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The Rule of Three

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EDITOR'S MESSAGE

Words Matter

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

Words matter. In fact, Merriam-Webster added 520 new words to their dictionary earlier this year. Not surprisingly, words related to the pandemic, such as "long hauler" and "COVID-19" made the cut, and the latter word added to the specious arguments on Twitter related to "what happened to COVID-1 to 18?"

Added words tend to reflect societal happenings or perhaps the normalization of events within our culture. Online communication and terms that were until recently only online have spilled over IRL (in real life). Many people will take a "hard pass" at the "flex" using these new words may produce in casual conversations. I particularly enjoy the crossover "@," as in "don't @ me bruh," especially when speaking with my teenage daughter. Not sure whether her perception of her father has been improved or damaged through my expanded vocabulary. The newly added words of gig worker and gig economy reflect the changes to the way people work and the influences of mobile technology in the workplace. Occupations have been changing over the past few years, and the coronavirus has hastened this change.

Expanding the dictionary to include words that are related to identity and self-identification have been added recently. Some of this year's inclusions are "BIPOC" (abbreviation for black, indigenous and people of color) and "folx," a version of folks that is used to explicitly signal the inclusion of groups commonly marginalized. This issue contains a very interesting research article regarding physician beliefs related to identity. For self-identification, I am happy for my future self for the addition of "silver fox" to the dictionary and hope my sapiosexual spouse appreciates the intelligence displayed by knowing these terms.

Within this issue, we tackle some of the pandemic complications, especially related to behavioral health. After coping with an incredibly stressful year, we take comfort in many things. The novel dictionary terms help provide words for this comfort. ASMR (autonomous sensory meridian response) is a pleasant tingling sensation that originates on the back of the scalp and often spreads to the neck and upper spine, that occurs in some people in response to a stimulus—such as a particular kind of sound or movement—and that tends to have a calming effect) is a wonderful

term that hopefully reflects some thoughtful OMT. Another comfort term introduced included hygge (a cozy quality that makes a person feel content and comfortable), which seems to be more suited to something found at lkea than the dictionary.

I hope you find comfort in this issue's words and find a time to use your newfound vocabulary in a non-stressful manner. Enjoy the journal, and have a good start to the summer of 2021!



FROM THE PRESIDENT'S DESK



Innovating Amid Continued Uncertainty: Progress in a Virtual World

Nicole Heath Bixler, DO, MBA, FACOFP ACOFP President

The month of May brings the end of the school year, summer vacation plans and sunny days. It is typically when we see our many state ACOFP chapters hold their annual meetings as a time to gather with colleagues and their families for education and fun. As this will be the start of our second COVID summer, these celebrations, plans and gatherings are still veiled in uncertainty, facemasks and more virtual interactions. It is fair to say we are in a much better place than last year, not only in our fight to end the pandemic, but also in our capabilities and creativity in making our virtual world more inclusive and interactive. The ACOFP Annual Convention & Scientific Seminars, held virtually in March, highlighted our efforts to enlighten, celebrate and educate our collective family in new formats to foster connectivity and a sense of normality.

The first order of business was the delivery of a participatory Congress of Delegates led by Speaker Elizabeth A. Palmarozzi, DO, FACOFP, and Vice Speaker Antonios J. Tsomponidis, DO, FACOFP. They masterfully navigated the Lumi platform that allowed more than 200 votes cast on 19 resolutions. Delegates had the opportunity to listen to pre-recorded messages from our dignitaries and special guests at their convenience. Additionally, a combined ACOFP President and Executive Director video paralleled the newly created 30-page annual report that highlighted the work of ACOFP in 2020. For many, this format was more efficient, accessible and engaging than our traditional two-day Congress.

Then we moved into our programming with a dynamic and thought-provoking keynote presentation from Sekou Andrews, a Grammy-nominated poetic voice artist, sharing Power Through the People: Diversity Is Disruption. In his unique format, our eyes, hearts and minds were opened by his forthright depiction of cultural, generational and racial differences. He challenged our thinking about the continuum of love represented as hate. He inspired while making some feel uncomfortable, a good sign seeing that some form of disruption is needed for positive change. He delivered exactly what was needed to result in over 50 pages of real-time chat dialogue and praise. The momentum continued as we introduced the inaugural Diversity, Equity & Inclusion (DEI) Award honoring Tejal R. Patel, DO. This award was established to recognize a physician's commitment to enhancing DEI in osteopathic education and practice. The combination of these events set the stage for three days of lectures, discussions and accolades. Many thanks to the Program Committee, Program Chair Matthew W. Told, DO, and Program Vice Chair Robert Danoff, DO, MS, FACOFP, FAAFP, for developing an outstanding CME program with various tracks of learning to meet the individual needs of our attendees. If you were not there, you missed out on

the full experience—but maybe not completely (read on to learn more).

The utilization of the Pathable platform gave attendees the opportunity to tour a virtual exhibit hall with access to vendors in between the informative and diverse lectures, as well as a chance to chat with new and old colleagues through the Idea Exchanges and Conversation Circles. Throughout the entire event, there was an underlying Connect the Dots & Collect the Dots game that sparked friendly rivalry in obtaining the most points to win coveted prizes. The chat function that accompanied every lecture and event worked seamlessly to answer questions, provide insight, banter with good humor and congratulate award recipients. The recognition of our deserving physicians with personal introductions and acceptance speech videos throughout the convention was just a slight variation from our traditional awards program. The following individuals were recognized:

- Bruce C. Brink, Jr., DO, FACOFP | Osteopathic Family Physician of the Year
- Joel M. Feder, DO, FACOFP dist. | Lifetime Achievement Award
- Robert C. DeLuca, DO, FACOFP dist. | Certificate of Special Recognition
- Barbara E. Walker, DO, FACOFP, FAAFP | Outstanding Female Leader Award
- Ira P. Monka, DO, MHA, FACOFP | Excellence in Advocacy Award
- Rachel A. Young, DO | New Physician of the Year
- Peter F. Bidey, DO, MSEd, FACOFP | Osteopathic Family Medicine Educator of the Year
- Carol L. Henwood, DO, FACOFP dist. | Distinguished Service Award
- Steven Legault, MSW | Distinguished Service Award

The honored tradition of the Fellows ceremony was magically created with academic regalia and videos from Florida to Colorado and everywhere in between. Once again, congratulations to the 2021 class of ACOFP Fellows:

- Eileen Conaway, DO, FACOFP
- · Paula Gregory, DO, MBA, FACOFP
- Mark Kauffman, DO, MSMEd, FACOFP
- Anthony Leazzo, DO, FAOASM, FACOFP

- Rebecca D. Lewis, DO, FACOFP
- · Priscilla Tu, DO, FAOASM, FAAFP, FAAMA, FACOFP
- John C. Welch, Jr., DO, FACOFP
- · Hallie Y. Zwibel, DO, MPH, FAAFP, FACOFP

The awards continued as the ACOFP Education & Research Foundation and Auxiliary to the ACOFP bestowed their honors on the following residents and students:

- David Tyler King, DO | Sander A. Kushner, DO, FACOFP Memorial Osteopathic Family Medicine Resident Award
- Heather McGuire, OMS-IV | Marie Wiseman Outstanding Osteopathic Medical Student of the Year
- Athena Chatzigiannidis, DO; Kendall Harris, DO; and Dustin Beck, DO | Namey/Burnett Preventive Medicine Writing Award, First Place
- Colleen Maher, OMS-IV | Namey/Burnett Preventive Medicine Writing Award, Second Place
- Shikha Patel, OMS-IV | Namey/Burnett Preventive Medicine Writing Award, Third Place
- Seema Mehta, OMS-III; Vikesh Shrestha, OMS-II; and Jasmine Nguyen, OMS-II | Emerging Leader Awards
- 19 Osteopathic Family Medicine Student Awards

And on Sunday morning, the Student Association of the ACOFP elected their new National Student Executive Board:

- Joe Li, OMS-III | President
- · Ashley Beckham, OMS-II | Vice President
- Rachel Souza, OMS-II | Secretary
- Kensley Grant, OMS-I | Parliamentarian
- James Wyatt Eikermann, OMS-IV | Student Governor

Additionally, there were nearly 100 scientific posters submitted and available for viewing throughout the convention. The future of osteopathic family medicine is in good hands with these student and resident leaders.

To say the least, besides the lack of physical connection with osteopathic hugs, OMT Boot Camp and procedural workshops, this virtual meeting was the closest I have felt to my osteopathic family since the start of the COVID-19 pandemic. To make that happen took the work of a forward-thinking Board of Governors, a dedicated and visionary ACOFP staff, engaged speakers, and—for the individual attendee—good bandwidth and a WiFi connection. So, if you were not one of the almost 2,800 participants that joined us live for this history-making event—you have not completely missed out. You will have the opportunity to use our eLearning Center to purchase this on-demand and obtain CME as if you were at a live event. There is also our upcoming Intensive Osteopathic Update that will be held virtually this summer as another opportunity to see our platforms and innovation work in

real-time.

Whichever you choose, thank you for your confidence in ACOFP to provide you with your educational needs and connection to your colleagues during this challenging time. I hope this summer brings all of us more certainty and increased opportunities for in-person engagement while not losing sight of the gains we have made in our virtual environment.

Osteopathically,

Nicole Heath Bixler, DO, MBA, FACOFP

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LETTER TO THE EDITOR

THE RULE OF THREE

To the OFP Editor:

Good Morning! I'm Dr. Abend, and I'll be treating you today. I am a DO.

A DO? What's that?

It's the acronym for doctor of osteopathic medicine. I'll be performing osteopathic manipulative treatment as part of my special training and hands-on skills.

Oh, you mean you can prescribe medicine and make referrals?

Yes, I am a fully licensed physician and can prescribe medication and physical therapy and refer patients to different specialists.

What about the chiropractic manipulations you do all the time?

The manipulations I perform are not chiropractic; instead, these are osteopathic and unique to what we do as DOs. They were developed to avoid medication and augment other therapies.

So, you're like a chiropractor?

No, it's the other way around. Chiropractors are like DOs. Most people know what a chiropractor is because they perform hands-on or manipulative techniques, but DOs are a hybrid. It's likened to having a chiropractor and an MD wrapped into one.

This type of conversation happens to me almost weekly when encountering new patients, as it has for the past 30 years of my experience as a practicing osteopathic physician. I usually describe to the patients the current statistics describing the exponential growth of DOs, which now comprises approximately 11% of the U.S. physician population, with 150,000 doctors currently in our ranks and another 25,000 students in medical school training.¹ If patients want to learn more, I refer them to the American Osteopathic Association website, specifically for patients,² or Wikipedia.³⁴ When disseminating this information, I carefully avoid using archaic terms such as osteopathy or therapy when describing osteopathic manipulative treatment (OMT). Ironically, due to its MD orientation, one of the best DO descriptions is offered by the Cleveland Clinic.⁵ With my facile hand manipulations and my explanations to patients, staff and students come readily. If they are willing, I demonstrate my skills and let the results speak for themselves. Although osteopathic practices have been in existence for over 128 years, recently, my conversations with patients had taken an interesting turn at a time when osteopathic physicians did not ask or even need public relations. It was thrust upon us after a curious Rule of Three in 2020. I was reminded of my mother's religious superstition that things always seem to happen in three.

The Oxford Dictionary of Quotations lists third-time lucky in its Proverbs section and says it goes back to the mid-19th century. The number three is much more often associated with good luck than bad. There's an old soldiers' superstition, variously said to date from the Crimean or Boer Wars, that it is bad luck to light three cigarettes with one match. That would give any would-be sniper a good sight at a target. However, I have also seen a suggestion about a Russian Orthodox prohibition on lighting the three altar candles with one taper.

Rule of Three #1: After then-President Donald Trump was diagnosed with COVID-19, I sat watching the October 3, 2020, national television broadcast of the physician press conference outside Walter Reed Naval Medical Center where the then-President was being treated. The cameras focused on the left-hand pocket of Dr. Sean Conley's starched crisp white coat, clearly reading Sean P. Conley, DO, Physician to the President, as he updated the nation on then-President Trump's condition after being admitted to the hospital.⁸

Rule of Three #2: A short time later, I read an article about then-President-Elect Joe Biden and his physician, Dr. Kevin O'Connor, who is also a DO.9

Rule of Three #3: Then, also in October 2020, NBC News reported Figs®, a manufacturer of medical scrub wear, posted a video advertisement insensitively targeting not just DOs but female DOs by specifically featuring a woman in neon pink scrubs reading an upside-down book titled "Medical Terminology for Dummies." ¹⁰

Suddenly, osteopathic medicine is taking center stage and in the national spotlight. Evidence of this could be seen after Sean Conley, DO, gave his update from Walter Reed Naval Medical Center. Despite his impressive background—consisting of an undergraduate degree from Notre Dame in 2002, graduation from The Philadelphia College of Osteopathic Medicine, and service in Afghanistan in active duty in the U.S. Navy and attaining the rank of Commander—the media seemed to focus solely on defining osteopathic medicine and DOs. As mentioned above, Dr. O'Connor is now President Biden's physician, a DO, a member of the George Washington University Medical Faculty Associates, a graduate of the New York College Osteopathic Medicine and a decorated flight surgeon and colonel in the U.S. Army.

Once again, the media spent its energy highlighting the osteopathic community. News media sources from all over the U.S., using quotes from leaders in our medical profession, juxtaposed us with our MD counterparts. But their efforts fell far short of the mark. Some news outlets referred to us as holistic and labeled us as osteopaths or delved into politics after a cursory and superficial discourse, thereby further confusing the public. 11,12,13 The Atlantic published a well-researched piece with a rich history of the osteopathic medical profession and a little-known Irish publication/newsletter published a piece that described Dr. Conley's osteopathic medical training in some detail. 15

With decades of experience, I have provided medical care to thousands of patients as a primary care physician. I've also proudly integrated the gift of hands-on skills learned from my medical school training of over 700 hours in Kirksville, notably OMT taught throughout my medical training and beyond. This unique hands-on skill forms the backbone of our profession's deep roots as developed by the founder, Andrew Still, an MD. An American-born physician, Dr. Still sought to improve upon the primitive and barbaric practices of medicine at the turn of the century in the late 1800s/early 1900s. This difference in utilizing our own hands helps heal the human body to support other traditional medical options—such as pharmacologic, interventional and surgical—that I have always championed. For more than a quarter of a century, other types of hands-on arts and sciences, such as physical therapy, chiropractic, massage, and even some sports medicine MDs, have incorporated OMT.¹⁶

While 11% of the nation's medical doctors are DOs, less than 10% use their hands and a lesser fraction of those are using their handson OMT skills. Moreover, DOs and MDs are generally indistinguishable today because the lines are blurred with the new Accreditation Council for Graduate Medical Education guidelines creating one universal residency matching program. In my opinion, these factors are fostering the public's misperception of our profession.¹⁷

We need to teach and reinforce our medical students and residents how important our hands-on osteopathic skills are to diagnose better and heal our patients. By doing so, we can create the necessary dialogue and recognition our medical profession deserves. The Venn diagram center connects the five clinical models: biomechanical, neurological, respiratory-circulatory, metabolic and behavioral, which form the basis—or root core—of osteopathic principles and philosophy.¹⁸ They provide the foundation of the basic and clinical sciences integrated into osteopathic medicine in all 37 osteopathic medical schools in 58 different locations.¹⁹

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RESEARCH ARTICLE

PHYSICIAN BELIEFS CONCERNING STRUCTURAL AND INSTITUTIONAL RACISM IN HEALTH CARE

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KEYWORDS:

Beliefs

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Institutional Racism

Race

ABSTRACT:

Perceived discrimination in medical settings remains prevalent within the U.S. health care system. However, the details of these experiences and their associations with perceived quality of care are not well understood. This study evaluates any potential difference in African Americans' systemic health care discrimination and Latinx perceived by African American and Latinx patients and physicians. The New England physician alumni from the University of New England College of Osteopathic Medicine were sent surveys. Two hundred fifty-one practicing physicians' responses to the 2018 study address their beliefs toward African Americans and Latinx' racism within the health care system. High scores indicate more significant perceived discrimination among these groups. Physicians have lower discriminatory belief scores across gender, patient racial distribution and specialty.

