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CONTENTS

EDITOR'S MESSAGE

Caring as a Community

Paula Gregory, DO, MBA, FACOFP

There is nothing that evokes such an emotional response as the illness and near death of a patient or loved one, and certainly illness in our practices' families and children are times when we reach deep to understand and help our practice families cope.

Children are a special case, as their lives have just begun, and they have so much future potential. The new and emergent viruses require us to keep up with the current recommendations for surveillance and treatment. Now with COVID-19, there is uncertainty of the long-term effects of the viruses. Unrecognized, untreated or even treated patients are at risk for long-term effects of most diseases that can be deadly if missed. This is our encouragement to keep abreast of the recommendations.

Although there has never been a time where we can relax and not worry about patients, the new, emergent and challenging infections are upon us as we learn how to recognize and treat unexpected complications, as it is with the multisystem inflammatory syndrome in children you will read about in this edition.

As family physicians we don't need reminding that when a child is ill, the entire community is involved. The parents, siblings and healthcare system, as well as the child's school, teachers and classmates, are upfront in the concern and caring of the patient, who may need additional services such as physical therapy and training, at which point other healthcare discipline support will be enlisted.

Even if for a single event in care, the mental and physical stress involved in being a parent or sibling bystander is evident. These effects can last for years into the future. The parents who helplessly stand by the bedside and the brothers and sisters who whisper in the hall will remember and have emotionally driven expectations of the healthcare system and physician. Educators who are wondering how to catch up the child as they return to class speculate if they missed sending the child home or if, in some way, they could have helped the child. And as physicians, we question ourselves and relearn as much as possible to recognize and treat illness.

Caring is a community event, and nowhere is there more concern than when it's a child.

Along with other important educational topics in this issue, a must-read article addresses how to avoid MIS-C misdiagnosis, as currently, there is not a clearly defined process that can predict which children will be at risk. We must be ever vigilant when a child presents with symptoms post-COVID-19 infection, especially because COVID-19 can be mild or unrecognized, so knowing when to investigate or hospitalize gains more importance.

Please take a moment to refresh your knowledge as you read this information.

FROM THE PRESIDENT'S DESK

Making a Statement to Make an Impact

Bruce R. Williams, DO, FACOFP

"I do hereby affirm my loyalty to the profession I am about to enter. I will be mindful always of my great responsibility to preserve the health and the life of my patients, to retain their confidence and respect both as a physician and a friend who will guard their secrets with scrupulous honor and fidelity, to perform faithfully my professional duties…"

These are the words that begin the osteopathic oath—the words that every osteopathic physician has publicly stated and sworn to. But what does it mean? What are we committing ourselves to?

We are committing to advocating for our patients. We are saying we will do the best we can to look out for the best interest of our patient. As osteopathic physicians, we took that oath, and as ACOFP members, we are keeping that commitment to our patients.

Advocacy is a significant part of ACOFP, as we are the voice for our patients. Advocacy means educating our patients on good and poor health choices; getting what our patients need from employers, insurance carriers and legislators; and volunteering on medical staff committees, healing arts boards, and local, state and national organized medicine committees and boards to educate others as to what our patients need. **Advocacy means being engaged and involved**.

Advocacy also involves getting your hands dirty. It means politics—writing letters, attending rallies and signing checks. It has been said many times and in many places: "If you are not at the table, you are on the menu." Unfortunately, that is a true statement. But what can you do for your patients?

For me, I look back at the oath I took as an osteopathic physician, and I look at the faces of my patients and feel their pain. I have the resources to do what is needed. I can be a member. I can write letters. I can visit legislators. I can sign a check. I can make a statement. I can be a voice.

A single voice makes a statement. Multiple voices make an impact. ACOFP can make an impact. When we say we represent over 20,000 osteopathic family physicians, residents and students, that gets attention. When we combine our voices with other family medicine organizations, that voice multiplies even further. When we are combined with the American Osteopathic Association, the American Medical Association and the House of Medicine, that voice becomes thunder—a force to be reckoned with. Voices are votes, and we represent more than one voice and more than one vote.

Family medicine needs to be recognized as the major specialty. We provide the prenatal care; we deliver the babies; we administer our children's immunizations; we set the broken bones; we remove the skin lesions; we provide the family counseling; we treat the back pain; we complete the workers compensation and disability forms; we treat the chronic conditions; we provide the palliative care; and we are there for the patient and their family for their last day. We advocate for our patients in listening to them, advising them, directing them, treating them, referring them and speaking for them. Family physicians treat the family, and we need to be recognized and reimbursed for the work we do.

Most recently, ACOFP championed the introduction of the *Rural Physician Workforce Act of 2021* in the U.S. House of Representatives, as an expansion of our efforts to promote graduate medical education to rural and underserved areas. We also have publicly opposed—and continue to oppose—Medicare Payment Fee Schedule proposed cuts to physician payments, launching call-to-action campaigns, submitting our own comment letters and partnering with other organizations to maximize our voice. Finally, in early August, we responded to the U.S. Health and Human Services' initiative to strengthen primary care.

For me, I look back at the oath I took as an osteopathic physician, and I look at the faces of my patients and feel their pain. I have the resources to do what is needed. I can be a member. I can write letters. I can visit legislators. I can sign a check. I can make a statement. I can be a voice.

To provide guidance on ACOFP's advocacy priorities and positions—in collaboration with advocacy firm Alston & Bird—we have developed the 2022 Principles of Healthcare System Reform. This document gives direction on issues for Alston & Bird to lobby and advocate for, such as preserving the family medicine model of care, addressing the primary healthcare workforce shortage, addressing reimbursement policies, reducing unnecessary paperwork requirements, and promoting and supporting osteopathic manipulative treatment.

It does take a village—members, committees, the Board of Governors, Alston & Bird and you! ACOFP will reach out to you. We will ask you to complete those forms, make those phone calls, document those issues. We will ask you to connect with your legislator through an ACOFP communication. We will ask you to write, call, visit and contribute to your legislators.

But what is important, is that you consider the oath you took as an osteopathic physician. Are you living up to that oath: "To affirm my loyalty to the profession. I will be mindful always of my great responsibility to preserve the health and the life of my patients, to retain their confidence and respect both as a physician and a friend who will guard their secrets with scrupulous honor and fidelity, to perform faithfully my professional duties?" I know you are.

Osteopathically yours,

Bruce R. Williams, DO, FACOFP

2022–23 ACOFP President

CALENDAR OF EVENTS

OCTOBER 27–30, 2022
OMED 2022
American College of Osteopathic Family Physicians
Boston, MA
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DECEMBER 2–4, 2022
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Chicago, IL
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JANUARY 20–21, 2023
IACOFP Midwinter Osteopathic Family Practice Conference
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JANUARY 26–29, 2023
Winter Family Medicine Update
Missouri Society of the ACOFP
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JANUARY 27–29, 2023
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REVIEW ARTICLE

AN OSTEOPATHIC APPROACH TO ANEMIA

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KEYWORDS:

Anemia

Folate deficiency

Iron deficiency anemia

Vitamin B12 deficiency

Abstract

With close to 2 billion people affected globally, anemia is a commonly seen condition worldwide. Diagnosed by a patient's low hemoglobin, and then subsequently differentiated through red blood cell indices, a complete blood count should be performed on every patient presenting with the classic symptoms of anemia. Iron studies, as well as the corrected reticulocyte count and peripheral blood smears, can also be of use to further specify the exact type of anemia. Additionally, tests including colonoscopies, upper endoscopies and gynecologic procedures should be considered to identify the different underlying causes of the disease. The most common microcytic anemias include iron deficiency, thalassemia and anemia of inflammation. Deficiencies in folate and B12—also known as cobalamin—are the most common etiologies of macrocytic anemia. Treatment of each of these types of anemia is tailored to the individual patient based on the severity of their condition as well as the specific underlying cause. Osteopathically, anemia falls largely into the respiratory-circulatory model, as well as the metabolic-energy model, which can also be used to guide treatment. For a family physician, identifying symptoms, making accurate diagnoses and properly treating patients with anemia is of the utmost importance.

INTRODUCTION

Anemia can be broadly defined as any condition that results in a deficiency of red blood cells (RBCs) or a decreased amount of hemoglobin, an iron-rich protein that binds oxygen. Anemia causes decreased oxygen delivery to tissues and can result in symptoms including lethargy, dyspnea, weakness and pallor. Anemia impacts approximately one-third of the world's population.[1] Estimations of the global prevalence suggest that 1.93 billion people are affected by anemia with iron deficiency being the most prominent cause, contributing to more than 60% of cases.[1] Other common causes include nutritional deficiencies, such as folate and B12, and conditions that result in prolonged inflammation. Understanding this complex etiology is crucial for the diagnosis and management of anemia.

