: chemotherapy, radiotherapy

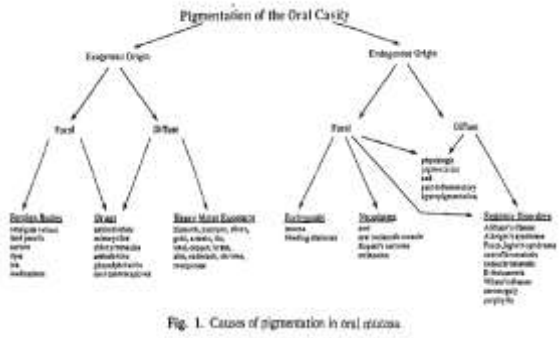


Fig. 1. Causes of pigmentation in oral mucosa

Adapted from: Eisen D, Voorhees J: Oral melanoma and other pigmented lesions of oral cavity. JAAD 1991; 24:527-37

AIDS Hairy Leukoplakia

- This variety of leukoplakia was first recognized in HIV-infected patients
- Lateral tongue is most common location
- Lesions are rough texture, adherent and asymptomatic
- Etiology:
  - Immunocompromised patients
  - Epstein-Barr herpesvirus

AIDS Hairy Leukoplakia

- Prognosis:
  - Improve with antiviral therapy
- Treatment:
  - Antifungal therapy first. If fail to resolve, biopsy
  - Treat the underlying cause: anti viral therapy

Conclusion

- Oral mucosal is not usually examined during dermatologic visit. Therefore, I hope this presentation will bring some awareness on the normal, normal variants, and pathological conditions to the audiences.

References

- 1. McKee P, Calonje E, and Granter S: *Pathology of Skin with Clinical Correlation* Volume 1, 385 – 472
- 2. Dunlap C, Barker B: *A Guide to Common Oral Lesions* 1 -46
- 3. Ferlio A, Rinaldo A, Mannara: Is primary radiotherapy an appropriate option for the treatment of verrucous carcinoma of the head and neck? *Journal of Laryngol Otol*, 112, 132-139
- 4. Eisen D, Voorhees J: Oral melanoma and other pigmented lesions of oral cavity. JAAD 1991; 24:527-37
- 5. Patrick R, Fenske N, Messina J: Primary Mucosal Melanoma, JAAD 2007, 56:828-34.

Thank You

Sunday, February 23, 2014
(4 CME)

7:30 a.m. to 8:00 a.m.	Breakfast
8:00 a.m. to 9:00 a.m.	*Safety and Continuous Improvement in Dermatology* **Kelly Nelson, MD**
9:00 a.m. to 10:00 a.m.	*Update on the Appropriate Use Criteria for Mohs Micrographic Surgery* **Rene Bermudez, DO, FAOCD**
10:00 a.m. to 11:00 a.m.	*Update on Cutaneous Lymphomas* **Scott Wickless, DO, FAOCD**
11:00 a.m. to 12:00 p.m.	*Pitfalls in Personal Finance and Investing* **James Dahle, MD**
12:00 p.m.	End of Meeting

8 Pearls in Personal Finance and Investing

James M. Dahle, MD, FACEP

AOCD Mid Year Meeting

February 22, 2014

- How I Got Started
- Disclosures/Conflicts of Interest
- Disclaimer

An Important Caveat

- Money Doesn't Bring Happiness (at least beyond $75K)
- You didn't go into medicine primarily for the money and neither did I
- Ignore money at your own peril

8 Pearls

- 1) You have a second job
- 2) Four ways to eliminate student loans
- 3) Get good advice at a fair price
- 4) Buy the right insurance
- 5) No one has a crystal ball
- 6) Your biggest tax break
- 7) The safe withdrawal rate
- 8) The good news of physician retirement

Your Second Job

- Med School/Residency makes you a clinical expert
- No business training
- No personal financial or investment training
- Being a Pension Manager in a 401K World
- Family CFO
- Not automatic