INTRODUCTION

Physicians from distinct racial minorities have the privilege of being highly educated professionals, often with power dynamics and societal respect. On the other hand, we are part of a system that provides unequal treatment to people of our same skin color and recognize there are significant perceived racial biases in the health care system. Populations in the U.S. that experience the greatest health disparities also suffer from negative cultural stereotypes, and implicit bias among physicians may impact clinical decision-making in ways that perpetuate health care disparities.¹⁻¹⁴

The perception of racism in the health care system by African Americans and Latinx is not unfounded and contributes to empirically demonstrated racial disparities in health and health care in the U.S.¹⁴ Structural issues act as real obstacles appropriate to care and contribute to the perceptions of racism that result in health care avoidance. Recent studies show that physicians continue to make decisions along racial lines and demonstrate acts of unconscious bias and microaggression.¹⁵⁻¹⁹ These subconscious acts can inadvertently undermine African American and Latinx patients' comfort in their care.²⁰ Therefore, it is at this interface between patients and their providers where improvements in racial bias perception can occur. A 2011 study by Todd found that

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experiences can combat automatic expressions of racial biases.²¹ In addition, a 2016 study demonstrated perspective-taking efficacy in reducing transphobia within its study cohort.²² Empathic feelings contribute to pro-social behavior.²³ Therefore, a physician's ability to show empathy for the African American and Latinx experience in health care might indicate the potential to perform acts of unconscious bias.

perspective-taking or actively contemplating others' psychological

In 1999, the Henry J. Kaiser Family Foundation surveyed 1,189 African Americans and 983 Latinx, which revealed significant perceived racial biases within the health care system.^{22,23} Frederick M. Chen, MD, MPH, utilized this data to quantify the degree to which African Americans and Latinx perceived racism and correlated those perceptions with physician preference and satisfaction with care.^{24,25} The degree of perceived racism was quantified into what was termed a "discriminatory belief score." Subsequent studies have found further evidence that perceived racial biases inform patient choices within health care and can result in negative health outcomes.^{24,25} Perceived discrimination is antecedent to disparities in cardiovascular health in minorities and poor glycemic control in diabetic African Americans. 25,26 These outcomes and others may occur because perceived discrimination modifies behaviors by decreasing preventive health services contributing to poor medication adherence and influencing chronic engagement in unhealthy behaviors to cope with stress.²⁷⁻³¹ The Henry J. Kaiser Family Foundation survey findings may have some degree of validity today, as perceptions of racial discrimination in health care persist. Furthermore, that perception may continue to guide health care.32-35

This current study aimed to ask whether physicians share the perspective of African Americans and Latinx about the degree of racial bias against them in the health care system. A physician's discriminatory belief scores could potentially identify physicians at high risk for committing acts of unconscious bias. Discriminatory belief scores could then become a tool for improving the physician/ patient relationship, lessening the bias perceived by minority patient cohorts. We sought to meet these aims by utilizing the discriminatory belief scoring system derived by Chen.²³

METHODS AND RESULTS

The initial hypothesis was that physicians believe less strongly that racial discrimination exists within the health care system than that thought by African American and Latinx patients. Therefore, physicians expect to have lower average discriminatory belief scores than African American and Latinx patients. Research is needed to understand racial and ethnic discrimination in the health care setting, which likely impacts health care perceptions and outcomes.

Chen *et al.* devised a formula to quantify discriminatory beliefs using the Henry J. Kaiser Family Foundation survey.²³ His team of authors independently identified survey items that they believed reflected patients' beliefs about racism. They identified nine survey items. Each item had been responded to by an African American or Latinx patient during the Kaiser Family Foundation survey using scaled Likert categories. These categories allowed for these items to be quantified and combined into a summated discriminatory belief scale. The items-chosen by the authors for their purposes-focused on various aspects of racism in health care, including unfair treatment, access to services, quality of care and cost.

The current study used the same nine items and Likert categories. However, we modified the survey's wording to assess physician perspectives on patient experience. The physician's views could be ascertained independently of one another to determine any differences in their own perceived discrimination. No question assesses specific patient-physician interactions or evaluates whether the physicians' practice knowingly or unknowingly discriminates against African American and Latinx patients. We instructed the physicians to assess their health care system experiences and their interaction with African Americans and Latinx patients. Table 1 shows the survey questions.

This study maintained the Kaiser Family Foundation's standards and Chen *et al.* by scaling with three or four Likert categories.²³ One item had respondents answer a binary yes or no. The raw scale score ranged from 9–30. The scores were then transformed by subtraction from the maximum score. This transformation allowed higher scale values to signify more significant racial discrimination of African American and Latinx patients by the health care system. The target cohort included physicians currently in active practice in New England. The alumni association from the University of New England College of Medicine (UNE-COM) distributed the survey to maintain their physician members' confidential email contacts. The doctors were faculty

TABLE 1:

Survey items for calculating discriminatory scores

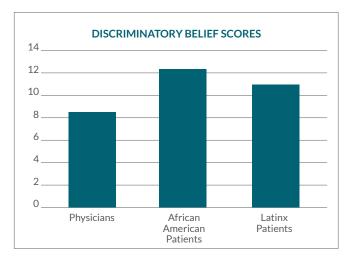
- 1. How often do you think our health care system treats people unfairly based on what their race or ethnic background is?
- 2. How often do you think a person's race or ethnic background affects whether they can get routine medical care when they need it?
- 3. How often do you think racism occurs when a patient and doctor are of different racial or ethnic backgrounds?
- 4. How often does racism occur if the patient and doctor are of the same racial or ethnic backgrounds?
- 5. Do you think most African Americans/Latinx receive the same quality of health care as whites?
- 6. Is racism a major problem in health care?
- 7. For the average African American/Latinx, how big a problem is being able to afford the cost of health insurance and medical care?
- 8. For the average African American/Latinx, how big a problem is having enough physicians and other health providers near where they live?
- 9. For the average African American/Latinx, how big a problem is having difficulty getting care because of their race or ethnic background?

of the medical school, regional clinical sites and local medical practices. The organizations did not have permission to access the survey responses and, therefore, were anonymous. The design of the electronic study could be completed once by a given email address. An email with the survey link included a statement of consent. Physicians could either provide consent and complete the survey, decline consent and not complete the survey or ignore the link altogether. Consenting physicians received demographic and survey questions.

These questions asked about the age, gender, race, ethnicity, medicine, specialty, level of training and average daily patient racial distribution in their current practices. Survey links remained open so physicians could complete them at a time and setting of their choosing. The survey was closed once we had 250 responses. Overall, the survey platform was open for 10 weeks, and 251 completed surveys were received. In addition, two declinations of consent and one survey were deemed invalid because the respondent was no longer in active practice. Comparisons were quantified using a one-way analysis of variance. A p-value of less than 0.05 is defined to be statistically significant.

The physicians demonstrated an average discriminatory belief score of 8.59. These were lower scores found for African American (12.4) and Latinx (11.0) patients in Chen *et al*'s 2005 study²³ (Table 2). We could not determine the significance of these scores in the absence of the raw data and standard deviations for African American and Latinx patients. No significant group within the physician cohort showed the same average discriminatory belief score as African American or Latinx patients. The one African American respondent in this physician cohort had a discriminatory belief score of 13.0. The four physicians who identified as Hispanic or Latinx had an average discriminatory belief score of 8.25. These scores were not statistically significant.

TABLE 2:Discriminatory belief scores for physicians with those obtained for African American and Latinx patients



Significant differences in the mean discriminatory belief score were found based on gender, patient population and specialty (Table 3). Females (9.30) had higher discriminatory belief scores than males (7.78, p<0.001). Physicians with only white patients, mostly white patients, half white/half African American and/or Latinx patients and primarily African American and/or Latinx patients reported scores of 10.2, 8.76, 7.23 9.21, respectively (p<0.01). There were no physicians with only African American and/or Latinx patients. [The respondents' specialties were medical, surgical, both and neither. These specialties are compared in Table 3. Medical (8.68), Surgical (7.92) Both (5.25) and Neither (9.14), respectively (p<0.05)].

There were no significant differences in discriminatory belief scores based on age, level of training, race and ethnicity of the responding physician (Table 3). There was also no significant difference between physician discriminatory belief scores against African Americans (8.58) and Latinx (8.60). Therefore, the mean discriminatory belief scores are the combined perception of the African American and Latinx experience.

DISCUSSION

The findings of this study suggest that physicians believe that the health care system discriminates against African American and Latinx patients to a lesser degree (discriminatory belief score: 8.59) than do African American (12.4) and Latinx patients (11.0). This finding is consistent with the current hypothesis. This is the first study to quantify physician beliefs about the degree of systemic racism encountered by African American and Latinx patients in their utilization of health care. Even though we did not have a broad diversity among the doctors surveyed, the conclusions are still valid. Two hundred fifty doctors who are alumni from of UNE-COM responded to this survey. Many of these physicians practice in Maine, which is known to have a racial composition of 94.48% white, 1.34% African American and 2.19% of two or more races. The UNE-COM currently uses the survey questions and methods. Chen's surveyed a national sample of 3,884 telephone interviews with adults 18-years-old and older, including 1,479 whites, 1,189 African Americans and 983 Latinx. Research studies about patient discrimination and racism in our health care system continue to be published. Racism and discrimination in health care continue to be a big issue; what has changed is our awareness and our ability to address these issues.

The difference in belief scores could be due to a deficit in physicians' education about health care disparities. There may be an in-group bias preventing admissions of the fault within the health care system. Furthermore, automatic biases and microaggressions occur subconsciously, so there may be an inherent lack of awareness of biased interactions between physicians and minority patients. Studies have attempted to address the presence of these social cognitions in physician care of patients. To fight racism, we all need to identify our own implicit bias. Methods have been proposed to increase awareness and overcome racism and discrimination in health

 TABLE 3:

 Discriminatory belief scores of physician respondents

	DISRIMINATORY BELIEF SCORE					
AGE	(20–29) 9.13	(30-39) 8.96	(40-49) 8.03	(50–59) 8.28	(60-69) 9.16	(70+) 7.6
GENDER	F 9.30	M 7.73	Decline 5			
RACE	African American 13	American Indian 9.25	Asian 9.57	Other 6.8	Caucasian 8.56	
ETHNICITY	Non-Hispanic or Latinx 8.59	Hispanic or Latinx 8.25				
SPECIALTY*	Both 5.25	Internal Medicine 8.68	Surgical 7.92	Neither 9.14		
LEVEL OF TRAINING	Attending 8.46	Fellow 8.08	Resident 9.25			
PATIENT RACE*	Caucasian 10.23	Mostly Caucasian 8.76	Half AA and LA 7.23	Mostly AA/or LA 9.21	Only AA and or LA 0	

The specialties are designated 'Both' for interventional radiology or anesthesiology subspecialties. 'Internal Medicine' designation is defined for an internist, internal medicine subspecialty, pediatrics or pediatric subspecialty, emergency medicine or specialties with an internal medicine intern year as radiology or dermatology. A 'Surgical' designation is for a general surgeon or surgical subspecialty and 'Neither' is for family medicine or osteopathic manipulative medicine specialist. AA – African American, LA – Latinx. *statistically significant.

care.⁴⁶⁻⁵⁰ The American Medical Association (AMA) has developed a Health Disparities Toolkit. This kit focuses on DVD interviews with physicians, nurses and patients on cultural competence and literacy topics. The integration of community health care workers on inter-professional teams is another promising strategy. Community health training for medical students, nurses, doctors and other community health workers improves our awareness. Whether the discriminatory belief scores we found relate to implicit biases remains to be seen.

Physician demographics stratified discriminatory belief scores. Female physicians believe there is health care discrimination against African American and Latinx patients to a significantly greater degree than male physicians.⁵¹ Studies that find a difference across genders in racial attitudes suggest that women have a more favorable opinion of minority groups, their experiences and policies designed to improve their general condition.^{49,50} These findings and those of the current discriminatory belief scores may be influenced by gender socialization, wherein women are expected to be more compassionate toward others than men.⁵⁰ Women's awareness of their vulnerabilities to discrimination may contribute to our results. Studies demonstrate female physicians experience their share of discrimination throughout their medical training.^{51,52} These scores suggest that perspectivetaking to decrease automatic, unconscious biases may be a more straightforward exercise for women.⁵³ However, more research is necessary to verify this conclusion.

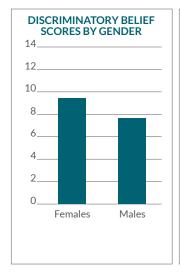
Physicians who exclusively saw white patients perceived more discrimination against African American and Latinx patients than those who saw mostly African American and Latinx patients. ^{30,42,44} In contrast, those whose average daily patient racial distribution was approximately half white, half African American and/or Latinx

perceived less discrimination against these groups. 43.44 These findings are influenced by cognitive biases like group attribution error and the availability heuristic. 53,54,55 Physicians may have been strongly influenced by their personal experiences—or lack thereof—with these racial and ethnic groups in their practice rather than considering the broader trends. Those who saw exclusively white patients may have been more objective in assessing the African American and Latinx experience because they could answer without implicating themselves as potential racial bias sources, while those whose average daily patient racial distribution was approximately half white, half African American and/or Latinx saw African Americans and Latinx and presumed that they had equitable health care encounters as white patients. It is possible they then attributed this experience to these racial and ethnic groups at large. More research is needed to ascertain how physician-patient profile impacts discriminatory belief scores.

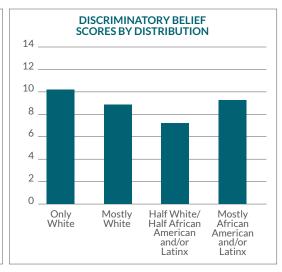
Specialities differ significantly in their discriminatory belief scores (Table 4). The discriminative belief scores were lower in interventional radiology and anesthesiology specialties. These doctors tend to have transient relationships with their patients. The lack of physician involvement in these patients' longitudinal care may consider their patients' socioeconomic status. The questionnaire instructed respondents to view the entire health care system; however, their personal experience may have heavily informed our participants' responses. Those in family medicine had a mean score of 9.14—the closest in value to African American and Latinx patients in our specialty groupings. Family medicine and primary care doctors spend a considerable amount of time developing positive relationships with their patients. Primary care doctors in rural and underserved communities establish long-term relationships with their patients. They provide comprehensive care to patients of all ages and genders throughout all stages of life.