Risk factors for anemia include female sex, increased age, nutritional deficiencies, heavy menstruation and pregnancy.[2] Anemia can develop by means of ineffective erythropoiesis, hemolysis and blood loss.[3] Though anemia can be classified by its cause, it is typically differentiated based upon the size, shape and color of RBCs. Hemoglobin levels that fall below given thresholds in both men and women are indicative of anemia. These thresholds, established by the World Health Organization, are 12 g/dL in women and 13 g/dL in men.[4,5]

COMMON ETIOLOGIES

Iron deficiency anemia (IDA) is most often a result of conditions such as malabsorption, gastrointestinal bleeding and heavy menstrual periods.[5,6] Folate and B12 deficiencies, which interrupt DNA synthesis, are grouped under megaloblastic anemia. B12 deficiency is common in malabsorptive states, such as malnutrition. Folate deficiency is most often seen in alcoholism, malnutrition and states of increased folate requirement, such as pregnancy. Non-megaloblastic anemias include deficiencies that are not due to a breakdown in DNA synthesis, such as liver disease and cancer.[7] Anemia of inflammation (AI), previously known as anemia of chronic disease, is caused by underlying conditions which result in a decrease in RBC synthesis or an increase in RBC loss.[8,9] Table 1 highlights various underlying causes of AI.

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TABLE 1:

Potential causes of anemia of inflammation[8–12]

Infection (viral, bacterial, parasitic, fungal)
Rheumatoid arthritis
Systemic lupus erythematosus
Inflammatory bowel disease
Sarcoidosis
Vasculitis
Chronic kidney disease
Chronic inflammation
Chronic rejection post organ transplant
Malignancy

CLINICAL MANIFESTATIONS

General symptoms are common among all anemias and are seen due to the body's lack of oxygenated blood resulting from reduced hemoglobin levels. These symptoms include fatigue, dizziness, lightheadedness, dyspnea, exercise intolerance, weakness, palpitations, headache and difficulty concentrating.[13] Often, these symptoms appear when hemoglobin levels fall below 7.0 g/dL, though comorbidities, the duration of anemia and its underlying etiology have a significant impact as well.[14] Symptoms specific to each type of anemia can be determined based on their underlying etiology as shown in Table 2.

TABLE 2:

Clinical manifestations of anemia[5,13–20]

	UNIQUE SYMPTOMS/SIGNS	SPECIAL CONSIDERATIONS
IDA	Pica Restless leg syndrome Brittle integument Cheilosis Spooning of the fingernails	Symptoms can occur prior to a change in the patient's hemoglobin level.
B12	Loss of proprioception Loss of vibratory senses Areflexia Irritability Acute psychosis Gait abnormalities	Gait abnormalities can be in the form of sensory ataxia that manifests as a positive romberg sign.
Folate	None	None

DIAGNOSTIC WORKUP

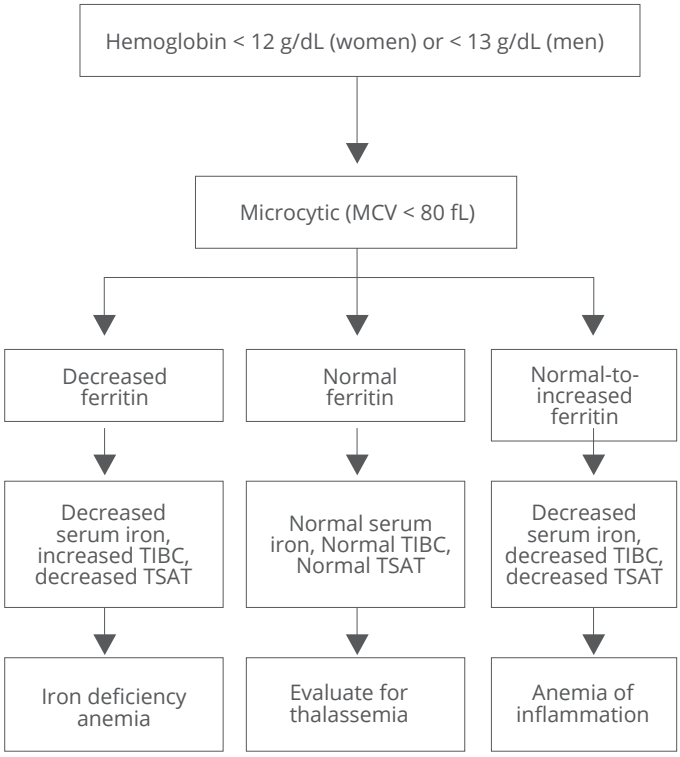
The initial workup of anemia is commonly done through the evaluation of hemoglobin concentration. A hemoglobin value indicative of anemia can only diagnose anemia and cannot determine the exact cause. Once established, the mean corpuscular volume (MCV) is assessed, which categorizes the anemia as microcytic (<80 fL), normocytic (80–100 fL) or macrocytic (>100 fL), which then allows for a more tailored evaluation.[21]

Microcytic

Once the anemia has been determined to be microcytic, iron studies—which include serum iron, ferritin, total iron binding capacity (TIBC) and transferrin saturation (TSAT)—are conducted. Figure 1 outlines the lab values that are used to further differentiate the 3 common causes of microcytic anemia.

FIGURE 1:

Diagnostic algorithm for microcytic anemia [23,26,27]



Ferritin levels, which serve as a measure of iron stores, below 45 µg/mL and above 100 µg/L are associated with IDA and AI, respectively.[9] Traditionally, a threshold of under 15 µg/mL can diagnose IDA, but a concentration of less than 45 µg/mL has a higher sensitivity with only a mild decrease in specificity.[22] The upregulation of ferritin, noted in AI, is due to ferritin being an acute-phase protein whose secretion is promoted by inflammatory mediators.[9,23] However, the inflammatory cytokines of AI reduce the levels of transferrin. The functional capacity of transferrin to bind iron is represented by the TIBC. The transferrin saturation, which is calculated by dividing serum iron by the TIBC, will be low in both IDA and AI.[18,24]

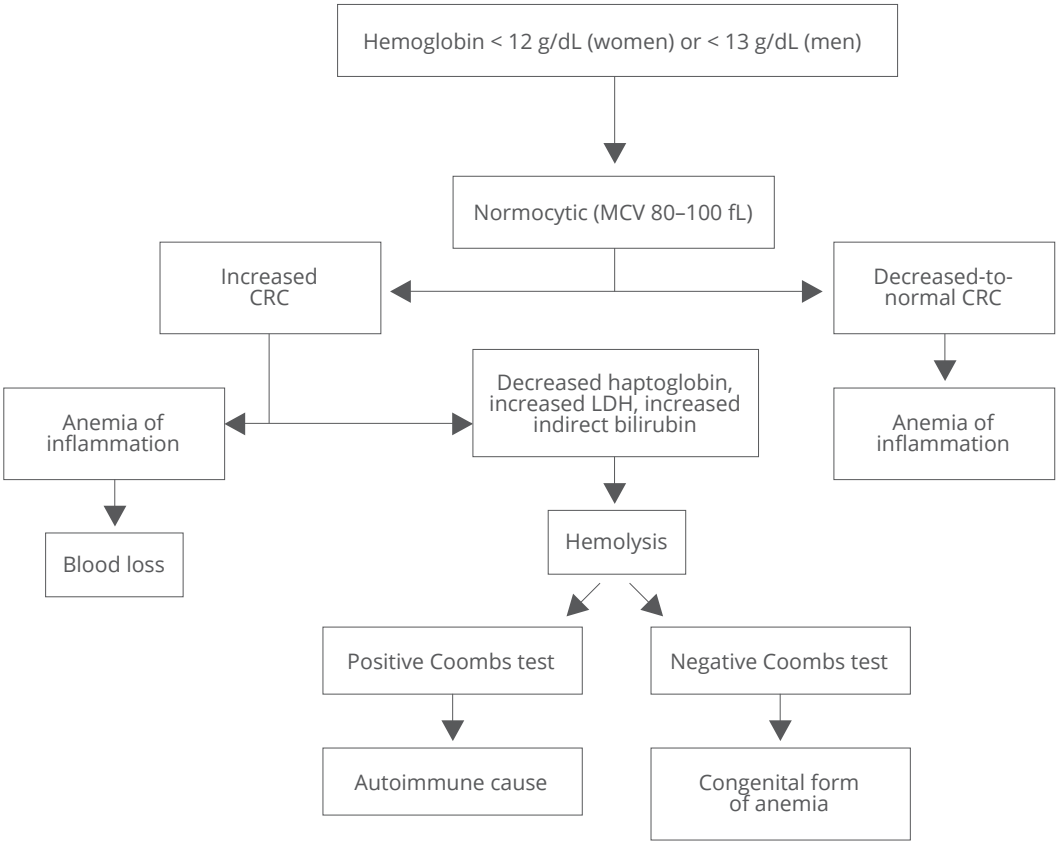
If all iron studies are normal, then thalassemia should be part of the differential diagnosis. Thalassemia can be further differentiated by hemoglobin electrophoresis. The Mentzer index, which is calculated by dividing the MCV by the RBC count, helps differentiate thalassemia from IDA. A Mentzer index value of <13 is indicative of thalassemia.[23,25]

