OFP

Osteopathic Family Physician

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

SEPTEMBER/OCTOBER, 2019

Volume 11 | Number 5

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. Periodicals 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 East Algonquin Rd, Suite 1
Arlington Heights, IL, 60005
membership@acofpca.org

CUSTOMER SERVICE

(orders, claims, online, change of address)

American College of Osteopathic Family Physicians

330 East Algonquin Rd, Suite 1
Arlington Heights, IL 60005

800-323-0794 | 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/resident rate, orders must be accompanied by name of affiliated institution, date of orders must be accompanied by name of affiliated institution, date of term and the signature of program/residency 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 800.323.0794 or email ashleyd@acofp.org.

EXAM SCHEDULE

CERTIFICATION & OCC (RECERTIFICATION)

AOBFP EST. 1972

EXAMS	LOCATIONS	POSTMARK DATE
Family Medicine / OMT Certification / OCC Cognitive Exam	**Electronic Testing** Regional Sites September 28, 2019	**April 1, 2019** *Late fee through June 1, 2019*
Family Medicine / OMT Certification / OCC Performance Evaluation Only	**AOA OMED Conference** Fall, 2019 exam dates TBD	**April 1, 2019** *Late fee through June 1, 2019*

AMERICAN OSTEOPATHIC BOARD OF FAMILY PHYSICIANS
If you have questions, please call 847.640.8477 or email aobfp@aobfp.org.

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

SEPT/OCT, 2019
VOLUME 11 | NUMBER 5

CONTENTS

OSTEOPATHIC FAMILY PHYSICIAN SPECIALTY PEER REVIEWERS

Nazem Abdelfatta, MD
Family Medicine, Obstetrics, Women's Health

Richard L. Averitte, Jr, MD
Dermatology

Jeffrey Benseler, DO
Radiology

Shagun Bindlish, MD
Diabetes and Endocrinology

Warren Bodine, DO
Sports Medicine & Family Medicine

Grace Brannan, PhD
Statistics/Design

Natasha Bray, DO
Ethics

Omar Bukhari, DO
Family Medicine, Obstetrics

Janis Coffin, DO
Practice Management

Philip Collins, DO
Patient Education

Danielle Cooley, DO
OMM

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

Rob Danoff, DO
Emergency Medicine, Preventive

Robin Devine, DO
Statistics/Design

Brian Downs, DO
HIV, Wound Care

Dennis Eckles, DO
Diabetes, Rural Medicine

Gail Feinberg, DO, FACOFP
Academic

Ron Gubb, DO
Diabetes, Sports Medicine

Patricia Happel, DO
Nutrition and Obesity

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

Ronald P. Januchowski, DO
Military & Rural/Underserved

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

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

Uzma Khan, DO
Family Medicine

Frank Komara, DO
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

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
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

Frederick Stine, DO
Pediatrics, Nephrology, Emergency & Critical Care

Lindsay Tjiattas-Saleski, DO
Clincial Images, Emergency Medicine

Johnathon Torres, DO
OMM

Chad Uptigrove, DO
Obstetrics, Residency Training

Michael Watkins, DO
OB/GYN & Women's Health

William Woolery, DO, PhD, FACOFP
Geriatrics

Julian Vega, DO
Clinical Images

Sheldon Yao, DO
Cardiology

Nicholas Pennings, DO, FOMA
Obesity

2019 STUDENT ACADEMIC & PEER REVIEW WRITING INTERNS

Michael Anderson
William Carey University College of Osteopathic Medicine

Steven Bean
William Carey University College of Osteopathic Medicine

Alex Belote
William Carey University College of Osteopathic Medicine

Anmol Bhatia
A.T. Still University - School of Osteopathic Medicine in Arizona

Lindsay Bigham
William Carey University College of Osteopathic Medicine

Shelbi Bolton
William Carey University College of Osteopathic Medicine

Johnny Campbell Jr.
William Carey University College of Osteopathic Medicine

Tessa Cucurullo
William Carey University College of Osteopathic Medicine

Alice Doong
Michigan State University College of Osteopathic Medicine

Angelic Dye
William Carey University College of Osteopathic Medicine

Zachary D. Ellis
William Carey University College of Osteopathic Medicine

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

Joanna Gobrial
A.T. Still University - School of Osteopathic Medicine in Arizona

Kathryn Johnson
A.T. Still University - School of Osteopathic Medicine in Arizona

Chris Koerber
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

Liana Kobayashi
A.T. Still University - School of Osteopathic Medicine in Arizona

Luiza Mnatsakanyan
William Carey University College of Osteopathic Medicine

Amelia Ni
A.T. Still University - School of Osteopathic Medicine in Arizona

Abi Moeller
A.T. Still University - School of Osteopathic Medicine in Arizona

Hennah Patel
William Carey University College of Osteopathic Medicine

Amena Payami
William Carey University College of Osteopathic Medicine

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

Mike Ramalia
Michigan State University College of Osteopathic Medicine

Shivani Reddy
William Carey University College of Osteopathic Medicine

Syed Danyal Raza
William Carey University College of Osteopathic Medicine

Diana Roy
William Carey University College of Osteopathic Medicine

Aryan Sharif
A.T. Still University - School of Osteopathic Medicine in Arizona

Sara Shu
Western University of Health Sciences College of Osteopathic Medicine of the Pacific

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

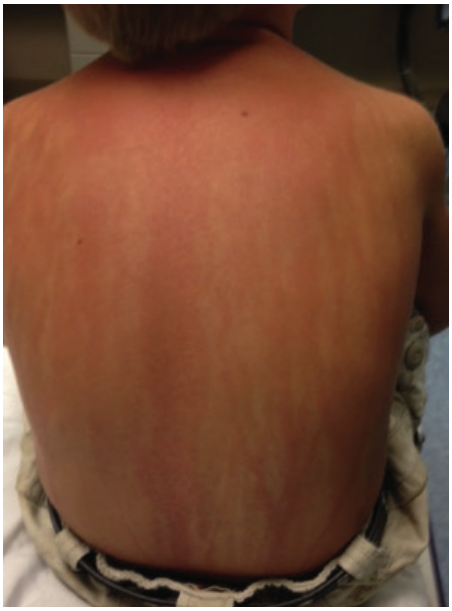
Nicholas S. Tito
William Carey University College of Osteopathic Medicine

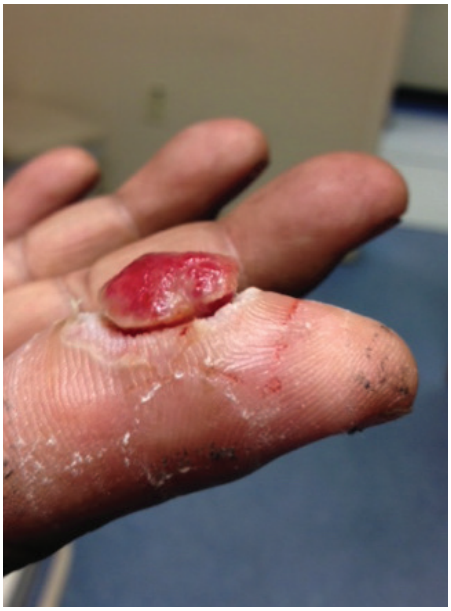
Elysia Tjong
A.T. Still University - School of Osteopathic Medicine in Arizona

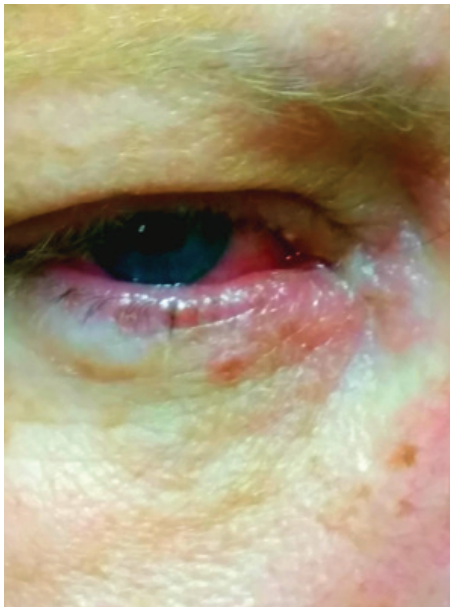
Nusrat Uddin
William Carey University College of Osteopathic Medicine

NOW SEEKING

CLINICAL IMAGES







OSTEOPATHIC FAMILY PHYSICIAN

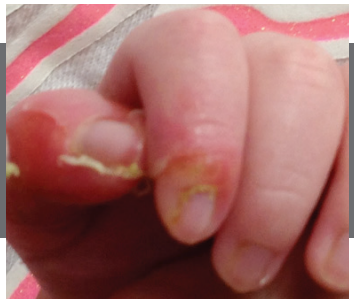
ACCEPTING SUBMISSIONS FOR THE SECTION TITLED "CLINICAL IMAGES."

This section showcases clinical images from the wards that cover essential concepts or subject matter to the primary care physician.

Each installment of "Clinical Images" comprises 1 or 2 medical images along with 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.

Submissions should be submitted online at ofpjournal.com via our Scholar One publication process.

OFP
OSTEOPATHIC FAMILY PHYSICIAN
The Official Peer-Reviewed Publication of the
American College of Osteopathic Family Physicians



New Orleans, LOUISIANA

ACOFP 57th Annual Convention & Scientific Seminars

acofp '20

MARCH 19 - 22, 2020

Over 30 Category 1-A CME Credits anticipated!

Register online this fall at www.acofp.org.

EDITOR'S MESSAGE

Tradition

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

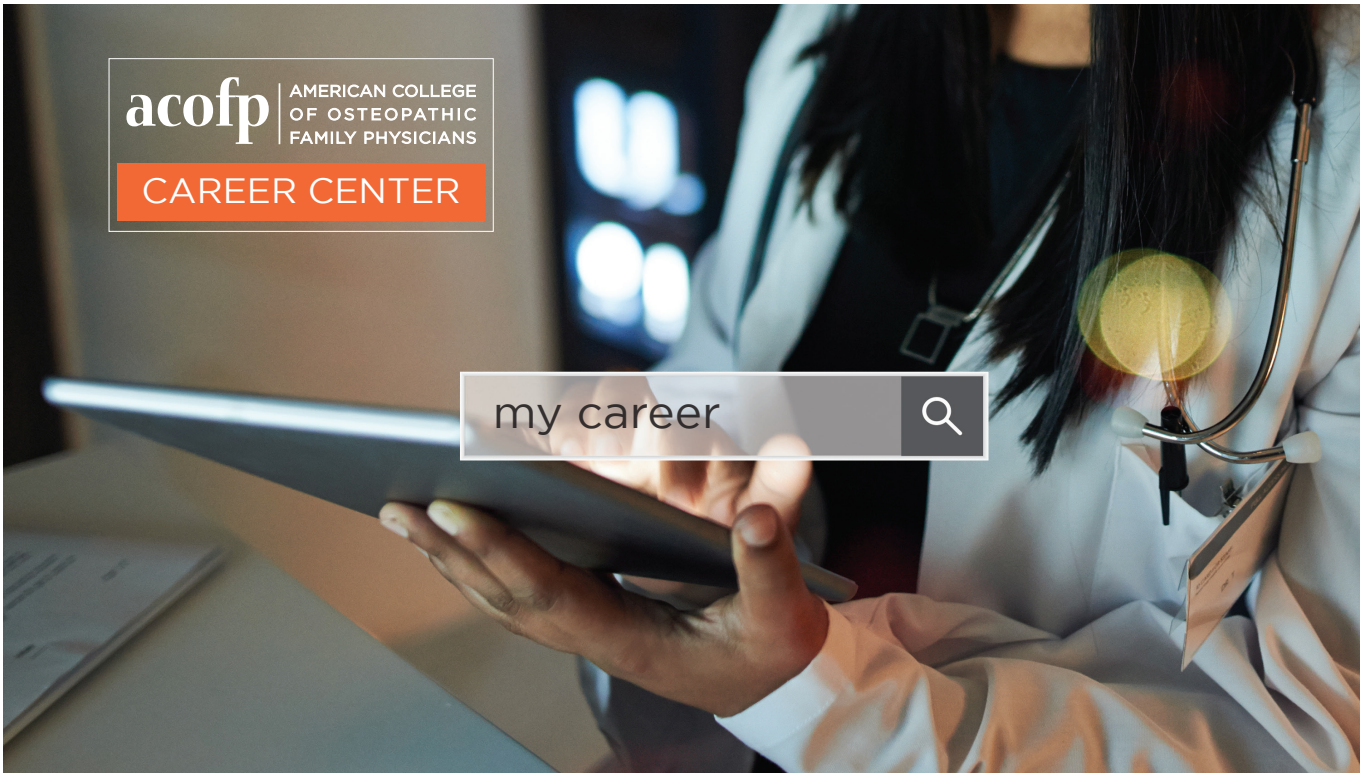
There have been plenty of signs in the past few weeks that the summer of 2019 is winding down. School sports physicals, preseason football and the fall issue of the *Osteopathic Family Physician* in your mailbox. As a lifelong Buffalo Bills fan, the second item gives me a bit of heartburn, but tradition would have me recognize the good entertainment provided and perhaps cloud over some of the more sad performances of the past. On the opposite end of poor performances, this issue of OFP may evoke some feelings of excitement in Family Medicine. The authors have submitted some excellent Osteopathic-based articles covering common diagnoses in Primary Care. Incorporating the tradition of the Osteopathic tenets along with some novel ideas, the authors have helped create a very unique issue containing relevant topics I hope you can use in practice before summer ends officially.

Speaking of combining tradition with forward-thinking ideas, congratulations go out to Jeffrey S. Grove, DO, FACOFP *dist*., chosen by *Crain's Chicago Business* as a notable LGBTQ Executive. Dr. Grove has been a champion for diverse populations in *Osteopathic Family Medicine* and for the LGBTQI+ community. The OFP article last year related to increasing the awareness of Osteopathic medical students of LGBTQ patient issues through a standardized patient program is hopefully one of many articles that will be here in the journal. I would like to add a call for papers related to this and other diversity issues to create a new tradition within our profession as the world changes around us.

With apologies to Tevye: "Who has the right to have the final word here? The editor, the editor! Tradition."

Enjoy the start of autumn and this issue of *Osteopathic Family Physician*!

 Print ISSN: 1877-573X



The ACOFP Career Center can help you find your perfect job. You can inventory your skills and accomplishments, proactively manage your career, and create a professional action plan tailored to your goals. Jump start your career by adding or updating your professional profile today and gain access to valuable tools and resources.

FROM THE PRESIDENT'S DESK

Exciting Developments in Osteopathic Medicine

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

There are big changes happening in the osteopathic family medicine profession right now and I'm happy to say that the new developments will be great for ACOFP members!

ACOFP RESOLUTIONS AT THE AOA HOUSE OF DELEGATES

ACOFP attended the American Osteopathic Association (AOA) House of Delegates meetings at the end of July in Chicago. It was a very successful, positive meeting this year. There was an air of change and cooperation. The new AOA CEO made the announcement of an open, direct and transparent relationship with members and staff.

The 2019-2020 AOA President, Ronald R. Burns, DO, FACOFP, was also sworn in at the House of Delegates. Dr. Burns outlined three areas that he'll focus on this year, which all align very well with the goals and strategies of ACOFP:

1. The certification process

2. Affiliate relations

3. Member benefits

ACOFP submitted resolutions on several issues that are important to ACOFP member physicians, residents and students.

Resolution 1. The AOA Board of Trustees, through the AOA Bureau of Osteopathic Specialists (BOS), shall ensure that osteopathic principles and practices (OPP) remains an integral and required part of AOA board certification and re-certification examinations as appropriate for each specialty.

This Resolution was signed by seven other specialty colleges and passed with the four strong policies:

a. Continued osteopathic content in the certification process as appropriate to the specialty

b. Continued opportunity for an OMM practical by any specialty

c. Continued specialty-specific content

d. Continued osteopathic content in the osteopathic recognition (OR) training programs

Resolution 2. The AOA shall require the certifying boards to notify the physician of their score within eight weeks of taking the test.

Resolution 3. The resolution on utilizing the OMT Boot Camp for partial fulfillment of OCC component four was referred to the BOS. The issue is now in the hands of AOBFP and ACOFP to work out the details and present to the BOS for approval.

EARLY ENTRY CERTIFICATION PROGRAM

ACOFP is excited that the American Osteopathic Association (AOA) and the American Board of Osteopathic Family Physicians (AOBFP) have moved forward with new Early Entry Certification (EEC) program!

The EEC program will allow a resident to take a shortened AOBFP initial certification exam. The residents that take this exam will have early entry into Osteopathic Continuous Certification (OCC), which reduces the requirements they need to meet in their first certification cycle. As further detailed in the AOA announcement, a resident only needs to take two (2) ACOFP/AOBFP In-Service exams (ISEs) prior to being eligible for the EEC.

There are several major benefits to this new exam format:

• The EEC exam will consist of fewer questions and be available at a lower cost than the traditional cognitive exam for board certification.

• The OMT performance exam is now optional.

• The OMM practical will be optional for the initial certification. If the physician chooses to take the OMM practical, then it will be reflected in the certificate. If the resident does not take the OMM practical on the initial certification, they have the option to do so later.

• There will be a way for a resident to register for the ISE as an individual so that their ability to take advantage of this EEC will not be determined solely by their institution.

AOBFP is currently finalizing other important details regarding the EEC and will announce them soon.

In addition to this great news, the ACOFP Education and Research Foundation has pledged to financially support third-year family medicine residents with the cost of their unreimbursed expenses. While details are still being completed, grants will be made available to residents taking their initial AOBFP exam to subsidize expenses not covered by their institution.

All these enhancements to the AOBFP certification process make it a very easy decision for osteopathic family medicine residents

when it comes to which certification board to choose…OF COURSE, IT IS THE AOBFP!

We believe that these changes will foster a refreshed sense of unity within the AOA, affiliate specialties and the profession. We hope that you share our excitement for these game-changing opportunities!

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

Rocky Mountain OPTI/Sky Ridge Medical Center
Neuromusculoskeletal Medicine + 1 Residency

Our program was established to enable physicians who have already completed a residency in an approved specialty to spend an extra year enhancing their skills in neuromusculoskeletal medicine and osteopathic manipulative medicine (NMM/OMM). Our goal is to develop highly trained physicians who can act as both clinicians and academicians. Our program places a significant emphasis on the integration of osteopathic manipulative medicine and the principles of primary care sports medicine. Our residents develop their Osteopathic clinical skills by providing inpatient care at Sky Ridge Medical Center and outpatient care at the Rocky Vista Health Center and other associated outpatient clinics.

Our program also includes such rotation choices as neurological surgery, occupational medicine, orthopedic spine surgery, podiatric medicine, primary care sports medicine, neurology, physical medicine and rehabilitation, rheumatology, musculoskeletal radiology, medical acupuncture, family medicine, integrative medicine, functional medicine, hospice and palliative care, internal medicine, obstetrics and gynecology and pediatrics. Academic development occurs through the Rocky Vista University College of Osteopathic Medicine in Parker, Colorado. Successful program completion will allow the physician to apply for the Neuromusculoskeletal Medicine/Osteopathic Manipulative Medicine certification examination.

Kenneth A. Ramey, DO, FACOFP serves as the program director and is a 1994 graduate ofthe Chicago College of Osteopathic Medicine. He is board certified in family medicine/osteopathic manipulative treatment, neuromusculoskeletal medicine/osteopathic manipulative medicine and has a certificate of added qualification in sports medicine. Dr. Ramey is a member of the medical staff at Sky Ridge Medical Center and has served as a team physician at the high school, college and semi-professional levels. He is an Associate Professor of OPP at Rocky Vista University and serves as the Director of the Sports Medicine and Osteopathic Manipulative Medicine Program at the Rocky Vista Health Center.

We have received ACGME Pre-Accreditation and would be honored to consider your application for our program. Please send a current CV, letter of interest and three letters of recommendation (including one from your residency director) to Dr. Ramey at kramey@rvu.edu. Please call Dr. Ramey at (720) 874-2421 if you need additional information.