Pearl 1 You Have A Second Job

Your Second Job

- You must spend time learning about finances/business
  - Continuing financial education
    - Follow a blog or two
    - Read a financial book each year – The $2M Book
  - Hire professionals to teach you, not just do it for you
- You must also spend the time to take care of your finances/business
  - You cannot be "100% clinical" and be financially successful

Student Loans Suck

- Started Med School in 1999- Tuition was $10K per year
- Mean debt in 1999 was $117K (2011 dollars) vs $161K in 2011. $300-$450K is becoming more common
- No more subsidized loans starting 2012
- No more consolidating at lower rates
- Radiologist next door- 0.9% student loans
- Current resident loans? 6.8%-9%

Student Loans Suck

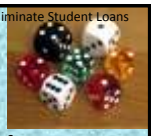
- Monthly payment on $117K at 0.9% = $1020.
- Monthly payment on $300K at 7.5% = $3561
- That's $2500 a month (after-tax) that you cannot spend or put toward retirement. On a $300K salary, that's 10% of your income going toward student loans that wouldn't have a decade ago.
- It's only getting worse

1 IBR + PSLF

- But at least you have IBR and PSLF
- IBR- Payments limited to 10-15%* of discretionary income (AGI minus 150% of poverty line)- typically ~$10K per year, or around $130 a month.
- Subsidized interest forgiven, unsubsidized tacked on
- Payments have no relationship to amount owed

*(10% for new borrowers as of 2008 who take out a loan in 2012 or later)

1 IBR and PSLF



- PSLF- A Roll Of The Dice
- Possible to get hundreds of thousands forgiven, but many docs will have little to none forgiven
- If no IBR, there will be nothing left to forgive
- Key is to make IBR payments for a long time- long residency, fellowship, and then a low income
- Must work for a 501(c)3 or the government for all 10 years
- Government may change the program
- Decide at residency graduation

2 Live Like A Resident

- The secret to becoming the rich doctor everyone thinks you are
- Don't grow into your income all at once
- If income goes from $50K to $250K, increase your lifestyle from $50K to $75K, pay $50K in taxes, and use the other $125K to build wealth
  - Pay off loans
  - Max out retirement accounts
  - Save up a down payment
- With in 5-10 years you can have student loans paid off, be living in your dream house, and be a millionaire.

3 Student Loan Refinancing

- Refinancing now possible again
- Darien Rowayton Bank
  - 4.75% fixed, 2.99% variable
- SoFi
  - 4.99% fixed, 2.91% variable
- Refinanced loans not eligible for PSLF

4 Reduce Cost Of Loan

- Refinance your house
- Student loans
  - High rates
  - Not deductible
  - Not dischargeable in bankruptcy
- Mortgage
  - Low rates
  - Usually fully deductible for doctors
  - Usually dischargeable in bankruptcy/foreclosure

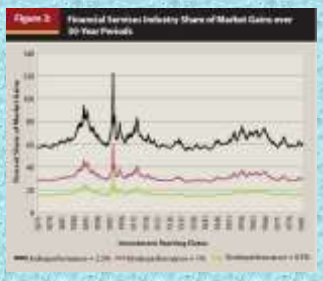
How Stockbrokers differ from Kindergarten Teachers

- Remember that personal statement
- "You are engaged in a life-and-death struggle with the financial services industry. ... If you act on the assumption that every broker, insurance salesman ... and financial advisor you encounter is a hardened criminal, you will do just fine."- William Bernstein, MD
- In investing, you get what you DON'T pay for

The Cost of Financial Advice

- If you pay just 2% of your portfolio each year in fees, commissions, and expenses, how much less would you end up with?
  - 30 years, 8% pre-fee returns, saving $50K a year.
  - $6.12M vs $4.19M
  - Is that advisor really worth nearly $2M to you?
    - 5+ years of your gross salary?
    - $80K/year in retirement?
  - Even after-inflation it's still > $1M
    - ($3.49M vs $2.45M)