Normocytic

When the MCV is within 80–100 fL, the corrected reticulocyte count (CRC)—also known as the reticulocyte index—and peripheral blood smear are then evaluated to find the root cause of the anemia. Typically, normocytic anemia is further subdivided by the CRC, which is derived from the reticulocyte count. The CRC adjusts for the degree of anemia and better reflects the state of erythropoiesis.[18,28] A decreased CRC is indicative of an inadequate bone marrow response to the anemia.[28] Though AI can be found in microcytic anemia, it is commonly the cause of normocytic anemia with a decreased or normal CRC.[9,13,18,29] Alternatively, an elevated CRC implies increased RBC turnover due to blood loss or hemolysis.[23] Hemolysis is supported with labs of increased indirect bilirubin, decreased haptoglobin and increased lactate dehydrogenase, and hemolysis can be further subdivided into congenital or acquired by a Coombs test. To determine the etiology of the hemolysis, a peripheral blood smear should be completed.[24] Figure 2 illustrates the lab evaluation for normocytic anemia.

FIGURE 2:

Diagnostic algorithm for normocytic anemia [13,27,29]

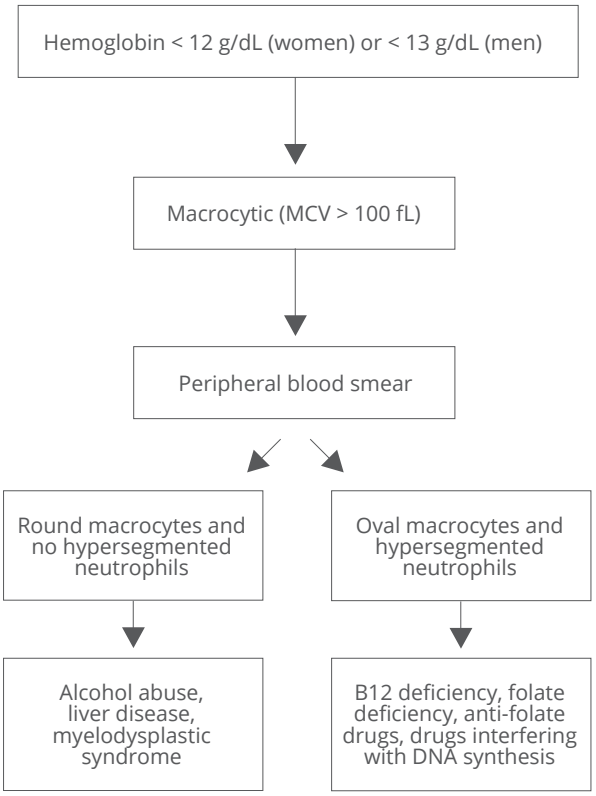


Macrocytic

Macrocytic anemia is subdivided into megaloblastic and non-megaloblastic anemias based on a peripheral blood smear. Hypersegmented neutrophils and macro-ovalocytes will be found with megaloblastic anemia, while morphological abnormalities are not present with non-megaloblastic anemia.[18,24] Serum homocysteine and methylmalonic acid levels can be obtained to further differentiate between folate or B12 deficiencies. Only homocysteine levels will be increased with folate deficiency, whereas both homocysteine and methylmalonic acid will be elevated in B12 deficiency.[18] Figure 3 highlights the workup for macrocytosis.

FIGURE 3:

Diagnostic algorithm for macrocytic anemia [21,27]



TREATMENT

Treatment of anemia is guided by the underlying cause. Oral iron therapy is typically prescribed for patients diagnosed with nutritional IDA. Ferrous salts are the standard first line oral iron therapy because of their high bioavailability, cost effectiveness, and accessibility.[5,30,31] Among the ferrous iron compounds, their side effects, bioavailability and efficacy are similar though their elemental iron content varies as shown in Table 3. The recommended daily dose of elemental iron for IDA patients is 150–200 mg.[18] It is recommended to avoid consumption of inhibitors of iron absorption such as whole grains, legumes, tea, coffee, red wine, hot chocolate, as well as proton pump inhibitors and antacids.[5,30] Common side effects with iron supplementation include metallic taste, epigastric pain, nausea, vomiting, constipation and dark stools.[16,21]

TABLE 3:

Oral iron therapy for iron deficiency anemia [5,30,31]

ORAL IRON FORMULATION	DOSE PER TABLET	ELEMENTAL IRON PER TABLET	SPECIAL CONSIDERATIONS
Heme Iron Polypeptide	398 mg	11 mg	Can be taken with food Acidic environment not required for absorption
Ferrous Gluconate	240 mg 325 mg	27 mg 38 mg	Best absorbed on empty stomach
Ferrous Sulfate	325 mg	65 mg	Best absorbed on empty stomach
Ferrous Fumarate	325 mg	106 mg	Best absorbed on empty stomach
Polysaccharide Iron Complex	150 mg	150 mg	Can be taken with food Acidic environment not required for absorption

In 2019, the FDA approved ACCRUFeR®, a new oral iron therapy for adults with IDA. This ferric maltol based compound represents a comparably efficacious and well-tolerated alternative for those who experience treatment-limiting intolerance issues such as nausea, abdominal discomfort, and constipation.[32,33] Other advancements in the treatment of IDA include Injectafer®, a ferric carboxymaltose based compound that offers an alternative parenteral option for treating patients who are refractory to or cannot tolerate conventional oral iron therapy.[34]

Treatment options for B12 deficiency anemia include supplementation with either 1 mg intramuscular (IM) injections or 1–2 mg oral formulations[19]. Dosing schedule and duration depend on the patient's symptomatic state as well as the underlying cause of the deficiency. If the patient's underlying cause is reversible and the patient is without severe neurologic symptoms, then dosing 3 times per week is warranted.[19] In cases with severe neurologic deficits, the frequency of dosing should increase to every other day.[19] For patients with a reversible condition, such as a nutritional insufficiency, supplementation should be discontinued following a resolution of symptoms or a correction of deficiency, whichever occurs first.[19] If the cause of deficiency is irreversible, such as malabsorption, then the treatment continues indefinitely.[19] Oral supplementation is non-inferior to IM injections throughout the first 8 weeks of treatment. After 8 weeks, IM injections were found to be superior.[35]

Folate deficiency anemia is generally treated with oral folate supplementation due to the underlying cause of the deficiency

typically being a lack of dietary intake. Folic acid, the oral supplement for folate replacement, is dosed up to 5 mg per day. The duration of treatment continues until resolution of the anemic state or until the underlying cause of the deficiency is addressed. If the cause of the deficiency is irreversible, such as a malabsorptive state, then treatment continues indefinitely.[11,14]

AI and macrocytic non-megaloblastic anemias are treated by controlling the underlying cause of disease or by removing the offending agent. Referral to hematology may be considered in some circumstances.

OTHER STUDIES

Given that anemia is a disease of multiple potential etiologies, numerous evaluative techniques can be performed to find the root cause for each patient. Determining the underlying cause, such as folate, B12 or iron deficiencies, or malabsorption is key to coordinating treatment. Beyond those already mentioned, other studies should be considered to evaluate the various causes. Since IDA can be due to blood loss, either gross or occult, further work-up should include evaluations of the gastrointestinal tract with both colonoscopy and upper endoscopy.[36] If neither evaluation identifies the cause, small bowel investigation is warranted. In women, heavy menstrual bleeding is a common cause of IDA.[37] Pelvic ultrasonography, saline infusion ultrasonography and hysteroscopy can be used to screen for common causes of heavy menstrual bleeding, such as endometrial polyps, intracavitary lesions or adnexal lesions.[38]

OSTEOPATHIC CONSIDERATIONS

Anemia primarily involves the metabolic-energy and respiratory-circulatory osteopathic models. This model aims to restore optimal function of metabolic processes while replenishing energy loss and fatigue due to ineffective metabolism.[39] Including more leafy green vegetables, for example, can help prevent recurrence of iron-deficiency anemia. There have been numerous studies conducted investigating the relationship between veganism, Mediterranean diets, and anemia.[40,41] Veganism is frequently associated with the development of mineral deficiencies, and it is even recommended that vegans should also receive B12 supplements regularly.[42]

The respiratory-circulatory model aims to restore vascular, gaseous and lymphatic movement.[39] It is understood that nutrition and blood flow create an environment that can facilitate or impede organ function.[19] The circulation absorbs nutrients from our diets and is distributed systemically. An anemic state can markedly disturb this circuit.