"The purpose of Osteopathy is to make life a little more comfortable for the patient."

"What are the limits of Osteopathy? No one knows the limits of Osteopathy."

John Martin Littlejohn, DO

REVIEW ARTICLE

A Literature Review of Osteopathic Manipulative Techniques for Otalgia

Tom Lindsey, DO, FACOS[1]; Ryan Lawson, OMS II[1]; Franklin Hiffernan, OMS II[1]

[1]Edward Via College of Osteopathic Medicine-Carolinas

KEYWORDS:

Eustachian Tube

Non-Opioid Pain Management

Osteopathic Manipulative Medicine

Osteopathic Manipulative Technique

Otalgia

ABSTRACT: Otalgia is a common painful condition of the ear that can stem from multiple etiologies, including, but not limited to infectious, mechanical or inflammatory conditions. The intricate anatomy of the ear and eustachian tube offer numerous avenues for pathophysiology to manifest. While the precise mechanism of otalgia has not been entirely elucidated, it is widely accepted that pressure is one common denominator. A potential source of pressure variations within the middle ear relies on pathology of the eustachian tube, making it a target for treatment with Osteopathic manipulative techniques (OMT). OMT offers mechanical solutions to mechanical problems within this complex anatomic system. With this literature review we have three goals: first, to provide an in-depth review of the existing Osteopathic manipulative techniques to treat otalgia; second, to present a case report of a novel Osteopathic manipulative technique for otalgia; and lastly, to encourage further data driven research for the use of OMT for otalgia.

Otalgia is a painful condition related to pathology of the ear or surrounding structures. The differential diagnoses for otalgia include categories such as infectious, inflammatory, and mechanical etiologies. Common diagnoses that are often associated with ear pain include: acute otitis media, serous otitis media, eustachian tube dysfunction, and post-tonsillectomy. Theories exist that otalgia may be directly related to pressure in the eustachian tube or referred pain from inflammation/inflection of the surrounding tissues. Osteopathic manipulative techniques offer a treatment of otalgia without the need for potential side effects of medical management, including unnecessary exposure to narcotic pain medication. This article is a review of the scientific literature involving manipulative treatment of otalgia, including historical references. In this article, we will describe the anatomy of the region and discuss the potential mechanisms of otalgia. In addition, we will delineate the various Osteopathic and other manipulative treatments of otalgia and detail their data driven outcomes. Finally, we will report a novel Osteopathic manipulative treatment and encourage further studies to evaluate the manipulative treatment of otalgia.

CORRESPONDENCE:
Tom Lindsey, DO, FACOS | tlindsey@carolinas.vcom.edu

METHODS

A thorough review of the literature was conducted using standard procedures[1] and the following databases and journals: *PubMed*, *MEDLINE*, *Osteopathic Medical Digital Repository*, *Journal of the American Medical Association*, and *Journal of the American Osteopathic Association*. A standard protocol for searching each of the databases was followed, which included using a universal set of terms to be searched listed in *Figure 1*. There were no date boundaries set for the searches conducted. In total, seven studies/case reports were selected for inclusion based on relevance to the osteopathic treatment of otalgia or otitis media. The types of literature included are either case reports, pilot studies or peer-reviewed journal articles.

FIGURE 1 :

Universal set of terms to be searched

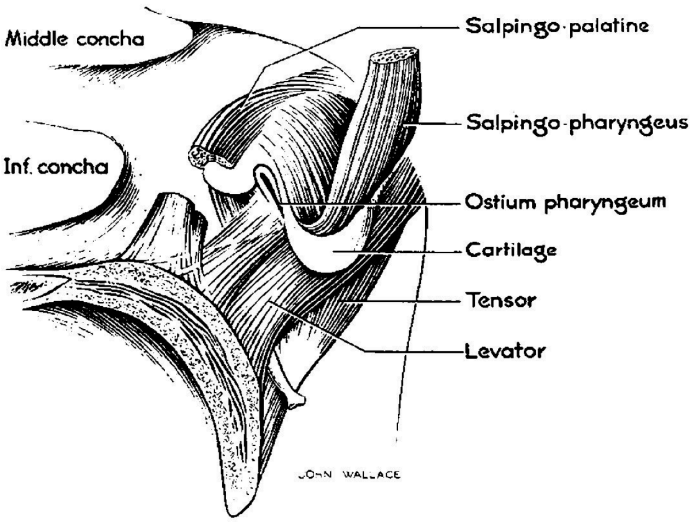
Terms Searched			
Osteopathic treatment of ear pain	Osteopathic treatment of otalgia	Manual ear therapy	Osteopathic treatment of eustachian tube
Osteopathic treatment of otitis media	Galbreath technique	Muncie technique	Modified Muncie technique
Treatment of otalgia	Otalgia	Ear pain	Osteopathic manipulative medicine (OMM)
High velocity low amplitude treatment of ear	Alternative treatment of otalgia	Eustachian tube treatment	Eustachian tube dysfunction

ANATOMY AND EMBRYOLOGY

"The pharyngotympanic tube serves to ventilate the middle ear, exchanging nasopharyngeal air with the air in the middle ear, which has been altered in its composition via transmucosal gas exchange with the hemoglobin in the blood vessels of the mucosa. The tube also carries mucus from the middle ear cleft to the nasopharynx as a result of ciliary transport."[2] Measuring, on average, 36mm in adults and 18mm in children, the tube has two distinct components: the lateral bony portion and the medial fibrocartilaginous portion.[3] In addition to the differences in length, the eustachian tube of a child is more horizontal with an angle of only 10 degrees with respect to the horizontal plane, compared to 45 degrees in adults, which increases the likelihood of otitis media due to inadequate clearance of secretions.[4] Embryologically the eustachian tube is derived from the proximal portion of the 1st pharyngeal pouch and is therefore endodermal in origin.[5] The cartilage and muscles associated with the eustachian tube are derived from mesoderm.[5] There are four muscles that are associated with the function of the eustachian tube: tensor veli palatini, levator veli palatini, salpingopharyngeus, and tensor tympani *(Figure 2)*.[6] According to Ars[6], the tensor veli palatini muscles plays the most significant role in the open and closure of the eustachian tube by tensing the anterolateral membranous wall during chewing, yawning or swallowing. Throughout the literature the levator veli palatini muscle has disputed function in opening or closing of the eustachian tube. Lastly, the salpingopharyngeus muscle is considered to serve an anchoring role as opposed to actively opening or closing the eustachian tube.[6] The innervation of the eustachian tube is complex and includes maxillary and mandibular branch of the trigeminal nerve as well as the tympanic plexus derived from the glossopharyngeal nerve. Arterial blood supply is derived from the ascending pharyngeal and middle meningeal arteries respectively.[7] Venous drainage passes through the pterygoid plexus, while lymphatic drainage flows to the deep cervical lymph nodes.[7] With an adequate understanding of the structure of function of the eustachian tube the mechanism of otalgia is more clear.

FIGURE 2 :

Four muscles that are associated with the function of the eustachian tube



This work has been released into the public domain by its author, S. SIMKINS, PH.D.

MECHANISM OF OTALGIA

There are multiple theories about the exact mechanism of otalgia in the literature. According to *Stanford Ear Institute*, blockage of the eustachian tube isolates the middle ear and traps air within this confined space.[8] Subsequently the mucosa of the middle ear absorbs the air, creating a negative pressure in the middle ear, which applies inward traction to the tympanic membrane.[8] Due to the dense innervation of the tympanic membrane the sensation of pain will occur. The sensory fibers for the inner surface of the tympanic membrane will be carried on the glossopharyngeal nerve.[3] Long term blockage of the eustachian tube will lead to a transudation of fluid into the middle ear space creating a situation known as serous otitis media.[9] There are numerous mechanisms by which the eustachian tube becomes obstructed, leading to the pathogenesis of otalgia described above. Inflammation of the nasopharynx, allergic rhinitis, influenza, cigarette smoke, post-tonsillectomy inflammation are examples of potential precipitating factors in eustachian tube obstruction.[8] According to Kujawski et al,[10] in a study of 200 patients, post-tonsillectomy otalgia was reported in 41%-69% of patients depending on the technique utilized.

REVIEW OF TECHNIQUES FOR OTALGIA

Find below the description of four specific techniques[1-4], followed by three studies with their supporting data[5-7].

Muncie Technique

The Muncie technique was developed by *Curtis H. Muncie, DO*, in the 1920's to address eustachian tube dysfunction. The technique is performed as follows: "the osteopathic physician should insert a gloved right index finger into the patient's mouth, placing the finger against the inferior part of the posterior pillar of the palatine tonsil. Moving the finger tip cephalad and slightly lateral to the

Rosenmüller fossa, posterior to the opening of the eustachian tube, the osteopathic physician should apply a pumping motion with the finger pad to lyse any adhesions and, ultimately, restore the eustachian tube opening."[7] The major disadvantage of this procedure is the lack of patient tolerance secondary to gagging. This technique was taught in osteopathic medical schools through the 1960's, however the procedure was seldom used in clinical practice due to limitations previously mentioned.[11] No studies measuring the effectiveness of the Muncie technique were discovered during the literature review.

Modified Muncie Technique

The Modified Muncie technique was introduced in the literature for the first time in 2008 via a case report of a patient with vertigo. One of the modifications to the original Muncie technique, is the patient is laid supine or reclined to increase head stabilization.[7] The technique is performed as follows: "First insert the index finger, gloved, into the patient's mouth. Place the finger against the posterior pillar of the palatine tonsil. Lastly, apply lateral pressure while making a circular motion into the soft tissue."[7] Channell notes that applying the motion to this specific point exerts traction to the ostium of the eustachian tube allowing it to open. Opening of the eustachian tube allows for equalization of pressure and drainage of fluid. The patient in the case study was a 37-year-old female presenting with difficulty hearing out of the right ear and subjective vertigo symptoms. On exam, she had a mildly retracted right tympanic membrane with serous fluid noted. Pressure measurements were not documented due to lack of instrumentation. She was diagnosed with serous otitis media secondary to seasonal allergies. The patient was subsequently treated with the Modified Muncie technique and tolerated the procedure well. The patient returned two weeks later with complaints of recurrent symptoms for approximately one week after initial treatment. The patient was treated with the Modified Muncie technique again with complete resolution of her symptoms. No studies measuring the effectiveness of the Modified Muncie technique were discovered during the literature review.

Galbreath Technique

The Galbreath Technique was first described by *William Otis Galbreath, DO* in 1929 and has been taught in osteopathic medical schools for the treatment of otitis media and otalgia. The technique was well described by *Dale Pratt-Harrington, DO* in a review article published in the *JAOA* in October of 2000. The technique is performed as follows: "The physician can perform this technique by either placing the child in the supine position (as originally described) or in the physician's or parent's lap). The physician then turns the child's head so that the affected ear faces away; with the operator's hand that is opposite of the affected ear (that is, if the child has otitis media on the right side, the operator uses the left hand), the operator contacts the child's mandible on the affected side and applies a downward and transverse mild force on the mandible that crosses the face. This is repeated in a slow rhythmic application of force (about 3 to 5 seconds per round) for 30 to 60 seconds. Drainage resulting from this technique provides relief of pain and of the infection."[11,12] No studies measuring the effectiveness of the Galbreath Technique were discovered during the literature review.

Manual Therapy (HVLA)

A high-velocity, low-amplitude (HVLA) technique was described by *Donald R. Murphy, DC* in T*he Journal of the Canadian Chiropractic Association* in March of 2011. The article described the treatment of four cases of idiopathic otalgia. The technique is performed as follows: "The technique used in the cases reported here was one in which the thumb is placed just inside the intertragic notch, with the proximal interphalangeal joint of the index finger contacting just inside the lobule. A gentle lateral movement is applied and the patient is asked whether this produces pain. The practitioner also attempts to assess the degree of resistance to the movement (the reliability and validity of this assessment is unknown). If manipulation is deemed indicated, a high-velocity, low-amplitude thrust is performed in a straight lateral direction. An audible release typically occurs. The patient can then be taught self-mobilization in the same direction, applying low-velocity, low-amplitude oscillatory maneuvers."[13] No studies measuring the effectiveness of the Manual Therapy (HVLA) were discovered during the literature review.

Integrated Osteopathic Treatment

In 1989 *Dr. William Pintal, DO*, published a case report in The Journal of the *American Osteopathic Association* detailing an integrated osteopathic treatment plan for otitis media. He utilized Cefaclor dosed appropriately along with the following osteopathic techniques:" deep soft tissue releases at both mandibular angles to increase blood supply and facilitate drainage around the eustachian tubes, hyoid release using direct articulatory approach, with subsequent alternating pressure to the lateral anterior aspect of the neck to stimulate eustachian tube drainage along with generalized lymphatic and venous drainage, bilateral shoulder raising to act as a lymphatic pump, direct muscle energy approach to the cervical spine was used, specifically at the level of C-1 and C-2, myofascial release technique to soft tissues, deep to the angles of the mandible, generalized anterior cervical soft tissue technique to facilitate arterial, venous, and lymphatic circulation in and about the head and neck."[14] The patient was treated for 5 days with this regimen and reported resolution of otalgia by fourth day of treatment. At a 9-month follow up, the patient had no recurrence of symptoms. Outside of Dr. Pintal's singular case report, no studies measuring the effectiveness of these specific techniques were discovered during the literature review.

Steele, DO, et al Pilot study

In May of 2014 *Dr. Karen Steele, DO*, et al published results of a pilot study designed "as a dual-site, prospective, randomized, blinded, controlled clinical trial on the efficacy of a standardized OMM protocol on middle ear effusion (MEE) in young children with acute otitis media (AOM)."[15] The authors set out to improve upon the historical limitations in studies of Osteopathic manipulative treatment such as lack of patient recruitment, insufficient standard treatment protocol, and results based only on subjective features. Treatment plans lasted 15-30 minutes and were based on a combination of osteopathic manipulative techniques including bilateral ligamentous tension, myofascial release, and supoccipital inhibition.[15] In an effort to report more objective data, they collected data using tympanometry and

acoustic reflectometry. Tympanometry reports on a tympanogram the ability of the tympanic membrane to vibrate at different pressures, while acoustic reflectometry reports the likelihood of middle ear effusion. There were 43 participants that completed the study aged 6 months-2 years. There were 2 groups in this study, either standard care (antibiotics) or OMT in addition to standard care. The findings of the study were reported as follows: "standard OMT protocol administered adjunctively with standard care for patients with AOM resulted in faster resolution of MEE at 2 weeks than standard care alone."[15] The evidence behind this assertion is that in the general US pediatric population after acute otitis media, roughly 70% of patients will have persistent MEE by 2 weeks as compared to 18.5% noted in the patients receiving OMT along with standard care.[15,16] Limitations of this study include the small sample size and the lack of a sham OMT group to compare against. Prakash[17] wrote in an article reviewing the study by Steele, DO, et al: "Many manipulation techniques were performed in the study by Steele et al, making interpretation of results difficult—especially considering the possible low enrollment of study participants."

Mills, MD, et al OMT study

In September 2003 *Miriam Mills, MD*, published a study in *The Archives of Pediatrics & Adolescent Medicine* investigating the effects on osteopathic manipulative treatment as adjuvant therapy for pediatric patients with recurrent otitis media. Patients for this study were aged 6 months to 6 years old and split into two group: either routine care or osteopathic manipulative treatment in addition to routine care. "Children in both groups were scheduled for 9 visits during the study: approximately 3 weekly, 3 biweekly, and 3 monthly."[18] This study reports that they followed the designed model of Steele, DO, et al by using tympanometry, however did not use acoustic reflectometry.[18] This study had a total of 57 patients that followed through to completion. The osteopathic treatments described in this study lacked specificity and are listed as follows: "Treatments lasted 15 to 25 minutes, which is usual in most practices. Treatments were gentle techniques on areas of restriction consisting of articulation, myofascial release, balanced membranous tension (according to teachings of William Garner Sutherland, DO, and others), balanced ligamentous tension, facilitated positional release, and/or counterstrain treatments."[18] Results from the study showed that the group receiving adjuvant osteopathic manipulative medicine had fewer episodes of AOM, required fewer prescriptions for antibiotics, and required fewer surgical placement of tubes.[18] This study reported similar limitations to previous studies due to the lack of a sham OMT group. In addition, this study reported a higher dropout rate than Steele, DO, et al. In a review of this study by Hollis King, DO, PhD commented: "My opinion is that we have proven the benefit of OMT in musculoskeletal disorders. Next, we need to develop and fund well-designed studies that demonstrate the benefit of OMT in physiologic functions and systemic disorders such as otitis media."[19]

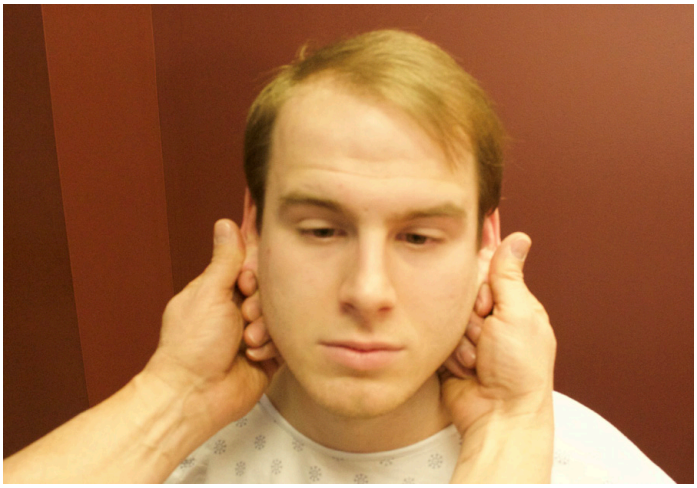
Case report of a novel Osteopathic Manipulative Treatment: Eustachian tube traction technique

A 35-year-old male presented to the urgent care clinic with three-day history of continuous right ear pain. Patient history revealed that he had no trauma, no recent air travel and was a non-smoker. The patient had no past history of surgery. He reported no other symptoms including sore throat, hearing loss or tinnitus. Otoscopic examination revealed right serous otitis media as evidenced by bulging right tympanic membrane with clear fluid noted. He was diagnosed with otalgia secondary to right serous otitis media. Standard of care for this diagnosis would be a 10-day course of anti-inflammatory medication. In addition to oral anti-inflammatory therapy, the patient was treated with the novel osteopathic manipulative technique titled Eustachian tube traction that has not been documented in osteopathic literature. He experienced immediate relief of his right ear pain and left the clinic pain free. On follow up the next day the patient reported that he remained pain free and was taking oral anti-inflammatory medication as prescribed.

The novel Eustachian tube traction technique was taught to the author during his third year of medical school in 1986 by an osteopathic clinical instructor. The Eustachian tube traction technique has been used for the treatment of idiopathic otalgia, otitis media (serous and infectious), vertigo, and post-tonsillectomy otalgia. The technique is performed as follows: the physician grasps the pinna of the ear with the thumb and index finger of each hand. The fifth metacarpal of the physician's hand is placed against the corner of the mandible of the patient *(Figure 3)*. The hand is rotated around a vertical axis to an end-point and then the Eustachian tube is distracted with force along its axis. There is often an audible pop heard by both the patient and the physician. The authors concede that physicians will become more proficient with application of this technique. Often the patient will report immediate relief of their pain and the sensation of fluid draining from the Eustachian tube into the posterior pharynx.

FIGURE 3 :

Eustachian tube traction technique



CONCLUSION

Otalgia is a mechanical problem and as such may be treatable by mechanical means. This literature search was undertaken to determine the full spectrum of manual treatments that exist and their supporting studies. Otalgia itself seems poorly understood, including the etiologies and mechanisms of the pain, despite a detailed understanding of the anatomy of the region. Review of the literature reveals four singular and three combination manual techniques.[7,12,14,16,18] Additionally, we submit a novel Osteopathic manipulative treatment, the Eustachian tube traction technique, into the literature. As a result of the review there is demonstrated a history of manual treatments without studies to support there reported, successful outcomes. These reports of successful management of otalgia with manual therapies are encouraging. A review of the literature on the manual treatment of otalgia leads to two conclusions. There is a need for a better understanding of the etiologies of otalgia and there is a need for further study of Osteopathic manipulative treatment in otalgia, specifically the Eustachian tube traction technique.