The Tyranny of Compounding Fees



- Neufeld- Journal of Financial Planning 2014

Financial Advisory Models

- 4 Ways To Pay For Finance Advice and Investment Management
- 1) Commissions – loaded mutual funds and commissions on insurance-based investing products (3-8% load, high expenses, bad products)
- 2) Asset Under Management Fee (0.15%-2%) ($1500-20,000 on a $1M portfolio)
- 3) Annual retainer ($1000-5000) or set fee for plan ($500-2000)
- 4) Hourly rate (typically $150-300/hour)
- All introduce their conflicts of interest, but look at the bottom line – how much per year for how much work

The Alphabet Soup of Advisers

- CFA
- ChFC
- CFP
- The rest aren't worth much.
- You can become a "financial advisor" in less than a week.
- A CFP requires 3 years of experience, but only 2-3 months of studying.

Image Credit: Stawberryblues, wikimedia

Avoid Responsibility For Financial Catastrophes

- Insure against catastrophes
  - Your life during your earning years
  - Disability during your earning years
  - Malpractice
  - Personal Liability
  - Property
  - Health

Insurance Guidelines

- Self-insure when possible
  - Emergency Fund
  - High deductibles
  - Avoid consumer insurance
    - Phone, computer, appliances, collision/comprehensive
  - Death or disability AFTER your earning years
    - Don't mix insurance and investing
  - Avoid stupid insurance- cancer, accident, vacation, consumer products

How To Buy Life Insurance

- 1) Decide how much to buy ($1-$3 Million)
- 2) Decide how long until you won't need it (20-30 years)
- 3) Go to term4sale.com to get quotes and print them out (healthy 30 yo F = $550 per year per million)
- 4) Take to agent. Tell him you don't want whole life insurance. Fill out application.
- 5) Move on with life.

How To Buy Disability Insurance

- Independent Agent- Guardian, Standard, Principal, Metlife, Massmutual, Ameritas
- Specialty-specific, Individual (not group) policy as a resident
- Buy more upon residency graduation
- You get what you pay for, but ask for discounts
- The definition of "disability" is all-important

Disability Insurance

- Sticker shock – 2-5% of income covered
  - $5000 per month benefit costs $100-250/month
- Pay annually (5% discount)
- Buy it together with others for a discount
- Disability insurance is complicated- use the agent

Riders

- Future Purchase Option
- Residual Disability
- Cost of Living
- Non-cancelable vs guaranteed renewable
- Catastrophic disability
- Retirement

Liability Insurance

- State minimums are way too low
- $300K or so on house and cars
- Umbrella policy $1-5M ($2M = $404/year)
- Malpractice- Don't stand out
  - Bigger the group, better the deal
  - Very rare to get sued above limits

Whole Life Insurance

- A life long death benefit combined with a low return investment
- Takes about 10 years to break even
- Guarantees life long returns of 2%
- Probable return of 3-5% if held until death
- Over 80% of policies are surrendered prior to death

Whole Life Insurance

- Dozens of uses for it
- Not the best financial product for any given purpose
- Commissions are 50-110% of the first year's premium
- Don't surrender it if you've already had it for 15+ years
- A product designed to be sold, not bought
- Universal life and variable life are similar

No One Has a Crystal Ball

- You need a plan likely to succeed no matter what happens in the future
- Nobody knows nothing
- CXO Advisory group evaluated stock market predictions
  - 6,582 stock market predictions
  - 1998 to 2012
  - 68 gurus
  - 47.4% accurate

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You Don't Have A Crystal Ball Either

- Downfall of physician investors
  - Overconfidence
- Intellectual failure
  - Investing is a science with its own literature
    - Journal of Investing
    - Journal of Financial Planning
    - Journal of Investment Management
    - Journal of Alternative Investments
    - Journal of Finance
  - Evidence-based investing

Mutual Fund Managers Don't Have A Crystal Ball

- On Persistence in Mutual Fund Performance, Carhart, 1997
  - Analyzed 1892 funds from 61-93
  - Average actively managed fund underperformed by 1.8%.

