OFP
Osteopathic Family Physician

THE OFFICIAL PEER-REVIEWED PUBLICATION OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

MAY/JUNE, 2020
Volume 12 | Number 3
ofpjournal.com

acofp | AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

www.acofp.org

Guide for...

READERS

Osteopathic Family Physician (ISSN 1877-573X) is published bimonthly by the American College of Osteopathic Family Physicians. Postage paid at Arlington Heights, IL and additional mailing offices.

USA POSTMASTER

Send address changes to:

American College of Osteopathic Family Physicians
Membership Department:

330 E. Algonquin Rd., Ste. 1
Arlington Heights, IL, 60005

CUSTOMER SERVICE

(orders, claims, online, change of address)

American College of Osteopathic Family Physicians

330 E. Algonquin Rd., Ste. 1
Arlington Heights, IL 60005

847-952-5100 | membership@acofp.org

YEARLY SUBSCRIPTION RATES

United States & Possessions:
Individual $116 | Institution $208 | Student $57

All other countries: *(prices include airspeed delivery)*

Individual $146 | Institution $26 | Student $74
Single issues $42

To receive student rate, orders must be accompanied by name of affiliated institution, date of term and the signature of program coordinator on institution letterhead. Orders will be billed at the individual rate until proof of status is received. Current prices are in effect for back volumes and back issues.

ADVERTISING INFORMATION:

Advertising orders and inquiries can be sent to:

Matt Van Wie
804-550-2312 | matt@esvw.com

AUTHOR INQUIRIES

For inquiries relating to the submission of articles (including electronic submission), please visit www.ofpjournal.com.

Content details for questions arising after acceptance of an article, especially those relating to proofs will be provided by the publisher.

You can track accepted articles and view Author Guidelines through Scholar One at mc04.manuscriptcentral.com/ofp.

The paper used in this publication meets the requirements of ANSI/NISO Z39.48-1992 (Permanence of Paper).

AUTHORS

For a full and complete Guide for Authors, please go to: mc04.manuscriptcentral.com/ofp.

REPRINTS:

For queries about author reprints, or to order 100 or more reprints for education, commercial or promotional use, contact ACOFP at 847-952-5100 or email tamic@acofp.org.

OFP
Osteopathic Family Physician
JOURNAL

2020 CALL FOR PAPERS

Osteopathic Family Physician is the ACOFP's official peer-reviewed journal
The bi-monthly publication features original research, clinical images and articles about preventive medicine, managed care, osteopathic principles and practices, pain management, public health, medical education and practice management.

RESERVE A TOPIC

Reserve a review article topic today by emailing ACOFP Managing Editor, Belinda Bombei at belindab@acofp.org. Please provide your name and the review title you would like to reserve. Once you reserve a review article topic, you will receive an email confirmation from ACOFP. This will initiate a three-month deadline for submission. If the paper is not received within three months, the system will release the review article topic for other authors to reserve. Articles submitted for publication must be original in nature and may not be published in any other periodical. Materials for publication should be of clinical or didactic interest to osteopathic family physicians. Any reference to statistics and/or studies must be footnoted. Material by another author must be in quotations and receive appropriate attribution. ACOFP reserves the right to edit all submissions. Visit ofpjournal.com to view author guidelines, policies, and manuscript checklist.

CLINICAL IMAGES

We are seeking clinical images from the wards that covers essential concepts or subject matter to the primary care physician.
Please provide a brief synopsis of how the case presented along with 1-4 questions and approximately 1 page of education with reference to the image and questions.

REVIEW ARTICLE TOPICS

- Disorders of Puberty: An Approach to Diagnosis and Management with an osteopathic component
- Lupus: Review Article with osteopathic component
- Depression in Children and Adolescents: Evaluation and Treatment with an osteopathic component
- Polypharmacy in the Elderly: Evaluating Risk and Deprescribing
- Prostate Disorders Diagnosis and Management review with an osteopathic component
- The impact of climate change on our patients' health and the Family Physician's role

RESEARCH TOPICS

We are seeking original clinical or applied research papers. Original contributions include controlled trials, observational studies, diagnostic test studies, cost-effectiveness studies, and survey-based studies. The OFP will accept basic scientific research only if the work has clear clinical applications. For randomized controlled trials, study flow diagrams must be submitted. For all other types of original contributions, flow diagrams are encouraged. Original contributions should be 3000 words with no more than 50 references and 5 tables or figures. OFP requires you to submit a 250-word abstract, along with four to six keywords.

The content should include the following:

Abstract
Introduction
Methods
Results
Discussion
Conclusions
Acknowledgments

Ronald Januchowski, DO, FACOFP
Editor-in-Chief

Paula Gregory, DO, MBA, CHCQM, FAIHQ
Associate Editor

acofp AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

OFP
Osteopathic Family Physician
The Official Peer-Reviewed Publication of the
American College of Osteopathic Family Physicians

MAY/JUNE, 2020
VOLUME 12 | NUMBER 3

CONTENTS

OSTEOPATHIC FAMILY PHYSICIAN SPECIALTY PEER REVIEWERS

Richard L. Averitte, Jr, MD
Dermatology

Jeffrey Benseler, DO
Radiology

Shagun Bindlish, MD
Diabetes and Endocrinology

Raj Brar, DO
Behavioral Health, Family Medicine, Geriatrics, OMT, Pain Management, Pediatrics

Natasha Bray, DO
Ethics

Omar Bukhari, DO
Family Medicine, Obstetrics

Janis Coffin, DO
Practice Management

Danielle Cooley, DO, FACOFP
OMM

Andrew Crow, DO
Academic, Emergency, Hospital Care, Military

Robin Devine, DO
Statistics/Design

Brian Downs, DO
HIV, Wound Care

Dennis Eckles, DO
Diabetes, Rural Medicine

Gail Feinberg, DO, FACOFP
Academic

Daniel Jason Frasca, DO
Behavioral Health, Addiction Medicine, Nutrition, Hypertension, Renal Disorders

Ron Gubb, DO
Diabetes, Sports Medicine

Patricia Happel, DO, FACOFP
Nutrition and Obesity

Robert Hunter, DO, CMD, FACOFP
Health Policy, Hospice/Palliative Care, ER, Diabetes, Wound Care

Ronald P. Januchowski, DO, FACOFP
Military & Rural/Underserved

Steve Kamajian, DO, CMD, FACOFP
Family Medicine, Geriatrics, Long Term Care

Amy Keenum, DO, PharmD
Healthy Literacy, International & Patient Education

Frank Komara, DO, FACOFP
Geriatrics

Mana Lazzaroto, DO
Clinical Images

Ehab Mady, DO
Vascular

Mohammad Mansour, MD
Inpatient Medicine, Cardiology, Pulmonary, Geriatrics, Obstetrics

Marjan Moghaddam, DO
Family Medicine

Merideth Norris, DO, FACOFP
Addiction

Jon Parham, DO
Preventive Medicine, Pulmonary, Public Health, Geriatrics, Medical Errors

Nicholas Pennings, DO, FOMA
Obesity

Raena Pettitt, DO
Disease Prevention & Wellness

Kim Pfotenhauer, DO
Diabetes

M. Jay Porcelli, DO, FACOFP *dist.*
Pain Management

Jill Yurko Porter, DO
Obesity, OMT, Physician Wellness and Women's Health

Joseph Reyes, DO
Pain Management

Bernadette Riley, DO, FACOFP
Medical Education, Academic, Simulation Medicine, Physician Leadership, Health Policy

Mark Rogers, DO, MA, CAQSM, FAAFP
Family Medicine, Sports Medicine, OMM, Medical Ethics

Kary Schroyer, DO
Direct Primary Care

Christopher Scuderi, DO
Family Practice, Practice Management

Jay Shubrook, Jr., DO, FACOFP
Endocrinology

Leslie Sleuwen, MD
Community Medicine

Lindsay Tjiattas-Saleski, DO, MBA, FACOEP
Clincial Images, Emergency Medicine

Johnathon Torres, DO, FACOFP
OMM

Chad Uptigrove, DO
Obstetrics, Residency Training

William Woolery, DO, PhD, FACOFP
Geriatrics

Julian Vega, DO
Clinical Images

Sheldon Yao, DO
Cardiology

2020 STUDENT ACADEMIC & PEER REVIEW WRITING INTERNS

Michael Anderson, DO
William Carey University College of Osteopathic Medicine

Jordan Burr
A.T. Still University - School of Osteopathic Medicine in Arizona

Alice Doong
Michigan State University College of Osteopathic Medicine

Angelic Dye
William Carey University College of Osteopathic Medicine

Zachary Ellis
William Carey University College of Osteopathic Medicine

Kimia Etemadi
A.T. Still University - School of Osteopathic Medicine in Arizona

Joanna Ghobrial, DO
A.T. Still University - School of Osteopathic Medicine in Arizona

Nadia Khan
Michigan State University College of Osteopathic Medicine

Matthew Kon
William Carey University College of Osteopathic Medicine

Luiza Mnatsakanyan
William Carey University College of Osteopathic Medicine

Sarah Jane Muder
New York Institute of Technology College of Osteopathic Medicine

Shikha Patel
Rowan University School of Osteopathic Medicine

Elenie Philippas
Western University of Health Sciences College of Osteopathic Medicine of the Pacific

Diana Roy, DO
William Carey University College of Osteopathic Medicine

Elysia Tjong
A.T. Still University - School of Osteopathic Medicine in Arizona

Nusrat Uddin
William Carey University College of Osteopathic Medicine

EDITOR'S MESSAGE

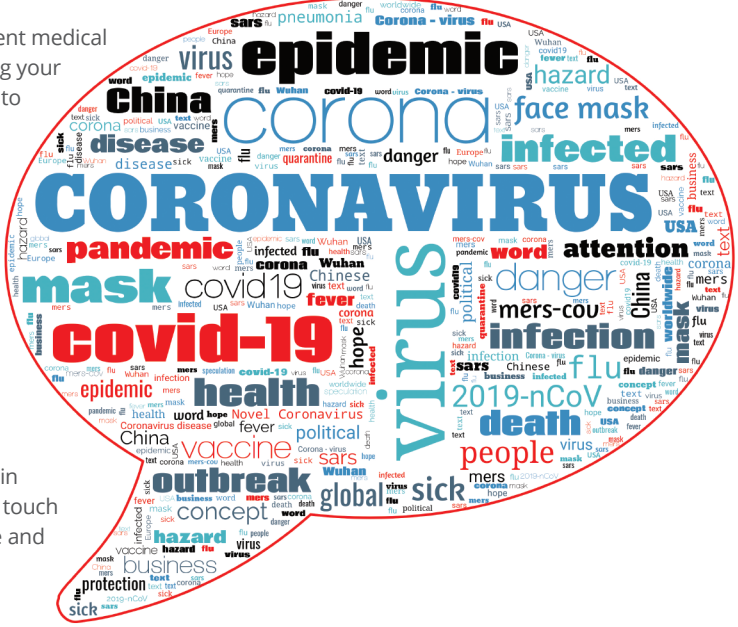
Quickly Quieting Quarantine Questions

Ronald Januchowski, DO, FACOFP, Editor, *Osteopathic Family Physician*

I wish I could tell you that this is a normal Editor's Message, but as you realize, it certainly is not. I am writing this message under the cloud of a worldwide pandemic that has created a new normal for society. Unprecedented, surreal, anomalous, and discombobulated all come back into the common vocabulary during this time. I hope you and the people around you are staying as safe as possible. I also hope you are doing everything possible to continue in your role as an Osteopathic Family Physician for your loved ones, your patients, and your community.

Social isolation has helped me have some time to learn more about topics that perhaps I would not have had time for previously. The origin of words has always been interesting to me. For example, learning about the difference between epidemic and pandemic. Both with roots from the Greek dēmos, "people of a district," the prefixes help distinguish the two words. The prefix of epi- refers to "upon or near" while the pan- prefix refers to "all." Both words, when they came into the English language, were originally used for the spread of diseases. Two other words with interesting etymology (bug lovers, don't confuse it with the entymology) are isolation and quarantine. Isolation, from the Latin insulātus, "made into an island," based on insula, "island," is related to but with a distinctly different root than quarantine. Quarantine, from the Italian quarantina was a period of forty days used to remove a potentially ill person from others to prevent the spread of disease, such as the plague in medieval Europe. Let us hope forty days will help flatten the curve during this current crisis.

I am pleased to provide you with some excellent medical information articles in this issue to read during your social isolation and distancing. You may want to review the clinical image first, in order to gain some perspective on the current medical situation. Physicians with more experience on Earth (aka older) may find the image to be very easy to diagnose. Other articles in this issue involve the integumentary system, including the Osteopathic management and treatment of hives and non-melanotic skin cancer. A joint pain related article rounds out the slate.



Remain diligent and optimistic in these times. How true are the words of Ulysses to Achilles in Shakespeare's play Troilus and Cressida "One touch of nature makes the whole world kin." Be safe and try to connect with others in the safest way possible. I wish the best for each of you.

OFP
Osteopathic Family Physician

2019 ATTENDING PAPER OF THE YEAR AWARD

"Primary Care Approach to Eye Conditions"

Presented to

Sharanjit Kaur, DO

Alanna Nattis, DO

Helaine Larsen, DO

2019 RESIDENT PAPER OF THE YEAR AWARD

"PCSK9 Inhibitors, The Most Significant Advance in Lipid Lowering Therapy Since Statins?"

Presented to

Andrew Wilson, DO

2019 STUDENT AUTHOR OF THE YEAR AWARD

"An Osteopathic Approach to Diagnosing and Treating Perimenstrual Disorders"

Presented to

James Docherty, OMS III

Suzanna Shermon, OMS III

FROM THE PRESIDENT'S DESK

Resilience During a Pandemic

Robert C. DeLuca, DO, MBA, FACOFP *dist.*
2019 - 2020 ACOFP President

These past two months have been challenging for people all over the world. As health care providers, we have not had the privilege to stay at home to avoid exposure. While we have worked to have our patients reduce their contact and have recommended the cancelling of local events including church services, meetings and dining in at restaurants, many of us have had to continue to see patients, attend to emergency rooms and care for those in hospitals and nursing homes. As family physicians we have made ourselves available by phone, online and, at times, in person. Our first duty has been to our communities and our patients.

ACOFP has worked to keep you updated not only with information concerning public safety and control measures, but also with information on billing, coding and Centers for Medicare & Medicaid Services rule changes that will assist physicians with managing their offices.

In the beginning of March, ACOFP had some very difficult decisions to make. At first, the Board of Governors felt that it might still be possible to continue plans to have our annual convention in New Orleans. At that time, the cases were localized to only a very small area of the country. We continued to monitor the progression and within a few days, the ACOFP board voted to cancel the convention.

We recognized that many physicians would have been unable to attend. Many worked for a college of osteopathic medicine or a large health care system that was already beginning to limit travel. The most important reason to cancel was that physicians were going to be needed in their own communities, and the risk of contracting the illness would remove them from the medical workforce.

While we understand the financial liability that this cancellation could have placed on ACOFP, we felt confident in the decision, particularly when within the next week cases of COVID-19 spiked in New Orleans. We were also fortunate enough to have had our staff add a communicable disease rider to our event insurance, which gave us an extra layer of protection. As the events unfolded, the conference headquarters hotel and the A/V company accepted the terms of our cancellation, waiving us of contractual liability.

The ACOFP board and staff quickly decided to move to a virtual platform for both the Faculty Development/Program Directors Workshop and the main session programming. Dr. Nicole Bixler had already developed a plan to launch the Task Force on Convention Innovation at ACOFP '20. Little did we know that circumstances would make this a reality before the task force could meet.

Under the direction of ACOFP Executive Director Bob Moore and Director of Knowledge, Learning and Assessment Steve Legault, ACOFP had five days to launch this plan. The staff was able to notify the registrants, provide options including the virtual convention, arrange for the speakers to be online, adapt the Zoom platform and find a suitable location from which to have unimpeded online access. As such, both the FD/PD Workshop and four days of CME went off perfectly. In fact, the live lectures had better daily attendance than the in-person events historically. Even Sunday's programming featured over 500 attendees at each lecture. The speakers did a fabulous job.

I would especially like to thank the Program Committee led by Joel Feder, DO, FACOFP *dist.*; Convention Education Program Chair Bernadette Riley, DO, FACOFP and Convention Education Program Vice-Chair Matthew Told, DO; as well as the FD/PD Committee led by Rob Danoff, DO, MS, FACOFP, FAAFP. Your leadership and commitment were instrumental in this ground-breaking endeavor.

The ACOFP Board of Governors wishes to thank the staff and volunteers for the amazing job they did to move our educational programs forward. We are going to review all the comments from attendees to build on this year's success. While we all missed the in-person comradery and fellowship (as well as the hugs), this virtual platform will certainly find its way into future educational endeavors.

The ACOFP Board also had to consider the other components of the meeting, including the Congress of Delegates. ACOFP Congress of Delegates Speaker Elizabeth Palmarozzi, DO, FACOFP, and Vice Speaker Antonio Tsompanidis, DO, FACOFP, worked on contingency plans for cancelling the convention. As part of their due diligence, ACOFP's legal counsel was consulted to learn what options existed. The attorney reviewed our bylaws and noted that there is a legal principle called "cy pres," which means when you can't do what you are required to do under your bylaws due to an emergency, you can do the next closest thing, such as an electronic vote.

The attorney suggested that the board make a motion clarifying important items of business that they request the speaker conduct

so that the board can continue the work of the organization. The board unanimously passed a motion asking the speaker to seek an electronic vote from Congress approving the 2020 budget. Secondly, they unanimously passed a motion asking the attorney to draft a temporarily bylaws amendment effectively staying the current board—with the exception of the student and resident governors who are graduating—until Congress next meets in person in March 2021. Additional information on this was sent to the membership on March 24. In summary, the board felt that the extreme circumstances we face as a country and organization requires consistency in leadership. The Congress of Delegates has until April 30, 2020 to cast their votes.

The ACOFP Board would like to thank all the members who have worked in their offices and communities during the COVID-19 crisis as a vital part of patient care. We also want to thank you for the support of the ACOFP '20 Virtual convention. We hope you all remain healthy and safe during this pandemic.

