OFP
Osteopathic Family Physician

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

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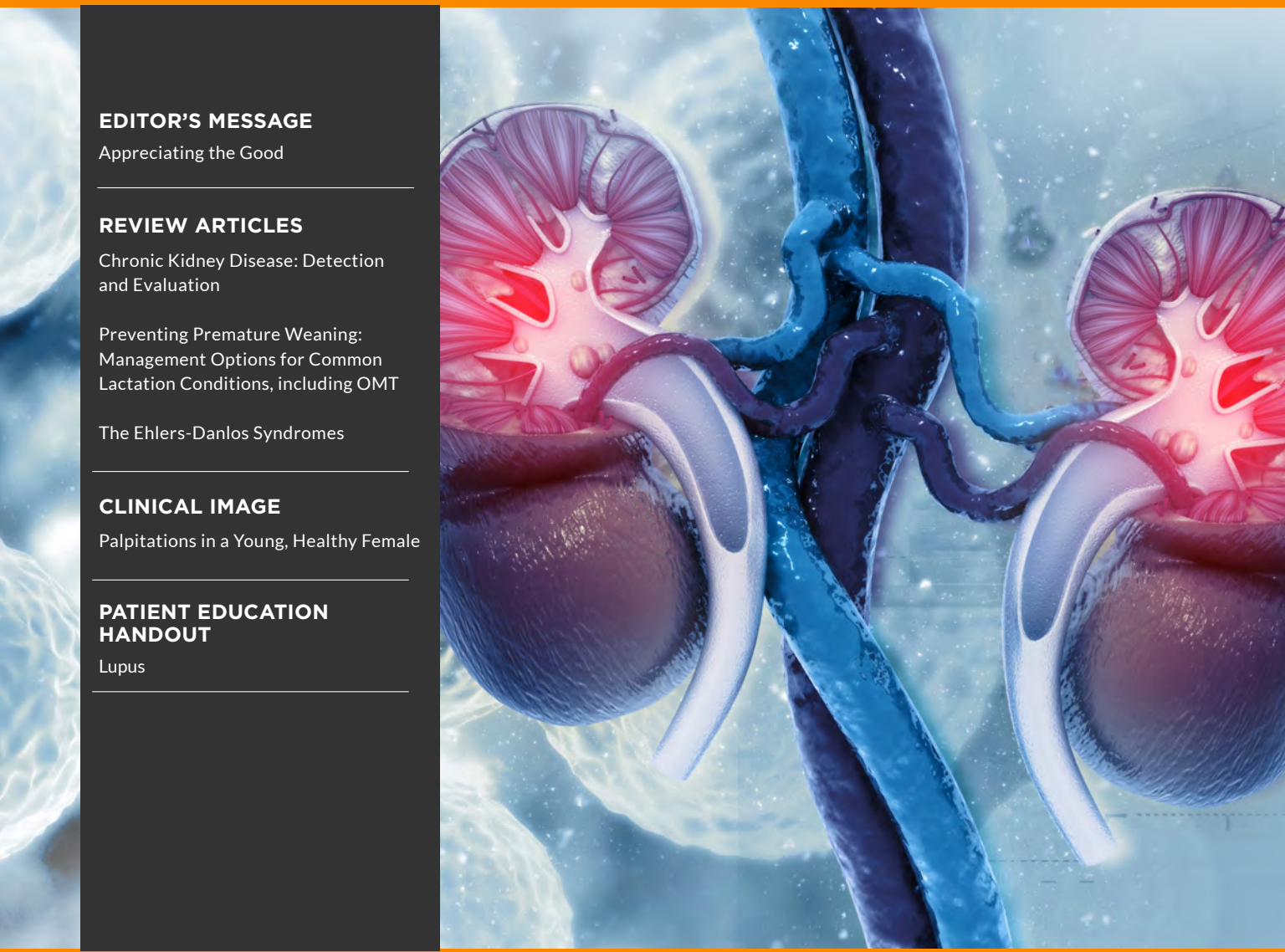

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OFP
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JOURNAL

2020 CALL FOR PAPERS

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

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 Articles submitted for publication must be original in nature and may not be published in any other periodical.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

CLINICAL IMAGES

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

REVIEW ARTICLE TOPICS

- Disorders of Puberty: An Approach to Diagnosis and Management with an osteopathic component
- Lupus: Review Article with Osteopathic Component
- CPPD: with an osteopathic component
- ADHD: Latest OptionsTreatment Review article with osteopathic component
- OMT treatments for pediatric conditions: a systematic review
- Insomnia Diagnosis and Management: An Osteopathic Perspective
- Non-Allergic Rhinitis with osteopathic component

RESEARCH TOPICS

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

The content should include the following:

Abstract
Introduction
Methods
Results
Discussion
Conclusions
Acknowledgments

Ronald Januchowski, DO, FACOFP
Editor-in-Chief

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

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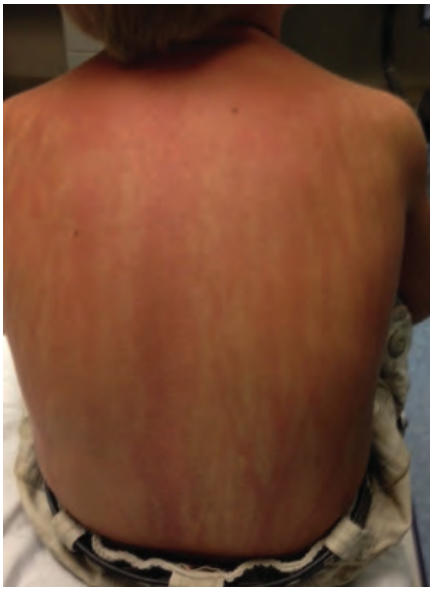
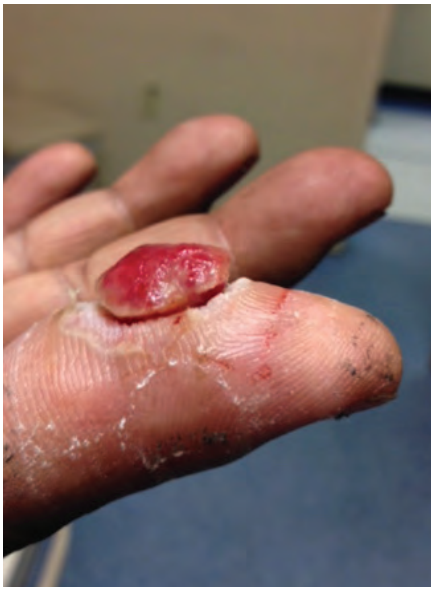
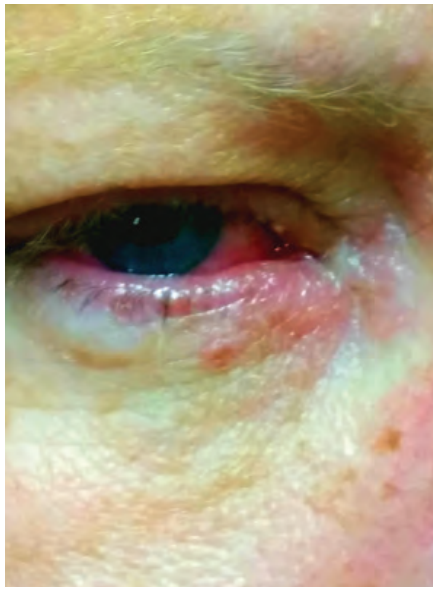
NOW SEEKING

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.

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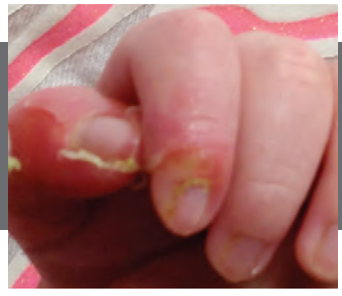

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Official Notice to the ACOFP Membership

Proposed Amendments to the ACOFP Constitution and Bylaws

Draft as of November 13, 2019

According to the Constitution of the American College of Osteopathic Family Physicians, Inc.

Article IX – Amendments: Section 1. *This Constitution may be amended at any annual meeting of the Congress of Delegates by a three-fourths vote of the total number of credentialed delegates in attendance for voting, provided that the proposed amendment shall have been filed with the Executive Director of the College at least 60 days before the first day of the meeting of the Congress of Delegates and that the Executive Director shall have notified the membership of the College in writing of the proposed amendment at least 30 days preceding the first day of the meeting of the Congress of Delegates.*

Section 2. *All amendments to the Constitution shall not be effective until they are submitted to and approved by the Board of Trustees of the AOA.*

The ACOFP Board of Governors proposes the following amendments to the Constitution as recommended by the 2019 Congress of Delegates. Approval of the amendments will be voted on at the ACOFP Congress of Delegates at its March 18-19, 2020 meeting. If adopted by the ACOFP Congress of Delegates, approval will be sent to the American Osteopathic Association Board of Trustees for approval. (New material in all caps and old material in strike out.)

CONSTITUTION OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS, INC.

ARTICLE II – MISSION & OBJECTIVES

Section 2. The objectives of the College are:

3. To support high standards of ongoing osteopathic education for ~~osteopathic~~ family physicians;

5. To encourage and improve the educational opportunities for the training of ~~osteopathic~~ family physicians in all branches of osteopathic medicine and surgery, including the osteopathic family medicine training programs WITH OSTEOPATHIC RECOGNITION STATUS;

ARTICLE IV – MEMBERSHIP

The membership of this College shall consist of osteopathic family physicians, ALLOPATHIC FAMILY PHYSICIANS and such other persons who have met the requirements of membership prescribed by the ACOFP Bylaws.

ARTICLE VII – BOARD OF GOVERNORS

Section 1. The Board of Governors shall be composed of the President, President-Elect, the Past Presidents for the preceding two years, Vice President, Secretary/Treasurer, six (6) Governors-at-large, one osteopathic RESIDENT GOVERNOR OR ALLOPATHIC Resident Governor IN OSTEOPATHIC FOCUSED EDUCATION AT A FAMILY MEDICINE RESIDENCY WITH ACGME OSTEOPATHIC RECOGNITION STATUS, one osteopathic Student Governor, and the Speaker of the Congress of Delegates, all to be selected as provided in the Bylaws. The Speaker has voice but no vote.

According to the Bylaws of the American College of Osteopathic Family Physicians.

ARTICLE XVI – AMENDMENTS

Article XVI – Amendments: Section 1. Notification – *These Bylaws may be amended at any annual meeting of the Congress of Delegates by a two-thirds vote of the total number of delegates credentialed for voting, provided that the proposed amendment shall have been filed with the Executive Director of the College at least 60 days before the first day of the meeting of the Congress of Delegates and that the Executive Director shall have notified the membership of the College in writing of the proposed amendment at least 30 days preceding the first day of the meeting of the Congress of Delegates.*

Section 2. Approval – *An amendment to these Bylaws shall not be effective until they are submitted to and approved by the Board of Trustees of the AOA.*

The ACOFP Board of Governors proposes the following amendments to the Bylaws as recommended by the 2019 Congress of Delegates. Approval of the amendments will be voted on at the ACOFP Congress of Delegates at its March 18-19, 2020 meeting. If adopted by the ACOFP Congress of Delegates, approval will be sent to the American Osteopathic Association Board of Trustees for approval. (New material in all caps and old material in strike out.)

BYLAWS OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS, INC.

ARTICLE III – MEMBERSHIP

Section 1. Qualifications

An applicant for membership, except as provided herein, shall be a graduate of a college of osteopathic medicine approved by the COMMISSION ON OSTEOPATHIC COLLEGE ACCREDITATION (COCA) ~~American Osteopathic Association~~ OR A GRADUATE OF A COLLEGE OF ALLOPATHIC MEDICINE APPROVED BY THE LIAISON COMMITTEE ON MEDICAL EDUCATION at the time of graduation and shall be licensed to practice ~~osteopathic~~ medicine. Each applicant shall be of good moral character and shall conform to the ACOFP Code of Ethics.

Section 3. Active Members in Good Standing

The phrase "in good standing" shall describe only those active members whose dues and assessments are current, and who document CME hours ~~earned within a three-year period of educational programs~~ consistent with the AOBFP OR AMERICAN BOARD OF FAMILY MEDICINE (ABFM) requirements, and who are in compliance with the ACOFP Code of Ethics. National officers, affiliate officers, and residency program directors must be members in good standing.

ARTICLE V – CONGRESS OF DELEGATES

Section 1. Composition

4. Each affiliate society shall be entitled to one voting ~~osteopathic~~ family medicine resident delegate who meets the following criteria.
   (a) Be currently enrolled and in good standing in an AOA or ACGME residency program in the state which the delegate represents
   (b) Be a member in good standing of the ACOFP affiliate society in the state (if such an affiliate society exists).
   (c) Be a member in good standing with ACOFP ~~and AOA~~.