The Index Fund Advantage

- Allan Roth Study (How a Second Grader Beats Wall Street)
- The probability an actively managed portfolio will beat index funds

	1 Year	5 Years	10 Years	25 Years
One Fund	42%	30%	23%	12%
Five Funds	32%	18%	11%	3%
Ten Funds	25%	9%	6%	1%

What Do The Experts Say?

- "Of the 355 equity funds in 1970, fully 233 of those funds have gone out of business. Only 24 outpaced the market by more than 1% a year. These are terrible odds." **Jack Bogle** (2007)

- "A low-cost index fund is the most sensible equity investment for the great majority of investors. My mentor, Ben Graham, took this position many years ago, and everything I have seen since convinces me of its truth." **Warren Buffet**

- "After a lifetime of picking stocks, I have to admit that Bogle's arguments in favor of the index fund have me thinking of joining him rather than trying to beat him." **Jim Cramer**

- "The statistical evidence proving that stock index funds outperform between 80% and 90% of actively managed equity funds is so overwhelming that it takes enormously expensive advertising campaigns to obscure the truth from investors." **Peter Lynch**

Taxes Aren't That Complicated

- 2012 I paid 9% of my income in Federal Taxes

- Saved for college - $500
- Started a business - $1,000
- Rental property- $1,500
- Have kids - $3,000
- Pay for health care - $3,000
- Own my house - $4,000
- Married - $7,000
- Give to charity - $7,000
- R.A. Contributions - $20,000
- R.A. Investments - $13,000

- Moral of the story?
  - If you want to lower your taxes, max out your retirement accounts.

Suitcases and Swimsuits

Roth IRA

401K

Cash Balance Plan

Stock

Bond

Mutual Fund

Tax Advantaged Accounts

- Tax-deferred – IRA, 401(k), 403(b), 457, Individual 401(k), SEP-IRA, SIMPLE IRA, Defined Benefit/Cash Balance Plan
- Tax-free – Roth IRA, Roth 401(k), Roth 403(b), Roth Individual 401(k)
- Others – 529 accounts, Coverdell ESAs, UGMA/UTMA, Taxable account

The Backdoor Roth IRA

- Attendings cannot deduct traditional IRA contributions
- Cannot contribute directly to a Roth IRA
- Can make personal and spousal non-deductible traditional IRA contributions for themselves and their spouse
- Can convert traditional IRAs to Roth IRAs.
- Beware the pro-rata rule

The Stealth IRA

- Health Savings Accounts
  - Pre-tax contributions
  - Untaxed growth
  - No taxes due at withdrawal if used for health care
  - Becomes a traditional IRA at age 65
  - Money need not be withdrawn in same year it is spent on health care
  - Triple Tax Free!

The Trinity Study

- How much money can you withdraw from your portfolio, adjusted upward with inflation each year, and have the money last?
- Advisors used to say 6%, 8%, or even 10%.
- The “Sequence of Returns” problem
- The 4% Rule

The Good News

- Using 4% rule, you need $250,000*25= $6.25 Million to replace a physician income
- With a 5% real return, that equals 25 years of saving 50% of your gross income
- Luckily, you don’t need to replace 100%

Item	Working Physician	Retired Physician
Working Income	300000	0
Portfolio Income	0	46600
SS Income	0	45000
Total Income	300000	91600
Taxes	75000	12000
Retirement Savings	60000	0
Mortgage	30000	0
College Savings	15000	0
Work expenses	2000	0
Children's expenses	15000	0
Life Insurance	2000	0
Disability Insurance	3000	0
Health Insurance and Health Care	7500	10000
H.S.A.	6400	0
Charity	30000	12500
Transportation	5000	3000
Travel	10000	15000
Other Expenses	39100	39100
Total Expenses	300000	91600

The Good News

- Instead of replacing 100%, you may only need to replace 25%.
- $75,000 * 25 = $1.88 Million
- 25 years, 5% real return, save 14% of your gross income
- Use the "Future Value" function to play with the variables

8 Pearls

- 1) You have a second job
- 2) Four ways to eliminate student loans
- 3) Get good advice at a fair price
- 4) Buy the right insurance
- 5) No one has a crystal ball
- 6) Your Biggest Tax Break
- 7) The safe withdrawal rate
- 8) The Good News of physician retirement