Osteopathically yours,

Robert C. DeLuca, DO, FACOFP *dist.*
2019 - 2020 ACOFP President

CALENDAR OF EVENTS

JULY 17 – 19, 2020
Direct Primary Care Summit
Kansas City, Missouri
www.dpc.org

JULY 29 – AUGUST 2, 2020
ACOFPCA 44th Annual Seminar & Convention
Anaheim, California
www.acofpca.org

JULY 30 – AUGUST 2, 2020
Michigan Association of Osteopathic Family Physicians
Traverse City, Michigan
www.maofp.org

AUGUST 7 – 9, 2020
POFPS Annual CME Symposium
Hershey, Pennsylvania
www.poma.org

AUGUST 13 – 16, 2020
North Carolina Society of the ACOFP
Pinehurst, North Carolina
www.nc-acofp.org

OCTOBER 16 – 19, 2020
OMED 2020
Austin, Texas
www.osteopathic.org

DECEMBER 4 – 6, 2020
Indiana Osteopathic Association
Indianapolis, Indiana
www.inostep.org

CME Resource: Osteopathic Family Physician Offers 2 Hours of 1-B CME

ACOFP members who read Osteopathic Family Physician can receive two hours of Category 1-B continuing medical education credit for completing quizzes in the journal. Visit the eLearning Center at www.acofp.org to access the quizzes.

REVIEW ARTICLE

Osteopathic Primary Care Treatment Options for Ulcerative Colitis

Amanda Fernandez, OMS IV[1]; Ronald Januchowski, DO, FACOFP[1]

[1]Edward Via College of Osteopathic Medicine-Carolinas Campus, Spartanburg, SC

KEYWORDS:

Drug Therapy

Osteopathic Manipulative Medicine

Ulcerative Colitis

ABSTRACT:

Introduction: Ulcerative colitis is a multifactorial, chronic inflammatory disease of the bowel that can cause physical, social and emotional injury to the patient. While perhaps not always making the initial diagnosis or providing primary treatment, the primary care physician can play a critical role in providing direction and clarity to the overall treatment plan for the patient. In addition, monitoring for complications or side effects of treatment will help maintain the patient's optimal health.

Methods: A literature search using PubMed, NCBI and WorldCat.org was done using the terms ulcerative colitis treatment, psychosocial association of ulcerative colitis, surgical management of ulcerative colitis, epidemiology of ulcerative colitis, the pathophysiology of ulcerative colitis, probiotics in ulcerative colitis, OMT for ulcerative colitis, and diagnosis of ulcerative colitis. A primary date range of 2015-2019 was used with a secondary search extending back to 1985.

Discussion: An Osteopathic approach to the treatment of ulcerative colitis will help the patient remain highly functioning and reduce complications of this disease. By being aware of the various pharmaceutical and non-pharmaceutical treatment options available, one can collaborate with the patient to create a treatment plan to minimize morbidity and increase functional days.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) affecting the intestinal mucosa that begins in the rectum and progresses proximally, usually not extending beyond the colon. The annual incidence rate in North America for UC is approximately 12.2 cases per 100,000 person-years with a gradual increase in incidence over time.[1] There is little difference in disease incidence concerning sex; however, there is a slight male predominance. The influence of race on disease incidence is also important to consider. In the United States, Caucasians have a higher incidence of UC than African Americans and other races. In addition, the incidence of UC is higher among Jewish populations everywhere worldwide.[2] A cohort study showed that racial and ethnic minority patients with UC, specifically Asians and Hispanics, had a more severe disease presentation than Caucasians.[3]

CORRESPONDENCE:
Ronald Januchowski DO, FACOFP
rjanuchowski@carolinas.vcom.edu

 Print ISSN: 1877-573X
DOI:10.33181/12031

Patients with UC most commonly present between 15 and 30 years of age with abdominal pain and discomfort, increased frequency of bowel movements, urgency of bowel movements, chronic and bloody diarrhea, and mucorrhea.[4] Extraintestinal manifestations include inflammatory arthropathies, osteoporosis, primary sclerosing cholangitis (PSC), erythema nodosum, pyoderma gangrenosum, uveitis, and nephrolithiasis. Common physical exam findings include diffuse abdominal tenderness without rebound or guarding, signs of anemia, signs of dehydration, gross or occult blood on digital rectal exam, and anal fissures present on rectal inspection. Additional physical exam findings include Chapman Reflex Points associated with the colon, particularly the anterior iliotibial band.

UC is understood to be a multifactorial immune-mediated disease due to genetic predisposition, defects in mucosal defense mechanisms, and environmental factors, such as immigration and depression.[5] The genetic component of UC is most closely associated with anti-neutrophil cytoplasmic antibodies (ANCA). ANCA positivity has a high specificity in the diagnosis of UC and is associated with more severe clinical symptoms. Psychosocial stress and depression have not only been shown to influence the pathogenesis of UC but also increase the risk of relapse. Patients with UC have an increased risk of colorectal cancer.

In a population-based meta-analysis the risk of colorectal cancer in IBD patients was over twofold compared to the general population.[6]

Diagnosis of UC is made by the combination of history, physical examination, endoscopy, histology, and ultimately by exclusion of all other differential diagnoses. Biomarkers, such as ANCA, and complete blood counts (CBC) can be performed to support diagnosis. Endoscopic evaluation by ileocolonoscopy and gastroduodenoscopy, followed by biopsies taken from all segments of the intestine, provides definitive diagnosis of UC. Endoscopic findings include diffuse continuous mucosal inflammation that involves the rectum with possible proximal intestinal involvement limited to the colon, loss of haustral folds, and pseudopolyps. Histologic features include crypt abscesses, goblet cell and mucin depletion, and mononuclear inflammation of the lamina propria. Endoscopic evaluation and biopsy help to definitively diagnose UC by identification of the hallmark features associated with the disease and by exclusion of features pathognomonic for alternate diagnoses.

The factors which mediate UC include genetic predisposition, autoimmune disease processes, psychosocial influences, and dietary triggers.[7] Utilizing an integrative approach when treating UC through consideration of each of these mediating factors is paramount to optimal patient outcomes.

NON-PHARMACOLOGICAL TREATMENT

UC is a multifactorial disease, which can be treated using non-pharmacological therapeutic modalities to augment pharmacological treatment. Osteopathic manipulative treatment (OMT), diet modification, probiotics and psychosocial interventions have proven successful in managing UC. The principle is that in treating the patient as a whole, the chronic inflammatory disease can be managed, and flares minimized.

OMT

In considering OMT, no reviews were published for the specific treatment of UC. However, a review was published for the treatment of generalized chronic inflammatory diseases. On a physiologic level, clinical studies of OMT proved to reduce cytokines, including substance P, demonstrating an anti-inflammatory effect of this non-invasive treatment modality.[8] The benefit of OMT is that it is a drug-free therapeutic modality that offers little side effect profile if any, with muscle soreness being the most common. OMT uses manual manipulation to treat somatic dysfunctions to restore physiologic function. Its ability to tune the autonomic nervous system and increase parasympathetic activity supports how OMT can be an alternative therapy in treating chronic inflammatory diseases such as UC. In patients with irritable bowel syndrome (IBS), who share similar somatic dysfunctions with UC patients, visceral, sacral, and other direct and indirect osteopathic techniques were shown to reduce symptoms of abdominal pain, diarrhea and cramps among others.[9] Although there is limited data on the direct effect of OMT on UC, the symptomatic improvement for patients with IBS who were treated with various osteopathic techniques is promising for the effects OMT may have on patients with UC.

Diet

Diet plays a major role in both the pathophysiology and management of IBD. Managing UC from a dietary standpoint requires the avoidance and addition of dietary triggers and therapies, respectively.

Tight junctions, found in the gut lumen, mediate the absorption of nutrients. These tight junctions are disrupted in IBD. An in vitro study showed that the addition of n-6 polyunsaturated fatty acids (PUFA), which include linolenic acid, arachidonic acid and docosapentaenoic acid, results in a decreased expression of tight junctions along the gut lumen, thereby worsening IBD. The study showed that the ingestion of n-6 PUFA is associated with a higher risk of developing IBD.[10] In a prospective, observational study evaluating the effects of certain compounds on UC patients in remission, intake of myristic acid and alpha linolenic acid (ALA) was associated with an increased risk of relapse. Myristic acid is a component of palm oil, coconut oil, and dairy fats, while ALA is a precursor to omega-3 fatty acids. UC patients should be advised to avoid foods and food products containing myristic acid and ALA in order to reduce the risk of relapse and flares. In addition, all patients should be advised to avoid n-6 PUFA as a preventative measure.

A case-control study investigating the link between diet and UC found that UC patients had a higher intake of total energy, protein, carbohydrates, total fat, SFA (saturated fatty acids), monounsaturated fatty acids (MUFA), and PUFA than those in the control group. Although this does not directly correlate a link between those food compounds and the development of UC, it does suggest that healthy patients and those with risk factors for developing UC should limit their consumption of them. The study also emphasized the importance of a diet rich in Vitamin C and folate, as consumption of these micronutrients in a nutrient-rich diet were found to lower the risk of UC.[11]

Curcumin, a component of the turmeric plant, is widely recognized for its health benefits, from its anti-inflammatory and antioxidant properties to its neuroprotective and cardioprotective uses. A less commonly recognized herbal medicine is asafetida (ASF); it is a common ingredient in Indian cuisine and is known to enhance the activities of digestive enzymes found in the pancreas and the small intestine. In an animal study, an encapsulated gut health product (GHP) was formulated using curcumin and ASF complexed onto turmeric nanofiber (TNF), a nanofiber prepared from turmeric containing dietary fiber. This novel GHP reduced the clinical symptoms of UC, the disease activity index, histopathologic lesions, and inflammatory mediator activity, such as myeloperoxidase, thereby elucidating the anti-inflammatory and antioxidant benefits of curcumin, ASF and turmeric.[12] This study suggests the supplementation of curcumin, ASF and turmeric into the diet can aid in managing flares and relapse of the disease. However, because this was an animal study, the authors cannot confidently recommend changes in patient management until human trials are performed.

Probiotics

Probiotics are living organisms that provide health benefits to the host, when consumed as part of a healthy diet. VSL#3 is unlike most probiotics, it is a highly concentrated probiotic consisting of eight live, freeze-dried bacterial strains, including Lactobacilli (L paracasei, L plantarum, L acidophilus, and L delbrueckii subspecies bulgaricus), Bifidobacteria (B longum, B breve, B infantis), and Streptococcus thermophilus. A meta-analysis demonstrated the effectiveness of VSL#3 at inducing remission in active UC and as a possible alternative to 5-aminosalicylic acid for maintenance therapy.[13] Moreover, there was a reduction in stool frequency and hematochezia, and an improvement in mucosal appearance. Escherichia coli Nissle 1917 (EcN), another type of probiotic, has been recommended for the treatment of ulcerative colitis (UC). It has proven to be equivalent to mesalazine in preventing relapse and inducing remission, as well as improving the composition of the natural gut microbiota in UC patients.[14]

The addition of probiotics to a UC treatment plan as a pharmacological adjuvant is not only beneficial for the possible synergistic effects, but also for its low side effect profile. Across multiple studies, the side effects were limited to abdominal bloating and discomfort for the first few days. Less common adverse effects were an unpleasant taste and an increase in flatulence.[13] Overall probiotics do not impose serious side effects, encouraging its addition to the pharmaceutical regimen of UC. The role of probiotics is efficacious in both the induction and maintenance of UC and should be utilized, in combination with other treatment modalities, in the treatment of UC.

Psychosocial

The Osteopathic principle which states that the body is a unit, in which the person is a combination of mind, body, and spirit requires consideration when treating patients with chronic illnesses, such as UC. Changes in body and behavior have psychological implications, just as the mind has effects on the body. Therefore, it is important to assess a patient with UC for the psychosocial effects that this lifelong and physically demanding condition can have on a person. There is a high prevalence of anxiety and depressive symptoms in IBD patients, particularly in adolescent and young adult patients.[15] In an animal study, experimental stress and depression negatively impacted immune function, by causing a reactivation of inflammation and altering the number and function of CD4 and CD8 lymphocytes. The treatment of those animal models with antidepressants such as the tricyclic antidepressants prevented reactivation of colitis, suggesting that treatment of UC through a biopsychosocial model helps to maintain remission.[16] In a study evaluating patient feedback about psychotherapy, patients reported improvement in their disease course as a result of reduced stress.[17] Psychological screening in adolescent and young adult IBD patients is recommended to improve the patient's quality of life and lessen health care costs. Screening for anxiety and depressive symptoms ensures early recognition and therefore early treatment of psychological conditions as a means to provide patients with the best chance at remission of UC.

PHARMACOLOGICAL TREATMENT

The pharmacological treatment of UC follows a step-up approach. Therapy should begin with the medications with the least invasive and lowest side effect profile and increase to the next management option only when intolerant or refractory to a particular therapy. Treatment options are separated into severity of symptoms and disease stage, i.e. acute versus maintenance. While not all medications mentioned will be used in the primary care setting, it is important to recognize complications or side effects from medications that may be prescribed by a referral physician.

Mild to Moderate Disease

Glucocorticoids

Glucocorticoids work to decrease inflammation by increasing the transcription of genes, which code for anti-inflammatory proteins, in addition to inhibiting the expression of various inflammatory cytokines. First generation glucocorticoids such as prednisone, methylprednisolone and hydrocortisone have been used for the induction of clinical remission of IBD since the 1970's. Systemic glucocorticoids serve as first line therapy for both acute flares as well as severe UC. [18]

Drawbacks associated with first generation glucocorticoids, limiting their long-term use, are their side effect profile. The most important adverse effects to be aware of include weight gain, Cushing's syndrome, steroid-induced diabetes, cataracts, glaucoma, gastric ulcer, gastrointestinal bleeding, osteoporosis, hypertension, insomnia, anxiety, and immunosuppression. This severe side effect profile drove the innovation of second-generation glucocorticoids.

Second-generation glucocorticoids include budesonide, budesonide MMX and beclomethasone dipropionate. Budesonide MMX works via a colonic delivery technology known as Multi-Matrix System (MMX), which allows for extended release in the colon. Budesonide MMX induces remission in patients with mild to moderate UC and is currently utilized for patients non-responsive to traditional maintenance therapy. The benefits of second-generation over first-generation glucocorticoids are their mild side effect profile, of which most commonly include headache, nausea and urinary tract infection.[18]

Aminosalicylates

Aminosalicylates represent a class that is inclusive of many preparations, with 5-aminosalicylic acid, mesalamine, balsalazide, sulfasalazine and olsalazine being the most commonly used. As a class, they have antibacterial and anti-inflammatory properties, making them effective for the short- and long-term treatment of IBD. Aminosalicylates decrease inflammation by preventing leukocyte recruitment in the bowel wall. These medications are available in both oral and topical forms for the purpose of achieving and maintaining remission of mild-moderate UC.

The most significant adverse effects in this class concern sulfasalazine. Due to its sulfapyridine moiety, patients commonly experience nausea, vomiting, dyspepsia, anorexia, headache, and abnormal sperm counts, motility and morphology. Less common reactions include allergic reactions, pancreatitis, hepatotoxicity,

drug-induced connective tissue disease, bone marrow suppression, interstitial nephritis and hemolytic anemia or megaloblastic anemia. Nephrotoxicity is not commonly seen, however it is recommended that serum creatinine be measured and followed, before and during treatment, respectively.[19]

Topical therapy has less systemic absorption and is thus better tolerated. Combination therapy with topical and oral aminosalicylates allows patients the ability to possibly achieve maximal response and remission.

Moderate to Severe Disease

Purine analogs

Azathioprine and 6-mercaptopurine are the two most commonly used purine analogs, also known as thiopurines, targeted for moderate-severe UC. Azathioprine and 6-mercaptopurine are effective maintenance therapies for those who have failed aminosalicylates. Purine analogs work to inhibit the immune response through a series of mechanisms including inhibiting cell receptors, inducing T cell apoptosis, inhibiting lymphokine release, reducing monocyte production and blocking lymphocyte and monocyte interaction. In a 20-year retrospective study, thiopurine therapy allowed patients to achieve long-term steroid-free remission and mucosal healing.[20]

Adverse effects associated with thiopurines most commonly include neutropenia and leukopenia, hypersensitivity, and liver dysfunction. Additional less common adverse effects include fever, alopecia, and indigestion. It is important to monitor liver function as well as complete blood count levels in patients on azathioprine or 6-mercaptopurine therapy.[21]

Methotrexate

Methotrexate works to decrease inflammation associated with IBD through various mechanisms including enhancing adenosine concentrations, inhibiting cellular proliferation, limiting the production of inflammatory mediators, and inducing apoptosis. Previous studies have shown methotrexate to be effective in the management of UC for those who failed or were intolerant to thiopurines and have a steroid sparing effect.[22] Newer studies indicate that methotrexate might not be indicated for induction or maintenance therapy in UC.[23] At present, the results from medical trials do not support the use of low dose oral methotrexate for the production of remission in active ulcerative colitis. It is not known whether a higher dose of oral methotrexate, or giving methotrexate by a different route (e.g. by injection), would increase the likelihood of remission.[24]

Although methotrexate is well tolerated in the majority of patients, due to the low dosage requirement for therapeutic benefit in IBD patients, it does bear significant adverse effects that should be closely monitored. The most commonly noted adverse effects associated with methotrexate include hepatotoxicity, dyspnea, bone marrow suppression, osteomyelitis, nausea, vomiting, hair loss, arthralgias and myalgias. Long-term use of methotrexate is more significant for a high side effect profile. In a study evaluating the long-term hepatic and hematologic effects of methotrexate adverse effects included leukopenia, pancytopenia, megaloblastic anemia, thrombocytopenia, elevated liver enzymes, hepatic fibrosis, portal hypertension, and fatty liver disease. Other systemic effects include pulmonary fibrosis, nephrotoxicity, and mucocutaneous reactions. It is important to monitor liver and kidney function as well as complete blood count levels in patients on methotrexate therapy.

Anti-Tumor Necrosis Factor

Antibodies against tumor necrosis factor (anti-TNF) include several formulations, with the most commonly used for the treatment of UC being infliximab and adalimumab. Anti-TNF therapies are useful for UC patients who fail conventional therapy. Tumor necrosis factor (TNF) is a pro-inflammatory cytokine that plays a strong role in the pathogenesis of several autoimmune diseases, such as IBD. Therefore, anti-TNF therapy has been utilized to suppress the inflammatory cascade driven by TNF. Treatment with these agents show good short-term and long-term resolution of clinical signs and symptoms, as well as decrease the colectomy rate.[25]

Mild adverse effects associated with anti-TNF agents include abdominal pain, nausea, arthralgias and upper respiratory tract infections, while severe adverse effects include pneumonia, sepsis, tuberculosis, drug-induced lupus and malignant tumors. Other adverse effects include tuberculosis, worsening neurological disease, psoriasis exacerbations, liver function test abnormalities, hepatitis, thrombocytopenia and neutropenia. In addition, patients can experience infusion reactions that can present with symptoms of fever, chills, headache, pruritis, nausea, flushing, dizziness, dyspnea, chest pain, changes in blood pressure and anaphylaxis.