AUTHOR DISCLOSURES:
No relevant financial affiliations

REFERENCES:

1. Pautasso M (2013) Ten Simple Rules for Writing a Literature Review. PLoS Comput Biol 9(7): e1003149.
2. Standring, S. and Gray, H. (2008). Gray's anatomy. p.626, [Edinburgh]: Churchill Livingstone/Elsevier.
3. Moore KL, Agur AMR, Dalley AF. Clinically Oriented Anatomy. Eighth ed. Philadelphia: Wolters Kluwer; 2018.
4. Kim SJ, Donovan DM, Blanchard SB, Kowolik JE, Eckert GJ. The relationship between acute otitis media and the anatomic form of the hard palate. Pediatr Dent. 2008 Jan-Feb;30(1):9-14.
5. Sadler TW. Langman's Medical Embryology. 13th ed. Philadelphia: Wolters Kluwer; 2015.
6. Ars B, Dirckx J. Eustachian tube function. Otolaryngologic clinics of north america. 2016;49(5):1121-1133.
7. Channell MK, Modified Muncie technique: Osteopathic manipulation for eustachian tube dysfunction and illustrative report of case. J Am Osteopath Assoc. 2008 May;108(5):260-3.
8. Stanford Medicine Otolaryngology Head & Neck Surgery. Stanford Ear Institute website https://med.stanford.edu/ohns/healthcare/earinstitute/conditions/eustachian_tube_dysfunction.html , Accessed Oct. 6 2018.
9. Sproat R, Burgess C., Lancaster T., Martinez-Devesa P.. Eustachian tube dysfunction in adults; BMJ 2014; 348, pg1647.
10. Kujawski O, Dulguerov P, Gysin C, Lehmann W. Microscopic tonsillectomy: a double-blind randomized trial. Otolaryngol Head Neck Surg. 1997;117(6):641–647.
11. Pratt-Harrington D. Galbreath technique: a manipulative treatment for otitis media revisited. J Am Osteopath Assoc. 2000 Oct;100(10):635-9.
12. Patriquin D. Lecture notes on otitis media. Paper presented at: UAAO meeting; April 1993; Athens, Ohio.
13. Murphy DR, Gay CW. Manual therapy and ear pain: a report of four cases. The Journal of the Canadian Chiropractic Association. 2011;55(1):40-46.
14. Pintal WJ, Kurtz ME. An integrated osteopathic treatment approach in acute otitis media. J Am Osteopath Assoc. 1989 Sep;89(9):1139-41.
15. Steele KM, Carreiro JE, Viola JH, Conte JA, Ridpath LC. Effect of Osteopathic Manipulative Treatment on Middle Ear Effusion Following Acute Otitis Media in Young Children: A Pilot Study. J Am Osteopath Assoc 2014;114(6):436–447.
16. Bluestone CD, Klein JO. Otitis Media in Infants and Children. 3rd ed. Philadelphia, Pa: B Saunders Co;2001.
17. Prakash L, Michalik DE. Brief Report of a Clinical Trial on the Duration of Middle Ear Effusion in Young Children Using a Standardized Osteopathic Manipulative Medicine Protocol. J Am Osteopath Assoc 2010;110(12):738–739.
18. Mills MV, Henley CE, Barnes LLB, Carreiro JE, Degenhardt BF. The Use of Osteopathic Manipulative Treatment as Adjuvant Therapy in Children With Recurrent Acute Otitis Media. Arch Pediatr Adolesc Med. 2003;157(9):861–866.
19. King HH. Systematic Review of CAM Approaches to Otitis Media: The Otolaryngology Perspective. J Am Osteopath Assoc 2013;113(10):795.

Lightbeam Health Solutions

- Population Health Management
- Value-Based Care Guidance
- MIPS Quality Manager
- Proven Clinical & Financial Results

Need Help With Your Quality Payment Program Strategy?

Lightbeam is for anyone who has to satisfy CMS Quality Payment Program requirements. Whether you're a solo practitioner, large hospital or ACO, Lightbeam enables you to manage complex patient populations easily and accurately in order to improve outcomes and reduce costs.

ACOFP members will have access to the Lightbeam Platform at a reduced member price. For more information, email advocacy@acofp.org.

acofp | AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

Lightbeam Health Solutions

REVIEW ARTICLE

Physician Wellness, Osteopathic Principles, and Strategies for Change

Katherine Lincoln, DO, FACOFP, FAAFP

Guthrie Center for Wound Care and Hyperbaric Medicine, Sayre, PA

KEYWORDS:

Burnout

Disease Prevention and Wellness

Physician Engagement

Physician Wellness

ABSTRACT: Physician burnout has been identified in the US Healthcare system at alarming rates. Osteopathic Family Physicians can reflect on the Osteopathic Principles as a foundation of improving physician wellness. Physician engagement can be used as an antidote to physician burnout and help physicians recapture meaning in the work of medicine.

In modern America, physicians are facing burnout at an extraordinary rate.[1] These physicians can suffer depression, premature loss of their careers, disruption or destruction of their families and also face the highest risk of suicide of any profession.[2] In order to stem the rising tide of physician burnout and the wake of its destructive effects, time must be taken to reflect on the sources of burnout. As Osteopathic family physicians, we should also take time to reflect on our osteopathic principles as a powerful core of treatment for this malady. Moving forward, strategies can be developed to thwart burnout in the career of Osteopathic family physicians.

Most Osteopathic physicians take the Osteopathic oath at the conclusion of the Osteopathic educational experience. In this Oath, it is affirmed, "...to perform faithfully my professional duties, to employ only those recognized methods of treatment consistent with good judgment and with my skill and ability, keeping in mind always nature's laws and the body's inherent capacity for recovery." When this Oath is reflected though the lens of physician burnout, it is clear that Osteopathic physicians suffering through burnout are struggling with good judgment, forgetting nature's laws, and putting up walls against the body's inherent capacity for recovery.

CORRESPONDENCE:
Katherine Lincoln, DO, FACOFP, FAAFP
Katherine.Lincoln@guthrie.org

 Print ISSN: 1877-573X

As the oath goes on, “I will endeavor to work in accord with my colleagues in a spirit of progressive cooperation.” It is through the long-term effects of burnout, this desire to learn and grow with colleagues is often lost. Physicians begin to lose passion for the role each play in the healthcare system. It can become a slippery slope to not feel like work matters. It can begin to feel like a factory job, just adding a widget to a greater machine without greater purpose, self-satisfaction and contemplation. As physicians see their jobs released to non-physician providers, they can lose sight of the patient care that was the motivation for their education in the first place. As service lines begin to compete for the healthcare dollar, the desired progressive cooperation can be lost.

Physician burnout has been written about extensively by Dike Drummond, MD. Dr. Drummond is a Mayo Clinic trained family physician who is a teacher and trainer on stress management, burnout prevention, physician engagement, and tools for effective physician leadership. In one of Drummond’s articles, he writes “The difference between stress and physician burnout is this ability to recover in your time off. Physician burnout begins when you are NOT able to recharge your batteries between call nights or days in the office. You begin a downward spiral that has three distinct symptoms.

1) Physical and Emotional Exhaustion

2) Depersonalization

3) Reduced Sense of Personal Accomplishment[3]

It must be noted that burnout is not fatigue. Burnout is not physician laziness. Burnout is not young doctors being "soft." Burnout lasts for months or even years. Burnout can make a physician feel like a failure and can manifests itself in the physician creating a cynical attitude and feelings of hopeless. According to multiple sources[4,5] it is an emotional exhaustion that is not replenished after a vacation or other restful activities. Callousness and exhaustion brought on by burnout cannot be cured with a mandatory class in patient satisfaction surveys or institutionally required courses and activities.

The average modern physician is overwhelmed with administrative tasks, unprecedented educational debt, increasing patient demands, and the struggle with work/life balance. After years of training, Osteopathic physicians have many choices: they may choose to practice in a private practice setting or as employees to a large groups or companies. Each choice comes with a downside. Private practice focus may have to be on maximizing revenue and minimizing cost just to survive. Private physicians may be responsible for taxing and overly burdensome administrative roles within the practice. On the other hand, employed physicians may feel that their work doesn't matter, that they have little control over their time and patient interaction or they have become "just a worker," having lost their passion for patient care.

According to the article, "Physician Burnout: It Just Keeps Getting Worse,"[6] the top four key areas of physician burnout were identified as (in order from worst to least): too many bureaucratic tasks, spending too many hours at work, income not high enough, and the increasing computerization of practice.

Those in private practice may work longer hours compared to peers to attain higher income goals. The benefits of this are higher incomes and more autonomy. However, by pushing oneself to maximize benefit, a balance between work and non-work can be lost. The act of leaving work to exercise or to spend time with family is sacrificed in order to earn more. When physicians are pushed to maximize work time, sleep time is lost to charting and other non-paid administrative tasks. As Osteopathic physicians, it is clear that nature's laws dictate that humans have a sleep-wake cycle. When physicians ignore the laws of nature, just like in every human, the results can be devastating; physicians can lose their sense of purpose in medicine and in their personal lives.

In employed settings, physicians may have waived their rights to autonomy in exchange for fewer administrative burdens. Physicians may be able to come to the office or other practice setting, see the patients to whom they are assigned, finish their charts, then simply go home. Though it removes these time consuming tasks of scheduling, marketing, oversight, and day-to-day practice operations from the family physician it also places these administrative duties on someone outside the control of the employed physician. By exchanging control for a regular paycheck and benefits, autonomy is lost. The physician relinquishes control to terminate patients for bad behavior or fire staff for misconduct.

A tenet of Osteopathy states "the Body is a unit, and the person represents a combination of body, mind, and spirit." Taking this tenet and applying it to physician burnout, it can be seen how the inherent flaws of the current physician practice models can lead to burnout. If a physician in the workplace is forced to complete meaningless tasks, such as trivial but "required" documentation into an EMR, the unit of a mind, body, and spirit breaks down. The mind of an Osteopathic physician seeks to restore health through natural processes, such as sleep, leisure time and laughter. The mind of an Osteopathic physician sees the patient as an integrated collection of parts, each with dependent structures and functions. The mind of an Osteopathic physician seeks to find meaning for the ill as the illness plays a role in the patient's own family and society. As the body is forced to click EMR tabs and sign forms, the mind and spirit become disconnected from the root of health. While the body is typing charts for hours, the mind can wander and the spirits wither.

In Osteopathic medical students, their minds are engaged in high endeavors with visions of charity and mercy when they become attending physicians. Collaboration is held up as a desired part of their chosen field. The student spirit is filled when senior doctors make students feel like a part of the team, each person sharing the collective responsibility of care. As training ends and attending to life begins, a physician can feel like a silo of medical care. Osteopathic family physicians see patients daily with multiple complex comorbidities and handle their patient's care with grace and dedication. As the months and years of "real life" wear on, the spark of spirit filling love of medicine can wane. The mind can start to dull and wander. It can become easy to wonder if the prescriptions and the phone calls and missed lunches and late nights of patient care matter at all. A great divide can occur between an active mind filled with medicine and the physical body being pushed, insulted, micromanaged, and fatigued from late night documenting. The spirit, previously engaged and filled with intellectual curiosity, now goes dormant. Life goes on. Time goes by. Patients are born and patients die. Physician families age and grow, contract and expand. Without intervention, physician burnout can cause the rifts between the physician's mind, body, and spirit to expand.

In order to reintegrate, Osteopathic physicians need to identify the problem. For this, the Maslock Physician Burnout Inventory can be very useful. It is free and can be found at ***mindgarden.com/117-maslach-burnout-inventory***.[7] This validated inventory can be taken periodically by physicians as a touch point for personal wellness. Once physician burnout is identified, the Osteopathic physician should be allowed to decipher which people, conditions, episodes, and locations of patient care are most meaningful to him/her. It has been demonstrated that when people find meaning in their work at least 20% of the time, they are willing and able to suffer with less engaging work the rest of their work life.[8] As leaders of the Osteopathic family physicians, the ACOFP should encourage physicians to screen themselves with standardized tools such as Maslock Inventory and others. Once a physician acknowledges personal burnout, it can help move the needle back toward physician wellness and away from the many malignant manifestations of burnout.

The Mayo Clinic has constructed work levels in which to analyze strategies for change.[9] When a physician accepts burnout data in the self and in the work group, it can be helpful to have a

framework for the institution of change. This framework can view options for change at the individual level, work unit factor, organizational level, and the national level.[9]

At an individual level, Osteopathic physicians can analyze their specialty and practice location. Each can assess their personal efficiency and organizational skills. Each person can identify meaning in work and use self-awareness to shape career interests.[9] Individual physicians can assess their personality traits and relationship building skills. Each can integrate work and life outside work by using personal priorities and values.[9]

As strategies for physician engagement are created, work unit factors must be considered. Work units are the local teams which physician's work and exist in every day during work. It may include nursing support, clerical staff, other professionals, and administrative assistants. These are the team units which have their own culture in the daily experience of work. Areas of analysis should include team structure and productivity goals.[9] To assess efficiency and resources, daily huddles are found to be helpful. These huddles can address "pebbles in my shoe,"[10] small frustrations which may have simple solutions once they are clearly identified. For example, if a front desk staff member identifies it is very frustrating when the phone is ringing when she is trying to assist a patient in from of her, routing some calls to an alternate person during a high-volume time, some angst may be alleviated. Guthrie Medical Group in Sayre, Pennsylvania encourages each work unit to hold these huddles with pebble in my shoe on the agenda at least weekly. It allows the physicians and staff to have a space for change, using concrete elements to change work flow.

From an institutional perspective, group leaders should seek to help physicians reengage in the Osteopathic oath's "progressive cooperation." Institutions can create initiatives to engage physicians to reintegrate body, mind, and spirit. One way is to encourage reintegration is through fellowship with physicians centering around a common cause, such as interest in special areas of patient health, legislative medical issues or women in medicine special interest groups. When physicians engage in meaningful, cooperative dialog with near peers, they feel like their opinions matter. They feel like they want to move forward, move ahead, and move on, instead of staying stagnant. When leadership of influential medical groups encourages finding meaning in one's work, it helps struggling individuals feel less alone.

Nationally, changes can be made to reduce physician burnout.[11] A healthcare model which encourages quality care over EMR box clicking would be a reasonable start. The United States has had a third-party payer system for healthcare since Medicare and Medicaid was enacted. As years have passed, the Centers for Medicaid and Medicare (CMS) have continued to support legislation requiring increasing mandates on physicians. This burden has mounted to a new high as MIPS (Merit-based Incentive Payment System) and MACRA (Medicare Access and CHIP Reauthorization Act of 2015) reporting will most likely cause small, private, rural medical practices to surrender to local Accountable Care Organizations (ACOs)[12] or other financial models that destroy physician autonomy. Presently there is a CMS awareness of the excessive burden that has been generated by the new MIPS payment system and legislation to curb the burdens are being encouraged by the present Administration of the United States.[13] If a national payer consensus does occur and reduces the administrative burden on physician practices, physicians could spend more time engaged in patient care.

As previously noted, the major causes of physician burnout are too many bureaucratic tasks, spending too many hours at work, income not high enough, and the increasing computerization of practice. Each of these is closely tied to national healthcare policy. If future national legislation effectively reduces required bureaucratic tasks, physicians could spend less time at work. As these tasks were streamlined, the over-"computerization" of medicine and the depersonalization that occurs with that activity would decline. Osteopathic physicians should "employ only those recognized methods of treatment consistent with good judgment and with my skill and ability." Depersonalization of direct patient care brought about by the bureaucratic requirements just mentioned is surely not consistent with the Osteopathic Family Physician's best judgment, skill or ability.

As the future of physician wellbeing is sought out, reflection should be taken from Osteopathic history. By examining the Osteopathic oath and Osteopathic tenants, guideposts can be created for sculpting the future. By embracing treatment of good judgment and a spirit of progressive cooperation, the future can focus on healthy, content, well balanced Osteopathic family physicians who will be able to bring best care to their patients during long and fulfilling careers.

AUTHOR DISCLOSURES:
No relevant financial affiliations

REFERENCES:

1. AAFP Physician Burnout (Position Paper). Retrieved May 21, 2018 from https://www.aafp.org/about/policies/all/physician-burnout.html.
2. Anderson, P. "Physicians Experience Highest Suicide Rate of Any Profession" posted on May 07, 2018, retrieved on May 14, 2018 from https://www.medscape.com/viewarticle/896257.
3. Drummond, MD, Dike. "Physician Burnout: Why it's not a Fair Fight" retrieved on May 14, 2018 from https://www.thehappymd.com/blog/bid/295048/Physician-Burnout-Why-its-not-a-Fair-Fight.
4. "Physician Burnout". Agency for Healthcare Research and Quality. Retrieved May 21, 2018 from https://www.ahrq.gov/professionals/clinicians-providers/ahrq-works/burnout/index.html.
5. "Leadership Survey: Why Physician Burnout Is Endemic, and How Health Care Must Respond". New England Journal of Medicine Catalyst. Published December 8, 2016. Retrieved May 21, 2018 from https://catalyst.nejm.org/physician-burnout-endemic-healthcare-respond/.
6. Peckham, Carol. "Physician Burnout: It Just Keeps Getting Worse" Medscape Family Medicine January 26, 2015 retrieved on My 14, 2018 from https://www.medscape.com/viewarticle/838437.
7. Maslach Burnout Inventory. Retrieved on May 14, 2018 from https://www.mindgarden.com/117-maslach-burnout-inventory.

8. Friedman, U. "7 Ways to Find Meaning at Work," posted July 4, 2016, The Atlantic. Retrieved May 14, 2018 from https://www.theatlantic.com/business/archive/2016/07/meaning-work-happiness-brooks/489920/. https://www.cms.gov/Research-Statistics-Data-and-Systems/Monitoring-Programs/Medicare-FFS-Compliance-Programs/ReducingProviderBurden.html

9. Shanafelt, Tait and Noseworthy, J. "Executive Leadership and Physician Well-being: Nine Organizational Strategies to Promote Engagement and Reduce Burnout". Mayo Clin Proc. Jan 2017:92(1):129-146.

10. (10) TD Jakes. "What are the Pebbles in your Shoe?". Retrieved on May 13, 2019 from https://www.tdjakes.com/posts/what-are-the-pebbles-in-your-shoe

11. "Reducing Provider Burden". Center for Medicare and Medicaid Services. Updated May 1, 2018. Retrieved May 21, 2018 from https://www.cms.gov/Research-Statistics-Data-and-Systems/Monitoring-Programs/Medicare-FFS-Compliance-Programs/ReducingProviderBurden.html

12. Belliveau, Jacqueline. "Is MACRA a Trojan Horse for Small Practices, Value-Based Care?" RevCycle Intelligence. Retrieved May 21, 2018 from https://revcycleintelligence.com/news/is-macra-a-trojan-horse-for-small-practices-value-based-care.

13. "Administrative Simplification Overview". Center for Medicare and Medicaid Services. Retrieved May 21, 2018 from https://www.cms.gov/Regulations-and-Guidance/Administrative-Simplification/HIPAA-ACA/index.html.

REVIEW ARTICLE

Probiotic Use in Gastrointestinal Conditions: An Overview of Efficacy and Evidence

Royce Toffol, DO[1]; Stephen Stacey, DO[1]; Paul Cump, DO[1]

1. Peak Vista Community Health Centers, Colorado Springs, Colorado

KEYWORDS:
Diarrhea
Gastroenterology
Microbiome
Probiotics
Supplements

ABSTRACT: Probiotics are collections of live bacteria that are meant to be ingested for beneficial purposes. Many different preparations are widely available over-the-counter and used to improve or stabilize gastrointestinal flora. Studies have shown promise for probiotic use in a number of gastrointestinal diseases, treating medication side effects, and in healthy individuals with minor GI upset. Investigators continue to evaluate the effects the gastrointestinal microbiome has on homeostasis and methods by which probiotics may beneficially influence the microbiome. Long term efficacy, choice of species, dosage, and concentration of available preparations also remain areas of evolving study. This article will discuss probiotic regulation and formulations, review current understanding of mechanisms of action, and summarize recent study data in regards to clinically relevant GI disorders.

