OFP

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

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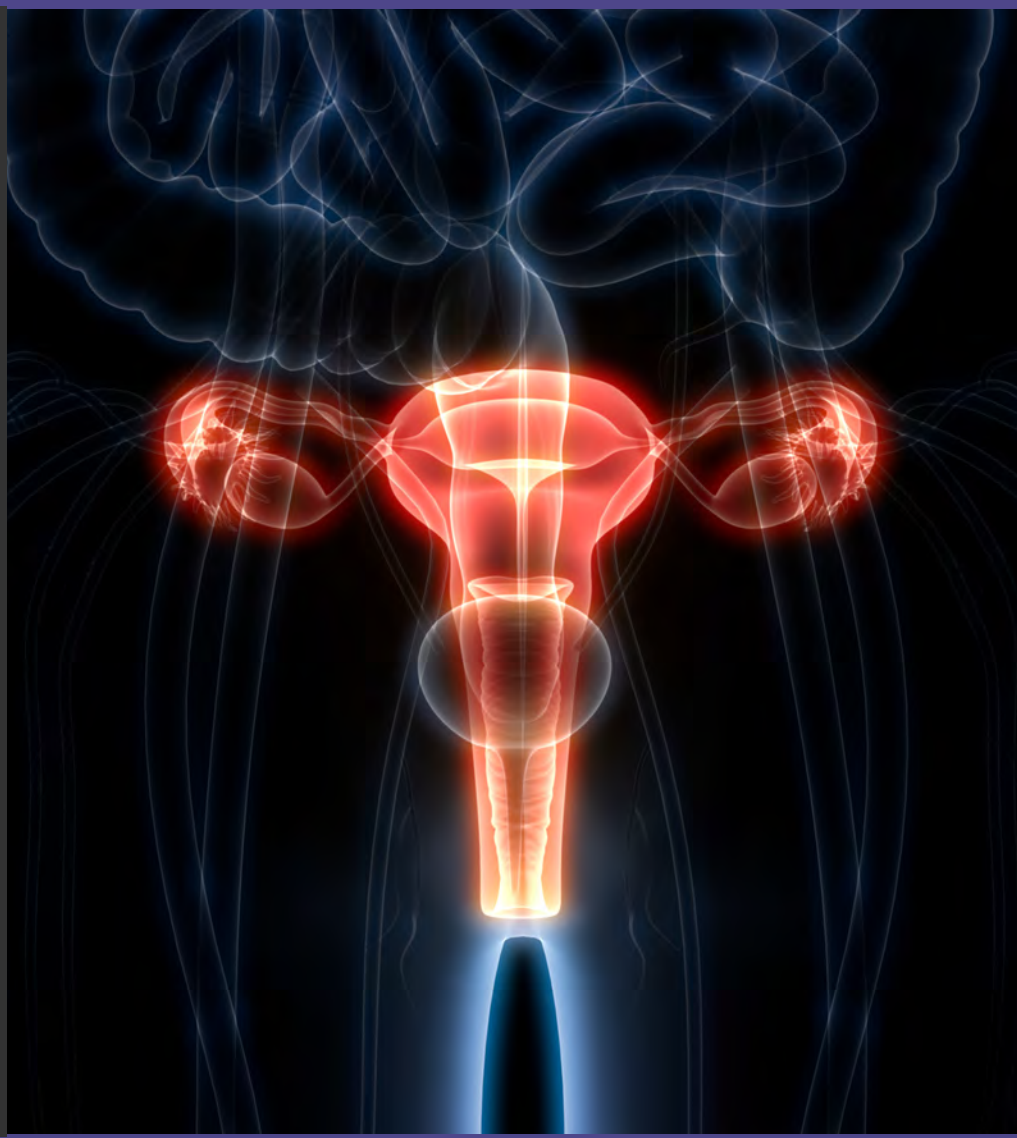

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EXAMS	LOCATIONS	POSTMARK DATE
Family Medicine / OMT Certification / OCC Cognitive Exam	**Electronic Testing** Regional Sites September 28, 2019	**April 1, 2019** *Late fee through June 1, 2019*
Family Medicine / OMT Certification / OCC Performance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

ACOFP SEEKS NOMINEES FOR 2020 - 2021 BOARD OF GOVERNORS

ACOFP is **now accepting nominations** for the positions of *Governor*, *Resident Governor*, and *Student Governor* for the 2020 - 2021 ACOFP Board of Governors. These positions will be elected by the ACOFP Congress of Delegates in March 2020 according to the Nominating Committee process.

Please visit acofp.org to submit your nominations by August 15, 2019.

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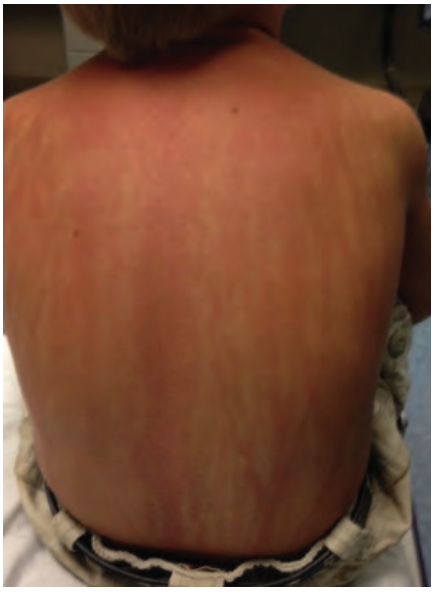

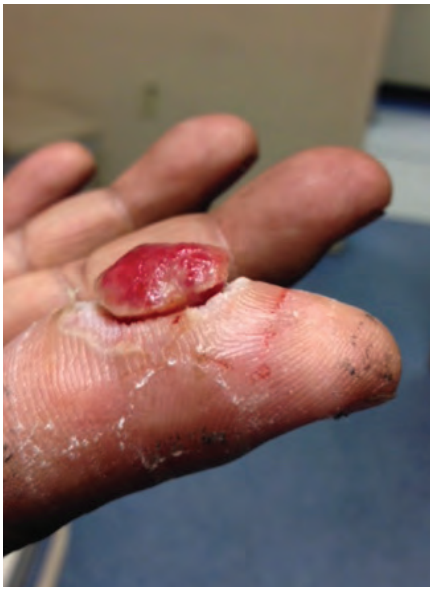

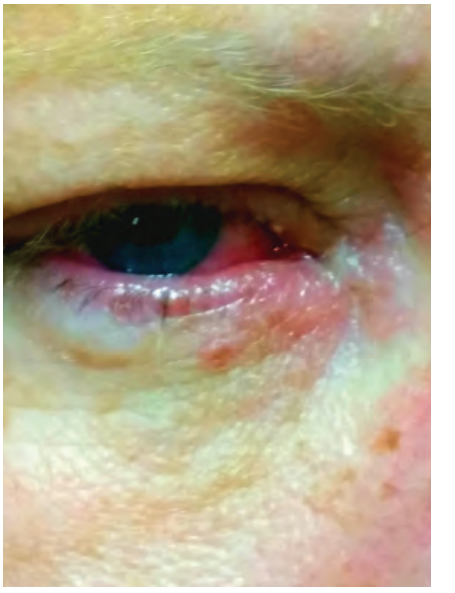

OSTEOPATHIC FAMILY PHYSICIAN

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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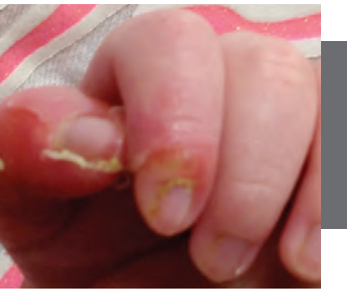

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EDITOR'S MESSAGE

Students of Family Medicine

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

Welcome to another issue of *Osteopathic Family Physician*.

The past month, I have been honored to be a part of a graduation ceremony for over 150 new Osteopathic physicians. Over 65% were going into Primary care and nearly a quarter of the graduates were going into Family Medicine – I'm hoping a wonderful group of new readers for the OFP! Being around students interested in Osteopathic Family Medicine and working with Family Medicine residents has helped me remain optimistic about the future of Osteopathic Family Medicine and allowed me to meet an incredible cohort of individuals with talents above and beyond taking another test. One of those students of Family Medicine submitted the poem below and I felt it to be appropriate for this journal. In the end, we are all students of Family Medicine – enjoy the learning!

AT THE CROSSROADS OF EMPATHY

I walk into the room,
"what brings you in?"
attempting to box
the pain I see
in your eyes
into a 30-minute encounter

and there
I feel it instantly,
the heaviness you carry inside
but where, where do I put it down?

you apologize to me
for taking up my time,
for not holding back the tears
and for a second,
I realize, how truly
insignificant
are my own worries
and my own fears

as I begin to tell you,
don't be sorry, this is exactly
what my time belongs to
from the moment
I took an oath to
help you heal you

you feel ashamed for your pain
and I feel hypocritical
telling you not to be ashamed
when I don't tell
my own heart
the same

you finally find the
words to speak
you tell me
you lost your son
when all your life
you thought it would be
the other way around

I tell you death
doesn't care about age
and still I can't save you
from the aching
from the rage

so all I do is listen

and I listen:
I place this stethoscope
on your chest, and I can hear your heart
pounding, telling me—
"I just don't know
where to put it down.
please tell me,
where I can put it down"

By Anusha Abbas, OMS III
College of Osteopathic Medicine of the
Pacific Western University of Health Sciences

FROM THE PRESIDENT'S DESK

Pathways to Certification

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

The osteopathic family medicine profession is currently experiencing a period of change that can understandably be confusing to everyone. ACOFP has received questions and comments from members and the Board is relaying those concerns to AOBFP and AOA. ACOFP will keep members up to date on new developments regarding certification and exam opportunities. ACOFP aims to instill the osteopathic philosophy by emphasizing the importance of choosing osteopathic recognition in residency programs and the pathway to certification that includes OMT.

ACOFP EXAM OPTIONS

ACOFP is committed to being the go-to resource for osteopathic family medicine residency programs and those that have Osteopathic Recognition (OR). To help programs meet the AOA and ACGME basic standard or OR requirements, ACOFP has the following programs available. As you'll see below, we have enhanced our program offerings to provide "one stop shopping" for residency programs that have OR with the ability to have residents just take one formative assessment and meet two standards. ACOFP is also committed to maintaining our osteopathic distinctiveness. All programs include some level of OPP/OMM content.

In-Service Exam Plus

The In-Service Exam Plus (ISE+) is a new formative exam that will fulfill the AOA basic standard and ACGME requirements. It also includes an osteopathic component that will fulfill ACGME's OPP/OMM formative assessment requirement for programs that have OR.

In-Service Exam

The traditional In-Service Exam (ISE) is a formative exam that will fulfill the AOA basic standard and will fulfill ACGME's formative assessment requirement for programs without OR.

CORTEx

The Clinical Osteopathic Recognition Training Exam (CORTEx) is a formative stand-alone OPP/OMM exam that will fulfill the Osteopathic Recognition ACGME requirement. This formative assessment is perfect for OR programs in other osteopathic specialties or for those that only offer the ABFM In-Training Exam. *(See chart on the next page for an exam comparison to help navigate options available to residency programs.)*

AOBFP CERTIFICATION

While the ACOFP does not manage the American Osteopathic Board of Family Physicians (AOBFP) certification, we have been actively involved in conversations with the AOBFP and AOA, who do oversee it. We remain committed to being an advocate for current and future AOBFP diplomates to ensure high-quality certification that is both streamlined and cost-effective. ACOFP and AOBFP have had terrific conversations over the last year and we are very excited about changes coming to the AOBFP certification process. While details will be announced by AOBFP and AOA, the AOBFP has developed a plan to offer an early entry exam for residents. There will also be two pathways for initial certification with an option to take the OMT practical exam or not. While we hope all residents take the practical exam to demonstrate their abilities and commitment to the practice of OMM, this will be optional. AOBFP also works closely with us on the In-Service Exams to ensure a strong and positive alignment with the board certification.

The key take-away on this subject is that positive change is coming soon and positive collaboration with AOBFP and AOA is helping this become a reality.

ACOFP BOARD OUTREACH HUB PROGRAM

The ACOFP Board of Governors has created a hub program in an effort to connect with members, assigning a Governor to an area of the country. They will contact residency program directors (PDs) across the country, provide accurate information about certification, clarify ACOFP's exam resources and options available residents, and answer questions that may help residency PDs make exam decisions. The Board also aims to instill osteopathic philosophy and potentially engage residents to remain committed to the same.

Each Governor is also responsible for communicating with the ACOFP Resident Council members in their geographical area. The Resident Council members can then forward information on to residents. Next, the Governors will contact medical schools in their hubs through ACOFP Student Chapter leadership so they are aware of the new hub program and know who on the Board can serve as a resource to them. As often as possible, the Governors will attend local student functions such as monthly student chapter meetings, state meetings, white coat ceremonies, NOM week and more. Since many students have not yet declared their specialty, Governors will highlight positive aspects of family medicine, osteopathic philosophy, and the practice of OMT.

The last goal of the hub structure is to establish a connection with new physicians. ACOFP recognizes the importance of developing a network of mentorship with physicians who are in the first few years of practicing family medicine. The Governors will be available to provide information about ACOFP opportunities, such as the New Physician Program and Committee participation, CME resources, and recertification options.

COMMITTEES TO HELP STUDENTS, RESIDENTS & PDS

ACOFP has created Committees to provide information and mentorship to students, residents and program directors regarding ACOFP exams, certification and continuing education. Also, residents can reach out to the ACOFP Resident Council for peer-to-peer support. The mission of the Committee on Osteopathic Recognition & Development (CORD) & Program Directors strives to maintain and advance the process of osteopathically-focused graduate medical education and increase the number of programs that enhance in this process. This is accomplished by supporting the development of quality osteopathic family medicine residency training programs through its basic standards, program director training, the In-Service exams, CORTEx and program reviews.

The Preceptorship Committee has been charged with identifying and educating high-quality preceptors to promote excellence and innovation with third and fourth-year osteopathic medical students to enhance their interest in osteopathic family medicine.

FOUNDATION SUPPORTS RESIDENTS

The ACOFP Education and Research Foundation recently created the Resident AOBFP Initial Certification Fund to support the ongoing participation of osteopathic family medicine residents in the American Osteopathic Board of Family Physician's (AOBFP) Initial Certification Exam. Grants will be made available from this fund for unreimbursed examination fees and airfare to qualifying residents taking the exam.

Continuing to have osteopathically trained residents become AOBFP certified is critically important to growing our profession and creating a bright future for the next generation of osteopathic physicians. Terms and conditions will be posted on the website in the coming months.

To support this critically important certification initiative, the Education and Research Foundation has set an ambitious annual goal of $400,00 and has already raised $150,000. Gifts of any size are greatly appreciated to help reach this target!

Visit acofpfoundation.org to learn more and donate.

The ACOFP Board hopes that these resources provide the information needed to clarify the certification and exam processes for all members, but of course, please contact ACOFP at any time with questions.

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

SEE CHART FOR REQUIREMENTS FULFILLED BY EACH EXAM.	**ACOFP IN-SERVICE EXAM PLUS (ISE+)**	**CORTEx**	**TRADITIONAL ACOFP IN-SERVICE EXAM (ISE)**	**ABFM IN-TRAINING EXAM (ITE)**
Meets AOA's Basic Standard for Residency Training in Osteopathic Family Medicine and Manipulative Treatment	X		X	
Meets ACGME's Basic Requirement	X		X	X
Meets ACGME's Osteopathic Recognition Requirement	X	X		
Number of exam questions	**265** (190 ISE & 75 OPP/OMM)	**75** (OPP/OMM)	**220** (190 ISE & 30 OPP/OMM)	**245** (Approximately)

Please see the ACOFP website for exam pricing.

RESEARCH ARTICLE

Coaching, Health, and Movement Program (CHAMPS) Taught by Medical Students: A Didactic Curriculum and Program Analysis

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KEYWORDS:

Disease Prevention and Wellness

Medical School Curriculum

Medical Students

Nutrition

Pediatric Obesity

ABSTRACT:

Purpose: The prevalence of pediatric obesity is increasing in the United States. While physicians are in a unique position to address pediatric obesity, nutrition education and counseling is insufficiently addressed in medical school curriculums. To fill this gap, one Midwest medical school piloted CHAMPS (Coaching, Health, and Movement Program with Students), a program where medical students learn about pediatric obesity and nutrition and coach families toward healthier lifestyle goals.