ARTICLE VI – BOARD OF GOVERNORS

Section 2. Composition

A. The Board of Governors shall consist of the President, President-Elect, the Past Presidents for the preceding two years, Vice President, Secretary/Treasurer, six (6) Governors-at-large, one Osteopathic RESIDENT GOVERNOR OR ALLOPATHIC Resident Governor IN OSTEOPATHIC FOCUSED EDUCATION AT A FAMILY MEDICINE RESIDENCY WITH ACGME OSTEOPATHIC RECOGNITION STATUS, and one Osteopathic Student Governor as provided for in the Bylaws.

ARTICLE X – DEPARTMENTS AND COMMITTEES

Section 2. Qualifications of ~~Standing~~ Committee CHAIRS AND Members

~~Standing c~~Committee chairs ~~and committee members~~ shall be OSTEOPATHIC PHYSICIANS WHO ARE active members of this College in good standing, or academic or associate members of this College., OR ALLOPATHIC PHYSICIANS WHO MEET THESE REQUIREMENTS AND HAVE COMPLETED OSTEOPATHIC FOCUSED EDUCATION AT RESIDENCY PROGRAMS WITH ACGME OSTEOPATHIC RECOGNITION STATUS.COMMITTEE MEMBERS SHALL BE OSTEOPATHIC OR ALLOPATHIC PHYSICIANS WHO ARE ACTIVE MEMBERS OF THIS COLLEGE IN GOOD STANDING, OR ACADEMIC OR ASSOCIATE MEMBERS OF THIS COLLEGE.

ARTICLE V – CONGRESS OF DELEGATES

Section 1. Composition

B. ONE VOTING DELEGATE AND ONE ALTERNATE DELEGATE SHALL REPRESENT THE RESIDENT MEMBERS OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS. THE DELEGATES SHALL BE APPOINTED ANNUALLY BY THE RESIDENT COUNCIL OF THE ACOFP. THE RESIDENT COUNCIL SHALL CERTIFY ITS DELEGATE AND ALTERNATE DELEGATE TO THE ACOFP EXECUTIVE DIRECTOR IN WRITING AT LEAST 30 DAYS PRIOR TO THE FIRST DAY OF THE ANNUAL MEETING OF THE CONGRESS OF DELEGATES.

Section 1. Composition

C. ONE VOTING DELEGATE AND ONE ALTERNATE DELEGATE SHALL REPRESENT THE STUDENT ASSOCIATION OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS (STUDENT ASSOCIATION OF THE ACOFP). THE DELEGATES SHALL BE APPOINTED ANNUALLY BY THE NATIONAL STUDENT EXECUTIVE BOARD. THE NATIONAL STUDENT EXECUTIVE BOARD SHALL CERTIFY ITS DELEGATE AND ALTERNATE DELEGATE TO THE ACOFP EXECUTIVE DIRECTOR IN WRITING AT LEAST 30 DAYS PRIOR TO THE FIRST DAY OF THE ANNUAL MEETING OF THE CONGRESS OF DELEGATES.

OFFICIAL CALL – 2020 CONGRESS OF DELEGATES OF THE ACOFP

You are hereby notified that the ACOFP Congress of Delegates will convene on March 18-19, 2020 at the Hilton New Orleans Riverside in New Orleans, Louisiana.

Credentialing of Delegates and Alternates will take place on the afternoon of March 18th before the start of Session I, and Session II which will convene on the morning of March 19th. Each ACOFP Affiliate State Society shall certify the names of its Delegates and Alternate Delegates to the ACOFP Executive Director by February 1, 2020.

Any reports, resolutions, or other business for this meeting should be submitted by February 1, 2020 to Annie DeVries at annied@acofp.org so that it can be posted on the ACOFP website and available for Delegates to review in advance.

Elizabeth A. Palmarozzi, DO, FACOFP
Speaker of the Congress of Delegates

Osteopathic Family Physician is looking for . . .

SPECIALTY PEER REVIEWERS

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- Computer literacy, Microsoft Word, Adobe PDFs and working with the Scholar One electronic submission process is required.
- Respect the confidentiality inherent in the review process.
- A good article takes 1-3 hours to review and a flawed article may take up to 10 hours.

CALL FOR SPECIALTY REVIEWERS IN THE FOLLOWING TOPICS:

- Behavioral Health
- Family Medicine
- Geriatrics
- OMT
- Pain Management
- Pediatrics
- Women's Health

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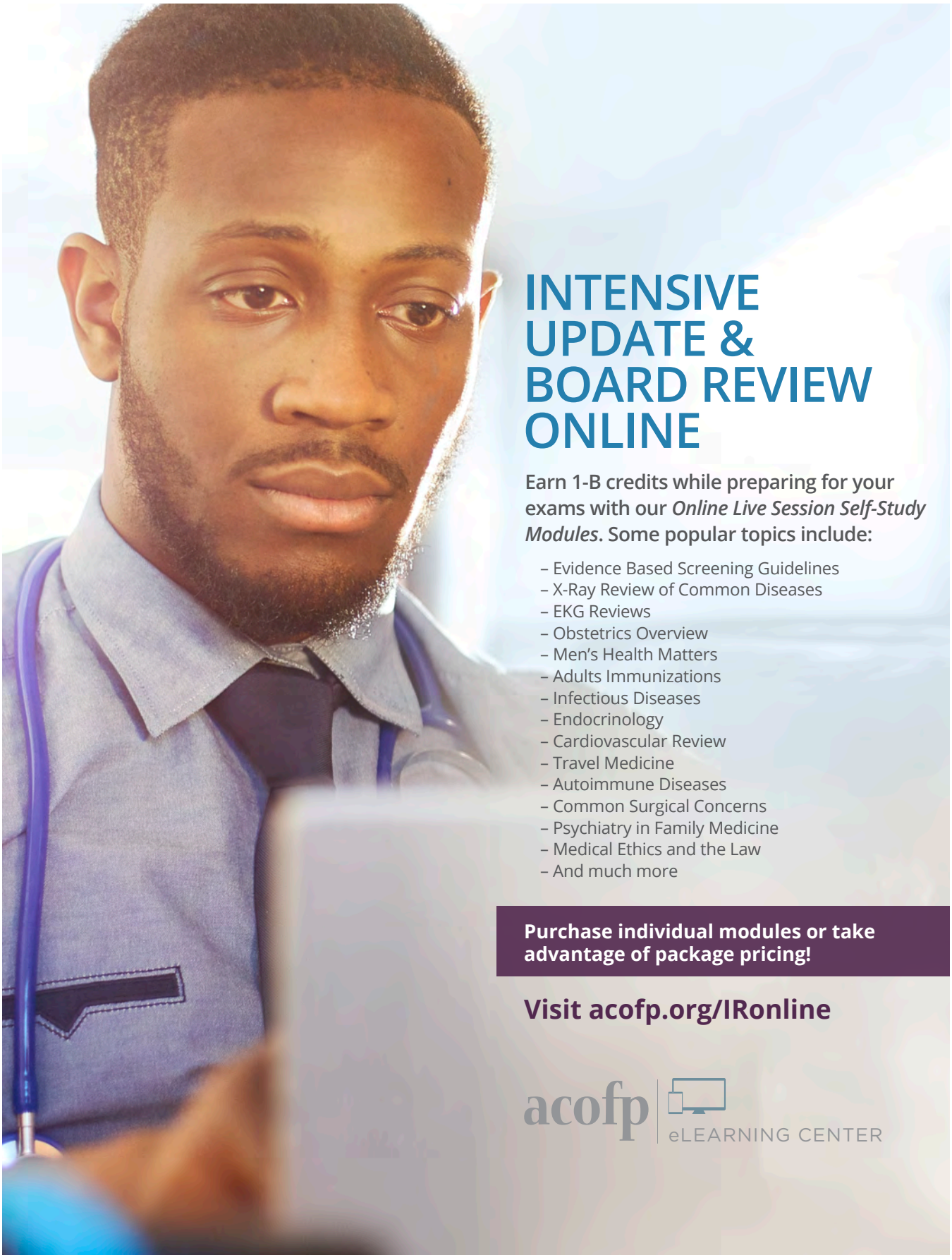
Email **belindab@acofp.org** your CV and what type of articles you are qualified to peer review based on your specialty area(s).



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EDITOR'S MESSAGE

Appreciating the Good

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

As we enter into 2020, I would like to extend a huge "thank you" to the people that make *Osteopathic Family Physician* an incredible resource for our profession. I appreciate ACOFP President DeLuca's support of the journal as well as all of the support provided by ACOFP's past presidents. As managing editor, Belinda Bombei has done an incredible job organizing the submissions and coordinating with the authors to create each issue. I appreciate the work of Associate Editor, Paula Gregory, DO in providing input and suggestions to authors as well as her efforts in making each issue special. The time and effort of the members on the Editorial Committee cannot be overlooked. Their energy provided the impetus for the PubMed listing as well as the improvement of the journal as a whole. Special appreciation to all of the authors that provided valuable additions to the medical literature last year. The Osteopathically unique submissions provided the medical field with great information that will help improve patient care.

With these appreciations, I hope to highlight the positive actions that happened in 2019 and set an optimistic view for this year. Positive thoughts create positive emotions. These emotions then should lead to actions affecting not only us personally but those around us. On a selfish note, providing appreciation and thanks to others has been shown to improve brain functioning and overall mood – critically crucial in post-holiday months with a paucity of sunshine.

Have a wonderful start to your 2020, and thanks for reading the *Osteopathic Family Physician*!

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FROM THE PRESIDENT'S DESK

The Next Decade in Osteopathic Medicine

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

Happy New Year and welcome to the 2020s! With the current rate of osteopathic students going into family medicine at 27 percent and the increase in the number of DO graduates in the next five years of around 12,000, we have the opportunity to welcome over 3,000 family medicine residents into the profession and ACOFP family. Compare that to only 1,600 MD graduates choosing family medicine in 2018.

Some exciting things are developing in osteopathic family medicine over the next few years. I hope that innovation, technology, and the need for more family physicians across the country will inspire even more students and residents to choose osteopathic family medicine through 2030 and beyond.

IMPORTANT INITIATIVES OF THE 2020s

Innovation in Osteopathic Certification

I have covered the new changes in initial certification and recertification requirements in previous *OFP* issues, so I won't go into detail again here. One new development is the Initial Certification Grant being offered by the ACOFP Education & Research Foundation. The grant will award up to $1,400 for exam fees and travel expenses to residents, who don't otherwise have funding support from their program, to be used for the AOBFP exam. You can find details on the Foundation website.

Family Medicine Leading in Technology and AI

Health data technology has become more complicated and detailed with advances in imaging, the measurement of vital signs, biochemical analyses such as blood glucose levels, augmented intelligence (AI) in several areas of medicine and much more. AI is ideal for information on patients and patient populations by using tools such as pattern identification, location knowledge and eliminating bias with an endless capacity for machine learning. Family physicians can take advantage of these AI functions, combining them with human characteristics of compassion, morals, imagination and common sense.

There are countless opportunities to use AI for increased efficiency in diagnosis and treatment, predicting and preventing complications, and the integration of disparate health information. By using these tools in the family medicine setting, physicians and clinicians will save time on administrative tasks and be able to perform at the highest level of their license.

Practicing at the Top of Our Profession

The time saved with technology allows physicians to practice at the top of their profession, rather than spending countless extra hours on EHRs and following cumbersome requirements for the Centers for Medicare and Medicaid Services (CMS). Additionally, CMS has initiated a series of sweeping changes regarding health record documentation and payment level scoring. The CMS "Patients Over Paperwork" initiative seeks to cut the red tape and streamline regulations with goals to reduce unnecessary burden, increase efficiencies and improve the beneficiary experience.

In May, the ACOFP Board approved a white paper produced by the Public Health & Wellness Committee that highlights an emerging outpatient E/M workflow process that fulfills "Patients Over Paperwork" goals while also accommodating proper compliance with federal rules and regulations. Of note, the new rules allow medical students, ancillary staff members and patients to fill out patient history information, which does not need to be re-entered over time by an attending physician. This helps both the physicians and the students while making patients happy that they won't have to provide the same information several times.

Focus on the One-on-One Doctor-Patient Relationship

As osteopathic family physicians, we pride ourselves on creating lasting relationships with our patients. It is a main reason many students and residents choose family medicine. The purpose of new technology and CMS changes is to reduce the burden of paperwork and save time for physicians, allowing meaningful conversations and establishing trust between physicians and patients. Office visits can be about listening to and examining the patient; not entering data on the computer. There is even a movement to bring back the old-time house calls, but only time will tell if that practice could be feasible.

Physician Wellness and Fitness

This leads us to physician wellness. Eliminating some causes of physician burnout should help to alleviate stress and depression within the family physician community. ACOFP recognizes the need for a healthy lifestyle on several fronts. Its Board Task Force

on Physician Wellness is working to find ways to help members and eliminate the stigma of seeing a mental health physician. Several Namey Burnett Preventive Medicine Writing Award blog submissions cover how exercise and eating healthy can help with depression, diabetic symptoms and much more. These posts can be found on the ACOFP website. Also, ACOFP '20 will feature fun exercise classes and healthy activities in the Health Expo's third year at convention.