INTRODUCTION

Probiotics are collections of bacterial flora that are meant to be ingested for beneficial purposes. Most varieties of probiotics are normally present in healthy gastrointestinal tracts and have become a popular research target over the past two decades for the treatment of nearly every gastrointestinal issue. Probiotics come in many forms, including pills, additives in water, cultured milk, yogurt, and other foods. They are currently treated as a supplement, and thus are not required to prove safety or efficacy to be sold to consumers.[1] The FDA has not approved any probiotics for the treatment of disease.

Probiotic research runs parallel to the effects of the gut microbiome on overall health. Healthy GI flora has been shown to play a role in metabolism, immune response, cardiovascular disease, and even mental health. A study of Americans not taking antibiotics found that most patients have stable levels of the same fecal bacteria over at least five years, while other studies indicate these bacteria levels may stay steady over an individual's lifetime. The effects of diet, race, and genetic factors on the microbiome requires more research. However, if the healthy microbiome becomes affected by antibiotics or disease, we may be able to return it to baseline with probiotic supplementation and have positive effects on overall health.[2]

CORRESPONDENCE:
Royce Toffol, DO, OGME | Royce.Toffol@peakvista.org

 Print ISSN: 1877-573X

MECHANISM OF ACTION

There is no consistently-proposed mechanism of action by which probiotics exert their effects, although several hypotheses have been put forth.[3,4] It is thought that beneficial bacteria contained in probiotics compete for nutrients, starving out pathogens, or that they are able to bind invaders for a direct antagonistic effect. Probiotics may be able to exert antimicrobial effects on harmful bacteria, or stimulate an immune response to better fight off pathogens with the proper antibody response, increasing mucosal immune products such as IgA. Some species may be able to aid in digestion of products such as gliadins in gluten and decrease inflammation in autoimmune disease. They may be able to repair defects in GI permeability, or simply compete for adhesion sites, affecting which bacteria survive.[3,4,10]

FIGURE 1 :

Proposed Mechanisms of Action [43]

Downregulation of proinflammatory cytokines in the GI tract
Strengthening or enhancing the epithelial barrier in the GI tract
Displacing pathogenic bacterial species or competing for adhesion sites
Beneficial changes to GI flora through acidification and fermentation of nutrients

DOSING

There is little consensus about the ideal concentration for probiotics, and studies vary in the number of colony forming units (CFUs) studied. Most over-the-counter preparations contain around 106 CFUs. *(Figure 2)* Study treatment times have ranged

anywhere from one week to three months, raising the question of long term viability of probiotics as a treatment. Due to the wide variation of data, it is difficult to determine which species, preparation, concentration, and duration of probiotic treatment to use specific GI disorders. Most studies are small and have poor outcomes regarding efficacy, but there are some promising formulations for certain diseases. Generally, broad spectrum combinations such as VSL#3 and products containing 10 billion CFUs appear to be most effective.

FIGURE 2 :

Commonly found formulations and pricing

Brand	Culture	CFUs	Price
Align	B. infantis	$1x10^7$	$50/ 56 count package
Culturelle	L. rhamnosus	$1x10^{10}$	$30-$40/ 60 capsules
DanActive	L. casei	$1x10^{10}$	$4-$5/bottle
Florastor	S. boulardii	$5x10^9$	$25/ 20 capsules
Mutaflor	E. coli	$1x10^9$	$75/ 60 capsules
VSL#3	Bifidobacterium breve, B. longum, B. infantis, Lacto-bacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus	$1x10^{11}$ $9x10^{11}$	$60 for 60 capsules $50-$90 for 60 capsules

SPECIFIC CONDITIONS

Antibiotic-Associated Diarrhea

Diarrhea is an extremely common side effect of antibiotic use. The clinical impact of antibiotic-associated diarrhea (AAD) ranges from mild, self-limited disease to life-threatening illness such as Clostridium difficile diarrhea. Probiotics are effective in maintaining gut flora during antibiotic treatment in children and adults and can be prescribed with the antibiotic course to increase patient compliance.

A Cochrane database review of twenty-three studies targeting children assessed the use of probiotics during antibiotic administration on prevention of AAD. Various probiotic formulations were used, including eight different strains across studies. The incidence of AAD in the treatment group was 8% compared to 19% in the control group. Analysis of this meta-analysis noted that this evidence was only moderate quality.[5]

A meta-analysis of adult and pediatric patients prescribed Lactobacillus for prevention of AAD during antibiotic treatment showed that those receiving Lactobacillus had a significantly lower risk of AAD (reported NNT ranging from 8-13). Subgroup analysis found this to be effective for adults but not pediatric patients.[6]

Acute Pancreatitis

Patients suffering from acute pancreatitis incur a risk of necrosis and subsequent infection and mortality. Studies analyzing the effect of probiotics on acute pancreatitis have been inconclusive or show increases in mortality and complications. They generally conclude that probiotics are not effective in treatment of acute pancreatitis.

One multicenter, randomized, double-blind, placebo-controlled study involved patients with APACHE II severe acute pancreatitis. Patients received probiotics or placebo within three days of symptom onset. Infectious complications occurred at a higher rate in the probiotics group compared to placebo. In addition, 16% of patients in the probiotics group died compared with 6% in the placebo group. Some patients in the probiotic group developed bowel ischemia while none in the placebo group did.[7,8]

Clostridium difficile Associated Diarrhea

Clostridium difficile associated diarrhea (CDAD) remains a troublesome inpatient and outpatient issue causing considerable mortality and health care spending. Probiotic use in CDAD remains controversial due to inconsistent evidence regarding treatment initiation and variability in data collection.

A meta-analysis of nineteen studies consisting of a cohort receiving probiotics and antibiotics and a control group receiving antibiotics alone showed decreased incidence of CDAD in the probiotic group. Results showed 1.6% of patients in the probiotic group contracted CDAD vs. 3.9% in the control group ($p < 0.001$). The most benefit was seen when probiotics were given within two days of antibiotic administration.[9]

In 2012, a meta-analysis of 20 trials involving adult and pediatric patients was performed to assess prevention of CDAD with the use of probiotics. Probiotic administration reduced CDAD by 66%. Those treated with probiotics also experienced less adverse events at 9.3% compared to 12.6% in the control group. In a population experiencing an incidence of CDAD at 5%, it was extrapolated that the use of probiotics for prophylaxis may prevent 33 episodes of CDAD per every 1000 patients. There was missing outcome data in 13 of the trials with up to 45% of data missing for some patients.[9]

Celiac Disease

Trials of probiotics for celiac disease have assessed probiotics' ability to hydrolyze gliadins in preventing symptoms. VSL#3 probiotics were used to pre-digest gliadins and compared to laboratory digestion of gliadins. Celiac jejunal biopsies were exposed to the pre-digested VSL#3 gliadin and showed a decrease in inflammatory cell infiltration, indicating possible benefits and immune modulation.[10]

Another study involved 22 patients with laboratory confirmed celiac disease. They were randomized to receive B. infantis or placebo two times a day for three weeks. Baseline intestinal permeability was not significantly affected by either treatment arm, but there was subjective improvement in symptoms.[11] Using probiotics in patients with celiac disease may provide subjective

improvement if patients have failed other options as adverse effects are minimal.

Constipation

Constipation can be induced by medication or diet. Although it is often self-limited, constipation can cause significant impairment through impaction or obstruction. Probiotics are effective in increasing stool frequency and are well tolerated although treatment with polyethylene glycol (PEG) may be just as effective.

A systematic review and meta-analysis of 21 studies that involved patients treated with either Lactobacillus or Bifidobacterium determined there was an increase in weekly stool frequency ($p<0.001$) although the effects varied depending on which ROME criteria was used. The meta-analysis observed high heterogeneity and publication bias, and when corrected for this, the effects on stool frequency were less apparent.[12]

Treatment of constipation with probiotics in pediatric patients was studied using Lactobacillus reuteri in a trial involving 121 patients ages 3-7. Patients with functional constipation were treated with a Lactobacillus formulation or PEG. There was no significant difference in number of bowel movements at two months and no difference in reported abdominal pain, pain with defecation, withholding, or hard stool.[13]

Healthy Patients

Patients without chronic gastrointestinal conditions may be prescribed probiotics to maintain healthy gut flora and prevent general GI upset. The available data involved non-primary outcomes and featured small sample sizes, but probiotics remain a viable and safe choice for healthy patients looking to use them as a supplement.

Two identical trials that involved treatment of healthy female patients with mild GI upset using Bifidobacterium lactis in fermented milk were assessed in 2013. Study groups were given fermented milk containing the probiotic or a control dairy drink for four weeks. A repeat study was designed to emulate the original study. No significant difference in GI wellbeing between the treatment and control groups was observed, but there was improvement when both studies were included in pooled analysis.[14]

A 2017 study that involved healthy elderly patients assessed the effects of Bifidobacterium lactis on cellular immune function. There was an increase in PMN phagocyte capability and NK cell tumoricidal activity, though no patient-oriented outcomes were assessed. Data quality was low, as only four studies were included in the final meta-analysis.[15]

Hepatic Encephalopathy

Lactulose and Rifaximin are proven therapies for hepatic encephalopathy (HE), and probiotics have been proposed as an adjunctive treatment. Probiotics are well tolerated and effective in improving symptoms and quality of life, but data is low quality with high associated bias and should be interpreted in this light.

A meta-analysis that included 21 trials compared probiotic with placebo or no treatment. Some of the trials also compared lactulose to probiotics. VSL#3 was the most commonly used probiotic, and duration of treatment was highly variable. There was low quality evidence of no effect on all-cause mortality in the treatment group. There was moderate quality evidence of incomplete or no resolution of HE symptoms in the treatment group. Adverse events were lower in the treatment group, quality of life was better, and ammonia levels were lower.[16]

A study from the *American Journal of Gastroenterology* in 2012 assessed lactulose vs. probiotics vs. placebo for secondary prophylaxis in cirrhotic patients who had already recovered from HE. Patients treated with lactulose probiotics saw a significant benefit when compared with placebo. There was no difference between patients treated with lactulose vs. probiotics.[17]

In a 2004 study, 97 patients with cirrhosis were randomized to receive either placebo or a "synbiotic" treatment of probiotics with fiber. The treatment group had a significant increase in stool Lactobacillus species and a decrease in E. coli, Staphylococcus species, and blood ammonia levels.[18]

H. Pylori Infection and Eradication

Helicobacter pylori is commonly encountered in primary care and ensuring eradication is central to preventing further gastric mucosal damage. Current studies show risk of bias, and show only modest benefit to using probiotics in conjunction with recommended treatment.

Infectious Diarrhea

Probiotic use has been shown to have beneficial effects on infectious causes of diarrhea and can decrease severity and duration of symptoms. Use in treatment of rotavirus induced diarrhea has produced inconsistent results.

A Cochrane review in 2010 collected 63 trials comparing probiotics with placebo in patients with acute infection diarrhea. Fifty-six studies enrolled infants and children. There was wide variation in species, dosage, and patient medical characteristics. Mean duration of diarrhea was reduced by 24.76 hours, and there was a reduction in stool frequency by day 2 in the treatment groups. There were no adverse events reported in the treatment group.[21]

A meta-analysis that included 12 studies showed that Saccharomyces boulardii, Lactobacillus acidophilus, and Bifidobacterium bifidum had statistically significant effects on reducing or preventing traveler's diarrhea ($P< 0.001$). There were no adverse events reported across all 12 trials.[22]

One meta-analysis collected 14 studies that involved treatment of children with acute diarrhea due to rotavirus. Lactobacillus rhamnosus significantly reduced duration of diarrhea in some studies while others did not show any significant difference.[23]

A multi-center, randomized controlled trial evaluated Lactobacillus reuteri use in children with acute infectious diarrhea in an outpatient setting. One group was treated with oral rehydration

solution (ORS) and probiotics and compared to a control group receiving ORS alone. Duration of diarrhea was reduced by 15 hours in the treatment group ($p<0.05$). There was no difference in the percentage of children with diarrhea after 72 hours. There were no reported adverse effects related to probiotic administration.[24]

Inflammatory Bowel Disease

Probiotics have been heavily targeted for treatment and symptomatic relief of IBD to promote beneficial immune modulation in the GI tract and help maintain healthy mucosal barrier function. They are effective for symptom control in patients with ulcerative colitis (UC) and are well tolerated. Their use in Crohn's disease (CD) has been shown to be ineffective, so probiotics should not be used in this patient population.

A meta-analysis of 23 randomized controlled trials looked at the effect of probiotics on inducing remission and maintaining therapy in UC, CD, and pouchitis. Remission rates were found to be significantly higher in patients with active UC treated with probiotics than with placebo. Subgroup analysis found that only VSL#3 probiotics significantly increased the remission rates compared to controls in patients with active UC. VSL#3 was beneficial for maintaining remission in patients with pouchitis, and probiotics can provide the similar effect as 5-aminosalicylic acid on maintaining remission of UC without additional adverse events.[25]

Analysis of 18 trials revealed that VSL#3 had significant effect ($P<0.01$) in patients with UC. In children with IBD, the combination of Lactobacillus with VSL#3 probiotics had significant positive effect ($P<0.01$). In conclusion, it was stated that probiotics are beneficial in IBD, especially the combination ones in UC.[26]

Review of 22 RCT's showed that with the exception of VSL#3, probiotics held no benefit over placebo in inducing remission in active UC. They concluded that VSL#3 may be effective in inducing remission in active UC and that probiotics may be as effective as 5-ASAs in preventing relapse of quiescent UC. There was no benefit of probiotics in inducing remission of active CD, in preventing relapse of quiescent CD, or in preventing relapse of CD after surgically induced remission.[27]

Irritable Bowel Syndrome

Probiotics are a safe option for treatment of IBS and have been shown to be somewhat effective. Available trials are short in duration, have low sample sizes, and show mixed results or only modest benefit. When treating IBS with probiotics, patients should be instructed to continue treatment symptomatically as needed.

One study that involved 122 patients randomized to receive placebo vs. Bifidobacterium bifidum once daily for four weeks resulted in beneficial response in 57% of patients receiving Bifidobacteria compared to only 21% in the placebo group.[28]

Another study involved 100 subjects randomized to receive placebo or a combination of probiotics for four weeks. The placebo group did not experience relief of symptoms compared with the probiotic combination, and there was a decrease in subjective abdominal pain in the treatment group.[29]

A trial in which 25 patients with IBS were randomly assigned treatment with VSL#3 or placebo twice a day for eight weeks showed no significant difference in GI transit, bowel function scores, or global symptom relief. There was statistically significant relief of abdominal bloating in the treatment group.[30]

Another study enrolled 70 patients with IBS and randomly assigned them to receive Lactobacillus plantarum and Bifidobacterium breve, Lactobacillus plantarum and Lactobacillus acidophilus, or a placebo powder for four weeks. Pain score and IBS severity scores decreased significantly in the treatment group after 14 weeks compared to placebo.[31]

Seventy-seven patients with IBS were randomized to receive Lactobacillus salivarius, Bifidobacterium infantis or placebo for eight weeks. Patients receiving B. infantis reported reduction in symptoms with easier bowel movements and less abdominal discomfort compared to placebo. In addition, patients with IBS had abnormal IL-10/IL-12 ratios at baseline that were found to be normalized in patients receiving B. infantis.[32]

One large study involving 362 patients with IBS were randomized to get placebo or a freeze-dried B. infantis for four weeks. Patients were given three different CFU concentrations. Only the middle-concentration group receiving a concentration of 1 x 10(8) CFU of B. infantis had significantly reduced symptoms. The lack of benefit observed at other dosage levels indicates the need for more trials regarding formulation.[33]

A study performed in early 2018 was the first to assess probiotic efficacy on small intestinal bacterial overgrowth (SIBO) in patients with IBS. Five patients with IBS and SIBO and 21 patients with IBS without SIBO were enrolled. Patients were given a capsule containing Saccharomyces boulardii, Bifidobacterium lactis, Lactobacillus acidophilus and Lactobacillus plantarum twice a day for 30 days. There was a 71% decrease in total IBS score in the IBS plus SIBO group compared to a 10.6% decrease in the IBS group. The IBS scoring is highly subjective, sample size was small, and results should be interpreted carefully.[34]

Lactose Intolerance

A systematic review performed to evaluate the role of probiotics in lactose intolerance involved 10 RCTs. The researchers concluded that probiotics did not alleviate symptoms of lactose intolerance. There were some strains and concentrations that may be effective, but further research is necessary.[35]

Necrotizing Enterocolitis in Preterm Infants

Neonatal necrotizing enterocolitis (NEC) is a condition of ischemic necrosis of the bowel due to the proliferation of enteric gas-forming microorganisms. It occurs in approximately 1–3 infants per 1,000 live births,[36,37,38] and is much more common in preterm infants.[39] It is thought that administration of probiotics should reduce the development of the altered gut microbiome that predisposes preterm infants to NEC.

Two meta-analyses have reviewed the usefulness of probiotics for preventing severe NEC. They concluded that probiotics led to a reduction in the incidence of NEC and mortality associated

with NEC in very-low birth weight (VLBW) infants. They also found that feeding with human breast milk worked synergistically with probiotics to protect against NEC. Based off a subgroup analysis, Thomas et al. concluded that Lactobacillus and Bifidobacterium species led to the best reduction in NEC-related mortality and all-cause mortality. They did not find that probiotics prevented the incidence of surgical NEC.[41] Given the fragility of the patient population most at risk for NEC (VLBW and preterm infants), there is a magnification of common problems facing probiotics, including poor quality control and lack of standardization of the specific products offered.[40,41] Considering the current state of evidence, probiotics have not been routinely adopted as a preventive strategy for the development of NEC.

Pouchitis

An ileal pouch-anal anastomosis is performed in some patients that require a total proctocolectomy. Inflammation of this pouch can occur, and treatment with probiotics has been shown to be effective in reducing inflammatory cytokines and improving stool consistency.

A study performed in 2017 used Lactobacillus acidophilus to treat pouchitis in rats that had undergone a colectomy and ileal pouch-anal anastomosis. Dextran sulfate sodium was administered to the rats to induce pouchitis. End points involved reduced weight loss associated with pouchitis ($p<0.05$), rate of hematochezia disappearance and stool consistency. There was an observed reduction of pro-inflammatory factors such as TNF-alpha, IL-1B, and IL-6 in the treatment group ($p<0.05$).[42]

CONTRAINDICATIONS

Probiotic preparations carry minimal risk of side effects and are well tolerated. Clinicians should prescribe probiotics when indicated in generally healthy patients if there is the possibility of symptom relief. There are situations in which probiotics are contraindicated, as there have been reported incidences of sepsis and fungal overgrowth. Those with acute pancreatitis should not receive probiotics as they may increase mortality.[7,8] Patients with immunocompromising conditions such as cancer and those on immunosuppressive drugs like transplant recipients should not receive probiotics.[43] Further studies are needed to assess other areas where probiotics may be contraindicated, if clinicians have concern for harm or mortality they should not be prescribed.