 TABLE 4:

 Discriminatory belief scores based on gender, specialty and patient racial distribution







These graphs show statistical differences found based on gender. Significant differences (p < 0.001) between female and male physician scores, with females having a score of 9.30 (SD = 3.14) and males having a score of 7.78 (SD = 3.45) are shown.in the graphs. These graphs show statistical differences found based on physician specialty (p < 0.005) with scores of 8.68 (SD = 3.33), 7.92 (SD = 3.00), 5.25 (SD = 4.24) and 9.14 (SD = 3.26) and differences (p < 0.01) between physicians with varying patient populations: Discriminatory belief scores by patient populations shows white patients, mostly white patients, half white/half AA &/or LA reported scores of 10.2 (SD = 3.06), 8.76 (SD = 3.30), 7.23 (SD = 3.37), 9.21 (SD = 3.41) respectively.

There are not as many doctors around in rural areas and certainly fewer specialties. Family medicine doctors do more than they would in an urban neighborhood because they have fewer colleagues to assist them. Patients with a high level of trust in their family doctor had the highest level of satisfaction. The question is whether family medicine doctors show less racism and discrimination to their patients. Many African Americans and Latinx perceive racism in the health care system and those who do are more likely to prefer a physician of their race or ethnicity. African Americans who have preferences are more often satisfied with their care when their physicians match their preferences.

CONCLUSION

Physicians have lower mean discriminatory belief scores than African American and Latinx patients. This finding may suggest that physicians struggle with perspective taking a behavior shown to lessen acts of automatic, unconscious racial bias. Further research is necessary to link discriminatory belief scores and actions of automatic, unconscious racial bias.

AUTHOR DISCLOSURE(S):

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REVIEW ARTICLE

THE OSTEOPATHIC APPROACH TO TREATING DEPRESSION IN CHILDREN AND ADOLESCENTS

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ABSTRACT:

Evidence confirms that children and adolescents can experience the whole spectrum of mood disorders and suffer from the significant morbidity and mortality associated with them. Effective treatment often relies on physicians developing advanced communication skills with their patients. Enhanced communication will help decipher the etiology of the patient's depression and, in addition to serotonin-regulating medications, will optimize treatment. Osteopathic medicine offers an effective treatment model through osteopathic manipulative treatment (OMT) because of the inseparability of physical and mental health. Osteopathic medicine takes a holistic view in which somatic, visceral and psychological dysfunction are united. Thus, physicians who incorporate OMT into their practice will help treat psychopathologies, such as depression and its accompanying somatic dysfunctions. This paper discusses the epidemiology of depression, the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) depression criteria, screening algorithms, current treatment protocols, osteopathic considerations to treating depression, and lastly, OMT and its role in treatment.

INTRODUCTION

Depression is often thought of as an adult problem when many children and adolescents suffer from depression. The condition interferes with their ability to perform daily life tasks, create and maintain relationships, and perform in school. Additionally, in children and adolescents, depression is often accompanied by behavioral problems, substance abuse and/or other mental disorders. Complicating matters, in children and adolescents, depression can manifest differently than it does in adults, making the ability to recognize this problem and start interventions more difficult.1 Forty years ago, many physicians doubted the existence of significant depressive disorders in children because they believed that children lacked the mature psychologic and cognitive structures necessary to experience these emotions.² However, evidence has confirmed that children and adolescents not only can experience the whole spectrum of mood disorders but also can suffer from the significant morbidity and mortality associated with them.2

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The 2005–2014 National Surveys on Drug Use and Health, which included 172,495 adolescents 12–17 years of age, found that the percentage of adolescents who experienced one or more major depressive episodes in the previous 12 months increased from 9% in 2005 to 11% in 2014.³ In 2016, this percentage was approximately 13% (5% in 12-year-olds, 13% in 14-year-olds and 17% in 17-year-olds). Depression, in this paper, will be defined by using the DSM-5 criteria.⁴ It should also be noted that children and adolescents may display symptoms and signs of depression that are different than that of adults and we will further elaborate on this.

DISCUSSION

Background

The exact cause of depression is unknown. However, twin studies suggest that genetics and environmental influences both play important roles in developing depression.¹ Biologically, neurotransmitters (i.e., serotonin, norepinephrine and dopamine) are thought to be involved in the onset of depression.¹ Normally, neurotransmitters allow neurons to communicate with each other and play an essential role in all brain functions, including movement, sensation, memory and emotions.¹ Moreover, an individual's behaviors and thoughts play a role in the development and course of depression.¹ However, many external risk factors have been studied in children and adolescents that put them at risk for depression. Typically, these risk factors are broken down into three domains:

Biological

Being overweight,⁵ chronic illness (i.e., diabetes mellitus, asthma, cancer),⁶ early puberty,⁷ family history of depression,⁸ female sex,⁹ high-functioning autism,¹⁰ LGBTQ status¹¹ and any genetic abnormalities in the serotonin, dopamine or monoamine oxidase genetic pathways.¹²

Psychological

Body dissatisfaction and early dieting, ¹³ dysfunction in emotion regulation, ¹⁴ video game addiction, ¹⁵ less attachment to parents, ¹⁶ problems with peers to peer interactions, ¹⁷ low self-esteem, ¹⁸ having an overall negative thought process, ¹⁹ previous depression, ²⁰ substance use disorder (i.e., alcohol), ²⁰ problematic use of and addiction to social media outlets (i.e., Facebook) ²¹ and extreme worry about school grades or standardized testing. ⁹

Environmental

Academic difficulties,⁹ being bullied or witnessing violence,²² physical, sexual or emotional abuse,²³ loss of a loved one,⁹ exposure to natural disasters,²⁴ few opportunities for physical activity,²⁵ greater than two hours per day of leisure-time screen use,²⁵ low socioeconomic status,²⁶ low parental involvement,⁷ poor family functioning and caretaker depression.⁷

DIAGNOSIS

With all these possible risk factors, the diagnosis of depression in children and adolescents can often be a challenge due to multifaceted social situations and comorbidities. The presenting signs of major depressive disorder (MDD) in children and adolescents include, but are not limited to, insomnia or hypersomnia, weight loss or gain, difficulty concentrating, loss of interest in school, sports or other previously enjoyable activities, increased irritability or a constant feeling of sadness or worthlessness.4 To distinguish MDD from normal grief (such as after the loss of a loved one), it is helpful to determine whether the predominant symptom is a sense of loss (more typical of grief) versus a persistent depressed mood in which one cannot anticipate future enjoyment (more typical of depression). However, if a clinician suspects a child or adolescent having MDD, they may use a screening tool, such as the patient health questionnaireadolescents (PHQ-A) and/or the Beck Depression Inventory, second edition (BDI-II). If the child or adolescent presents with symptoms indicating a possible depressive disorder, the primary care physician should assess whether the symptoms are truly the result of a major depressive episode and not better explained by another condition or substance that may mimic these symptoms. Criteria from the DSM-5 must be met to diagnose MDD.4

One important factor to consider is that children and adolescents may have more than one psychiatric diagnosis concurrently, such as co-occurring depression and anxiety (or behavioral problems).²⁷ In fact, about three in four children aged 3–17 years with depression also have anxiety (73.8%) and almost one in two have behavioral problems (47.2%).²⁷ Thus, it is understandable why the United States Preventive Services Task Force (USPSTF) dictates annual depression screening in adolescents because of the prevalence of comorbidities.²⁸ The importance placed

on screening youth and being aware of potential depression symptoms is because of the significant negative consequences depression can have on this population. One of the significant negative consequences of missing or delaying the diagnosis of MDD would be the risk of suicide—the second leading cause of death for individuals 10-24-years old—after unintentional injury.²⁹ Depression is a major risk factor for suicide, yet at-risk youth can still be easily missed without specific suicide screening, as well as depression screening.³⁰ Nevertheless, early diagnosis and treatment can improve outcomes and possibly even resolve the issue.²⁸

CURRENT TREATMENT OF DEPRESSION IN CHILDREN AND ADOLESCENTS

As many as 70% of youths with depression experience severe impairment from the condition, yet only about 40% received treatment.³ Treatment rates have changed little since 2005, raising concern that adolescents are not receiving needed care for depression.³ Thus, a thorough assessment of symptoms is warranted through a clinical interview that is aided by the physician, patient and parents' clinical relationship and through the use of assessments, such as the PHQ-A and BDI-II. If a child or adolescent has a positive screen on the PHQ-A and meets the diagnostic criteria for MDD, the next step for the patient should be to use the tools provided by the Guidelines for Adolescent Depression in Primary Care (GLAD-PC), as well as the following a suggested protocol from the International Classification of Diseases, 10th revision (ICD-10).³¹

Pharmacotherapy Monotherapy

Fluoxetine (Prozac®) and escitalopram (Lexapro®) are the only two medications approved by the U.S. Food and Drug Administration to treat MDD in children and adolescents. Three systematic reviews of randomized controlled trials, including children and adolescents with MDD, support fluoxetine as the first-line antidepressant medication.³³⁻³⁴ Fluoxetine is approved for patients eight years and older, and escitalopram is approved for patients 12 years and older. Moreover, in trials of children and adolescents taking antidepressants, although there were no suicides, suicidal thoughts and behaviors were increased compared with placebo (4% vs. 2%).³² Thus, children and adolescents who are taking these medications should be monitored for suicidality and a possible "flip" into a manic state, as there could be an underlying bipolar disorder not yet diagnosed. The frequency of monitoring should be based on the individual patient's risk.

Psychotherapy Monotherapy

Cognitive behavioral therapy (CBT) is a form of talk therapy that focuses on changing behaviors by correcting faulty or potentially harmful thought patterns. Whereas CBT focuses on cognition and behaviors, interpersonal psychotherapy (IPT) concentrates on improving interpersonal relationships. Evidence is mixed for the use of CBT as monotherapy in children and adolescents with depression, with one study observing inconsistent effects on symptoms, response and functioning,³⁵ another observed shorter remission times,³⁶ and another observed a small positive effect on depressive symptoms in children and adolescents.³⁷

With IPT, current evidence indicates it has superior efficacy and acceptability compared with controls in treating adolescents with depression.³⁸

Combined Therapy

Evidence from a randomized trial suggests that adolescents are most likely to achieve remission with 12 weeks of combined fluoxetine and CBT therapy (37%; NNT = 4) compared with either therapy as a stand-alone (23% with fluoxetine; NNT = 11; 16% with CBT) or placebo (17%).³⁹ In addition, suicidality declined with the duration of treatment for all therapies, but the decline was less significant for fluoxetine alone (26.2% at baseline to 13.7% at week 36) vs. combination therapy (39.6% to 2.5%).39 In another trial of adolescents who achieved at least a 50% decrease in depression scores following six weeks of fluoxetine mono treatment, those who were randomized to receive the addition of CBT to fluoxetine therapy for six months were less likely to relapse 1.5 years later when compared with continued fluoxetine monotherapy (36% vs. 62%).40 Thus, children and adolescents with moderate, severe or persistent mild depression are usually treated with fluoxetine or escitalopram in conjunction with CBT or other talk therapy.³⁹ If combination therapy is not used, monotherapy with an antidepressant or psychotherapy is recommended, although the likelihood of benefit is lower.³⁷ In addition to the therapy, one trial found that constantly re-evaluating the treatment plan is one of the most important factors in how one's treatment course will work.41

THE OSTEOPATHIC APPROACH

Central to Andrew Taylor Still, MD, DO's philosophy of osteopathic medicine, the goal of OMT is to provide patients with the tools they need to restore and maintain their natural, self-healing state. Therefore, any alterations in any part of the system, including an individual's mental and spiritual health, will affect the body's function as a whole. Hence, we must treat a person's psychological state and accompanying somatic dysfunctions to optimize health. Along with these tenets, there are five osteopathic care models that osteopathic physicians use to facilitate diagnosis and treatment by applying understanding of the various anatomical, psychological and physiological substrates of disease: biopsychosocial, respiratory-circulatory, neurologic, biomechanical and metabolic-nutritional.

Treating Depression in Children and Adolescents Through the Biopsychosocial Model

This 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. Irritability, tension, difficulty concentrating, diminished interest, feeling overwhelmed and sleep disturbances are all common in those suffering from mental dysfunction, including depression.^{44,45} The application of the biopsychosocial model is knowledge and skill-based. Childhood depression should receive special attention, considering the serious and lasting consequences of the disease to child development,⁴⁶ ranging from physiological changes to the impairment of social and cognitive functions.⁴⁷ In the short

term, depressive disorders might be a source of psychological suffering for these children; whereas, in the long term, they can compromise social, cognitive and emotional aspects of child development,⁴⁶ becoming an important predictor of the patient's psychopathologies in adulthood.⁴⁸

More attention must be placed on health promotion and disease prevention, that is, providing more time to educate patients about their disease and to tell the patient and their parents about the symptomatology, the treatment plan and physician's assurance. This proactive approach leads to a healthier lifestyle for the patient but demands more time from the physician. ^{49,50} Also, an essential component of depression treatment is to reassure the patient that they have a disorder and that they are not at fault for these behaviors. ⁴⁹ Moreover, because children or adolescents may not completely understand or articulate their feelings and the details of their economic, environment, and social status, it is important to have their parents/or guardian cooperate with the treatment plan. With this focus, the patient (and their caregiver) becomes part of the treatment team to promote a more comprehensive and unified treatment strategy. ⁴⁹

OMT: DEPRESSION AND ITS SOMATIC DYSFUNCTIONS

Although depression is considered a mental health issue, it may bring on somatic manifestations. Therefore, it is justified to use OMT as a potential tool in the treatment plan for depression. Here we will discuss functional anatomic disturbances possibly due to depression's effect on the mind, known as either a "viscerosomatic reflex" or, more specifically, a "psycho-somatic reflex."

A decreased cranial motion has been reported in patients with depression and other psychological disturbances.⁵¹ Along with this, we will discuss the ramifications of depression on the central nervous system (CNS). The CNS has a valveless venous plexus and any passive congestion can compromise the CNS circulation and accumulate waste products in the CNS.⁵² In fact, studies have shown the complex interplay of psychological state and neuroendocrine-immune function. This includes alterations in rates of healing, immune function and autonomic tone during psychological disturbances.⁵³

Other somatic manifestations in depression are related to postural changes.⁵⁴ The depressed patient tends to adopt a slouched forward posture, which leads to the development of exhalation dysfunctions in the ribcage (and shallow breathing) and shortening of the psoas muscles, lower back pain, with partial un-doming of the abdominal diaphragm.⁵⁴ Additionally, there is hyperflexion of the cervical spine as well as increased kyphosis in the thoracic spine and a dropped sternum allowing for less full breaths.⁵⁴ Patients suffering from depression and other psychological disturbances often have shallow and rapid breathing, causing a dysfunction of the respiratory-circulatory system to effectively return lymph to the central circulation and venous blood to the heart.⁵² This change in posture can also lead to chronic pain along with the affected, slouched regions. Hence, an OMT focus on these systems would aid in treatment.

The above considerations provide a rationale for the efficacy of OMT in the treatment of depression. Using OMT to improve respiratory-circulatory efficiency and decrease sympathetic hyperactivity can be used as an adjunct to counseling, pharmacotherapy, and engaging the patient in a therapeutic process where the depression is being treated.⁵¹ Additionally, OMT can effectively give short term relief of somatic issues that accompany depression such as muscle aches, headaches, musculoskeletal pain, abdominal pain and excessive sweating.⁵¹

OMT TECHNIQUES TO TREAT PATIENTS WITH DEPRESSION

The contraindications for each technique are all the same: do not use any of the following techniques if there is no somatic dysfunction and if there is regional pathology or the somatic dysfunction suggests an underlying pathology that should be further evaluated before rendering OMT.