OMT: The Hands-On Approach to the Opioid Crisis

With health risks and dependence on opioids so often in the news, more patients are searching for opioid alternatives for pain management. OMT can reduce pain and improve function in both acute and chronic pain patients. OMT is associated with significant measures for recovery from chronic lower back pain. It can restore mobility and normal movement, and in turn, reduce pain.

The new ACOFP OMTotal Video Library, which you can find in the eLearning Center, is a great way to practice and learn OMT techniques.

OMT Boot Camps

Of course, another great way to brush up on your OMT skills, or learn new techniques, is the OMT Boot Camp. ACOFP offers these useful hands-on sessions throughout the year: at ACOFP annual conventions, at the ACOFP Intensive Update and Board Review and at OMED.

Bringing Obstetrics Back to Family Medicine

For several years, the importance of training family physicians in obstetrics, including preconception, prenatal, delivery and postpartum care, has been documented repeatedly but not acted upon by many health care systems throughout the country. Unfortunately, the number of family physicians providing maternity care continues to decline. Family medicine with obstetrics has become a cost-effective solution offering improvements in access, cost and quality of care in underserved areas.

ACOFP promotes training for family physicians and provides several OB/GYN sessions for CME and general training in its programs at the annual events and in its eLearning Center. Also, the *OFP* journal regularly features research and case study articles that keep members up to date on OB/GYN issues.

ACFOP will continue to be your source of updates to keep you in the loop on all that is happening in the profession. I hope that you are as excited for the next decade in osteopathic family medicine as I am!

Osteopathically yours,

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

REVIEW ARTICLE

Chronic Kidney Disease: Detection and Evaluation

Raena M. Pettitt, DO[1]; Alonna P. Brumbaugh, OMS-I[1]; Michaela F. Gartman, OMS-I[1]; Alyssa M. Jackson, OMS-I[1]

[1]Liberty University College of Osteopathic Medicine, Lynchburg, VA

KEYWORDS:

CKD

Chronic Kidney Disease

Nephrology

ABSTRACT: Chronic kidney disease (CKD) is a prevalent disease that continues to affect more than one-tenth of the American population. Early detection is essential to slow the natural progression of CKD. This can be accomplished by urine and blood screening tests, which are analyzed for creatinine, urine albumin, and urine protein. Screening is often indicated for individuals with known comorbidities such as cardiovascular disease, mineral and bone disorders, and diabetes. Asymptomatic patients with early renal disease can make detection problematic, requiring clinicians to recognize risk factors that may warrant further testing. When symptoms do appear, the renal manifestations are often broad, including changes in kidney size, electrolyte abnormalities, and proteinuria. Changes in biomarkers may be evaluated in the early stages of CKD before significant kidney damage. The current, most accurate determination of renal function is the estimated glomerular filtration rate (GFR), which must be less than 60 mL/min to prompt further testing for CKD. Novel biomarkers may allow for earlier diagnosis of CKD as they can be detected at lower levels than standard biomarkers. Biomarkers such as homocysteine, cystatin C, and kidney injury molecule-1 are predicted to become more prevalent in a clinical setting. The current gold standard for diagnosis of CKD is a renal biopsy, but MRI is a less invasive alternative. Proper staging of CKD allows for appropriate evaluation and treatment of the patient. The early stages of CKD should be treated to limit complications and to prolong the life and health of patients.

INTRODUCTION

Chronic kidney disease (CKD) is among the most prevalent chronic diseases in the United States, affecting approximately 11% of the adult population.[1] It results from disease pathways that persistently change the structure and function of the kidneys.[1] The presence of CKD has been associated with chronic comorbidities such as hypertension, diabetes, cardiovascular disease, and anemia. Complications frequently arise in CKD management due to low detection rates and comorbidities. As a result, renal disease often goes undetected until the damage has become symptomatic or has progressed to end-stage renal disease.

Chronic kidney disease is defined as the progressive loss of kidney function, causing a decrease in glomerular filtration rate (GFR) of less than 60 mL/min or producing biomarkers of kidney damage, which persist for a minimum of three months.[1] GFR remains the best indicator currently available to determine overall kidney function. This criterion can be used to further subdivide CKD into five stages.

Chronic kidney disease is a significant health care burden for the US population. According to the most recent annual data report from the US Renal Data System, Medicare expenses for chronic kidney disease were 79 billion dollars.[2] As CKD progresses, treatment expenses increase, especially in stages 3-5[3]. The average patient with end-stage renal disease is admitted to the hospital twice a year, with 30% of patients readmitted within 30 days of discharge. Inpatient treatment of these patients accounts for 40% of total yearly Medicare expenses for patients on dialysis.[4] Additionally, in 2016, 83,000 deaths occurred due to CKD in the United States alone.[5]

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The growing knowledge and proper management of comorbidities have caused the incidence rate of CKD to stabilize since 2004. Specifically, improved protocols for the management of hypertension, cholesterol levels, and obesity contribute to the incidence rate stability. Nevertheless, continuously increasing prevalence and disease progression may test the capacity to treat and bear the economic burden of the late stages of CKD. By detecting CKD earlier, prompt and effective preventive treatment can slow the progression of the disease. Opportunities for clinical planning, resource allocation, and patient outcomes can also be improved with early detection.[3]

DETECTION

Early detection of CKD is imperative due to the potential of progression to end-stage renal disease and death.[6] With early detection, therapeutic measures can reduce nephrotoxicity and prevent decreases in glomerular filtration rate, thus inhibiting CKD progression in an attempt to prevent future need for kidney transplantation or dialysis.[6,7] Screening tests are regularly employed for patients with diabetes, hypertension, and other CKD risk factors to ensure that treatment is initiated promptly.[6] Blood work or a urine sample should be used to screen anyone suspected of kidney dysfunction who presents with clinical manifestations of CKD.[7] It can be noted that when a patient does not have hypertension or diabetes mellitus, random measurement of blood glucose and blood pressure can serve as useful tools to identify patients who need further screening for CKD.[7]

COMORBIDITIES

Among the most strongly associated CKD comorbidities is cardiovascular disease. CKD is a known complication of uncontrolled hypertension.8 Inadequacy to control blood pressure among hypertensive diabetic patients with CKD is common and may be attributable to unawareness of target levels and effective management approaches.[9]

CKD is associated with an increased risk for the development of normochromic, normocytic anemia.[10] Kidneys produce erythropoietin, which is key to red blood cell development. Due to the role of the kidney in erythropoietin synthesis, anemia is frequently observed in patients with kidney dysfunction.[10]

Studies have indicated a correlation between mineral and bone disorders and CKD. Patients with early CKD, as defined by a GFR no less than 45 mL/min, who have not previously been diagnosed with a mineral and bone disorder, can be screened for osteoporosis using the standard of care methods for the general population.[11] For patients with CKD and a GFR less than 45 mL/min, bone densitometry is less accurate for determining fracture risk prediction. Metabolic bone diseases, such as renal osteodystrophy, are not detectable by densitometry.[11] A bone biopsy is necessary to evaluate for such diseases in patients with advanced CKD. Serum calcium, phosphorus, 25-hydroxyvitamin D, parathyroid hormone, and alkaline phosphatase levels should be checked regularly in patients in CKD stages 3 to 5 in order to monitor the possibility of mineral kidney disease.[11]

A positive correlation between kidney disease prevalence in diabetic patients has been proven.[12] Diabetic nephropathy accounts for 40% of CKD and 50% of end-stage renal disease cases.[13] Patients with diabetes and CKD face higher risks of morbidity and mortality, making detection of CKD even more critical among these patients.

CLINICAL MANIFESTATIONS

Patients with early renal disease often do not experience symptoms, thus increasing the diagnostic challenge.[7] Many early cases of CKD are diagnosed as incidental findings during routine visits. Without proper screenings, such as urine and blood testing, early detection of CKD may be problematic.[7] Clinicians often use risk factors such as hypertension, diabetes, obesity, cigarette smoking, ethnicity, age, family history, and socioeconomic status to influence the chosen screening modalities.[7]

Since the body is interconnected and the kidney interacts closely with numerous organ systems, several characteristics can be assessed to support a diagnosis of CKD. The first objective manifestation of kidney disease is the basic decline of kidney function. Uremic retention solutes accumulate as a complication of CKD and contribute to inflammation, immune dysfunction, vascular disease, platelet dysfunction with increased bleeding risk, dysbiosis in the gut, and altered drug metabolism.[1] Uremic toxins result from these solutes causing immediate adverse biochemical or physiological effects. These effects can be systemic and often vague.[1] The mechanisms affecting the integumentary system are not fully understood, but it is suggested that the symptoms are results of the deregulation of immune responses and opioid receptors caused by advanced-stage renal disease.[1] Hypoalbuminemia in CKD causes nephrotic syndrome, which increases sodium retention and perpetuates cardiopulmonary deficits by causing edema. These cardiopulmonary symptoms can be further amplified by a decreased oncotic gradient.[1]

Renal manifestations of CKD are broad. Evaluation of kidney size from imaging studies can prove useful for determining the underlying cause of disease. Bilateral small kidneys can indicate intrinsic disease, whereas a unilateral small kidney is suggestive of renal arterial disease.[1] In addition, clubbed calyces and cortical scarring point to reflux, infection, or ischemia, while an overall enlarged cystic kidney suggests cystic kidney disease.[1] Impairment of solute diuresis or edema can lead to damaged tubular concentration ability within the kidney and is indicated by persistent frothy, proteinated urine.[1] Immune-mediated damage to the capillary walls within the kidney can also lead to hematuria from glomerular bleeding.

CKD can also affect the nervous system by increasing the risk of cognitive impairment by 65%. CKD-induced cognitive impairments often present as language and attention deficits.[1] A summary of systemic manifestations is shown in *Table 1*.

LAB AND BIOMARKERS

Standard and novel biomarkers found in urine and plasma are used to screen for fluctuations in kidney function, as summarized

TABLE 1 :

Systemic Manifestations of CKD [1,4,14]

System	Manifestations
Integumentary	Pallor, Unexplained pruritus
Cardiopulmonary	Primary or secondary hypertension, Shortness of breath, Ischemic heart disease, Anemia, Cardiomyopathy, Peripheral edema
Renal	Polyuria, Oliguria, Nocturia, Proteinuria, Hematuria
Muscular	Cramps (typically at night)
Nervous	Cognitive deficits
Gastrointestinal	Anorexia, Vomiting, Taste disturbances, Uremic odor in breath

in *Table 2*. When compared to standard CKD evaluation, novel biomarkers suggest earlier detection of renal pathology with future tests promising higher specificity in diagnosis and prognosis of CKD.

EVALUATION

In 2016, the Evidence Based Practice Project implemented a clinical decision tool for CKD into the electronic medical record system of primary care physicians, physician assistants, and nurse practitioners.[21] One of the goals of this program is to educate providers on the risk factors, staging, management, and outcomes of their patients with CKD in order to improve early detection rates and long term management.[21] As a result of this project, more patients were correctly diagnosed with CKD, detection rates improved, and appropriate referrals to nephrologists increased. This showed that evidence-based medicine is a valuable tool for primary care providers, especially when implemented into electronic medical record systems.[21]

While the current gold standard for diagnosis of CKD is a renal biopsy, recent studies present magnetic resonance imaging (MRI) as a less invasive alternative.[22] Implementation of a non-invasive modality, such as MRI, is proposed to decrease the number of undiagnosed cases of CKD in the population.[22] The magnetic resonance (MR) technique provides broad spatial coverage compared to traditional tissue biopsy and allows for detailed analysis of atherosclerosis associated with CKD.[22] By applying image restoration to dynamic T1-weighted images, MRI researchers were able to match MR biomarkers to those from tissue biopsy samples. Significant correlations were also found between deformation, volume change, and pressure gradient in atherosclerotic kidneys.[22] Staging is required for appropriate diagnosis, evaluation, and treatment of CKD. *(Table 3)*

The 2017 Kidney Disease Improving Global Outcomes (KDIGO) Guidelines contain a framework for the classification of CKD using albuminuria. They address prognosis as well as follow-up frequency and referral recommendations.[6,23] KDIGO recommends that primary care providers use GFR and urine albumin levels to appropriately stage CKD and use albuminuria, urine sediment changes, electrolyte abnormalities, tubular disorders, histologic changes, structural deficiencies, and history of transplantation as a means for assessing subjects with CKD.[7,11,23] Renal fibrosis is the final histologic indication of CKD and presents when the kidneys become unable to properly heal from injury, leaving behind scarred kidney tissue. In the early stages, renal fibrosis contributes to the development of interstitial fibrosis, tubular atrophy, and glomerulosclerosis. Proliferating smooth muscle cells, endothelial damage, and podocyte effacement prompt the development of glomerulosclerosis. Such conditions are often caused by smoking, dyslipidemia, and hypertension.