CONCLUSION

When used in conjunction with standard treatment, probiotics can be useful in symptom management of several frequently encountered GI disorders. Although cost remains an issue, probiotics have minimal side effects and are well tolerated by most patients. What species to use should be taken into consideration when choosing to prescribe probiotics for patients with specific GI disorders.[Fig.4] VSL#3 probiotics may be effective in the short-term for treatment of pouchitis. Patients with ulcerative colitis who cannot tolerate traditional treatments may respond well to E. coli probiotics. There has been no benefit seen in trials involving patients with Crohn's disease. Adult and pediatric patients who are assumed to have infectious diarrhea may respond to probiotic treatment with Lactobacillus GG and S. boulardii. Results of trials analyzing treatment of IBS with probiotics have been inconclusive as to which formulation may be effective. There are very few studies on lactose intolerance, and no benefit has been seen so far. Trials of probiotic use for patients with hepatic encephalopathy have shown no benefit in regards to mortality. Probiotics should be avoided in patients who are critically ill or have immunocompromising conditions.[43]

FIGURE 3 :

Probiotic efficacy by disease type [25,43,44,45]
Evidence ratings of A through D per GRADE rating scale

Condition	Efficacy	Evidence rating
Antibiotic associated diarrhea	May be effective for treatment and prevention	A[44]
Clostridium difficile colitis	May be effective for prevention but not treatment	A[44]
Infectious diarrhea	May be effective for treatment	A[44]
Ulcerative Colitis	May be effective for treatment	A[25]
Crohn's disease	No proven benefit	C[44]
Pouchitis	May be effective for treatment	C[25]
Irritable Bowel Syndrome	May be effective for symptom relief	B[45]
Lactose intolerance	No proven benefit	Insufficient studies to provide rating
Hepatic encephalopathy	No proven benefit, may decrease hepatic encephalopathy but no more effective than lactulose and rifaximin	C[44]
Necrotizing Enterocolitis	No proven benefit, but may reduce mortality in very low birth weight infants	C[44]

AUTHOR DISCLOSURES:
No relevant financial affiliations

REFERENCES:

1. Venugopalan V, Shriner KA, Wong-Beringer A. Regulatory Oversight and Safety of Probiotic Use. Emerging Infectious Diseases. 2010;16(11):1661-1665. doi:10.3201/eid1611.100574.
2. Shreiner AB, Kao JY, Young VB. The gut microbiome in health and in disease. Current opinion in gastroenterology. 2015;31(1):69-75. doi:10.1097/MOG.0000000000000139.

FIGURE 4 :

Strains that may be effective for certain conditions

Condition	Probiotic strain
Antibiotic- associated diarrhea[44]	Lactobacillus acidophilus, L. casei, L. rhamnosus, Saccharomyces Boulardii
Clostridium difficile associated diarrhea[44]	Lactobacillus acidophilus, L. casei, L. rhamnosus
Celiac disease[10,11]	Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus
Infectious diarrhea[44]	Lactobacillus reuteri. L. protectis, L. casei, Saccharomyces. Boulardii
Irritable Bowel Syndrome[43]	Bifidobacterium spp., Lactobacillus spp.
Necrotizing enterocolitis[41]	Bifidobacterium spp., Lactobacillus acidophilus, L. casei, L. rhamnosus
Pouchitis[43]	Bifidobacterium breve, B. longum, B. infantis, Lactobacillus acidophilus, L. plantarum, L. paracasei, L. bulgaricus, Streptococcus thermophilus
Ulcerative colitis[43]	Bifidobacterium longum, B. breve, B. bifidum, E. coli Nissle 1917, Lactobacillus acidophilus, L. GG

3. Hemarajata P, Versalovic J. Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuromodulation. Therapeutic Advances in Gastroenterology. 2013;6(1):39-51. doi:10.1177/1756283X12459294.
4. Gill HS. Probiotics to enhance anti-infective defences in the gastrointestinal tract. Best Pract Res Clin Gastroenterol. 2003 Oct;17(5):755-73. Review. PubMed PMID: 14507586.
5. Goldenberg JZ, Lytvyn L, Steurich J, Parkin P, Mahant S, Johnston BC. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. Cochrane Database Syst Rev. 2015 Dec 22;(12):CD004827. doi: 10.1002/14651858.CD004827.pub4. Review. PubMed PMID: 26695080.
6. Kale-Pradhan PB, Jassal HK, Wilhelm SM. Role of Lactobacillus in the prevention of antibiotic-associated diarrhea: a meta-analysis. Pharmacotherapy. 2010 Feb;30(2):119-26. doi: 10.1592/phco.30.2.119. PubMed PMID: 20099986.
7. Capurso G, Marignani M, Piciucchi M, Merola E, Delle Fave G. Probiotics and severe acute pancreatitis. J Clin Gastroenterol. 2008 Sep;42 Suppl 3 Pt 1:S148-51. doi: 10.1097/MCG.0b013e318169e935. Review. PubMed PMID: 18806709.
8. Besselink MG, van Santvoort HC, Buskens E, Boermeester MA, van Goor H, Timmerman HM, Nieuwenhuijs VB, Bollen TL, van Ramshorst B, Witteman BJ, Rosman C, Ploeg RJ, Brink MA, Schaapherder AF, Dejong CH, Wahab PJ, van Laarhoven CJ, van der Harst E, van Eijck CH, Cuesta MA, Akkermans LM, Gooszen HG; Dutch Acute Pancreatitis Study Group.. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. Lancet. 2008 Feb 23;371(9613):651-659. doi: 10.1016/S0140-6736(08)60207-X. Epub 2008 Feb 14. Erratum in: Lancet.2008 Apr 12;371(9620):1246. PubMed PMID: 18279948.
9. Johnston BC, Ma SS, Goldenberg JZ, Thorlund K, Vandvik PO, Loeb M, Guyatt GH. Probiotics for the prevention of Clostridium difficile-associated diarrhea: a systematic review and meta-analysis. Ann Intern Med. 2012 Dec 18;157(12):878-88. Review. PubMed PMID: 23362517.
10. De Angelis M, Rizzello CG, Fasano A, Clemente MG, De Simone C, Silano M, De Vincenzi M, Losito I, Gobbetti M. VSL#3 probiotic preparation has the capacity to hydrolyze gliadin polypeptides responsible for Celiac Sprue. Biochim Biophys Acta. 2006 Jan;1762(1):80-93. Epub 2005 Oct 21. PubMed PMID: 16311022.
11. Smecuol E, Hwang HJ, Sugai E, Corso L, Cherñavsky AC, Bellavite FP, González A, Vodánovich F, Moreno ML, Vázquez H, Lozano G, Niveloni S, Mazure R, Meddings J, Mauriño E, Bai JC. Exploratory, randomized, double-blind, placebo-controlled study on the effects of Bifidobacterium infantis natren life start strain super strain in active celiac disease. J Clin Gastroenterol. 2013 Feb;47(2):139-47. doi: 10.1097/MCG.0b013e31827759ac. PubMed PMID: 23314670.
12. Miller LE, Ouwehand AC, Ibarra A. Effects of probiotic-containing products on stool frequency and intestinal transit in constipated adults: systematic review and meta-analysis of randomized controlled trials. Ann Gastroenterol. 2017;30(6):629-639. doi: 10.20524/aog.2017.0192. Epub 2017 Sep 21. PubMed PMID: 29118557; PubMed Central PMCID: PMC5670282.
13. Wegner A, Banaszkiewicz A, Kierkus J, Landowski P, Korlatowicz-Bilar A, Wiecek S, Kwiecien J, Gawronska A, Dembinski L, Czaja-Bulsa G, Socha P. The effectiveness of Lactobacillus reuteri DSM 17938 as an adjunct to macrogol in the treatment of functional constipation in children. A randomized, double-blind, placebo-controlled, multicentre trial. Clin Res Hepatol Gastroenterol. 2018 Apr 9. pii: S2210-7401(18)30047-0. doi: 10.1016/j.clinre.2018.03.008. [Epub ahead of print] PubMed PMID: 29650440.
14. Marteau P, Guyonnet D, Lafaye de Micheaux P, Gelu S. A randomized, double-blind, controlled study and pooled analysis of two identical trials of fermented milk containing probiotic Bifidobacterium lactis CNCM I-2494 in healthy women reporting minor digestive symptoms. Neurogastroenterol Motil. 2013 Apr;25(4):331-e252. doi: 10.1111/nmo.12078. Epub 2013 Mar 11. PubMed PMID: 23480238.
15. Miller LE, Lehtoranta L, Lehtinen MJ. The Effect of Bifidobacterium animalis ssp. lactis HN019 on Cellular Immune Function in Healthy Elderly Subjects: Systematic Review and Meta-Analysis. Nutrients. 2017 Feb 24;9(3). pii: E191. doi: 10.3390/nu9030191. Review. PubMed PMID: 28245559; PubMed Central PMCID: PMC5372854.
16. Dalal R, McGee RG, Riordan SM, Webster AC. Probiotics for people with hepatic encephalopathy. Cochrane Database Syst Rev. 2017 Feb 23;2:CD008716. doi: 10.1002/14651858.CD008716.pub3. Review. PubMed PMID: 28230908.
17. Agrawal A, Sharma BC, Sharma P, Sarin SK. Secondary prophylaxis of hepatic encephalopathy in cirrhosis: an open-label, randomized controlled trial of lactulose, probiotics, and no therapy. Am J Gastroenterol. 2012 Jul;107(7):1043-50. doi: 10.1038/ajg.2012.113. Epub 2012 Jun 19. PubMed PMID: 22710579.

18. Liu Q, Duan ZP, Ha DK, Bengmark S, Kurtovic J, Riordan SM. Synbiotic modulation of gut flora: effect on minimal hepatic encephalopathy in patients with cirrhosis. Hepatology. 2004 May;39(5):1441-9. PubMed PMID: 15122774.

19. Zhang MM, Qian W, Qin YY, He J, Zhou YH. Probiotics in Helicobacter pylori eradication therapy: a systematic review and meta-analysis. World J Gastroenterol. 2015 Apr 14;21(14):4345-57. doi: 10.3748/wjg.v21.i14.4345. Review. PubMed PMID: 25892886; PubMed Central PMCID: PMC4394097.

20. Dang Y, Reinhardt JD, Zhou X, Zhang G. The effect of probiotics supplementation on Helicobacter pylori eradication rates and side effects during eradication therapy: a meta-analysis. PLoS One. 2014 Nov 3;9(11):e111030. doi: 10.1371/journal.pone.0111030. eCollection 2014. PubMed PMID: 25365320; PubMed Central PMCID: PMC4217763.

21. Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. Cochrane Database Syst Rev. 2010 Nov 10;(11):CD003048. doi: 10.1002/14651858.CD003048.pub3. Review. PubMed PMID: 21069673.

22. McFarland LV. Meta-analysis of probiotics for the prevention of traveler's diarrhea. Travel Med Infect Dis. 2007 Mar;5(2):97-105. Epub 2005 Dec 5. PubMed PMID: 17298915.

23. Ahmadi E, Alizadeh-Navaei R, Rezai MS. Efficacy of probiotic use in acute rotavirus diarrhea in children: A systematic review and meta-analysis. Caspian J Intern Med. 2015 Fall;6(4):187-95. Review. PubMed PMID: 26644891; PubMed Central PMCID: PMC4649266.

24. Dinleyici EC, Dalgic N, Guven S, Metin O, Yasa O, Kurugol Z, Turel O, Tanir G, Yazar AS, Arica V, Sancar M, Karbuz A, Eren M, Ozen M, Kara A, Vandenplas Y. Lactobacillus reuteri DSM 17938 shortens acute infectious diarrhea in a pediatric outpatient setting. J Pediatr (Rio J). 2015 Jul-Aug;91(4):392-6. doi: 10.1016/j.jped.2014.10.009. Epub 2015 May 16. PubMed PMID: 25986615.

25. Shen J, Zuo ZX, Mao AP. Effect of probiotics on inducing remission and maintaining therapy in ulcerative colitis, Crohn's disease, and pouchitis: meta-analysis of randomized controlled trials. Inflamm Bowel Dis. 2014 Jan;20(1):21-35. doi: 10.1097/01.MIB.0000437495.30052.be. Erratum in: Inflamm Bowel Dis. 2014 Dec;20(12):2526-8. PubMed PMID: 24280877.

26. Ganji-Arjenaki M, Rafieian-Kopaei M. Probiotics are a good choice in remission of inflammatory bowel diseases: A meta analysis and systematic review. J Cell Physiol. 2018 Mar;233(3):2091-2103. doi: 10.1002/jcp.25911. Epub 2017 May 3. Review. PubMed PMID: 28294322.

27. Derwa Y, Gracie DJ, Hamlin PJ, Ford AC. Systematic review with meta-analysis: the efficacy of probiotics in inflammatory bowel disease. Aliment Pharmacol Ther. 2017 Aug;46(4):389-400. doi: 10.1111/apt.14203. Epub 2017 Jun 27. Review. PubMed PMID: 28653751.

28. Guglielmetti S, Mora D, Gschwender M, Popp K. Randomised clinical trial: Bifidobacterium bifidum MIMBb75 significantly alleviates irritable bowel syndrome and improves quality of life--a double-blind, placebo-controlled study. Aliment Pharmacol Ther. 2011 May;33(10):1123-32. doi: 10.1111/j.1365-2036.2011.04633.x. Epub 2011 Mar 21. PubMed PMID: 21418261.

29. Drouault-Holowacz S, Bieuvelet S, Burckel A, Cazaubiel M, Dray X, Marteau P. A double blind randomized controlled trial of a probiotic combination in 100 patients with irritable bowel syndrome. Gastroenterol Clin Biol. 2008 Feb;32(2):147-52. doi: 10.1016/j.gcb.2007.06.001. Epub 2008 Mar 4. PubMed PMID: 18387426.

30. Kim HJ, Camilleri M, McKinzie S, Lempke MB, Burton DD, Thomforde GM, Zinsmeister AR. A randomized controlled trial of a probiotic, VSL#3, on gut transit and symptoms in diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther. 2003 Apr 1;17(7):895-904. PubMed PMID: 12656692.

31. Saggioro A. Probiotics in the treatment of irritable bowel syndrome. J Clin Gastroenterol. 2004 Jul;38(6 Suppl):S104-6. Erratum in: J Clin Gastroenterol. 2005 Mar;39(3):261. PubMed PMID: 15220671.

32. O'Mahony L, McCarthy J, Kelly P, Hurley G, Luo F, Chen K, O'Sullivan GC, Kiely B, Collins JK, Shanahan F, Quigley EM. Lactobacillus and bifidobacterium in irritable bowel syndrome: symptom responses and relationship to cytokine profiles.Gastroenterology. 2005 Mar;128(3):541-51. PubMed PMID: 15765388.

33. Whorwell PJ, Altringer L, Morel J, Bond Y, Charbonneau D, O'Mahony L, Kiely B, Shanahan F, Quigley EM. Efficacy of an encapsulated probiotic Bifidobacterium infantis 35624 in women with irritable bowel syndrome. Am J Gastroenterol. 2006 Jul;101(7):1581-90. PubMed PMID: 16863564.

34. Leventogiannis K, Gkolfakis P, Spithakis G, Tsatali A, Pistiki A, Sioulas A, Giamarellos-Bourboulis EJ, Triantafyllou K. Effect of a Preparation of Four Probiotics on Symptoms of Patients with Irritable Bowel Syndrome: Association with Intestinal Bacterial Overgrowth. Probiotics Antimicrob Proteins. 2018 Mar 5. doi: 10.1007/s12602-018-9401-3. [Epub ahead of print] Erratum in: Probiotics Antimicrob Proteins. 2018 Mar 28;:. PubMed PMID: 29508268.

35. Levri KM, Ketvertis K, Deramo M, Merenstein JH, D'Amico F. Do probiotics reduce adult lactose intolerance? A systematic review. J Fam Pract. 2005 Jul;54(7):613-20. Review. PubMed PMID: 16009090.

36. Holman RC, Stoll BJ, Curns AT, Yorita KL, Steiner CA, Schonberger LB. Necrotising enterocolitis hospitalisations among neonates in the United States. Paediatr Perinat Epidemiol. 2006 Nov;20(6):498-506

37. Stoll BJ, Hansen NI, Bell EF et al. Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993-2012. JAMA. 2015 Sep 8;314(10):1039-51

38. Rees CM, Eaton S, Pierro A. National prospective surveillance study of necrotizing enterocolitis in neonatal intensive care units. J Pediatr Surg. 2010 Jul;45(7):1391-7

39. Battersby C, Santhalingam T, Costeloe K, Modi N. Incidence of neonatal necrotising enterocolitis in high-income countries: a systematic review. Arch Dis Child Fetal Neonatal Ed. 2018 Mar;103(2):F182-F189

40. Rees CM, Hall NJ, Fleming P, Eaton S. Probiotics for the prevention of surgical necrotising enterocolitis: systematic review and meta-analysis. BMJ Paediatr Open. 2017 Nov 1;1(1):e000066

41. Thomas JP, Raine T, Reddy S, Belteki G. Probiotics for the prevention of necrotising enterocolitis in very low-birth-weight infants: a meta-analysis and systematic review. Acta Paediatr. 2017 Nov;106(11):1729-1741

42. Xu YY, Zhang YY, He AQ, Li KY, Gao SY, Liu G. Lactobacillus acidophilus alleviates pouchitis after ileal pouch-anal anastomosis in rats. World J Gastroenterol. 2017 Jul 14;23(26):4735-4743. doi: 10.3748/wjg.v23.i26.4735. PubMed PMID: 28765694; PubMed Central PMCID: PMC5514638.

43. Verna EC, Lucak S. Use of probiotics in gastrointestinal disorders: what to recommend? Therapeutic Advances in Gastroenterology. 2010;3(5):307-319. doi:10.1177/1756283X10373814.

44. Ciorba MA. A Gastroenterologist's Guide to Probiotics. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 2012;10(9):960-968. doi:10.1016/j.cgh.2012.03.024.

45. Ford AC, Moayyedi P, Lacy BE, Lembo AJ, Saito YA, Schiller LR, Soffer EE, Spiegel BM, Quigley EM; Task Force on the Management of Functional Bowel Disorders.. American College of Gastroenterology monograph on the management of irritable bowel syndrome and chronic idiopathic constipation. Am J Gastroenterol. 2014 Aug;109 Suppl 1:S2-26; quiz S27. doi: 10.1038/ajg.2014.187. Review. PubMed PMID: 25091148.

REVIEW ARTICLE

Ocular Manifestations of Obstructive Sleep Apnea

Leonid Skorin Jr., DO, OD, MS[1]; Amber Weimer, OD[2]

[1]Mayo Clinic Health System in Albert Lea, MN
[2]Pacific University College of Optometry, Forest Grove, OR

KEYWORDS:

Floppy Eyelid

Glaucoma

Nonarteritic Ischemic Optic Neuropathy

Obstructive Sleep Apnea

ABSTRACT: Obstructive sleep apnea (OSA) is a sleep disorder resulting in periods of breathing cessation secondary to upper airway collapse during sleep. The effects of OSA on a patient's cardiovascular and metabolic health are well known, though less recognized are OSA's associations with ophthalmic disease. The effects of OSA on the eye and ocular adnexa include floppy eyelid syndrome (FES), chronic eye irritation, glaucoma, nonarteritic anterior ischemic optic neuropathy (NAION), papilledema, keratoconus, central serous chorioretinopathy (CSCR), retinal vein occlusion (RVO), and complications with anti-vascular endothelial growth factor (anti-VEGF) injections. Sleep apnea is a common sleep disorder with a slew of ocular side effects, some of which are sight threatening, and many of which merit referral to an eye care provider.

INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep disorder resulting in periods of breathing cessation secondary to upper airway collapse during sleep. Apneic events in patients with OSA generally last from 10 to 30 seconds and result in numerous swings between hypoxia and reperfusion throughout the night. The effects of OSA on a patient's cardiovascular and metabolic health are well known and include an increased risk of hypertension, type II diabetes, cardiovascular disease, and changes in neurocognitive function.[1,2] Less recognized are OSA's associations with ophthalmic disease.

The prevalence of OSA is ever increasing along with the rise of obesity, societal aging, and improvements in screening and testing methods for the disorder; OSA is now considered an issue of global public health. Studies have found the prevalence of symptomatic OSA to range from 22% to 24% in men, 9% to 17% in women, and 6% in adolescents.[1,3,4] A 2014 study found 26 of 30 patients with OSA to have some form of ocular involvement.[2] The effects of OSA on the eye and ocular adnexa include floppy eyelid syndrome (FES), chronic eye irritation, glaucoma, nonarteritic anterior ischemic optic neuropathy (NAION), papilledema, keratoconus, central serous chorioretinopathy (CSCR), retinal vein occlusions, and complications with anti-vascular endothelial growth factor (anti-VEGF) injections.[5,6] Sleep apnea is a common sleep disorder with a slew of ocular side effects, some of which are sight threatening, and many of which merit referral to an eye care provider.