Method: This study evaluated the effectiveness of a 7-hour didactic curriculum and looked at changes in medical student knowledge, bias, and mentorship skills. The cohort included 35 first- and second-year medical students who completed a pre-test and two post-tests—one post-test after the didactic training and one after the 6-8 week coaching program with a family.

Results: After both the didactic curriculum and coaching sessions, medical students demonstrated statistically significant improvement in knowledge and mentorship skills with regards to pediatric obesity and nutrition. Medical students also reported feeling more confident answering questions and coaching families on healthy lifestyle choices. Medical student bias was unchanged after our intervention.

Conclusion: The CHAMPS program represents a promising experience for medical students and fills a gap in the traditional medical school curriculum.

INTRODUCTION

The prevalence of pediatric obesity, as defined by sex-specific BMI at or above the 95th percentile, was 18.9% or 13.7 million children between the ages of 2-19 years. Hispanics (25.8%) and African Americans (22.0%) were disproportionally affected.[1] Additionally, obesity prevalence was 18.9% among children and adolescents between 2-19 years in the lowest income group compared to 10.9% in the highest income group. Physicians are in a position to help guide patients and families toward healthier lifestyles, preventing obesity and decreasing morbidity. In 2013, several national societies issued guidelines for physicians to play a more active role in this public health concern. Recommendations included calculating the BMI (a screening tool for obesity) at each visit, informing patients of their BMI, advising lifestyle changes aimed at lowering BMI, and having regular conversations about healthy meals and exercise at each visit.[2] A 2014 study of over 5,000 participants in the National Health and Nutritional Examination Survey determined that patients are more likely to engage in lifestyle changes if physicians initiate conversations about their weight and health status. A meta-analysis completed in 2013 found that increased physician counseling and discussion during a patient encounter resulted in increased weight loss and better health outcomes.[2]

Unfortunately, nutrition education is lacking in the traditional medical school curriculum, leaving graduating physicians with less skills to address this topic in practice. The National Academy of Science (NAS) produced the Nutrition Education in U.S. Medical Schools report in 1985. It concluded medical students need a minimum of 25 hours of nutrition instruction over four

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years to be adequately prepared to address patient concerns. However, students were only receiving an average of 19 hours over four years.[3] One 10-year research study between 1999-2009 found that 62%-73% of medical schools were not meeting the minimum suggested hours by NAS.[3] With less than twenty-five hours of required nutrition education at graduation, new resident physicians cannot expect to address nutrition concerns of patients or be competent to provide advice.

Kansas City University of Medicine and Biosciences (KCU) is one medical school located in Kansas City, Missouri hoping to address this gap in nutrition education and pediatric obesity. The school offers an innovative program called Score 1 for Health, which provides free medical screenings by supervised medical students and practitioners to low-income students at community schools. The Score 1 for Health team piloted CHAMPS in 2010 with a grant from the Health Care Foundation of Kansas City. Students under the age of 18 were identified at Score 1 health screenings or referred by physicians as having a BMI 95th percentile for age and sex and likely to benefit from a healthy lifestyle program. The pilot mentorship program was first conducted at local schools and involved group classes with a registered dietician and registered nurse. In 2015, CHAMPS was redesigned to be a partnership program between one medical student and one family; first- and second-year medical students at KCU were paired with families to mentor and discuss healthy nutrition and exercise options. In addition to facilitating wellness for family participants, the program aimed to enhance medical students' nutrition knowledge, increase preparedness with mentorship skills, and reduce negative bias.

To be a CHAMPS mentor, a 7-hour didactic training is completed prior to working with families. An example curriculum is detailed in *Table 1*. This curriculum incorporates a variety of teaching methodologies: lecture, question-and-answer sessions, mock training sessions, and review sessions. The goal is for medical students to gain a foundation in nutrition topics and be prepared to convey this knowledge to families. The medical students guide the families using recommendations adapted from the "5-4-3-2-1 Go!" program created by the Consortium to Lower Obesity in Chicago Children (CLOCC). These were first launched as a mass-media campaign and counseling program in 2009 and later evaluated as a promising intervention in a 2011 community trial.[4] It recommends the following daily goals for children and families: consume 5 servings of fruits and vegetables and 3 servings of low-fat dairy, drink 4 servings of water, experience at most 2 hours of screen time, and engage in at least 1 hour of physical activity (at least 3 times per week). Topics discussed in the didactic curriculum include: appropriate vocabulary, structuring and organizing sessions, facilitating the creation of a family-centered goal, barriers to effective coaching, motivational interviewing skills, relationship skills, and staying motivated. After completion of the 7-hour training session, medical students implement their skills during weekly 2-hour sessions with an assigned family for 6-8 weeks.

In this study, we sought to determine if this curriculum (created by an interdisciplinary team of medical doctors, registered dieticians, registered nurses, and program coordinators at KCU) was effective in improving medical student knowledge and mentorship skills. Knowledge about pediatric obesity and nutrition and mentorship skills to convey this knowledge were two skills to be obtained from CHAMPS curriculum. We also evaluated if intrinsic biases of medical students changed over the course of the program.

TABLE 1:

Example CHAMPS curriculum

NAME OF SESSION	DELIVERY OF SESSION (SUGGESTED)	DESCRIPTION OF SESSION	TIME OF SESSION
"Childhood Obesity: What Can We Do?"	MD/DO with specific interest in primary care	Background information about BMI, definition of obesity, history of obesity, social determinants of health, and current issues in the United States.	1 hour, Day 1
CHAMPS Background	Registered Dietician/Registered Nurse (RD/RN) or MD/DO	History of Score 1 for Health and the program, family-centered goals and treatment strategies.	1 hour, Day 1
CHAMPS Coaching Advice	Prior CHAMPS medical students who have completed the training and program	Medical students discuss their experience with CHAMPS, question and answer session.	30 minutes, Day 2
Nutrition Knowledge and Anticipatory Guidance	RD/RN/MD/DO or MEd	Specific content of knowledge and anticipatory guidance that will be presented to families at sessions.	1 hour, Day 2
Nutrition Coaching and Review	RD/RN/MD/DO or MEd	Considerations in coaching, finding motivation, overcoming barriers, leading a coaching session, appropriate language, reviewing knowledge and reviewing coaching strategies.	2 hour, Day 2
Mock Training Session	Medical Student, RD/MD/DO/ RN, Program Coordinator, Practice Interpreter	Medical students are paired and enter room with mock family and interpreter, example scenario occurs, medical students switch, allotted time for feedback.	1 hour, Day 3

Allocated Time for Questions and Breaks –30 Minutes
6-8 Week Program: After completing the 7-hour training session, 1-hour per week is spent with a family (including the referred child/children) addressing a family-centered goal.

METHODS

Survey Design

We evaluated our CHAMPS curriculum with first- and second-year medical students from Kansas City University of Medicine and Biosciences. Students were given a survey and asked to complete it three separate times: (1) before the completion of the CHAMPS 7-hour didactic session, (2) after the completion of the CHAMPS 7-hour didactic session, and (3) after the completion of the 6-8 week sessions with families. These were each titled (1) pre-test, (2) post-test #1, and (3) post-test #2, respectively.

The survey was 23 questions divided into two sections: 13 multiple-choice questions (Section 1) and 10 Likert-style questions *(Section 2)*. Knowledge multiple-choice questions focused on definitions of pediatric obesity, common nutrition vocabulary and concepts, and components of the "5-4-3-2-1 Go!" model. Multiple-choice mentorship skill questions focused on developing family-centered goals, leading coaching sessions, having appropriate language, developing relationships with families, and answering challenging questions from families. The Likert-style questions evaluated knowledge, mentorship skills, and biases. Bias questions evaluated how medical students perceive patients and families with obesity, what factors have caused obesity, and how patient care may be affected by bias.

The survey was qualitatively validated using both face and content validity. A group of 3 students (past CHAMPS participants) and 2 faculty members were asked to evaluate for ease of use and evaluate each question for clarity and readability. Each question was also evaluated for relevance, accuracy, and breadth of knowledge. Questions that did not meet each of these criteria were either dropped (two questions) or rewritten (three questions). Another separate group of 4 CHAMPS participants and 2 faculty members evaluated the revised survey for face and content validity using the factors described above. The final instrument incorporated revisions based on both validity screens. The instrument was approved as part of the overall study plan by Kansas City University of Medicine and Biosciences IRB.

Participant Selection

First- and second-year medical students were first informed about CHAMPS through the Pediatrics Club and Score 1 for Health Organization. Participants were also emailed about the opportunity after orientation. Students filled out an application and were asked to discuss their interest in pediatrics and their goal to promote health and wellness in the community. In order to be chosen as a mentor, the medical student had to be in good academic standing with the Dean's Office and agree to the program's time commitment. A total of 35 students were chosen and agreed to participate in one of three cohorts in September 2017, December 2017, or March 2018.

Data Analysis

Section 1: Multiple Choice Questions

One-Way Repeated Measures ANOVA was completed using ANOVA: Single Factor on Excel to check for differences in the mean multiple-choice test scores across the three-survey series. If significance was found, we utilized a Bonferroni correction in Excel to determine which pairs showed significant differences. The correction of our p-value allowed us to account for the number of pairwise comparisons ran by the Repeated Measures ANOVA. Lastly, we used t-test: Two-Sample Assuming Equal Variances in Excel to compare pre-test and post-test #1 data from excluded participants with data from included participants to account for possible non-response biases.

Section 2: Likert Scale Questions

We analyzed the data for the Likert Scale Questions of the survey using the non-parametric Friedman Test for repeated-measures in Excel. If significance was found, we utilized subsequent Wilcoxon Signed-Rank tests in R to determine which paired survey iterations showed significant differences. The dependent variables chosen for this study were Bias, Knowledge, and Mentorship Skills. A Likert-type scale was utilized to measure items associated with each variable.

RESULTS

Out of 36 students who began the study, 25 completed the three-survey series (pre-test, post-test #1, and post-test #2), resulting in a 69.44% response rate. Results from 11 students were excluded from the final data analyses due to partial completion of the three-survey series. There were 5 students who completed only pre-test, and 6 students completed only pre-test and post-test #1. Characteristics of participants are detailed in *Table 2*.

TABLE 2:

Characteristics of participants in the CHAMPS program

CHARACTERISTIC	NUMBER(S)
Gender	
Male	14 (56%)
Female	11 (44%)
Year in School	
1st	22 (88%)
2nd	3 (12%)

Multiple Choice Test Scores—Before and After Didactic Course, Family Sessions

Prior to beginning the 7-hour didactic course, participants averaged a score of 63.69% (13.96%, n = 25) on Section 1 of the pre-test. After completion of the didactic curriculum, the same participants scored an average of 82.46% (9.29%, n = 25) on Section 1 of post-test #1. After participating in the 6-8 week program with their paired families, the participants scored an average of 78.77% (11.16%, n = 25) on Section 1 of post-test #2. One-Way Repeated Measures ANOVA showed significant variation

TABLE 3:

Section 1 – Multiple-choice test scores for pre-test and post-tests

GROUP	MEAN SCORE (SD)*	MEAN % (SD)*	MEDIAN	MINIMUM	MAXIMUM
Pre-Test (n=25)	8.28 (1.81)	63.69% (13.96)	8	8	8
Post-Test #1 (n=25)	10.72 (1.21)	82.46% (9.29)	11	11	11
Post-Test #2 (n=25)	10.24 (1.45)	78.77% (11.16)	10	10	10

Total correct responses scored from 0 to 13 correct (0 – 100%). *Repeated Measures ANOVA showed significant variation amongst pre-test, post-test #1, and post-test #2 performance, $F(2, 72) = 18.27$, $p < 0.001$. Bonferroni correction showed difference between pre-test and post-test #1 ($p < 0.001$), as well as between pre-test and post-test #2 ($p < 0.001$).

amongst pre-test, post-test #1, and post-test #2 performance, $F(2, 72) = 18.27$, $p < 0.001$. Subsequent Bonferroni correction with adjusted alpha level of 0.017 revealed that the mean score for pre-test was significantly different than the mean score for post-test #1 ($p < 0.001$). It also revealed that the mean score for pre-test was significantly different than the mean score for post-test #2 ($p < 0.001$). No statistically significant difference was found between the mean scores of post-test #1 and post-test #2 ($p = 0.80$). Results for the Section 1 of surveys are presented in *Figure 1 and Table 3*.

In order to account for possible non-response bias due to removing data of participants that did not fully complete the three-survey series, we conducted additional analyses to compare results of included versus excluded participants. First, we compared the mean pre-test score of participants who only completed the pre-test with the mean pre-test score of participants who completed the entire three-survey series. The independent-samples t-test comparing the two showed no significant difference in pre-test performance of Included participants (Mean = 63.69%, SD = 13.96%, n = 25) and pre-test performance of Excluded participants (Mean = 67.13%, SD = 13.36%, n = 11); $t(34) = 2.03$, $P = 0.50$. Next, we compared the mean post-test #1 of participants who only completed the pre-test and post-test #1 with the mean post-test #1 score of participants who completed the study. The independent-samples t-test comparing the two showed no significant difference in post-test #1 performance of Included participants (Mean = 82.46%, SD = 9.29%, n = 25) and post-test #1 performance of Excluded participants (Mean = 87.18%, SD = 7.94%, n = 6); $t(29) = 2.05$, p value = 0.26. Comparison is shown in *Table 4 and Table 5*.

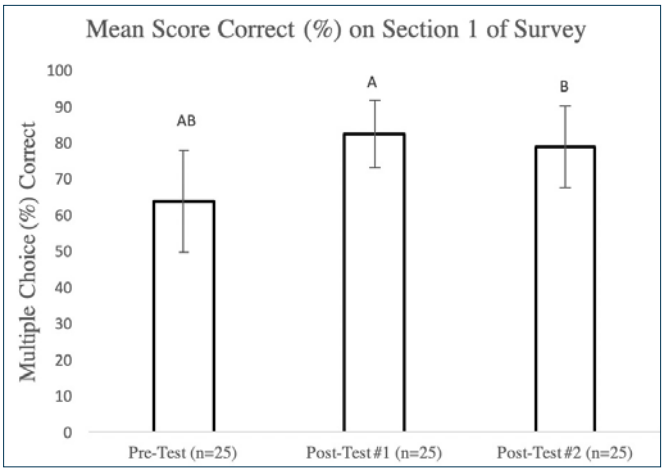
Student Agreeability Before and After Didactic Course, Family Sessions

In individual items testing for mentorship skills, non-parametric Friedman Test for Repeated-Measures showed significant variation amongst pre-test, post-test #1, and post-test #2 responses. Items with significant Friedman Test were further analyzed by Wilcoxon Signed-Rank Test, all showing differences between the pre-test and post-test #1 responses, as well as between the pre-test and post-test #2 responses. For whether "I feel confident answering questions about pediatric obesity," the Median score increased from a 3 (Neutral) in the pre-test to a 4 (Agree) in both post-test #1 and post-test #2; $X2=26.42$, $p<00001$. In addition, significance for this item was also found between post-test #1 and post-test #2 responses. For whether "I feel prepared to discuss with a family the prevalence of pediatric obesity and the importance of being healthy," the Median score increased from a 3 (Neutral) in the pre-test to a 4 (Agree) in both post-test #1 and post-test #2; $X2=25.62$, $p<00001$. For whether "I feel prepared to coach a family on healthy lifestyle choices," the Median score increased from a 3 (Neutral) in the pre-test to a 4 (Agree) and 5 (Strongly Agree) in post-test #1 and post-test #2, respectively; $X2=32.46$, $p<00001$.

In individual items testing for knowledge, significant variation was found amongst pre-test, post-test #1, and post-test #2. Further analysis showed differences between the pre-test and post-test #1 responses, as well as between the pre-test and post-test #2

FIGURE 1:

Mean Score Correct (%) on Section 1 of Survey



Mean test scores (%) (+SD) on Section 1 of survey. Statistically significant differences between groups are noted via same letters (Bonferroni correction, $p < 0.001$).