If a CKD diagnosis is found in the early stages (stages 1-3), the progression and complications of CKD can be altered with proper intervention.[27] Once CKD has reached stage 4, renal replacement therapy should be considered, which includes methods such as dialysis or renal transplant.[18,27] Stage 5 CKD is also referred to as end-stage renal disease as the kidneys are no longer functioning adequately to support life.[1] Although small fluctuations in GFR are common and generally unalarming, higher frequency monitoring is suggested for those at risk of disease progression. Progression is defined as a decline in GFR ≥ 25% from baseline.[1]

Once a patient is diagnosed with CKD and staged using biomarkers or GFR, the next step is to evaluate disease progression. If the GFR remains abnormal or worsens over the subsequent three months, then it is necessary for physicians to further evaluate for potential causes. Common etiologies of CKD include hypertensive kidney disease, diabetic nephropathy, and primary or secondary glomerulonephritis.[1] Minimal change disease or focal point glomerulonephritis should also be considered. Exposure to potential nephrotoxins, current and historical blood pressures, family history of CKD, dietary history, and weight measurements should all be investigated during a full medical history, followed by a complete physical exam.[1]

TREATMENT AND REFERRAL

The Cockcroft-Gault equation is used only to estimate GFR and determine dosing of medications for first line therapy and management in a primary care setting.[6] Clinical practice guidelines

TABLE 2 :

Biomarkers of CKD [6,7,12-20,24-26]

STANDARD		
Marker	**Application**	**Measurement**
Albumin/ Creatinine Ratio	First line CKD screen	Mild: <30 mg/g, Moderate: 30-300 mg/g , Severe: >300 mg/g Assessed in early morning urine sample
Proteinuria	Indicative of renal injury at any GFR	Urinary protein levels exceeding 300 mg are considered clinically significant
Glomerular Filtration Rate (GFR)	Most accurate determination of renal function	Mild: 60-89 mL/min, Mild-Moderate: 45-59 mL/min, Moderate-Severe: 30-44 mL/min, Severe: 15-20 mL:/min, Failure: <15 mL/min Estimated from serum creatinine levels, with adjustments for age, BUN, gender, and race
Serum Creatinine	Lacks predictive value when assessed alone	Used with serum assessment of electrolytes, fasting lipids, A1C, and albumin/creatinine ratio
Urinalysis and Microscopy	Adjunct for diagnosis Can be indicative of kidney dysfunction	Determines presence of increased or abnormal sedimentation, hematuria, chronic pyuria, cellular casts, urine concentration, and urine acidification Assessed in early morning urine sample

NOVEL		
Marker	**Function**	**Application**
Kidney Injury Test (KIT)	Used when concern of comorbidity is present	Performed on urine samples and requires no additional processing at the site of collection Emerging as an alternative standard of care test to monitor dysfunction burden as well as therapy efficacy
Serum Cystatin C	Used to estimate GFR in patients with no known structural kidney disease or risk factors Supplemental confirmatory test	Not reliable in patients with a high body mass index, thyroid abnormalities, acute kidney injury, or general inflammatory conditions
Homocysteine	Increased concentration predicts diminished GFR	Maintains high predictive value after adjustments for age, smoking history, and body mass index are made to GFR
Asymmetric Dimethylarginine (ADMA)	Increased levels indicates decreased renal function	Increased levels correlate to a more aggressive course of renal damage leading to glomerular hypertension, endothelial damage, cell senescence, and salt build-up
Symmetric Dimethylarginine (SDMA)	Increased levels indicates decreased renal function	Increased levels coincide with kidney dysfunction as determined by GFR and creatinine clearance
Uromodulin	Reduced level correlates with decreased number of functioning nephrons	Glycoprotein likely engaged in the defense of tubular cells from ascending urinary tract infections, chronic pyelonephritis, and urolithiasis Patients with renal interstitial fibrosis or tubular atrophy due to CKD are shown to have reduced levels
Kidney Injury Molecule 1 (KIM-1)	Upregulated after ischemic or toxic injury of proximal tubular epithelial cells	Only detectable in dysfunctional kidneys Levels seen prior to detectable changes in GFR
Neutrophil Gelatinase Associated Lipocalin (NGAL)	Associated with innate kidney dysfunction	Predictive power for patients at higher risk for faster progression of CKD Increased levels associated with damage in the loop of Henle and distal convoluted tubule

TABLE 3 :

Stages of Chronic Kidney Disease According to Current National Guidelines [12,14,24,25,26]

Stage	GFR Descriptor	GFR Range (mL/min)	Suggested Treatment
G1*	Normal or high	≥ 90	Manage comorbid conditions and reduce cardiovascular risk
G2*	Mildly decreased	60-89	Evaluate progression potential
G3a	Mild-moderately decreased	45-59	Evaluate progression and treat complications
G3b	Moderately-severely decreased	30-44	Evaluate progression and treat complications
G4	Severely Decreased	15-29	Prepare for renal replacement therapy
G5	Kidney Failure	<15 (or receiving dialysis treatment)	Renal replacement therapy if uremia is present

*(GFR= glomerular filtration rate) *= biomarkers of kidney damage such as proteinuria, albuminuria, and abnormalities in urinary sediment or electrolytes are required for a diagnosis of stage 1 or 2 CKD.*

recommend that primary care physicians discuss those patients at risk for progression of CKD with their local nephrologist. It is highly encouraged to refer a patient during and after stage 3 CKD. Absolute referral indications are summarized in *Table 4*.

CONCLUSION

CKD continues to impact the health of a significant portion of American society even with improved detection practices. Standard biomarkers are only useful to detect significant damage, but novel biomarkers have promise for earlier detection. Additionally, estimates of GFR and creatinine must be corrected for risk factors such as race, age, and gender, which may change the indications of results. Thus, the development of more efficient and sensitive methods of early detection is essential to aid primary care physicians in their key role in slowing the progression of CKD.

Studies are currently underway to identify additional sensors for key biomarkers such as cystatin C and KIM-1. As continued research uncovers more effective detection methods, patients with early CKD may be diagnosed before the presence of symptoms, promoting long-term well-being among patients.

TABLE 4 :

Absolute referral indications [1,25,26,28]

Diagnosis of CKD from AKI that is unresponsive to initial management
Diagnosis of anemia with CKD
Presence of red blood cell casts in the urine
Management of CKD when hemoglobin <10 g per dL
CKD and refractory hypertension
Mineral and bone disorders diagnosis with CKD
Persistent abnormalities in serum potassium
Persistently elevated albuminuria with the albumin/creatinine ratio >300 mg/g
Refractory proteinuria with urinary protein/creatinine ratio >500:1000 mg/g
Recurrent nephrolithiasis
Concern for nephrocalcinosis
Preparation for renal replacement therapy

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REVIEW ARTICLE

Preventing Premature Weaning: Management Options for Common Lactation Conditions, including OMT

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KEYWORDS:

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Women's Health Issues

ABSTRACT: The benefits of breastfeeding are well established. The World Health Organization and the Centers for Disease Control and Prevention recommend that mothers breastfeed infants for at least one year, but most children are not breastfed that long because of many factors. Breastfeeding mothers face many challenges to continued breastfeeding, including medical conditions that arise during this period, such as postpartum depression and lactational mastitis. Because of a perceived lack of consistent guidance on medication safety, it can be difficult for the family physician to treat these conditions while encouraging mothers to continue breastfeeding. The purpose of the current review is to summarize and clarify treatment options for the osteopathic family physician treating lactating mothers. We specifically focus on the pharmacological management of contraception, postpartum depression, and lactational mastitis.

The benefits of breastfeeding are well established. Breastfeeding reduces mortality from infectious disease in childhood, provides a protective effect against the development of diabetes and obesity, and increases cognition.[1] The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) recommend breastfeeding for the first year of life. However, most children are not breastfed that long.[2] Breastfeeding mothers face challenges in fulfilling this recommendation, including medical conditions that can arise during this period such as postpartum depression and lactational mastitis.

Furthermore, physicians may feel uncomfortable providing pharmacotherapy, the primary therapeutic intervention for these conditions because of the risk of effects on milk supply and to the baby. Therefore, the family physician must be equipped to treat these conditions in such a way as to facilitate continued breastfeeding. Providing quality care for breastfeeding mothers can enable the maintenance of breastfeeding and result in improved outcomes for the mother and baby. The purpose of the current review is to clarify treatment options for the family physician treating lactating mothers, specifically contraception, postpartum depression, and lactational mastitis.

BARRIERS TO TREATMENT

Treatment of the breastfeeding mother presents many challenges for the physician and the most significant challenge may be lack of knowledge. In general, medical education provides little training in breastfeeding. This deficiency may arise from limited availability of references and resources regarding the pharmacologic treatment of lactating women.[3,4] Anecdotally, another deficiency may arise from limited educational hours to teach students about treatment during lactation. A Canadian study from 2014 found that three hours of training in this area improved attitudes and knowledge about breastfeeding issues in participating physicians.[5] Fortunately, educational opportunities exist for those interested in furthering their knowledge. The Academy of Breastfeeding Medicine offers excellent resources, including protocols, but it has only been in existence since 1993.[6] The WHO offers a 40-hour course on common breastfeeding issues, such as latch problems, but it does not address breastfeeding in the context of medical conditions and their pharmacologic treatment.[7]

The paucity of safety data about medication use in breastfeeding mothers can be an obstacle to effective treatment.[3] Most testing of medications is performed in healthy individuals and not in

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breastfeeding mothers. Therefore, the drug package insert or manufacturer information may have limited information for breastfeeding populations. As such, physicians may be reluctant to treat breastfeeding mothers because they lack safety information for prescribed medications.[3] This situation may prompt physicians to err on the side of caution and recommend weaning or "pump and dump" until breastfeeding is a reasonably safe option to support.[3]

Treatment of breastfeeding mothers can be challenging for mothers as well. Six weeks after delivery, mothers are typically discharged or transitioned from the care of their obstetrician. After that time, breastfeeding mothers may find themselves in a medical "no man's land" for care.[8] Pediatricians are more concerned with the weight gain and growth of the infant, so they are less likely to address breastfeeding from the maternal viewpoint.[9]

Lactation consultants are readily available in the hospital. However, after discharge, postpartum mothers may have difficulty locating a new provider and determining their insurance coverage of lactation. A discontinuity of care arises with each provider relying on another to care for mothers during this crucial time.[9] Because the family physician may assume the care of the infant and the mother after the six-week postpartum visit, family physicians are the best-positioned specialty to assist both the mother and child and, thus, should be equipped to handle concerns that arise during lactation.[9]

OVERVIEW OF GENERAL PRESCRIBING GUIDELINES

Given these barriers, it may be helpful to readjust the mindset of physicians regarding medication safety. Because no medication is without risk, the patient can be a helpful ally for the physician to determine which medications are compatible with her desires to breastfeed and her comfort level regarding risk. Therefore, physicians should listen to the patient about her comfort level with various medications and help her consider personal risks and benefits. Because of the many benefits of breastfeeding, physicians should not recommend cessation of breastfeeding unless there is evidence that a drug will be harmful to the infant.

Several factors influence the transfer of a drug from the maternal serum into breast milk: oral availability, lipid solubility, molecular weight, protein binding, and half-life.[10] During breastfeeding, drugs from the maternal bloodstream are filtered through the breast, resulting in a lower concentration in the breast milk. Therefore, when deciding which drug to prescribe, physicians usually begin with a risk/benefit comparison that includes consideration of absorption and pharmacokinetics. When weighing the risks and benefits of medication when breastfeeding, the American Academy of Pediatrics recommends assessing the mother's therapeutic need for the drug, the potential effects on lactation, the drug passage into the breast milk, the absorption, and the potential adverse effects on the infant.[10]

Fortunately, for the treatment of specific conditions, useful resources exist for physicians beyond the medication package insert.[11] LactMed is a database from the National Institutes of Health that contains detailed information about medication safety during lactation.[12] LactMed is peer-reviewed, fully referenced, and continually updated. More specifically, it provides summaries of use during lactation, data on detectable levels in breast milk, effects on the infant, effects on lactation and breast milk production, and alternative drugs to consider when necessary. Physicians can use this information to make the best medical decisions for the patient that are compatible with breastfeeding.[11] General prescribing guidelines for breastfeeding mothers are summarized in *Table 1*.

TABLE 1 :

General guidelines for prescribing medications to breastfeeding mothers

Use drugs only when unavoidable.
Consider alternative, nonpharmacological treatment when possible
Delay initiation until the infant is older when possible.
Problems may be lessened in an older infant.
Use the lowest possible dose for the shortest possible time.
Avoid drugs with long half-lives or sustained-release preparations.
Use non-gastrointestinal formulations, such as topical or inhaled/nasal medications.
Schedule doses so that the lowest amount appears in breast milk.
Consider recommending "pump and dump" if drug is indicated with no alternative.
Monitor infant reactions, such as somnolence, fussiness, gastrointestinal upset, and rash.
If the drug is commonly prescribed for infants, it is generally safe for breastfeeding mothers.
If the drug is commonly safe in pregnancy, it is often safe in breastfeeding mothers.