CORRESPONDENCE:
Leonid Skorin Jr., DO, OD, MS

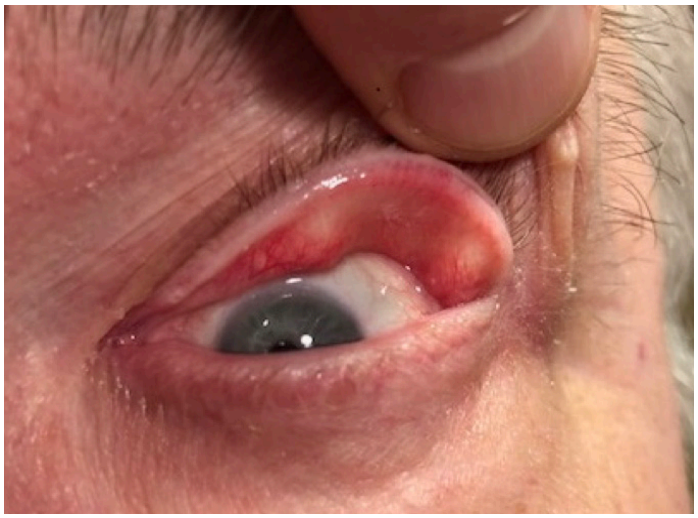
 Print ISSN: 1877-573X

FLOPPY EYELID SYNDROME

Floppy eyelid syndrome is a condition in which the upper eyelids become more elastic and more easily everted with upward traction *(Figure 1)*. Lid eversion most commonly occurs while sleeping, secondary to traction of a pillow against the patient's eyelids. Eversion of the upper lid during sleep leaves the eye exposed and susceptible to mechanical trauma, papillary conjunctivitis, and eyelid edema. One study found 96% of patients with FES have OSA,[7] while the reported prevalence of patients with OSA who have FES ranges from 2% to 25.8%.[7,8] The likelihood of concurrent FES increases with the severity of the patient's OSA symptoms.[8]

FIGURE 1:

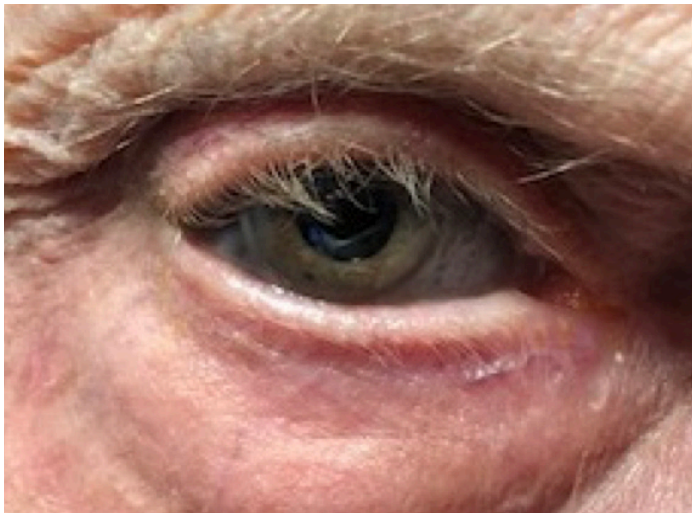
Eyelid eversion with floppy eyelid syndrome



Exposure of the cornea during sleep results in ocular surface disorders including punctate epithelial erosions, dry eye, exposure keratopathy, corneal scarring, neovascularization, ulceration, and rarely microbial infections that may lead to corneal perforation.[9-11] Eversion of the upper eyelid and rubbing of the conjunctiva against the pillow can result in conjunctival irritation and chronic papillary conjunctivitis. This mechanical trauma to the eyelid can over time result in lid edema, dermatochalasis, blepharitis, meibomianitis, ectropion, eyelash ptosis *(Figure 2)*, and trichiasis. Repeat mechanical trauma to the exposed cornea can also result in keratoconus.[10,11]

FIGURE 2:

Eyelash ptosis



Two mechanisms have been proposed to explain the etiology of FES, these being mechanical stress and transient tissue ischemia. Histological studies of affected eyelids reveal decreased elastin and increased matrix metalloproteinase (MMP) activity in lid connective tissue, and chronic inflammation.[12] Patients with FES are often more symptomatic on the side they sleep on. Traction of the lid against a pillow weakens lid connective tissue over time, providing support for the mechanical stress theory. Additionally, transient tissue ischemia secondary to hypoxia followed by periods of reperfusion that are characteristic of apneic events in patients with OSA have been shown to result in vascular damage and chronic lid inflammation.[12] The combination of these two mechanisms results in the connective tissue damage and increased lid elasticity seen in patients with FES. Eyelid laxity can be quantified through measurement of vertical eyelid pull. The eyelid is measured in resting position and at maximal manual displacement superiorly.[5] Normal eyelids can be stretched 5 to 10 mm vertically, though in eyes with FES this vertical pull ranges from 15 to 25 mm.[11]

Treatment of OSA via continuous positive airway pressure (CPAP) has been shown to improve the signs and symptoms associated with FES.[7] Treatments specific to FES should focus on treating any ocular surface disease and advising the patient against sleeping on their side or face. The patient can wear an eye shield at night to protect their lids, and use ocular lubricants and artificial tears to maintain the health of the ocular surface. Surgical intervention can be employed to shorten the upper eyelids, effectively tightening its apposition to the globe.

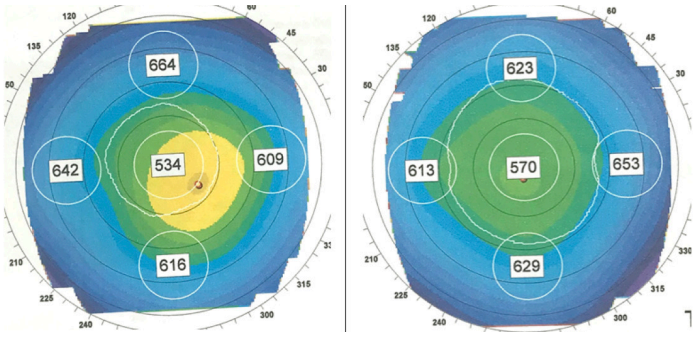
KERATOCONUS

Keratoconus is a condition characterized by progressive thinning and protrusion of the cornea, resulting in a cone-shaped corneal surface and a high degree of irregular corneal astigmatism *(Figure 3)*. These irregularities in the corneal surface result in decreased vision that is often difficult to correct without specialty contact lenses and is progressive in nature. Studies have found 18% to 20% of obese patients with keratoconus to have OSA, while the prevalence of keratoconus in the general population is cited at only 0.054%.[13,14] When obesity is controlled for, non-obese patients with keratoconus were not found to have an increased prevalence of OSA.[15]

The mechanism for developing keratoconus in patients with OSA is unknown, though it is theorized that mechanical trauma to the cornea results in the breakdown of corneal collagen fibers and progressive thinning of corneal tissue.[16] Additional theories propose that increased corneal MMP activity similarly results in chronic inflammation and tissue damage. In patients with OSA, keratoconus is seen more frequently in patients who also have FES,[17] leaving the corneal surface exposed with lid eversion during sleep. This exposure makes the cornea more susceptible to damage and provides further support for the mechanical trauma theory.

FIGURE 3:

Keratoconic corneal topography (L) versus normal corneal topography (R). Yellow center of the keratoconic cornea indicates corneal steepening.



Treatments for keratoconus include fitting the patient in a specialty contact lens such as a scleral or hybrid contact lens. In more advanced cases, surgical intervention in the form of corneal cross-linking or corneal transplant may be required to improve the patient's vision and stabilize their condition.

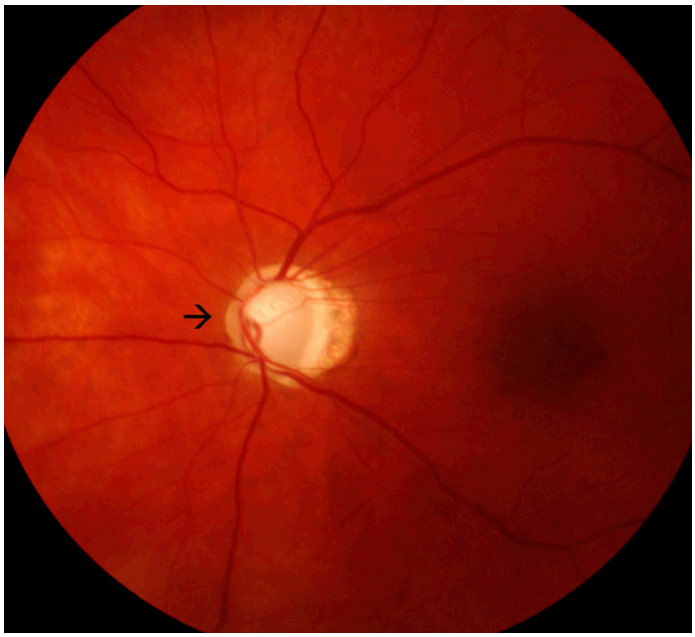
GLAUCOMA

Glaucoma is a chronic, progressive optic neuropathy resulting in thinning of the nerve fiber layer of the retina and increased cupping of the optic nerve on fundus examination *(Figure 4)*. Patients with glaucoma are often asymptomatic in the early stages

of the disease, slowly developing defects in their peripheral visual field over time as the condition progresses. Without treatment, patients develop complete loss of their peripheral field, (tunnel vision) and reduced visual acuity. Glaucoma is the second leading cause of blindness worldwide and has been shown to have a positive association with OSA.[18,19] Studies have found the prevalence of glaucoma in patients with OSA to range from 2% to 27%, while in the general population glaucoma has a prevalence of only 2% to 3%.[20]

FIGURE 4:

Fundus photo of glaucomatous optic nerve head



The mechanism for glaucomatous damage to the optic nerve remains unclear, however two leading theories exist. The mechanical theory proposes that elevated intraocular pressure (IOP) compresses the optic nerve resulting in damage to nerve fibers, while the vascular theory proposes that it is poor perfusion to the optic nerve head that results in glaucomatous damage.[5] The most likely explanation for nerve fiber loss in glaucoma is a combination of these two mechanisms, and OSA may contribute to both. A 2016 study found IOP to decrease in patients with OSA during apneic events, potentially resulting in periods of optic nerve head hypoxia.[21] Regardless the mechanism controlling glaucomatous damage, stabilization of glaucomatous visual field loss with treatment of OSA has been reported in the literature.[22] In light of the association between glaucoma and OSA, it is important that all patients with OSA undergo regular eye examinations including IOP checks and assessment of the optic nerve. Management of glaucoma involves the use of eye drops to reduce intraocular pressure. Numerous methods of surgical intervention exist that can be used to reduce eye pressure either by selectively targeting the ocular tissues responsible for creating the aqueous humor of the eye, or by promoting drainage of the aqueous humor.[6]

NONARTERITIC ANTERIOR ISCHEMIC OPTIC NEUROPATHY

Nonarteritic anterior ischemic optic neuropathy is characterized by a sudden, painless, unilateral loss of vision that occurs most frequently upon waking *(Figure 5)*.[23] NAION is caused by ischemia of the short posterior ciliary arteries that supply the optic nerve head and can result in irreversible loss of vision. Risk factors for NAION include vascular disease such as hypertension, atherosclerosis, vasculitis, and diabetes as well as the anatomical risk factors of a small optic nerve head and small optic cup.[24] The loss of vision occurring upon waking suggests that nocturnal hypotension plays a role in the development of NAION, a finding commonly seen in patients with OSA. Studies show the prevalence of OSA in patients who have had a NAION is 71% to 89%, and meta-analysis reveals patients with NAION are five times more likely to have OSA than the general population.[23,25,26]

The mechanism for developing NAION in patients with OSA is unknown though several theories exist. One theory proposes that vascular dysregulation of the optic nerve, coupled with the oxidative stresses of hypoxia and reperfusion as seen in apneic events, results in damage to the optic nerve and characteristic loss of vision.[25] Another theory proposes it is the increase in intracranial pressure (ICP) seen during these events that results in NAION.[23] The most likely etiology is a combination of these factors.

NAION is a sight-threatening condition that may result in significant visual field defects *(Figure 6)* and even bilateral blindness without proper management of risk factors. Although the presentation of NAION is generally unilateral, both eyes are at risk. Management of risk factors involves the treatment of underlying systemic disease. In patients with OSA, studies show a decreased risk of developing NAION in patients who are treated with CPAP.[27]

FIGURE 5:

Fundus photo showing localized disc edema (arrow) in a patient with nonarteritic ischemic optic neuropathy.

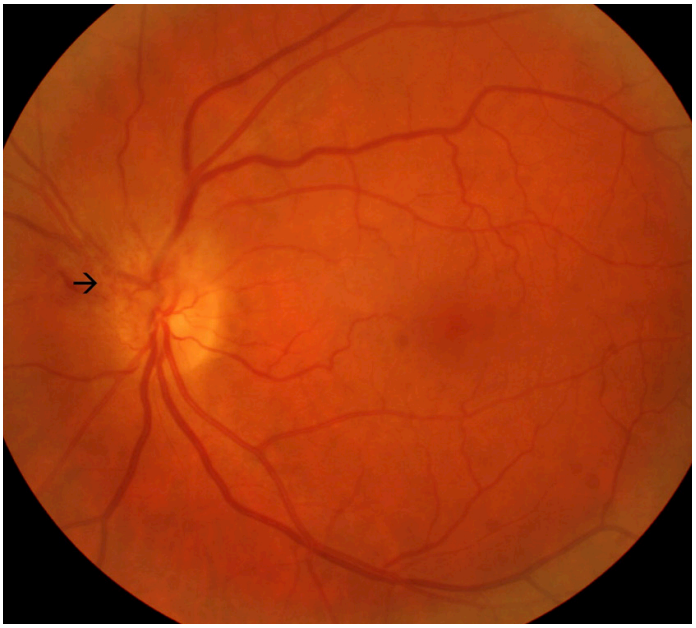
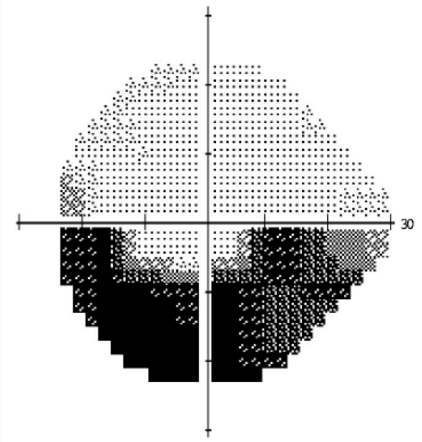


FIGURE 6:

Characteristic altitudinal visual field defect in nonarteritic ischemic optic neuropathy



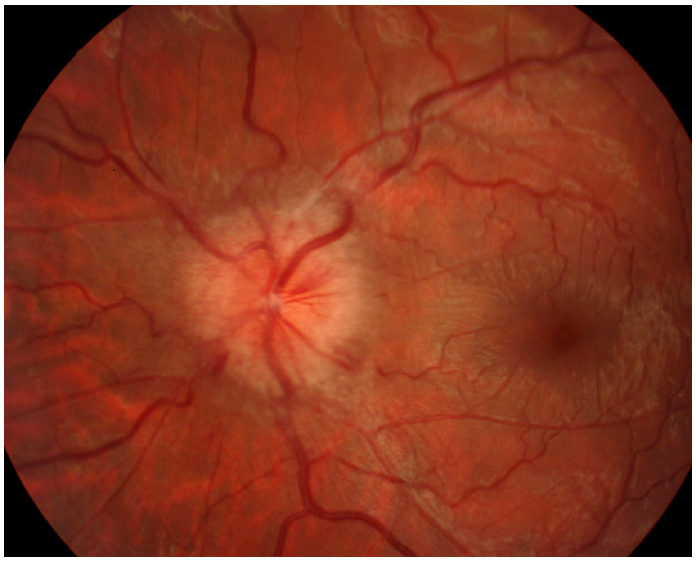
PAPILLEDEMA

Papilledema is the bilateral swelling of the optic discs secondary to increased ICP. Edematous optic discs appear elevated, with dilated capillaries and blurred disc margins *(Figure 7)*. The cause of increased ICP can be a mechanical blockage of intracranial fluid drainage (intracranial tumor), central nervous system (CNS) inflammation, or can be idiopathic in nature. Idiopathic cases are referred to as idiopathic intracranial hypertension (IIH) and are the form of papilledema associated with OSA. One study found 33% of individuals with IIH to have concurrent OSA.[27] Patients with papilledema may experience headache that is often worse in the morning, nausea, vomiting, and an increase in the size of the blind spot on formal visual field testing.

During apneic events blood oxygen levels decrease and carbon dioxide levels increase, resulting in cerebral vasodilation and a subsequent increase in intracranial blood volume. This increase in blood volume can over time result in venous sinus stenosis and the sustained increase in ICP we see in IIH.[28]

FIGURE 7:

Fundus photo of papilledema



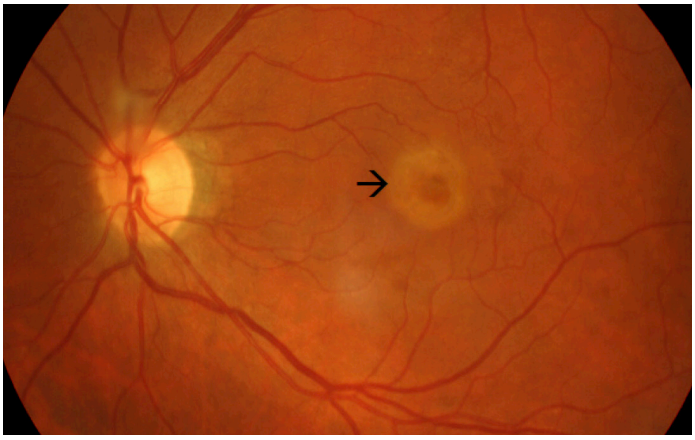
The preferred treatment for IIH is weight loss; studies show reducing body fat by 6% is generally successful in resolving IIH symptoms.[29] Diuretics such as acetazolamide, or surgical intervention by lumboperitoneal shunt or optic nerve sheath fenestration can be utilized in more severe or persistent cases to decrease ICP. Studies show that in patients with OSA and papilledema, CPAP can be used to reduce ICP.[15]

CENTRAL SEROUS CHORIORETINOPATHY

Central serous chorioretinopathy is the fourth most common form of retinopathy, and is typically found in middle-aged males.[30] CSCR results in a serous detachment of the sensory retina in the location of the macula *(Figure 8)*. This can result in a mild reduction in visual acuity (20/30 to 20/60), central visual distortions, a reduction in contrast sensitivity and color vision disruption.[30] Meta-analysis has found a statistically significant association between OSA and CSCR.[31] One study found 66% of patients with CSCR to have OSA,[32] though additional research shows that when obesity is controlled for, there is no increase in the prevalence of CSCR for patients with OSA.[33]

FIGURE 8:

Fundus photo of central serous chorioretinopathy



The mechanism for CSCR is unknown, though elevated levels of endogenous cortisol have been found in affected individuals. It is theorized that vasospasm and endothelial dysregulation of choroidal vessels, as mediated by cortisol, increases vascular permeability. This allows for fluid leakage from retinal capillaries and a buildup of osmotic pressure beneath the retina. This pressure gradient pulls fluid through the retinal pigment epithelium into the choroid, resulting in CSCR's characteristic serous retinal detachment.[34] In patients with OSA, the oxidative stress of hypoxia and reperfusion results in vascular endothelial cell dysregulation and has also been shown to result in fluid leakage.