Treating the Sympathetic Nervous System at T1-T6

These regions are the major points of viscero-somatic reflexes of the head and neck, as well as heart and lungs.⁵⁶

- Rib raising bilaterally to normalize the sympathetic inputs to this region.
- Direct balanced ligamentous tension (BLT) to directly work on any thoracic, lumbar or rib dysfunctions.
- Counterstrain, facilitated positional release (FPR) and other soft tissue techniques that most primary care providers typically feel comfortable doing and most patients feel comfortably receiving. Additionally, thoracic high-velocity, low amplitude (HVLA) could be used if deemed necessary.

Rib raising, a technique that is very commonly used in practice and will be suggested several times throughout this article, has studies that back up its efficacy in regulating the sympathetic nervous system. One study suggests that sympathetic nervous system activity may decrease immediately after rib raising, which was confirmed through the usage of salivary alpha-amylase as a biomarker.⁵⁶

Treating the Exaggerated Thoracic Kyphosis, Dropped Neck Posture and Lower Back Pain

Treatment of rib dysfunctions resulting from the kyphosis improves the circulatory and oxygenation status and often has the effect of patients having more energy. Many of these techniques will be like those mentioned in the first point, with a few additions:⁵⁴

- · Rib raising
- Direct BLT
- Muscle energy technique (MET) of the cervical, rib, thoracic and lumbar regions.
- Counterstrain, FPR and other soft tissue techniques.
- Thoracic, cervical and/or lumbar HVLA could be used if deemed necessary.

Studies show muscle energy and counter strain techniques can play a significant role in treating lower back pain injuries.⁵⁷ They can lead to a reduction in pain and disability and even an increase in lumbar flexion range of motion (ROM) immediately upon one treatment session.⁵⁷ Moreover, these techniques can lead to a reduction of pain and disability.⁵⁷ Patients with depression often experience these somatic pains, and relief of them would be an integral part of their treatment plans to possibly encourage performing activities.

Treating the Lymphatic System

Depression may lead to shallow and rapid breathing, which can cause a dysfunction of the respiratory-circulatory system to effectively return lymph to the central circulation and venous blood to the heart. Treating the thoracic inlet and performing other lymphatic techniques will assist lymph flow.⁵⁵

- First rib MET bilaterally to free up restrictions in the thoracic inlet, as well as sympathetic influences.
- Clavicle MET bilaterally to free up restrictions in the thoracic inlet, as well as sympathetic influences.
- Thoracic outlet release to open the thoracic inlet and allow for better lymphatic drainage.
- Upper and lower extremity wobble techniques to allow for proper lymphatic flow through the extremities.
- Hepatic and splenic pumps to support organ function and support fluid circulation.
- Counterstrain, FPR and other soft tissue techniques.
- Additionally, thoracic and/or lumbar HVLA could be used if deemed necessary.

While there are currently no studies discussing the direct effects of OMT on depression-induced lymphatic stasis, what is known is that many conditions that lead to lymphatic stasis commonly present with depression as a comorbidity. Lymphatic filariasis⁵⁸ and post-surgical lymphedema⁵⁹ following a mastectomy are conditions in which the lymphatic system performs sub-optimally and many of these patients present with depression. A study that looked at the comorbidity between post-mastectomy lymphedema and depression found that lymphatic massage and relaxation techniques reduced anxiety and depression levels.⁵⁹ Looking into the relationship between using OMT as a supplemental treatment to encourage lymphatic drainage in those with depression is a possible future study of relevance.

Secondary Respiration Through Diaphragm Release

Treating the abdominal diaphragm helps to normalize lymphatic flow, which, as discussed, should have an overall positive effect.⁵⁵ Due to the diaphragm's connection to the sternum, if the diaphragm is flat, it prevents sternal elevation, further inhalation is prevented, which leads to less oxygenation.⁵⁴

- · Re-doming of the diaphragm
- Pelvic diaphragm release

- · Rib raising
- Direct BLT
- MET of the cervical, thoracic and lumbar regions.
- Counterstrain, FPR and other soft tissue techniques.
- Thoracic, cervical and/or lumbar HVLA could be used if deemed necessary.

Shortness of breath is a significant predictor of depressive symptoms. Given that shortness of breath is responsive to therapeutic intervention, active intervention to relieve the symptom could reduce the incidence of depressive symptoms.⁶⁰ In addition, one study found there is potential for diaphragmatic breathing practice to improve cognitive performance and reduce negative subjective and physiological consequences of stress in healthy adults.⁶¹

While no studies have been done on OMT regarding assisting respiratory changes in depression specifically, studies show OMT effectively assisting respiration in other pathologies such as pneumonia. These protocols all take advantage of the importance of the diaphragm and include it in the treatment. Thus, in treating a patient with depression who displays suboptimal breathing, we can help to increase this respiratory excursion through doming of the diaphragm to help alleviate downstream symptoms of poor respiration. ⁶²

Sacroiliac (SI) Joint Treatment

Treating the SI joint will treat the "core" link between the sacrum, spinal column and dura mater. By releasing this tension, you decrease restrictions along the CNS, which may have passive congestion at this time due to depression. 63

- SI joint exaggeration
- Sacral rock
- Sacral MET

There are no OMT studies that discuss the effects of sacral OMT treatments concerning depression. However, sacral techniques are used in many other protocols to normalize parasympathetic influences and CNS-based congestion.

Treating Cortical Tissue

The goal is to assess tension, restriction laxity and seek balance to affect the tissues themselves directly.⁵⁵ It is important to remember that these techniques are contraindicated if the patient had a recent vascular event. The techniques include:

- Suboccipital release
- Cranial vault hold
- CV4 technique
- Myofascial release to the C1-C2 region
- · Balanced membranous tension

Many studies have shown the effectiveness of sub-occipital release on the autonomic nervous system due to its effect on the vagus nerve. Studies show that suboccipital release has the capacity to modulate autonomic control and regulation, ⁶⁴ as well as affect heart rate variability acutely. ⁶⁵ This would be extremely beneficial as we discussed how depression could affect the CNS and its effects. One study observed an association between patients who received cranial field osteopathy and lower depression rates, higher satisfaction with life and higher meaningfulness of daily activities. ⁶⁶ This would have clinical relevance for managing patients, particularly those who are depressed, not satisfied with life or do not perform meaningful daily activities. ⁶⁶

OMT overall can have positive effects on a patient's condition overall and improvement of clinical signs and symptoms. This, in turn, may translate to increased compliance with medications and psychotherapy as well and, thus, more positive outcomes.

OMT RESULTS ON DEPRESSION

Current literature regarding OMT in depression treatment is limited and even more so in the pediatric and adolescent population. However, preliminary data regarding OMT and depression overall is encouraging.

A study in 2001 by Plotkin *et al.*, which has yet to be re-done, assessed the impact of OMT as an adjunct to standard psychiatric treatment of premenopausal women with depression and found that OMT may be a useful adjunctive treatment for alleviating depression in this population.⁵³ Another study found that OMT produced a statistically significant decrease in self-perceived fatigue in first-year osteopathic medical students. Thus, OMT represents a potential modality to reduce self-perceived distress in medical students.⁶⁷ However, a thorough literature review does not display any results for how OMT treatment would compare to the mainstay treatment of depression. Thus, we have included a possible sample study design to view OMT's effect on depression against standard treatment.

OMT STUDY DESIGN

A possible cohort study looking at the effects of OMT on children and adolescents with MDD may be conducted by dividing participants into three groups. One group is treated with selective serotonin reuptake inhibitors (SSRIs) and therapy (mainstay treatment), another with SSRI, therapy and OMT and the last group with SSRI, therapy and a sham OMT (performed by a Ph. non-health care professional or student). The BDI-II, as discussed previously, would be used to measure the patient's MDD at three different time points: pre-treatment, three months into treatment and six months into treatment. A repeated-measures analysis of variance (ANOVA) could be used to analyze statistical differences between the time points. The comparison of these results would give an interesting perspective regarding the treatment of MDD patients with osteopathic manipulative medicine (OMM). In addition, a qualitative component to our study design could be interjected by monitoring the participants for irritability, tension, anxiety, difficulty concentrating, diminished interest, feeling overwhelmed and sleep disturbances that they felt throughout the treatment course at those same three-time points.

CONCLUSION

Children and adolescents are affected by depression, often accompanied by behavioral problems, substance abuse and/or other mental disorders. Many risk factors have been studied in children and adolescents that put them at risk for depression, usually broken down into biological, psychological, and environmental domains. Complicating matters, in children and adolescents, depression can manifest differently than it does in adults, making the ability to recognize this problem and start interventions more difficult. Early recognition, while challenging, is essential in the treatment of these individuals. Regular screening plays an important role.

Moreover, the better the connection that a physician, parent and patient has, the more likely the patient and their parents will come in earlier with their concerns. The most effective treatment for children or adolescents with depression is a combination therapy of psychotherapy, IPT or CBT and pharmacotherapy. OMT should be considered as a supplemental treatment for depression. Ultimately, if treatment is done with all these considerations accounted for, the patient will more likely have positive results. It is important to note that OMT affects the somato-visceral and somato-psychological pathways and somatic dysfunctions caused by depression and should be considered in the treatment of depression. The biopsychosocial model is significant with an understanding that enhanced communication is vital. OMT plays a role in its varied applications, which can positively impact the somatic, visceral systems affected by this condition and thus is a viable treatment modality. Studies are warranted and greatly encouraged to expand on OMT's role in depression.

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IOA '21 Virtual Live Annual Spring Update Indiana Osteopathic Association Virtual

inosteo.org

JUNE 12-13, 2021

MOA 110th Annual Convention Maine Osteopathic Association Virtual

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JUNE 19, 2021

2021 Virtual Summer Family Medicine Update Missouri Society of the ACOFP Virtual msacofp.org

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REVIEW ARTICLE

WHAT THE PAST HAS TAUGHT US: BEST PRACTICES FOR OFPS TO MANAGE STRESS DURING A VIRUS OUTBREAK

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KEYWORDS:

Virus Outbreaks

Psychological Distress

Physician Wellness

Stress

ABSTRACT:

OFPs and other health care professionals experience increased rates of stress, anxiety, fatigue and burnout in the face of pandemics. Historically, this has been observed with other pandemics, such as the influenza pandemic, HIV/AIDS, SARS, H1N1, Ebola virus disease and, more recently, COVID-19. Research about physician wellbeing during prior pandemics has informed recent practices and provides more guidance on how larger health care entities can provide for employees and how physicians can care for themselves. Here, we explore best practices for emotional/spiritual wellbeing, physical wellbeing, maintaining a healthy family life and wellness during a virus outbreak.

INTRODUCTION

Osteopathic family physicians (OFP) play a large part in public health crises, such as infectious disease outbreaks. However, many OFPs report not feeling prepared. Research shows that OFPs express concerns for the limit of support from health authorities on education, training and supply of personal protective equipment (PPE).¹ This can lead to significant long-term stressors, so managing the stress and psychological distress during infectious disease outbreaks will be an integrative part of preventing burnout and improving wellness.

HISTORICAL PERSPECTIVE

There have been multiple historical accounts of health care provider distress in times of pandemics. These include influenza pandemics, the spread of HIV/AIDS and newer pandemics, such as H1N1 influenza, SARS-associated coronavirus and Ebola virus.

Influenza pandemic of 1918

Also known as the Spanish Flu, the H1N1 influenza outbreak of 1918 lasted over two years and infected 500 million people—roughly one-third of the world's population.² This particularly virulent strain of influenza placed enormous strain on the health care system worldwide. Although more than a century has passed, health care providers' sentiments caring for these influenza patients and those caring for COVID-19 patients are eerily similar.

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In a letter written from Dr. Norman Roy Grist in 1918, a physician stationed at Camp Devens, Massachusetts, to a fellow physician, he states:

"We have lost an outrageous number of nurses and doctors and the little town of Ayer is a sight. It takes special trains to carry away the dead. For several days there were no coffins and the bodies piled up something fierce.

We have no relief here; you get up in the morning at 5:30 and work steady till about 9:30 p.m., sleep, then go at it again. Some of the men of course, have been here all the time and they are tired."

A 21-year-old Jean Curlewis, who was volunteering as a nurse's aide away from her family during the influenza outbreak of 1918, writes to her mother about the fear of spreading the virus to her family if she were to return home.

"On the whole, though I long to see you all, I think I would rather not spend the subsequent nights worrying myself sick for fear I had given it to you. You know I am not given to imaginations in worrying, but up here, all the girls find it almost unbearable to think that people belonging to us might get this awful thing, through lack of precaution." 4

During the COVID-19 pandemic, health care workers (HCW) have gone to great lengths to protect themselves and contacts from becoming ill. Yet, many health care providers have been infected with COVID-19 or know of health care providers who have been ill. This is much like what was seen at the onset of the COVID-19 pandemic when HCWs exposed to the virus often separated from their families to keep them safe.

HIV/AIDS pandemic

There are multiple accounts of physicians providing care to patients at the onset of the human immunodeficiency virus (HIV) pandemic who grappled with fear of dying, fear of acquiring the virus themselves and fear of lifestyles that were considered "alternative." Stressors on the job included feeling manipulated by patients who did not change their high-risk behaviors, did not heed precautions, arrived late for appointments or took advantage of physicians by selling their medication or using them for social benefits. Additionally, physicians noted that receiving decreased institutional support was a major source of stress. Partially brought on by changes in health care—namely the transition to managed care—decreased institutional support included fiscal cutbacks, decreased nursing and support staffing and lack of resources for patient care. 5 Physicians endorsed burnout exacerbated by the demands of managed care and distress over-discharging patients early from the hospital, despite their persistent needs for substantial nursing and medical care. Clinical depression, emotional distancing and marital issues were also manifestations of physician burnout. Coping strategies included taking more time away from work, saying "no" to additional obligations, sharing their workload, leaning on others for support and getting better at work-life balance.4

SARS pandemic

In 2003, severe acute respiratory syndrome (SARS-associated coronavirus) spread to more than two dozen countries in North America, South America, Europe and Asia. Wong et al. 5 describe how primary care physicians of the Hong Kong and Toronto health systems responded to the outbreak. In Hong Kong, physicians endorsed little guidance regarding diagnosis and treatment of the virus and had difficulty advising anxious patients. In Toronto, three major hospitals were closed and HCWs were quarantined, resulting in staffing shortages. In both cities, 80% of the practitioners surveyed experienced reduced incomes and increased overhead costs. Approximately 50% of the practitioners from both cities were considered high anxiety.⁶ Family physicians in Hong Kong were significantly less satisfied with how their government handled the outbreak than those in Toronto. This dissatisfaction was related to a younger age, more clinical duties and increased frequency of changing screening tools. The authors infer that primary care physicians would benefit from increased training and communication during pandemics.