POSTPARTUM CONTRACEPTION

The choice of contraception method is important because it can influence a mother's ability to breastfeed. Natural family planning, the lactational amenorrhea method (LAM), barrier methods, surgical sterilization, or copper intrauterine devices (IUDs) can be used during the postpartum period,[13] but the current review will focus on pharmacologic hormonal medications. One of the primary treatment considerations for contraception is the potential for hormonal methods to disrupt milk synthesis.[13] Because a variety of hormonal changes after birth are necessary for the onset of milk production, initiation of hormonal contraception before lactation is established can be a problem.[13, 14] Breastfeeding is generally well established by four to six weeks after birth, but this timing can vary.[13] Physicians should consider the breastfeeding goals of the mother, the number and timing of wanted pregnancies, previous birth control methods and results, and partner satisfaction with the birth control method. Many mothers use LAM for contraception, and this method is approximately 98% effective for the first six months after birth if mothers adhere to the method closely.[14] Alternative methods to LAM should be discussed at or before six

months after birth in women who choose LAM initially.

Hormonal methods may be used in place of LAM. The WHO and CDC have slight variations in their recommendations, but in general, patients should remain abstinent for 6 weeks after birth for healing.[13] Because of limited interference with the breast milk supply, progesterone-only birth control methods can be safely used at any time after six weeks, such as progesterone-only oral medication, the mini pill, or levonorgestrel-releasing IUDs.[14] However, research suggests that the levonorgestrel IUD may be associated with a shorter duration of breastfeeding when placed immediately after birth.[13] No adverse effects on breastfeeding have been reported when the IUD is placed four to six weeks after birth or later.[13] Progesterone-only options have the least impact on breast milk supply.[13] However, estrogen-containing products are an option after breastfeeding is well established. Combined oral contraceptives (COCs), which contain estrogen and progesterone, have a risk of decreasing breast milk supply, especially with older pills that have higher estrogen levels than current products. Because of the potential to interrupt milk supply before the establishment of breastfeeding, COCs should definitely not be started earlier than six weeks after birth.[15] For COC use between 6 weeks and 6 months after birth, there is limited data about their use.[15] Therefore, during that time frame, the risk of diminished breast milk supply must be weighed against the advantage of protecting against unplanned pregnancy. These factors must be considered with the mother so that she can make an autonomous and informed decision. Beyond six months after birth, COCs in general can be safely used.[15] Contraceptive options for breastfeeding mothers are summarized in *Table 2*.

TABLE 2 :

Contraceptive options for the breastfeeding mother by postpartum period

Less Than 6 Weeks	6 Weeks to 6 Months	Greater Than 6 Months
Abstinence[13]	**Lactational amenorrhea method[14]** **Progesterone-only medication[14]** **Levonogestrel-releasing intrauterine device[14]** **Combined oral contraceptive (with risk/benefit analysis)[15]**	**Progesterone-only medication[14]** **Levonogestrel-releasing intrauterine device[14]** **Combined oral contraceptive[15]**

POSTPARTUM DEPRESSION

Postpartum mood disorders are common in the first six months after delivery and occur in up to 15% of women.[16] Nonpharmacologic therapy is preferred when symptoms are mild to moderate.[17] Physicians should not avoid pharmacologic treatment when indicated since there is little evidence of serious adverse effects in infants exposed to antidepressants in breast milk.[18] Therefore, the antidepressant that is most effective for the mother should be considered.[18]

There is no widely accepted algorithm for treatment of this condition and prescribing patterns are inconsistent.[16,19] Breastfeeding support for those with postpartum depression (PDD) involves individualized therapy, medication dose titration with close follow-up, and monitoring. Historically, PDD treatment was restricted to the use of the well-studied drug class of selective serotonin reuptake inhibitors, which are still considered to pose the least risks. Sertraline and paroxetine are considered the first-line treatment for PDD because they have virtually undetectable levels in breast milk.[18] Fluoxetine and citalopram reach higher levels in breast milk; therefore, fluoxetine should not be used during lactation.[18,19] Overall, sertraline has the best safety profile for lactating mothers with evidence of lower drug levels in breast milk and in infant serum.[19] The recommended starting dose is 25 mg for five to seven days to avoid side effects; it can be increased to 50 mg/day if indicated.[19]

Guidance for the treatment of PDD has evolved over the past decade. Currently, serotonin and norepinephrine reuptake inhibitors are also useful in the treatment of PPD. Selective norepinephrine reuptake inhibitors, such as venlafaxine, have slightly higher risks but may still be considered for treatment.[16,18] Venlafaxine is present in breast milk, but no drug-related side effects have been proven. Therefore, venlafaxine can be used with caution and close monitoring of the infant for sedation and weight gain.[19] Bupropion may be considered, but data about its effects are limited and another drug may be preferred if effective.[19] In the tricyclic antidepressant class, there is enough data to substantiate the use of nortriptyline. Nortriptyline is undetectable in infant serum and has no reported adverse events.[19] Physicians should not use doxepin because of documented adverse effects.[19]

According to Sriraman et al.,[19] "If a mother has been successfully treated with a particular selective serotonin reuptake inhibitor, tricyclic antidepressant, or serotonin-norepinephrine reuptake inhibitor in the past, the data for that particular antidepressant should be reviewed and considered as a first-line treatment if there are no contraindications." Mothers successfully treated with any of these three classes of medications during pregnancy should continue using the same medication during breastfeeding.[19] However, both mother and infant should be monitored for side effects.[19] Ultimately, drug choice is often based on successful previous treatment, and previous treatment success is the best predictor of clinical response.

Because of risks to the mother and infant, treatment of PDD is essential for the overall health of the family unit. Further, because of its positive effect on neurodevelopment and other benefits, breastfeeding should be continued during PDD treatment. Breastfeeding mothers need to work closely with their physicians when taking psychotropic medications since some medications have better safety profiles than others. In nearly all cases, an effective medication can be safely taken while continuing to breastfeed. Pharmacological options for treatment of PPD for breastfeeding mothers are summarized in *Table 3*.

TABLE 3 :

Pharmacological options for treatment of postpartum depression in breastfeeding mothers

First-Line Treatment	Use with Caution	Limited Data for Safe Use	Avoid
Sertraline[11]	Venlafaxine[16,18]	Bupropion[19]	Fluoxetine[18]
Paroxetine[11]			Citalopram[18]
Nortriptyline[19]			Doxepin[19]

LACTATIONAL MASTITIS

Lactational mastitis (LM) is the most common issue experienced by postpartum women.[20] Worldwide, it has an incidence of 15%-20% in the first six months after birth.[21]

This condition is characterized by inflammation of the mammary tissues, and this inflammation may be the result of a bacterial infection or from a noninfectious source.[1, 20] Clogged mammary ducts, prolonged breast tissue engorgement, milk stasis, nipple damage, and maternal fatigue have been cited as predisposing factors for LM.[9,22-25] The effects of LM on a breastfeeding mother should not be underestimated and may lead to premature weaning. The condition is quite painful and the suggestion to continue nursing or pumping through it can be difficult to unsustainable for some mothers. This can be complicated by the potential sequelae of a breast abscess, which can discourage nursing mothers from continuing to breastfeed.[26, 27] Therefore, prompt and effective treatment is imperative, and if symptoms are mild and less than 24 hours in duration, supportive care is indicated. When LM develops into a bacterial infection or acute maternal illness, antibiotics are indicated. Empiric therapy antibiotic choice should be directed at common microorganisms, such as Staphylococcus aureus, including methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus, and Escherichia coli.[28] Physicians should also check local patterns for community prevalence of MRSA. Dicloxacillin, amoxicillin-clavulanic acid, or cephalexin should be considered for empiric therapy for non-severe infections without risk factors for MRSA.[20,21,29] When allergies to these antibiotics are present, physicians should use clindamycin.[28] When MRSA is strongly suspected or confirmed, physicians should use trimethoprim-sulfamethoxazole or clindamycin.[30, 31] To safely use trimethoprim-sulfamethoxazole, the infant must be at least one month old; and if a severe infection is present, vancomycin can be used.[28, 32] If there is a lack of response to treatment, a culture of breast milk can guide further treatment selection. In general, the length of therapy should be 10-14 days to reduce the risk of relapse.[30, 31] Antibiotic options for treatment of LM for breastfeeding mothers are summarized in *Table 4*.

TABLE 4 :

Antibiotic options for treatment of lactational mastitis in breastfeeding mothers

First-Line Agents	To Treat for MRSA	For Allergies to First-Line Agents
Dicloxacillin[28]	Trimethoprim-sulfamethoxazole[28]	Progesterone-only medication[14]
Amoxicillin-clavulanic acid[28]	Clindamycin[20]	Levonogestrel-releasing intrauterine device[14]
Cephalexin[28]		Combined oral contraceptive[15]

Abbreviation: MRSA, methicillin-resistant Staphylococcus aureus.

OSTEOPATHIC MANIPULATIVE TREATMENT IN LACTATION ISSUES

Lactation problems can be treated with an osteopathic manipulative treatment approach. However, statistical data supporting the efficacy of such treatment of the breast for lactation issues, as well as treatment for the infant for breastfeeding and suckling issues is limited.[33,34] Treatment goals should include decreasing the biomechanical restrictions that are limiting or affecting normal blood flow and lymphatic return.[35] When there is a lack of proper tissue motion, disease processes can develop. Restoring normal motion will result in improved circulation, improved nervous function, decreased venous/lymphatic stasis, improved drug delivery, and optimal breast function.[35] Osteopathic techniques that improve localized motion of the breast and the surrounding tissue include lymphatic techniques, myofascial release, balanced ligamentous tension, and counterstrain. As an example, a lymphatic treatment protocol would begin by removing tissue tension around the proximal return into the subclavian vein by performing a release of the thoracic inlet.[35,36] From there, lymphatic treatment generally moves from a proximal to a distal position and may include techniques around the shoulder, such as pectoral lift/traction, shoulder myofascial release (the Chila method), and scapular release in a lateral recumbent position. Treatment of diaphragm restriction is important for any lymphatic protocol, so a thoracic pump technique may be used as a finishing technique.[35] Autonomic and hormonal balance can be achieved by such techniques as occipitoatlantal decompression/release to affect vagal influences and rib raising or balanced ligamentous tension to T1-T7 to affect upper extremity and thoracic viscera sympathetic innervation.[36] Finally, anterior and posterior thoracic or rib tender points should be diagnosed and treated with counterstrain. In general, osteopathic treatment of the breast tissue itself is avoided. If it is performed, treatment should be done by someone with expertise and with a chaperone.

CONCLUSION

Although the benefits and recommendations for breastfeeding are clear, few breastfeeding mothers can comply with the recommended one-year duration of sustained breastfeeding. Family physicians are ideally placed to help breastfeeding mothers cope with the challenges of breastfeeding, such as managing LM and related issues. For instance, regarding contraception use while breastfeeding, progesterone only options or IUDs have the least possible impact on milk supply and should be considered after the first six weeks of abstinence.[13,14] After six months, COCs can safely be used.[15] Between six weeks and six months postpartum, physicians should weigh the risks versus benefits of the use of COCs.[15] For the treatment of PPD during lactation, sertraline and paroxetine are first-line treatment,[18] but certain serotonin-norepinephrine reuptake inhibitors and tricyclic antidepressants can also be used. For individual cases, previous successful treatment with an antidepressant should prompt its use for PPD if it has been demonstrated to be safe during lactation.[19] For the treatment of LM, dicloxacillin, amoxicillin-clavulanic acid, or cephalexin are first-line antibiotic agents.[20,21,28] When MRSA is suspected or confirmed, treatment with trimethoprim-sulfamethoxazole or clindamycin should be initiated if the infant is at least one month old.[28,30,31] Ultimately, appropriate treatment of these common problems encountered by lactating mothers can ease their breastfeeding journey. By providing their support, physicians can help prevent premature weaning and increase the well-being of mothers and infant health.

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REVIEW ARTICLE

The Ehlers–Danlos Syndromes

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KEYWORDS:

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hEDS

Hypermobility

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ABSTRACT: An Osteopathic Family Physician will encounter hypermobile patients. Hypermobility is a symptom of many of the subtypes of the Ehlers Danlos Syndromes (EDS). With the updated classification system (the 2017 International Classification of the Ehlers-Danlos Syndromes) it is important for the osteopathic family physician to become familiar with the EDS patient. The classification system identifies 13 subtypes of EDS.[1] Of these 13, 12 have a recognized genetic basis. Hypermobile EDS (hEDS) has a clinical diagnosis criteria checklist (Figure 1, page 29). There is opportunity for the osteopathic family physician community to help diagnose and treat the EDS population. This article seeks to have the osteopathic family physician become familiar with the Ehlers-Danlos Syndrome, and provide an overview of all of the subtypes of EDS, including hEDS and discusses signs, symptoms, and risks associated with the syndrome.