Anti-Integrins

Anti-integrins, also known as selective leukocyte adhesion molecule inhibitors, like TNF antagonists, are another type of infusion therapy useful for the induction and maintenance of UC. This treatment option is superior to anti-TNF agents for patients with an increased risk of infection, such as the elderly or those with immunocompromised states and is indicated for those who have failed or are intolerant to TNF antagonists.[26] Anti-integrins work by disrupting intravascular lymphocyte adhesion to the gastrointestinal tract thereby inhibiting the inflammatory immune cascade. The most commonly used anti-integrins indicated for UC induction and maintenance include natalizumab and vedolizumab.

Reported adverse effects associated with natalizumab include worsening of UC symptoms, headache, vomiting, lethargy, sore throat, Campylobacter jejunii enteritis and opportunistic infections such as progressive multifocal leukoencephalopathy (PML). Adverse effects associated with vedolizumab most commonly include lethargy, headache, arthralgias, nausea, pyrexia, nasopharyngitis, upper respiratory tract infection, cough, sinusitis, oropharyngeal pain, bronchitis, influenza, rash, pruritis, back pain and extremity pain. Mild infusion-related and hypersensitivity reactions have also been reported. Serious infections associated with vedolizumab therapy include abscess, sepsis, tuberculosis,

Salmonella, listeria meningitis, giardiasis and cytomegaloviral colitis. While no cases of PML have been reported with vedolizumab to date, the risk of PML cannot be ruled out; signs and symptoms for this disease process should be monitored.

Tofacitinib

Tofacitinib was approved for use in patients with moderate to severe rheumatoid arthritis in 2012 and was approved in 2018 for the treatment of treatment-resistant UC. Tofacitinib works by inhibiting janus kinase (JAK), most specifically JAK1 and JAK3. It decreases the signaling of inflammatory cytokines, thereby reducing inflammation associated with inflammatory diseases such as rheumatoid arthritis and IBD. Onset of action is rapid showing significant improvement in symptoms in just two weeks, with a reduction in baseline C-reactive protein levels in four weeks.[27]

Adverse effects reported in recent studies include increased overall rate of infections, especially herpes zoster, nonmelanoma skin cancer, cardiovascular events, and abnormal lipid levels. Tofacitinib remains a new UC therapy and therefore its studies are limited. The long-term safety and efficacy of tofacitinib for the treatment of UC requires close follow-up and ongoing data collection.[27]

Fulminant Disease

Cyclosporine

Cyclosporine is most commonly utilized as rescue therapy for UC patients who are steroid-resistant. It is effective at inducing remission in UC patients due to its rapid response time, as well as lasting effects. Cyclosporine works by mediating anti-inflammatory effects by lowering T cell activity and inducing apoptosis of lamina propria mononuclear cells. Severe adverse effects associated with cyclosporine include nephrotoxicity, infection, seizures and death. Less severe adverse effects include paresthesias, hypertension, hypertrichosis, headache, abnormal liver function tests, hyperkalemia and gingival hyperplasia. Renal function monitoring is important in patients receiving cyclosporine therapy.

Tacrolimus

Tacrolimus is used for patients with moderate to severe active UC whom are resistant to most therapies. It has proven to be a safe long-term therapeutic option that should be utilized prior to considering surgery for the management of UC. Tacrolimus is a macrolide antibiotic with an immunosuppressive role that works by inhibiting calcineurin, which results in the interruption of T cell signal transduction and prevention of inflammatory cytokine transcription.

Tacrolimus and cyclosporine share a similar side effect profile and thus patients on either therapy should be monitored the same way.[28] Adverse effects associated with tacrolimus include elevations in creatinine, tremor, cytomegalovirus colitis and esophagitis, herpes zoster, urinary tract infections, venous thrombosis, hypertension, headache, nausea, acquired thrombotic thrombocytopenia, and hypomagnesemia. *(Table 1, page 15)*

SURGICAL REFERRAL

Medical management of UC has advanced over time, however many patients that become refractory to pharmaceutical intervention or develop serious complications require surgery for definitive treatment. The indications for surgical referral include acute colitis associated with severe complications or nonresponsive to medical management, chronic disease resulting in steroid dependency in adults, chronic disease resulting in growth or pubertal delay in children, colon dysplasia or cancer, and reconstruction after previous colectomy.[29] Absolute indications for surgery in the case of acute colitis are toxic megacolon, perforation, and severe colorectal bleeding. Cancer of the colon or rectum is an absolute indication for surgical management, with the standard procedure being ileal pouch anal-anastomosis (IPAA). Although surgical intervention carries its own risks, when indicated and utilized appropriately, surgery can prevent further complications, improve quality and longevity of life, and in some circumstances even save lives. Surgery, as a treatment option, should be viewed as an additional treatment modality that complements other forms of therapy rather than a 'failure of medical management.' Close communication between the primary care physician, gastroenterologist, and colorectal surgeon is imperative in order to achieve safe and efficacious outcomes that improve the quality of life for patients with UC.

DISCUSSION

Ulcerative colitis is a disease that will be commonly encountered in the primary care setting. An Osteopathic approach to treatment will involve collaborating with the patient to develop a comprehensive, patient-centered treatment care plan that minimizes side effects and improves overall function. Monitoring for adverse effects to pharmaceutical treatment along with providing additional treatment options beyond medications will help the patient have reduced symptoms and an improved quality of life. The osteopathic family physician can provide excellent care to patients with ulcerative colitis to reduce the emotional and social impact associated with this lifelong illness.

TABLE 1 :

Summary of Pharmacological Treatment

Pharmaceutical	Mechanism of Action	Adverse Effects	Notes
Mild to Moderate			
Glucocorticoids First generation: prednisone, methylprednisolone, hydrocortisone Second generation: budesonide, beclomethasone	Increase transcription of genes that code for anti-inflammatory cytokines.	Weight gain, Cushing's syndrome, steroid-induced diabetes, cataracts, glaucoma, gastric ulcer, gastrointestinal bleeding, osteoporosis, hypertension, insomnia, anxiety, immunosuppression, urinary tract infection.	Second generation glucocorticoids have a milder side effect profile as opposed to first generation glucocorticoids.
Aminosalicylates 5-aminosalicylic acid, mesalamine, balsalazide, sulfasalazine and olsalazine	Decrease inflammation by preventing leukocyte recruitment in the bowel wall.	Dyspepsia, anorexia, abnormal sperm counts, motility and morphology, allergic reactions, pancreatitis, hepatotoxicity, drug-induced connective tissue disease, bone marrow suppression, nephrotoxicity, hemolytic anemia, megaloblastic anemia.	Topical formulations are better tolerated. Monitor serum creatinine.
Moderate to Severe			
Purine analogs Azathioprine, 6-mercaptopurine	Inhibit the immune response through a series of mechanisms.	Neutropenia, leukopenia, hypersensitivity, liver dysfunction, fever, alopecia and indigestion. Hepatotoxicity associated with 6-mercaptopurine.	Monitor liver function and complete blood
Methotrexate	Enhance adenosine concentrations, inhibit cellular proliferation, limit the production of inflammatory mediators, and induce apoptosis.	Hepatotoxicity, dyspnea, bone marrow suppression, megaloblastic anemia, elevated liver enzymes, hepatic fibrosis, portal hypertension, fatty liver disease, osteomyelitis, hair loss, arthralgias, myalgias, pulmonary fibrosis, nephrotoxicity, muco-cutaneous reactions.	Monitor liver and kidney function, as well as complete blood count levels
Anti-Tumor Necrosis Factor Infliximab, adalimumab	Suppress the inflammatory cascade driven by TNF	Infusion reactions, abdominal pain, nausea, arthralgias, upper respiratory tract infections, pneumonia, sepsis, tuberculosis, drug-induced lupus, malignant tumors, liver function test abnormalities, hepatitis, thrombocytopenia and neutropenia.	
Anti-Integrins Infliximab, adalimumab	Disrupt intravascular lymphocyte adhesion to the gastrointestinal tract thereby inhibiting the inflammatory immune cascade.	Lethargy, upper respiratory tract infections, Campylobecter jejunii enteritis, opportunistic infections such as PML, and arthralgias. Serious infections associated with vedolizumab therapy include abscess, sepsis, tuberculosis, Salmonella, Listeria meningitis, giardiasis and cytomegaloviral colitis.	Monitor for signs and symptoms of PML.
Tofacitinib	Inhibitor of janus kinase (JAK), thereby inhibiting the signaling of inflammatory cytokines.	Increase in the overall rate of infections, especially herpes zoster, non-melanoma skin cancer, cardiovascular events, and abnormal lipid levels.	Long-term safety and efficacy require close follow-up.
Fulminant			
Cyclosporine	Suppresses T cell activity and induces apoptosis of lamina propria mononuclear cells.	Nephrotoxicity, infection, seizures, death, paresthesias, hypertension, hypertrichosis, headache, abnormal liver function tests, hyperkalemia and gingival hyperplasia.	Monitor kidney function.
Tacrolimus	Macrolide antibiotic that prevents transcription of inflammatory cytokines.	Elevated creatinine, tremor, cytomegalovirus colitis and esophagitis, herpes zoster, urinary tract infections, venous thrombosis, hypertension, headache, nausea, acquired thrombotic thrombocytopenia, and hypomagnesemia.	Monitor kidney function.

AUTHOR DISCLOSURES:
No relevant financial affiliations or conflicts of interest.

REFERENCES:

1. Shivashankar, R., Tremaine, W., Harmsen, W., & Loftus, E. (2017). Incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota from 1970 through 2010. Clinical Gastroenterology and Hepatology, 15(6), 857-863. doi:10.1016/j.cgh.2016.10.039
2. Karlinger, K., Györke, T., Makö, E., Mester, A., & Tarján, Z. (2000). The epidemiology and the pathogenesis of inflammatory bowel disease. European Journal of Radiology, 35(3), 154-167. doi:10.1016/S0720-048X(00)00238-2
3. Castaneda, G., Liu, B., Torres, S., Bhuket, T., & Wong, R. (2017). Race/ethnicity-specific disparities in the severity of disease at presentation in adults with ulcerative colitis: A cross-sectional study. Digestive Diseases and Sciences, 62(10), 2876-2881. doi:10.1007/s10620-017-4733-5
4. Ungaro, R., Mehandru, S., Allen, P., Peyrin-Biroulet, L., & Colombel, J., Department of Gastroenterology, University Hospital of Nancy-Brabois, Vandoeuvre-les-Nancy, France. (2017). Ulcerative colitis. The Lancet, 389(10080), 1756-1770. doi:10.1016/S0140-6736(16)32126-2
5. Bye, W., Ma, C., Nguyen, T., Parker, C., Jairath, V., & East, J. (2018). Strategies for detecting colorectal cancer in patients with inflammatory bowel disease: A cochrane systematic review and meta-analysis. The American Journal of Gastroenterology, 113(12), 1801-1809. doi:10.1038/s41395-018-0354-7
6. Hartnett, L., & Egan, L. (2012). Inflammation, DNA methylation and colitis-associated cancer. Carcinogenesis, 33(4), 723-731.
7. Barnes, E., Nestor, M., Onyewadume, L., De Silva, P., Korzenik, J., Aguilar, H., Waldholtz, B., Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, Boston, Massachusetts. (2017). High dietary intake of specific fatty acids increases risk of flares in patients with ulcerative colitis in remission during treatment with aminosalicylates. Clinical Gastroenterology and Hepatology, 15(9), 1390-1396.
8. Licciardone JC, Kearns CM, Hodge LM, Bergamini MV. Associations of cytokine concentrations with key osteopathic lesions and clinical outcomes in patients with nonspecific chronic low back pain: results from the OSTEOPATHIC Trial. J Am Osteopath Assoc. 2012; 112: 596–605.
9. Cicchitti, L., Martelli, M., Cerritelli, F., & D'Acquisto, F., Academic Editor. (2015). Chronic inflammatory disease and osteopathy: A systematic review. Plos One, 10(3).
10. Balzola, F., Cullen, G., Ho, G., & Russell, R. (2013). Effect of polyunsaturated fatty acids on tight junctions in a model of the human intestinal epithelium under normal and inflammatory conditions. Inflammatory Bowel Disease Monitor, 14(1), 28-29.
11. Hou, Jason, Abraham, Bincy, El-Serag, Hashem (2011). Dietary Intake and Risk of Developing Inflammatory Bowel Disease: A Systematic Review of the Literature. The American Journal of Gastroenterology, 106 (4), 563-573.
12. Gopi, S., Amalraj, A., Jude, S., Varma, K., Sreeraj, T., Haponiuk, J., & Thomas, S. (2017). Preparation, characterization and anti-colitis activity of curcumin-asafoetida complex encapsulated in turmeric nanofiber. Materials Science & Engineering C, 81, 20-31. doi:10.1016/j.msec.2017.07.037
13. Derwa, Y., Gracie, D., Hamlin, P., & Ford, A. (2017). Systematic review with meta-analysis: Efficacy of probiotics in inflammatory bowel disease. Alimentary Pharmacology and Therapeutics, 46(4), 389-400.
14. Graziani, C., Petito, V., Del Chierico, F., Mangiola, F., Pecere, S., Schiavoni, E.,et al. Bologna Italy 20170329-20170401. (2017). Oc.14.6: Escherichia coli Nissle 1917 modulate gut microbiota composition in ulcerative colitis patients. Digestive and Liver Disease, 49, 119. doi:10.1016/S1590-8658(17)30390-0
15. Van den Brink, G., Stapersma, L., Vlug, L., Rizopolous, D., Bodelier, A., Wering, H., Escher, J. (2018). Clinical disease activity is associated with anxiety and depressive symptoms in adolescents and young adults with inflammatory bowel disease. Alimentary Pharmacology & Therapeutics, 48(3), 358-369.
16. Ananthakrishnan, A., Khalili, H., Pan, A., Higuchi, L., De, S., Richter, J.,Chan, A. (2013). Association between depressive symptoms and incidence of Crohn's disease and ulcerative colitis: Results from the nurses' health study. Clinical Gastroenterology and Hepatology: The Official Clinical Practice Journal of the American Gastroenterological Association,11(1), 57-62.
17. Mikocka-Walus, A., Gordon, A., Stewart, B., & Andrews, J. (2013). 'Just to get it off my chest': Patients' views on psychotherapy in inflammatory bowel disease. Counselling and Psychotherapy Research, 13(3), 227-234.
18. Dubois-Camacho K, Ottum PA, Franco-Muñoz D, De la Fuente M, Torres-Riquelme A, Díaz-Jiménez D, Olivares-Morales M, Astudillo G, Quera R, Hermoso MA. Glucocorticosteroid therapy in inflammatory bowel diseases: From clinical practice to molecular biology. World J Gastroenterol 2017, 23(36): 6628-6638.
19. Kornbluth, A., Sachar, D., & Practice Parameters Committee of the American College of Gastroenterology. (2010). Ulcerative colitis practice guidelines in adults: American college of gastroenterology, practice parameters committee. The American Journal of Gastroenterology, 105(3), 501-23.
20. Daniela, P., Annalisa, A., Stefano, F., Pietro, M., Rita, M., Luisa, G., Alessandro, A. (2018). Sustained clinical efficacy and mucosal healing of thiopurine maintenance treatment in ulcerative colitis: A real-life study. Gastroenterology Research and Practice, (2018). doi:10.1155/2018/4195968
21. Kakuta, Y., Kawai, Y., Okamoto, D., Takagawa, T., Ikeya, K., Suzuki, Y. (2018). Nudt15 codon 139 is the best pharmacogenetic marker for predicting thiopurine-induced severe adverse events in Japanese patients with inflammatory bowel disease: A multicenter study. Journal of Gastroenterology, 53(9), 1065-1078. doi:10.1007/s00535-018-1486-7.
22. Wahed, M., Louis-Auguste, J., Baxter, L., Limdi, J., McCartney, S., Lindsay, J., & Bloom, S. (2009). Efficacy of methotrexate in crohn's disease and ulcerative colitis patients unresponsive or intolerant to azathioprine / mercaptopurine. Alimentary Pharmacology and Therapeutics, 30(6), 614-620.
23. Herfarth, H., Barnes, E., Valentine, J., Hanson, J., Higgins, P., Isaacs, K., Lewis, J. (2018). Methotrexate is not superior to placebo in maintaining steroid-free response or remission in ulcerative colitis. Gastroenterology, 155(4), 1098-1108. doi:10.1053/j.gastro.2018.06.046
24. Macaluso, F., Renna, S., Cottone, M., & Orlando, A. (2016). The meteor trial: The burial of methotrexate in ulcerative colitis? Gastroenterology, 151(1), 211-2. doi:10.1053/j.gastro.2016.02.085
25. Ruxi, L., Weiguang, Q., Zhiyong, W., Yinjun, W., Shixue, D., Qiang, L., & Xuebao, Z. (2014). Tumor necrosis factor alpha blocking agents as treatment for ulcerative colitis intolerant or refractory to conventional medical therapy: A meta-analysis. Plos One, 9(1). doi:10.1371/journal.pone.0086692
26. Khanna, R., Mosli, M., & Feagan, B. (2016). Anti-integrins in ulcerative colitis and Crohn's disease: What is their place? Digestive Diseases (Basel, Switzerland), 34(1-2), 153-9.
27. Pouillon, L., Bossuyt, P., & Peyrin-Biroulet, L. (2017). Tofacitinib is the right octave for ulcerative colitis. Gastroenterology, 153(3), 862-864. doi:10.1053/j.gastro.2017.07.027
28. Weigmann, B., Mott, S., Atreya, R., & Neurath, M. (2017). A mechanism of action for cyclosporine a in ulcerative colitis: The role of the TEC kinase ITK in disease pathogenesis. Gastroenterology, 152(5), 758.
29. Gallo, G., Kotze, P., & Spinelli, A. (2018). Surgery in ulcerative colitis: When? how? Best Practice & Research Clinical Gastroenterology, 32-33, 71-78. doi:10.1016/j.bpg.2018.05.017

OMTotal

A comprehensive, on-demand collection of OMT training videos

Special Introductory Price

SAVE $25

on your subscription to OMTotal when you use the code **OMTOTAL25** at checkout!

Refine your skills with step-by-step demonstrations of over 150 osteopathic manipulative treatment (OMT) procedures. Sort and select the videos according to anatomic area to be treated, type of OMT procedure (muscle energy, counter-strain, HVLA, etc.) or chapter in the ACOFP publication *Somatic Dysfunction in Osteopathic Family Medicine*.