H1N1 (Swine Flu) pandemic

During pandemic times, there is an increased demand for HCWs, as was seen with the H1N1 influenza pandemic in 2009. Several studies have evaluated the factors that influence HCWs' willingness to work during pandemics. These factors include type of disaster, concern for family or personal safety, education and training, belief in a duty of care, access to PPE and basic needs (water, food, rest, electricity, shelter and communication tools). ^{7,8}

Aoyagi *et al.*⁸ found that health care willingness to work during the H1N1 influenza pandemic ranged from 23.1% (in community nurses during the 2009 H1N1 pandemic in Hong Kong) to 95.8% (seen in a study of U.S. medical students presented with a case of hypothetical H1N1 outbreak). Their analysis shows that HCWs

are more likely to work if presented with hypothetical influenza scenarios and limited details. Lower levels of willingness were associated with precise scenarios and information on the influenza virus's strain and virulence. More so, they found that factors associated with being more willing to work in an influenza pandemic included: being male, being a physician (compared to nursing and other HCWs), working in a rural environment, being a full-time employee, not having children or childcare obligations and not being pregnant.

Ebola epidemic

Health care workers caring for patients through the Ebola epidemic faced known challenges, such as deprivation of resources, mistrust of the medical community and lack of public health funding. However, the more recent outbreak spanning 2014–2016 posed unique challenges—mainly spreading within urban areas, overwhelming individual health care providers. Fatality rates among the public were less than that of HCWs—41% in the general population and 58% of HCWs, although the proportion of HCWs who died is much smaller. Nevertheless, physicians and other HCWs caring for sick patients incur substantial risks doing so. This is compounded when basic supplies such as water, power and PPE are lacking.

At the American Society for Nephrology's annual conference in 2014, Dr. Nicolas Evans discussed the ethics of treating patients with Ebola virus disease (EVD) on an ad hoc panel. They concluded that physicians and other HCWs have a duty to provide for patients, colleagues and the community. Yet, professional duties may be conflicting with the duty to their wellbeing or family. However, the risks HCWs take honoring the duty to treat must be mitigated by better planning for public health emergencies, particularly in resource-rich countries where there is more capacity to do so. The committee acknowledged that areas where resources are limited have providers "are likely to find themselves in untenable positions, where their rights to welfare are overshadowed by the compelling need to treat patients and respond to an outbreak. The right to welfare means little, even to the most self-interested person, if absenteeism only risks the individual more through the continuation of an emergency." 9

COVID-19 pandemic

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), now simply known as coronavirus disease 2019 (COVID-19), has become a global pandemic that overwhelmed health care systems worldwide. Globally, there have been over 40 million cases of COVID-19 and 1.12 million deaths. In the United States, there have been over 29 million cases and over 573,000 deaths. 10 Before the pandemic, rates of physician "burnout" in the United States neared 50%11 and rates have increased in the face of COVID-19related stressors. These include fear of infection and putting self or family at risk, lack of PPE and changing of U.S. Centers for Disease Control and Prevention (CDC) guidelines for recommended PPE, ethical dilemmas regarding resuscitation status and distribution of medication and ventilators, 12 feeling physically and emotionally drained as a result of being "over-worked" and not having access to usual coping mechanisms, such as a gym, movies or social gatherings with family and friends.

It is important to recognize that the responses to disasters such as COVID-19 can vary and span from an acute stress reaction to post-traumatic stress disorder (PTSD). The physical, cognitive, behavioral and emotional manifestations that result from these conditions are vast and can include pain, palpitations, detachment, substance use, mood disturbance, flashbacks, poor concentration and rumination, among other symptoms.¹³ As a result, individuals, as well as whole organizations, have been organizing to call for support of physician wellness at the policy and institutional level.¹⁴

With a better understanding of the scope of physician wellness, we hope to help identify barriers and promote solutions. Here, we outline several subsets of wellness—emotional and spiritual wellness, physical wellness; family life; and resident wellness—and propose strategies for managing stress and duress during the COVID-19 pandemic.

WELLNESS

Emotional/spiritual wellness

Research has shown that staff who have been quarantined reported psychological symptoms including emotional disturbance, depression, stress, low mood, irritability, insomnia, anger, emotional exhaustion and post-traumatic stress symptoms.¹⁵ Individuals who respond to natural or humanmade disasters experience death, injury and destruction with prolonged work environments. Research studies identify these individuals at risk for psychological distress and posttraumatic stress.¹⁶ Furthermore, a study after the severe acute respiratory syndrome outbreak showed a positive association with guarantined health care workers and alcohol abuse or dependency symptoms, especially in those who worked in a high-risk location.¹⁷ Providers can fear their own health or fear infecting others, such as family members, friends and co-workers. Financial loss can lead to anxiety. Quarantined HCWs may feel stigma for creating understaffing or extra work for colleagues.1 To prevent these concerns, mental health care for OFPs should be emphasized. OFPs should remember to take breaks and schedule time for themselves. There should be a focus on healthy meals, rest and sleep. Spending time with family and friends by phone or videoconferencing can help alleviate isolation. Additionally, seeking support through therapy or group sessions can be a way to focus on mental health.

Physical wellness

Exercise has been shown to improve mood, cognitive function and alleviate social withdraw. Several types of aerobic exercises, like jogging, walking and dancing, can reduce anxiety and depression. During a pandemic, normal exercise routines may be disrupted when facilities are closed. OFPs who routinely use exercise facilities should develop at-home exercise regimens. Investing in equipment, such as exercise bikes and weights, can help OFPs keep a physical activity schedule. Additionally, outdoor activities like jogging and running are a safe way to distance themselves socially. Mobile health and fitness applications can help OFPs find home exercises and participate in virtual exercise routines.

Family life

OFPs experience stressors with marriage, children and family regularly. During an infectious outbreak, these stressors may be heightened. A supportive home environment is essential in maintaining physician wellbeing. A survey of family medicine graduates found that most OFPs manage stress by talking to family or friends. OFPs should communicate with their partners regularly about work schedules to adjust to frequent changes. Families should work out a childcare schedule, especially as there is a shift toward virtual learning. Many OFPS may also struggle with caring for patients and returning home to families with fears of infecting loved ones. To reduce anxiety about spreading the virus, OFPs can take several precautions like changing clothing before entering homes and good hand hygiene.

Residency wellness

Family medicine residency training programs require three years of training with rotations into ambulatory, community and inpatient settings.²¹ During pandemics, duty obligations increase mental and physical strain for residents. Family medicine residents are at increased risk because of their exposure to viral outbreaks in various settings. Residents may be working in the inpatient sites, including intensive care units and ambulatory sites, evaluating sick patients. Therefore, prioritizing wellness for residents is very important. The surgical program at the University of British Columbia evaluated their program for the efficiency of practice, the culture of wellness and personal resilience during the COVID-19 pandemic. Their strategies to improve resident wellness include talking about signs of burnout, establishing committees to support residents, regular virtual meetings, maximizing safety with PPE and journaling. They also established a reserve team to minimize resident-to-resident contact and rotated their residents into different blocks.²² These methods can be initiated in family medicine residencies to help manage stress and alleviate psychological distress.

CONCLUSION

OFPs and other health care professionals are in increased demand during pandemics and observe a duty to provide care. However, this is often at the expense of their wellbeing and health. While this has been observed and studied through several pandemics over the last century, newer data has emerged that can be used to help mitigate stress, fatigue and burnout observed with the COVID-19 outbreak. Physician emotional/spiritual wellness can improve by focusing on a healthy lifestyle (healthy meals, rest and sleep) and maintaining relationships with friends and families through videoconferencing and phone calls. OFP wellness can improve by establishing at-home gyms, using fitness applications and exercising outdoors. OFPs can maintain a strong family life by keeping open communication about changing work schedules and other work-related stressors. For OFPs, it is important to recall how the tenants of osteopathic medicine and the osteopathic oath promote wellbeing. In the 2019 Osteopathic Family Physician article "Physician Wellness, Osteopathic Principles and Strategies for Change," Dr. Katherine Lincoln²³ demonstrates that working

past one's physical, emotional and spiritual threshold can violate the osteopathic tenant that "the body is a unit and the person represents a combination of body, mind and spirit." It is critical that health care providers do not sacrifice their own health when providing care and providers should seek help from their communities.

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REVIEW ARTICLE

INGROWN TOENAIL MANAGEMENT

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KEYWORDS:

Ingrown Toenails

Matricectomy

Onychocryptosis

Onychomycosis

ABSTRACT:

Ingrown toenails are a common condition in general medicine and dermatology, and they occur when the nail curves inward and pierces the nail fold. Symptoms include pain in the affected toe, erythema and edema. The diagnosis is made clinically and, if left untreated, ingrown toenails can lead to infections and even cellulitis and osteomyelitis. Conservative treatments involve clipping on the spicule and topical antibiotics. However, the mainstay of treatment is matricectomy to reduce the recurrence rate. The risk of ingrown toenail development can be reduced by wearing proper footwear, keeping toenails cut straight and overall foot hygiene. Ingrown toenails can affect various patient populations but are more prevalent in males, young adolescents and pregnant patients. Risk factors include obesity, diabetes, improper toenail clipping and improper footwear. This review explores the clinical manifestations of ingrown toenails, along with their diagnosis and treatment, providing a concise review for physicians to accurately identify and effectively treat patients with ingrown toenails or their resultant complications.

INTRODUCTION

Ingrown toenail, also known as onychocryptosis or unguis incarnatus, is the most common nail problem in general medical practice and nail dermatology settings. It occurs when a spicule on the side of the nail curves inward and pierces into the nail folds. This causes an inflammatory response and can lead to a secondary infection. The nail's lateral side is usually affected and it occurs most commonly in the hallux toenail. Reports indicate ingrown toenails have a prevalence of 2.5-5%, which has increased in recent years, possibly due to lifestyle factors and increased awareness of health among patients.1 Ingrown toenails are more prevalent in young adolescents and pregnant women; however, generally, men are more commonly affected than women. Furthermore, preexisting conditions like diabetes and vascular conditions can negatively affect presentation.² This review provides insight into the pathophysiology, clinical manifestations, diagnosis, complications, treatment, recurrence and prevention of ingrown toenails.

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PATHOPHYSIOLOGY

Ingrown toenails occur when the edge of a toenail penetrates the skin. The edge of the toenail will curve into the nailbed, and if penetration occurs, it will cause an inflammatory cascade and secondary bacterial infections. One of the more common causes is irregular nail trimming. This occurs when the nail is trimmed unevenly and the patient might tear off a piece of the nail. Other factors include poor footwear, poor foot hygiene, anatomical deformities, trauma and genetic predisposition. 1 Obesity, diabetes and thyroid, renal or cardiac disorders can cause lower extremity edema, increasing the risk of development of an ingrown toenail. Adolescents are prone to hyperhidrosis, which can cause nails to become soft and split easily. Toenails become thicker and more challenging to maintain as patients age.3 Some medications can increase the risk of developing an ingrown toenail, including isotretinoin and epidermal growth factor receptor inhibitors like gefitinib and cetuximab (albeit rarely).1,4

SYMPTOMS

Common symptoms of patients presenting with an ingrown toenail include a painful affected toe, erythema and edema. The pain can vary in severity and may affect the patient's ability to walk. An ingrown toenail can present as mild (Stage 1), moderate (Stage 2) or severe (Stage 3). Symptoms of a mild ingrown toenail are erythema, edema and minimal pain. Moderate ingrown toenails present with more severe pain, along with ulceration and drainage. Severe cases usually present with the formation of granulation tissue and hypertrophy of the nail fold.¹

DIAGNOSIS

An ingrown toenail diagnosis is almost always clinical, based on the presenting symptoms and a physical examination of the toenail and the surrounding skin. This includes inspection of the nail's lateral edge and determining if the nail is growing underneath the skin. The penetration of the nail bed can be visualized in some cases. Inflammation and redness of the area are usually present and infection is denoted by apparent drainage. Testing is usually unnecessary, but potassium hydroxide treatment and fungal culture may be performed when a fungal infection is suspected.⁵ Other conditions that can mimic this presentation include cellulitis, osteomyelitis, tumors, exostosis and foreign bodies. X-rays, cultures and failure of treatment can help rule out these other conditions.⁶

COMPLICATIONS

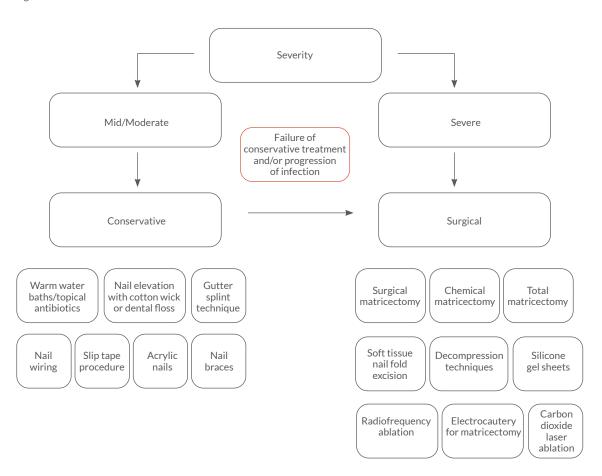
Untreated or improperly treated ingrown toenails can cause a variety of complications. Paronychia is possible and is usually caused by staphylococcus, pseudomonas, candida or superficial

dermatophytes. There can also be scarring of the skin surrounding the nail and nail fold. More severe infections can lead to cellulitis and osteomyelitis. If diabetes is also present, there is a notable risk of severe infection and amputation. Other complications include foot ulcers, sores, loss of blood flow to the foot, tissue damage and tissue death.⁶ Dadaci *et al.* reported a 17-year-old boy who noticed an ingrown toenail lasting three years. The delay in treatment was due to the patient's phobia of needles, which likely worsened his condition. It was left untreated, resulting in extensive hypertrophy. The excess skin growth epithelialized and moved past the midline on the nail, further enveloping it.⁷ Patients may be genetically predisposed to recurrent ingrown toenails, lowering their quality of life due to pain, recurrent infections and other foot complications. In these cases, matricectomy may be recommended, as it can decrease the rate of recurrence.

TREATMENT

Management of an ingrown toenail depends on the presentation's stage and severity, as shown in Figure 1.

FIGURE 1:
Approach to ingrown toenail treatment. ^{6,8}



Ghafoor, Paracha, Goldstein Ingrown Toenail Management

Stages 1 and 2 usually involve conservative management, while a Stage 3 ingrown toenail will require surgical intervention. The first step in treatment is providing symptomatic relief. This includes removing the spicule that is growing into the skin. It is essential to clean the area with an iodine or hydrogen peroxide solution to reduce infection risk. Patients can massage the area of inflammation as well. Silver nitrate can be used to reduce granulation tissue formation; however, it is recommended that physicians remove any granulation tissue during surgery.⁹

Underlying conditions that add to disease burden (i.e., hyperhidrosis, onychomycosis) should be treated. Gupta *et al.* conducted a meta-analysis of 28 studies on onychomycosis treatments. They found that topical amorolfine, ciclopirox, tavaborole and efinaconazole were common treatments for mild and moderate toenail onychomycosis efinaconazole showing the highest rate of improvement. Treatments lasted for approximately 24—48 weeks and the antibiotics were applied topically daily. More prolonged treatment and follow-up monitoring demonstrated better results. ¹⁰ Warm water baths followed by topical antibiotics can offer relief. This method can also reduce inflammation.