A significant consequence of anemia is fatigue. The CV4 technique increases parasympathetic activity and decreases sympathetic activity. For this technique, with the patient supine, the physician cradles the occipital bone laterally while easing the cranium into extension. This results in a decrease in sleep latency, thus improving fatigue.[43]

Occipitoatlantal decompression is another technique used to increase parasympathetic activity.[44] For this treatment, with the patient supine, the physician's fingers balance the patient's head at the occipital condyles. The physician then applies a superior tractional force, decompressing the condylar region.[45]

CONCLUSION

Anemia continues to affect a widespread population around the world. While various treatments have been instituted, investigation remains both about the origins of the disease and its pathophysiology. Due to its multifaceted etiologies, anemia remains elusive in terms of its root causation in many patients. Continued studies of micronutrients could be analyzed to further manage this disease state. Increasing awareness of appropriate nutrition and lifestyle habits will help to alleviate the burden of anemia.

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REVIEW ARTICLE

IDENTIFYING MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN AFTER COVID-19 INFECTION

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MIS-C

Severe acute respiratory system

Introduction: Since its discovery, the novel coronavirus disease 2019 (COVID-19) has evolved into a global pandemic that has affected millions. The pediatric population was once thought to be mostly spared from the SARS-CoV-2 virus. However, a severe hyperinflammatory sequela of the virus known as multisystem inflammatory syndrome in children (MIS-C) has since been identified and poses a great risk to pediatric morbidity and mortality. The goal of this manuscript is to clarify and characterize MIS-C as a diagnosis, including current management and future considerations.

Methods: A thorough literature search was performed using Google Scholar and PubMed databases for articles published January 2020 through August 2021.

Results: A two-tiered diagnostic approach was created for any pediatric patient presenting with fever and an epidemiologic link to SARS-CoV-2. The mean age at time of diagnosis was 9.3 years old, with 56.8% of patients identifying as male and the majority identifying as either Hispanic (36.5%) or Black (35.1%). Common signs and symptoms included fever, cough, tachycardia and tachypnea. Current treatment recommendations included IVIG, glucocorticoids, and aspirin, with the more severe cases needing hospitalization and immune modulator therapy. Discussion: MIS-C is a serious and potentially fatal sequelae after COVID-19 infection in the pediatric population. Much is still unknown regarding the long-term effects of MIS-C. Further emphasis should be placed on identifying definitive treatment and preventative strategies. Osteopathic family physicians are the primary providers for many of the patients who may present with signs and symptoms of MIS-C, and familiarity with the workup and treatment can help improve care.

INTRODUCTION

On December 31, 2019, the World Health Organization (WHO) was first notified by a group of scientists in China of a group of unexplained cases occurring in Wuhan, China and presenting as a pneumonia-like illness. Over the next 18 months, this unknown illness would become known around the world as the novel coronavirus disease 2019 (COVID-19), which has developed into a global pandemic with almost 200 million confirmed cases and over 4 million reported deaths as of the start of August 2021.[1]

During this time, much surrounding COVID-19, including its diagnosis, management and prevention, has continued to evolve. The causative agent—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—continues to spread across the globe despite continued efforts to contain the virus.[2,3,4] The development of a vaccine has helped to decrease transmission rates, hospital admissions and overall mortality.[4] However, new COVID-19 variants, skepticism and misinformation surrounding the vaccine, and social and political biases, have made controlling the spread of SARS-CoV-2 difficult.[5,6]

While in adults the presentation and severity of COVID-19 can vary greatly, it was initially thought that children were mostly spared from showing signs and symptoms of the virus, and therefore assumed to have lower rates of infectivity.[7,8] In an early study of 171 children with confirmed COVID-19 diagnoses, it was found that only 3 cases needed intensive care unit admission and only 1 case resulted in death.[9] These results suggested that children were less likely to be infected by SARS-CoV-2, and those who were infected had a milder clinical course when compared to adults. However, most of the children in these studies were symptomatic when diagnosed, and therefore only followed until symptom

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resolution. Because many children infected with COVID-19 are asymptomatic, this made determining an exact rate of infectivity difficult for this patient population, as well as challenging when trying to identify any possible negative effects the virus could have in both symptomatic patients and asymptomatic carriers.

In April 2020, a United Kingdom report highlighted a group of 8 previously healthy children presenting with a hyperinflammatory state and signs of multiple-organ damage.[10] While never tested directly, all of these cases were linked to recent COVID-19 exposure. This newly identified hyperinflammatory syndrome associated with COVID-19 was eventually named by the U.S. Centers for Disease Control and Prevention (CDC) as multisystem inflammatory syndrome in children (MIS-C) and has become a serious complication of the virus with morbidity and mortality rates in children much higher than previously suspected.[11,12]

With the discovery of new variants, rates of COVID-19 and MIS-C diagnosis in children have only continued to increase. Since there is currently no diagnostic testing for MIS-C, it presents a major public health concern for the pediatric population. The authors wish to clarify and further characterize the epidemiology, pathogenesis, clinical identification, symptomatology, diagnostic criteria, management and long-term outcomes of MIS-C, including new advancements and understanding of this novel syndrome since its discovery.

METHODS

A thorough search of available literature in the English language was performed using Google Scholar and PubMed databases for articles published from January 2020 through August 2021. Due to the rapidly changing and continued evolving understanding of COVID-19 and MIS-C, multiple various search criteria were used, including "coronavirus disease 2019;" "severe acute respiratory syndrome coronavirus 2;" "multisystem inflammatory syndrome in children;" "hyperinflammatory syndrome;" "Kawasaki disease;" "toxic shock syndrome;" "shock;" "children;" "pediatrics;" "pandemic;" and "vaccine."

RESULTS

Several meta-analyses and systematic reviews[13–18] have been conducted since the discovery of MIS-C, encompassing over 500 published articles to date. A summary of findings is detailed below, including diagnostic criteria, demographics, clinical characteristics, laboratory and imaging findings, treatment and management, and clinical outcomes and complications of patients with MIS-C.

Diagnostic criteria

The CDC and WHO have similar case definitions for diagnosing MIS-C, both of which are outlined in Table 1.[19,20] While these criteria were initially used to make a formal diagnosis, as MIS-C became more widespread, a tiered diagnostic approach was adopted for any patient presenting to the emergency department with unremitting fever and an epidemiologic link to SARS-CoV-2.[16,21]

TABLE 1:
CDC and WHO case definitions of multisystem inflammatory syndrome in children.

CRITERIA	CDC CASE DEFINITION	WHO CASE DEFINITION
Age	<21 years old	<19 years old
Fever	Fever >38.0°C (100.4°F) for ≥24 hours **or** subjective fever lasting ≥24 hours	Fever for ≥3 days
Clinical Presentation	**2 or more** organ system involvement: o Cardiac o Renal o Respiratory o Hematologic o Gastrointestinal o Dermatologic o Neurological	**2 or more** of the following: o Rash or non-purulent conjunctivitis or muco-cutaneous inflammation o Hypotension or shock o Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities o Evidence of coagulopathy o Acute gastrointestinal problems
Inflammatory Laboratory Evidence	Including **any** of the following: Elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, LDH, IL-6, neutrophilia, lymphocytopenia or hypoalbuminemia	**1 or more** of the following: Elevated markers of inflammation such as ESR, CRP **or** procalcitonin
Diagnosis of Exclusion	No alternative plausible diagnoses	No other obvious microbial cause of inflammation (including sepsis, or bacterial shock syndromes)
Link to SARS-CoV-2	Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test **or** COVID-19 exposure within the 4 weeks prior to onset of symptoms	Evidence of COVID-19 (RT-PCR, antigen test, or serology positive) **or** likely contact with patients with COVID-19

This includes performing an initial evaluation screen (tier 1) through measuring a complete blood count (CBC), complete metabolic panel (CMP), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and SARS-CoV-2 PCR laboratory values. If these results are consistent with MIS-C diagnosis, a complete diagnostic evaluation (tier 2) should be performed. Tier 2 evaluation consists of more complex testing, including measuring brain natriuretic peptide (BNP), troponin-T, procalcitonin, ferritin, prothrombin time (PT), partial thromboplastin time (PTT), D-dimer, fibrinogen, lactic dehydrogenase (LDH) and triglyceride levels, as well as a cytokine panel, SARS-CoV-2 serology, blood smear, electrocardiogram (ECG) and echocardiogram.[21] Blood cultures are also indicated for patients presenting with severe symptoms, such as fever and 2 or more organ systems involvement.