TABLE 4:

Section 1 - Multiple choice test scores, included versus excluded pre-test performance

GROUP	MEAN SCORE (SD)*	MEAN % (SD)*	MEDIAN	MINIMUM	MAXIMUM
Included Pre-Test (n=25)	8.28 (1.81)	63.69% (13.96)	8	4	12
Excluded Pre-Test (n=11)	8.73 (1.74)	67.13% (13.36)	8	6	11

Total correct responses scored from 0 to 13 correct (0 – 100%). * No significant difference between Included and Excluded pre-test performance, t(34) = 2.03, p value = 0.50.

responses. For whether "I understand the coaching strategy of 5-4-3-2-1 and how to set a goal with a family," the Median score increased from a 1 (Strongly Disagree) in the pre-test to a 4 (Agree) in both post-test #1 and post-test #2; X2=30.62, p<00001. No significant difference was shown between responses from post-test #1 to post-test #2.

In individual items testing for biases, no significant variation was found amongst pre-test, post-test #1, and post-test #2 responses. Median scores are presented in Supplemental Appendix 1, with full individual item results reported in Supplemental Appendix 2.

DISCUSSION

Given the lack of nutrition education and experiences available in United States medical schools, we sought to create a curriculum that filled this gap. We evaluated the CHAMPS curriculum based on medical student knowledge and mentorship skills before and after this intervention. With participants acting as their own controls, we can make several deductions based on the data.

Immediately following the completion of the didactic curriculum, participants demonstrated statistically significant improvement in performance on the multiple choice section of post-test #1, scoring 18.77% higher than pre-test scores. Additionally, participants continued to perform higher on the multiple choice section of post-test #2 after conclusion of the mentoring sessions with families, scoring 15.08% higher than the pre-test. It should be noted that although performance between post-test #1 and post-test #2 dropped by 3.69%, this difference was not statistically significant. This slight decrease was expected as students had been apart from the formal didactic curriculum for 6–8 weeks while mentoring their families. Furthermore, the comparable performances on both post-tests showed that knowledge and skills were neither significantly lost nor gained during the time working with families. These results show support for the applicability of our curriculum as an intervention that can solidify understanding of nutrition education over a long-term period. In addition, our survey only measured two skills (medical student knowledge and mentorship skills) gained throughout the CHAMPS experience. It is likely that medical students gained other skills and strategies that were not targeted in this survey while working with their families. To account for possible non-response bias, an additional statistical analysis was completed comparing included versus excluded participants. We were able to infer from this data that our study would not have been significantly different if all starting participants had completed the entire three-survey series.

With the agreeability questions, student's knowledge, mentorship skills, and biases were all evaluated. After completion of the CHAMPS curriculum, participants reported feeling more confident with their mentorship skills in answering questions about pediatric obesity and nutrition, discussing the prevalence of pediatric obesity, and coaching families on healthy lifestyles choices. Interestingly, there was also statistical improvement in feeling comfortable answering questions about pediatric obesity and nutrition between post-test #1 and post-test #2, which we attribute to the hands-on nature of working with real families during the family sessions. In regards to knowledge, students reported greater understanding of the coaching strategy of 5-4-3-2-1 and goal-setting with their families after the didactic portion. Our results from the agreeability questions show that participants' perceptions of their mentorship skills and knowledge were improved by completion of the didactic curriculum and were maintained, or even further improved upon, throughout the 6-8 week family sessions.

One portion of this study involved evaluating medical student bias. Research has shown that physicians and medical students both hold significant bias against obese patients compared to patients below the 95th percentile for BMI.[5,6] One study on medical student bias revealed that students showed biases in their belief, attitudes, and interactions on the basis of patient weight alone.[6] Because biases can undermine the patient-provider relationship, delay treatment, and lessen the quality of care, we decided to see if biases changed after the CHAMPS curriculum or sessions with families. Our results indicated that there was no variation in biases between any of the surveys. The fact that bias can be present and affect obese pediatric patient care was never discussed with medical students during this study. Additionally, bias was never directly addressed during the curriculum, so a lack of bias variation is not surprising. What is important to note, however, is that students did not develop increased negative bias after completion of the curriculum.

The present study does have some limitations. First, our sample size was limited to a group of 35 students completing the CHAMPS program between 2017-2018. This limits generalizability regarding knowledge and mentorship skills gained from our intervention. However, the preliminary results are very promising. Second, only medical students from KCU were included in this initial study,

and it would be beneficial to evaluate this curriculum at other institutions.

In conclusion, the CHAMPS curriculum is an effective program to improve medical student knowledge and mentorship skills based on the results from our survey. The additional 6-8 weeks working with the families provides additional opportunities for interacting with patients, including answering questions regarding pediatric obesity. Overall, this extracurricular opportunity is one way to fill a gap in nutrition education in medical school.

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Ethical Approval: *Ethical approval has been granted for this study involving human subjects. The reviewing body was the IRB Board at Kansas City University of Medicine and Biosciences. Dates of approval were July 2017-June 2019 . Reference number (via IRBNet) is [897971].*

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REVIEW ARTICLE

Fat Shaming in Medicine: Overview of Alternative Patient Strategies

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KEYWORDS:

Behavior Change

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Overweight

ABSTRACT: As the rate of obesity-related diseases rise, physicians are spending more time in their practices working to motivate patients to lose weight. Historically, to change the lifestyle behaviors of patients, physicians have detailed the consequences of excess weight gain and offered predictions of obesity-related complications and early demise. Although this motivational technique has been widely used in medicine, this "tough love" educational approach can have unintended consequences and be ineffective or even harmful in some patients. Behavioral change models and the positive psychology literature provide tools and methods to assist providers in the care of patients living with or at risk of weight-related morbidity and mortality. These techniques motivate patients without unintentionally disempowering them or their families.

WHAT IS FAT SHAMING?

Recently, a patient said, "I went to the cardiologist, but all he did was fat shame me." The initial reaction was to bristle. The cardiologist, of all medical specialists, had legitimate reasons to address the patient's weight status. The patient had a body mass index (BMI) of 38 (kg/m2). with past medical history significant for diabetes mellitus type 2 and obstructive sleep apnea. But this patient was not done with her account. She further related that after she left the cardiologist's office, because of feeling fat shamed, she ate most of a pumpkin pie. Clearly, weight loss would have a beneficial effect on her health conditions. So what caused this patient to have a negative response to weight loss counseling?

The next day, the author came across an article in a popular women's fitness magazine in which a patient complained about being fat shamed by all but one of her doctors.[1] As a result, the patient stopped seeing the physicians who told her to lose weight and only continued seeing the one who did not bring it up.[1] Her BMI was 35 (kg/m2).[1] This behavior was truly perplexing and had a paradoxical effect. The physicians who counseled the patient in weight loss had her best interests in mind and were providing evidence-based information, so why did she stop seeing them?

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A quick Internet search revealed additional articles with similar themes in prominent magazines in the last few months.[2,3] Was the medical community truly fat shaming or were these patients' reactions the result of societal stigmas? We began to wonder whether we had ever harmed a patient by providing evidence-based weight loss counseling? If doctors and patients have a shared goal, namely, optimal health and vitality, then what is the disconnect on this issue? More importantly, how can we, the medical community, fix it?

WEIGHT LOSS PROMOTION AND LIFESTYLE CHANGES MOTIVATION

Until recently in medical training and practice, physicians attempted to motivate patients by discussing the progression of disease resulting from lack of behavior change. To motivate patients to change their lifestyle behaviors, providers detailed the consequences of excess weight, including predictions of severe complications and early demise. Even though the description of factual consequences as a weight loss counseling approach can induce fear and shame in some individuals, the application of "tough love" was considered acceptable if done for the right reasons.

However, these techniques are not always effective and can be detrimental as suggested at the American Psychology Association (APA) conference.[4] At the 125th Annual Convention of the APA, Joan Chrisler asserted that fat shaming or sizism "is stressful and can cause patients to delay health care encounters or avoid interacting with providers."[4] After receiving weight loss advice, patients may delay seeking healthcare or avoid necessary

return visits when they feel judgment, rejection, or shame. Despite the best of intentions, the medical community may not be consistently inspiring patients to make lifestyle changes, so healthcare providers should consider using strategies that avoid the unintended consequences of weight loss counseling.

FACTORS INFLUENCING BODY MASS INDEX

There is an association between elevated BMI and health-related problems. Diseases related to weight gain include but are not limited to hypertension, diabetes mellitus, coronary artery disease, stroke, osteoarthritis, sleep apnea, gall bladder disease, hyperlipidemia, and fatty liver disease.[5,6]

Multiple factors contribute to elevated BMI. For instance, food intake and physical activity can have a profound effect on weight and BMI. External physical environment also plays a significant role in predisposing people to obesity because of lack of access to parks, sidewalks, and supermarkets with healthy food.[7] Other factors that increase obesity are lack of resources to join a gym, oversized serving portions, and food advertising that encourages increased caloric consumption and normalizes overeating.[7-10] Furthermore, larger food portions habituate large caloric intake, and the direct consumer advertising of high sugar, high saturated fat foods increase awareness and temptation for these food that can adversely affect overall wellbeing and health. From the physician's viewpoint, societal pressures from food advertising that recommends unhealthy, sugary foods create a difficult battle when encouraging patients to follow healthy behaviors. This viewpoint is supported by the literature, which suggests that food, activity, environment, genetics, environmental stress, emotional factors, and poor sleep contribute to weight-related disease.[10-12] It is important to clarify with patients the limitation of using BMI to assess for healthy weight status. To get more comprehensive evaluation, physician can also follow waist circumference and body fat percentage.

While genetics, stress, emotions, and poor sleep quality can increase risk of obesity, research also suggests that race and social class are important contributing variables.[13] For example, families may reside in an area without safe areas with parks or sidewalks, making physical activity difficult. Low socioeconomic status may make joining a gym or purchasing affordable healthy food unattainable. Poor access to affordable healthy food may lead to patients feeling incapable of eating for optimal health. Taken altogether, multiple and complex factors contribute to an individual's interactions with environment, body weight, and BMI.

PROVIDER STRATEGIES

Barriers can arise when dealing with obesity in the clinic. For instance, patients with unsuccessful attempts at losing or maintaining weight may develop mistrust of doctors and have poor adherence.[13] Additionally, unintended stigmatization by physicians may result in increased patient shame of weight status, thus reducing the quality of care. As a result, discussing diet, exercise, and weight with patients can seem like walking through a minefield. However, studies show that education and training in compassionate speech, slow incremental changes, a wellness approach, and motivational interviewing may help healthcare providers to provide the highest quality care for these patients.[14,15] Because of social stigmas and personal self-esteem issues associated with weight status, physicians need to develop skills that compassionately encourage better health in these patients. Specifically, physicians can use holistic, osteopathic wellness strategies to help patients achieve optimal health without feeling shame *(Table 1)*.

TABLE 1:

Strategies for Preventing Patient Perception or Interpretation of Fat Shaming

Optimal health, vitality, wellness, and prevention are more important goals than body size
Complete a full diagnostic workup regardless of weight
Avoid blame, shame, or guilt
Make office visits nonthreatening and comfortable
Use sensitivity in your word choices
Assess and address self-stigmatization like weight-bias internalization
Use the readiness assessment technique of the motivational interviewing paradigm
Offer patients an incentive agreement
Inform yourself and patients about treatment options and resources

Use Wellness and Prevention as Targeted Outcomes

Healthcare providers can reduce the focus on body weight or BMI as an endpoint and concentrate instead on screening for and preventing the diseases related to obesity. In this manner, the provider can present a wellness philosophy for all patients, regardless of weight, with a weight-inclusive approach that views health and wellness as multifaceted. From an osteopathic perspective, physicians can see the health in patients. Physicians could also inform patients about the metabolically healthy obesity. In one study, 30% of individuals with an overweight or obese BMI were determined to be metabolically healthy after completing cardiovascular factor evaluation.[16] The distinguishing feature in these patients was regular physical exercise.[16] This finding suggests that exercise may mitigate the cardiovascular risk factors associated with BMI elevation. Furthermore, the study found that 30% of normal weight individuals were metabolically unhealthy.[16] In this context, an individual's BMI becomes a poor predictor of cardiovascular health. Thus, a high percentage of people with normal or low BMI are at risk of cardiovascular events. In fact, in a large prospective cohort study of Korean adults, a metabolically unhealthy risk profile contributed more to risk of death from cardiovascular disease and all causes than BMI alone.[17]

The use of a weight-inclusive approach to lifestyle medicine emphasizes the importance of wellbeing to all patients regardless of their weight. This positive focus on wellness may reduce discouraging conversations about weight or weight loss and increase the likelihood of behavior change and maintenance.

For instance, physicians could promote wellness behaviors that improve health by encouraging patients to focus on the multitude of health benefits of better nutrition, exercise, meditation, and mindfulness rather than focusing exclusively on weight loss.

To address prevention, physicians can assess and determine the patient's expectations, knowledge, and preconceptions. Once patients are aware of risks associated with certain behaviors, they can be informed about the impact of a healthy lifestyle to treat and prevent disease. Families of patients should also be educated about how reducing risk factors is a healthier goal than the number on the scale. Further, lifestyle activities can be determined with consideration of patient preferences within the context of what the physician deems most appropriate. Ultimately, healthcare providers need to work together with patients utilizing shared decision-making to set incremental lifestyle behavior changes and achievable goals toward the common purpose of optimal health and vitality.

Perform Consistent Diagnostic Evaluations

Obese patients can face obstacles when seeking medical care, such as being told that obesity is the cause of their concerns and weight loss is the only treatment. In the absence of a complete investigation, important considerations in the patient could be missed. For example, if a patient with an elevated BMI is complaining of knee pain, some physicians might attribute the condition to weight alone and fail to obtain x-rays. The patient might also be informed that weight loss is the only treatment for the knee pain. However, it is unfair and negligent to attribute a patient's pain to weight status without a proper workup, making obesity a diagnosis of exclusion. Patient evaluation should include the appropriate investigation even when elevated BMI, in theory, could possibly be the cause of the signs and symptoms.[10]

Avoid Assigning Blame

The world around us challenges our ability to maintain a healthy weight. As mentioned previously, multiple factors can contribute to obesity.[18] Given these constant challenges, physicians can avoid assigning blame by acknowledging the difficulty of lifestyle changes and by not perpetuating the incorrect stereotype that obesity results from a lack of personal willpower. Physicians can also acknowledge and validate those patients who have tried to lose weight repeatedly and feel a sense of failure because of their lack of ability to lose weight. Furthermore, the process of behavior changes and health determinants can be used as the outcome goal rather than weight loss. Educating patients to set achievable short-term goals that emphasize small weight losses can improve compliance and sustainability. To encourage health improvements, physicians should validate patient worth outside of weight and body size.

Provide a Comfortable and Nonthreatening Office

To make office visits more comfortable, the office and waiting room suite should accommodate patients of all body habitus. For instance, armless chairs in the waiting room would be more comfortable for larger patients, and a range of gown sizes and medical equipment would be suitable for patients of varying sizes.

Although we do not advocate skipping the weight measurement at office visits, patients can be offered the option to not view their weight at every visit. This practice takes the focus off weight and instead emphasizes physical health and emotional wellness. In patients with weight-related anxiety, decreasing the emphasis on weight by not allowing them to see their weight or BMI during the visit can help them focus on optimal health and decrease anxiety.

Choose Words Carefully

A favorite question to open a discussion on weight management is to ask the patient, "How do you feel about your weight?" By using a kind word choice or tone, physicians may make a patient more open to discussing weight-related issues. One study showed a preference for the terms weight, BMI, weight problem, excess weight, unhealthy body weight, and unhealthy BMI and a distaste for the terms obesity, heaviness, large size, excess fat, and fatness *(Table 2)*.[14] By using open-ended questions and seeing failures as a normal part of the personal development process, physicians can empower patients to persevere when conditions are not ideal.