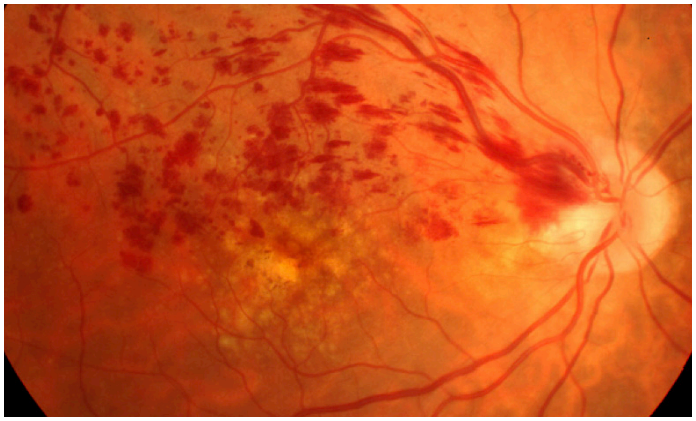
Most cases of CSCR are self-resolving, with patients recovering the majority of their visual acuity within three months.[30] If CSCR is recurrent however, permanent reduction can occur. Treatment for chronic or recurrent cases includes the use of laser and intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) to reduce retinal swelling. Systemic medications such as aldosterone inhibitors, beta-blockers, and carbonic anhydrase inhibitors have also been found to be effective in resolving CSCR.[30]

RETINAL VEIN OCCLUSION

Retinal vein occlusion (RVO) is the second most common vascular cause of blindness after diabetic retinopathy.[35] Vein occlusion most commonly presents as a branch retinal vein occlusion (BRVO) wherein only a portion of the retina is affected, though central retinal vein occlusion (CRVO) affecting the entire retina may also occur *(Figure 9)*. Patients that have a RVO often experience a sudden, painless, unilateral loss of vision or new visual field defect. These visual findings are a result of retinal ischemia following venous occlusion, as well as subsequent retinal hemorrhaging and edema. Studies suggest that there is an increased risk of RVO in patients with OSA.[35-37] A 2012 study found 37% of patients with RVOs to have sleep-disordered breathing, including sleep apnea.[36]

FIGURE 9:

Fundus photo of branch retinal vein occlusion



The mechanism for RVOs in patients with OSA is theorized to be hypercoagulability and vascular inflammation of retinal vessels secondary to increased nocturnal ICP and changes in retinal microcirculation.[37] Hypoxic conditions, as experienced in an apneic event, result in increased hematocrit levels and a predisposition for clot formation.[38] Patients with OSA have also been found to have an increase in blood viscosity independent of cardiovascular risk factors such as hypertension.[39]

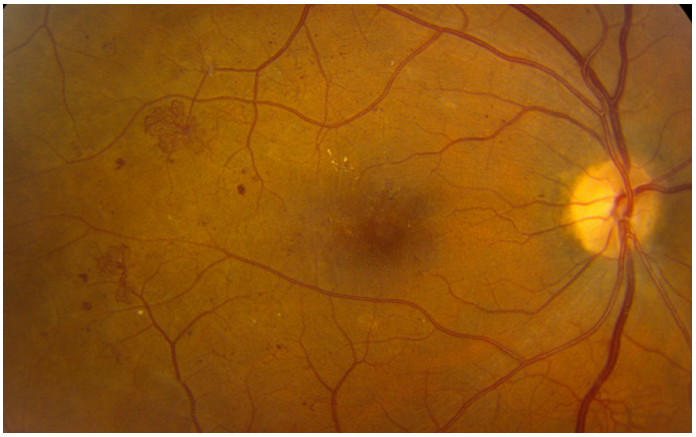
A study conducted in 2001 found that consistent use of a CPAP machine in patients with OSA reduced blood hypercoagulability, thus reducing the patient's risk of developing a stroke including a BRVO.[40] Treatment of RVOs after they have occurred consists of laser photocoagulation for patients with macular edema, as well as intravitreal steroid or anti-VEGF injections.[37]

COMPLICATIONS WITH ANTI-VEGF

Studies have found an increased prevalence of diabetic macular edema (DME) in patients with OSA.[41] Macular edema is the buildup of fluid within the macula, the area of the retina responsible for central vision. Damage to retinal blood vessels results in fluid leakage and swelling of the macula *(Figure 10)*. Patients with DME may experience reduced visual acuity and visual distortions, known as metamorphopsia. The treatment for DME is intravitreal injections of anti-VEGF. Studies have shown that patients with OSA are more resistant to this anti-VEGF treatment.[42,43] Hypoxia experienced during apneic events results in oxidative stress, inflammation, and vascular endothelial cell dysfunction of retinal vessels, all of which encourage the release of VEGF. Anti-VEGF resistance in patients with OSA is likely due to this increased retinal VEGF secretion.

FIGURE 10:

Fundus photo of diabetic retinopathy with macular edema



Although the link between OSA and other causes of intraretinal edema and neovascularization has not been studied, anti-VEGF resistance has implications for the treatment of numerous ocular diseases. Conditions such as exudative age-related macular degeneration and RVOs are also treated with intravitreal anti-VEGF injections. Management of OSA with CPAP however, has been shown to decrease retinal anti-VEGF resistance.[43]

CONCLUSION

Sleep apnea is a common sleep disorder associated with numerous ophthalmic conditions that merit co-management with eye-care providers.[1,3,4] Physicians should be aware of the many ocular side effects of OSA, some of which are sight threatening, so that appropriate referrals can be made, and damage to the patient's ocular health and vision prevented.

AUTHOR DISCLOSURES:

No relevant financial affiliations

REFERENCES:

1. Lee W, Nagubadi S, Kryger MH, Mokhlesi B. Epidemiology of obstructive sleep apnea: a population based perspective. Expert Rev Respir Med. 2008;2(3):349-364. doi:10.1586/17476348.2.3.349.
2. Barewal RM. Obstructive sleep apnea: the role of gender in prevalence, symptoms, and treatment success. Dent Clin North Am. 2019;63(2):297-308.
3. Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population-a review on the epidemiology of sleep apnea. J Thorac Dis. 2015;7: 1311–1322.
4. Johnson EO, Roth T. An epidemiologic study of sleep-disordered breathing symptoms among adolescents. Sleep. 2006;29:1135–1142.
5. Skorin L, Knutson R. Ophthalmic diseases in patients with obstructive sleep apnea. J Am Osteo Assoc. 2016;116(8):522-529.
6. Santos M, Hofmann RJ. Ocular manifestation of obstructive sleep apnea. J Clin Sleep Med. 2017;13(11):1345-1348.
7. McNab AA. The eye and sleep apnea. Sleep Med Rev. 2007;11(4):269–276.
8. Chambe J, Laib S, Hubbard J, Erhardt C, Ruppert E, Schroder C, Malan A, Bourcier T, Bourgin P. Floppy eyelid syndrome is associated with obstructive sleep apnoea: a prospective study on 127 patients. J Sleep Res. 2012;21(3):308–315.
9. Ezra DG, Beaconsfield M, Collin R. Floppy eyelid syndrome stretching the limits. Surv Ophthalmol. 2010;55(1):35-46. doi:10.1016/j.survophthal.2009.02.025.
10. Leibovitch I, Selva D. Floppy eyelid syndrome: clinical features and the association with obstructive sleep apnea. Sleep Med. 2005;(7)2:117-122. doi:10.1016/j.sleep.2005.07.001.
11. Moscato EE, Jian-Amado A. Floppy eyelid syndrome. Compr Ophthalml Update. 2007;8(2)59-65.
12. Miyamoto C, Espirito Santo LC, Roisman L, Moreno Pde A, Cariello AJ, Osaki MH. Floppy eyelid syndrome: review. Arq Bras Oftalmol. 2011;74(1):64–66.
13. Saidel MA, Paik JY, Garcia C, Russo P, Cao D, Bouchard C. Prevalence of sleep apnea syndrome and high-risk characteristics among keratoconus patients. Cornea. 2012;31(6):600-603. doi:10.1097/ico.0b013e318243e446.
14. Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiologic study of keratoconus. Am J Ophthalmol.1986;101(3):267-73.
15. Javaheri S, Quereshi L, Golnik K. Resolution of papilledema associated with OSA treatment. J Clin Sleep Med. 2011;7(4):399-400. doi:10.5664/JCSM.1202.
16. Gupta PK, Stinnett SS, Carlson AN. Prevalence of sleep apnea in patients with keratoconus. Cornea. 2012;31(6):595-599. doi:10.1097/ico.0b013e31823f8acd.
17. Gencer B, Ozgurhan EB, Kara S, Tufan HA, Arikan S, Bozkurt E, Demirok A. Obesity and obstructive sleep apnea in patients with keratoconus in a Turkish population. Cornea. 2014;33(2):137-140. doi:10.1097/ico.0000000000000024.
18. Lin CC, Hu CC, Ho JD, Chiu HW, Lin HC. Obstructive sleep apnea and increased risk of glaucoma: a population based matched cohort study. Ophthalmology. 2013;120(8):1559-1564.
19. Blumen OE, Blumen MB, Blowol E, Derri M, Chabolle F, Nordmann JP. Primary open angle glaucoma and snoring: prevalence of OSAS. Eur Ann Otorhinolaryngol Head Neck Dis. 2010;127(5):159-164.
20. Perez-Rico C, Gutierrez-Diaz E, Mencia-Gutierrez E, Diaz-de-Atauri, Blanco R. Obstructive sleep apnea hypopnea syndrome (OSAHS) and glaucomatous optic neuropathy. Graefes Arch Clin Exp Ophthalmol. 2014;252(9):1345-1357.
21. Shinmei Y, Nitta T, Saito H, Ohguchi T, Kijima R, Chin S, Ishida S. Continuous intraocular pressure monitoring during nocturnal sleep in patients with obstructive sleep apnea syndrome. Invest Ophthalmol Vis Sci. 2016;57(6):2824–2830.
22. Kremmer S, Selbach JM, Ayertey HD, Steuhl KP. Normal tension glaucoma, sleep apnea syndrome and nasal continuous positive airway pressure therapy--case report with a review of literature. Klin Monbl Augenheilkd. 2001;218(4):263–268.
23. Archer EL, Pepin S. Obstructive sleep apnea and nonarteritic anterior ischemic optic neuropathy: evidence for an association. J Clin Sleep Med. 2013;9(6):613-618. doi:10.5664/jcsm.2766.
24. Campion E, Biousse V, Newman N. Ischemic optic neuropathies. N Engl J Med.2015;372(25):2428-2436. doi:10.1056/NEJMra1413352.
25. Aptel F, Khayi H, Pépin JL, Tamisier R, Levy P, Romanet JP, Chiquet C. Association of nonarteritic ischemic optic neuropathy with obstructive sleep apnea syndrome: consequences for obstructive sleep apnea screening and treatment. JAMA Ophthalmol. 2015;133(7):797-804. doi:10.1001/jamaophthalmol.2015.0893.
26. Gaier ED, Torun N. The enigma of nonarteritic anterior ischemic optic neuropathy: an update for the comprehensive ophthalmologist. Curr Opin Ophthalmol. 2016;27(6):498–504.
27. Thurtell MJ, Trotti LM, Bixler EO, Rye DB, Bliwise DL, Newman NJ, Biosse V, Bruce BB. Obstructive sleep apnea in idiopathic intracranial hypertension: comparison with matched population data. J Neurol. 2014;260(7):1748-1751.
28. Jennum P, Børgesen SE. Intracranial pressure and obstructive sleep apnea. Chest. 1989;95(2):279-83.
29. Johnson LN, Krohel GB Madsen RW, March GA. The role of weight loss and acetazolamide in the treatment of idiopathic intracranial hypertension (pseudotumor cerebri). Ophthalmology. 1998;105(12):2313-2317.
30. Liegl R, Ulbig MW. Central serous chorioretinopathy. Ophthalmologica. 2014;232(2):65-76.
31. Huon LK, Liu SY, Camacho M, Guilleminault C. The association between ophthalmologic diseases and obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath. 2016;20(4):1145–1154.
32. Yavas GF, Kusbeci T, Kasikci M, Gunay E, Dogan M, Unlu M, Inan UU. Obstructive sleep apnea in patients with central serous chorioretinopathy. Curr Eye Res. 2014;39(1):88-92. doi:10.3109/02713683.2013.824986.
33. Brodie FL, Charlson ES, Aleman TS, Salvo RT, Gewaily DY, Lau MK, Farren ND, Engelhard SB, Pistilli M, Brucker AJ. Obstructive sleep apnea and central serous chorioretinopathy. Retina. 2015;35(2):238-243.
34. Nicholson B, Noble J, Forooghian F, Meyerle C. Central serous chorioretinopathy: update on pathophysiology and treatment. Surv Ophthalmol. 2013;58(2):103-126. doi:10.1016/j.survophthal.2012.07.004.
35. Glacet-Bernard A, Leroux les Jardins G, Lasry S, Coscas G, Soubrane G, Souied E, Housset B. Obstructive sleep apnea among patients with retinal vein occlusion. Arch Ophthalmol. 2010;128(12):1533–1538.
36. Kanai H, Shiba T, Hori Y, Saishin Y, Maeno T, Takahashi M. Prevalence of sleep-disordered breathing in patients with retinal vein occlusion. Nippon Ganka Gakkai Zasshi. 2012;116(2):81–85.
37. Grover DP. Obstructive sleep apnea and ocular disorders. Curr Opin Ophthalmol. 2010;21(6):454-458.

38. Liak C, Fitzpatrick M. Coagulability in obstructive sleep apnea. Can Respir J. 2011;18(6):338-348. doi:10.1155/2011/924629.

39. Nobili L, Schiavi G, Bozano E, De Carli F, Ferrillo F, Nobili F. Morning increase of whole blood viscosity in obstructive sleep apnea syndrome. Clin Hemorheol Microcirc. 2000;22:21.

CLINICAL IMAGE

Patchy Hair Loss

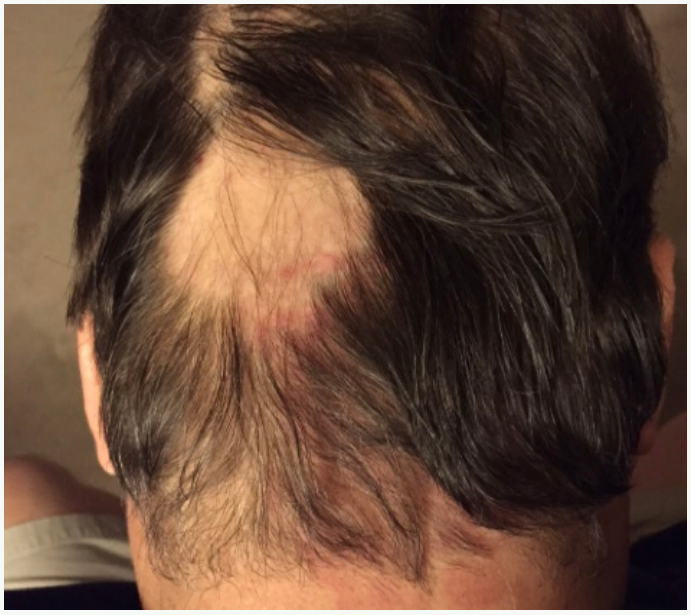
Caitlin Purvis MS[1]; Lindsay Tjiattas-Saleski DO, MBA, FACOEP[1]

[1]University of South Carolina School of Medicine Greenville, South Carolina
[2]Prisma Health, Greenville South Carolina

A 64-year-old male presented with a small patch of hair loss on his left occipital scalp. He stated that it started about one-month prior as a small quarter sized patch, which was initially recognized by a barber. There was no scaling, itching, or other associated symptoms. The patch progressively enlarged in size *(Figure 1)* and more patches developed on the scalp. The hair loss stopped after three months with no apparent regrowth. The patient was referred to a dermatologist by his PCP for further evaluation. Prior to these symptoms, the patient had typical male pattern baldness, which he stated runs in the family. Patient denied previous episodes of similar, or other hair loss. He denied pain or pruritis to the area, rash, fevers, chills, or arthralgias.

FIGURE 1:

Hair loss on the left occipital scalp



QUESTIONS

1. What is the most likely diagnosis?

A. Alopecia areata
B. Alopecia neoplastica
C. Lichen planopilaris
D. Tinea capitis
E. Trichotillomania

2. Which of the following statements is most correct?

A. Intralesional corticosteroids are usually the first line treatment.
B. This condition is often a side effect of treatment with Janus kinase inhibitors.
C. This condition results from an underlying malignancy.
D. This condition will occasionally respond to behavior modification therapy.
E. Wood's light examination sometimes shows florescence of surrounding hairs.

CORRESPONDENCE:
Lindsay Tjiattas-Saleski DO, MBA, FACOEP
Lindsay.Tjiattas-Saleski@Prismahealth.org

 Print ISSN: 1877-573X

ANSWERS:

1. What is the most likely diagnosis?

Correct Answer:
A) Alopecia areata

This sharply demarcated patch of non-scarring hair loss is most consistent with a diagnosis of alopecia areata. This may be difficult to distinguish from trichotillomania, which results from habitual pulling of hairs. However, in trichotillomania, patients are often not able to pull all hairs completely, broken hairs are commonly seen, and the distribution is usually in the frontotemporal scalp.[1,2] In tinea capitis, there is inflammation that is usually evident by scaling in some types or frank abscesses (kerion) in others.[3] Scarring, never seen in alopecia areata, is evident in lichen planopilaris, where the follicular orifices are obliterated.[4] Alopecia neoplastica is alopecia secondary to an underlying malignancy, usually metastatic, and is also a scarring process.[5] Lesions may be single or multiple plaques having a red-pink color and may be smooth or uneven and are often associated with telangiectasia.[5]

2. Which of the following statements is most correct?

Correct Answer:
A) Intralesional corticosteroids are usually the first line treatment.