The tier approach is a good evaluation design, as it permits effective and cost-efficient screening for patients who may have MIS-C. Since MIS-C is still a rare complication of SARS-CoV-2 infection with a current estimated incidence rate of 2 out of 200,000 individuals,[22] it is not necessary to perform a full work-up on each patient. However, in patients who exhibit signs and symptoms of MIS-C, a second, more thorough evaluation should be completed due to the severe cardiovascular and respiratory complications that MIS-C can cause.

Demographics

The mean age of patients at time of diagnosis of MIS-C was 9.3 years old, with 56.8% of patients identifying as male.[17] Patient race/ethnicity varied, with 36.5% identifying as Hispanic, 35.1% Black, 25.2% white, 16.2% Asian, and 14% other.[18] Of all patients diagnosed with MIS-C, 31% reported a previous comorbid condition, the most common being a past medical history of obesity or asthma.[1]

Clinical characteristics

All patient presentations met the criteria for MIS-C diagnosis. The most common symptoms present at time of diagnosis were fever, diarrhea, cough and abdominal pain. Common clinical signs were mainly cardiovascular dysfunction (tachycardia, hypotension) followed by respiratory dysfunction (tachypnea, low oxygen saturation).[14]

Laboratory and imaging findings

The most common laboratory findings were elevated inflammatory markers. Of these, the most elevated were ESR and CRP, albeit these are considered non-specific markers of inflammation for a variety of disease processes.[17] While imaging was rarely necessary at time of diagnosis, the most commonly performed was echocardiography, and it frequently demonstrated decreased cardiac ventricular function.

Because the clinical presentation and laboratory findings of MIS-C can closely mimic other pediatric inflammatory diagnoses, most especially Kawasaki disease, careful consideration must be given in order to make the correct diagnosis. Kawasaki disease is an acute inflammatory illness of unknown origin that was originally founded in Japan in 1967 and primarily affects children 5 years of age and younger.[12] Common initial signs and symptoms include fever, a classic "strawberry" red tongue, rash, irritability and fatigue,[12] many of which are also seen in patients with MIS-C.

TABLE 2:
Comparison of MIS-C and Kawasaki Disease.

	MIS-C	KAWASAKI DISEASE
Age	Older children and adolescents with median ages of 8–11 years	Infant and younger children, 76% of affected children <5 years
Race and Ethnicity	Black and Hispanic descent	Asian descent
Clinical Presentation:		
GI Symptoms	GI symptoms very common (53%–92%)	GI symptoms less common (20%)
Myocardial Dysfunction and Shock	Myocardial dysfunction common, elevated BNP (73%), troponin (50%), 48% receive vasoactive support	Myocardial dysfunction much less common, normal troponin, 5% receive vasoactive support
Organ Dysfunction	Multiorgan dysfunction common	Multiorgan dysfunction uncommon
Inflammatory Markers	Highly elevated CRP, ferritin, procalcitonin and D-dimer, lymphopenia and thrombocytopenia	Elevated CRP and D-dimer, normal ferritin, thrombocytosis
Treatment	IVIG, corticosteroids, IL-1 blocker, IL-6 inhibitors	IVIG, corticosteroids, IL-1 blocker
Average Outcomes	Fatality rate: 1.4%–1.7%	Fatality rate: 0.01%

Table 2 below compares the most common presentations and objective data for both MIS-C and Kawasaki disease.[23,24] Utilizing similar guidelines and algorithms as seen in Table 2 can greatly impact patients' medical decision making by allowing for accurate diagnosis and subsequent management.

Symptomatic treatment, clinical management and complications

The overall goal of MIS-C treatment is to stabilize the patient and prevent life-threatening long-term complications, especially any cardiac manifestations such as myocardial fibrosis/scarring and coronary artery aneurysms. To prevent these complications, most patients with confirmed MIS-C diagnosis were initially stabilized with intravenous immune globulin (IVIG) as well as adjunctive high-dose glucocorticoids for more severe cases.[15–17] Daily therapeutic aspirin was also given to patients who had an increased risk for coagulation and thrombosis, seen with elevated D-dimer and fibrinogen.[25]

According to several recent studies, IVIG and steroids are considered mainstay therapy for all patients diagnosed with MIS-C.[15–17] IVIG therapy has been shown to reduce inflammatory markers in MIS-C patients post-infusion, as well as result in overall decreased rates of myocarditis compared to those who did not receive IVIG.[16,26] In a study that compared the use of combination IVIG and steroid therapy versus IVIG monotherapy on the development of cardiac dysfunction, it was found that there was a 44% risk reduction in those patients receiving combination therapy.[2]

In more severe treatment-resistant cases of MIS-C, additional treatment modalities should be initiated. For those patients presenting with severe multisystemic shock, empiric broad-spectrum antibiotic therapy should be started following a blood culture draw.[16,17,27] In the pediatric setting, an appropriate antibiotic regimen of ceftriaxone plus vancomycin is usually sufficient.[27] If blood culture results are negative infection, antibiotic therapy should be discontinued. Furthermore, in patients who continued to worsen with decreased responses to IVIG, steroids and/or aspirin alone, it is recommended that immune modulators be initiated. These include anakinra (IL-1 receptor blocker), tocilizumab (IL-6 inhibitor) and infliximab (anti-TNF-α), which can be added to the treatment regimen and has been shown to have improved outcomes in some patients.[27] The efficacy of these medications in the treatment of MIS-C, as well as other immune modulators, are currently still being tested.

Finally, serial laboratory testing of systemic inflammatory markers (ESR and CRP) and cardiac monitoring (troponin-T and BNP) were performed to track the progress of the patient. Additionally, other systemic complications, such as respiratory distress, signs of hypercoagulability and development of systemic shock were frequently monitored and evaluated.[15–17]

Prevention

There is still much to elucidate surrounding the pathogenesis and possible transmission of MIS-C. Because studies have shown that MIS-C symptoms only present in relation to either active COVID-19 infection or recent exposure, SARS-CoV-2 may act as a trigger for immunomodulator in the development of MIS-C.[28] There is still confusion regarding why some children develop MIS-C, while others do not. Some researchers suggest that pre-existing conditions, race and severity of inflammatory response to COVID-19 may play a role in its development.[29] However, no definitive cause or explanation has yet been proven. Therefore, it is important to focus on preventative public health policies that decrease transmission of SARS-CoV-2 to decrease the incidence of MIS-C. These include strategies such as wearing masks, socially distancing, proper hand hygiene and encouraging COVID-19 vaccination.

Comparison to adults

As knowledge surrounding MIS-C continues to evolve and expand across the globe, there have been a few, rare, documented cases of a similar hyperinflammatory response in connection with recent COVID-19 exposure/diagnosis in adults.[30] So called "MIS-A" because they are occurring in adults at least 21 years of age, these cases are being considered the same as MIS-C, with similar treatment and management strategies. While MIS-C has been recognized as a true syndrome in the pediatric population, MIS-A is not as well defined.[31]

DISCUSSION

Since the first diagnosed cases in 2020, COVID-19 has rapidly developed into a very serious global health concern. In part due to its high infectivity rate, the SARS-CoV-2 virus has spread to nearly every country in the world, resulting in hundreds of millions of positive cases, and almost 4 million deaths worldwide. As a relatively new pandemic, new discoveries about the virus and a better understanding of its potential impact are continuing to evolve. What was once thought of as a disease that mainly impacted adult patients and the immunocompromised, it is now known that COVID-19 also greatly impacts the pediatric population, with hundreds of new cases occurring in the United States alone. Even as variants spread, they are affecting many children, resulting in increased pediatric morbidity and mortality rates.[32]

MIS-C, a very serious sequelae of SARS-CoV-2 infection, is quickly becoming a public health concern. Due to the severity of symptoms, as well as a current lack of understanding surrounding future complications from the disease, much has been discussed as to the best diagnostic, management and preventative measures for children against MIS-C.