TABLE 2:

Terms/Verbage

PATIENT PREFERRED TERMS	PERCEIVED SHAMING TERMS
Weight	Obesity
BMI	Heaviness
Weight problems	Large size
Excess weight	Excess fat
Unhealthy body weight	Fatness
Unhealthy BMI	

As physicians, we should strive to be aware of our biases and overcome our preconceptions, effectively build rapport, and avoid having patients paradoxically terminate the provider relationship. When healthcare providers have obesity-related biases, patients may be perceived as lazy or unmotivated. In one study, the authors found that "More than 40% of physicians had a negative reaction towards obese patients, only 56% felt qualified to treat obesity, and 46% felt successful in this realm."[19] In spite of our preconceptions, when words are chosen carefully, they can contribute to a more productive alliance with the patient.

Address Weight-Bias Internalization

External weight-based stigmatization is pervasive, but weight-bias internalization (WBI), self-directed fat shaming, and self-deprecation can also lead to self-harm and a poor cardiometabolic profile.[15] In one study, individuals who self-stigmatized had an amplified cardiometabolic risk profile score when compared with individuals with obesity who did not have WBI.[15] In addition, WBI has been associated with increased risk of eating disorders.[15] Patients should be taught to not judge themselves and to de-emphasize failures. When WBI is noted in patients, physicians should encourage self-forgiveness and moving forward with the next task or goal.

Using this strategy, patients can be encouraged to adopt a proactive philosophy instead of reactive behavioral changes by anticipating failures and relapses as part of the weight loss process. Hence, patients should focus on proactive planning rather than depend on willpower alone. For instance, patients can be taught how to use meal planning and proactive eating when unplanned food is present. They should also be taught that WBI is a harmful response to weight gain and can have dire consequences. With proper identification, physicians can address and mitigate this maladaptive behavior quickly.

Utilize Motivational Interviewing Techniques

Another strategy to help patients with obesity and overweight status achieve better health is to consistently use the readiness assessment component of the motivational interviewing paradigm. Motivational interviewing uses guided questions that allow patients to verbalize their preferences for change. Instead of the usual direct instructions from physicians, patients are able to decide the best methods to motivate change and avoid ambivalence.[20] Because these communication strategies are patient-centered, patients seem more comfortable and less threatened by them. In contrast to simply informing patients of the consequences of weight gain, research suggests using motivational interviewing techniques for weight loss can have positive results.[21] In a systematic review,[21] more than a third of studies found participants using motivational interviewing for weight loss lost significantly more weight than controls. Other outcomes related to weight, such as physical activity, food intake, and metabolic measurements, also improved when participants using motivational interviewing were compared with controls.[21] About half of the reviewed studies indicated that motivational interviewing helped participants lose 5% of their initial weight.[21] Although more research is necessary to identify effective motivational interviewing strategies and approaches for weight loss, this technique can be used successfully by physicians *(Table 3)*.[22]

Another benefit of the use of motivational interviewing for weight loss is that it can be performed in the primary care clinic without having to refer to a weight loss specialist. Indeed, various members of the healthcare team can conduct the interview, giving the physician more time to focus on specific health concerns. Because motivational interviewing is an accessible and versatile technique, it may have benefits beyond the predicted loss of weight. For instance, this technique may be useful for effecting changes that help patients forego more invasive treatments, such as surgery. More physicians should use the interviewing techniques of motivational interviewing to improve health outcomes and patient adherence.

Offer Patients an Incentive Agreement

Patient empowerment and shared decision-making can help patients take accountability and pride in their compliance and self-care. As an example of an incentive agreement, the physician could agree to do a trial of decreasing or stopping a patient's medication for hypertension or lipids if the patient lost a specified amount of weight. Because many patients prefer to avoid medications for a plethora of reasons, this kind of incentive can be a powerful motivator.[23] Further, incentive agreements position the physician and patient as allies working toward achievement of a common goal.

TABLE 3:

Sample Motivational Interviewing Questions for Patients with Abnormal Weight

MOTIVATIONAL QUESTIONS
How important is your health to you?
How have you been doing with taking care of yourself?
Have you been treating yourself well?
What are the biggest barriers to taking care of yourself?
What does self-care mean to you?
What self-care activities would you like to do?
On a scale from 1-10, how motivated do you feel to improve your health and vitality?
How much of you is not wanting to change?
What was your life like before you gained weight?
What are your hopes for the future if you are able to become healthier?
What kinds of small healthy changes do you think you could make this week?
REFLECTIVE LISTENING
You are thinking about losing weight but you are not sure if you are ready to take action right now. Would you be willing to talk about this again at our next visit?
It sounds as if you are concerned about your weight and that you would like to start making some changes in your lifestyle.
It is up to you to decide if and when you are ready to make lifestyle changes. I am here to support you.
It can be hard to initiate changes in your life. I want to thank you for talking with me about this today.
It is great that you feel good about your decision to make some lifestyle changes; you are taking important steps to improve your health.

Educate Yourself on Options and Resources

Finally, physicians should educate themselves on weight loss diets, weight loss medications, and bariatric surgery options so they are comfortable discussing these options with patients. Physicians should investigate the community resources that are available locally. With that knowledge, they can educate patients on available support and resources. For instance, some patients are not aware of the resources available to them, such as seeing a dietitian to help with weight loss concerns. Healthcare providers do not have unlimited time or knowledge, so referring complex issues, such as obesity, to other healthcare professionals may be best for the patient. Further, interprofessional collaborations may be very beneficial for the busy physician and the patient with multifaceted needs.

Another option is to discuss weight loss treatment options with the patient. Many patients are not aware of the newer weight loss medications that have better safety profiles than earlier

medications used for weight management.[24] Making patients aware of the newer medications may make them more willing to discuss weight loss because of the accessibility of novel options. Diet is a frequently discussed treatment, and most diets will lead to weight loss. It is important to choose one that fits the patient's needs and preferences and results in sustainable weight loss in the long term. Weight Watchers is the longest existing successful support and nutrition-based weight loss program,[25] and it has affordable online options.

Another way to help patients is to develop a self-care plan using the wellness wheel and the eight dimensions of wellness developed by the Substance Abuse and Mental Health Services Administration.[26] Explain to patients the importance and meaning of healthy lifestyle from a wellness perspective in the eight dimensions including emotional, environmental, financial, intellectual, occupational, physical, social and spiritual. Patient education regarding healthy lifestyle should include the comprehensive perspective towards nutrition, physical movement, mindfulness with a self-care focus. Self-care seems to be a growing reform in the healthcare community. Therefore, physicians should empower patients to take the lead in their care, set incremental goals, maintain a positive attitude, and encourage them to identify social and community support systems. In this manner, self-compassion assessment and training may be useful tools to support this empowerment and provide stories of hope and inspiration.[26] Communication in an open, shared decision-making paradigm can encourage patients to prioritize self-care, develop perseverance, and maintain resilience during the challenging task of weight loss to achieve optimal health and vitality.

CONCLUSION

There are many ways we can help our patients lose weight and achieve better health without adding shame. Using the strategies described above, healthcare providers should be able to effectively communicate their concerns to patients without the patients feeling bullied, threatened, or shamed. Hopefully in the future, patients will believe that when their physician discusses weight with them it is because the physician cares about their health. The physician is not fat shaming them; the physician is just doing her job.

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REVIEW ARTICLE

PCSK9 Inhibitors, The Most Significant Advance in Lipid Lowering Therapy Since Statins? A Literature Review

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KEYWORDS:

Alirocumab

Cardiology

Evolocumab

Lipid Lowering

PCSK9 Inhibitor

OBJECTIVE: The purpose of this study was to evaluate efficacy, safety and cost of PCSK9 inhibitors.

METHODS: PubMed was used to search for literature regarding PCSK9 inhibitors up to May 1, 2018. Clinical trials, systematic reviews, meta-analyses and prescribing information were utilized for this review. Inclusion criteria was Phase II, III randomized control trials (RCT) and review articles comparing treatment of hypercholesterolemia in adults with and without PCSK9 inhibitors. All studies were completed from 2012-2017 and were conducted primarily in America.

RESULTS: Evolocumab and alirocumab are the only FDA approved PCSK9 inhibitors and have been shown to reduce baseline LDL-C by 50-60% in multiple clinical trials. Although there is no proven all-cause or cardiovascular mortality benefit associated with these drugs, there is a significant reduction in myocardial infarction (MI), stroke and coronary revascularization in treatment groups.

DISCUSSION: Low-density lipoprotein cholesterol (LDL-C) is a well characterized risk factor for cardiovascular disease (CVD). While hypercholesterolemia is often well controlled with statins, there remains a need for additional lipid lowering therapy in select patients. PCSK9 inhibitors represent a novel approach to lowering LDL-C in patients with familial hypercholesterolemia and clinical atherosclerotic cardiovascular disease (ASCVD) alone or in combination with other cholesterol lowering medications. PCSK9 inhibitors are well tolerated, with the most common side effects being local injection site reactions and flu-like symptoms. High cost remains the most significant obstacle for widespread use. PCSK9 inhibitors have a valuable role in the lipid lowering treatment algorithm with their full therapeutic potential yet to be realized.

INTRODUCTION

Heart disease, with the most common type being coronary artery disease (CAD), remains the leading cause of death in the United States as of 2016 and has been so for the past 40 years, according to the CDC[1]. It is well known that elevated levels of low-density lipoprotein cholesterol (LDL-C) increase the risk of developing atherosclerotic cardiovascular disease (ASCVD). When atherosclerotic plaques occlude coronary vessels, it often results in ischemic heart disease and life-threatening myocardial infarctions. Primary care physicians are predominantly responsible for managing patients with elevated LDL-C and its comorbidities, making it essential for them to be aware of all advances in treatment of hypercholesterolemia. Statins have long been the mainstay of lipid lowering therapy and have been shown to decrease morbidity and mortality associated with cardiovascular disease. Other adjunct agents such as fenofibrates, bile acid resins, omega 3 fatty acids and niacin are frequently used in combination with statins but have not shown consistent additional cardiac risk reduction in clinical trials[2]. The most recent lipid lowering guidelines from the *American College of Cardiology/American Heart Association* (ACC/AHA) in 2014 do not recommend initiating statin therapy based on absolute LDL-C levels, but rather calculating the 10-year risk of cardiac events defined as myocardial infarction (MI) or cerebrovascular accident (CVA). The 10-year risk is based on the following risk factors: sex, race, smoking status, presence of diabetes, high density lipoprotein cholesterol (HDL) level, total cholesterol level and systolic blood pressure. In general, statin therapy is indicated when the 10-year risk is > 7.5%[3]. Overall, the ACC recommends aggressively lowering LDL-C below 70 mg/dL in patients with high risk of developing adverse CV events[4]. Even with maximal statin therapy there is strong evidence to show that residual risk for cardiovascular disease (CVD) remains, especially in patients who are statin intolerant and do not have adequate reduction in LDL-C[2]. As early as 2007, inhibition of an enzyme called proprotein convertase subtilisin/kexin type 9 (PCSK9) was being proposed as a target for lipid lowering therapy[5]. Nearly a decade of research and clinical trials later resulted in the FDA approval

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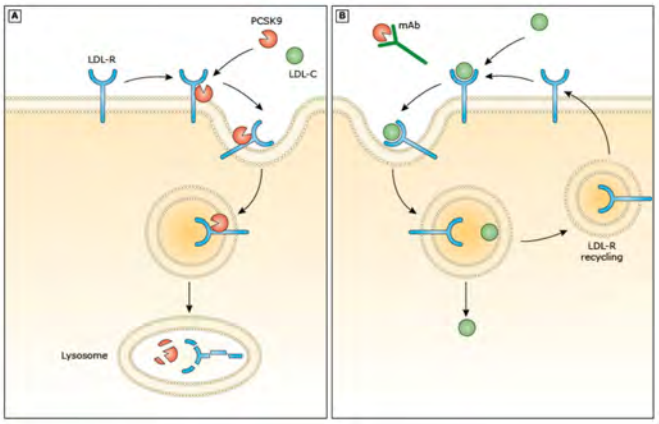
of the first PCSK9 inhibitors in 2015, Repatha (evolocumab) and Praluent (alirocumab) both indicated for the treatment of hypercholesterolemia[6,7]. This article aims to explore the role of PCSK9 inhibitors in lipid lowering therapy and investigate their efficacy, safety and cost effectiveness.

MECHANISM OF ACTION AND PHARMACOLOGY

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a serine protease produced primarily in the liver. PCSK9 binds to the low-density lipoprotein receptor (LDL-R) on the hepatocyte cell surface causing degradation of the LDL-R and subsequent elevated plasma levels of LDL-cholesterol (LDL-C). PCSK9 inhibitors, including alirocumab and evolocumab, are fully humanized monoclonal antibodies against the PCSK9 enzyme. Once bound, degradation of the enzyme follows and results in decreased PCSK9 available to bind LDL-R. The outcome is more recycled LDL-R expressed on the surface of hepatocytes and less degradation of the receptor, allowing the liver to remove more LDL-C from circulation and lower its plasma levels *(Figure 1)*. PCSK9 inhibitors bind quickly, inactivating the PCSK9 enzyme within 4-8 hours of the first subcutaneous injection. They prevent availability of PCSK9 for 2-3 weeks following administration. Regarding drug interactions, statins have been shown to increase PCSK9 levels making its inhibition an effective target for further lowering of LDL-C. Combination therapy with statin and PCSK9 inhibitor is considered safe and produces a synergistic reduction of serum LDL-C. Since monoclonal antibodies are eliminated through the reticuloendothelial system, dose adjustment in patients with renal or hepatic impairment is not necessary[8].

FIGURE 1:

Mechanism of action for PCSK9 inhibitors



[A] PCSK9 binds to LDL-R and promotes lysosomal degradation
[B] PCSK9 inhibitor is a monoclonal antibody (mAb) that blocks the action of PCSK9

EFFICACY OF PCSK9 INHIBITORS

An initial study in 2009 targeting PCSK9 showed success in lowering LDL-C levels[9]. Phase I and II trials followed demonstrating adequate safety and up to 70% reduction in LDL-C at high dose administration in addition to substantially increasing high density lipoprotein (HDL) and decreasing total cholesterol, triglycerides, apolipoprotein B and lipoprotein(a)[10]. Extensive phase III trials have since been conducted with promising results, consistently reducing baseline LDL-C 50-60% over a wide spectrum of pretreatment LDL-C levels, CVD risk, as monotherapy, adjunct to statin therapy and in patients with familial hypercholesterolemia *(Table 1)*. Of note, it is estimated that 15-20% of patients being treated with statins suffer from intolerance secondary to muscle aches, pains, cramps or weakness[33]. In the GAUSS-2,3 clinical trials, PCSK9 inhibitors were shown to have superior LDL-C lowering efficacy (52.8% reduction LDL-C) in patients with clinically diagnosed statin intolerance compared to treatment with ezetimibe (16.7% reduction LDL-C). Furthermore, fewer patients had to discontinue evolocumab therapy due to associated adverse muscular events (0.7%) versus ezetimibe (6.8%)[17,18]. It is important to recognize that evolocumab has recently been FDA approved for secondary prevention of CV events in patients with established CVD, while this indication was denied for ezetimibe[34,35]. The FOURIER phase III RCT completed in 2016 recruited 27,564 patients 40-85 years old with known ASCVD, LDL-C > 70 mg/dL undergoing statin therapy and compared outcomes with evolocumab verses placebo. Those treated with evolocumab showed a 59% decrease in baseline LDL-C in addition to a 15% reduction in primary end points of cardiovascular death, MI, coronary revascularization, unstable angina and stroke. Despite this, there was no benefit in all-cause mortality (p=0.54) or cardiovascular mortality (p=0.62)[11]. One meta-analysis made up of 35 RCTs looking at all-cause and cardiovascular mortality benefits gained from treatment with PCSK9 inhibitor compared to no treatment with PCSK9 inhibitor showed similar results. Inhibition of PCSK9 was not associated with a statistically significant change in either outcome (all-cause mortality=0.3% reduction, p=0.12, cardiovascular mortality=0.2% reduction, p=0.95). However, multiple RCTs included in the meta-analysis showed a statistically significant reduction in myocardial infarction (MI) (1.3% reduction, p<0.001), stroke (0.4% reduction, p=0.02) and coronary revascularization (1.6% reduction, p<0.001) with PCSK9 inhibitor therapy[36]. The efficacy of PCSK9 inhibitors has been addressed by the American College of Cardiology in a 2016 expert consensus decision pathway for treatment of hypercholesterolemia with non-statin therapies. It stated PCSK9 inhibitors should be considered first or second line treatment for patients with clinical ASCVD or a baseline LDL-C > 190 mg/dL not due to secondary modifiable etiology who have not reached an ideal reduction in LDL-C on maximum tolerated statin (<50% or <70-100 mg/dL)[37]. According to Navarese et al, more intensive compared with less intensive LDL-C lowering therapy correlates with greater risk reduction of total and cardiovascular mortality (7.08% more intensive therapy vs 7.70% low intensive therapy) in patients with elevated baseline LDL-C levels > 100 mg/dL. The systematic review/meta-analysis defined more intensive therapy as statin in combination with PCSK9 inhibitor and less intensive therapy as statin monotherapy or combination of statin and ezetimibe. This substantiates a significant cardiovascular mortality benefit with use of PCSK9 inhibitors in patients with elevated baseline LDL-C > 100 mg/dL[38].