When used, oral antibiotics have not been shown to improve healing times significantly. Reyzelman *et al.* conducted a study amongst 45 individuals with no preexisting conditions. Individuals were divided into three groups. Group 1 received one week of antibiotics concurrently with a chemical matricectomy, Group 2 received one week of antibiotics followed with a chemical matricectomy and Group 3 only had a chemical matricectomy done. While Group 1 healed faster than Group 2, there was no significant difference in the healing times of Groups 1 and 3.¹¹ The most common organisms for an ingrown toenail infection are staphylococcus, pseudomonas and streptococcus species.⁵

Conservative measures

For mild or moderate cases, there are several different types of conservative treatment modalities available. A cotton wick or dental floss can be inserted into the corner of the affected nail will elevate the nail to alleviate the pressure and prevent further curving. Another technique involves splinting the nail's lateral edge with a vinyl intravenous infusion tube and then securing it with tape, known as the gutter splint technique. The taping procedure simply involves taping the ingrown toenail under and around to the other side of the nail, which lifts the affected region and relieves pressure, restricting the nail's inward curve. This can also allow any pus to drain so the wound can dry. Nail wiring is another conservative method where two holes are placed at the distal end of the nail and wires are inserted to cover the deformity. Less common modalities include slip tape-strap procedure, acrylic nails and nail braces.¹

Surgical interventions

Severe cases of ingrown toenail require surgical intervention. Matricectomy is the partial or complete ablation of the nail matrix and it can be done surgically (mechanically) or chemically. Chemical matricectomy is preferred over surgical matricectomy, given it is a simple procedure with little blood loss, is cosmetically appealing and can be performed in a short time.8 Most chemical

matricectomies are done using phenol, which yields a low recurrence rate and favorable cosmetic outcomes.² However, phenol can cause tissue destruction and drainage, which can result in delayed healing time. Other chemicals have been explored, such as sodium hydroxide and trichloroacetic acid, due to these adverse effects. Tersi *et al.* conducted a study of 30 patients with ingrown toenails treated with chemical matricectomy using 90% bichloracetic acid. They reported minimal pain and drainage postoperatively. After 12 months, 29 of the 30 patients had no recurrence, demonstrating that bichloracetic acid is a viable alternative to phenol.¹²

Matricectomies can be combined with spicule excision or wedge resections of the toenail, depending on the presentation. Excising the entire affected toenail with a total matricectomy is reserved for advanced-stage presentation, onychogryphosis and onychodystrophy.¹ A soft-tissue nail fold incision is preferred when the soft tissue surrounding the nail is the ingrown toenail's causative agent. Therefore, wide excision of the soft tissue surrounding the ingrown toenail is needed. Some other modalities that are not commonly used include electrocautery, radiofrequency ablation, carbon dioxide laser ablation, decompression techniques and silicone gel sheets.6

Singal *et al.* conducted a study on eight adult patients with Stage 2 ingrown toenails who failed to find relief with conservative procedures using radiofrequency ablation. Radiofrequency ablation first involves a partial nail avulsion. A nail elevator is used to elevate the nail plate on the affected side and a spicule of the nail is removed. Then, an electrode is placed on the matrix over the lateral horn of the nail for approximately 3–5 seconds and repeated 2–3 times. The mean postoperative healing time was 7.5 days. By day four, oozing was absent and erythema, pain and edema had significantly improved. No postoperative complications were observed and no recurrences were noted at 3-to-6-month follow-up evaluations.¹³

Uygur *et al.* investigated placing the skin under the ingrown toenail during surgery due to the pathophysiology involving the lateral edge of toenail curving inward and invading the nail fold's skin. Two groups were studied, one with the traditional suturing technique and the other with the new suturing technique. Both groups used the Winograd procedure (i.e., partial plate excision followed by the nail matrix's destruction) as the initial treatment.¹⁴ For patients receiving the new technique where skin was placed under the nail, the recurrence rate was significantly reduced (p-value = 0.011).¹⁴

RECURRENT INFECTIONS

Recurrence can occur from a variety of factors. These include genetic predispositions, preexisting conditions, immunosuppression, advanced age, untreated infection, lack of foot hygiene, poor footwear and trauma. Recurrence can be caused by a lack of fungal infection clearance, which can lead to reinfection.¹⁵ Regardless of the type of fungal infection treatment used, there has been a reported rate of recurrence ranging from 10–53%.¹⁶ Surgical interventions have lower recurrence rates than nonsurgical treatments.¹ This includes surgical

excision with chemical matricectomy. Eekhof *et al.* conducted a meta-analysis that concluded that nail avulsion combined with chemical matricectomy reduced the recurrence of ingrown toenails by 75–91% compared to surgical matricectomy.¹⁷

PREVENTATIVE MEASURES

There are several preventative measures to help reduce the risk of developing ingrown toenails. One method is the use of proper footwear that does not constrict around the toes. Another preventative measure is trimming toenail edges in a straight line instead of curved through proper toenail clipping. Good foot hygiene, including cleaning under the toenails, can also reduce the risk.⁶

CONCLUSION

Ingrown toenails are common nail pathology. This review explored the clinical manifestations of ingrown toenails along with their diagnosis and treatment, providing a concise review for physicians to accurately identify and effectively treat patients with ingrown toenails or their resultant complications. Prompt diagnosis and appropriate treatment can mitigate the risks of infection or other compilations and foster optimal patient outcomes.

AUTHOR DISCLOSURES:

No relevant financial affiliations or conflicts of interest. If the authors used any personal details or images of patients or research subjects, written permission or consent from the patient has been obtained. This work was not supported by any outside funding.

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BRIEF REPORT

MULTISYSTEM INFLAMMATORY SYNDROME IN AN INFANT WITH NEGATIVE SARS-COV-2 RT-PCR AND ANTIBODIES

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KEYWORDS:

COVID-19

Infectious Disease

MIS-C

Pediatrics

SARS-COV-2

ABSTRACT:

Since the declaration of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in March 2020 by the World Health Organization (WHO), there has been an emergence of a new syndrome termed multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19. MIS-C is defined by the presence of fever, systemic inflammation and multiorgan dysfunction in association with SARS-CoV-2 infection or COVID-19 exposure. Knowledge of this syndrome's presentation and pathophysiology is constantly evolving as more cases are reported in the literature. This case identifies a 3-month-old patient who tested negative for SARS-CoV-2 antigen, reverse transcriptase polymerase chain reaction (RT-PCR) and antibodies but qualified for MIS-C diagnosis. To the best of our knowledge and through extensive research at the time of diagnosing and reporting this condition to the healthcare authorities, we report the youngest pediatric patient with MIS-C diagnosis. We document this case to contribute to further understanding the variable manifestations of MIS-C and the importance of early diagnosis and treatment with intravenous immunoglobulin (IVIG).

INTRODUCTION

A pandemic was declared by the WHO in March 2020 of COVID-19 due to the development of a novel coronavirus designated SARS-CoV-2.¹ The clinical course of the disease in the majority of pediatric cases has been asymptomatic or mild.²-⁵ In more recent literature, it has become apparent that some children may develop a more severe clinical course with a MIS-C. This syndrome is defined as systemic hyper inflammation with fever and multiorgan dysfunction in relation to COVID-19 exposure.⁶ The average age of MIS-C patients is eight-years-old but typically ranges from 1-14-years-old.⁶ Clinical presentation is variable, with most cases reporting significant gastrointestinal symptoms, cardiac disease, skin rash, conjunctivitis, absent or mild respiratory symptoms and oral mucous membrane changes.

Many of the cases reported in the literature identify MIS-C with overlapping symptoms of Kawasaki disease (KD) or toxic shock syndrome (TSS).⁸⁻¹⁵ KD and MIS-C share several common symptoms, including skin rash, lymphadenopathy, strawberry

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tongue and an elevation of inflammatory biomarkers. These similarities likely suggest that MIS-C exhibits the same excessive inflammatory cytokine production in response to an infectious trigger observed in KD. However, the exact pathophysiology is still under investigation. Previous reports have shown that MIS-C differs from KD by the older age of onset, abdominal symptoms and left ventricular systolic dysfunction.

RT-PCR has been effective in identifying active COVID-19 cases and the more recent antibody tests may aid in identifying cases with related post-infectious complications. There was a question of whether MIS-C is a primary complication of infection with SARS-CoV-2 or a post-infectious complication; however, it either occurs 2–4 weeks following exposure or is associated with positive antibody markers, which supports the conclusion that it is likely a post-infectious complication. This brief report intends to describe the clinical presentation and successful treatment of an infant diagnosed with MIS-C.

CASE PRESENTATION

A three-month-old African American male with no significant past medical history presented to urgent care with a two-day history of fever and rash, accompanied by abdominal pain, dry cough, diarrhea and lethargy. Physical examination was benign other than an erythematous rash on the face and chest with papules on the torso and axilla. The patient was up-to-date on immunizations with no recent exposure to sick contacts. He was diagnosed with a

viral illness and viral exanthem with a possible allergic component. The parents were instructed to continue supportive care at home.

The patient presented to the emergency department the next day with a high-grade fever that did not resolve with multiple doses of acetaminophen. The mother reported associated symptoms of cough and a new bilateral eye discharge with eye redness. Vital signs showed a temperature of 103.3°F and a heart rate of 195 beats per minute. Physical examination showed bilateral conjunctivitis and purulent eye discharge. No rash was evident at this visit. He was treated with acetaminophen and, once stable, discharged home on supportive management for a viral syndrome.

The patient returned to the emergency department on day four of his illness with unresolved fever, abdominal pain, diarrhea, conjunctivitis and irritability. The mother reported a significant decrease in the patient's oral intake and urine output. Physical examination showed an ill-appearing, nontoxic infant with 10% loss of body weight over two days, evidence of severe dehydration and diffuse abdominal tenderness. Lungs were clear to auscultation with no respiratory distress. The patient received two normal saline fluid boluses 20 mL/kg each without resolution of the tachycardia. The patient was then admitted to the general pediatric floor for fever of unknown origin and dehydration with COVID-19 precautions.

The patient's parents denied the patient having any recent illnesses or sick contact but reported a positive COVID-19 case at the father's job at a steel plant. The mother stays at home with the patient and his six older sisters, who were reported to be well and healthy with no recent illnesses. None of the family members had recently been tested for COVID-19.

Goal-directed investigation for MIS-C through testing aimed at:

- 1. Evidence of current or recent infection with SARS-CoV-2
- 2. Laboratory markers of inflammation
- 3. Multisystem organ involvement
- 4. Exclusion of other etiology and diagnosis

During the patient's hospital stay, a full sepsis workup was completed and empiric antibiotics, which included ampicillin, ceftriaxone and vancomycin, were given. Laboratory studies were notable for leukocytosis with neutrophil predominance, thrombophilia, lymphocytopenia, hypoalbuminemia, elevated inflammatory markers, elevated D-dimer, hypertriglyceridemia, sterile pyuria and cerebrospinal fluid (CSF) pleocytosis (Table 1). An echocardiogram was performed to assess cardiac function and any coronary artery involvement and revealed normal results. Gallbladder ultrasound was ordered to rule out hydrops of the gallbladder, which showed gallbladder wall thickening (Figure 1) with pericholecystic and perisplenic edema. Chest radiography was normal. Microbiological investigations included blood culture, stool culture, conjunctiva secretion culture, CSF fluid culture with gram stain, FilmArray Respiratory Panel, FilmArray Meningitis/ Encephalitis Panel, Epistein Barr Virus DNA PCR, and SARS-CoV-2 RT-PCR, antigen, IgG and IgM were all negative.

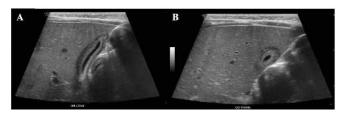
TABLE 1:

TABLE I:				
Lab	Value	Reference Range	Unit	
WBC count	21.1	6.0-17.5	x 103/uL	
Hemoglobin	10.6	9.5-13.5	g/dL	
Hematocrit	31.7	29.0-41.0	%	
Platelets	472	130-400	x 103/uL	
Segmented neutrophils	86	16-60	%	
Lymphocyte count	8	19-50	%	
Creatinine	0.3	0.3-0.6	mg/dL	
BUN	10	5-27	mg/dL	
BUN/Creatinine ratio	33	8-23	-	
Albumin	2.5	2.7-4.8	g/dL	
AST	19	22-58	IU/L	
ALT	14	11-39	IU/L	
CRP	24.90	0.00-0.60	mg/dL	
ESR	82	0-15	mm/hour	
Procalcitonin	0.81	Non-ICU patients: < 0.25 bacterial infection unlikely ≥ 0.25 bacterial infection likely ICU patients: < 0.50 bacterial infection unlikely ≥ 0.50 bacterial infection unlikely	ng/mL	
D-Dimer	3.54	0.00-0.46	ug/mL	
Ferritin	222.6	22.0-322.0	ng/mL	
Lactate Dehydrogenase	292	140-304	IU/L	
Troponin	<0.006	0.000-0.040	ng/mL	
Triglycerides	Triglycerides 129		mg/dL	
Urine WBC	10	0 -8	Per hpf	
CSF WBC	14	0-5	Per hpf	
CSF RBC	5	<1	/cmm	
CSF glucose	63	50-80	mg/dL	
CSF protein	35	15-45	mg/dL	

(WBC: white blood cell, RBC: red blood cell, BUN: blood urea nitrogen, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, AST: aspartate aminotransferase, ALT: alanine aminotransferase, CSF: cerebral spinal fluid)

FIGURE 1:

Longitudinal (A) and transverse (B) view of gallbladder demonstrating gallbladder wall thickening



On day seven of symptoms, because the patient was not clinically improving and met all of the criteria for MIS-C diagnosis, he received a 2 g/kg dose of IVIG. The patient showed significant clinical improvement and laboratory values began to normalize. CRP decreased markedly. High-dose acetylsalicylic acid (ASA) of 80 mg/kg/day was given until he remained afebrile for 48 hours. The patient was discharged (Figures 2 and 3) home to continue ASA of 5 mg/kg/day.

FIGURE 2: Fading of skin rash

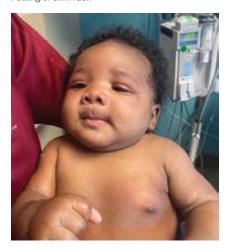


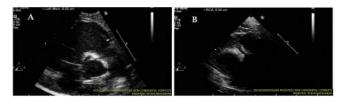
FIGURE 3: Absence of oral mucosal inflammation



Four days after discharge, the patient returned to his pediatrician with a fever of 100.7°F, persistent cough, congestion and irritability. Laboratory investigation showed an elevated white blood cell count of 30.9 x 103/uL. Repeat echocardiogram showed initial signs of coronary artery dilation formation (Figure 4). He received a second dose of IVIG in addition to corticosteroids and continued high-dose ASA. The patient responded well to treatment, fever subsided and laboratory values returned to normal limits.

FIGURE 4:

Repeat echocardiogram showing Initial signs of coronary artery dilation. (A) Left main coronary artery 0.25 cm (normal 0.11-0.23), (B) proximal right coronary artery 0.24 cm (normal 0.08-0.19), left anterior descending artery 0.19 cm (normal 0.08-0.14).