Questions

- Email me at editor@whitecoatinvestor.com
- Or come by the website: http://whitecoatinvestor.com

PROGRAM EVALUATION

AOCD Midyear Meeting
February 20-23, 2014
Dallas, TX

1. What was your reason for enrollment?
   __Program topics
   __Location of the program
   __Desire to broaden your knowledge
   __Needed CME hours
   __Other _____

2. Were you interested in a specific speaker?
   __Yes, If so, who _____
   __No

3. Have you previously attended an AOCD CME program?
   __Yes __No

4. What is the population of the city in which you practice?
   __ under 10,000 __ 10,000-30,000 __30,000-50,000 __50,000-100,000
   __ over 100,000

5. What type of practice are you currently engaged in?
   __ solo __ group __ hospital __ military __ retired

6. List the subjects you felt were most valuable to you.

   _____

7. List the subjects you felt could have been omitted.

   _____

8. If you could choose ONE location to attend a CME program, where would it be?

   _____

9. List three topics you would like to see presented at a future meeting and why.

   1._____

   2. _____

   3._____

10. What was the best part of your experience at this meeting?

_____

11. What was the worst part of your experience at this meeting?

_____

12. Overall, was the activity commercially biased? _____ YES _____ NO

General Evaluation (please circle one)	**Excellent**	**Good**	**Average**	**Fair**	**Poor**
Program content	5	4	3	2	1
Scheduling	5	4	3	2	1
Length of program	5	4	3	2	1
Program publicity	5	4	3	2	1
Facilities	5	4	3	2	1
Overall rating of program	5	4	3	2	1

Thank you for taking the time to complete this evaluation. It is greatly appreciated and will facilitate planning for future meetings.

Marsha A. Wise
Executive Director

American Osteopathic College of Dermatology
Continuing Medical Education
Attendance Documentation & Program Evaluation

Name:_____ AOA#/AAD#:_____

Address:_____ Date: Thursday, February 20, 2014

City: _____ST._____ ZIP_____ __Physician __Non-Physician

_____
Signature

Please rate speakers on the following scale:

Speaker Evaluation

AREAS OF WEAKNESS

Excellent (5) Good (4) Average (3) Fair (2) Poor (1)		Delivery	Audiovisual	Content
Holly Kanavy, D.O.	5 4 3 2 1	D	AV	C
Trey Haunson, D.O.	5 4 3 2 1	D	AV	C
Samuel Wilson, D.O.	5 4 3 2 1	D	AV	C
Faith McNicholas, CPC	5 4 3 2 1	D	AV	C
John Coppola, D.O., FAOCD	5 4 3 2 1	D	AV	C
Jennifer Cather, M.D.	5 4 3 2 1	D	AV	C
Teresa Ishak, D.O.	5 4 3 2 1	D	AV	C
Michael Kassardjian, D.O.	5 4 3 2 1	D	AV	C
Emily Matthews, D.O.	5 4 3 2 1	D	AV	C
Aaron Bruce, D.O., FAOCD	5 4 3 2 1	D	AV	C

Evaluation of Content	**Excellent (5)**	**Good (4)**	**Average (3)**	**Fair (2)**	**Poor (1)**
Presentation met your needs.	☐	☐	☐	☐	☐
Presentation provided usable ideas and/or techniques.	☐	☐	☐	☐	☐
Program will improve professional effectiveness.	☐	☐	☐	☐	☐
Time for questions & answers was sufficient.	☐	☐	☐	☐	☐
Handouts were useful.	☐	☐	☐	☐	☐
Seminar met your expectations.	☐	☐	☐	☐	☐
Format and organization were effective.	☐	☐	☐	☐	☐

Did these lectures meet the objectives of this CME program?	☐ YES	☐ NO
Would you attend a similar conference next year?	☐ YES	☐ NO
Did the activity remain commercially unbiased?	☐ YES	☐ NO

American Osteopathic College of Dermatology
Continuing Medical Education
Attendance Documentation & Program Evaluation