These videos are ideal for preparing to take practical portion of the AOBFP recertification exam or simply brushing up on your OMT techniques, with the convenience of a comprehensive on-demand collection—there when you need them most on whichever device you choose.

www.acofp.org/OMTotal

acofp AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

REVIEW ARTICLE

Urticaria: Diagnosis and Treatment with Osteopathic Considerations

Stephen Stacey, DO[1]; Daniel Burke, DO[1]; Timothy Brininger, DO[1]

[1]Peak Vista Community Health Centers, Colorado Springs, CO

KEYWORDS:

Antihistamines

Dermatology

Family Medicine

Primary Care

Urticaria

ABSTRACT: Urticaria is a common benign dermatologic condition. It is primarily manifested by well-marginated pruritic wheals typically surrounded by erythema caused by the release of histamine into the skin. Urticaria may occur with or without angioedema and typically resolves within 24 hours. Urticaria that persists or recurs past six weeks is known as chronic urticaria. Urticaria may be caused by various medications and illnesses, though in most cases, a trigger cannot be identified. Certain forms of urticaria may be triggered by physical stimuli such as pressure, heat, cold, water, or sunlight. Antihistamines are the mainstay of pharmacotherapy for acute and chronic urticaria. Trigger avoidance should be emphasized when a trigger is identified. Other treatments include oral steroids, doxepin and omalizumab. Topical steroids are ineffective. This article reviews the presentation, diagnosis and treatment of acute and chronic urticaria.

Urticaria (also known as hives) is a common benign dermatologic condition caused by histamine released into the skin. It appears as well-demarcated, raised pruritic pale, pink or red wheals typically surrounded by erythema. Lesions can appear on any part of the skin and may range in size from millimeters to centimeters with well-demarcated, serpiginous borders. They may rapidly change size and coalesce or be separate. The lesions are blanching, are not tender and resolve without residual skin changes. *(Figures 1—4)*

The onset of urticaria to maximal spread usually takes from minutes to hours. They typically resolve without treatment in less than 24 hours. Lesions that recur within six weeks are considered recurrent acute urticaria.[1] Lesions that repeatedly occur over a period lasting more than six weeks are called chronic urticaria. Lesions that last longer than 24 hours, do not blanch or leave behind pigment changes following resolution are atypical and may be associated with urticarial vasculitis.[2,3]

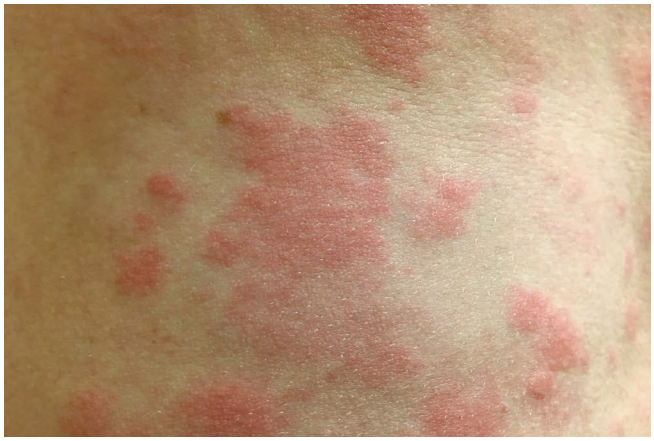
Acute and chronic urticaria may occur with or without angioedema. Angioedema is swelling that occurs deeper in the tissues without any overlying skin changes. The discussion of urticaria in this paper includes both urticaria without angioedema as well as urticaria with angioedema. Angioedema occurring without urticaria is a separate clinical entity and is not addressed in this paper. This paper also does not discuss other conditions relating to the release of histamine, such as anaphylaxis.

EPIDEMIOLOGY

Urticaria is a common disorder, and the prevalence varies from 20% spontaneous acute urticaria, to 1% of the general population with chronic recurrent urticarial symptoms (depending on the which

FIGURE 1:

Urticaria on the flank of an adult male



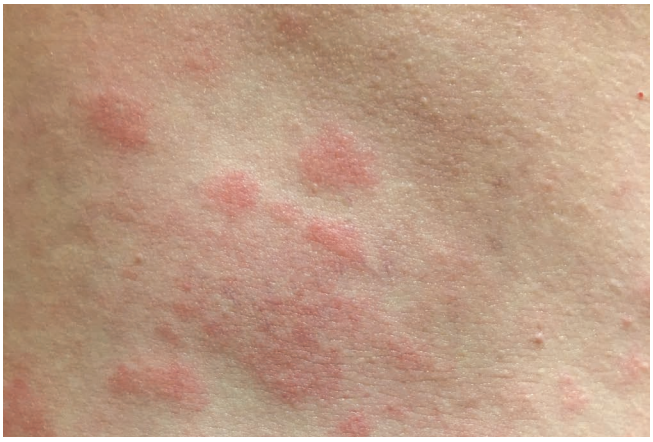
Stephen K. Stacey, DO (Photographer)

CORRESPONDENCE:
Stephen Stacey, DO | stacey.stephen@mayo.edu

 Print ISSN: 1877-573X
DOI:10.33181/12035

FIGURE 2:

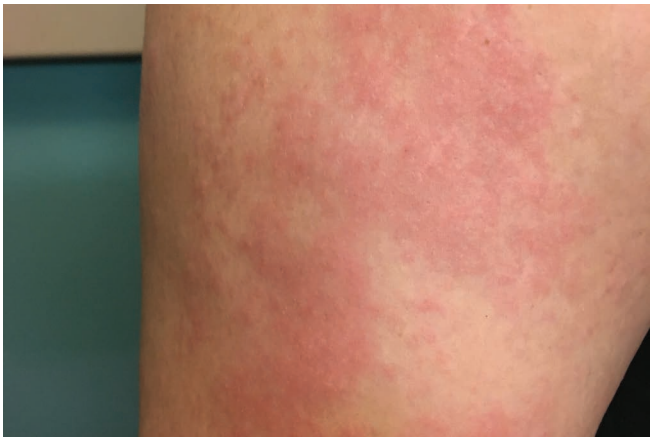
Urticaria on the back of an adult male



Stephen K. Stacey, DO (Photographer)

FIGURE 3:

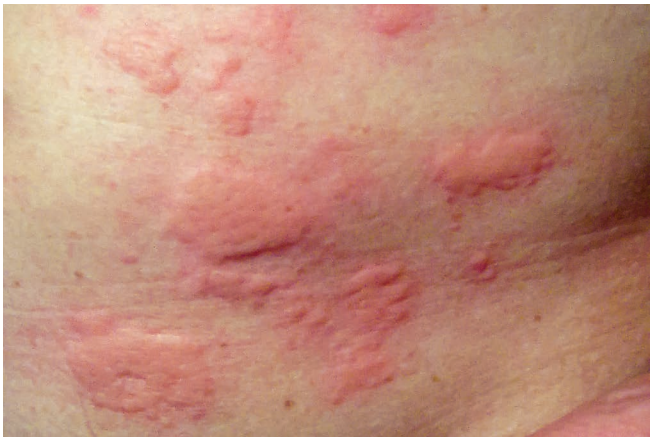
Urticaria on the arm of an adult female



Stephen K. Stacey, DO (Photographer)

FIGURE 4:

Erythematous wheals of urticaria



Enoch Lau (Photographer). Licensed under CC by 3.0.

trigger the patient is susceptible).[3,4] Approximately 16-20% of those with recurrent acute urticaria will go on to develop the chronic form.[5] Chronic urticaria is noted in approximately 0.6-1% of the general population, with similar reports from multiple countries.[3,4,5,6] Prevalence is higher in women and adults in the third or fourth decade of life. Chronic urticaria may resolve spontaneously in up to 50% within the first year and in up to 80% by five years.

ETIOLOGY

The wheals of urticaria result from the release of histamine into the epidermis by mast cells and basophils. Histamine release into the deeper tissues such as the dermis and subcutis results in angioedema. This histamine release is typically IgE mediated in response to allergens that stimulate an immune response. However, non-IgE histamine release may result from proteases from aeroallergens, complement activation and autoantibodies to IgE. Systemic conditions are uncommon causes of urticaria and include mastocytosis, Hashimoto thyroiditis, hypothyroidism, Sjögren syndrome, SLE, RA, celiac, vasculitis, lymphoma, and viral infection such as hepatitis B and C. Medications may cause urticaria either through sensitization and IgE-mediated allergic response or direct stimulation of mast cell degranulation. Other common causes include insect bites, pruritic urticarial papules and plaques of pregnancy (PUPPP), physical urticaria and cholinergic urticaria.[7]

Acute urticaria typically results from exposure to a specific trigger. Patients may report a history of being exposed to drugs, environmental allergens, arthropod bite, food or specific contact allergen. Common offending drugs include penicillins, sulfonamides, NSAIDs, diuretics, muscle relaxants, and contrast dye. Common offending foods include milk, eggs, shellfish, peanuts, and tree nuts. They may also develop as a response to acute viral infection. Strong emotions are even purported to play a role in many cases. However, in approximately 30-50% of cases, no specific trigger is found.[8,9] The etiology of chronic urticaria is not well-understood. A specific trigger is rarely found even after a thorough search. It is likely caused by an autoimmune process involving IgG autoantibodies against IgG.[10]

Physical urticarias are a subset of urticaria caused by physical triggers. Physical triggers include physical pressure, heat, cold, water, or sunlight. Significant diagnostic uncertainty may exist in the diagnosis of physical urticarias because in certain patients the urticaria develops after a considerable delay following exposure to the offending process.[11,12,13]

WORKUP

The initial evaluation of urticaria involves a thorough history and general physical exam. The typical history of urticaria is of characteristic lesions that are very pruritic and arise over several hours and typically resolve within 24 hours without treatment. No labs or imaging are required to establish the diagnosis of urticaria but may help rule-out alternative diagnoses if indicated. Evaluation begins by establishing whether the urticaria are acute or chronic. Chronic urticaria are defined as recurring for over six weeks. History should also focus on identifying possible triggers

of urticaria as discussed above under "etiology".[14,15]

During the physical exam, lesions on any affected skin surface should be evaluated. The character and distribution of the lesions should be described. If the lesions have resolved before the evaluation, it can often be helpful to ask whether the patient has taken a picture of the lesions. In the case of recurrent urticaria, patients should be encouraged to take pictures of active lesions. Also note the presence of any excoriations in addition to the primary lesions. Urticaria should typically resolve without any residual skin changes, and the presence of remaining hyperpigmentation or other effects should prompt consideration of an alternate diagnosis such as urticaria pigmentosa.[16]

Several forms of physical urticaria can be elicited during the physical exam. The performance of each of these exam maneuvers is typically not indicated for acute urticaria. However, during the evaluation of chronic urticaria it can be helpful to evaluate whether a form of physical urticaria is the cause of the patient's symptoms. These are discussed in greater detail under "physical urticaria."

Laboratory evaluation and biopsies are not required to make the diagnosis of urticaria. They may be obtained to rule-out other diagnoses. No imaging is required. Skin prick testing is likewise not indicated as it has not been shown to improve outcomes or significantly alter management in either acute or chronic urticaria.[17,18] As part of their Choosing Wisely campaign, the American Academy of Allergy, Asthma & Immunology has stated: "Don't routinely do diagnostic testing in patients with chronic urticaria." They further state that "Routine extensive testing is neither cost effective nor associated with improved clinical outcomes. Skin or serum-specific IgE testing for inhalants or foods is not indicated, unless there is a clear history implicating an allergen as a provoking or perpetuating factor for urticaria."

PHYSICAL URTICARIA

Physical urticaria are a subset of urticaria caused by an identifiable physical trigger *(Table 1)*. Such triggers include physical pressure, heat, cold, water and sunlight. In general, physical urticaria may be evaluated by exposing the patient to the suspected trigger and observing the response. Care should be taken not to confound exposures, which may complicate the clinical assessment. For example, when assessing cold urticaria, if ice is placed directly on the skin then the patient has been exposed to both low temperature as well as water.[19] *(Table 2)*

Dermatographism is a condition in which physical pressure elicits the direct release of histamine, creating a wheal. It can be elicited by gently stroking the patient with a sharp object such as the wooden end of a cotton-tipped applicator. The wheals will typically appear within minutes over the area with or without pruritus. In delayed-pressure urticaria, the wheals may not appear until 6-12 or even 24 hours later, so the patient should be asked to continue to monitor the area for development of lesions if none are seen during exam.[20]

Cholinergic urticaria (sometimes known as generalized heat urticaria) is a condition in which hives develop diffusely in response to increased body temperature. Triggers may include exercise, hot water, ingestion of spicy foods, high ambient temperatures, or even strong emotions. The diagnosis can be clinical based off a history of suspicious lesions in the appropriate context. However, if the diagnosis is in question or requires confirmation, induced heat can be applied in the office. One method involves submerging the patient's arms in 40°C (104°F) hot water until the core temperature has elevated by at least 0.7 °C. The diagnosis is confirmed by the appearance of lesions in sites other than those directly exposed to the water.[21]

Local heat urticaria is a condition caused by heat applied to a focal area of skin. Unlike cholinergic urticaria, only the portions of skin exposed to the head manifest symptoms. This can be induced by applying a container of water heated to approximately 110 °F. Care should be taken to not accidentally burn the patient while still applying heat strong enough to induce symptoms.[22]

Cold urticaria may be elicited by conducting a cold stimulation test. One way to perform this test is to expose a portion of the patient's skin (such as the volar forearm) to ice in a plastic bag. The ice should be applied for five minutes. The skin should be observed after about ten minutes for the development of urticaria.[23]

Aquagenic urticaria may be elicited by placing one of the patient's extremities into a basin filled with water for 20–30 minutes. The water should be lukewarm to avoid confusion with local heat urticaria or cold-induced urticaria.[24]

Solar urticaria is a rare cause of urticaria. It is provoked by exposure to sunlight. Concerning clinical history with lesions of appropriate clinical appearance are enough to secure the diagnosis in most cases. If uncertainty exists, patients can be tested with controlled light exposure, which requires specialty equipment.[25]

TABLE 1:

Common urticaria treatments

TREATMENT	DESCRIPTION
Trigger avoidance	Indicated for all cases in which a trigger is identified.
Non-sedating H1 antihistamines	First-line therapy. Examples include loratadine, fexofenadine, cetirizine. May titrate dose to effect.
First-generation (sedating) H1 antihistamines	These agents possess a higher side-effect potential when compared with non-sedating antihistamines and should only be used at approved doses. Examples include diphenhydramine or hydroxyzine.
H2 antihistamines	Used in conjunction with H1 antihistamines as second-line therapy. Examples include ranitidine, cimetidine, famotidine.
Systemic steroids	May be used for refractory or severe cases. One sample regimen is prednisone 0.5—1 mg/kg as a single or divided dose daily for 3—5 days.
Topical steroids	Play no role in the management of urticaria.

TABLE 2:

Physical urticaria types

CONDITION	DESCRIPTION	EVALUATION
Dermatographism	Physical pressure elicits the direct release of histamine, creating a wheal.	Gently stroke the patient with a sharp object. Wheals typically appear within minutes.[20]
Cholinergic urticaria	Diffuse wheals develop in response to elevated body temperature.	Increase the patient's core temperature and observe for urticaria at sites not directly exposed to heat.[21]
Local heat urticaria	Wheals develop in areas of skin directly exposed to heat.	Apply dry heat (e.g., warm dry compress) to the patient's skin. Lesions are observed only at the area of exposure (contrast with cholinergic urticaria).[22]
Cold urticaria	Wheals develop in areas of skin directly exposed to cold.	Apply dry cold (e.g. ice covered in a bag) to the patient's skin. Lesions are observed at the area of exposure.[23]
Aquagenic urticaria	Wheals develop in areas of skin directly exposed to water.	Apply lukewarm water to patient's skin. Lesions are observed at the area of exposure.[24]
Solar urticaria	Wheals develop in areas of skin directly exposed to sunlight.	Clinical history with typical lesions in appropriate distribution. May attempt controlled exposure using specialty equipment.[25]

TREATMENT

Treatment options have variable efficacy and sometimes numerous agents may need to be tried to find the most efficacious plan. *(Table 1)* Avoidance of the inciting agent is fundamental as it is the single most effective therapy. It should be emphasized with all patients, but is sometimes difficult to accomplish. Many of the triggers for the various forms of physical urticaria such as sunlight, heat, cold, water, exercise and vibration can be avoided only to a limited extent.[26,27]

First-line pharmacotherapy for acute urticaria is to use a non-sedating H1-antihistamine such as fexofenadine, cetirizine, loratadine, or desloratadine. There is no evidence that any agent is superior to any other. Dosing can safely be titrated up to as high as four times the usual dose.[28] If symptoms are still not controlled, the addition of a histamine H2-receptor antagonist such as ranitidine, cimetidine, or famotidine may be attempted. A first-generation H1-antihistamine such as diphenhydramine or hydroxyzine may prove beneficial, especially if dosed at bedtime. Sometimes using a non-sedating antihistamine in the AM and a sedating antihistamine in the evening may prove effective.

For cases that do not respond to antihistamines, a short course of systemic corticosteroids (e.g. prednisone 0.5 to 1 mg/kg/d as a single or divided dose) may be attempted. Topical steroids are not an effective treatment for urticaria and should not be used.[29]

Treatment of chronic urticaria again focuses primarily on trigger identification and avoidance. Recurrent episodes may be treated individually as per treatment of acute urticaria above. If episodes are frequent, daily use of antihistamines may be required to reduce symptom burden. In these patients, steroids should be avoided if possible as the benefits of chronic steroid use may not outweigh the risks. Alternative treatments include doxepin, a tricyclic antidepressant with very potent antihistaminic effects. If all these treatment options are ineffective then omalizumab, cyclosporine and other anti-inflammatory/immunosuppressive agents have been advocated by many and found to be effective in select cases.[30]

FOLLOW-UP

Patients with acute urticaria typically do not require routine follow-up as the vast majority of cases resolve completely within 24–48 hours and do not recur. They should be advised that if lesions persist and become chronic, they should return for further evaluation. Patients with chronic urticaria should be monitored regularly for compliance and response to therapy.[31]

Lesions that do not blanch or leave behind pigment changes following resolution are atypical and may be associated with urticarial vasculitis. These lesions may require a biopsy.