BARRIERS TO TREATMENT

During the course of a career, the osteopathic physician will encounter a patient with hypermobility. It is important for the osteopathic family physician to become familiar with the difference between hypermobility and Ehlers Danlos Syndrome (EDS). Hypermobility may be localized to a specific joint or can be generalized throughout many joints. Based on the accompanying symptoms, the osteopathic family physician can become familiar with when to differentiate between the hypermobile patients verses the patient with EDS. This article seeks to introduce all of the subtypes of EDS and the symptoms that the patient may present to the osteopathic family physician with.

The Ehlers Danlos Syndromes are a type of connective tissue disorders that have certain defining features.[1] EDS has recently been reclassified into 13 subtypes, (the 2017 International Classification of the Ehlers-Danlos Syndromes) and includes a type, which is diagnosed clinically.[1] In 2018, an EDS spectrum connective tissue disorder was identified by a genetic mutation found in four individuals.[2] This subtype is due to an AR mutation in the AEBP1 gene, and these patients have joint hypermobility, skin elasticity, osteoporosis and poor wound healing.[2] The importance of identification of a specific type of EDS is imperative, as there are a multitude of risks, some life threatening, that need proper surveillance.[1] This article seeks to give the family physician an overview of each type of EDS, so that the osteopathic family physician can become familiar with each subtype and learn when to look for EDS in the hypermobile patient.

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CLASSICAL EDS

Classical EDS (cEDS) is thought to be of an Autosomal Dominant (AD) pattern of inheritance is associated with skin issues and hypermobility (major criteria) as well as minor criteria (including but not limited to easy bruising, soft skin, hernias, or family history).[1] Skin is especially fragile and "wound healing is poor."[3] The Beighton score (which measures joint hypermobility on a 9 point scale) for patients with cEDS is "5 or greater."[4] This type of EDS is diagnosed clinically and by genetic testing. The "pathologic variant in COL5A1, COL5A2, or (less commonly) COL1A1" is seen.[3]

CLASSICAL-LIKE EDS

Classical-like EDS (clEDS) patients typically have mutations in the TNXB gene, in an autosomal recessive (AR) manor.[1] The mutations seen in the TNXB gene are varied and their symptoms are usually more severe than seen in the hypermobile EDS (hEDS) subtype.[5] clEDS patients present with manifestations of skin issues and hypermobility, and this subtype can be challenging to differentiate from hEDS.

CARDIAC-VALVULAR EDS

Patients with cvEDS typically present with "severe progressive cardiac-valvular problems"[1] as well as musculoskeletal and skin issues. Cardiac-valvular EDS (cvEDS) has an Autosomal recessive inheritance pattern.[1] "The biallelic COL1A2 mutations result" in

absence of a collagen chain. This subtype of EDS is considered rare.[6] "Absence of confirmatory genetic findings does not exclude the diagnosis as specific types of mutations may go undetected by standard diagnostic molecular techniques."[1]

VASCULAR EDS

Vascular EDS (vEDS) is inherited in an AD pattern of inheritance and is thought to be caused by a mutation in the COL3A1 or COL1A1 gene, which affects collagen.[1] "vEDS is typified by a number of characteristic facial features (eg, large eyes, small chin, sunken cheeks, thin nose and lips)."[7] It is important for clinicians to recognize a vEDS patient, as proper surveillance needs to be followed. vEDS patients are at risk for arterial or organ rupture.[8] vEDS patients may present with aneurysms or bleeding issues.[8] Since vEDS is a rare disease with serious co morbidities and complications, genetic testing is recommended.[10] "Absence of confirmatory findings does not exclude diagnosis, as specific types of mutations may go undetected by standard diagnostic molecular techniques."[1] The importance of working with a Geneticist and Cardiovascular specialist in these cases are imperative.

ARTHROCHALASIA EDS

Arthrochalasia EDS (aEDS) is an AD genetic disorder, thought to be caused by a mutation in the COL1A1 or COL1A2 gene.[1] The main features of this disorder are hypermobility, skin issues, congenital hip dysplasia, and muscle weakness.[11] "In addition to fragility of skin and joint laxity that are observed in other forms of EDS," patients usually have distinct facial features.[11] "As patients get older the hypotonia decreases and the facial features become less distinct."[11]

DERMATOSPARAXIS EDS (DEDS)

Dermatosparaxis EDS (dEDS) is an AR genetic disorder involving the ADAMTS2 gene.[1] Patients with this rare subtype of EDS present with extremely lax skin.[1] Some features seen in dEDS patients include a swelling on the forehead at birth, skin fragility, ocular issues, and umbilical hernia.[12] Patients with dEDS are also at risk for "visceral complications due to connective tissue fragility."[12]

KYPHOSCOLIOTIC EDS (KEDS)

Patients with Kyphoscoliotic EDS (kEDS) have genetic mutations in PLOD1 or FKBP14 genes in an AR fashion.[1] These patients present with skin fragility, hypermobility and kyphoscoliosis.[13] The kyphoscoliosis can be severe, causing organ compromise.[13] Patients with genetic variations in the FKBP14 gene can also have hearing impairment.[1]

BRITTLE CORNEA SYNDROME (BCS)

Patients with BCS have an AR pattern of inheritance and present with ocular issues.[1] The genes affected in this subtype are usually ZNF469 or PRDM5.[1] Sometimes a blue sclera is seen, and ocular issues could be serious (including potential for ocular rupture or blindness).[6] Hearing impairment and hearing loss can also be seen in patients as well.[6]

SPONDYLODYSPLASTIC EDS (SPEDS)

Patients with the rare subtype spEDS, have inherited a probable AR genetic variant in B4GALT7, B3GALT6, or SLC39A13.[1] Two major criteria, (i.e., short stature muscle hypotonia, and bowing of limbs plus characteristic radiographic abnormalities) and three minor criteria (skin hyper extensibility, pes planus, motor or cognitive delay, and osteopenia are suggestive for spEDS.[14] "Confirmatory molecular testing is obligatory to reach a final diagnosis."[1]

MUSCULOCONTRACTURAL EDS (MCEDS)

mcEDS patients present with cranial facial features, and musculoskeletal features that are inherited in an AR fashion with a genetic basis in CHST14 and DSE.[1] Contractures and finger/hand characteristics are seen.[6] Cardiovascular, urological, ophthalmological and auditory issues are also seen in mcEDS patients.[6] This is in addition to the cutaneous symptoms seen in the EDS. Absence of these confirmatory findings does not exclude the diagnosis of mcEDS, as specific types of mutations may go undetected by standard diagnostic molecular techniques."[1]

MYOPATHIC EDS (MEDS)

Patients with myopathic EDS (mEDS) have "muscle weakness, hypotonia, myopathy, and connective tissue symptoms."[6] mEDS is caused by defects in genes for collagen or affecting the muscles and is thought to have a genetic basis in the COL12A1 gene possibly AR or AD in inheritance pattern.[1] Many patients report severe hypotonia or contractures.[6] The skin scarring typical of EDS patients can also be seen. Absence of these confirmatory findings does not exclude the diagnosis, as specific types of mutations may go undetected by standard diagnostic molecular techniques."[1]

PERIODONTAL EDS (PEDS)

Periodontal EDS is characterized by severe periodontal disease, as well as hypermobility and skin issues.[6] These type of patients were found to have bone loss even after restorative surgery for patients' periodontal disease.[15] The severe periodontal disease seen in this disorder starts in childhood or adolescence.[16] The disease is passed AD and in the C1R or C1S genes.[1] Specific craniofacial features including long, prominent nose, short philtrum and triangular face has been observed.[16]

HYPERMOBILE EDS (HEDS)

hEDS, "probably the most common EDS subtype",[17] has a criteria associated with diagnosis as per the 2017 International Classification of the Ehlers-Danlos Syndromes (EDS)[1] *(see Figure 1)*. No distinct genetic mutation has been found to cause this type, as of publication. Research is ongoing on the genetic basis, and is

thought to have an AD form of inheritance.[1] Many patients with hEDS present with joint hypermobility, skin issues, fatigue and chronic pain.[17]

Many patients with hEDS can also have a variety of co-morbidities.[18] Along with hypermobility, there could be chronic pain, cardiovascular issues, psychological issues, bone mass issues and GI symptoms.[18] Since there is a variety of symptoms the osteopathic family physician should become familiar with the presentation.

For the osteopathic family physician who sees pediatric patients, hEDS and hypermobility may be difficult to diagnose for children, as children are typically more flexible and hypermobile than adults.[18] It is particularly important to rule out a HCTD in children, as some of the signs and symptoms of hEDS overlap with other connective tissues disorders.[18]

Since there are many systems that the hypermobile patient may present with, it is important the osteopathic family physician become familiar with EDS. There is a chance that the osteopathic family physician may be the first provider the EDS patient contacts. Due to the diverse nature of the EDS and hEDS in particular, a multidisciplinary approach to the EDS patient including Primary Care, pain management, Cardiology, Physical Therapy, Occupational Therapy, Psychology, and Geneticist (if applicable) is needed.[17] Since EDS affects many systems of the body, and there is currently no genetic basis of hEDS it is important for the osteopathic family physician to become familiar with the Ehlers Danlos Syndromes as they may be the first one to recognize some of the signs, symptoms and co-morbid conditions seen in this condition. The osteopathic family physician may also be the one in contact with a geneticist to assist in the identification of a specific subtype. The importance of the diagnosis and proper surveillance for the EDS patient is imperative. With further research, the osteopathic family physician can be helpful in treating an EDS patient. Literature and education is needed for providers to become aware of this condition and this article seeks to be an introduction for the osteopathic family physician to all the EDS subtypes.

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FIGURE 1:

Diagnostic Criteria for Hypermobile Ehlers-Danlos Syndrome (hEDS)[19]

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The International Consortium on Ehlers-Danlos Syndromes & Related Disorders
In Association with The Ehlers-Danlos Society

Diagnostic Criteria for Hypermobile Ehlers-Danlos Syndrome (hEDS)

This diagnostic checklist is for doctors across all disciplines to be able to diagnose EDS

Distributed by The Ehlers Danlos Society.

Patient name: _____ DOB: _____ DOV: _____ Evaluator: _____

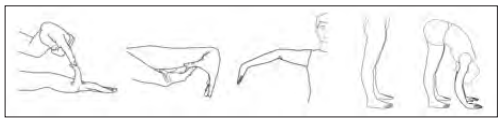
The clinical diagnosis of hypermobile EDS needs the simultaneous presence of all criteria, 1 ***and*** 2 ***and*** 3.

CRITERION 1 – Generalized Joint Hypermobility

One of the following selected:

- ☐ ≥6 pre-pubertal children and adolescents
- ☐ ≥5 pubertal men and woman to age 50
- ☐ ≥4 men and women over the age of 50

Beighton Score: _____/9



If Beighton Score is one point below age- and sex-specific cut off, two or more of the following must also be selected to meet criterion:

- ☐ Can you now (or could you ever) place your hands flat on the floor without bending your knees?
- ☐ Can you now (or could you ever) bend your thumb to touch your forearm?
- ☐ As a child, did you amuse your friends by contorting your body into strange shapes or could you do the splits?
- ☐ As a child or teenager, did your shoulder or kneecap dislocate on more than one occasion?
- ☐ Do you consider yourself "double jointed"?

CRITERION 2 – Two or more of the following features (A, B, or C) must be present

Feature A (five must be present)

- ☐ Unusually soft or velvety skin
- ☐ Mild skin hyperextensibility
- ☐ Unexplained striae distensae or rubae at the back, groins, thighs, breasts and/or abdomen in adolescents, men or pre-pubertal women without a history of significant gain or loss of body fat or weight
- ☐ Bilateral piezogenic papules of the heel
- ☐ Recurrent or multiple abdominal hernia(s)
- ☐ Atrophic scarring involving at least two sites and without the formation of truly papyraceous and/or hemosideric scars as seen in classical EDS
- ☐ Pelvic floor, rectal, and/or uterine prolapse in children, men or nulliparous women without a history of morbid obesity or other known predisposing medical condition
- ☐ Dental crowding and high or narrow palate
- ☐ Arachnodactyly, as defined in one or more of the following:
  (i) positive wrist sign (Walker sign) on both sides, (ii) positive thumb sign (Steinberg sign) on both sides
- ☐ Arm span-to-height ratio ≥1.05
- ☐ Mitral valve prolapse (MVP) mild or greater based on strict echocardiographic criteria
- ☐ Aortic root dilatation with Z-score >+2

Feature A total: _____/12

Feature B

- ☐ Positive family history; one or more first-degree relatives independently meeting the current criteria for hEDS

Feature C (must have at least one)

- ☐ Musculoskeletal pain in two or more limbs, recurring daily for at least 3 months
- ☐ Chronic, widespread pain for ≥3 months
- ☐ Recurrent joint dislocations or frank joint instability, in the absence of trauma

CRITERION 3 – All of the following prerequisites MUST be met

1. Absence of unusual skin fragility, which should prompt consideration of other types of EDS
2. Exclusion of other heritable and acquired connective tissue disorders, including autoimmune rheumatologic conditions. In patients with an acquired CTD (*e.g.* Lupus, Rheumatoid Arthritis, etc.), additional diagnosis of hEDS requires meeting both Features A and B of Criterion 2. Feature C of Criterion 2 (chronic pain and/or instability) cannot be counted toward a diagnosis of hEDS in this situation.
3. Exclusion of alternative diagnoses that may also include joint hypermobility by means of hypotonia and/or connective tissue laxity. Alternative diagnoses and diagnostic categories include, but are not limited to, neuromuscular disorders (*e.g.* Bethlem myopathy), other hereditary disorders of the connective tissue (e.g. other types of EDS, Loeys-Dietz syndrome, Marfan syndrome), and skeletal dysplasias (*e.g.* osteogenesis imperfecta). Exclusion of these considerations may be based upon history, physical examination, and/or molecular genetic testing, as indicated.