A two-tier diagnostic approach to MIS-C is the current recommendation to minimize costs, time, and resources.[16,21] Any pediatric patient who presents with fever, multi-organ

symptoms, and recent association with COVID-19 should be tested for SARS-CoV-2 infection and referred to a pediatric infectious disease specialist/hospital unit. Symptomatic treatment with IVIG, glucocorticoids, and/or aspirin, as well as close monitoring for specific organ system findings is recommended while serial inflammatory marker labs are performed to aid in monitoring disease progression.[17,26]

Because MIS-C is a relatively new diagnosis, future emphasis needs to be placed on monitoring the evolution of MIS-C diagnosis, including more definitive testing and treatment options. Additionally, future research should focus on determining any sequalae for children who are diagnosed with MIS-C, including possible organ system complications, weakened immune systems, or risk for future infections. As current vaccines are being authorized for children aged 12–18 years (as well as possible authorization for younger ages in the future), it is important to determine the efficacy of these vaccines in preventing not only SARS-CoV-2 infection, but also in preventing MIS-C diagnosis. As more is discovered surrounding the pathogenesis and clinical outcomes of MIS-C, it is important to consider new treatment and management strategies, including immune modulators such as anakinra, tocilizumab, infliximab and others, which are currently undergoing clinical trials.[33]

CONCLUSION

Since its discovery in late 2019, COVID-19 infection from the SARS-CoV-2 virus continues to pose a serious epidemiologic threat to most of the world. The pediatric population faces a unique and unexpected sequela of being infected by the virus after the discovery of MIS-C hyperinflammatory syndrome, which has affected more than 6000 pediatric individuals in the United States alone. Due to the severity of symptoms, as well as a current lack of understanding surrounding future complications from the disease, much has been discussed as to the best diagnostic, management, and preventative measures for children against MIS-C. Following a two-tiered approach to diagnosis MIS-C is critical for accurate identification of the syndrome. Current evidence suggests symptomatic patients should be treated with IVIG and glucocorticoids, as well as monitoring for worsening organ dysfunction. As new discoveries and understandings of MIS-C continue to evolve, it is important to continue following the latest CDC and WHO guidelines for appropriate treatment and management. The osteopathic family physician plays a key role in primary care in the United States, and prompt identification and treatment of this disorder is critical.

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BRIEF REPORT

LEVERAGING PRIMARY CARE, PUBLIC HEALTH AND SOCIAL CONTEXT DURING THE COVID-19 RESPONSE WITHIN A UNIVERSITY SETTING: CONSIDERATIONS FOR THE OSTEOPATHIC FAMILY PHYSICIAN

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The COVID-19 pandemic placed a spotlight on both the successes and the needs across the spectrum of the healthcare system. The trusting, enduring relationships developed within the primary care setting served as an important foundation on which to build response strategies throughout the pandemic. Early detection and testing, implementation of telehealth, delivery of continuous comprehensive care, and vaccine education and administration are all key areas where primary care and public health systems successfully served patients and community. Emerging national research from the COVID-19 pandemic experience has also demonstrated the reduction in COVID-19 infection and death rates through the synergy between primary care, public health and social factors, emphasizing once again the critical role these services play and the importance of developing integration strategies for the future. In particular, the COVID-19 experience within the university setting served as a key example of this integration and synergy in action. As osteopathic family physicians, these experiences can serve as lessons learned toward embracing the opportunity afforded by our unique training, expertise and commitment to the osteopathic philosophy.

During the 2-year span of the COVID-19 pandemic, the efforts and impacts of healthcare professionals at the emergency front lines who responded to the urgent surges of disease and death have been appropriately recognized and applauded. However, as peaks and nadirs of illness continue to evolve over time, we have seen a shift—both inside and outside the healthcare system—from emergency and crisis management toward a renewed focus on preventive community health interventions. Throughout this time, osteopathic family physicians responded as we always do: by adapting to the needs of our patients and communities, quickly determining where gaps existed in the systems and swiftly implementing protocols and services to address the holistic needs of our patients and communities. Many have highlighted the intensity of the emergency response, but how did the pandemic impact the practice of and experience within the world of primary care?

As we transition into the next phases of the COVID-19 pandemic, it is crucial to understand and appreciate the components of our systems that contributed to success in order to build upon these elements in the future. This paper places a spotlight on the role of the primary care system during the COVID-19 pandemic. Using a combination of practical experience within the university-based health center, review of leading and emerging literature, we will highlight the success of community partnerships between primary care and public health, the importance of continued focus on health equity and the social determinants of health, and the opportunity they present for osteopathic family physicians in the future.

THE ROLE OF PRIMARY CARE

We know from practice that primary care is the foundation of our healthcare systems and communities. Decades of research prior to the pandemic have shown that primary care is the most equitable, efficient and cost-effective way of enhancing the health of populations.[1–2] Recent studies have demonstrated that key public health measures—including symptomatic and asymptomatic testing, vaccine delivery, and patient counseling and education, among others—are routinely delivered within primary care practices.[3] These hallmarks of the primary care system are proving vital to the delivery of health care during the COVID-19 pandemic,[4] and were outlined in real time through surveys of primary care clinicians as the pandemic unfolded.[5–6] With a recent Doximity survey revealing that 60% of polled

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another pandemic is possible within this lifetime, the importance of primary care clinicians cannot be understated.[7]

Early detection and testing

When the pandemic began in early 2020, primary care clinics were among the first to detect infection and disease. Within university-based health centers, for example, COVID-19's beginning coincided with the start of the 2020 spring semester when students were returning to campus from around the world. In January 2020, COVID-19, a novel virus associated with a market in a small village in Asia evolved into a potential infectious disease outbreak on a residential college campus in the northeastern United States. Students were learning while in transit back to college that they might have been exposed. Calls to our local public health departments during a weekend clinic jump-started the testing procedures in our health centers, setting off a firestorm of activity within our local community. As students who returned to campus sought treatment for respiratory illnesses in January and February 2020, the clinical presentations seemed different from what we would expect during the normal flu season but testing for the novel coronavirus was restricted.

As testing technology and availability ramped up within the state and nation, our protocols changed and adjusted as often as several times per day. Quickly recognizing the exponential increase in work to be done, we in primary care continually found ways to work with public health agencies that made us more efficient and effective. For example, testing could initially only be done with the approval of the local public health authorities, which necessitated a call to a public health nurse each time we needed to administer a test. Over time, we worked with the public health departments to develop testing protocols that eliminated the need for these repetitive calls. This protocol evolved to include a daily briefing call between the health department and our health center to debrief the day's events and plan for the next situation or developing issue. This partnership was critical to our collective ability to stay vigilant for our shared community.

Telehealth

When the U.S. Centers for Disease Control and Prevention shifted to a pandemic operations model, outpatient practices were forced into a reality of strict building entry protocols, PPE assignments and stay-at-home orders.[8] Primary care practices quickly leveraged telehealth technologies, implementing software and platforms within days to ensure that patients' acute and chronic care needs would be met.[9] During this time, emergency departments and acute care centers were overwhelmed—not only by volume, but also by the risk of exposure.[10] As osteopathic family physicians, we considered the risk/benefit ratio of bringing our patients in for care compared to treating empirically through telehealth.[10]

Within the university setting, using telehealth resulted in improved access to care for students on our residential campuses. In mid-March 2020, as universities across the country closed and sent students home, we worked diligently to continue to care for patients' needs via telehealth. Many primary care practices throughout the country launched these programs even before formal payment models developed billing and coding procedures.[10–13] These actions represent key factors for the solidification and strengthening of trust in the primary care system. Our patients knew they could depend on our practices and on us as physicians to meet them where they were: in their homes during the lockdown phase of the pandemic.[14]

Continuous & comprehensive care

At a time when many specialty services were forced to shut down or restrict services, the primary care field continued to communicate the importance of holistic care. We knew from experience, from our commitment to the osteopathic philosophy and from knowing our patients, that the inability to treat one part of the system would affect a whole person's health. For example, the importance of continued screening, testing, vaccination and mental health care were recognized and emphasized throughout the pandemic. This meant that many family physicians were managing complex and complicated clinical scenarios over telehealth, with or without the benefit of quick access to specialty care.