TABLE 1:

Phase III clinical trials for Evolocumab and Alirocumab

STUDY	DRUG AND DOSE	DESCRIPTION	NUMBER OF PATIENTS	POPULATION	WEEKS	BASELINE E. LDL	MEAN % LDL LOWERING
FOURIER[11]	Evolocumab 420 mg q4w/140 mg q2w	Maximum statin vs placebo	27,564	HC	48	92	59
YUKAWA II[12]	Evolocumab 420 mg q4w/140 mg q2w	Statin therapy vs placebo	404	HC	12	128	67
MENDEL-2[13]	Evolocumab 420 mg q4w/140 mg q2w	Monotherapy vs ezetimibe and placebo	614	HC	12	140-144	55-57
DESCARTES[14]	Evolocumab 420 mg q4w	Long term efficacy/ tolerability atorvastatin 10-80 + ezetimibe	901	HC	52	104 (95-120)	55-57
RUTHERFORD-2[15]	Evolocumab 420 mg q4w/140 mg q2w	LDL-C goal reached in HeFH with statin	331	HeFH	12	151-161	59-61
LAPLACE-2[16]	Evolocumab 420 mg q4w/140 mg q2w	Combination with different statins vs ezetimibe and placebo	2067	HC	12	108	55-76
GAUSS-2[17]	Evolocumab 420 mg q4w/140 mg q2w	Statin intolerance vs ezetimibe	307	HC-statin intolerant	12	192-195	53-56
GAUSS-3[18]	Evolocumab 420 mg q4w	Statin intolerance vs ezetimibe	511	HC-statin intolerant	24	212-219	53
TESLA PART B[19]	Evolocumab 420 mg q4w	HoFH on stable lipid lowering therapy vs placebo	49	HoFH	12	348	30.9
TAUSSIG[20]	Evolocumab 420 mg q4w/140 mg q2w	Homozygous FH statin + ezetimibe, open label	94	HoFH	12	321	20.9
ODYSSEY ALTERNATIVE[21]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	Statin intolerance vs ezetimibe	361	HC-statin intolerant	24	191.3	45
ODYSSEY JAPAN[22]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	Maximum statin therapy vs placebo	216	HC	52	141.2	62.5
ODYSSEY OPTIONS I[23]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	High intensity statin vs ezetimibe	355	HC	24	105.1	44-54
ODYSSEY OPTIONS II[24]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	High intensity statin vs ezetimibe	305	HC	24	111.3	36.3-50.6
ODYSSEY FH I[25]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	HeFH vs ezetimibe	486	HeFH	24	145	58
ODYSSEY FH II[25]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	HeFH vs ezetimibe	249	HeFH	24	135	51
ODYSSEY-High FH[26]	Alirocumab 150 mg q2w	HeFH on statin vs placebo	106	HeFH	24	196-201	46
ODYSSEY-COMBO I[27]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	Hypercholesterolemia vs placebo	316	HC	24	95-100	48
ODYSSEY-COMBO II[28]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	High CVD risk with ezetimibe vs placebo/ ezetimibe	707	HC	24	105-109	51
ODYSSEY CHOICE I[29]	Alirocumab 75 mg q2w/up-titration 150 mg q2w	Maximum statin or statin intolerant vs placebo	803	HC	24	112-148	52 (no statin) 59 (+ statin)
ODYSSEY CHOICE II[30]	Alirocumab 75 mg q2w/up-titration 150 mg q2w b	Combination with ezetimibe or fenofibrate or as monotherapy vs placebo	233	HC-statin intolerant	24	154-164	56
ODYSSEY LONG TERM[31]	Alirocumab 150 mg q2w	Maximum statin therapy vs placebo	2341	HC	78	122.4	62
ODYSSEY MONO[32]	Alirocumab 75 mg q2w/up titration 150mg q2w	Monotherapy vs ezetimibe	103	HC	24	139.7	47.2

CVD = cardiovascular disease; HC=Hypercholesterolemia; FOURIER=Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk; YUKAWA II= Study of LDL-Cholesterol Reduction Using a Monoclonal PCSK9 Antibody in Japanese Patients with Advanced Cardiovascular Disease Risk; MENDEL-2=Monoclonal Antibody Against PCSK9 to Reduce Elevated LDL-C in Subjects Currently Not Receiving Drug Therapy for Easing Lipid Levels-2; DESCARTES = Durable Effect of PCSK9 Antibody Compared With Placebo Study; Rutherford-2=Reduction of LDL-C With PCSK9 Inhibition in Heterozygous Familial Hypercholesterolemia Disorder Study-2; Laplace-2=LDL-C Assessment w/ PCSK9 Monoclonal Antibody Inhibition Combined With Statin Therapy-2; GAUSS-2 = Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects-2; GAUSS-3 = Goal Achievement After Utilizing an Anti-PCSK9 Antibody in Statin Intolerant Subjects-3; HeFH = heterozygous familial hypercholesterolemia; HoFH= homozygous familial hypercholesterolemia; TESLA PART B= Trial Evaluating PCSK9 Antibody in Subjects With LDL Receptor Abnormalities Part B; LDL-C = low-density lipoprotein cholesterol; TAUSSIG = Trial Assessing Long Term Use of PCSK9 Inhibition in Subjects With Genetic LDL Disorders ODYSSEY ALTERNATIVE= Efficacy and Safety of Alirocumab vs Ezetimibe in Statin-Intolerant patients, with a Statin Rechallenge Arm; ODYSSEY JAPAN= Efficacy and Safety of Alirocumab in Japanese Patients with Heterozygous Familial Hypercholesterolemia or at High Cardiovascular Risk With Hypercholesterolemia Not Adequately Controlled With Statins; ODYSSEY OPTIONS I, II=Alirocumab as Add-On to Atorvastatin Versus Other Lipid Treatment Strategies I and II; ODYSSEY FH I,II= Efficacy and Safety of Alirocumab (SAR236553/REGN727) Versus Placebo on Top of Lipid-Modifying Therapy in Patients With Heterozygous Familial Hypercholesterolemia Not Adequately Controlled With Their Lipid-Modifying Therapy; ODYSSEY-High FH = Efficacy and Safety of Alirocumab (SAR236553/REGN727) Versus Placebo on Top of Lipid-Modifying Therapy in Patients With Heterozygous Familial Hypercholesterolemia; ODYSSEY COMBO I = Efficacy and Safety of Alirocumab (SAR236553/REGN727) Versus Placebo on Top of Lipid-Modifying Therapy in Patients With High Cardiovascular Risk and Hypercholesterolemia; ODYSSEY COMBO II = Efficacy and Safety of Alirocumab (SAR236553/REGN727) Versus Ezetimibe on Top of Statin in High Cardiovascular Risk Patients With Hypercholesterolemia; ODYSSEY CHOICE I = Study to Evaluate the Efficacy and Safety of an Every Four Weeks Treatment Regimen of Alirocumab (REGN727/SAR236553) in Patients With Primary Hypercholesterolemia; ODYSSEY CHOICE II = Phase III Study To Evaluate Alirocumab in Patients With Hypercholesterolemia Not Treated With a Statin; ODYSSEY LONG TERM= Long-term Safety and Tolerability of Alirocumab SAR236553 (REGN727) Versus Placebo on Top of Lipid-Modifying Therapy in High Cardiovascular Risk Patients With Hypercholesterolemia; ODYSSEY MONO= Efficacy and Safety of Alirocumab Versus Ezetimibe in Patients With Hypercholesterolemia

PCSK9 INHIBITORS IN LIPID LOWERING THERAPY

Current indications from the FDA for the use of PCSK9 inhibitors evolocumab and alirocumab in lipid lowering therapy are as follows: an adjunct to diet, alone or in combination with maximum tolerated dose of statin for treatment of adult patients with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) who require additional reduction of LDL-C. Evolocumab is also used for the treatment of homozygous familial hypercholesterolemia (HoFH) for additional lowering of LDL-C. In adults with known cardiovascular disease, PCSK9 inhibitors are indicated as preventative therapy to reduce risk of MI, coronary revascularization and stroke. The only known contraindication for use of evolcumab and alirocumab is serious hypersensitivity reactions (urticaria, rash) occurring with administration that cannot be tolerated by patients[6,7].

SAFETY AND DOSING INFORMATION

Both FDA approved PCSK9 inhibitors are administered as subcutaneous injections with variable dosing. Repatha (evolocumab) is formulated into a single-use prefilled autoinjector 140 mg/mL dosed every 2 weeks or a single-use on-body infusor with a prefilled cartridge 420 mg/3.5 mL dosed once monthly [6]. Praluent (alirocumab) is also formulated as a single-dose prefilled pen autoinjector with 75 mg/ml or 150 mg/ml. Either dose can be administered every two weeks although the manufacturer recommends starting with the 75 mg/ml dose and titrating up as necessary. Alternatively, 300 mg/2mL can be dosed every 4 weeks as two consecutive injections at different sites on the body, recommended injection sites include thighs, stomach and upper arms[7]. The most common side effects of both drugs are nasopharyngitis, flu or flu-like symptoms, common cold symptoms and local injection site reactions including erythema/redness, itching, swelling, pain and tenderness. Transaminitis, hyperglycemia and neurocognitive events such as confusion and memory impairment are other adverse events associated with these drugs[6,7]. A recent meta-analysis made up of 35 RCTs extensively characterized the safety profile of PCSK9 inhibitors. Neurocognitive adverse events defined as memory loss and confusion was analyzed over 21 RCTs comparing PCSK9 inhibitors with placebo. There was no statistically significant change in neurocognitive adverse events associated with PCSK9 inhibitors (1.2% incidence with and without PCSK9 inhibitor therapy, p=0.37). In the context of diabetes mellitus (DM), there was no statistically significant change in newly manifested or worsening of preexisting DM (0.3% increased incidence with PCSK9 inhibitor therapy, p=0.32). Other adverse events studied included increased creatine kinase, increased alanine or aspartate aminotransferase, myalgias or treatment-emergent serious adverse events. Compared to placebo, PCSK9 inhibitors were associated with fewer elevations of creatine kinase. There was no statistically significant increase in any of the other adverse events described above as well[36].

COST AND VALUE

The efficacy and benefits of PCSK9 inhibitors in CVD has been well established, but what about the cost and accessibility to patients? Priced at over $14,000 in the US and $5580 in the UK annually, affordability is a significant barrier to treatment. Initially, many patients in the US were provided financial assistance for PCSK9 inhibitor therapy from the Patient Access Network (PAN) foundation funded by pharmaceutical companies. Much of this financial aid has since decreased and patients are now responsible for significantly higher copays[39]. Compared to the cost of generic statin therapy at $48-120 annually and newer brand name agents like Livalo (pitavastatin) priced at $3840 yearly, these novel medications are quite a bit more expensive. Ezetimibe, a non-statin therapy often compared with PCSK9 inhibitors, has now become available in generic form. It ranges in cost from $552 to $2544 annually, also significantly cheaper than PCSK9 inhibitor therapy[4]. In addition, coverage by healthcare plans is often difficult to obtain, with payer rejections upwards of 80% for first time prescriptions and overall approvals of only 40%.

A potential solution to the high out of pocket costs PCSK9 inhibitors place on patients is utilization of specialty pharmacy programs. Specialty pharmacy programs are found primarily at large medical institutions that are sites for research on pharmaceutical usage and cost control. The data collected from these programs are relayed to the FDA who can expand access to specialty drugs by expediting approvals, making it less difficult for patients that will benefit most from these medications to be started on therapy[39]. Considering the high financial burden that major adverse cardiovascular events (MACE) place on the healthcare system, it can be argued that a medication that decreases these events is worth the cost. The widespread benefit of PCSK9 inhibitors will likely not be realized until they are more readily available to patients and more affordable for third-party payers. Responses from physicians and patients alike about the use of alirocumab has been positive as described in clinical trials by Roth et al. Physicians and patients stated devices were easy to operate, with the majority of patients willing to self-inject after an initial demonstration and counseling. The study was limited by patients injecting the device into a prosthetic pad rather than themselves in order to assess their willingness to use the device. A brief survey was filled out after the finishing the practice exercise bringing into question the validity of the feedback versus actual administration of the medication. Out of the 200 physicians selected for this study, 99 were primary care physicians further highlighting the importance of using PCSK9 inhibitors in a primary care setting, rather than referring to subspeciaties for treatment[40].

CONCLUSION

The high morbidity and mortality associated with atherosclerotic cardiovascular disease (ASCVD) are being driven in large part by hyperlipidemia, specifically elevated LDL-C. Statin therapy remains the gold standard for treatment of hypercholesterolemia due to its LDL-C lowering capabilities and proven CVD risk reduction. However, there remains a significant patient population that does not reach adequate LDL-C treatment goals with statins alone or combination therapy or who are completely statin intolerant. PCSK9 inhibitors offer a new approach to lipid lowering therapy that have been shown to reduce LDL-C levels by 50-60% in multiple clinical trials. These drugs have also proven to significantly reduce MI, stroke and coronary revascularization in treatment groups. They are well tolerated according to current data and do not cause intolerance secondary to myalgias typical of statins. The definitive clinical role of PCSK9 inhibitors must be based on LDL-C reduction, CVD events reduction, long-term safety, tolerability versus their high annual cost of $14,000 in the US, insurance coverage and overall benefit when added to conventional therapies. Current data are promising and suggests these drugs may be the greatest advance in lipid lowering therapy since statins. Advantages and disadvantages of PCSK9 inhibitors are summarized in *Table 2*.

TABLE 2:

Advantages and Disadvantages of PCSK9 inhibitors

ADVANTAGES
• Consistently lowers LDL-C by 50-60% in multiple phase III randomized control trials [36]
• Increases HDL, decreases triglycerides and total cholesterol [10]
• Significantly reduces MI, coronary revascularization and stroke in patients with clinical ASCVD and familial hypercholesterolemia[36]
• Evolocumab is FDA approved for secondary prevention of MI, coronary revascularization and stroke in patients with established cardiovascular disease[34]
• Few adverse effects associated, effective treatment option for patients with statin intolerance
• Can be used as monotherapy or in combination with other lipid lowering medications
DISADVANTAGES
• High annual cost, $14,000 US and $5580 UK[39]
• Most third-party payers will not provide coverage
• Only available as subcutaneous injection, may not be tolerated by some patients
• Has not been proven to reduce all cause or cardiovascular mortality[36]

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

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

John Martin Littlejohn, DO

REVIEW ARTICLE

An Osteopathic Approach to Diagnosing and Treating Perimenstrual Disorders

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KEYWORDS:

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Premenstrual Dysphoric Disorder

Women's Health

ABSTRACT: Premenstrual syndrome (PMS), premenstrual dysphoric disorder (PMDD), and dysmenorrhea are Perimenstrual disorders that cause significant physical and emotional distress to reproductive-aged women. The hormonal imbalance associated with perimenstrual disorders impacts multiple organs and somatic structures throughout the body. Many pharmacologic treatments are currently used to treat the various symptoms of perimenstrual disorders, however, these treatments can have a multitude of undesirable side effects. Osteopathic manipulative treatment (OMT) can be incorporated in the treatment of somatic and visceral components of PMS, PMDD, and dysmenorrhea. Osteopathic treatments can target multiple organs and structural components affected by these disorders holistically and with limited potential side effects to the patients. This article describes relevant OMT techniques, which encompass the five models of osteopathic medicine that can be used for specific perimenstrual symptoms.