Diagnosis: _____

v9

CLINICAL IMAGE

Palpitations in a Young, Healthy Female

Maricel Dela Cruz, DO, MPH, FAWM[1];Megan Gillespie, DO[2]; Seng Yue Joshua Foong, DO, MS[2]; Robert Danoff, DO, MS, FACOFP, FAAFP[2]

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A 26-year-old African American female presented to her family medicine office with a recent pre-syncopal event that occurred early that day. Symptoms included intermittent dizziness, lightheadedness, and palpitations of a two-hour duration. She otherwise had a negative review of systems.

During the previous two months, the patient had experienced similar but less severe episodes of dizziness, lightheadedness and palpitations, which self-resolved within thirty minutes. The patient denied having an increased caffeine or other stimulant intake, and denied any alleviating factors.

An office electrocardiogram *(Figure 1)* was performed. Based upon the patient's symptoms of near syncope in conjunction with an abnormal ECG demonstrating a shortened PR interval, less than 0.12 seconds, and an associated slurred upstroke of the QRS complex, known as a delta wave, the patient was sent for an immediate assessment in the emergency department.

Upon presentation to the emergency department, the patient was found to be afebrile with a blood pressure of 112/72, heart rate regular at 102 beats per minute, and a respiratory rate of 22 breaths per minute with a pulse oximetry on room air at 98%. Physical examination revealed a patient in mild distress, but otherwise awake, alert, oriented, well developed, and well nourished. She was normocephalic and atraumatic with moist mucous membranes and normal tympanic membranes bilaterally. Pupils were equal, round and reactive, extraocular eye movements intact, no nystagmus, and no proptosis. No palpable neck masses were noted. Heart rate was regular and no murmurs, rubs, or gallops were appreciated. Lungs were clear to auscultation without wheezing, rales, or rhonchi. Abdomen was soft, non-tender, and without distention. Distal pulses were strong and symmetric bilaterally without peripheral edema. No exanthems, petechiae, or ecchymosis was noted.

In addition to the office ECG that accompanied the patient upon presentation to the emergency department, two department ECG's were performed *(Figures 2 and 3)*. Significant department diagnostic results included a negative urine pregnancy test, and unremarkable complete blood count, complete metabolic panel and thyroid stimulating hormone, and troponins. Her chest radiograph was unremarkable.

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FIGURE 1:

Office electrocardiogram

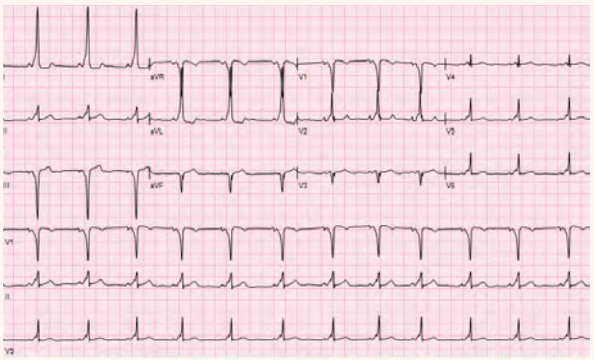


FIGURE 2:

ER Department ECG 1

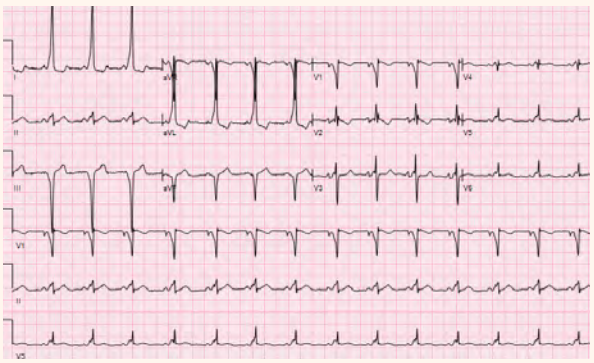
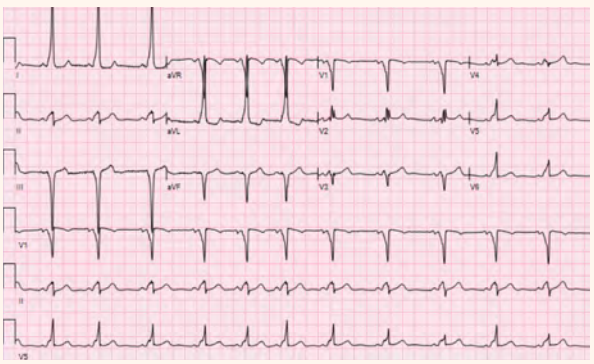


FIGURE 2:

ER Department ECG 2



QUESTIONS:

1. **What is the diagnosis based upon the electrocardiogram (ECG) findings?**

   A. Brugada syndrome
   B. Left bundle branch block
   C. Wolff-Parkinson-White pattern
   D. Myocardial infarction
   E. First degree atrioventricular block

2. **What is the most serious complication of this condition?**

   A. Sudden cardiac death
   B. Heart failure
   C. Syncope
   D. Cardiomyopathy
   E. Palpitations

3. **What is the preferred long-term management of this condition to reduce frequency and intensity of symptoms and decrease mortality?**

   A. Oral doses of verapamil
   B. Oral doses of amiodarone
   C. Mitral valve replacement
   D. Catheter ablation
   E. Digoxin

ANSWERS:

1. **What is the diagnosis based on ECG findings?**

   Correct Answer:
   C. Wolff-Parkinson-White Pattern

Wolff-Parkinson White (WPW) pattern is ventricular pre-excitation with characteristic ECG findings including a short PR interval, less than 0.12 seconds, and slurring of the QRS upstroke, known as a delta wave, which results in a widened QRS complex, lasting greater than 0.10 seconds.[1,2,3]

Incorrect answers:

Brugada syndrome has a characteristic ECG finding of coved ST elevation in leads V1-V3 followed by a negative T wave and is caused by sodium channelopathy.[4]

Left bundle branch block has a characteristic ECG with widened QRS, greater than 120ms, tall broad or notched "M-shaped" R waves in lateral leads (I, V5-6) and deep S waves in right precordial leads (V1-3).[5]

First degree AV block is defined as prolonged PR interval on ECG greater than 200ms.[6]

2. **What is the most serious complication of this condition?**

   Correct Answer:
   A. Sudden cardiac death (SCD)

For an individual with WPW syndrome, there is an estimated annual 0.25% per year risk of SCD, or about a 4% lifetime risk of SCD.[7] SCD in WPW syndrome occurs in most cases because of the rapid ventricular response due to conduction from the AP during atrial fibrillation that deteriorates into ventricular fibrillation.[2,3]

Incorrect answers:

Palpitations and syncope are symptoms associated with WPW, not complications. Cardiomyopathy is not a complication of WPW syndrome. Heart failure is an infrequent complication of WPW syndrome that is not as serious as sudden cardiac death.[2,3]

3. **What is the preferred long-term management of this condition to reduce frequency and intensity of symptoms and decrease mortality?**

   Correct Answer:
   D. Catheter ablation

In patients with WPW syndrome, non-pharmacologic therapy, namely catheter ablation of the accessory conduction pathway, is the current first-line therapy to decrease frequency and severity of symptoms and prevent SCD.[1,2,3,8]

Incorrect answers:

Oral verapamil, amiodarone, and digoxin are contraindicated in patients who have atrial fibrillation (AF) as these AV nodal blocking agents could enhance conduction over the AP and cause increased ventricular contraction, thus increasing the risk to the patient for developing ventricular fibrillation or SCD.[2]

HOSPITAL COURSE OF PATIENT

The 26-year-old female was admitted to the hospital for her symptoms and concerning changes on ECG. The patient was evaluated by cardiology and had successful treatment of her Wolff-Parkinson White (WPW) syndrome with catheter ablation by an electrophysiologist. The ablation was successful in reducing her symptoms of intermittent dizziness, lightheadedness, and palpitations. Key components of the successful outcome included appropriate ECG screening and interpretation by her family physician, appropriate emergent referral to the emergency department, and expedited evaluation by cardiology, resulting in ultimate management via catheter ablation by an electrophysiologist.

DISCUSSION

The patient described above presented to her primary care physician's office with a relatively common chief complaint of pre-syncopal symptoms including dizziness, lightheadedness, and palpitations. These symptoms are frequently brought to the family physician's attention for evaluation by patients of all

ages, gender, race, and with various medical comorbidities. The differential diagnosis for pre-syncope and syncopal symptoms is broad, and includes reflex mediated, cardiac causes, orthostatic hypotension, neurologic causes, endocrinologic causes, psychiatric disorders, and drug induced.[9,10] Of note, patients found to have a cardiac cause of pre-syncope or syncopal symptoms had a higher annual mortality rate.[9,10] Initial evaluation of patients with similar chief complaint of pre-syncope with lightheadedness, dizziness, and palpitations as the presented young female in this case report should include a thorough history and physical exam and ECG in the family physician office setting. Initial screening ECG can aid in assessing for dysrhythmia as source of symptoms. A differential of dysrhythmias or ECG changes that can cause pre-syncope or syncopal symptoms includes atrial fibrillation, atrial flutter, supraventricular tachycardia, pre-excitation syndromes including Wolff-Parkinson White, atrioventricular block, bifascicular block, sinus pause, Brugada syndrome, prolonged QT, ventricular dysrhythmias, bradyarrhythmias, arrhythmogenic right ventricular dysplasia, myocardial infarction, etc.[1,2,11]

WOLFF-PARKINSON WHITE SYNDROME

Wolff-Parkinson White (WPW) syndrome is the cardiac diagnosis responsible for the pre-syncopal symptoms and ECG changes noted of the patient presented in this case report. WPW syndrome is defined as the combination of ventricular pre-excitation pattern on ECG in combination with symptoms of tachyarrhythmia.[12] The characteristic ECG findings of short PR interval, less than 0.[12] seconds, and an associated slurred upstroke of the QRS complex, referred to as a delta wave, are known as the WPW pattern and can be observed in this patient's above ECGs in *Figure 1, 2, and 3*.[1,12,13] This distinct WPW pattern with a delta wave noted on ECG was first identified and documented by Drs. Louis Wolff, John Parkinson, and Paul White in 1930 in a group of patients with the common symptom of intermittent episodes of palpitations or pre-syncope.[13] The prevalence of this distinct WPW pattern is found on ECG in about 0.1-0.3% of the general population.[12,14,15]

WPW PATHOPHYSIOLOGY

The WPW pattern on ECG is the result of conduction via an accessory pathway (AP), known as the Bundle of Kent. This bundle arises from the abnormal differentiation of myocardial tissue during embryonic development.[16] This congenital AP tract forms abnormal conductive cardiac tissue between the atria and ventricles, thus providing an alternative tract for conduction, leading to early ventricular depolarization.[1,16]

In contrast to the AV node, the AP has rapid anterograde and retrograde conduction without rate limitation.[1] This rapid, bidirectional conduction of the electrical stimulus between the atria and ventricles causes ventricular depolarization immediately after atrial depolarization. The result is a pre-excitation pathway that contributes to reentrant tachycardia.[1] This more rapid electrical stimulus conduction over the AP is the reason for the classic ECG findings of the WPW pattern consisting of a short PR interval (less than 0.12 seconds) and slurring of the QRS upstroke (known as a delta wave), and a widened QRS complex lasting more than 0.10 seconds.[1,2,3]

Accessory pathway (AP) and WPW pattern are typically found at random in young healthy patients without structural cardiac abnormalities. However, there have been infrequent case reports of familial WPW and WPW associated with Ebstein's anomaly, as well as structural changes from myocardial ischemia.[17,18]

WPW CLINICAL PRESENTATION

About 60% of patients with WPW pattern on ECG experience symptoms, with the remaining 40% being asymptomatic.[3] Symptoms associated with WPW syndrome include palpitations, episodic lightheadedness or dizziness, pre-syncope, syncope, and, rarely, sudden cardiac death (SCD).[2,3] While SCD can infrequently be the presenting symptom, especially in children or young adults, the overall incidence of SCD in patients with WPW is estimated to be about 0.15-0.39%.[3,19]