Name:_____ AOA#/AAD#:_____

Address:_____ Date: Friday, February 21, 2014

City: _____ ST._____ ZIP_____ __Physician __Non-Physician

_____
Signature

Please rate speakers on the following scale:

Speaker Evaluation

AREAS OF WEAKNESS

Excellent (5) Good (4) Average (3) Fair (2) Poor (1)		Delivery	Audiovisual	Content
Lise Brown, D.O.	5 4 3 2 1	D	AV	C
Panagiotis Mitropoulos, D.O.	5 4 3 2 1	D	AV	C
Justin Rubin, D.O.	5 4 3 2 1	D	AV	C
Steven Grekin, D.O., FAOCD	5 4 3 2 1	D	AV	C
Stuart Brown, M.D.	5 4 3 2 1	D	AV	C
Ronald Rapini, M.D.	5 4 3 2 1	D	AV	C
Jared Heaton, D.O.	5 4 3 2 1	D	AV	C
Julian Ngo, D.O.	5 4 3 2 1	D	AV	C
Clayton Schiltz, D.O.	5 4 3 2 1	D	AV	C
Adam Friedman, M.D.	5 4 3 2 1	D	AV	C
James Del Rosso, D.O., FAOCD	5 4 3 2 1	D	AV	C
Michelle Foley, D.O., FAOCD	5 4 3 2 1	D	AV	C

Evaluation of Content	**Excellent (5)**	**Good (4)**	**Average (3)**	**Fair (2)**	**Poor (1)**
Presentation met your needs.	☐	☐	☐	☐	☐
Presentation provided usable ideas and/or techniques.	☐	☐	☐	☐	☐
Program will improve professional effectiveness.	☐	☐	☐	☐	☐
Time for questions & answers was sufficient.	☐	☐	☐	☐	☐
Handouts were useful.	☐	☐	☐	☐	☐
Seminar met your expectations.	☐	☐	☐	☐	☐
Format and organization were effective.	☐	☐	☐	☐	☐

Did these lectures meet the objectives of this CME program?	☐ YES	☐ NO
Would you attend a similar conference next year?	☐ YES	☐ NO
Did the activity remain commercially unbiased?	☐ YES	☐ NO

American Osteopathic College of Dermatology
Continuing Medical Education
Attendance Documentation & Program Evaluation

Name:_____ AOA#/AAD#:_____

Address:_____ Date: Saturday, February 22, 2014

City: _____ST._____ ZIP_____ __Physician __Non-Physician

_____
Signature

Please rate speakers on the following scale:

Speaker Evaluation

AREAS OF WEAKNESS

Excellent (5) Good (4) Average (3) Fair (2) Poor (1)		Delivery	Audiovisual	Content
Jordan Fabrikant, D.O.	5 4 3 2 1	D	AV	C
Matthew Zarraga, D.O.	5 4 3 2 1	D	AV	C
Suzanne Micciantuono, D.O.	5 4 3 2 1	D	AV	C
David Fivenson, M.D.	5 4 3 2 1	D	AV	C
Amy Spizuoco, D.O., FAOCD	5 4 3 2 1	D	AV	C
Mariel Bird, D.O.	5 4 3 2 1	D	AV	C
Christina Feser, D.O.	5 4 3 2 1	D	AV	C
Jesse Jensen, D.O.	5 4 3 2 1	D	AV	C
Alan Menter, M.D.	5 4 3 2 1	D	AV	C
Lloyd Cleaver, D.O., FAOCD	5 4 3 2 1	D	AV	C
Raymond Knisley, D.O.	5 4 3 2 1	D	AV	C
Ryan Pham, D.O.	5 4 3 2 1	D	AV	C
Tang Le, D.O.	5 4 3 2 1	D	AV	C
Cliff Lober, M.D., JD	5 4 3 2 1	D	AV	C