OSTEOPATHIC CONSIDERATIONS

Lesions are distressing to the patient and often interrupt normal function. When patients experience severe pruritus, they naturally scratch the symptomatic area. The resultant structural changes (i.e. microtrauma from scratching) can interfere with the regulatory functions of the skin. This allows release of moisture and causes local irritation with inflammation. The resulting skin changes can cause a concomitant acute irritant dermatitis and, if continued, may even result in lichen simplex or other neurodermatoses. Understanding the psychological effects of the dermatologic disease is extremely important in providing whole-person healthcare. Urticarial lesions are temporarily disfiguring, and the patient's perception of a deteriorating appearance may contribute to or exacerbate underlying emotional stress or anxiety. Also, patients are often worried that the lesions may represent a severe condition, which can further exacerbate any mental condition.

CONCLUSION

For most cases of urticaria, the diagnosis is straightforward. Trigger identification should be attempted, and avoidance advised when able. Extensive diagnostic testing beyond a thorough history and physical is rarely indicated. In the cases where the diagnosis is in question, limited diagnostic testing should be performed to rule out alternative causes of the patient's symptoms. Treatment with antihistamines is usually successful. When needed, dosing may be safely titrated up to four times the typical level. Multiple forms of antihistamines may be attempted, beginning with non-sedating H1-antihistamines and adding H2-antihistamines or sedating (first-generation) H1-antihistamines as needed. Advise patients to avoid scratching the lesions. Cases of acute urticaria rarely need follow up as they typically resolve within 24–48 hours. Regularly monitor patients with chronic urticaria for response and adherence to treatment.

AUTHOR DISCLOSURES:
No relevant financial affiliations or conflicts of interest.

REFERENCES:

1. Magen E, Zueva E, Mishal J, Schlesinger M. The clinical and laboratory characteristics of acute spontaneous urticaria and its progression to chronic spontaneous urticaria. Allergy Asthma Proc. 2016 Sep;37(5):394-9.
2. Grattan C, Powell S, Humphreys F. Management and diagnostic guidelines for urticaria and angio-oedema. Br J Dermatol. 2001 Apr;144(4):708-14.
3. Umer N, Bajwa Z, Ostro M, Sheikh J. A retrospective review of clinical presentation, thyroid autoimmunity, laboratory characteristics, and therapies used in patients with chronic idiopathic urticaria. Ann Allergy Asthma Immunol. 2009 Dec;103(6):496-501.
4. Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006 Feb;117(2):391-7.
5. Fonacier L, Aquino M, Kim B. Clinical evaluation and treatment of chronic urticaria. Postgrad Med. 2010 Mar;122(2):148-56.
6. Gaig P, Olona M, Muñoz Lejarazu D, et al. Epidemiology of Urticaria in Spain. J Investig Allergol Clin Immunol. 2004;14(3):214-20.
7. Lapi F, Cassano N, Pegoraro V, et al. Epidemiology of chronic spontaneous urticaria: results from a nationwide, population-based study in Italy. Br J Dermatol. 2016 May;174(5):996-1004.
8. Taylor D, Pappo E, Aronson IK. Polymorphic eruption of pregnancy. Clin Dermatol. 2016 May-Jun;34(3):383-91. Kim MH, Park CH, Kim DI, et al. Surveillance of contrast-media-induced hypersensitivity reactions using signals from an electronic medical recording system. Ann Allergy Asthma Immunol. 2012 Mar;108(3):167-71.
9. Ellis AK, Day JH. Diagnosis and management of anaphylaxis. CMAJ. 2003 Aug 19;169(4):307-11.
10. Hernandez RG, Cohen BA. Insect bite-induced hypersensitivity and the SCRATCH principles: a new approach to papular urticaria. Pediatrics. 2006 Jul;118(1):e189-96.
11. Panaszek B, Pawłowicz R, Grzegrzółka J, Obojski A. Autoreactive IgE in Chronic Spontaneous/Idiopathic Urticaria and Basophil/Mastocyte Priming Phenomenon, as a Feature of Autoimmune Nature of the Syndrome. Arch Immunol Ther Exp (Warsz). 2017 Apr;65(2):137-143.
12. Chen Q, Zhong H, Chen WC, Zhai Z, et al. Different expression patterns of plasma Th1, Th2, Th17 and Th22related cytokines correlate with serum autoreactivity and allergen sensitivity in chronic spontaneous urticaria. Journal Of The European Academy Of Dermatology And Venereology. 2018;(3):441.
13. Waserman S, Chad Z, Francoeur MJ, Small P, et al. Management of anaphylaxis in primary care: Canadian expert consensus recommendations. Allergy. 2010 Sep;65(9):1082-92.
14. Lieberman P, Nicklas RA, Oppenheimer J, Kemp SF, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 update. J Allergy Clin Immunol. 2010 Sep;126(3):477-80.
15. Brown AF, McKinnon D, Chu K. Emergency department anaphylaxis: a review of 142 patients in a single year. J Allergy Clin Immunol. 2001 Nov;108(5):861-6.
16. Simons FE. Anaphylaxis, killer allergy: long-term management in the community. J Allergy Clin Immunol. 2006 Feb;117(2):367-77.
17. Greaves, MW. Chronic Idiopathic Urticaria. Curr Opin Allergy Clin Immunol. 2003 Oct;3(5):363-8.
18. Sánchez-Borges M, González-Aveledo L, Caballero-Fonseca F, Capriles-Hulett A. Review of Physical Urticarias and Testing Methods. Curr Allergy Asthma Rep. 2017 Aug;17(8):51.
19. Lang DM, Hsieh FH, Bernstein JA. Contemporary approaches to the diagnosis and management of physical urticaria. Ann Allergy Asthma Immunol. 2013 Oct;111(4):235-41.
20. Fukunaga A, Washio K, Hatakeyama M, et al. Cholinergic urticaria: epidemiology, physiopathology, new categorization, and management. Clin Auton Res. 2018 Feb;28(1):103-113.
21. Bullerkotte U, Wieczorek D, Kapp A, Wedi B. Effective treatment of refractory severe heat urticaria with omalizumab. Allergy. 2010 Jul;65(7):931-2.
22. Boyce JA. Successful treatment of cold-induced urticaria/anaphylaxis with anti-IgE. J Allergy Clin Immunol. 2006 Jun;117(6):1415-8.
23. Shelley WB, Rawnsley HM. Aquagenic Urticaria Contact Sensitivity Reaction to Water. JAMA. 1964 Sep 21;189:895-8.
24. Monfrecola G, Masturzo E, Riccardo AM. Solar Urticaria: A Report on 57 Cases. Am J Contact Dermat. 2000 Jun;11(2):89-94.
25. Kulthanan K, Chiawsirikajorn Y, Jiamton S. Acute urticaria: etiologies, clinical course and quality of life. Asian Pac J Allergy Immunol. 2008 Mar;26(1):1-9.
26. Baiardini I, Braido F, Molinengo G, et al. Chronic Urticaria Patient Perspective (CUPP): The First Validated Tool for Assessing Quality of Life in Clinical Practice. J Allergy Clin Immunol Pract. 2018 Jan - Feb;6(1):208-218.
27. Ortonne JP. Chronic urticaria: a comparison of management guidelines. Expert Opin Pharmacother. 2011 Dec;12(17):2683-93.
28. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014 May;133(5):1270-7.
29. Maurer M, Rosén K, Hsieh HJ, et al. Omalizumab for the Treatment of Chronic Idiopathic or Spontaneous Urticaria. N Engl J Med. 2013 Mar 7;368(10):924-35.
30. Kozel MM, Mekkes JR, Bossuyt PM, Bos JD. Natural course of physical and chronic urticaria and angioedema in 220 patients. J Am Acad Dermatol. 2001 Sep;45(3):387-91. Confino-Cohen R, Chodick G, Shalev V, et al. Chronic urticaria and autoimmunity: Associations found in a large population study. J Allergy Clin Immunol. 2012 May;129(5):1307-13.
31. Rance K, Goldberg P. The Management of Chronic Urticaria: A Clinical Update and Review. J Allergy Clin Immunol. 2013 Nov;4(6): 305-9.

Forging Our Osteopathic Future: Donor Honor Roll

ACOFP Foundation leaders would like to recognize the following individuals for their tremendous contributions to the Forging Our Osteopathic Future fundraising initiative.

Thank you all for your support.

Pinnacle Donors ($50,000+)
Jeffrey S. Grove, DO, FACOFP *dist.*

Diamond Donors ($25,000+)
Eugene M. DiBetta, Jr., DO
Carol L. Henwood, DO, FACOFP *dist.*
Paul A. Martin, DO, FACOFP *dist.*

Emerald Donors ($15,000+)
Larry W. Anderson, DO, FACOFP *dist.*
Nicole H. Bixler, DO, MBA, FACOFP
Greg D. Cohen, DO, FACOFP *dist.*
Robert C. DeLuca, DO, FACOFP *dist.*
John J. Dougherty, DO, FACOFP
Kenneth Heiles, DO, FACOFP *dist.*
Brian A. Kessler, DO, FACOFP *dist.*
Dewey McAfee, DO, FACOFP
Saroj Misra, DO, FACOFP
Kevin V. de Regnier, DO, FACOFP *dist.*
Thomas N. Told, DO, FACOFP *dist.*
Nicholas Tyszka, JD and Alicia A. Martin, DO
Bruce R. Williams, DO, FACOFP

Ruby Donors ($10,000+)
Katherine Galluzzi, DO, FACOFP *dist.*
David J. Park, DO, FACOFP

Sapphire Donors ($5,000+)
Clinton Adams, DO
Guatam J. Desai, DO, FACOFP
Gary Edwards, DO, FACOFP *dist.*
Joel M. Feder, DO, FACOFP *dist.*
James E. Froelich, III. DO, FACOFP *dist.*
Ronnie B. Martin, DO, FACOFP *dist.*
Rance McClain, DO, FACOFP
Joseph P. Molnar, DO, FACOFP *dist.*
Bob Moore, CAE
Jennifer M. Olson, DO
Elizabeth Palmarozzi, DO, FACOFP
Sonia Rivera-Martinez, DO, FACOFP
William M. Silverman, DO, FACOFP *dist.*
Antonios J. Tsompanidis, DO, FACOFP
Rodney M. Wiseman, DO, FACOFP *dist.*

*As of 4/1/20

For more information, please contact us at foundation@acofp.org or (254) 624-3219.

acofp EDUCATION & RESEARCH FOUNDATION

REVIEW ARTICLE

Approach To Joint Pain In The Elderly For Osteopathic Providers

Syna Daudfar, OMS-IV[1]; Natalia Nakajima, OMS-IV[1]; Khristopher Faiss, OMS-IV[1]; Luke Tegeler, OMS-V[1]; Jessica Kuo, OMS-III[2]; Robyn Dreibelbis, DO[1]; Edward Goering, DO[1]; Emmanuel Katsaros, DO[1]; John T. Pham, DO[1]

[1]Western University of Health Sciences, College of Osteopathic Medicine of the Pacific-Northwest, Lebanon, Oregon
[2]Midwestern University-AZCOM, Glendale, AZ

KEYWORDS:
Arthritis
Geriatrics
Inflammation
Joint Pain
Rheumatology

ABSTRACT: Joint pain in the elderly is becoming ever more ubiquitous in the primary care setting. Primary care providers, especially in rural communities, may be required to manage patients with rheumatologic conditions because consultation is unavailable. Literature supporting the approach to the diagnosis of joint pain in the elderly population is limited. The purpose of this manuscript is to present a case-based learning opportunity for osteopathic primary care providers, residents, and medical students regarding an elderly male with joint pain. In this manuscript, the authors have presented an advanced organizer to be used in the medical education setting which differentiates patients suffering from joint pain based on timing, the number of joints involved, and the size of the joint affected. We conclude with osteopathic considerations in evaluating an elderly patient with joint pain and the tools available to appropriately evaluate and treat the patient.

INTRODUCTION

In the United States, joint pain has been estimated to affect 52.5 million adults, with projections upwards of 78.4 million adults by 2040. The significant inflation is attributed to a baby boomer generation, which will enter the high-risk group of patients above the age of 65.[1] Most of these cases are noninflammatory in nature, but joint pain in the elderly otherwise becomes a difficult and frustrating diagnosis for primary care providers because of its broad differential diagnosis and nonspecific presentation.[2,3] Unfortunately, providers cannot always depend on rheumatologic markers because most lack the specificity necessary to solely contribute to a reliable diagnosis.[4] Experience in rheumatologic diseases and guidance from rheumatologic specialists play a valuable role in the identification and treatment of inflammatory joint pain, however their resources in rural communities are overwhelmed by the demand for consultation.[5] For these reasons, the onus may fall on primary care providers to have a systematic approach in identifying conditions requiring expedient management to minimize patient morbidity.[6,7] The purpose of this manuscript is to present an approach to joint pain to be used by Osteopathic providers, residents and medical students with a focus on the elderly population. The authors will briefly discuss the role of osteopathy in evaluation and appropriate diagnosis in these patients.

CASE PRESENTATION

An otherwise healthy 70-year-old Caucasian male with a history of osteoarthritis and peripheral neuropathy presented to the family medicine office complaining of “arthritis” flares for the past two months. He had just returned from a trip to Hawaii when he started noticing increasing groin, shoulder and low back pain which was sudden in onset and worsened after long periods of rest. He could not sit or lay down for longer than 30 minutes, otherwise his pain and stiffness significantly worsened. He denied any trauma. Prior to the onset of his symptoms, he was able to run four miles a day. In the last month, the pain and stiffness had caused him to only be able to walk a mile with a cane. He recently started taking over-the-counter naproxen with some improvement in his symptoms. He admitted to muscle aches, arthralgias, and back pain but denied fevers, chills, night sweats, or significant weight changes. He had no chest pain, shortness of breath, palpitations, or leg swelling. He denied dizziness, numbness, or headaches. He had no muscle spasms.

On examination, the patient was mildly uncomfortable yet well-appearing 70-year-old male with vital signs which were within normal limits. He had normal mood and affect and is alert and oriented. He had no petechiae, ecchymosis or hematomas. He had 2+ radial and dorsalis pedis pulses bilaterally without cyanosis

CORRESPONDENCE:
John T. Pham, DO | jtpham@westernu.edu

 Print ISSN: 1877-573X
DOI:10.33181/12033

or edema. The patient ambulated with a slight preference for his left leg. He had normal range of motion of his wrists, ankles, and phalanges bilaterally with no bony hypertrophy or deformities and no objective signs of synovitis. There were contractures and limited range of movement in his shoulders and hips bilaterally, and lower back pain but no joint tenderness or erythema. Patrick's test was positive with pain in the hips bilaterally and straight leg test is negative bilaterally. His quadriceps and hamstrings were hypertonic bilaterally. There was paravertebral lumbosacral spasms and tenderness. No lumbar spinous process tenderness was noted.

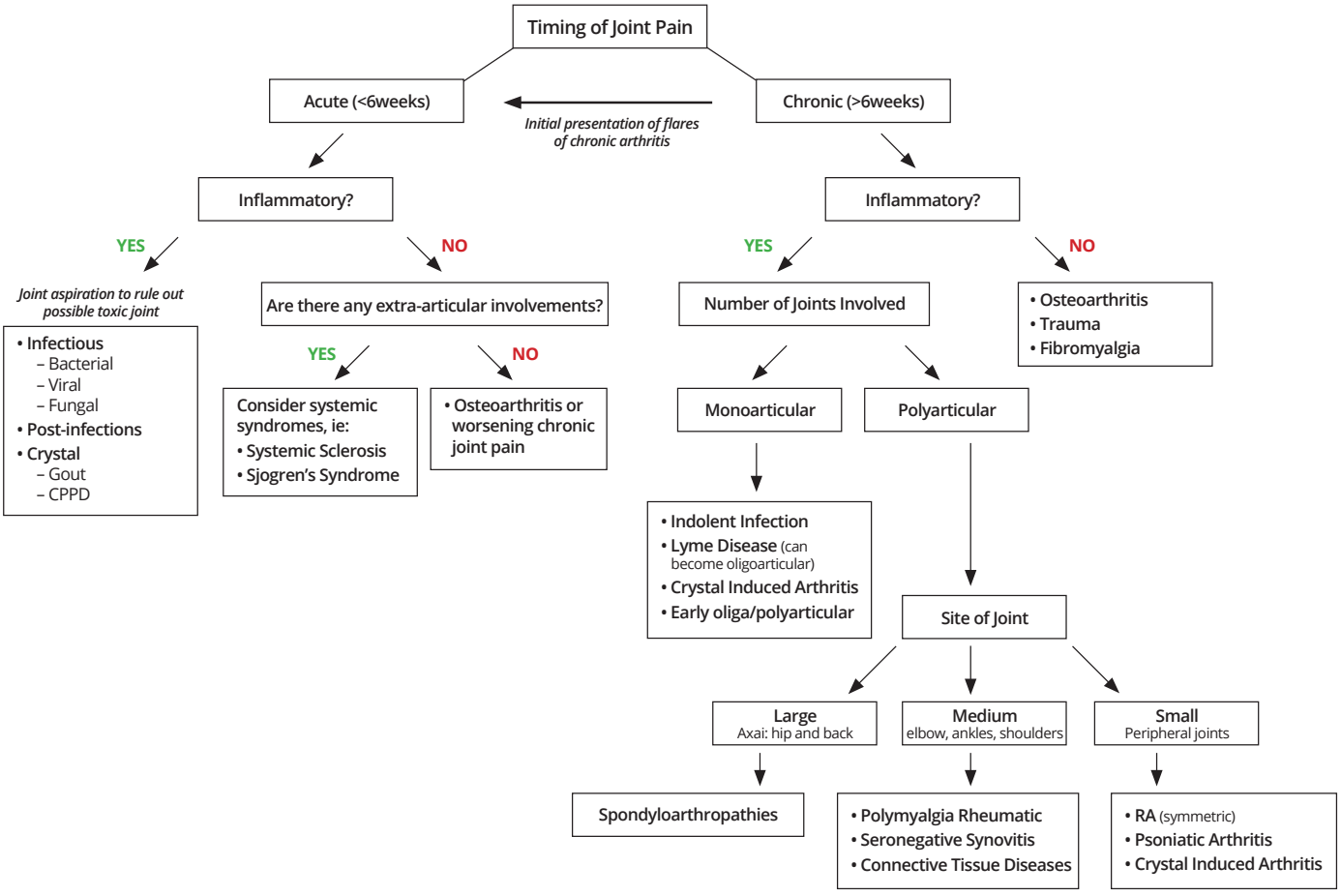
Laboratory evaluation revealed negative rheumatoid factor, HLA-DR4, TSH and ANA screen. ESR and CRP were elevated at 56 mm/h and 6.08 mg/dL, respectively. The patient was presumed to have a diagnosis of polymyalgia rheumatica and was started on prednisone 20 mg once daily for 30 days. On the second day of treatment, the patient reported complete resolution of his pain and stiffness. Repeat laboratory evaluation two weeks later revealed a WBC of 15.9 and his ESR had normalized to 2 mm/h. He was instructed to begin tapering his prednisone by 1 mg per week after his one-month prescription and to contact the office if he developed worsening pain or increased stiffness in his shoulders or hips.