INTRODUCTION

Premenstrual Syndrome (PMS), premenstrual dysphoric disorder (PMDD), and dysmenorrhea are a spectrum of menstrual disorders that share pelvic pain as a symptom. PMS and PMDD both present with somatic and emotional symptoms that may last throughout the menstrual cycle. Common somatic symptoms found in each disorder include pelvic pain, abdominal bloating, breast tenderness, and edema. Emotional symptoms such as anxiety, depression, and irritability are also commonly present in both disorders. Unlike PMS and PMDD, dysmenorrhea usually presents only with somatic symptoms such as pelvic pain and only occurs during menstruation.[1,2]

PMS and PMDD have been associated with a reduced quality of life (QOL) in reproductive-age females. Women affected with these disorders have increased costs, including ambulatory care visit costs, decreased productivity at work, and increased missed workdays. Women also report decreased interest in hobbies, impairment to social activities, and general impairment throughout the day while symptoms are present.[3] Another major concern is the association between major depressive disorder and PMS and PMDD.[4] Dysmenorrhea is suggested to be a leading causes of recurrent missed days at school and/or work in reproductive-age females and can be debilitating.[5,6] Over-the-counter (OTC) medication is of limited effectiveness, not to mention side effects of nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen including gastroesophageal reflux disease (GERD), stomach pain, increased blood pressure, fluid retention and liver injuries: This further supports incorporation of osteopathic treatment for perimenstrual dysfunctions. [3,6,7]

The authors believe osteopathic manipulative treatment (OMT) has a significant role in treating women with PMS, PMDD, and dysmenorrhea, and therefore, this article will focus on osteopathic findings in these disabling conditions, and the manual approach thereof.

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EPIDEMIOLOGY

The prevalence of PMS is difficult to measure as the ICD-10 definition differs than the American College of Obstetricians and Gynecologists (ACOG), in addition to failure to apply strict criteria by evaluating severity or impairment to function. Studies have found the prevalence of PMS to be 3-98.6% depending on which diagnostic criteria is used, however, research using strict ACOG criteria have found the prevalence to be 3-8%.[3,8,9] Clearly, there are extraordinary differences between these percentages, which may call into question the validity of these statistics and the number of women who are not properly diagnosed. In the experience of these authors, perimenstrual disorders affect a majority of women. PMDD was only added to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) in 2013 (previously a provisional diagnosis) with prevalence estimated to be 1-5%.[3,10] Studies measure the prevalence of dysmenorrhea to be much higher estimating 45-60%.[11–13]

DIAGNOSTIC CRITERIA

The definition and diagnostic criteria of PMS have evolved over the years, but several key features have remained the cornerstone of diagnosis. These include:

1) The luteal timing of symptom onset, beginning after cycle day 13 and subsiding within 4 days after the onset of menses.

2) Symptoms occurring in at least 2 sequential cycles.[7,14]

ACOG sets the standard for diagnostic criteria of female reproductive disorders and diseases in the United States and they stipulate that an identifiable dysfunction in social, academic, or work performance must be present as well. Together with the above criteria, one of the affective or somatic symptoms in *Table 1* must be reported during the appropriate time and without any separate identifiable causes.[1]

TABLE 1:

Diagnostic criteria for premenstrual syndrome[1]

AFFECTIVE SYMPTOMS	SOMATIC SYMPTOMS
Angry outbursts	Abdominal bloating
Anxiety	Breast tenderness or swelling
Confusion	Headache
Depression	Joint or muscle pain
Increased irritability	Swelling of extremities
Social withdrawal	Weight gain

The diagnostic criteria for PMDD is set by the American Psychiatric Association (APA) in DSM-5 and has seven criteria that must be met (A-G). (A) Similar to PMS, the timing must be luteal with five symptoms presenting in the week before the onset of menses, improving within a few days after the onset of menses, and being minimal or absent in the week after menses. Symptoms must be present in more than 50% of menstrual cycles. (B, C) A total of at least five symptoms must be present and contain at least one symptom from criterion B and at least one symptom from criterion C *(Table 2)*. (D) The symptoms must cause significant distress and interference with regular activities (social, work, academic, or relationships). E) Symptoms must not be an exacerbation of another disorder. (F) Symptoms should be confirmed by prospective daily ratings during at least two symptomatic cycles. (G) No other attributable cause can be found (medications, recreational drugs, other medical conditions).[2]

TABLE 2:

Diagnostic criteria for premenstrual dysphoric disorder[2]

CRITERION B	CRITERION C
Mood swings, sudden sadness, increased sensitivity	Difficulty concentrating
Anger, irritability	Diminished interest in usual activities
Sense of hopelessness, depressed mood, self-critical thoughts	Easy fatigability, decreased energy
Tension, anxiety, feeling on edge	Marked changes in appetite
	Sense of being overwhelmed
	Changes in sleep
	Physical symptoms, such as those seen in PMS

Dysmenorrhea diagnosis is made clinically in patients with recurrent, crampy, midline, pelvic pain that starts just before or with the onset of menses and then diminishes over 12-72 hours with no other attributable cause.[15]

PATHOGENESIS

The exact pathophysiology of PMS and PMDD is still unknown and under investigation, however, multiple neurotransmitters and hormones have been implicated in playing a role. The latest theories suggest the serum level changes of estrogen and progesterone are the root causes of PMS and PMDD. One study showed that patients with PMS who received leuprolide, which decreases estrogen and progesterone levels, had decreased symptoms. These symptoms returned when estrogen or progesterone therapy was introduced. Contrastingly, women without PMS who received the same interventions had no response to treatment.[16] This evidence suggests that imbalances in both estrogen and progesterone are involved in the disease process, further suggesting an abnormal response to these hormones with downstream players involved.

Multiple neurotransmitters have been identified as having a possible role in the PMS and PMDD disease process, including gamma-Aminobutyric acid (GABA), opioids, and serotonin. The role of GABA needs additional research; however, benzodiazepines, which agonize the GABA receptor, have shown benefit to patients afflicted with PMS.[17] Opioids also have limited research, but several studies have found reduced peripheral beta-endorphin levels in

patients with PMS and PMDD.[18–20] Serotonin has been found to play a significant role in PMS and PMDD. Cerebrospinal fluid (CSF) serotonin levels were estimated to be negatively correlated with serum estradiol, progesterone, and testosterone. CSF serotonin levels were also estimated to be decreased in patients with PMS.[21] These findings are supported by the effectiveness of selective serotonin reuptake inhibitors (SSRIs) in reducing symptoms of PMS and PMDD.[22,23] Furthermore, tryptophan (serotonin precursor) restriction worsens PMS symptoms and the serotonin antagonist, metergoline, causes a return of symptoms in patients previously effectively treated with SSRIs.[24,25] Altogether, this evidence strongly supports serotonin as a downstream effector of PMS and PMDD.

In contrast to PMS and PMDD, the etiology of dysmenorrhea is less complex. Increased serum prostanoids during menses cause frequent, irregular contractions of the uterus. These contractions increase the uterine pressure, which may overcome arterial pressure to the organ, leading to ischemia and pain.[15] The pathogenesis and symptoms of PMS, PMDD, and dysmenorrhea affect all the osteopathic models, including the biomechanical, respiratory-circulatory, neurological, metabolic-nutritional, and biopsychosocial models. Osteopathic structural exam (OSE) is a key component in revealing areas of somatic dysfunctions that can be addressed by osteopathic manipulative techniques (OMT).

HORMONAL AND ORGAN SYSTEM ONSIDERATION IN PREMENSTRUAL SYNDROME AND PREMENSTRUAL DYSMORPHIC DISORDER (PMS/PMDD)

Multiple organs and structures contribute to the pain and symptoms associated with PMS and PMDD. Organs and structures that play a significant role in these disorders and that require special attention when performing the OSE and OMT are as follows: thyroid, ovaries, uterus, broad ligaments, kidneys, pelvic lymphatic glands, kidneys, adrenals, breasts, sacroiliac area, and the occipital-atlantal (OA) joint.

The thyroid contains sex hormone receptors for estrogen, progesterone, and testosterone.[26] These hormones influence thyroid stimulating hormone (TSH) production.[27] Prior studies have found that both estrogen and progesterone are imbalanced in a patient with PMS, which in response may alter TSH levels.[28] Borderline thyroid function with TSH in the middle to high range and active T3 in the low normal to below normal range have been associated with increased PMS symptoms.[29] Thyroid disease has often been found to lead to menstrual disturbances, reduced fertility, and pelvic pain. Hyperthyroidism is associated mainly with hypomenorrhea and polymenorrhea, whereas hypothyroidism is associated mainly with oligomenorrhea and menorrhagia.[28] For these reasons, a proper history with deviations of normal reproductive gland activity should follow-up with a thyroid workup.

The ovaries are potentially the most vital organs when considering PMS and PMDD due to their role in estrogen and progesterone production.[30] Abnormal production of both hormones has been found in women with PMS.[31,32] Estrogen has been found to increase baroreflex regulation of sympathetic outflow, increasing norepinephrine activity and can lead to vasoconstriction of blood flow to major pelvic organs thereafter.[33] Vasoconstriction and the resulting ischemia can result in lower thresholds in nociception. In a patient with PMS, it is important to check luteinizing hormone (LH) and follicular stimulating hormone (FSH), estrogen, and progesterone levels to rule out hormonal imbalance.

The effects of imbalanced estrogen also extend to the uterus. Many women with dysmenorrhea and chronic pelvic pain have been found to have uterine fibroids. Estrogen has proliferating effects on fibroids, which may lead to pelvic pain or pressure, heavy menstrual bleeding, and in rare cases, reproductive dysfunction.[34] These fibroids may interfere with uterine contractions and restrict uterine blood vessels, resulting in ischemia, pain, and excessive menstrual bleeding. Heavy menstrual bleeding can still occur in women with PMS who do not have fibroids. Estrogen controls the amount of uterine shedding during the menstrual period. Abnormal estrogen may lead to increased endometrial thickness that leads to increased sloughing and therefore bleeding during menses.[30] Women with PMS are recommended to receive abdominal ultrasounds to rule out uterine fibroids.

The broad ligament is thick mesentery that encapsulates the uterus, ovaries, and fallopian tubes in the pelvis.[35] As mentioned previously, the organs that the broad ligament surrounds contribute to the symptoms of PMS and PMDD. Treating the broad ligament osteopathically to reduce some of its tension may increase blood flow, allowing more oxygen to reach these organs, reducing some of the pain caused by ischemia in PMS. The Chapman's reflex for the broad ligament to enhance lymphatic flow is located on the outer thigh, along the iliotibial band.[36]

The kidneys can contribute to PMS/PMDD pain and bloating via fluid retention through the renin-angiotensin-aldosterone-system (RAAS). During the luteal phase, when estrogen is at its peak, RAAS components also rise.[37] Increased RAAS components lead to vasoconstriction and fluid retention, increasing pelvic pressure and leading to pain.[30] The water retention caused by the elevated RAAS components may also lead to bloating, a common symptom found in women with PMS/PMDD.[14] Renin and angiotensin II levels should be assessed in women suffering from PMS/PMDD who present with bloating or edema. The chemical axis of the RAAS not only involves the kidneys and adrenals, but also the liver and lungs, supporting the osteopathic principal of body unity.

The adrenal glands, which are small glands that produce stress hormones such as cortisol and aldosterone, are also impacted by the imbalanced estrogen levels in PMS.30 Replacement estrogen therapy leads to a rise in the cortisol levels produced by the adrenal glands, leading to hypertension, suppressed immunity, hyperglycemia, and carbohydrate cravings.[38] Abnormal estrogen and progesterone levels can also result in a rise in aldosterone levels produced by the adrenal glands, leading to salt and water retention, bloating, and possibly edema.[39] Further workup of cortisol and aldosterone may be needed if women who suffer from PMS have alterations in electrolytes such as sodium and potassium or corresponding adrenal symptoms such as hirsuitism.

Breast tenderness is a common symptom of PMS/PMDD. Hormonal imbalance may contribute to breast fullness and tenderness.[14] OMT addressing lymphatic drainage and associated chapman points may decrease the severity of this symptom.

OSTEOPATHIC STRUCTURAL EXAM AND PHYSICAL EXAM FOR THE PATIENT SUFFERING FROM PREMENSTRUAL SYNDROME AND PREMENSTRUAL DYSMORPHIC DISORDER (PMS/PMDD)

Patients with PMS, PMDD, or dysmenorrhea should have a complete and thorough osteopathic structural exam (OSE) and physical exam prior to initiating OMT. On OSE, women diagnosed with any of these conditions may demonstrate abnormalities with their biomechanics, circulation, lymphatics, and autonomics.

Biomechanically, physicians should examine the abdomen, lumbar spine, pelvis, sacrum, and paraspinal musculature for somatic dysfunctions. A gentle palpatory evaluation of the abdomen should be performed to reproduce and localize any pain. Abdominal evaluation can also reveal specific pathology such as uterine or adnexal enlargement or nodularity. The innominates are another important region for osteopathic consideration as it has significant pelvic fascia connections and houses the organs most severely affected by PMS, PMDD, and dysmenorrhea. Additionally, the pelvis is the source of most sex hormones, which, as discussed above, interact with the major glands of stress and exacerbate symptoms. Fascial connections and autonomics also extend to and from the lumbar spine and the sacrum. On OSE, lumbar spinal curves, paravertebral muscle contractions, and sacral base leveling should be assessed for somatic dysfunctions. Abnormal lumbar spine curvature or lumbar paravertebral contraction can reveal whether the dysfunction is acute or chronic, the level of neuromuscular hyperactivity, and which organs are affected based on viscerosomatic reflexes and chapman points. An unlevel sacral base can be indicative of abnormal autonomics.[40]

The parasympathetic nervous system and inflammatory response play a role in PMS. It has been demonstrated that women with PMS had elevated inflammation markers that correlate with the severity of symptoms.[41] The vagus nerve inhibits inflammation via the cholinergic anti-inflammatory pathway (CAP) by interacting with the alpha7 subunit found on the surfaces of macrophages.[42] In addition, the activation of the parasympathetic nervous system leads to vasodilation to pelvic organs, increasing oxygen perfusion, and thereby decreasing ischemia-induced pain. The parasympathetic pathways affecting the abdominopelvic organs, specifically the ovaries, proximal fallopian tubes, kidneys and upper ureters, arise from the vagus nerve. The vagus nerve leaves the cranium through the jugular foramen, accessible to the hands of the operator in the occipital, temporal, occipitoatlantal (OA), and suboccipital regions. Splanchnic nerves from the sacrum innervate the lower uterus and inferior reproductive system.[29] Therefore, diagnosing and treating the jugular foramen and sacral junctional and diaphragmatic areas is vital in women with PMS.