For an individual with WPW syndrome, there is an estimated annual 0.25% per year risk of SCD, or about a 4% lifetime risk of SCD.[7] SCD in WPW syndrome occurs in most cases secondary to the rapid ventricular response due to conduction from the AP that deteriorates into ventricular fibrillation. High risk factors for SCD include male sex, age less than thirty years, history of atrial fibrillation, family history of WPW, prior syncope, and presence of congenital heart disease, in particular Ebstein's anomaly.[20]

WPW MANAGEMENT

Treatment of WPW is dependent on hemodynamic stability, severity of symptoms, assessed risk for sudden cardiac death, and location of patient presentation.[2] If a patient presents as an outpatient to the non-acute setting of a primary care physician office, is hemodynamically stable, and has intermittent mild symptoms or if the patient is asymptomatic with incidentally discovered WPW pattern on ECG, a history and physical with non-invasive testing are useful for initial risk-stratification of SCD. Supplemental non-invasive testing includes ECG, ambulatory electrocardiography monitoring, echocardiogram, and exercise stress testing. Electrophysiology study should also be considered to risk-stratify for potential arrhythmic events. The loss of conduction over the AP during exercise testing, or sporadic loss of pre-excitation during ambulatory monitoring indicate lower risk of arrhythmias.[2,3] Asymptomatic WPW pattern patients are determined to be at higher risk for SCD if the shortest pre-excited RR interval is less than 250 milliseconds in AF, if the patient has a history of symptomatic tachycardia, if the patient is found to have multiple AP during an electrophysiology study, or if the patient has a history of Ebstein's anomaly.[2,3,12]

In WPW pattern patients deemed to be at low risk for SCD, close monitoring and observation as an outpatient without further treatment is reasonable.[2,8] In patients with chronic WPW syndrome, or frequent cumbersome symptoms, catheter ablation of the accessory pathway is the current first-line approach to decrease frequency and severity of symptoms as well as to prevent SCD.[1,2,3,8] Catheter ablation is indicated in asymptomatic patients both at higher risk for SCD and in low-risk asymptomatic patients with WPW pattern whose employment requires the treatment of pre-excitation, such as pilots.[2,3] As in this case report, referral of the

patient with WPW syndrome who presents to the primary care office to the emergency department can expedite the evaluation and testing and determination of treatment plan.

In the acute setting, such as in the emergency department, if a patient with known WPW pattern presents with a tachyarrhythmia with a pulse but is hemodynamically unstable, cardioversion is indicated.[2] In hemodynamically stable patients with acute tachyarrhythmia such as supraventricular tachycardia (SVT) or atrioventricular reentrant tachycardia (AVRT) caused by the AP in WPW, pharmacologic agents designed to slow ventricular heart rate and cease arrhythmias are commonly used in the acute setting.

Vagal maneuvers such as the Valsalva maneuver or carotid massage and/or intravenous (IV) adenosine are recommended initial treatments. If vagal maneuvers and IV adenosine are unsuccessful, then IV verapamil, diltiazem or beta blockers are indicated in a hemodynamically stable patient with symptomatic tachyarrhythmia.[2] If these pharmacologic treatments fail to control the ventricular heart rate or cease the arrhythmias, synchronized cardioversion is indicated.[2] It should be noted that in patients who have atrial fibrillation (AF) with pre-excitation, IV or oral verapamil, diltiazem, beta-blockers, IV adenosine, IV amiodarone, and IV digoxin are contraindicated. The reason: these AV nodal blocking agents could enhance conduction over the AP and cause increased ventricular contraction, thus increasing the risk to the patient for developing ventricular fibrillation or SCD.[2] Instead, IV ibutilide or IV procainamide are used to restore sinus rhythm in hemodynamically stable patients with pre-excited AF.[2]

Once the tachyarrhythmia of the symptomatic patient is restored to sinus rhythm and stabilized in the acute setting, the ultimate treatment of WPW syndrome is catheter ablation of the accessory pathway.[1,2,3,8]

CONCLUSION

Although rare, Wolff-Parkinson White pattern and WPW syndrome patients can initially present in the primary care setting. Thus, it is important to be aware this differential diagnosis when evaluating patients with a chief complaint of palpitations, lightheadedness, dizziness, pre-syncope, or syncope. It is also crucial that primary care physicians are able to recognize the characteristic ECG findings for WPW pattern consisting of a short PR interval, less than 0.12 seconds, and slurring of the QRS upstroke (delta wave), resulting in a widened QRS complex.

Family physicians can and should assess for these ECG findings, especially since approximately 40% of patients with WPW pattern are asymptomatic.

Further vigilance to these ECG patterns are especially important in young patients with a history of intermittent palpitations or pre-syncope, in patients with a history of Ebstein's anomaly, and in patients with a familial history of WPW. Referral of WPW pattern or WPW syndrome patients by primary care physicians to cardiology/electrophysiology should be prompt for further evaluation and treatment planning.

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

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CALENDAR OF EVENTS

JANUARY 10 – 12, 2020
Iowa ACOFP 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 23 – 26, 2020
MSACOFP - Annual Winter Family Medicine Update
Independence, Missouri
www.msacofp.org

JANUARY 30 – FEBRUARY 2, 2020
TOMA Midwinter Conference
Irving, Texas
www.txosteo.org

FEBRUARY 6 – 8, 2020
MAOFP Winter Family Medicine Update
Boyne Falls, Michigan
www.maofp.org

FEBRUARY 7 – 9, 2020
MOA Midwinter Symposium
Portland, Maine
www.mainedo.org

MARCH 18 – 19, 2020
ACOFP Congress of Delegates
New Orleans, Louisiana
www.acofp.org

MARCH 19 – 22, 2020
ACOFP '20 Annual Convention and Scientific Seminars
New Orleans, Louisiana
www.acofp.org

APRIL 4, 2020
Arizona ACOFP Annual Meeting & Social
Scotsdale, Arizona

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

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

JUNE 5 – 7, 2020
Maine ACOFP
Rockport, Maine
www.mainedo.org

JUNE 10 – 14, 2020
Toma/Texas ACOFP
San Antonio, Texas
www.txacofp.org

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

JULY 29 – AUGUST 2, 2020
FS ACOFP Family Medicine Update + Convention
Orlando, Florida
www.fsacofp.org

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

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

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

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

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.

PATIENT EDUCATION HANDOUT

Lupus

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

Systemic lupus erythematosus (commonly called Lupus) is a disease in which your body's own immune system attacks many different organs such as the heart, kidneys, lungs, blood, brain, skin and reproductive organs. The number of organs involved decides how bad the Lupus is and this is different for every person. Some people with Lupus have symptoms all the time while others only sometimes. A flare-up is when the disease, along with symptoms, gets worse. Flare-ups happen unexpectedly and can last for a short or long time. When you experience a flare-up you may require treatment changes to help control symptoms.

WARNING SIGNS OF A FLARE-UP

- Lupus diagnosed before the age of 25 increases the risk of flare-ups.
- Previous disease of your kidneys, blood vessels, or brain increases the risk of flare-ups.
- Your doctor may do blood tests during a flare-up.
- The onset of mild Lupus flare-up symptoms includes fever, a red or purple rash on the face that resembles the shape of butterfly wings (malar rash) and muscle aches.
- Moderate Lupus flare-up symptoms include chest pain and swelling in the wrists or other joints.
- Severe Lupus flare-up symptoms include kidney problems that can lead to protein in the urine and chemical imbalances in the blood.

PREVENTING A FLARE-UP

- Sun sensitivity can make your symptoms worse. Avoid too much time in the sun and wear sunblock with a Sun Protective Factor (SPF) above 55.
- Eating healthy and regular exercise can help prevent or reduce being tired from a flare-up.
- Avoiding tobacco will help keep your lungs and blood vessels healthy.
- Proper use of Lupus medications from your physician can help prevent a flare-up.
- As Lupus gets worse, you may need to use medications that suppress the immune system.
- Check in with your doctor every 3-4 months to talk about how you are feeling and to check laboratory tests for blood and urine.
- Call your doctor or 911 right away if you have chest pain, trouble breathing, severe headaches, or dizziness, or high fever as Lupus may lead to neurologic, kidney or cardiovascular complications or even death. In case of any emergency, you should call your doctor or 911 right away.

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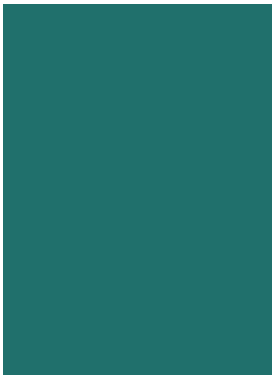
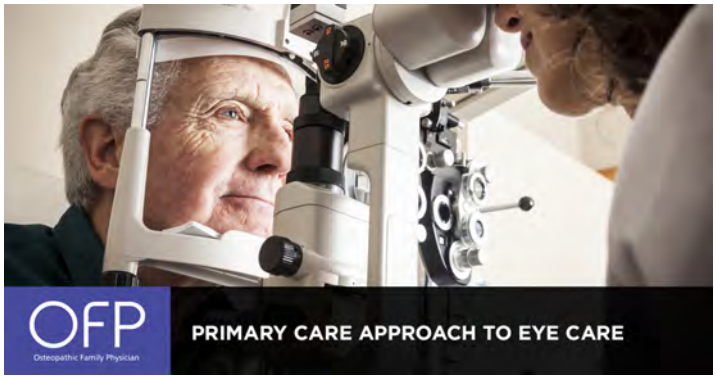
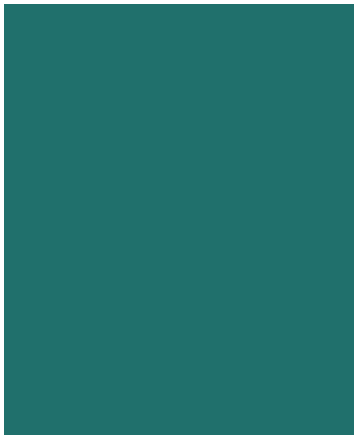
SOURCE(S): *American Academy of Family Physicians, Up To Date*







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Published six times a year, Osteopathic Family Physician (OFP) offers continuing medical education (CME) in each issue. ***Physicians may earn two hours of AOA Category 1-B CME credit per issue*** by reading the designated article and successfully completing a corresponding quiz.

OFP quizzes are located in our eLearning Center at www.acofp.org.

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To receive credit, members are required to complete the CME quiz within one year of the issue's publication date, receive a grade of 70 percent or better, and submit it to ACOFP. OFP is the ACOFP's official peer-reviewed journal featuring original research, case reports and articles about preventive medicine, managed care, osteopathic principles and practices, pain management, public health, medical education and practice management.

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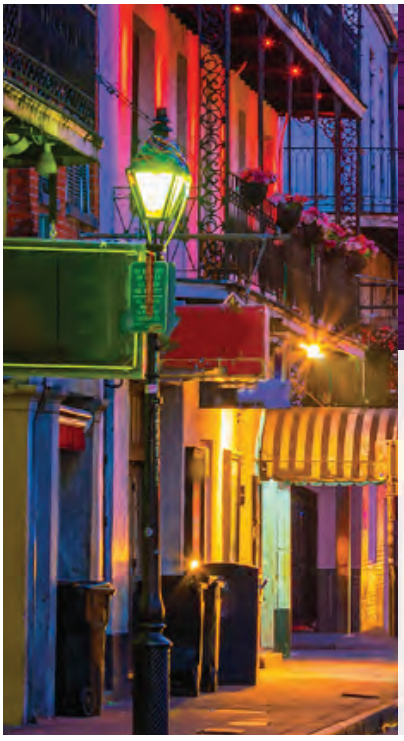

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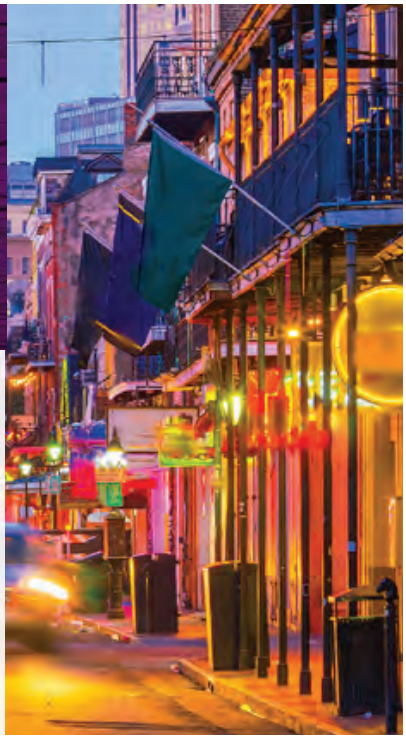
MARCH 18-19:
Congress of Delegates

MARCH 19-22:
Convention



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