On university campuses, where the strain of student burnout and concerns of campus climate led to mental health challenges, university health centers also needed to retain a holistic approach to care. When COVID-19 surged, staff were redeployed into COVID-19 testing, positive case investigations, isolation and quarantine functions, while temporarily reducing services for general primary care. After COVID-19 surges resolved, the needs for general primary care subsequently surged in response. Over time, it became essential to ensure that basic primary care, screening, testing and access to holistic services, especially related to mental health, remained consistently available.[11,12] In community medicine and primary care practices alike, our practices remained essential locations for continuous, holistic care, hallmarks of the osteopathic philosophy that rang true throughout the pandemic.[10]

The combination of these experiences also revealed one of the true joys of primary care and osteopathic family medicine—the continuity that results from trust and shared ownership of health care. Due to the establishment of trusting relationships with their providers and teams, patients continued to rely on the primary care system for many of their questions about both COVID-19 and their holistic health.[13]

Vaccine education & administration

Vaccine education, as part of a comprehensive health maintenance plan, rests squarely within the scope of primary care.[15] Due to the holistic and trusting relationships built within primary care practices, many patients seek the opinion of their family physician, pediatrician or primary care provider regarding issues of vaccine hesitancy or safety.[15] The COVID-19 pandemic proved no different, with primary care offices being a key location for patients to receive answers to their vaccine questions as well as vaccine administration.[16]

Though large-scale vaccine distribution sites comprised the early volume of vaccine delivery, this mode of administration soon

proved to be cumbersome and of unclear overall value given the investment of staff time and resources. Nevertheless, primary care professionals continued to contribute to the public health effort by volunteering their time or resources to community vaccine pop-ups, in addition to obtaining and administering vaccines within the practice setting as soon as a supply became available.[16] After vaccination centers began to close, family physicians were able to smoothly transition vaccinations from a large-scale clinic location to local family medicine offices within the local community. The ability to have direct conversations with vaccine-hesitant patients, with instantaneous access to the vaccine, allowed for the delivery of comprehensive preventive care the outpatient setting.

In some demographic regions adjacent to schools of osteopathic medicine, physical campuses became key sites for state-designated large vaccination centers. As family physicians, we served as the lead onsite physicians, which required up-to-date knowledge of vaccine product specifics, relative and absolute contraindications, and current vaccination guidelines. In addition, we were responsible for leading the response to vaccine urgencies or emergencies and training volunteer resident or specialist physicians in response strategies. We were also called upon by the local community and the media to represent the vaccination effort and the evolution of the COVID-19 pandemic.

This critical relationship and trust built between these partners allowed vaccination centers the flexibility to institute pop-up sites for special populations, including the local community, as well as the university campus itself. During these events, thousands of doses were administered to undergraduate and graduate students in addition to any interested party in the surrounding community. Within university settings, vaccine delivery was also a critical example of how shared resources, time and staffing enabled widespread vaccination on residential campuses.[17] In this setting, the trusting relationships became increasingly reciprocal. When students and community members experienced their health center staff contributing to a large-scale vaccine effort, it helped improve trust in the health systems around them as well as in the public health system as a whole.[17]

THE IMPACT OF SYNERGY BETWEEN PRIMARY CARE, PUBLIC HEALTH AND SOCIAL DETERMINANTS OF HEALTH

In October 2021, the Primary Care Collaborative and the Graham Center published the report Primary Care and COVID-19: It's Complicated—Leveraging Primary Care, Public Health and Social Assets.[3] The goal of this research was to examine each of these entities—primary care, public health and social drivers—as a group, looking for synergistic effects of their efforts in combination, rather than as related siloes.[3] Its findings demonstrate that communities with the combination of the most robust primary care, strongest public health infrastructure and fewest social vulnerabilities had lower COVID-19 infection and death rates as compared to communities without the combination of these factors.[3] These results validate existing literature indicating that the integration of primary care systems with public health infrastructure, while using a guiding set of principles in social justice, can improve the health of patients and communities.[18–22]

Health care delivered in university settings is a key example of this synergy in action. Residential college campuses have a unique responsibility for the protection from harm and safety of students who choose to study during these unprecedented times. For example, students infected with or exposed to COVID-19 required access to safe isolation and quarantine locations, including access to necessities such as meals, bathroom facilities and the healthcare system for both basic health questions and coordination of care in the event of severe illness.

Our experience throughout the pandemic was that many public health systems were already overwhelmed, making partnerships and shared protocols essential. Without them, duplication of work would cause delays and mistakes. Using shared commitment to patient wellbeing and keen process improvement strategies, we worked together to eliminate waste, reduce redundancies and enhance efficiency for deployment of testing, contact tracing, and isolation and quarantine protocols to the community by medical services partnering with laboratory personnel, as well as necessary social service organizations, such as housing, transportation and informational technology.[23] In each of our university practices, we are fortunate that no severe morbidity or incidents of mortality were reported or experienced among students.

This synergy was also at work during outbreak investigations, where understanding social connections between student groups was crucial to controlling surges in infection. As we learned about positive cases, we used outbreak identification technology to create social networks and web-diagrams, a standard rubric from public health practice. However, it was health center staff's partnerships with campus leaders, advisors to student groups and academic staff that helped us identify connections between students based on social factors. These connections allowed us to find exposure points or risk factors—such as shared study locations, social gatherings or areas within residence halls—where environmental infection controls could be strengthened. This became an iterative process of identifying opportunities for engagement through potential or discovered surges, delivering community prevention education and collaborating with public health entities to ensure coordinated efforts.[24]

Local communities surrounding universities also benefitted from the early and ongoing engagement of family physicians, especially where osteopathic medical schools were located. Lead family physicians were often called upon by public health entities to engage with specific communities, especially those with risk factors related to social determinants of health, to learn about specific challenges, provide education and risk mitigation interventions, improve safety, and enhance overall health. While university-based health centers across the nation vary in scope, size, service population and resources, re-opening of institutions of higher education has required organizational commitment to these key mitigation and treatment strategies, including early detection, testing, vaccination, contact tracing, and isolation and quarantine procedures.[25] In our experience, osteopathic family physicians, together with interprofessional colleagues within primary care and public health, continue to discover creative solutions to providing this level of service given the challenges to scope, services and resources within community and university-based settings.

The COVID-19 pandemic tested our societal and organizational systems and connections, and yet as we collectively process our experiences in the primary care system, public health sector and social community, we must continue our future work in an integrated way, capitalizing on our shared success. The osteopathic oath itself calls us to "be ever vigilant in aiding in the general welfare of the community" in addition to "preserv[ing] the health and the life of [our] patients," and to "work in accord with… colleagues in a spirit of progressive cooperation."[26] As osteopathic family physicians, we have the opportunity to build bridges and take responsibility for creating these connections.

In practice, it often can be difficult to identify whose responsibility it should be to initiate these synergies, but our experience from the COVID-19 pandemic teaches us that these first steps can come from any of these three stakeholders: primary care, public health and the social community. Successful strategies exist at multiple levels, from the perspective of the individual physician to the scope of the organization or health system to facilitate these connections (Table 1). While these strategies do take time and initial investment in energy and buy-in, our experience has demonstrated that successful partnerships can lead to a decrease in wasted time and effort, enhanced efficiency and improved care for patients overall.

As the emergency preparedness adage says, "Disaster is the wrong time to exchange business cards."[27] Despite the demands on our time and energy, and in the face of increased levels of burnout and mental health concerns in our profession, we encourage colleagues to consider these approaches as opportunities to share and expand upon the successes that emerged during the pandemic.

TABLE 1:

Strategies at the level of the individual physician, the physician practice and the organization or health system that would create synergy between primary care, public health and social assets

FOR THE PHYSICIAN	Connect with your local public health department outside of times of crisis, looking for low-stakes opportunities to work on shared projects or goals
	Reach out to public health organizations to coordinate care with patients around reportable infectious diseases
	Consider volunteering for a public health distribution event (eg, vaccine pop-ups)
	Consider serving on a committee or board of directors to create connections with leadership and influence protocols and infrastructure. If osteopathic physicians are not represented on committees or boards within your community, consider serving as a representative.
FOR THE PRACTICE	Facilitate connections between professionals in your office with similarly trained professionals within the public health system (eg, social worker, registered nurses, front desk staff)
	Create protocols for public health processes that decrease the necessity for lengthy calls and approvals (eg, testing, treatment, isolation, quarantine)
	Consider partnerships with organizations whose needs relate to key social determinants of health and connect to osteopathic philosophy (eg, group homes, nursing homes, integrated mental health centers) to assist with decision-making at the intersection of clinical medicine and public health (eg, testing, quarantine, isolation protocols for shared residential spaces and related staff members)
FOR THE ORGANIZATION OR HEALTH SYSTEM	Develop models to share staff, cross-train or jointly deploy resources to higher need areas during surges in activity
	Explore models for shared savings or payment incentives for shared partnerships and programs

CONCLUSION

The continued COVID-19 pandemic reinforces the importance of appropriate systems within primary care, demonstrated the necessity of infrastructure for public health, and reveals the impact of health disparities related to social determinants of health. As osteopathic family physicians, we are existing through an incredibly challenging time that has required adjustment, flexibility, and continual adaptation to the ever-changing landscape in healthcare and public health.[28] As we evaluate the successes and lessons learned from these experiences, may we celebrate the ways in which we served our communities and heed the newfound opportunities to continue to serve, develop and improve ourselves, our patients and our communities.