Viscerosomatic reflexes are localized responses found on somatic structures that originated from visceral organ stimulation. The spine and surrounding tissues are common somatic sites to find visceral reflexes. The following spinal regions are important to evaluate during the osteopathic structural exam: T1-4 for reflexes from the thyroid and thoracolumbar region for sympathetic reflexes from abdominopelvic organs. Parasympathetic reflexes for the lower abdominal and pelvic organs are located from S2-S4 and are important to assess during the osteopathic structural examination (OSE) because the pelvic and abdominal organ reflexes are found there.[43] Details pertaining to each organ contributing to PMS can be found in *Table 3*.[36,44,45]

TABLE 3:

Osteopathic structural exam autonomic considerations[36,45]

AREA TREATED	VISCEROSOMATIC REFLEXES	CHAPMAN POINTS
Thyroid	T1-T5 bilaterally	**Anterior:** 2nd ICS **Posterior:** T2 transverse processes
Ovaries	**Sympathetic:** T10-T11 bilaterally **Parasympathetic:** S2-S4	**Anterior:** Superior and inferior to the pubic symphysis. **Posterior:** Between T9 and T10, and between T10 and T11.
Uterus	**Sympathetic:** T9-L2 bilaterally **Parasympathetic:** S2-S4	**Anterior:** Between pubic symphysis and obturator foramen. **Posterior:** Between spinous process of L5 and PSIS.
Broad Ligament	**Sympathetic:** T9-L2 bilaterally **Parasympathetic:** S2-S4	Laterally, along the ITB, from the greater trochanter to just superior to the lateral knee along the femoral condyle.
Pelvic (lymphatic) Glands	**Sympathetic:** T10-L2 bilaterally **Parasympathetic:** S2-4	**Anterior:** Along the lower 2/5th of the sartorius muscle (inner thigh) into the proximal, medial tibia. **Posterior:** At the iliosacral joint, near the PIIS (S3)
Kidneys	**Sympathetic:** T9-L1 ipsilaterally **Parasympathetic:** S2-S4	**Anterior:** 1-inch lateral and one inch superior to umbilicus. **Posterior:** Between T12-L1
Adrenals	**Sympathetic:** T8-T10 ipsilaterally **Parasympathetic:** S2-S4	**Anterior:** 1-inch lateral to and 2.5 inches superior to the umbilicus. **Posterior:** Between T11 and T12.
Breast	-----	**Posterior:** Angles of ribs 5 and 6

Abbreviations- ICS- intercostal space, PSIS- Posterior Superior Ischial Tuberosity, ITB- Iliotibial band, CPP- chronic pelvic pain

Chapman points are small gangliform, myofascial contractions that result in tissue texture changes found just underneath the skin in the fascia, muscle, periosteum, and bone. Posteriorly, these reflexes are found along the short restrictor muscles of the spine and are traditionally considered "stringy" in texture. They are a type of viscerosomatic reflex mediated by the sympathetic nervous system. Based on their location, these points are diagnostic for specific visceral organ problems. The innominate must be treated before directly treating Chapman points to ensure a freeing of the sympathetic trunk termini, named the ganglion impar, which is anterior to the sacrococcygeal joint. Chapman points are treated by applying gentle rotary motion with the endpoint being a reduction of fluid due to lymphatic edema anteriorly and relaxation of tissue texture changes in the muscle in the myofascial of the spinal region. The specific anterior and posterior points found in PMS/PMDD can be found in *Table 3*.[36,44,45]

Women with PMS, PMDD, or dysmenorrhea tend to have stasis in blood and lymph flow, which may lead to ischemic pain and edema, as mentioned in the previous sections.[15,40] Zink's patterns should be taken into account and the tentorium cerebelli, thoracic outlet, abdominal diaphragm, and pelvic diaphragm should be examined for rigidity and decreased movement. These diaphragms play a vital role in circulating blood and lymph throughout the body, meaning that stasis in any of these will lead to circulatory/lymphatic stasis. The attachment sites of these diaphragms are also important to examine as decreased motility in these sites will lead to diaphragmatic stasis. Therefore, somatic dysfunction of the cranium, spine, ribs, clavicle, and innominates should be a evaluated and treated to optimize diaphragmatic motion.[40]

The OSE will not only aid the physician in diagnosing the patient suffering from a perimenstrual disorder, but will also guide them in which treatments the patient would most benefit from based on the corresponding somatic dysfunction.

THE FIVE OSTEOPATHIC MODELS AND OMT TECHNIQUES FOR TREATING PMS, PMDD, AND DYSMENORRHEA

OMT targets specific organs and structures involved in PMS, PMDD, and dysmenorrhea with limited potential side effects making it a useful treatment compared to pharmacologic therapy. OMT and manual therapy have been effective in treating symptoms of PMS and PMDD.[46–48] Specifically manual therapy has shown to decrease PMS/PMDD symptoms such as fatigue, bloating, and pain.48 One systemic review concluded OMT to effectively decrease dysmenorrhea pain intensity and duration.[47] In addition to viscerosomatic reflexes from certain organs, chronic pelvic pain can result directly either from either structural or emotional changes, both in which OMT can be useful. Muscle imbalance and posture can affect the structure, and thus, the functioning of pelvic organs. Poor pelvic and lower extremity muscle tone may increase lumbar lordosis and exaggerate anterior pelvic tilt, with resultant crowding of viscera into the pelvic bowl. Repeated alternation of muscle tension and relaxation may lead to nerve entrapment or alteration of blood and lymph circulation to muscles or other body structures. Techniques that decrease muscle tone, improve lumbar lordosis, and increase lymphatic flow can improve these direct structural changes that lead to pelvic pain.[49]

In osteopathic manipulative treatment, there are five main models that osteopathic physicians adhere to: The Respiratory-Circulatory, Neurologic, Mechanical, Metabolic- Nutritional, and Biopsychosocial. The respiratory-circulatory model addresses respiratory and fluid mechanics in the body such as congestive changes, lymphatic flow, venous return, and edema formation. Treatment goals include restoring the body's ability to improve respiratory excursion, and thus, lymph and circulatory flow. PMS symptoms that can be addressed with this model include bloating, weight gain, pelvic and thoracic diaphragm pain, salt and water retention, breast tenderness/fullness, inflammation, and lymphatic stasis. The following OMT techniques address this model and can improve the resulting symptoms: pelvic diaphragm release, sacral rocking, ischial tuberosity spread, doming of the thoracic diaphragm, pedal pump, Marian Clark release, assessing and addressing Zink's patterns to decrease restrictions of the before-mentioned diaphragms. Treatment of the diaphragms can help to maintain appropriate pressures- such as negative intrathoracic- for better fluid movement. [29,50,51]

The Neurologic model addresses facilitated spinal cord segments, viscerosomatic and somatovisceral reflex phenomena, Chapman points, and abnormal parasympathetic effects resulting from cranial or sacral nerve entrapment syndromes. Treatment goals include restoring autonomic balance, alleviation of segmental facilitation, decreasing abnormal afferent signaling, and relief of pain. PMS and PMDD symptoms incorporated in this model include viscerosomatic reflexes to the spine (cervical, thoracic, and low back tenderness), Chapman sympathetic points, OA (vagus nerve) and sacral (splanchnic nerves) somatic dysfunctions that also commonly lead to autonomic para/sympathetic abnormalities. OMT techniques that can be used to resolve these symptoms include lumbosacral decompression, sacral rocking, ischial tuberosity spread, quadratus lumborum release, inhibitory sacral pressure, and suboccipital release. Treating Chapman points in the left 6th intercostal space, on T6-T7, and on the iliotibial band[58] to mobilize stasis of the upper and lower gastrointestinal tract can facilitate better gut motility, which should lead to less bloating.[29,50–52] Owen's An Endocrine Interpretation of Chapman's Reflexes discusses treating the ovarian reflex points during the LH surge in the middle of the menstrual cycle, which may alleviate perimenstrual discomfort.[45]

The Mechanical model addresses factors that alter posture, motion, and gait. The goal of treatment is the restoration of free motion within the musculoskeletal system. Cervical, thoracic, and lumbar pain from viscerosomatic reflexes, tender points found in the lumbar and pelvic regions, increased muscle tension, diaphragm restrictions, and lumbar lordosis are common complaints associated with PMS, PMDD, and dysmenorrhea that fall under this model. OMT techniques that can be used to treatment musculoskeletal restrictions include lumbosacral decompression, counterstrain for lumbar, sacral and pelvic tenderpoints, sacral rocking, ischial tuberosity spread, quadratus

lumborum release, inhibitory sacral pressure, myofascial release, and muscle energy.[29,50,51]

The Metabolic-Nutritional model addresses dietary deficiencies and excesses, food allergies, and effect of toxins. Treatment goals include promoting energy conservation/exchange and immune system enhancement. The Metabolic-Nutritional model encompasses many symptoms of PMS and PMDD, such as appetite, food cravings, overeating, fatigability, decreased energy, and increased inflammatory state. Nutritional counseling, exercise encouragement, and OMT techniques directed at somatic dysfunctions including compression of the fourth ventricle, can improve the cranial rhythmic impulse (CRI) and decrease musculoskeletal restriction that increase allostatic load and therefore energy expenditure and can thus help to address PMS and PMDD symptoms. The importance of utilization of muscular activity to modulate blood sugar levels and insulin sensitivity is also a bioenergetics consideration with OMT. [29,50,51]

The Biopsychosocial model addresses the psychological and social components of a patient's health, as stress is a well-known contributor to illness. Treatment goals include optimizing psychological and social components of a patient's health. Mood swings, anger, irritability, tension, anxiety, difficulty concentrating, diminished interest in usual activity, feeling overwhelmed, and sleep disturbances are all PMS and PMDD symptoms that fall under this model. Treatments can include teaching the patient stress reduction strategies, helping the patient improve his or her social interactions, and OMT including CV4 (compression of the fourth ventricle), and suboccipital release. All treatments are described in *Table 4*. [29,50,51]

Informed Consent

While OMT is a useful treatment for PMS, PMDD, and chronic pelvic pain, informed consent must always be obtained from the patient prior to starting treatment. PMS/PMDD is a condition of that mostly involves organs of sexuality. As with all informed consent, patients must be educated on what techniques they will receive in their treatment sessions, why these techniques are important for addressing their chief complaints, how each technique is performed, and what side effects can be expected after the treatment session is completed. The physician must also inform the patient of any contraindications to the technique *(listed in Table 4)* to assess whether this technique may bring harm to the patient. Lack of informed consent may be detrimental to both patient and physician and the professional relationship between both parties; an uncomfortable patient may tense up amid treatment, which may worsen, rather than alleviate, the original complaint. Finally, each patient should have the right to decline a technique that they are uneasy with and can only do so after being properly informed about it. In the opinion of this author, a choice for a chaperone should be available to the patient. It is the duty of the osteopathic physician to educate patients on treatment goals and OMT: This is best accomplished with a transparent patient-physician relationship.

Non-Osteopathic Treatments for PMS and PMDD- Pharmacologic and Non-Pharmacologic

The main treatment goals in pharmacologic therapy for PMS/PMDD include suppression of ovulation, suppression of physical symptoms, suppression of psychological symptoms, and potential surgery for intractable PMS/PMDD. For managing PMS/PMDD symptoms anti-depressants are often prescribed. Selective serotonin reuptake inhibitors (SSRIs) are the first line treatment, of which escitalopram seems to be consensus amongst the authors.[53] Serotonin and norepinephrine reuptake inhibitors (SNRIs) are also prescribed because action is quick and often found to be helpful. Sexual dysfunction, fatigue, and weight gain are the most common side effects associated with SSRIs and SNRIs.[54]

Various birth controls can be used including oral contraceptives, progestin only contraceptives, oral micronized progesterone, medroxyprogesterone, transdermal estradiol, and gonadotropin releasing hormone (GnRH) agonists to treat PMS/PMDD symptoms.[1,54] These medications take advantage of the hypothalamic–pituitary–gonadal axis to prevent ovulation from occurring. Despite their effectiveness, oral contraceptives have side effects, including weight gain, nausea, headache, breast tenderness, irritability, depression, vaginal dryness, and the potential for cancer and blood clots.[55]

For suppression of physical symptoms, spironolactone can be used.[56] Spironolactone is an aldosterone-antagonizing diuretic that can be used for water retention and increased aldosterone, both symptoms found in PMS.[54] Metorrhagia, gynecomastia, urticarial, and scalp hair loss are side effects of spironolactone.[56]

For intractable PMS and PMDD, bilateral oophorectomy with estrogen replacement post-surgery is recommended.[54] While all the aforementioned medications are useful in managing PMS, they have unwanted side effects. For this reason, OMT is a very useful treatment because not only can it achieve reductions in symptoms, but it does so with very few, temporary side effects.[29,46,50]

Non-pharmacologic therapy for PMS should address psychosocial and nutritional difficulties that are often present in PMS and PMDD. For psychosocial problems, physicians should educate patients on stress management and coping mechanisms. Physicians should discuss with their patients time management and realistic goals for incorporating exercise and adequate rest and sleep into their lifestyles. Encouraging patients to maintain a diet with adequate amounts of protein, fiber, and carbohydrates, but with low fat, can help promote energy and decrease water retention. Avoiding foods that are high in salt and sugar may also decrease water retention, which will lessen physical discomfort from bloating and edema. Iodine supplementation can be considered for those who experience breast tenderness, as this element prevents the formation of estrone (E1), which is one of the three molecules of estrogen that contribute to mastalgia.[57] Women with perimenstrual disorders should also avoid alcohol and illicit drugs as they often worsen emotional lability.[54]

TABLE 4:

OMT treatments for pelvic pain[29,50,51]

TECHNIQUE	BASIC STEPS	CONTRAINDICATIONS	OSTEOPATHIC MODEL
Pelvic Diaphragm Release	Can be performed in lateral, prone, or supine position. The physician's fingers are placed medial to the patient's ischial tuberosity. Patient then inhales and exhales slowly. With patient exhalation, the physician advances fingers cephalad.	Few contraindications but consider patient positioning.	Respiratory- Circulatory Metabolic-Nutritional
Lumbosacral Decompression	Patient is in lateral position. Place fingers of one hand on sacral base and the other on L5. Traction to separate fingers and gap the lumbosacral junction.	• Localized and unstable spinal fractures	Mechanical Neurologic
Anterior Counterstrain Points (Pelvis) 1. Psoas-2/3 distance from ASIS to midline 2. Iliacus-1/3 distance from ASIS to midline 3. Low Ilium- Superior surface of iliopectineal eminence 4. Inguinal- Lateral aspect of pubic tubercle.	Indirect technique. All treatments need to be placed into proper position and held for 90 seconds or until a change in at least two or three of the TART changes are palpated by the physician 1. Marked bilateral hip flexion and some external rotation with side bending toward side of tender point. 2. Marked bilateral flexion and external rotation of hips with knees flexed. 3. Marked ipsilateral hip flexion. 4. Flexion of hips with contralateral thigh crossed over ipsilateral thigh. Ipsilateral thigh is then pulled laterally for slight internal hip rotation.	Relative Contraindications: • Cannot voluntarily relax. • Cannot discern pain with positional change. • Cannot understand instructions. • Connective tissue disease (arthritis, Parkinson's) Absolute Contraindications: • Severely strained tissue. • Instability of treated area. • Vascular or neurologic disease. •Degenerative spondylosis.	Mechanical
Sacral Rocking	Patient is prone and physician should cup hands over sacrum. Gentle rocking into nutation and counter-nutation is performed.	• Pilonidal cyst	Mechanical Respiratory-circulatory Neurologic Metabolic-Nutritional
Ischial Tuberosity Spread	Patient is prone with the upper body elevated on the elbows and knees flexed. Place thumbs medial to the ischial tuberosities. Have the patient exhale slowly and apply lateral pressure. Repeat three times.	• Fractures • Cannot tolerate treatment position	Mechanical Respiratory-circulatory Neurologic
Doming of the diaphragm	Fingers are placed under xyphoid process pointing cephalad and posterior. Patient slowly inhales and exhales. Fingers are advanced cephalad with exhalation.	• Rib fractures	Mechanical Respiratory-circulatory Metabolic-nutritional
Quadratus lumborum release	Have patient lie on affected side. Lift both feet up to the ceiling. Ask patient to push down to the floor while applying isometric resistance. Re-engage the barrier three times while repeating the procedure.	Few contraindications	Mechanical Neurologic
Pedal Pump	Patient is supine and physician places hands on plantar aspect of feet and moves them rhythmically into dorsiflexion and plantar flexion as if sloshing saline in one total body biologic system. At first physician initiates bodily movement but then the fluid begins to move the physician's hands. The repeated dorsiflexion/plantar flexion should be at about 120 movements per minute. The end point of a true lymphatic pedal pump is that there is no resistance.	Contraindications: • Venous thrombosis • Ankle Sprain • Achilles strain • Post-surgical patient	Respiratory-circulatory
Marian Clark Release	Patient is semiprone on all fours with back arched. Physician places fingerpads medial to the patient's ASIS bilaterally. The physician then pulls hands cephalad and tractions abdomen upwards repeatedly.	Pre-existing condition that prevents her from attaining the treatment position.	Respiratory-circulatory
Inhibitory Sacral Pressure	Patient is prone as the physician maintains a steady pressure on the base of the sacrum until pain is relieved. The same may be done at the thoracolumbar region.	Fractures in surrounding area.	Mechanical Neurologic
Suboccipital Release	Patient is supine. Put fingers onto patient's suboccipital area. Apply gentle lateral and superior traction by pushing elbows together and tractioning backwards.	Few contraindications	Neurologic Biopsychosocial
Myofascial C1, C2, L1-5	Direct or Indirect Technique; Doctor places enough force to contact the patient's cervical fascia. The doctor then moves the fascia into either its restriction or ease and holds it in place for 20-60 seconds or until a release is felt.	Relative Contraindications: • Acute sprain • Fracture • Neurologic or vascular compromise • Osteoporosis or osteopenia. • Malignancy • Infection Absolute Contraindications: • None	Mechanical
Muscle Energy C1, C2	Direct technique; Patient is supine and physician brings neck to the edge of the restrictive barrier. The patient is then asked to move neck towards his or her direction of freedom while the physician applies an isometric force for 3-5 seconds. The patient then relaxes for 3-5 seconds and the patient is brought further into his or her restrictive barrier. Repeat 3 times and perform a passive stretch into the restrictive barrier at the end of treatment.	Relative Contraindications: • Severe muscle strain • Osteoporosis • Post-surgical or ICU patient Absolute Contraindications: • Fracture • Dislocation • Joint Instability • Lack of cooperation from patient.	Mechanical
Chapman Reflexes	Firm and gentle rotary motion on the point until the localized swelling is smoothened out or stringy muscles are relaxed.	Few contraindications	Mechanical Neurologic

CONCLUSION

The effects of the altered hormonal state in PMS and PMDD is vast and the inflammation pathways of menstruation can be excruciating. These effects extend to not only the soma but also to multiple organs including the thyroid, ovaries, uterus, kidneys, pelvic lymphatic glands, kidneys, adrenals, and breasts. Perimenstrual disorders result in a reduced quality of life for women suffering from them, having impact on their jobs, education, relationships, emotional state, and well-being. OMT can be useful for these patients because of the holistic approach to treating these distinct organs and the limited side effects that can be associated with pharmaceutical medications. OMT can be considered as an adjunctive means of treating perimenstrual disorders and improving the physical and emotional state of the women suffering from them.