DISCUSSION

MIS-C is a clinical diagnosis made by ruling out plausible alternative diagnoses and fulfilling the criteria defined by the U.S. Centers for Disease Control and Prevention (CDC) or the WHO.6,17 When this patient was admitted to the hospital, he was on day four of his fever. Laboratory values supporting signs of inflammation included lymphocytopenia at 8%, hypoalbuminemia of 2.5 g/dL, elevated CRP of 24.90 mg/dL, elevated ESR of 82 mm/ hour and elevated D-dimer of 3.54 ug/mL. Multisystem organ involvement included the gastrointestinal system with diarrhea, the dermatological system with a rash and the neurological system with aseptic meningitis. A full sepsis workup provided there was no explanation for another source of infection or fever.

After an extensive review of published MIS-C cases, it is important to note this case differs from others due to the lack of positive RT-PCR or antibody tests. Although the patient had no known sick contacts and no family members diagnosed with COVID-19, we suspect there may have been unknown exposure due to potential asymptomatic carriers and the continued increasing number of cases in the area.¹⁸ Two studies have shown that asymptomatic carriers of COVID-19 infection are likely to produce an infection in close contacts that are also asymptomatic. 19, 20 In conjunction with the evidence that children typically experience asymptomatic or mild symptoms during active SARS-CoV-2 infection, this would support our hypothesis that if anyone in contact with our patient over the prior four weeks had an asymptomatic COVID-19 infection, that unknown exposure is likely for this case. We hypothesize that the negative SARS-CoV-2 results seen in this patient could be attributed to several factors, including high falsenegative rates in the RT-PCR test and failure of detection in the antibody test. A study of 1,330 confirmed COVID-19 cases with RT-PCR revealed that the false-negative rate for SARS-CoV-2 RT-PCR was highly variable, with the highest rate of 67% within the first five days of exposure and the lowest rate of 21% on day eight after exposure. 21 IgM and IgG antibodies against SARS-CoV-2 have increased sensitivity after one week of symptom onset.²² This

highlights the importance of how the timing and sensitivity of these tests may affect the accuracy of the results. Although SARS-CoV-2 antibody testing has been shown to have high sensitivity and specificity, researchers are still discovering more about antibody response characteristics. Immune responses to SARS-CoV-2 can vary from person to person and currently are not well studied in infants due to the low incidence of COVID-19 cases in the younger population.

Our patient also lacked the criteria necessary to meet complete KD or TSS, unlike many other reported cases. A cohort study of Kawasaki-like disease cases in the Bergamo province reported a dramatic increase of new cases of KD with an increased incidence of nearly 30-fold over the past five years.14 The region observed for this study had the highest rate of COVID-19 infection and death in Italy. A retrospective cohort study of 33 pediatric patients diagnosed with MIS-C in Cohen Children's Medical Center revealed 64% fulfilled the complete criteria for KD.²³ Our patient met one out of five criteria for KD, although he had rapid clinical improvement when treated with KD protocol, which includes IVIG and ASA. The successful treatment, similar manifestations and occurrence after exposure to an infectious agent may suggest that KD and MIS-C may have similar pathophysiology. Although the older average age of onset in MIS-C and the high occurrence of gastrointestinal symptoms and incidence of left ventricular dysfunction warrants further investigation for other factors that may contribute to the severity and nature of the syndrome.

CONCLUSION

The number of cases of MIS-C associated with COVID-19 is expected to increase as the SARS-CoV-2 pandemic progresses. Our understanding of the underlying pathophysiology and potential manifestations will improve with additional reports and research. This is a pediatric case in an infant that meets MIS-C criteria with negative SARS-CoV-2 testing, which was successfully treated with IVIG. Our study's limitations include the absence of COVID-19 diagnosis due to two negative RT-PCR tests, a negative antigen test and negative IgG and IgM tests. There also was no presence of COVID-19 illness in the family which may reduce the likelihood of exposure in this patient. The timing and sensitivity of available SARS-CoV-2 tests may affect the accuracy of the results. Therefore, unknown exposure to COVID-19 should not exclude MIS-C from the differential diagnosis.

Given that the understanding of MIS-C is still evolving, it is important to closely follow potential MIS-C patients as the physical examination findings do not appear simultaneously but rather evolve over several days. Increased index of suspicion and early decision to initiate intensive care is critical in successfully treating MIS-C. In this case, treatment with two doses of IVIG was successful. If MIS-C goes undiagnosed, the deterioration can be quite rapid and severe, resulting in a significantly increased mortality rate. This case highlights the importance of high clinical suspicion for MIS-C and early treatment benefits with IVIG.

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BRIEF REPORT

NEW-ONSET DIABETIC KETOACIDOSIS SECONDARY TO NIVOLUMAB THERAPY IN A PATIENT WITH PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

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KEYWORDS:

Autoimmune

Diabetic ketoacidosis

Hyperglycemia

Insulin

Lymphoma

Nivolumab

ABSTRACT:

Introduction: Inhibitors of programmed cell death receptor (PD-1) and its ligand (PD-L1), such as nivolumab and pembrolizumab, confer anti-autoimmune activities and are therefore approved for anti-cancer therapy. Their mode of action removes autoimmunity checkpoints, thus increasing the risk of immune-related adverse events.

Case Presentation: This report describes a clinical case of life-threatening diabetic ketoacidosis (DKA) in a patient after long-term nivolumab administration to treat primary central nervous system lymphoma (PCNSL). The patient presented to the emergency department (ED) with symptoms of fatigue, along with nausea and vomiting for two days; laboratory testing revealed significant hyperglycemia (glucose 673 mg/dL), elevated anion gap (>27), metabolic acidosis, ketonemia, glucosuria and ketonuria, findings of which were consistent with DKA. Given no personal history of diabetes mellitus or other autoimmune conditions and additional tests ruling out alternative causes, the patient was suspected of having newly-onset DKA secondary to nivolumab treatment.

Management & Outcome: The patient was treated with fluids, electrolytes replenishments and insulin drip, which closed the anion gap and normalized electrolytes. She was transitioned to subcutaneous insulin. The patient recovered well and was discharged on Metformin and long-acting insulin, with close follow-up with endocrinology and oncology.

Discussion: Autoimmune endocrinopathies induced by checkpoint inhibitors for cancer treatment have been reported in the past. Newly-onset hyperglycemia and DKA are common autoimmune-mediated side effects of checkpoint inhibitor uses in patients without prior history of diabetes mellitus. Clinicians should be aware to prevent this potentially life-threatening condition.

INTRODUCTION

Cancer cells can evade the host's immune-mediated programmed cell death (apoptosis) signals. Programmed cell death receptor (PD-1) and its ligand (PD-L1) function as an inhibitory immune checkpoint for the activity of peripheral T-lymphocytes (T-cells) upon their interaction.¹ The checkpoint confers immunologic

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tolerance, which is essential for preventing the onset or progression of autoimmune disease.² A wide variety of immune cells present in tumor or cancer microenvironments, particularly tumor-reactive T-cells, B-cells, natural killer (NK) cells and activated monocytes, exhibit elevated levels of PD-1. PD-L1 binds tumor-reactive T-cells expressing PD-1 (CD279), thus tolerizing them by reverse signaling through T-cell-expressed CD80. This neutralizes the host's anti-tumor immune (CD8+T-cell) and Fas Ligand-mediated lysis signaling.³ Using PD-1/PD-1L as therapeutic targets, cancer immunotherapies that help restore anti-cancer immune responses have been developed. They include monoclonal antibodies against PD-1 (nivolumab and pembrolizumab) and the PD-L1 (avelumab, atezolizumab and durvalumab); with only nivolumab and pembrolizumab being

approved for the treatment of advanced non-small-cell lung cancer (NSCLC), melanoma, Hodgkin's lymphoma and bladder urothelial cancer including renal cell carcinoma (RCC) and other cancers. 4.5.6 Nivolumab, a PD-1 inhibitor, has been demonstrated to be effective against NSCLC, melanoma, RCC, head and neck cancer and Merkel cell carcinoma. 1.6 Both PD-1 and PD-1L confer their immunogenic effects by binding and inhibiting PD-1/PD-1L interactions, thereby preferentially reactivating tumor-reactive T-cells with high specificity for cancer. 7

However, PD-1/PD-1L inhibitors also remove the essential inhibitory autoimmune checkpoints, thus increasing the risk of immune-related adverse events (AE). A recent systematic review and meta-analysis have demonstrated increased rates of autoimmune endocrinopathies, including hypophysitis (Odds Ratio—OR: 3.38, 95% CI: 1.02 to 11.08), adrenal insufficiency, thyroid disorders—hypothyroidism (OR: 7.56, 4.53 to 12.61), pneumonitis (5.37, 2.73 to 10.56) and colitis (2.88, 1.30 to 6.37), following long-term administration of nivolumab compared to standard treatments.4 Nivolumab can induce autoimmune diabetes characterized by severe hyperglycemia or diabetic ketoacidosis (DKA).5,8 This report presents a clinical case of a 55-year-old female patient who presented to the emergency department (ED) with new-onset DKA, suspected to be induced by long-term nivolumab treatment for her primary central nervous system lymphoma (PCNSL).

CLINICAL PRESENTATION

A 55-year-old female with PMHx of PCNSL (status post-intermittent immunomodulatory treatment and stereotactic brain biopsy) presented to the ED with two days of generalized weakness and nausea with non-bloody non-bilious vomiting whenever she tried to eat. She also reported burning chest pain accompanied by intermittent palpitations. She denied fever, chills, headache, dizziness, cough, shortness of breath, abdominal pain, diarrhea, constipation and dysuria. Physical exams revealed that she had no acute distress as she laid calmly in bed. She was neuro-alert and oriented, with no focal deficits. HEENT was normal. Her mucous membranes were moist, no pharyngeal erythema or exudates; neck was supple and with no cervical lymphadenopathy and no facial flushing/redness. A heart exam revealed a regular rate and rhythm, S1S2 without murmurs, gallops or rubs. Her lungs were clear to auscultation bilaterally, with no wheezes, rales or rhonchi. The abdomen was soft, depressible, non-distended with normal bowel sounds, non-tender to palpation. Exams of lower extremities revealed no peripheral edema bilaterally with normal distal pulses. Her skin was normal without rash, generally warm and dry. In the ED, her vital signs were normal except for mild tachycardia and hypertension: 36.5°C, HR 106, BP 141/76, RR17 and oxygen saturation 97% on room air. Her clinical presentation prompted laboratory and imaging investigations.

LABORATORY INVESTIGATIONS AND FINAL DIAGNOSIS

Laboratory results (Table 1) revealed leukocytosis with left shift (WBC 29.1), abnormally low serum electrolytes (Na 126, Cl 90

and HCO3 <9.0) and significant hyperglycemia (673 mg/dL); ABG revealed low pH (7.298), low pCO2 (26.5mmHg), elevated pO2 (125.0 mmHg) and low HCO3 (12.6mmol/L). There was also an anion gap of >27, which suggested high anion gap metabolic acidosis. Urinalysis showed glucose >500 and moderate ketones. Blood cultures were drawn as well. No other precipitating factors were identified. The patient denied a medical history of diabetes mellitus or any use of steroids. She was admitted to MICU to manage a suspected new-onset DKA secondary to long-term nivolumab therapy (two years) for her PCNSL. Endocrinology was consulted and ordered GAD 65 antibody, β -hydroxybutyrate and C-peptide; results showed negative GAD antibody, low β -hydroxybutyrate (< 4.0) and low C-peptide (0.12).

TABLE 1:Relevant laboratory results drawn at admission

Venous blood gas		Blood cell coun	Blood cell count		
рН	7.03	Hgb (g/dL)	15.3		
Arterial blood gas		Hct (%)	45.1		
рН	7.298	WBC (×109/L)	29.10		
pCO2 (mmHg)					
pO2 (mmHg)	26.5				
125.0	Platelet (x 109/L)	236			
HCO3 (mEq/L)	12.6				
Serum electrolytes		Endocrine			
Na (mmol/L)	126	HgA1c	6.4		
K (mmol/L)	4.4	β-HB (mg/dL)	>4.5		
CI (mmol/L)	90	GAD-65 Ab	Negative		
HCO3 (mmol/L)	<9	C-peptide	0.12		
Anion gap	26	Urine analysis			
Glucose (mg/ dL)	673	Glucose(mg/ dL)	≥500		
Ca (mg/dL)	8.3	Ketones	Moderate		
Mg (mg/dL)	2.1	Protein (g/dL)	Nil		
Phos (mg/dL)	2.2				

 β -HB, beta-hydroxybutyrate; Ca, calcium; Cl, chloride; GAD-65 Ab, glutamic acid decarboxylase antibody; HCO3, bicarbonate; Hct, hematocrit; Hgb, hemoglobin; HgA1c, glycosylated hemoglobin; K, potassium; Mg, magnesium; Na, sodium; pCO2, partial carbon dioxide pressure; pO2, partial oxygen pressure; Phos, phosphorus; WBC, white blood cells.

MANAGEMENT AND OUTCOME

After initial laboratory confirmation of DKA, the patient was placed on IV hydration (NS boluses, which then transitioned to D5 ½ NS) and insulin drip (titrated according to protocol). Electrolytes were also replenished accordingly. The patient was transferred to the medical floor once being stabilized with a resolution of metabolic derangements. She was then started on mealtime insulin aspart (NovoLog®) and bedtime insulin glargine (Lantus®) injected subcutaneously upon normalization of anion gap, electrolytes and blood glucose. Regarding initial leukocytosis

(WBC 29.1) prior to admission, the patient received one dose of antibiotic (Cefepime) in the ED. However, CXR, UA and blood cultures were negative for any infectious etiologies and antibiotic was discontinued. WBC trended down without further use of antibiotics. This was unlikely the trigger for her ketoacidosis. The patient responded well to treatments, with a resolution of symptoms (nausea, emesis and abdominal discomfort) even after diet advancement. She was hemodynamically stable at the time of discharge. She was discharged on Metformin and Lantus® with follow-up recommendations with the endocrinologist and oncologist to manage central nervous system lymphoma with DKA.

DISCUSSION

This clinical case is among several other clinical cases of new-onset DKA secondary to cancer treatment with checkpoint inhibitors such as nivolumab. 9,13 The Naranjo Algorithm Assessment (Table 2) was used to assess for the likelihood of whether this patient's adverse drug reaction (ADR) of DKA was actually due to nivolumab rather than the result of other factors. The patient in our case received a final Naranjo score of 6, which is interpreted as a probable ADR.

In previously published and current case reports, the involved patients have no history of DM or hyperglycemia and only developed DKA after using checkpoint inhibitors. The overall evidence from these case reports strongly supports that DKA is a common autoimmune-mediated adverse effect induced by checkpoint inhibitors. While it appears that other common autoimmune endocrinopathies produced by checkpoint inhibitors—such as hypophysitis, adrenal insufficiency, thyroid disorders (hypothyroidism), pneumonitis and colitis—are well tolerated, finicians should be aware of the acute nature and severity of the autoimmune DKA. Immediate drug-induced hyperglycemia and autoimmune DKA has been reported in a

case report by Aziz et al., where a 48-year-old woman with no previous personal history of diabetes or previous use of potential diabetogenic corticosteroids presented with pembrolizimabinduced DKA barely two weeks after a single cycle of the therapy (2mg/kg).9 Other similar case reports have demonstrated an immediate onset after the patient received only two cycles of nivolumab, 10 and only three cycles of nivolumab. 13 In contrast, others have reported delayed onsets after one year⁵ or up to a couple of years, as with this clinical case reported in the current study, where acute autoimmune DKA occurred after two years nivolumab use. Stamatouli et al. demonstrated that the time to onset of acute autoimmune DKA presentation was longer than other common AEs, for which on average occur after one-three cycles of treatment or between three-eight weeks after treatment.11 DKA should always be considered one of the differential diagnoses for patients presenting with metabolic acidosis following treatment with checkpoint inhibitors. Where indicated, oncologists should consider modification or even discontinuation of cancer therapies involving checkpoint inhibitors, especially in cases of immediate onset of acute autoimmune DKA.