INITIAL EVALUATION OF JOINT PAIN

The appropriate initial evaluation of joint pain begins with an accurate history and physical examination to reduce the list of reasonable etiologies. As with any diagnosis in medicine, the definitive diagnosis of the etiology for joint pain depends on the provider's index of suspicion. To direct the provider towards certain causes of joint pain, the authors will focus attention on three advanced organizers for arriving at a thorough yet reasonable differential: timing of illness, number of joints involved, and the size of the joint in question.

FIGURE 1:

Flow Chart for Approach to Joint Pain in Elderly Male



Timing of illness

The first and most dichotomous method of evaluating a patient with joint pain, specifically with synovitis, is to define them as having either acute (<6 weeks) or chronic (>6 weeks) joint pain.[8,9] While uncommon in an ambulatory setting, a patient with an acute onset of joint pain may present with cardinal signs of inflammation (red, hot, swollen, painful joint that is limited in function) and thus should be considered to have a toxic joint until proven otherwise.[10] Joint aspiration should be performed in this setting to rule out crystal-induced or other inflammatory arthropathy, septic joint, or hemarthrosis.[10,11]Employing this diagnostic approach may incidentally offer pain relief with temporary restoration of function.[11]Chronic inflammatory processes that present with acute flares or intermittent arthritis (ex. rheumatoid arthritis, spondyloarthropathy, gout or palindromic rheumatism) complicate this clinical picture and should be considered acute presentations of their chronic disease. The index of suspicion for degenerative joint disease in that joint should be low unless the complete acute evaluation of the joint pain is inconclusive.[7,12]

As in the case presentation, if the joint pain is indolent or progressively worsening over several months to years, the provider should approach the clinical presentation with special attention to differentiating osteoarthritis from inflammatory arthropathy. One uncomplicated method for ruling out osteoarthritis is to ask for evidence of myalgias. Another way a primary care provider can discern the appropriate diagnosis is to ask for evidence of extra-articular involvement. If there is evidence of extra-articular involvement, the differential narrows further to rheumatologic diseases that cause systemic inflammation (ex. systemic sclerosis or Sjogren's syndrome). Also, a primary care provider can consider morning stiffness lasting longer than one hour as a clue for an underlying inflammatory and rheumatologic process.[3]

Number of joints involved

An alternative method of arriving to a similar conclusion is to focus attention to the number of joints involved. Generally, if a patient can localize their pain to one joint, the provider's index of suspicion for the aforementioned toxic causes of arthropathy should be heightened—particularly in weight bearing joints.[10] One toxic cause of monoarthritis which may be overlooked is consideration of a foreign body in the synovium, particularly in gardeners. An MRI may be warranted to identify the foreign material (plain radiographs are often normal).[13] If no history of such acute flares exist in an otherwise progressively worsening arthropathy, then appropriate plain films may confirm the diagnosis of degenerative joint disease.

The most challenging of the differentials is in the case of polyarticular joint pain. It may be necessary for a patient with polyarticular joint pain to have multiple visits before arriving at a diagnosis. These diseases are generally rheumatologic in nature, however viral etiology, crystal arthropathies, and serum sickness reactions should also be considered, especially in the case of an acute presentation.[14] Viruses which may manifest as polyarticular joint pain include Hepatitis B, Hepatitis C, EBV, CMV, and parvovirus B19, to name a few.[14-17] Because most of these etiologies are self-limited, managing their sequelae is more important than the management of the arthropathy in question. In the case presentation, this patient had polyarticular joint pain in his shoulders, hip girdles, and lower back. This increased our index of suspicion for polymyalgia rheumatica and seronegative spondyloarthropathies. In this case, our team examined the patient for the aforementioned inflammatory markers to improve our index of suspicion. With the patient's myalgias, and elevated ESR/CRP, empiric treatment was started.

The presentation of oligoarticular joint pain may be less specific to uncovering the disease process, and more often reflect the stage of the disease process being evaluated. The classic example includes the arthralgias of Lyme disease, which, in its chronic phase, may involve oligoarthropathy of the knees.[18] Another classic example is that of Neisseria gonorrhaeae, which is most often oligoarticular in nature, however in the acute flare of the disease, may present with monoarthritis. Other examples of disease processes which may present with an oligoarticular presentation include crystal arthropathy (which in its early stages is monoarticular) and seronegative disease processes (which in its chronic phase is polyarticular).[3,8]

Pattern of joint involvement

The third reliable method of uncovering the diagnostic clues necessary to arrive at the appropriate diagnosis is consideration of the joints involved in the disease presentation. The involvement of axial joints, like the back and hips, present with a difficult and broad differential for primary care providers to consider. A classic example includes lower back and sacroiliac joint pain and the associated presentation of ankylosing spondylitis.19Spondylo arthropathies most commonly have their effects on large joints like the spine and the lower extremity.[20-23] Of course, psoriatic arthritis complicates this picture, because patients with this disease manifestation can see arthropathy of their small joints as well.[14,20] Another example of disease process affecting the large joints include polyarticular crystal-induced arthropathy and bacterial infection, particularly in the knee.[16,24] Providers should note, however, that crystal-induced arthropathy most commonly affects the first metatarsophalangeal joint. If no suspicion for inflammatory processes exist, primary care providers should consider osteoarthritis and the degenerative effects on weight bearing joints as the cause of the joint pain.[25]

The involvement of the peripheral joints, like the interphalangeal joints, are classically described by the joints involved and spared. The most common example is involvement of the distal interphalangeal joints, seen in osteoarthritis, that is not commonly seen in rheumatoid arthritis.[9,25] In the case of distal interphalangeal joint involvement, primary care providers should note that psoriatic arthritis and chronic crystal-induced arthritis (especially in the elderly) should still be included in the differential as these diseases may affect any of the joints in the hand.[20,26,27] Ideally, a clinically skilled provider should be able to note the physical findings of bony hypertrophy associated with noninflammatory joint pain and the inflammatory synovitis which would be noted in the inflammatory conditions like gout and psoriatic arthritis in these joints.

Involvement of moderate sized joints, like the elbows, ankles, and shoulders, present an interesting new set of pathologies. These joints often present with myalgias and periarticular symptoms rather than synovitis. Symmetry should be considered in these patients to rule in diseases like polymyalgia rheumatica and maturity onset seronegative synovitis, and rule out more asymmetric causes of joint pain, like Lyme arthritis or deep vein thrombosis.[3,18,28] If purely articular joint pain exists in these joints, consideration for bursitis, tenosynovitis, or other orthopedic causes of joint pain should be explored. Physical therapy and consultation with orthopedic surgery may be necessary to further elucidate the cause of the joint pain.[29]

OSTEOPATHIC CONSIDERATIONS IN EVALUATION

Within the primary care setting, the osteopathic physician may approach the elderly male with joint pain using the distinct osteopathic philosophy. Along with a thorough history and physical focused on the relevant etiology, the physician may consider the broader contributing factors. The five-model system reminds the osteopathic physician of the unity of the body; how unique social, emotional, psychological, and physiological contributions extend and vary beyond the specific etiology and pathology to become a complex and individualized patient presentation. For example, while managing joint pain, the physician should consider possible social isolation of the patient, increased risk of depression, loss of family relationships, difficult access to health care, poor transportation abilities, compounding health complaints, and many other factors. Taking these biopsychosocial factors into account, the osteopathic physician then may address barriers to healing. Additionally, the osteopathic physician can consider structural limitations causing poor function, such as a large body habitus compounding joint irritation, venous stasis due to poor cardiac output limiting joint mobility, age-related spinal deterioration leading to poor mobility, along with a myriad of other possibilities. In short, the osteopathic physician seeks the health for the elderly patient presenting with joint pain, not merely focusing on the pain in the joint.

Osteopathic physicians also can use the osteopathic structural exam, using their observation and palpation skills to gain information for evaluation. Palpation may discern restriction of various tissues, tissue texture changes, the temperature, and asymmetry.[30] These characteristics provide information concerning the acuity of the insult, the severity, and possible structural contributions to the presentation. The physician may also discern the location and involved anatomy of the presenting arthropathy.[31,32] As arthropathies are typically painful, these will limit the function of the patient, leading to structural compensations, and consequently evaluation of the joints beyond the effected joint is imperative.[33] The Osteopathic physician should also examine both somato-visceral and somato-somatic reflexes. Heightened sympathetic tone due to nociceptive feedback may lead to lymphatic congestion around the joint, which could direct one's focus to lymphatic treatment. The palpatory examination will inform the osteopathic physician if and how OMT may help with the healing of the painful joint.

CONCLUSION

In the primary care setting, joint pain is a common complaint in the elderly population. The authors have presented a case-based learning opportunity for osteopathic primary care physicians, residents, and medical students to have a systematic approach to the diagnosis of joint pain in the elderly population. Osteopathic providers should consider the use of the osteopathic structural examination as an extra tool for improving accuracy in their diagnosis and improving overall holistic management of their elderly patients with joint pain.

AUTHOR DISCLOSURES:
No relevant financial affiliations or conflicts of interest.

REFERENCES:

1. Hootman JM, Helmick CG, Barbour KE, Theis KA, Boring MA. Updated Projected Prevalence of Self-Reported Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation Among US Adults, 2015-2040. Arthritis & rheumatology (Hoboken, NJ). 2016;68(7):1582-1587.
2. Helmick CG, Felson DT, Lawrence RC, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: Part I. Arthritis & Rheumatism. 2008;58(1):15-25.
3. Klinkhoff A. Rheumatology: 5. Diagnosis and management of inflammatory polyarthritis. Canadian Medical Association Journal. 2000;162(13):1833-1838.
4. Sox HC, Jr. Probability theory in the use of diagnostic tests. An introduction to critical study of the literature. Ann Intern Med. 1986;104(1):60-66.
5. Bamji AN. Waiting times and referrals. Rheumatology. 2000;39(4):349-352.
6. Lard LR, Visser H, Speyer I, et al. Early versus delayed treatment in patients with recent-onset rheumatoid arthritis: comparison of two cohorts who received different treatment strategies. The American Journal of Medicine. 2001;111(6):446-451.
7. Palmer T, Toombs JD. Managing joint pain in primary care. The Journal of the American Board of Family Practice. 2004;17 Suppl:S32-42.
8. Guidelines for the initial evaluation of the adult patient with acute musculoskeletal symptoms. Arthritis & Rheumatism. 1996;39(1):1-8.
9. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis & Rheumatism. 2010;62(9):2569-2581.
10. Singh N, Vogelgesang SA. Monoarticular Arthritis. Medical Clinics of North America. 2017;101(3):607-613.
11. Bettencourt RB, Linder MM. Arthrocentesis and Therapeutic Joint Injection: An Overview for the Primary Care Physician. Primary Care: Clinics in Office Practice. 2010;37(4):691-702.
12. Sanmarti R, Cañete JD, Salvador G. Palindromic rheumatism and other relapsing arthritis. Best Practice & Research Clinical Rheumatology. 2004;18(5):647-661.
13. Baskar S, Mann JS, Thomas AP, Newton P. Plant thorn tenosynovitis. Journal of clinical rheumatology : practical reports on rheumatic & musculoskeletal diseases. 2006;12(3):137-138.

14. Mies Richie A, Francis ML. Diagnostic approach to polyarticular joint pain. American family physician. 2003;68(6):1151-1160.
15. Gill K, Ghazinian H, Manch R, Gish R. Hepatitis C virus as a systemic disease: reaching beyond the liver. Hepatology international. 2016;10(3):415-423.
16. Pujalte GG, Albano-Aluquin SA. Differential Diagnosis of Polyarticular Arthritis. American family physician. 2015;92(1):35-41.
17. Sterling RK, Bralow S. Extrahepatic manifestations of hepatitis C virus. 2. 2006;8(1):53-59.
18. Arvikar SL, Steere AC. Diagnosis and treatment of Lyme arthritis. Infectious disease clinics of North America. 2015;29(2):269-280.
19. Deodhar A, Mittal M, Reilly P, et al. Ankylosing spondylitis diagnosis in US patients with back pain: identifying providers involved and factors associated with rheumatology referral delay. Clinical Rheumatology. 2016;35(7):1769-1776.
20. Jadon DR. Psoriatic arthritis and seronegative spondyloarthropathies. Medicine. 2018;46(4):237-242.
21. Kataria RK, Brent LH. Spondyloarthropathies. American family physician. 2004;69(12):2853-2860.
22. Malik TA. Inflammatory Bowel Disease. Surgical Clinics. 2015;95(6):1105-1122.
23. Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, Rogler G. Extraintestinal Manifestations of Inflammatory Bowel Disease. Inflammatory bowel diseases. 2015;21(8):1982-1992.
24. Ruddy S, Harris ED, Sledge CB, Kelley WN. Kelley's textbook of rheumatology. Philadelphia : W.B. Saunders Co., c2001.
25. Sinusas K. Osteoarthritis: diagnosis and treatment. American family physician. 2012;85(1).
26. Mudgal CS. Management of tophaceous gout of the distal interphalangeal joint. The Journal of Hand Surgery: British & European Volume. 2006;31(1):101-103.
27. Scarpa R, Soscia E, Peluso R, et al. Nail and distal interphalangeal joint in psoriatic arthritis. The Journal of Rheumatology. 2006;2(7):1315-1319.
28. González-Gay MA, Matteson EL, Castañeda S. Polymyalgia rheumatica. The Lancet. 2017.
29. Burbank KM, Stevenson JH, Czarnecki GR, Dorfman J. Chronic shoulder pain: part I. Evaluation and diagnosis. American family physician. 2008;77(4).
30. Snider KT, Johnson JC, Snider EJ, Degenhardt BF. Increased incidence and severity of somatic dysfunction in subjects with chronic low back pain. The Journal of the American Osteopathic Association. 2008;108(8):372-378.
31. Snider KT, Snider EJ, Degenhardt BF, Johnson JC, Kribs JW. Palpatory accuracy of lumbar spinous processes using multiple bony landmarks. Journal of manipulative and physiological therapeutics. 2011;34(5):306-313.
32. Shaw KA, Dougherty JJ, Treffer KD, Glaros AG. Establishing the content validity of palpatory examination for the assessment of the lumbar spine using ultrasonography: a pilot study. The Journal of the American Osteopathic Association. 2012;112(12):775-782.
33. Hashemirad F, Talebian S, Olyaei GR, Hatef B. Compensatory behavior of the postural control system to flexion-relaxation phenomena. Journal of bodywork and movement therapies. 2010;14(4):418-423.

Forging Our Osteopathic Future

The ACOFP Foundation recently launched the Forging Our Osteopathic Future Campaign. This is a $2 million fundraising effort to help strengthen the osteopathic medicine profession by ensuring the next generation of osteopathic family physicians are the most highly qualified in the nation. This is the first-ever major fundraising campaign in the organization's history.

What will $2 million fund?

The main goal of the campaign is to fund **300 Initial Certification Grants*** annually for the next five years.

Grant recipients will receive **up to $500 in travel reimbursements and $900 to cover fees** for the AOBFP cognitive and practical exams.

In addition to Initial Certification Grants, campaign funding will allow for enhancement and expansion of:

- Student and Resident Scholarships
- Preceptorship Fund
- Future Leaders Conference

$10,000
7 lives changed

$7,000
5 lives changed

$5,600
4 lives changed

$2,800
2 lives changed

$1,400
1 life changed

Commitments are tax-deductible and can be pledged over a five-year period.

Can my gift really make a difference?

Commitments as small as $0.77/day can change a life. If a contributor pledges $0.77/day for the next five years, that is enough to fund one Initial Certification Grant. $1.44/day can launch the careers of two osteopathic family physicians. No matter the size of your commitment, please know that it can make a demonstrable impact!

*Only residents sitting for both their AOBFP cognitive and practical certification exams for the first time are eligible for grant funding.

For more information, or to make a contribution to the Forging Our Osteopathic Future Campaign, please contact foundation@acofp.org.

acofp EDUCATION & RESEARCH FOUNDATION

REVIEW ARTICLE

Diagnosis and Management of Nonmelanoma Skin Cancer

Luis Perez, DO, FAAFP, FACOFP[1]

[1]Grand Lake Family Practice and Pediatrics | Celina, OH

KEYWORDS:

Basal Cell Carcinoma

Dermatofibrosarcoma Protuberans

Keratinocyte Carcinoma

Merkel Cell Carcinoma

Nonmelanoma Skin Cancer

Squamous Cell Carcinoma

ABSTRACT: Nonmelanoma skin cancer (NMSC) is the most common cancer in the world. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common types. SCC lesions are more likely to metastasize when compared to BCC, but due to low risk for metastasis, prognosis for NMSC is excellent. Ultraviolet radiation exposure is the main risk factor for developing NMSC. Merkel cell carcinoma and dermatofibrosarcoma protuberans are rare forms of NMSC. The most common BCC lesions types are nodular, superficial, and sclerosing. Nodular BCC typically consists of papular lesions with a pearly border. Superficial BCC lesions are flat or slightly raised, often red to brown. Sclerosing BCC lesions usually have nondiscrete margins. The gross appearance of SCC is that of an erythematous plaque with scale and/or ulceration. The diagnosis of NMSC starts with gross examination, followed by biopsy. Recommended biopsy techniques include punch, shave, and excisional biopsy. Dermatoscopy should also be used to aid in the evaluation of suspected NMSC and other skin cancers, as it greatly enhances the point-of-care diagnosis of skin malignancies. For low-risk lesions, surgical excision is the cornerstone of treatment, although depending on the clinical situation, curettage and electrodessication or non-surgical modalities may be used. Cryotherapy, topical treatments, photodynamic therapy, or radiation treatment can be used to treat BCC and SCC, but cure rates are lower than with surgical excision. High-risk lesions require specialist referral. All patients treated for NMSC should undergo regular complete skin exams, and counseling on the use of sun protection and avoidance.

INTRODUCTION

Nonmelanoma skin cancer (NMSC) is the most common cancer in the world. In the US, 97% of all skin cancers diagnosed are NMSCs. Of these, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common.[1,2] BCC and SCC lesions arise from keratinocytes, so these lesions are typically grouped under a subtype of NMSC called keratinocyte carcinomas. This is to differentiate them from other types of NMSC such as Merkel cell carcinoma or dermatofibrosarcoma protuberans, which are not of keratinocyte origin.