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CLINICAL IMAGE

Rash in an Elderly Bed-Bound Patient

William Webster, OMS IV[1]; Michaeleena Carr, DO[1]

[1]Prisma Health Tuomey - Sumter, SC

A 91-year-old afebrile female with a history of bilateral below-the-knee amputations and congestive heart failure presents to the emergency department by ambulance with a vesicular and excoriated rash to her upper and lower extremities *(Figure 1 and Figure 2)*. The patient was being evaluated by a wound care specialist and was advised to report to the emergency department for the possibility of infection. The vesicular lesions have been progressing in size and number for two weeks, although localized to the patient's upper and lower extremities.

The lesions have enlarged to bullae as large as 6 cm in diameter, with worsening pruritus and resultant excoriations. There is no induration, tenderness to palpation or surrounding erythema noted and very minimal pigmentation changes surrounding the lesions. Nikolsky sign is not present and there is no involvement of the oral mucosa, palms, or soles. Initial laboratory tests reveal an elevated C-reactive protein and are otherwise unremarkable. Medications include daily furosemide.

FIGURE 1:

Vesicular and excoriated rash to upper extremities

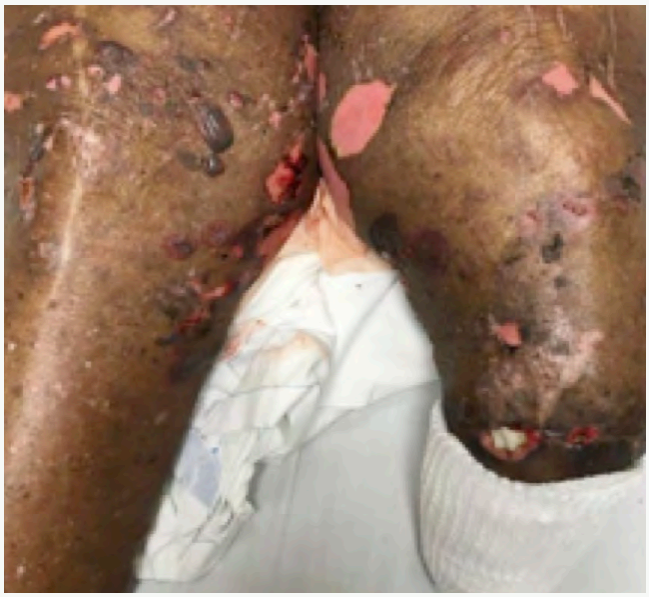

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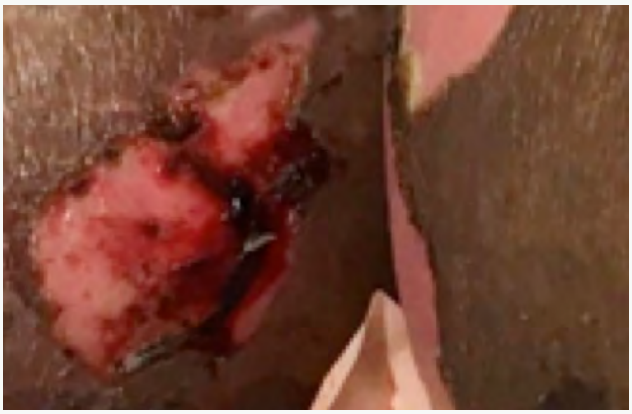
FIGURE 2:

Vesicular and excoriated rash to lower extremities



QUESTIONS

1. What is the most likely diagnosis?

A. Staphylococcal Scalded Skin Syndrome
B. Cellulitis
C. Bullous Pemphigoid
D. Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis
E. Pemphigus Vulgaris

2. What is the most common etiology of this rash in the patient's age group?

A. Autoimmune
B. Photosensitivity
C. Type IV Hypersensitivity reaction
D. Medication Induced
E. Fungal

3. Given that the patient has two below-the-knee amputations and is bedridden, what is the first line of treatment in this patient?

A. Symptomatic care
B. Topical corticosteroids
C. Oral terbinafine
D. Topical bacitracin
E. Oral corticosteroids

ANSWERS:

1. What is the most likely diagnosis?

Correct Answer: C) Bullous Pemphigoid

The fluid-filled blisters began developing with no known exposure to infectious or hypersensitivity agents. Originating as vesicles less than 1 cm in diameter, the lesions progressed over several days to bulla as large as 6 cm in diameter. This is the typical presentation of bullous pemphigoid.[1] Staphylococcal Scalded Skin Syndrome (SSSS) and cellulitis are both infectious processes, expecting erythema, induration, or warmth on physical exam. Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are serious, immune-mediated responses to medications or infection which result in confluent epidermal necrosis. Pemphigus vulgaris (PV) is an autoimmune blistering disease that can be differentiated from bullous pemphigoid based on unique autoantibodies as well as a physical exam.[2,3]

2. What is the most common etiology of this rash in the patient's age group?

Correct Answer: A) Autoimmune

It is characterized by subepidermal autoantibodies directed against two components of adhesion complexes promoting dermo-epidermal cohesion.[4] These autoantibodies can activate an inflammatory reaction that can cause epidermal-dermal splitting and resultant blistering.[1]

3. Given that the patient has two below-the-knee amputations and is bedridden what is the first line treatment in this patient?

Correct Answer: E) Oral corticosteroids

Topical clobetasol propionate 0.05% (40 grams per day) has been shown to be superior to oral prednisolone (0.5 mg/kg per day) in terms of overall survival, disease control and adverse event profile for patients with extensive BP.[4,5] However, due to poor practicality and compliance in bedridden patients, oral prednisolone or prednisone (0.5–1 mg/kg per day) is recommended as the initial therapy in this patient.[6,7]

DISCUSSION

Bullous pemphigoid (BP) is the most common subtype of autoimmune blistering disease, which although rare, can lead to fatal outcomes. Typically, it manifests with large, tense blisters preceded by urticarial plaques and severe pruritus.[7] BP ranges from mildly itchy welts to severe blisters that can be complicated by infection. It may affect a small area of the body or be widespread, commonly affecting the lower abdomen, inner or anterior thighs, and flexor forearms. The clear majority of those affected are elderly, but it has been seen at all ages.[6,8] Commonly progressing over several days to weeks, small vesicles progress to larger bullae accompanied by this severe pruritus.[8] This can inevitably lead to excoriation and infection if proper treatment is not initiated promptly.

The pathophysiology of this skin disease involves autoantibodies against hemidesmosomal antigens. The binding of autoantibodies leads to complement activation, recruitment of inflammatory cells, and release of proteolytic enzymes.[3] It is this onslaught of immunological and inflammatory mediators involving the hemidesmosome and its components that leads to urticaria and consequent subepidermal blisters.

Medical knowledge regarding bullous pemphigoid has progressed considerably over recent years, allowing for rapid detection and differentiation from other autoimmune blistering diseases such as pemphigus vulgaris. The location of blistering and immunoglobulin deposition distinguishes bullous pemphigoid from pemphigus vulgaris.[9]

In pemphigus vulgaris, blister formation and antibody deposition occur within the epidermis/epithelium, where keratinocytes in the epidermis and mucus membranes lose cell-cell adhesion from direct attack of autoantibodies to the desmosome.[9,10] Bullous pemphigoid differs because these autoantibodies fix complement and mediate inflammation secondary to binding to hemidesmosomal components. This differentiation has enabled diagnostic testing for these diseases by enzyme-linked immunosorbent assays and dissection of various pathophysiological mechanisms that have led to targeted therapeutic strategies.[9]

DIAGNOSIS

In a setting of tense bullae with dermal-epidermal separation on histology and positive direct immunofluorescence for IgG or C3, the diagnosis of bullous pemphigoid can be made if three of the four following criteria are present:

1. Age more than 70 years,
2. absence of atrophic scars,
3. Absence of mucosal involvement,
4. Absence of predominant bullous lesions on the head and neck.[7,11]

This has a sensitivity of 86%, specificity of 90%, and positive predictive value of over 95% when validated using immunoblotting as the gold standard.[7] Therefore, it is recommended to perform a direct immunofluorescent and serological analysis to exclude bullous pemphigoid in all patients with pruritic skin lesions who are at least 65-years-old.[12] ELISA can then be used to further confirm the diagnosis.[7]

There still exists clinical dermatological signs that can aid in the differentiation of blistering diseases. Nikolsky sign is present when slight rubbing of the skin results in exfoliation of the outermost layer, forming a blister within minutes.[4] This technique is useful in differentiating pemphigus vulgaris (positive Nikolsky sign) from bullous pemphigoid (negative Nikolsky sign). Asboe-Hansen sign is also useful clinically, characterized as the extension of a blister to adjacent unblistered skin when pressure is put on top of the bulla. While a regular rounded border is observed in bullous pemphigoid

and other subepidermal blistering disorders including dermatitis herpetiformis, an irregular angulated border is seen in pemphigus vulgaris.[4]

TREATMENT

The treatment of BP should be aimed at decreasing blistering formation and pruritus, promoting the healing of blisters, and improving QOL while having a minimally adverse profile.[13] As discussed before, topical clobetasol propionate 0.05% (40 grams per day) has been shown to be superior to oral prednisolone (0.5 mg/kg per day) and has thus taken over the previous benchmark of bullous pemphigoid therapy, oral corticosteroids, as first line therapy. Due to its impracticality and poor compliance in bed-ridden patients, oral prednisolone or prednisone (0.5-1 mg/kg per day) is recommended as the initial therapy in such cases.[5,6] It is important to note the importance of tapering oral corticosteroids, as a taper of 6-9 months can be initiated once there have been no new lesions or pruritis for at least two weeks.[1,6] Hydroxyzine 10-50 mg has been shown to symptomatically control pruritis when given every four hours as needed.[14,15]

Given the possible adverse side effects seen with oral corticosteroid therapy, alternative therapies have also been studied. A randomized controlled trial found that doxycycline(200 mg daily) was inferior to prednisolone, but such a reduction in effectiveness was acceptable given its favorable safety profile.[2,14] Nicotinamide has been shown to exhibit synergistic effects with antibiotics, as it should be started at 500 mg daily and gradually increased to 1500-2500 mg daily to minimize gastric side effects.[1,6,8,14] Antibiotics and nicotinamide can be continued for as long as one or two months until control is achieved and can be used as monotherapy, concomitantly with oral steroids, or after the disease has been initially controlled with oral steroids to maintain remission during steroid taper.[1,14]

Patients with a neutrophil predominate infiltrate or mucosal involvement have been shown to respond well to dapsone 50-200 mg daily.[6,14] In patients with inadequate response to the aforementioned treatments, further adjuvant therapy has been studied including methotrexate (5-25 mg/week), azathioprine (1-3 mg/kg/day), mycophenolate mofetil(1.5-3 g/day), and IVIG.[1, 6,8,14] Compared with placebo, IVIG at 400 mg/kg/day for five consecutive days is an effective therapeutic approach in such patients and can be repeated every four weeks until remission.[14,16] Cyclosporine and plasmapheresis have been used in patients with severe progressive disease but is seldom required.[1,14]

CONCLUSION

Bullous pemphigoid is an autoimmune blistering disorder, characterized by fluid-filled blisters(bullae) and pruritus. Common in elderly patients, the pruritus and eventual excoriation can be a concern for infection. For this reason, prompt diagnosis and treatment are important to prevent further complications and ensure a better quality of life for the patient. Frequent examinations of the trunk and upper and lower extremities are important to check for developing blisters, especially in elderly patients who live in a nursing home, as these patients may overlook the lesions or fail to mention them to the provider.

AUTHOR DISCLOSURE:
No relevant financial affiliations

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PATIENT EDUCATION HANDOUT

HIGH CHOLESTEROL

Fariha Siddiquie, OMS

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

High cholesterol is a risk factor for heart disease. It is a form of fat derived from the food we eat that can build up in blood vessels and create plaques. Plaques are large lumps of fat which stick to the vessel wall and obstruct the flow of blood, creating increased pressure.

THE NEGATIVE EFFECT OF HIGH CHOLESTEROL

Imagine the heart is like a water pump, you push down on the pump so that water can flow out through the pipe. Similarly, your heart works to push blood through little pipes called blood vessels throughout your body. If there is too much debris and rust within the pipe, you must work harder and faster at the pump to get the same amount of water flow. In the same way, cholesterol is like debris that builds up in the vessels and obstructs blood flow, causing the heart to pump harder.

MEDICATION OPTIONS FOR HIGH CHOLESTEROL

Your doctor will take a blood sample to measure the total amount of cholesterol in your blood, ideally it should be less than 200 mg/dl. If your total cholesterol is high, that does not mean you are automatically prescribed medication! First, your doctor will calculate your risk score, which factors in all proven risks associated with heart disease. If your score is above a 7.5%, drug therapy with a statin is started. This drug is also found with many other names including Lipitor, crestor, and altoprev. Statins are the first line medication as it can both decrease bad cholesterol, and increase good cholesterol. However, it also causes side effects of muscle pain and digestive issues. As cholesterol levels are regularly monitored, your doctor may add on other medication that lowers levels in different ways, until the best fit is found.

THE IMPORTANCE OF LIFESTYLE CHANGES BEFORE MEDICATION

Diet, weight loss, and physical activity are the greatest weapons we have against disease. To lower cholesterol naturally, decrease consumption of red meat and full fat dairy products. Look at food labels and avoid anything with "partially hydrogenated vegetable oil" or "trans fat." Fill your plate with high fiber foods such as oatmeal, beans, Brussel sprouts, apples and pears. Add at least thirty minutes of moderate aerobic activity to your schedule, five times a week. Physical activity and weight loss both decrease levels of bad cholesterol, and increase natural levels of good cholesterol, doubling the decrease in heart disease risk! Additionally, it is vital to quit any tobacco products. Just within a year of quitting, the risk of heart disease is cut into half.

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SOURCE(S): *Mayo Clinic, UpToDate; American College of Cardiology*

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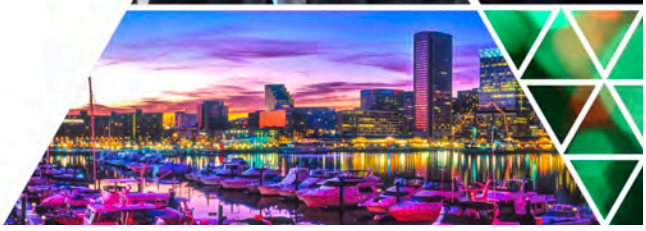

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