CONCLUSION

Immunomodulating therapies have demonstrated good efficacies in the management of multiple cancers. Discussing common AEs and potential acute autoimmune hyperglycemia and DKA with patients who are good candidates for checkpoint inhibitors is an ideal informed consent process. At the same time, clinicians should closely monitor such patients for potential drug-induced DKA, among other immune-mediated AEs.

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TABLE 2: Naranjo adverse drug reaction probability scale

QUESTION		No	Do not know	Score
1. Are there previous conclusive reports on th is reaction?		0	0	+1
2. Did the adverse event appear after the suspected drug was administered?		-1	0	+2
3. Did the adverse reaction improve when the drug was discontinuedor a specific antagonist was administered?		0	0	0
4. Did the adverse event reappear when the drug was re-administered?		-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?		+2	0	+2
6. Did the reaction reappear when a placebo was given?		+1	0	0
7. Was the drug detected in blood (or other fluids) in conentrations know to be toxic?		0	0	0
8. Was the reaction more severe when the dose was increased or less seevere when the dose was decreased?		0	0	0
9. Did the patient have a similar reaction to the same os similar drugs in any previous exposure?		0	0	0
10. Was the adverse event confirmed by any objective evidence?		0	0	+1
	TOTAL SCORE		6	

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CLINICAL IMAGE

FACIAL RASH WITH EYE SWELLING

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INTRODUCTION

A 60-year-old male presents to the office for a painful rash on his forehead and scalp associated with periorbital swelling. Initially, the patient noticed a slight headache on his head's right parietal aspect, described as aching and constant. Two days later, he developed blister-like lesions on his right upper forehead and scalp. These lesions subsequently spread to his face and nose, causing his right eye to become swollen (Figures 1 and 2). He denies any associated vision changes, but his eye was swollen shut and he noted that his conjunctiva became erythematous. The patient had obtained a shingles vaccination 10 years ago and recalled having chickenpox as a child around the age of seven. The visual acuity check was within normal limits. He denied headache, fever, trauma, known sick contacts or previous episodes of similar presentation.

FIGURE 1: Swollen eye and rash, left side



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FIGURE 2: Swollen eye and rash, straight on



QUESTIONS:

- 1. What is the most likely diagnosis?
 - A. Bacterial Conjunctivitis
 - **B.** Contact Dermatitis
 - C. Herpes Simplex Keratitis
 - D. Herpes Zoster Ophthalmicus
 - E. Ramsay Hunt Syndrome
- 2. What is the preferred initial treatment?
 - A. Acyclovir
 - B. Amoxicillin
 - C. Clotrimazole
 - D. Prednisone
 - E. Reassurance

Tjiattas-Saleski, Krueger Facial Rash with Eye Swelling 45

3. What is the most likely causative agent?

- A. Dimorphic Fungi
- B. Double-Stranded DNA
- C. Gram-Negative Bacilli
- D. Gram-Positive Cocci
- E. Positive-sense RNA

ANSWERS:

1. What is the most likely diagnosis?

Correct Answer:

D) Herpes Zoster Ophthalmicus

The lesions are present in a dermatomal distribution, along with the ophthalmic division of the trigeminal nerve. The patient's rash is vesicular, and there is also ocular involvement consistent with herpes zoster ophthalmicus.¹ Contact dermatitis is incorrect because the patient had no known exposures to irritants or allergens. The patient also has ocular involvement, which is not necessarily caused by contact dermatitis.² Herpes simplex keratitis is incorrect because the rash is presenting in a dermatomal distribution. Herpes simplex keratitis can cause a corneal infection and may cause periocular lesions, but this patient's rash expands beyond this region. Reactivation of the varicella-zoster virus also causes Ramsay Hunt syndrome.2 The vesicular rash on the ear or in the mouth may be accompanied by a facial nerve palsy and hearing loss.³ Bacterial conjunctivitis would typically present with conjunctival erythema, discharge, irritation, eyelid crusting and periorbital swelling.2

2. What is the preferred initial treatment?

Correct Answer:

A) Acyclovir

The preferred treatment is acyclovir. It is recommended to begin an antiviral medication- such as acyclovir, valacyclovir or famciclovir - within 72 hours of onset.⁴ Treatment has been shown to speed the resolution of skin lesions, reduce viral shedding and decrease the incidence of dendritic and stromal keratitis as well as anterior uveitis.⁴ Amoxicillin would be used for a bacterial infection and topical clotrimazole for a fungal infection. Corticosteroids will be indicated if there are acute retinal necrosis symptoms, including blurred vision and pain in the eye.⁴

3. What is the most likely causative agent?

Correct Answer:

B) Double-Stranded DNA

The diagnosis is herpes zoster ophthalmicus and is caused by the varicella-zoster virus. Herpes zoster is an enveloped virus that contains double-stranded DNA.⁵ Gram-negative bacilli is incorrect,

with examples of gram-negative bacilli include Escherichia coli, Pseudomonas aeruginosa and Bacteroides fragilis.5 Gram-Positive cocci would include Staphylococcus aureus, Streptococcus pyogenes and Streptococcus pneumoniae. ⁵ These organisms will not cause a vesicular skin reaction such as this. Positive-sense RNA viruses include those of the Picornaviridae family and Flaviviridae family.⁵ These viruses will not cause this presentation. Picornaviridae viruses include diseases such as Poliovirus, Coxsackievirus and Rhinovirus. Flaviviridae viruses include Yellow fever virus, West Nile virus, Dengue virus and Zika virus.⁵ Dimorphic fungi include Candida albicans, Blastomyces dermatitidis and Histoplasma capsulitis.5 DNA viruses replicate in the nucleus using host cell polymerases, except poxviruses.5 Many DNA viruses, including HSV can establish latent infections and later reactivate.⁵ In contrast, RNA viruses replicate in the cytoplasm, except for orthomyxoviruses and retroviruses.5

DISCUSSION

There are one million estimated cases of herpes zoster in the U.S. each year, with approximately 50% occurring in individuals 50 years and older.⁶ Only 10–20% of these infections are diagnosed as herpes zoster ophthalmicus, with an overall lifetime risk of herpes zoster ophthalmicus of 1%.7 Herpes zoster is a very prevalent infection and is also known as shingles, a reactivation of the varicella-zoster virus; it is part of the herpes virus family.8 In those that have previously been infected with the virus, it remains latent in the dorsal root ganglia. When the virus is reactivated, it typically results in a vesicular eruption along a specific dermatome that does not cross the midline. There can also be associated symptoms, including a viral prodrome of flu-like symptoms, such as fever and the disease's early stages. Postherpetic neuralgia is a common residual side effect of the varicella-zoster virus. This is a pain in the corresponding infected dermatome for months to years after the infection and appears to be due to damage of the nerve root.9

Herpes zoster ophthalmicus occurs when the varicella-zoster virus is reactivated from the trigeminal nerve, specifically the ophthalmic division.¹⁰ Herpes zoster ophthalmicus typically has a prodromal period including fatigue and fever that appears up to one week before the rash appears.¹¹ There is a pain in the distribution of the ophthalmic nerve in 60% of patients.12 It presents as fluid-filled vesicles that are unilateral, presenting over five to seven days.9 Seventy-one percent of individuals with herpes-zoster ophthalmicus develop ocular complications.¹³ Examples of ocular complications include corneal disease, uveitis, scleritis and ocular motor palsies.¹³ If there are vision changes, then there should be a referral to an ophthalmologist for further evaluation.¹⁴ It is important to check patients for Hutchinson's sign, which includes vesicles on the tip or side of the nose. When these vesicles are present, there is a high risk of ocular complications because of the shared innervation of the nasociliary branch of V1.14

Herpes zoster is typically diagnosed based on clinical assessment, but there are confirmatory tests such as immunofluorescence, immunoperoxidase staining and serological diagnosis. The U.S. Centers for Disease Control and Prevention (CDC) states that

polymerase chain reaction (PCR) is the most useful test when using laboratory testing to diagnose herpes zoster.¹⁵ The specimen's ideal sampling is obtained by swabbing unroofed vesicular lesions and scabs from the lesions.¹⁵ Samples are recommended to be collected in the first days of illness.¹⁶ Clinical diagnosis is usually enough to diagnose, but laboratory methods, such as PCR, are useful in situations in the absence of a rash.¹⁵ Clinical judgment is an effective method of diagnosis of herpes zoster. The rash presents unilaterally, which helps physicians make the diagnosis. In a study with 272 participants, clinical diagnosis was confirmed in 91% of patients with signs and symptoms of herpes zoster.¹⁷

The vaccine for herpes zoster can be effective in preventing the reactivation of the virus and a reduction in prodrome. The CDC recommendation is that healthy adults aged 50 or older should receive two doses of the Shingrix® vaccine separated by two to six months.¹8 In a case study of 266 herpes zoster patients and 362 matched controls, the vaccine was 54% effective at preventing herpes zoster in persons age 60 and older over three years following vaccination.¹9 There is also a reduction in the severity of prodromal discomfort as well as post herpetic neuralgia in patients who experience a herpes zoster event after having a vaccination.¹9

Herpes zoster ophthalmicus infections should be treated within 72 hours of the rash onset using acyclovir, valacyclovir or famciclovir.⁴ Early treatment improves skin lesions' healing time, reduces viral shedding and decreases keratitis and anterior uveitis incidence.⁴ Without antiviral treatment, half of the patients with herpes zoster ophthalmicus will develop an eye disorder.²⁰ Treatment with antivirals reduces the percentage of patients with eye disorders from 50% to 20–30%.²⁰ A patient who has Hutchinson's sign, visual complaints or an unexplained red eye indicates referral to an ophthalmologist.²⁰ Patients who develop uveitis or keratitis may require a topical corticosteroid such as prednisolone. If the patient has increased intraocular pressure, the patient should receive a topical corticosteroid and aqueous suppressant.²¹

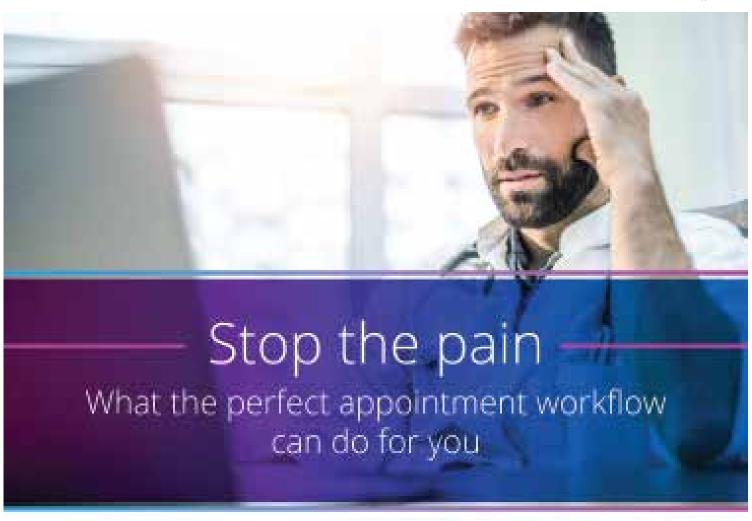
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Depression: Symptoms to Watch for and When to Contact Your Physician

Manoraj Ratnaraj, MD, PGY-1; Justine Monthony, OMS-III; Katherine Warden, PhD

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

Depression is a collection of symptoms people experience for weeks, months or years. Several causes for depression (vitamin deficiencies, thyroid problems, blood disorders, low self-esteem, alcohol or drug use, chronic medical conditions, pregnancy, grief, major life changes, etc.) have been well documented. Still, in some cases, it is not possible to identify one specific cause.

Since sadness is the major symptom of depression, it is often difficult to tell the two apart. Everyone can feel sadness, but normal sadness is often limited to a couple of days, while depression can persist for weeks, months or years. Depression is a common problem, and it is treated with a combination of medications and psychotherapy.

SYMPTOMS

If you experience one or more symptoms from this list, please seek help from your provider:

- Feeling sad or hopeless nearly every day for more than two weeks
- Low mood affecting your daily activity at home or work
- Feeling guilty, helpless or worthless for several days
- Difficulty falling asleep or staying asleep
- Decreased or increased appetite
- Feeling tired and/or loss of interest in sex
- Frequent thoughts about death
- Various body aches and pain nearly every day or most days
- Thinking about or making plans to hurt yourself or others

IDENTIFICATION AND TREATMENT

Early identification and treatment of depression are key to reduce symptoms and recurrence. You can also take steps to improve depression symptoms, such as mindfulness, regular exercise, developing a routine, staying connected with friends/family and keeping a healthy diet. Talk with your doctor to find the treatment that is right for you.







How to Identify and Handle Stress During COVID-19

Tania Ghazarian, OMS-III

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

For many, the COVID-19 pandemic has disrupted their normal daily routines and created new challenges to maintain social support. The combination of these life changes during a global pandemic has fueled feelings of stress.

HOW TO IDENTIFY STRESS

It is important to self-monitor and identify signs of increased stress levels in yourself and those around you. These signs commonly present as: constantly worrying about your health or the health of your loved ones, reporting changes in sleep or eating patterns, routinely feeling overwhelmed, worsening of chronic health issues, worsening of mental health conditions, increasing substance use and having difficulty sleeping or concentrating. There are many additional signs of stress, and it is important to be monitor changes in one's own behavior.

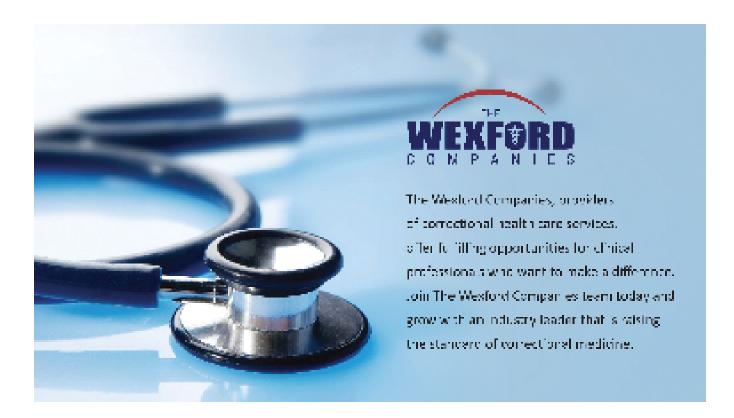
HOW TO HANDLE STRESS WITH COVID-19

Handling stress is a daily challenge that may be customized for each individual. Some steps to deal with stress during the COVID-19 pandemic include connecting with loved ones through video calls or phone calls, staying informed with accurate and reliable information, limiting screen time and maintaining a healthy lifestyle with diet and exercise. It is important to try different coping mechanisms and identify which approach works best for you.

WHEN TO CONTACT YOUR OSTEOPATHIC FAMILY PHYSICIAN

Please contact your osteopathic family physician if your stress level is interfering with your daily life activities or if coping mechanisms are proven unsuccessful.





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