It is imperative that family physicians feel comfortable with the diagnosis and treatment of these common skin malignancies. Although significant morbidity and mortality are rare with keratinocyte carcinomas, the early identification of these cancers is important given their rising incidence and the cost of late treatment.[3]

CORRESPONDENCE:
Luis Perez, DO, FAAFP, FACOFP | LP131304@ohio.edu

 Print ISSN: 1877-573X
DOI: 10.33181/12032

Epidemiology

BCC affects more than three million persons annually in the US and comprises more than half of all NMSC diagnoses. It is estimated that BCC affects more than 3.3 million people annually.[4] SCC is the second most common form of NMSC after BCC. In the US, the lifetime risk for developing SCC is estimated at 9-14% for men and 4-9% for women with approximately 300,000 new cases of SCC yearly.[5] Lifetime risk for developing BCC is estimated at 30%.[6]

Prognosis for keratinocyte carcinomas is excellent, due to low risk for metastasis. SCC lesions are more likely to metastasize when compared to BCC – 4% annual incidence of metastasis for SCC versus 0.55% or less for all cases of BCC.[3,7] Risk factors for NMSC metastasis are lesions >2cm in diameter, poorly-defined lesions, recurrent disease, immunosuppression, and high risk anatomic areas such as the central face, lips, ears, hands/feet, and genitalia.[5]

Risk Factors

Ultraviolet (UV) radiation exposure is the main risk factor for developing NMSC. This includes UV exposure from tanning beds. Intense intermittent exposure increases the risk for BCC, whereas cumulative UV exposure, especially in childhood and youth, increases the risk for SCC.[5]

Other significant risk factors for developing NMSC are fair skin, exposure to radiation such as X-rays, cigarette smoking, and immunosuppression.[8]

BASA CELL CARCINOMA

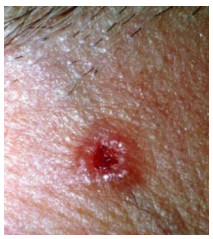
Diagnosis

The diagnosis of BCC or any NMSC starts with the gross examination of the lesion. The most common BCC lesions types are nodular, superficial, and sclerosing. Nodular BCC is the most prevalent type, comprising about 70% of all diagnosed BCC. It's usually found in the head and face. Superficial BCC is usually found on the trunk and extremities.[9]

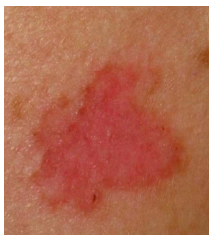
Nodular BCC typically consists of papular or raised lesions with a translucent, or pearly border. Central erosion, telangectasias, and bleeding are common. These lesions may be pigmented which make them look like a melanoma. Superficial BCC lesions are flat or slightly raised, often red to brown. Sclerosing BCC lesions usually have nondiscrete margins.[9,10] *See Table 1*.

TABLE 1:

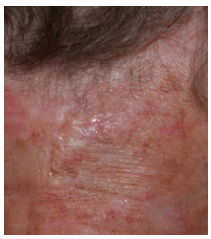
Common types of Basal Cell Carcinoma



Nodular



Superficial



Slerosing

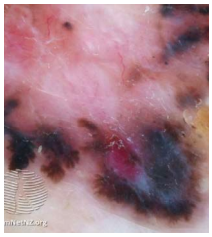
Images used with permission of Waikato District Health Board and DermNet New Zealand, www.dermnetnz.org.

Dermatoscopy should be used to aid in the diagnosis of BCC and other skin cancers, as it greatly enhances the point-of-care diagnosis of skin malignancies. Classic dermatoscopic features of BCC include leaf-like structures, spoke wheel-like structures, and more commonly, arborizing vessels. *See Table 2*.

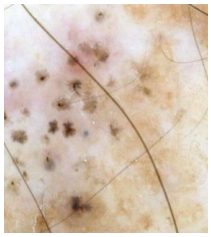
TABLE 2:

Common dermatoscopic features of Basal Cell Carcinoma

Arborizing vessels



Leaf-like structures and dark blotches



Spoke wheel-like structures

Images used with the permission of DermNet New Zealand, www.dermnetnz.org.

Biopsy

Once a lesion is suspected to be BCC by gross and dermatoscopic examination, a biopsy is needed to confirm the diagnosis. Recommended biopsy techniques include punch, shave, and excisional biopsy. There is no evidence that proves any particular biopsy technique superior or preferred for the biopsy of suspected BCC lesions. The choice of biopsy technique depends on the physician's experience, comfort level, and the lesion's size and location. If the biopsy specimen proves to be inadequate for accurate histologic diagnosis of the lesion, a repeat biopsy may be considered. There are no specific margin recommendations for the biopsy of suspected BCC. Enough tissue should be removed to ensure accurate histologic diagnosis.[11]

Treatment

The treatment of a confirmed localized BCC lesion is guided not by a staging system but by determining whether the lesion is at low versus high risk for recurrence. Currently, there is no formal staging system specific to BCC.[11]

Low-risk lesions are primary lesions that are <20mm and located on the trunk and extremities, or <10mm and located in the cheeks, forehead, scalp, neck or shins. They also have well-defined borders, are not located in areas of prior radiation therapy, and are present in a patient who's not immunosuppressed. Histologically, low-risk lesions have no perineural involvement.[12]

High-risk lesions are those that are recurrent, >20mm in the trunk and extremities, >10mm in the cheeks, forehead, scalp, neck or shins, or lesions of any size located in the central face, nose, eyelids, periorbital skin, ears, lips, chin, hands, feet, or genitalia. They may be poorly-defined and of an aggressive histological subtype and may have perineural involvement.[12]

For low-risk lesions, surgical excision is the cornerstone of treatment, although depending on the clinical situation, curettage and electrodessication (C&E) or non-surgical modalities may be used. Cryotherapy, topical treatments, photodynamic therapy (PDT), or radiation treatment can be used to treat BCC, but cure rates are lower when compared with surgical excision.[11]

The goal of cryosurgery for keratinocyte carcinomas such as BCC is to destroy the same amount of tissue as that which would have been removed with standard surgical excision.[11]

Topical therapies for BCC include imiquimod and 5-FU. Imiquimod can be applied once or twice daily, for six to 16 weeks. Local reactions are common and include skin redness and swelling, vesicles, and itching. 5-FU is typically applied twice daily for three to six weeks and causes skin reactions similar to those with imiquimod. Topical therapies should be reserved for the treatment of small primary lesions in low-risk areas, when surgical excision of the lesion is not feasible or declined by the patient.[11]

For low-risk primary BCC lesions, the American Academy of Dermatology (AAD) and the National Comprehensive Cancer Network (NCCN) recommend standard excision with a 4mm margin of uninvolved skin around the tumor and/or biopsy site to a depth of the mid-subcutaneous adipose tissue with histologic

margin assessment. If margins are positive after excision, re-excision is recommended, or the patient may be referred for Mohs micrographic surgery (MMS).[11,12]

A study showed that local recurrence rates after an excision with positive histologic margins was 27% compared with 6% following excision with histologically negative margins.[13] Research studies, however, consistently report low recurrence rates after standard excision of BCC with predominantly nonaggressive histologic growth patterns.[12]

For high-risk lesions, the AAD recommends MMS, so referral to a dermatologist is recommended for these types of lesions.

Follow-up

For patients treated for BCC, the NCCN recommends a complete skin exam every six to 12 months for five years, and then annually for life.[12] Any local recurrence with nodal or distant metastases requires referral to a multidisciplinary team for treatment, although as mentioned previously metastases are very rare with BCC.

All patients should also be counseled on the use of sun protection and avoidance.

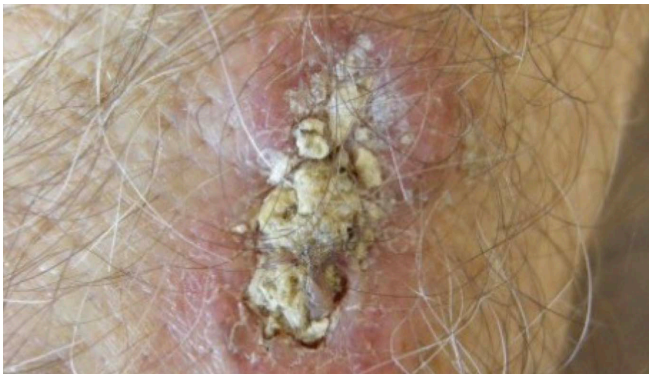
SQUAMOUS CELL CARCINOMA

Diagnosis

The gross appearance of SCC is that of an erythematous plaque with scale and/or ulceration. Keratoacanthomas, considered by some to be a variant of SCC, present as rapidly-enlarging, dome-shaped lesions, with a central keratin plug.[9,10] *See Figure 1*.

FIGURE 1:

Squamous Cell Carcinoma

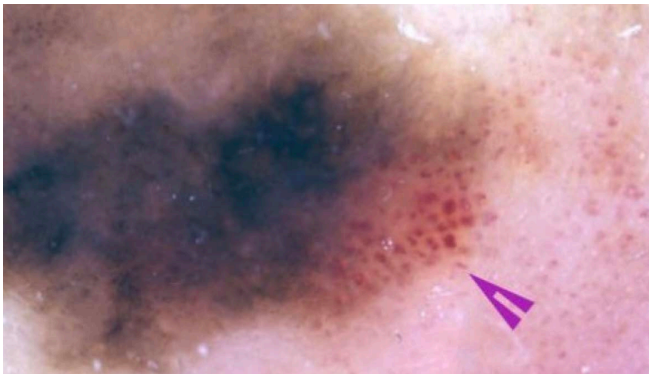


Images used with the permission of DermNet New Zealand, www.dermnetnz.org.

Dermatoscopy of SCC lesions may reveal focal glomerular vessels, rosettes, and peripheral brown dots and globules. *See Figure 2*.

FIGURE 2:

Glomerular vessels sometimes seen in dermatoscopy of Squamous Cell Carcinoma



Images used with the permission of DermNet New Zealand, www.dermnetnz.org.

Biopsy

As with BCC, no biopsy method for SCC has been shown superior, and biopsy method selection is based on lesion size, location, and the physician's experience and comfort level. Recommended biopsy techniques include punch, shave, and excisional biopsy, and a repeat biopsy should be considered if the specimen is inadequate for an adequate histologic analysis.[5]

Treatment

There's no universally accepted staging system for risk stratification of SCC. A stratification system developed at the Brigham and Women's Hospital that classifies SCC tumors according to the presence of several clinical and pathologic risk factors does show some promise, but at this time no system is universally accepted.[5,14]

An approach to stratifying low- and high-risk tumors, similar to that used for BCC, has been provided by the NCCN, and is primarily intended to provide guidance on treatment of SCC rather than in prognosis and outcomes.[5]

Low-risk SCC lesions are primary lesions are <20mm and located on the trunk and extremities, or <10mm and located in the cheeks, forehead, scalp, neck or shins. They also have well-defined borders, are not located in areas of prior radiation therapy, and are present in a patient who's not immunosuppressed. Histologically, low-risk lesions have no perineural, lymphatic, or vascular involvement, are moderately or well-differentiated, and have a depth <=6mm and don't invade beyond subcutaneous fat. Low-risk SCC lesions also exhibit no rapid growth.[15]

High-risk SCC lesions are those that are rapid-growing or recurrent, >20mm in the trunk and extremities, >10mm in the cheeks, forehead, scalp, neck or shins, or lesions of any size located in the central face, nose, eyelids, periorbital skin, ears, lips, chin, hands, feet, or genitalia. They may have ill-defined borders or be found

on an immunocompromised patient or be found in an area of prior radiation treatment. Histologically, high-risk lesions have poorly-differentiated features, or have perineural, lymphatic, or vascular involvement. These lesions may also go deeper than 6mm or invade beyond subcutaneous fat.[15]

For low-risk primary SCC lesions, the AAD and the NCCN recommend standard excision with a 4 to 6mm margin of uninvolved skin to a depth of the mid-subcutaneous adipose tissue with histologic margin assessment.[5,15] C&E may be considered for low-risk lesions, but there's no data to compare the efficacy of C&E with other treatment methods.[15] Non-surgical methods such as topical therapies, cryosurgery, and radiation therapy may be used to treat low-risk superficial lesions, but these methods achieve lower cure rates than surgical excision.[15]

High-risk SCC lesions should be referred to dermatology for MMS.

Follow-up

For patients treated for SCC, the NCCN recommends a complete skin exam every three to twelve months for two years, then every six to twelve months for three years, then annually for life. The ADD recommends skin exams at least annually but does not specify intervals as the NCCN does.[5,15] All patients should also be counseled on the use of sun protection and avoidance and performing a self-examination of the skin.

OTHER TYPES OF NMSC

MERKEL CELL CARCINOMA

Merkel cell carcinoma (MCC), a rare form of skin cancer, is an aggressive malignancy mainly seen in older adults. It primarily affects people with light skin and has a tendency for local recurrence.[16] Affected individuals tend to be in their 70s when they present with this form of skin malignancy and the risk of MCC is greatly increased in people that have had other malignancies.[17]

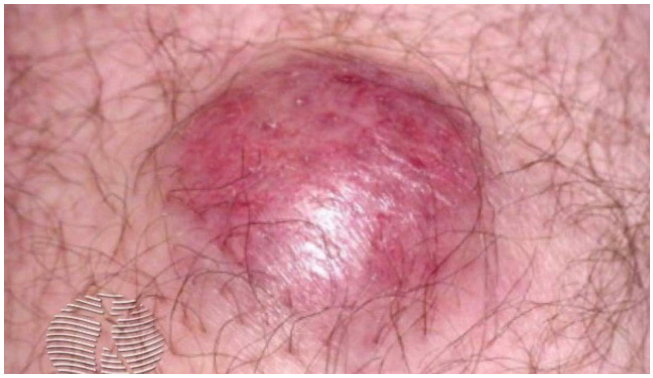
Skin mechanoreceptors, located in the basal layer of the epidermis as well as in hair follicles, contain Merkel cells. MCC is believed to arise from these cells. Malignant transformation of Merkel cells into MCC has been associated with sun exposure, immunosuppression, and the so-called Merkel cell polyomavirus, a virus thought to be part of the normal skin microbiome.[18]

MCC typically presents as a rapidly growing, painless, and firm skin nodule, usually in sun-exposed areas. Metastases are uncommon. *See Figure 3*.

Diagnosis is confirmed by histopathologic analysis of a biopsy sample. Immunoreactivity to CK20 is a fairly specific and sensitive marker for MCC. Once the diagnosis is confirmed by histopathology, and the primary tumor is removed by wide local excision, further treatment depends on results of sentinel lymph node (SLN) biopsy or the presence of metastatic disease.[19] If SLN biopsy is negative, radiation therapy to the tumor site is recommended. If SLN biopsy is positive and there are no metastases, lymph node dissection or nodal radiation therapy is indicated. If there are metastases then systemic therapy is the treatment of choice. Frequent follow-up is needed after treatment due to the high rate of recurrence of MCC.

FIGURE 3:

Merkel Cell Carcinoma



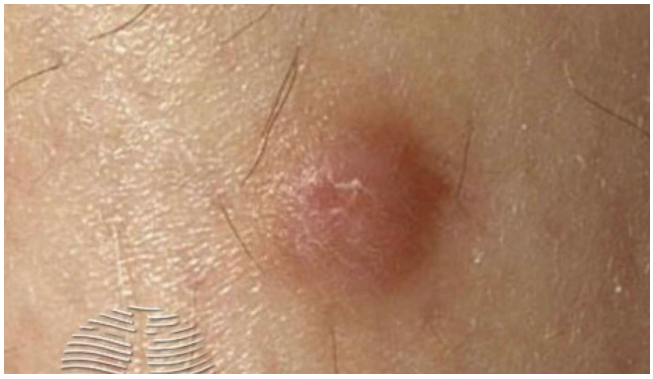
Images used with the permission of DermNet New Zealand, www.dermnetnz.org.

DERMATOFIBROSARCOMA PROTUBERANS

Dermatofibrosarcoma protuberans (DP) is rare soft-tissue sarcoma of fibroblast origin. Its incidence in the US is approximately 4.5 cases per million persons per year.[20] DP rarely metastasizes. Given their similar gross clinical appearance, differentiation of DP from dermatofibroma can be difficult, and a deep subcutaneous punch or incisional biopsy are recommended for initial diagnosis of these lesions. *See Figure 4*.

FIGURE 4:

Dermatofibrosarcoma Protuberans



Images used with the permission of DermNet New Zealand, www.dermnetnz.org.

Histologically, the vast majority of DP cases are CD34 positive and factor XIIIa negative.[21]

The treatment of DP is surgical, with repeat excision if histologic margins are positive. MMS or wide excision with 2-4 cm margins are recommended treatment strategies for this type of NMSC.[22]

Follow-up of patients after treatment of DP consist of office visits every six to twelve months.[23]

CONCLUSION

NMSC can be very effectively treated if diagnosed early. Primary care physicians are typically the first point of contact when a patient notices a "bump" on the skin they want evaluated. By becoming comfortable with the classic gross and dermatoscopic features of NMSC and the different available treatment modalities, Osteopathic family physicians can competently diagnose and treat NMSC and avoid unnecessary referrals.

AUTHOR DISCLOSURES:
No relevant financial affiliations or conflicts of interest.