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BRIEF REPORT

DERMOSCOPY CURRICULUM IN FAMILY MEDICINE RESIDENCY BRIDGES GAP BETWEEN DERMATOLOGICAL CARE OF SKIN MALIGNANCIES IN RURAL, UNDERSERVED MEDICAL COMMUNITIES

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An important aspect of any family medicine resident's training is the ability to competently diagnose and manage common skin conditions, including differentiating between benign and potentially malignant skin lesions. This is particularly important for residents planning to practice in rural or underserved areas where patients may have limited access to specialty dermatologists due to barriers related to their social determinants of health. The authors believe that training family medicine residents in the effective use of dermoscopy can improve the accuracy with which they are able to differentiate between benign and malignant skin lesions, and thereby reduce the need for unnecessary and burdensome referrals to dermatology specialists.

Use of the triage amalgamated dermoscopic algorithm (TADA) as part of a family medicine residency's dermatology curriculum is a simple and effective way to train residents in the use of dermoscopy, and could prove to be an important part of how FM GME programs produce a primary care workforce with the knowledge and skills required to care for the healthcare needs of rural and underserved patient populations.

INTRODUCTION

Skin conditions are among the top 20 reasons patients present to their family medicine physicians.[1,2] Commonly referred to as the largest organ system of the human body, skin cancer is currently the most common cancer diagnosed in the United States and the incidence of both nonmelanoma and melanoma skin cancers continues to rise.[3] According to the *American Journal of Preventive Medicine*, the number of adults treated with skin cancers increased from 3.4 million during 2002–06 to 4.9 million in 2007–11.[3] Nonmelanoma skin cancers (NMSC), including basal cell carcinoma and squamous cell carcinoma, now constitute more than 1 million new cases annually, while new reported cases of malignant melanoma (MM) was noted to be at over 85000 in 2017.[4,5]

Osteopathic physicians, with their unique training in structural physical exam and osteopathic manipulative medicine (OMM), have more opportunities to discover skin lesions than only using limited traditional problem-focused exams. Furthermore, DOs are more likely to choose to live and practice in rural communities than their MD counterparts.[6]

With a national shortage of dermatologists, patients living in rural and underserved areas of the country have the least access to dermatologists.[7,8] It is critical that family physicians—especially rural predominating osteopathic physicians—are well trained in the diagnosis and management of skin conditions.[7,8]

ADOPTING A SECONDARY PREVENTION METHOD FOR SKIN CANCERS

Clinical assessment of skin lesions in the primary care setting requires that the family physician understands how to consistently and accurately differentiate benign skin lesions from those suspicious enough to warrant biopsy or referral to a dermatologist.[8] With little time dedicated to teaching dermatology in medical school education and even post-graduate training, many primary care physicians acknowledge being ill-prepared for managing skin related conditions. Despite current "skin conditions" curriculum guidelines published by the American Academy of Family Physicians (AAFP), which state that family medicine residents should gain competency in using dermoscopy

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to complement physical exams, very few family medicine residency programs report including dermoscopy into their didactic curriculum.[2,8]

Dermoscopy involves use of a dermatoscope, a handheld light-emitting, cost-effective instrument that magnifies the skin; enhances characteristics of color and structure of the epidermis, dermis and papillary dermis; and has been proven to improve diagnostic accuracy, sensitivity, and specificity when attempting to differentiate suspicious and benign appearing skin lesions.[9–13] The triage amalgamated dermoscopic algorithm (TADA) is a simplified and easy to learn dermoscopic algorithm that can be used to diagnose both pigmented and nonpigmented skin cancers.[8] Teaching family medicine physicians to apply the TADA method has been shown to significantly improve primary care physicians' ability to safely and accurately differentiate benign from suspicious skin lesions, increasingly detect suspicious lesions that truly warrant referral, and reduce patient cost, inconvenience, unnecessary referrals and lack of follow-up.[8,14]

ENABLING FAMILY MEDICINE RESIDENTS TO DIAGNOSE PIGMENTED AND NONPIGMENTED SKIN CANCERS

TADA enables primary care physicians to confidently identify pigmented and nonpigmented skin cancers by recognizing architectural patterns such disorganized structure, asymmetric color, blue-black or gray color changes, "hair pin" vessels, ulceration or starburst patterns.[8] Additionally, users are taught to recognize the common features of benign skin lesions such as dermatofibroma, angioma and seborrheic keratosis.[8] Appreciation and recognition of these benign skin lesions helps reduce the number of unnecessary biopsy procedures and unwarranted referrals to dermatologist.[14] The subjective interpretation of architectural disarray using a dermatoscope has high interobserver agreement and discriminatory power for malignancy,[8] and improves diagnostic accuracy, sensitivity and specificity.[12] The TADA method of dermoscopy prompts users to study a lesion's architecture, assess for disorder or other malignant features and determine if the findings suggest the need for biopsy or a referral to specialist.[12]

IDENTIFYING BARRIERS TO USE OF DERMOSCOPY IN FAMILY MEDICINE

With dermoscopy being a best practices screening tool for family physicians, and the AAFP's skin conditions curriculum encouraging dermoscopy use, it is unfortunate that only 8% of family physicians are utilizing dermoscopy.[2,15] Barriers cited regarding use of dermoscopy included lack of training and access due to cost.[16]

DEVELOPING A SOLUTION TO OVERCOME BARRIERS

Research has proven that short dermoscopy workshops offered during residency training have a significant impact on how physicians perceive the barrier of lack of training.[15]

Georgia South Family Medicine Residency Program is located in a rural county of southwest Georgia where the median income is below $21,000 and the social determinants of health play a large role in patient access to care.[17] Consequently, it is the authors' belief that prior to having a dermatologist practicing in the area, limited access to advanced dermatological care resulted in delayed diagnosis and treatment of malignant and premalignant skin lesions.

As part of a joint resident and faculty scholarly activity project, a dermatology curriculum was developed to prepare family medicine residents to become competent in identification and differentiation of benign and suspicious/malignant skin lesions and to guide residents in decision making for biopsy, excision or referral of suspicious lesions. Competency is achieved by having a faculty member and an interested resident are tasked with teaching dermoscopy to other faculty members and residents in a 2-hour workshop utilizing materials and other didactic resources provided by dermatologist Elizabeth Seiverling, MD, at Maine Medical Center. Permission to use resources was granted to address the lack of training barrier commonly cited among family medicine physicians.[15]

The workshop required learners to complete a 30-minute timed pre-test in which they attempted to identify photos of various benign and malignant skin lesions.[15] Learners watched a 30-minute video, followed by a 30-minute educational PowerPoint presentation created by Maine Medical Center Dermatology Department on benign and malignant skin conditions. Residents completed a timed 30-minute post-test of the same lesions presented in a different sequence, which assessed improvement in ability to accurately differentiate benign from suspicious lesions.[15] Georgia South family medicine residents (n=9) were surveyed with pre-test scores averaging 59.7% and post-test scores averaging 73.6%. Longitudinal competency was fostered by having learners repeat and review the post-test at a minimum of 8 weeks later. Following the TADA workshop, residents were tasked with using the dermatoscope in clinic when assessing skin lesions and were required to describe features identified on dermoscopy that supported their decision to biopsy, excise, refer or offer supportive reassurance. Three months after the initial workshop, residents were provided an additional post-test, averaging 85.9%, further supporting that competency can be achieved with the dermoscopy workshop.[15]

CONCLUSION

Implementing an efficient, productive and safe dermoscopy curriculum in family medicine residencies supports the important role the osteopathic family physician has in early identification of potentially malignant skin lesions, especially in rural and underserved patient populations. Because dermatologist density is highest in urban areas and lowest in rural medically underserved areas, adding a family medicine dermatology curriculum that includes training and repetitive use of the TADA method of dermoscopy would allow family physicians to help serve as the part of the solution for unequal access to competent medical management of skin cancers in rural and medically underserved communities throughout the country.[16,18]

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