Evaluation of Content	**Excellent (5)**	**Good (4)**	**Average (3)**	**Fair (2)**	**Poor (1)**
Presentation met your needs.	☐	☐	☐	☐	☐
Presentation provided usable ideas and/or techniques.	☐	☐	☐	☐	☐
Program will improve professional effectiveness.	☐	☐	☐	☐	☐
Time for questions & answers was sufficient.	☐	☐	☐	☐	☐
Handouts were useful.	☐	☐	☐	☐	☐
Seminar met your expectations.	☐	☐	☐	☐	☐
Format and organization were effective.	☐	☐	☐	☐	☐

Did these lectures meet the objectives of this CME program?	☐ YES	☐ NO
Would you attend a similar conference next year?	☐ YES	☐ NO
Did the activity remain commercially unbiased?	☐ YES	☐ NO

American Osteopathic College of Dermatology
Continuing Medical Education
Attendance Documentation & Program Evaluation

Name:_____ AOA#/AAD#:_____

Address:_____ Date: Sunday, February 23, 2014

City: _____ST._____ ZIP_____ __Physician __Non-Physician

_____
Signature

Please rate speakers on the following scale:

Speaker Evaluation

AREAS OF WEAKNESS

Excellent (5) Good (4) Average (3) Fair (2) Poor (1)		Delivery	Audiovisual	Content
Kelly Nelson, M.D.	5 4 3 2 1	D	AV	C
Rene Bermudez, D.O., FAOCD	5 4 3 2 1	D	AV	C
Scott Wickless, D.O., FAOCD	5 4 3 2 1	D	AV	C
James Dahle, M.D.	5 4 3 2 1	D	AV	C

Evaluation of Content	**Excellent (5)**	**Good (4)**	**Average (3)**	**Fair (2)**	**Poor (1)**
Presentation met your needs.	☐	☐	☐	☐	☐
Presentation provided usable ideas and/or techniques.	☐	☐	☐	☐	☐
Program will improve professional effectiveness.	☐	☐	☐	☐	☐
Time for questions & answers was sufficient.	☐	☐	☐	☐	☐
Handouts were useful.	☐	☐	☐	☐	☐
Seminar met your expectations.	☐	☐	☐	☐	☐
Format and organization were effective.	☐	☐	☐	☐	☐

Did these lectures meet the objectives of this CME program?	☐ YES	☐ NO
Would you attend a similar conference next year?	☐ YES	☐ NO
Did the activity remain commercially unbiased?	☐ YES	☐ NO

MIDYEAR MEETING AND SCIENTIFIC SEMINAR
CONTINUING MEDICAL EDUCATION REPORTING FORM
Thursday, February 20 – Sunday, February 23, 2014
Dallas Texas

Maximum Credit: 26.5 credits Category 1A CME (Thursday – Sunday)

Instructions:

1. Check each session attended.
2. Insert total and sign form.
3. **Please fax this form to (660) 627-2623**

Thursday, February 20, 2014

_____ 12:00 pm - 6:30 pm	Dermatology CME	6.5 credits

Friday, April 20, 2012

_____ 7:30 am – 11:30 am	Dermatology CME	4 credits
_____ 1:00 pm - 2:00 pm	Dermatology CME	1 credit
_____ 2:30 pm – 5:30 pm	Dermatology CME	3 credits

Saturday, April 21, 2012

_____7:30 am -9:30 am	Dermatology CME	2 credits
_____9:30 am -10:30 am	Dermatopathology CME	1 credit
_____10:30 am -11:30 am	Dermatology CME	1 credit
_____1:00 am -2:00 am	Dermatology CME	1 credit
_____ 2:30 pm – 5:30 pm	Dermatology CME	3 credits

Sunday, April 22, 2012

_____ 8:00 am - 9:00 am	Dermatology CME	1 credit
_____ 9:00 am -10:00 pm	MOHS CME	1 credit
_____10:00 am -12:00 pm	Dermatology CME	2 credits

Total CME Credits _____

I attest to the accuracy of the total hours listed above.

Name *(print)* _____ AOA# _____

Signature_____ Date _____

Attendees should claim credit only for the portion of the program they attended and successfully completed.

2014 AOCD Midyear Meeting

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