REFERENCES:

1. Rigel DS, Friedman RJ, Kopf AW. Lifetime risk for development of skin cancer in the U.S. population: current estimate is now 1 in 5. J Am Acad Dermatol. 1996;35(6):1012-1013.
2. Rogers HW, Weinstock MA, Harris AR, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. Arch Dermatol. 2010;146(3):283-287.
3. Fahradyan A, Howell AC, Wolfswinkel EM, Tsuha M, Sheth P, Wong AK. Updates on the management of non-melanoma skin cancer (NMSC). Healthcare (Basel). 2017;5(4):82.
4. Rogers HW, Weinstock MA, Ferldman SR, Coldiron BM. Incidence estimate of nonmelanoma skin cancer in the US population, 2012. Jama Dermatol. 2015;151(10):1081-1086.
5. Alam M, Armstrong A, Baum C, et al. Guidelines of care for the management of cutaneous squamous cell carcinoma. J Am Acad Dermatol. 2018;78(3):560-578.
6. Miller DL, Weinstock MA. Nonmelanoma skin cancer in the United States: incidence. J Am Acad Dermatol. 1994;30:774-8.
7. Seo SH, Shim WH, Shin DH, Kim YS, and Sung HW, Pulmonary metastasis of basal cell carcinoma, Ann Dermatol. 2011;23(2):213-216.
8. Perez LL, Bashline B, Bruner P. Skin Cancer. FP Essent. 2019;481:1-44.
9. Usatine RP, Smith MA, Mayeaux Jr. EJ, Chumley HS, eds. The Color Atlas and Synopsis of Family Medicine. 3rd ed. New York: McGraw-Hill Education; 2019.
10. Usatine RP, Pfenninger JL, Sulberg DL, and Small R. Dermatologic and cosmetic procedures in office practice. Philadelphia, PA: Elsevier; 2012.
11. Bichakjian C, Armstrong, A, Baum C, et al. Guidelines of care for the management of basal cell carcinoma. J Am Acad Dermatol. 2018;78(3):540-559.
12. National Comprehensive Cancer Network, Basal Cell Skin Cancer. Available online: https://www.nccn.org/professionals/physician_gls/pdf/nmsc_blocks.pdf (accessed on 17 June 2019).
13. Codazzi D, Van Der Velden J, Carminati M, et al. Positive compared with negative margins in a single-centre retrospective study on 3957 consecutive excisions of basal cell carcinomas. Associated risk factors and preferred surgical management. J Plast Surg Hand Surg. 2014;48(1):38-43.
14. Nehal KS, and Bichakjian CK. Update on keratinocyte carcinomas. N Engl J Med. 2018 Jul 26;379(4):363-374.
15. National Comprehensive Cancer Network, Squamous Cell Skin Cancer. Available online: https://www.nccn.org/professionals/physician_gls/pdf/nmsc_blocks.pdf (accessed on 17 June 2019).
16. Tothill R, Estall V, Rischin D. Merkel cell carcinoma: emerging biology, current approaches, and future directions. Am Soc Clin Oncol Educ Book. 2015:e519-26.
17. Albores-Saavedra J, Batich K, Chable-Montero F, et al. Merkel cell carcinoma demographics, morphology, and survival based on 3870 cases: a population-based study. J Cutan Pathol. 2010 Jan; 37(1):20-7.
18. Rather D, Nelson BR, Brown MD, Johnson TM. Merkel cell carcinoma. J Am Acad Dermatol. 1993 Aug; 29(2 Pt 1):143-56.
19. National Comprehensive Cancer Network. Merkel Cell Carcinoma (Version 1.2017). https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf. Accessed June 29, 2017.
20. Criscione VD, Weinstock MA. Descriptive epidemiology of dermatofibrosarcoma protuberans in the United States, 1973 to 2002. J Am Acad Dermatol 2007;56:968-973.
21. Abenoza P, Lillemoe T. CD34 and factor XIIIa in the differential diagnosis of dermatofibroma and dermatofibrosarcoma protuberans. Am J Dermatopathol 1993; 15:429-434.
22. Stojadinovic A, Karpoff HM, Antonescu CR, et al. Dermatofibrosarcoma protuberans of the head and neck. Ann Surg Oncol 2000 Oct;7(9):696-704.
23. National Comprehensive Cancer Network, Dermatofibrosarcoma Protuberans. Available online: https://www.nccn.org/professionals/physician_gls/pdf/nmsc_blocks.pdf (accessed on 17 June 2019).


WE'RE HIRING FOR FAMILY MEDICINE POSITIONS
Air Force Civilian Service offers an alternative to the distractions of extensive paperwork and reporting in today's health care environment. It's attractive on every level and makes it possible to keep the focus on your calling and not on the paperwork.
DO WHAT YOU LOVE AT AFCS.
#ItsACivilianThing — email: afcs@us.af.mil
AFCivilianCareers.com/Medical
Equal Opportunity Employer. U.S. Citizenship required. Must be of legal working age.
AIR FORCE CIVILIAN SERVICE
Forces. Joined.

CLINICAL IMAGE

Rash on a Child

Chelsea Reynolds, OMS-III[1]; Ronald Januchowski, DO, FACOFP[1]; Hanna Sahhar, MD

[1]Edward Via College of Osteopathic Medicine-Carolinas Campus, Spartanburg, SC

An 11-month-old male presented to the emergency center with a two-day history of worsening cough, conjunctivitis, purulent runny nose, fever and the presence of a maculopapular rash as seen in *Figure 1 and 2*. Patient's mother noted that the rash started on the child's face and progressed down his body. Physical exam showed a diffuse erythematous, maculopapular rash present over the entire body with sparing of the palms and soles. He had fevers and malaise but denied gastrointestinal symptoms or genitourinary symptoms. The rash faded two days later and followed a similar pattern.

Social history includes a trip to Europe a month prior, no prior immunizations and a two-year-old sister with a similar presentation two weeks prior. She also had no prior immunizations.

FIGURE 1:

Rash on trunk of patient

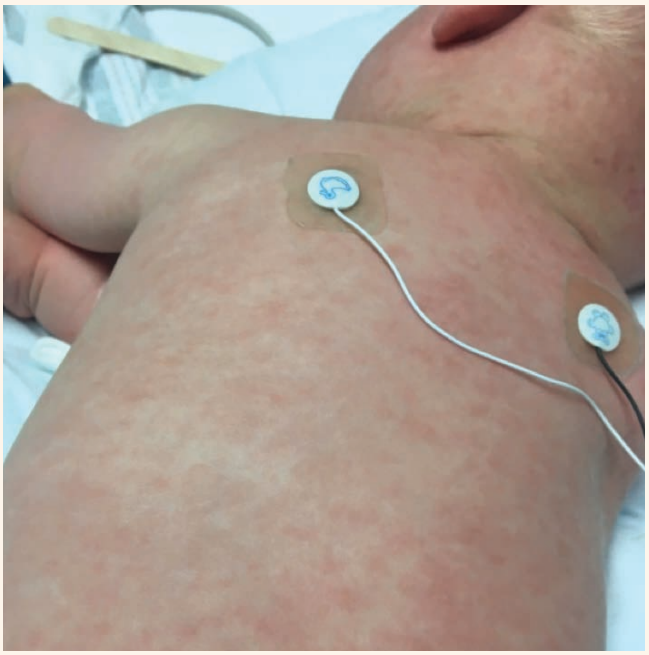
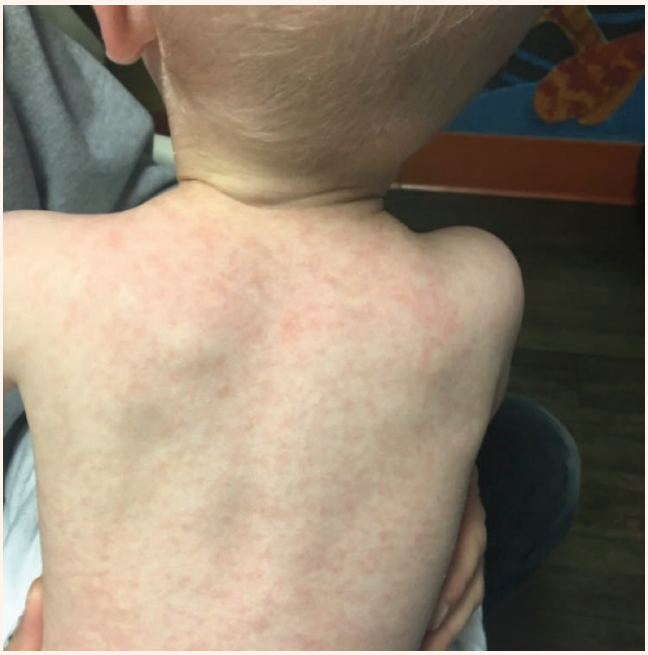


FIGURE 2:

Maculopapular rash on trunk of patient



CORRESPONDENCE:
Ronald Januchowski DO, FACOFP | rjanuchowski@carolinas.vcom.edu

 Print ISSN: 1877-573X
DOI: 10.33181/12034

QUESTIONS:

1. **What is the most likely diagnosis?**

   A. Erythema infectiosum

   B. Roseola

   C. Rubeola

   D. Varicella Zoster

2. **Besides supportive care, what treatment has been shown to reduce morbidity and mortality for this patient?**

   A. Acyclovir

   B. Corticosteroids

   C. Aspirin

   D. Penicillin G

   E. Vitamin A

ANSWERS:

1. **What is the most likely diagnosis?**

   Correct Answer:
   C. Rubeola

Rubeola (Measles) is characterized by cough, coryza, conjunctivitis, Koplik spots and the presence of a fever and a maculopapular rash. The rash appears as a non-pruritic, non-painful rash that begins at the hairline and spreads distally sparing the palms and soles. The rash fades in the same direction it appears. An important characteristic of measles infection includes the combination of fever and rash at the same time.

The differential diagnosis of measles includes Kawasaki disease, dengue fever, syphilis, roseola, erythema infectiosum, and primary varicella infection (chickenpox) as well as other viral diseases of childhood. Measles and chickenpox are the only rashes that present with fever along with body rash. Roseola presents as a lacy rash that starts on the trunk and appears after a fever break. Erythema infectiosum (parvovirus B19) is known for its "slapped cheek" rash that is prominent on the face and accompanied by a fever. The patient was brought to urgent care a day prior to being admitted to the hospital and was diagnosed with parvovirus B19. His sister presented two weeks prior with similar symptoms and was diagnosed with roseola. The diagnosis of measles in this case was made by clinical presentation as well as positive IgG testing for the measles virus.

2. **Besides supportive care, what treatment has been shown to reduce morbidity and mortality for this patient?**

   Correct Answer:
   E. Vitamin A

Supportive care to include hydration is the mainstay of treating measles. Vitamin A supplementation is associated with reduced morbidity and mortality in patients. It can also reduce eye damage and blindness associated with the disease. Dosing is based on age as noted in the discussion.

DISCUSSION

Rubeola, also known as measles, occurs from an infection caused by a single-stranded; negative-sense enveloped RNA virus of the genus Morbillivirus. The virus is transmitted through respiratory droplets. Patients infected will present with a prodrome of fever, anorexia, malaise and the classic triad of coryza, cough and conjunctivitis. One to two days prior to the onset of exanthem, bluish-white papules on an erythematous base can appear on the buccal mucosa mainly behind the molars (also known as Koplik spots). A maculopapular rash appears 3 to 4 days after onset of fever, classically beginning on the face, hairline, and neck. The rash will then spread distally with sparing of the palms of the hands and soles of the feet. The rash fades in the same pattern it appears. Uncomplicated measles generally lasts seven to ten days in immunocompetent individuals.[1]

The prevalence of measles in the United States population declined greatly after the introduction of the measles vaccination in 1971, but recent lack of immunization has led to a recurrence of the virus. Measles is highly contagious with up to 90% of susceptible contacts developing the disease.[2] In 2018-2019, there were 971 confirmed cases of measles infection in the United States.[3] Most cases of measles infection are due to improperly or non-vaccinated children, the majority of which are due to immigration from other countries.[4]

Diagnosis is typically clinical although it can be supported with an IgG and IgM antibody test. This test is confirmatory and positive results are mandated to report to the state health department.

Treatment is mainly supportive with the use of fluids for dehydration, acetaminophen to control fever and Vitamin A. The CDC found in a study that the use of Vitamin A decreases the morbidity and mortality in patients with measles infection.[5] Once daily doses for two doses of oral vitamin A are recommended at the following amounts: infants less than six months of age 50,000 IU/day; age 6-11 months – 100,000 IU/day; and older than one year – 200,000 IU/day.

Complications of measles are more likely to occur in immunocompromised patients, patients less than five years old or greater than 20 years old and malnourished patients, especially those with vitamin A deficiency.[5] Complications can include diarrhea, otitis media, pneumonia, meningitis, encephalitis and rarely, subacute sclerosing panencephalitis. Keratitis leading to vision loss can also occur. Careful monitoring of the patient must be performed for symptoms concerning for pneumonia or central nervous system infection, such as headache, confusion or vison changes.

CASE DISCUSSION

In this case, confirmation of rubeola was made via IgG rubeola antibody testing and was confirmed with IgM rubeola antibody testing a few weeks later. Treatment was mainly supportive. When the patient developed bilateral otitis media and lower lobe pneumonia, antibiotics were started. After discharge, parents were advised to vaccinate not only the patient, but his sister as well, and to follow up with a primary care physician. While the vaccine is routinely started at 12 months of age, it can be given as young as six months of age for post-exposure prophylaxis or if the child is at a high risk of exposure to the virus, such as with travel to an endemic area, such as with this case. The vaccine should be given within 72 hours of exposure. Alternatively, immunoglobulin can be used within six days post-exposure for immunocompromised individuals, pregnant females without evidence of measles immunity or infants less than 12 months of age. The vaccine and immunoglobulin should not be administered together, as this would cause the vaccine to be invalidated.[6]

Measles is a complex disease process. This photographic clinical case is meant to illustrate the basic presentation and progression of the disease in pictures and is not intended to cover all of the intricacies of this infectious process.

AUTHOR DISCLOSURES:
No relevant financial affiliations or conflicts of interest.

REFERENCES:

1. Centers for Disease Control and Prevention. "Measles: Epidemiology and Prevention of Vaccine- Preventable Disease," 13th Edition. (2015). 209-230.
2. Marcdante, Karen J., Kliegman, Robert, M. "Nelson Essentials of Pediatrics- Eighth Edition." Philadelphia (PA). Elsevier Saunders. 2019. 97: 373-375
3. Center for Disease Control and Prevention. "Cases and Outbreaks: Measles Cases in 2019". (2019).
4. Alexander, KC., KL Hon, KF Leong, CM Sergi. "Measles: A disease often forgotten but not gone." Hong Kong Academy of Medicine. (2018): 512-20.
5. Centers for Disease Control and Prevention. "Complications of Measles." (2018).
6. American Academy of Pediatrics. Measles. Pickering LK, ed. Red Book: Report of the Committee on Infectious Disease. 31st Edition. Elk Grove, Ill: AAP; 2018-2021. 537-550.

acofp | eLEARNING CENTER

We know you're busy.

The ACOFP eLearning Center offers a variety of educational opportunities that are priced right and fit easily into your busy schedule.

View ACOFP's expanding catalog of on-demand modules covering a variety of topics, from physician wellness to firearm safety to OMT procedures addressing specific symptoms, anatomic areas and manipulation types.

Check out the new modules in the eLearning Center:

- **OMTotal Video Library**
- **Intensive Update & Board Review Online**
- **Practice Questions for Board Prep**

Learn more at **acofp.org**.

Osteopathic Family Physician | Volume 12, No. 3 | May/June, 2020

PATIENT EDUCATION HANDOUT

Nonmelanoma Skin Cancer: Am I at Risk?

Luiza Mnatsakanyan, OMS-III

Ronald Januchowski, DO, FACOFP, Editor • Paula Gregory, DO, MBA, CHCQM, FAIHQ, Health Literacy Editor

Skin cancer is the most common malignancy that is diagnosed in the U.S. There are two types of skin cancer: melanoma or nonmelanoma.

Melanoma skin cancers are more aggressive and spread very fast. Nonmelanoma skin cancers (NMSC) occur at a slower rate and are usually only in the upper layers of the skin and do not spread to other areas. Nonmelanoma skin cancers are associated with low death rates and slow growth. The main mode of treatment for NMSC is the surgical removal of the malignant tissue. Some other alternative treatments include radiotherapy, chemotherapy, cryotherapy, certain creams and photodynamic therapy. The NMSC cure rate is around 90% and the risk of spreading to other parts is very low when caught early.

COMMON SIGNS OF NMSC

- Lumps and patches that are persistent for several weeks.
- Lumps will usually have a red and firm appearance and patches will look flat and feel scaly.
- Changes in the skin such as a new growth.
- Nonhealing sores that look like a freckle or a mole.

RISK FACTORS

- Environmental exposure to ultraviolet (UV) light. Family history of skin cancer, pale skin, freckles or moles, chronic wounds or a history of a lot of sunburns.
- Exposure to cancer causing chemicals.
- Human Papilloma Virus.
- Men are at a higher risk than women.
- Certain medications increase the sensitivity of the skin and put you more at risk of getting skin damage. Immunosuppressants can also put you at risk.

acofp AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

SOURCE(S): *American Academy of Dermatology; Centers for Disease Control; Up-to-Date*

PATIENT EDUCATION HANDOUT

Treatment Options for Ulcerative Colitis

Joanna Ghobrial, OMS-IV

Ronald Januchowski, DO, FACOFP, Editor • Paula Gregory, DO, MBA, CHCQM, FAIHQ, Health Literacy Editor

Ulcerative Colitis (UC) is an autoimmune disease that affects the large intestine. In UC, patients often have blood or mucus in their stool, frequent stools, and lower abdominal pain. Some non-gastrointestinal symptoms include inflammation of the skin, eye and/or joints. This is different from the other type of inflammatory intestinal disease, Crohn's Disease, as it does not affect any other part of the gastrointestinal tract, such as the mouth or small intestine. Early diagnosis and treatment mean recognizing abdominal symptoms and talking with your physician about your worries. Ulcerative colitis patients should avoid NSAID's (such as ibuprofen), opioids and anticholinergics in the case of severe disease. Working with your doctor will allow you to come up with the best treatment plan that is tailored to your case. A diagnosis of UC is often treated with medications. While these treatments are helpful, there are many things that you can do to help manage symptoms yourself.

TREATMENTS THAT A PERSON CAN TRY TO TREAT THEIR SYMPTOMS

- Antidiarrheal agents such as loperamide
- Anticholinergic medication such as propantheline or dicyclomine to relieve cramping

TREATMENT OPTIONS THAT REQUIRE DOCTOR MANAGEMENT

If You Have A Mild Case: A doctor might prescribe 5-aminosalicylic acid derivatives (5-ASAs) medication

- 5-ASAs can provide anti-inflammatory and immunosuppressive effects on the bowel
- 5-ASAs can be given by mouth or by suppository

If You Have a Moderate Case: A doctor might prescribe 5-ASAs, topical corticosteroids and/or anti-TNF therapy

- 5-ASAs can be given by mouth or topically
- An example of a topical corticosteroid is budesonide
- anti-TNF therapy includes adalimumab, golimumab, or infliximab

If You Have a Severe Case or Refractory Disease:

- A high-dose by mouth and topical 5-ASA's
- Systemic corticosteroids
- anti-TNF therapy
- Calcineurin antagonists (cyclosporine, tacrolimus)
- Thiopurines (but are not monotherapy)
- Last resort: referral for surgery

acofp AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

SOURCE(S): *Mayo Clinic, The American Journal of Gastroenterology, The National Library of Medicine, The New England Journal of Medicine*

American College of Osteopathic Family Physicians
330 East Algonquin Road, Suite 1
Arlington Heights, IL 60005

Non-Profit Org.
U.S. Postage
PAID
Carol Stream, IL
PERMIT NO.
1746

acofp | AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

www.acofp.org