Unless the alopecia is very extensive or total, intralesional steroids are usually the first option for treating alopecia areata.[6,7] Recent reports have shown promise in the treatment of alopecia areata with oral or topical Janus kinase inhibitors, but they have not been thought to be implicated in triggering the disease.[8] Behavior modification would be a more appropriate approach to the management of trichotillomania but is not likely to be very effective for alopecia areata.[6] Alopecia areata is not a scarring response to a malignancy, although there have been cases of concomitant malignancies such as lymphomas reported in association.[9,10] Wood's light examination would not be expected to reveal fluorescence in alopecia areata but would yield a green fluorescence with a dermatophyte infection with Microsporum canis.[3]

DISCUSSION

Alopecia areata is estimated to affect 6.8 million people in the United States and has a lifetime incidence of 2.1% worldwide.[11,12] While not a particularly severe health threat, it can be cosmetically disturbing as well as psychologically stressful for the patient.[6] Alopecia areata is a type of non-scarring hair loss which usually involves well circumscribed patches of nearly complete hair loss, but which can be more diffuse involving the entire scalp (alopecia totalis) or the entire scalp and body (alopecia universalis).[6] The affected skin can commonly present with slight redness but otherwise has no other abnormalities. Frequently, "exclamation mark" hairs, or short, broken hairs that are thicker at its damaged section and thinner proximally as it enters the scalp, can be seen around the margins of alopecia areata, specifically where it is expanding.[6,13] Nail changes, such as grid-like nail pitting, can also be seen in patients with alopecia areata.[13] It can be seen in all ages and there is no known prevention, race, or sex dominance and also has a variable occurrence of relapse.[6] A common practice in diagnosis involves the use of dermoscopy, a noninvasive handheld instrument with a transilluminating light source and magnifier, where one can see the presence of "round yellow dots" around the areas of hair loss which implies progression of alopecia areata.[6]

Roughly 20% of people with alopecia areata have a family history of the disease, therefore, it is believed that there is a genetic predisposition to the disease.[14] The direct cause of alopecia is unknown. Theories suggest that there is an autoimmune destruction of hair follicles due to chronic inflammation as evidenced by histopathologic examination, which reveals a dense lymphocytic infiltrate of T lymphocytes around the anagen follicular bulb referred to as a "swarm of bees" appearance.[15,16] There have been multifactorial associations with a variety of genes, including major histocompatibility complex (MHC) and cytokine genes.[14,17] Melanocytes, which are active during the anagen phase, could be responsible for the immune response against the hair follicles by expressing an autoantigen.[18] Since alopecia areata is associated with many autoimmune diseases, such as autoimmune thyroid disease, it is further believed that alopecia areata may be autoimmune in nature.[19]

The differential diagnosis of localized hair loss is vast. Compared to trichotillomania, an impulse-control disorder which can be mistaken for alopecia areata, the broken hairs are firmly attached to the scalp and remain in the growing phase (unlike exclamation mark hairs).[6] Unlike alopecia areata, the scalp in tinea capitis is often inflamed, erythematous, and scaly where hair loss is present.[20] Androgenetic alopecia, commonly known as male or female-pattern baldness, is distinguished by diffuse thinning of hair with either the frontal hairline still intact (female pattern) or an M pattern of hair loss (male) with both displaying a negative pull test away from hair loss.[20] A pull test is used to diagnose hair loss and involves grasping 40-60 hairs at the base using the thumb, index, and middle fingers and gently applying traction away from the scalp while lightly pulling on the hairs.[21] This process is usually repeated in two other areas of the scalp for confirmation.[21] A positive pull test results when more than 10% of hairs (4-6 hairs) are pulled from the scalp, indicating that the hair is actively shedding.[21] Telogen effluvium is a nonscarring and noninflammatory alopecia that presents suddenly but subtly involving hair loss on the entire scalp and primarily affects women ages 30-60 years.[18] Telogen effluvium is most commonly caused by physiologic changes in health status (infection, chronic illness, medication exposure, surgery, pregnancy, hypothyroidism) or even emotional stress that, once removed, hair typically regrows.[18,20,22] Trichorrhexis nodosa occurs when hairs break due to trauma, i.e. traction with tight braids, straightening, or hair product overuse.[20] Lastly, anagen effluvium is a diffuse hair loss caused most commonly by chemotherapy, which disrupts the mitotic activity of hair follicles.[20]

TREATMENT/PREVENTION

Patients may initially present to the family practitioner once they start to experience hair loss. It is recommended that a dermatologist evaluate more advanced hair loss cases or refractory

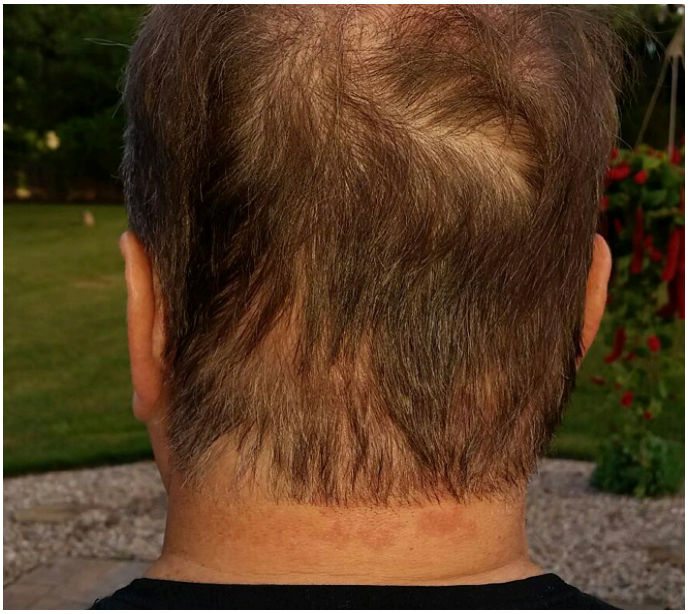
cases when necessary.[23] Since the hair follicles are preserved in nonscarring alopecia areata, recovering hair growth is possible in most cases, even in longstanding disease.[6] A study performed in Japan reported that spontaneous remission within a year was seen in 80% of patients who had small numbers of patches of hair loss.[6] Almost all patients with this disease will experience more than one episode of alopecia areata hair loss and 14-25% of these patients can progress to alopecia totalis or even alopecia universalis where treatment becomes more complex and a full recovery is difficult to achieve (< 10%).[24,25] Furthermore, the prognosis becomes even less favorable when the onset of alopecia areata develops during childhood as well as in ophiasis, or a wave-like presentation of hair loss.[24, 26-28]

The first line treatment for alopecia areata is multiple intralesional injections of corticosteroids every 4-8 weeks in the mid dermis, specifically triamcinolone acetonide (2.5-5 mg/mL) or hydrocortisone acetate (25 mg/mL)(5), which are given at monthly intervals.6,7,29 Studies report an injection of 0.05-0.1 mL will produce an area of regrowth of hair approximately 0.5 cm in diameter.6,7,29 This is most effective when treating patchy patterned hair loss with a limited extension, as well as for areas of cosmetic concern i.e. eyebrows, however, this practice is limited by patient discomfort.6 Needleless devices, such as a Dermajet™ exisit which make it more practical for diverse practitioner utilization.[6] High concentrations of corticosteroids should not be used in order to avoid excess skin atrophy at the sites of injection.[6] Systemic corticosteroids are sometimes given when the alopecia is exceptionally rapid.[6,30] A small study reported 30-47% of patients treated for 6-weeks with oral prednisolone (40 mg daily) showed 25% or more hair regrowth, but continued treatment was needed for maintaining the new growth.[30,31] Topical steroids and calcineurin inhibitors such as oral cyclosporine and topical tacrolimus are sometimes used but tend to be less beneficial as are topical retinoids and anthralin (0.5-1% cream applied daily). [6, 32-39] Reports of successful treatments with topical immunotherapeutic agents dinitrochlorobenzene (DNCB), diphenylcyclopropenone (DPCP), and squaric acid dibutylester (SADBE) have also been published.[6,40,41] Recently, there have been reports of alopecia areata responding to oral and topical Janus kinase inhibitors such as tofacitinib and ruxolitinib but relapse post discontinuation is a concern.[18,42,43] Patients can expect variable response to these treatment options. Comfort and supporting the patient is important during treatment in attempts to eliminate stress. If the patient does not retain hair growth, wigs, plugs, and distracting accessories such as eyeglasses can be recommended in concordance with the patients concern. Support groups (National Alopecia Areata Foundation) are also an option for discussion for patients suffering from psychological trauma from the hair loss.

Our Patient received intralesional triamcinolone acetonide (Kenalog – 10) injections, from 1ml to 2.5ml once a month in the patches of hair loss starting from the front (the most noticeable) then working towards the back. He received about 20 to 30 small injections around a patch each month until the full dose was administered. It took about 3 treatments (or about 3 months) in each patch site before hair started to grow and he received these injections for about a year.

FIGURE 2:

Regrowth



AUTHOR DISCLOSURE:
No relevant financial affiliations

REFERENCES:

1. Grant JE, Chamberlain SR. Trichotillomania. The American journal of psychiatry. 2016;173(9):868-874. doi:10.1176/appi.ajp.2016.15111432.
2. Ankad, B. S., Naidu, M. V., Beergouder, S. L., & Sujana, L. (2014). Trichoscopy in trichotillomania: a useful diagnostic tool. International journal of trichology, 6(4), 160-3.
3. Hay RJ. Tinea Capitis: Current Status. Mycopathologia. 2017;182(1):87-93. doi:10.1007/s11046-016-0058-8.
4. Soares VC, Mulinari-Brenner F, de Souza TE. Lichen planopilaris epidemiology: a retrospective study of 80 cases. Anais Brasileiros de Dermatologia. 2015;90(5):666-670. doi:10.1590/abd1806-4841.20153923.
5. Kim J-H, Kim M-J, Sim W-Y, Lew B-L. Alopecia Neoplastica due to Gastric Adenocarcinoma Metastasis to the Scalp, Presenting as Alopecia: A Case Report and Literature Review. Annals of Dermatology. 2014;26(5):624-627. doi:10.5021/ad.2014.26.5.624.
6. Messenger AG, McKillop J, Farrant P, McDonagh AJ, Sladden M. British Association of Dermatologists' guidelines for the management of alopecia areata 2012. Br J Dermatol 2012; 166: 916-926.
7. Porter D, Burton JL. A comparison of intra-lesional triamcinolone hexacetonide and triamcinolone acetonide in alopecia areata. Br J Dermatol 1971; 85:272–3.
8. Mackay-Wiggan, J., Jabbari, A., Nguyen, N., Cerise, J. E., Clark, C., Ulerio, G., . . . Clynes, R. (2016, September 22). Oral ruxolitinib induces hair regrowth in patients with moderate-to-severe alopecia areata. Retrieved from https://insight.jci.org/articles/view/89790

9. Pratt, C. H., King, L. E., Messenger, A. G., Christiano, A. M., & Sundberg, J. P. (2017). Alopecia areata. Nature reviews. Disease primers, 3, 17011. doi:10.1038/nrdp.2017.11
10. Ramot, Y., Gural, A., & Zlotogorski, A. (2016). Alopecia Areata as a Manifestation of Systemic Lymphoma: Report of Two Cases. Skin appendage disorders, 2(1-2), 63-66.
11. FAQ's. (n.d.). Retrieved from https://www.naaf.org/faqs
12. Villasante Fricke, A. C., & Miteva, M. (2015). Epidemiology and burden of alopecia areata: a systematic review. Clinical, cosmetic and investigational dermatology, 8, 397-403. doi:10.2147/CCID.S53985
13. Spano F, Donovan JC. Alopecia areata: Part 1: pathogenesis, diagnosis, and prognosis. Canadian Family Physician. 2015;61(9):751-755.
14. McDonagh AJG, Messenger AG. The pathogenesis of alopecia areata. Dermatol Clin 1996;14:661–70.
15. Gilhar A, Ullmann Y, Berkutzki T et al. Autoimmune hair loss (alopecia areata) transferred by T lymphocytes to human scalp explants on SCID mice. J Clin Invest 1998;101:62–7.
16. Rapini, R. P. (2012). Practical Dermatopathology. Elsevier Health Sciences.
17. Petukhova L, Duvic M, Hordinsky M et al. Genome-wide association study in alopecia areata implicates both innate and adaptive immunity. Nature 2010; 466:113–17.
18. Bolognia, J., Cerroni, L., & Schaffer, J. V. (2018). Dermatology (Fourth ed., Vol. One). Philadelphia: Elsevier.
19. Saif GAB. Severe subtype of alopecia areata is highly associated with thyroid autoimmunity. Saudi Medical Journal. 2016;37(6):656-661. doi:10.15537/smj.2016.6.13777.
20. Phillips TG, Slomiany WP, Allison R. Hair loss: common causes and treatment. Am Fam Physician 2017; 96(6):371-378.
21. Gordon, K. A., & Tosti, A. (2011). Alopecia: evaluation and treatment. Clinical, cosmetic and investigational dermatology, 4, 101-6.
22. Springer, Karyn, et al. "Common Hair Loss Disorders." AAFP Home, 1 July 2003, www.aafp.org/afp/2003/0701/p93.html.
23. Spano, F., & Donovan, J. C. (2015). Alopecia areata: Part 2: treatment. Canadian family physician Medecin de famille canadien, 61(9), 757-61.
24. Walker SA, Rothman S. Alopecia areata: a statistical study and consideration of endocrine influences. J Invest Dermatol 1950;14:403–13.
25. Gip L, Lodin A, Molin L. Alopecia areata. A follow-up investigation of outpatient material. Acta Derm Venereol1969;49:180–8.
26. Anderson I. Alopecia areata: a clinical study. Br Med J 1950;2:1250–2.
27. Muller SA, Winkelmann RK. Alopecia areata. Arch Dermatol 1963; 88:290–7.
28. De Waard-van der Spek FB, Oranje AP, De Raeymaecker DM et al. Juvenile versus maturity-onset alopecia areata – a comparative retrospective clinical study. Clin Exp Dermatol 1989;14:429–33.
29. Kubeyinje EP. Intralesional triamcinolone acetonide in alopecia areata amongst 62 Saudi Arabs. East Afr Med J 1994; 71:674–5.
30. Olsen EA, Carson SC, Turney EA. Systemic steroids with or without 2% topical minoxidil in the treatment of alopecia areata. Arch Der- matol 1992; 128:1467–73.
31. Winter RJ, Kern F, Blizzard RM. Prednisone therapy for alopecia areata. A follow-up report. Arch Dermatol 1976;112:1549–52.
32. Tosti A, Iorizzo M, Botta GL et al. Efficacy and safety of a new clob- etasol propionate 0Æ05% foam in alopecia areata: a randomized, double-blind placebo-controlled trial. J Eur Acad Dermatol Venereol 2006; 20:1243–7.
33. Charuwichitratana S, Wattanakrai P, Tanrattanakorn S. Randomized double-blind placebo-controlled trial in the treatment of alopecia areata with 0Æ25% desoximetasone cream. Arch Dermatol 2000; 136:1276–7.
34. Tosti A, Piraccini BM, Pazzaglia M et al. Clobetasol propionate 0.05% under occlusion in the treatment of alopecia totalis/univer- salis. J Am Acad Dermatol 2003; 49:96–8.
35. Gupta AK, Ellis CN, Cooper KD et al. Oral cyclosporine for the treatment of alopecia areata. A clinical and immunohistochemical analysis. J Am Acad Dermatol 1990; 22:242–50.
36. Price VH, Willey A, Chen BK. Topical tacrolimus in alopecia areata. J Am Acad Dermatol 2005; 52:138–9.
37. Fiedler-Weiss VC, Buys CM. Evaluation of anthralin in the treatment of alopecia areata. Arch Dermatol 1987; 123:1491–3.
38. Nelson DA, Spielvogel RL. Anthralin therapy for alopecia areata. Int J Dermatol 1985; 24:606–7.
39. Schmoeckel C, Weissmann I, Plewig G et al. Treatment of alopecia areata by anthralin-induced dermatitis. Arch Dermatol 1979; 115:1254–5.
40. Rosenberg EW, Drake L. Alopecia areata. Arch Dermatol 1976; 112:256.
41. Rokhsar CK, Shupack JL, Vafai JJ et al. Efficacy of topical sensitizers in the treatment of alopecia areata. J Am Acad Dermatol 1998; 39:751–61.
42. Crispin MK, Ko JM, Craiglow BG, et al. Safety and efficacy of the JAK inhibitor tofactinib citrate in patients with alopecia areata. JCI Insight 2016;1:e89790.
43. Mackay-Wiggan J, Jabbari A, Nguyen N, et al. Oral ruxolitinib induces hair regrowth in patients with moderate-to-severe alopecia areata. JCI Insight 2016;1:e89790.

CALENDAR OF EVENTS

OCTOBER 25 – 28, 2019
OMED
Baltimore, Maryland
www.poma.org

DECEMBER 6 – 8, 2019
Indiana Osteopathic Association 38th Annual Winter Update
Indianapolis, Indiana
www.inosteo.org

JANUARY 10 – 12, 2020
Midwinter Osteopathic Family Practice Conference
Des Moines, Iowa
www.ioma.org

JANUARY 17 – 19, 2020
ACOFP Future Leaders Conference
Phoenix, Arizona
www.acofp.org

JANUARY 24 - 27, 2020
MSACOFP - Annual Winter Family Medicine Update
Independence, Missouri
www.msacofp.org

MARCH 16 – 22, 2020
ACOFP ’20 Annual Convention and Scientific Seminars
New Orleans, Louisiana
www.acofp.org

APRIL 22 – 26, 2020
Ohio ACOFP
Columbus, Ohio
www.ohioacofp.org

APRIL 23 – 26, 2020
Oklahoma ACOFP
Norman, Oklahoma
www.okosteo.org

JULY 29 – AUGUST 2, 2020
California ACOFP
Anaheim, California
www.acofpca.org

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

OCTOBER 24, 2020
ACOFP OMT Boot Camp
Baltimore, Maryland
www.acofp.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.

acofp | eLEARNING CENTER

Support your ongoing medical education with essential CME tools.

- Earn 1-A and 1-B credits for attending live webinars
- View on-demand instructional OMT videos
- Choose from multiple helpful guides and self-study modules to prepare for board exams
- Access journal quizzes
- Utilize online practice questions for Board exams
- And much more

Visit the eLearning Center today at acofp.org.

PATIENT EDUCATION HANDOUT

INSOMNIA

Lauren Burns, DO; Kyle Addison Ward, DO

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

TIPS FOR A BETTER NIGHT'S SLEEP

Insomnia is a common condition when you have difficulty falling asleep, staying asleep and poor quality of sleep. It interferes with normal daily activities. Symptoms can include problems with attention, concentration or memory, poor performance at school or work, changes in mood, daytime sleepiness, and lack of energy or motivation. It has been linked to car accidents and errors at work including industrial disasters. People with insomnia are also more likely to suffer from other problems such as high blood pressure, diabetes, depression and obesity. It can decrease enjoyment of life and can cause work to suffer. The amount of sleep we need is different for all people and changes as we age. The NIH suggests school aged kids need at least 10 hours of sleep, teens about 9-10 hours and adults from 7-8 hours per night. Sleep hygiene is the adoption of good sleep habits every night to improve how you sleep. Healthy sleep habits (good sleep hygiene) can greatly improve people's enjoyment of life and daily functioning.

STRATEGIES FOR BETTER SLEEP:

- **Keep a regular sleep schedule by going to sleep and waking up at the same time every day, even on weekends.**
- **Develop a relaxing bedtime routine away from bright lights. Avoid watching television, phone or computer screens in the bedroom and right before bed. Bright lights and screens lead to excitement, stress or anxiety and make it more difficult to fall asleep.**
- **Keep your bedroom cool and comfortable, between 60-67 degrees and keep your bedroom free from any noise, distractions or excess lights that can disturb your sleep.**
- **Daily exercise has been shown to help people sleep better at night, preferably for at least 20 minutes per day more than 4-5 hours before bedtime.**
- **Avoid afternoon naps, even short ones because they disturb the normal sleep-wake cycle.**
- **Avoid alcohol, cigarettes, heavy meals and drinks with caffeine later in the day and before bed. Avoid eating large meals at least 2-3 hours before bedtime and avoid spicy meals that may cause upset stomach during the night.**
- **Make sure your mattress and pillows are comfortable and supportive. Most mattresses last about 9-10 years before you should replace it.**
- **Spend the last hour before bed doing a calming activity such as reading, taking a warm bath or meditating. If you find you cannot sleep when you lie down, go into another room and do something relaxing until you feel tired. Keep work materials, computers and televisions out of the sleeping area.**

TREATMENT

If you continue to have trouble sleeping despite healthy sleep hygiene habits, speak with your family doctor. They may recommend recording your sleep habits in a sleep diary to help evaluate common patterns or issues with your sleep hygiene. Your doctor may look for and treat an underlying problem causing your sleep disturbance.

acofp AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

SOURCE(S): *National Sleep Foundation, Centers for Disease Control and Prevention, and American Academy of Sleep Medicine*

OMED®19

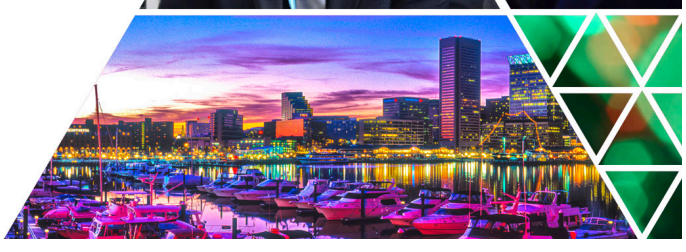
engage › empower › excel ›

OCTOBER 25-28, 2019 || BALTIMORE

Recharge and reconnect with thousands of your fellow physicians and medical students at the largest gathering of DOs in the world.

REGISTER TODAY!

omed.osteopathic.org



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

acofp | AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

ACOFP is looking for the future resident and new physician leaders of the osteopathic community.

Nominate an exceptional resident or new physician for the 2020 ACOFP Future Leaders Conference!

FUTURE LEADERS CONFERENCE

APPLICATION DEADLINE IS NOVEMBER 15, 2019.

Apply at www.acofp.org

The conference will be held

JANUARY 17-19, 2020

Sheraton Phoenix Downtown
Phoenix, Arizona