OFP

Osteopathic Family Physician

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

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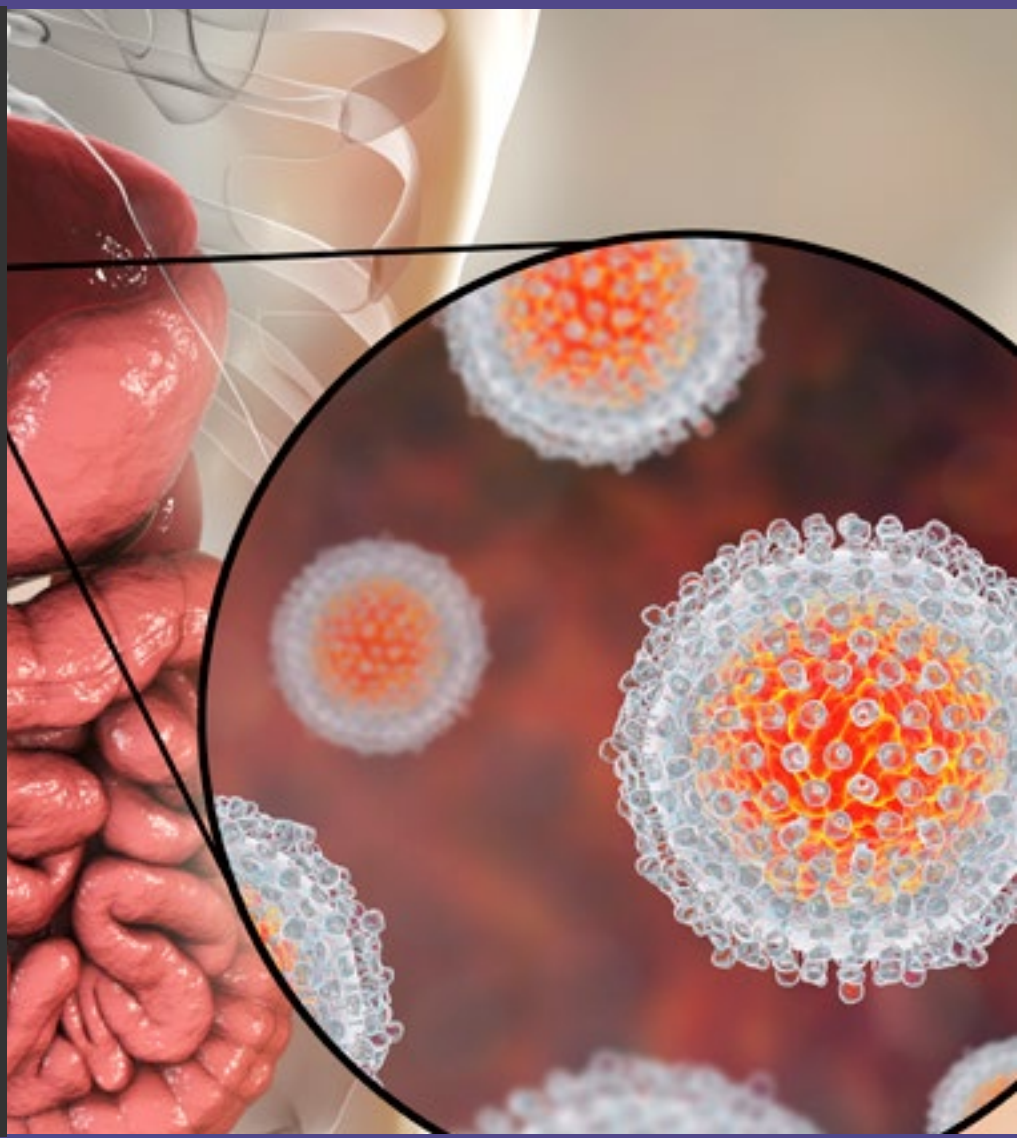

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Official Notice to the ACOFP Membership

Proposed Amendments to the ACOFP Constitution & Bylaws

Draft as of August 28, 2018

CONSTITUTION

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

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

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

The ACOFP Board proposes the following amendments to the Constitution to allow Medical Doctors (MDs) to be Active Members of the ACOFP, as recommended by the 2018 ACOFP Congress of Delegates. Approval of the amendments will be voted on at the ACOFP Congress of Delegates at its March 21, 2019 meeting. If adopted by the ACOFP Congress of Delegates, approval will be sent to the American Osteopathic Association Board of Trustees for approval. (New material in all caps and old material in strike out.)

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

ARTICLE II – MISSION & OBJECTIVES

Section 2

The objectives of the College are:

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

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

ARTICLE IV – MEMBERSHIP

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

ARTICLE VII - BOARD OF GOVERNORS

Section 1.

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

BYLAWS

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

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

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

The ACOFP Board proposes the following amendments to the Bylaws to allow Medical Doctors (MDs) to be Active Members of the ACOFP as recommended by the 2018 ACOFP Congress of Delegates, to create a Student Delegation in the ACOFP Congress of Delegates, and to include the Distinguished Fellow designation in the Bylaws. Approval of the amendments will be voted on at the ACOFP Congress of Delegates at its March 21, 2019 meeting. If adopted by the ACOFP Congress of Delegates, approval will be sent to the American Osteopathic Association Board of Trustees for approval. (New material in all caps and old material in strike out.)

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

ARTICLE III – MEMBERSHIP

Section 1. Qualifications

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

Section 3. Active Members in Good Standing

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

ARTICLE V - CONGRESS OF DELEGATES

Section 1. Composition

A. The ACOFP Executive Director shall provide to the Secretary of each ACOFP affiliate society in writing the number of delegates to which ~~that Society~~ EACH DELEGATION is entitled at least 60 days before the first day of the annual meeting of the Congress of Delegates.

(1) Each affiliate society shall be entitled to at least one voting delegate, who shall be a member in good standing, and shall be entitled to an additional voting delegate for every 25 members thereafter, or the majority fraction thereof, active members, plus one voting delegate from each approved undergraduate chapter located within the geographic boundaries served by the ACOFP affiliate society. IN ADDITION, A SEPARATE STUDENT DELEGATION SHALL BE ENTITLED TO ONE VOTING DELEGATE AND ONE ALTERNATE DELEGATE APPOINTED BY THE PRESIDENT OF THE STUDENT ASSOCIATION OF THE ACOFP FROM WITHIN THE STUDENT RESOLUTIONS COMMITTEE, WITH APPROVAL FROM THE NATIONAL STUDENT EXECUTIVE BOARD.

(4) Each affiliate society shall be entitled to one voting ~~osteopathic~~ family medicine resident delegate who meets the following criteria.

(a) Be currently enrolled and in good standing in an AOA or ACGME residency program in the state which the delegate represents.

(b) Be a member in good standing of the ACOFP affiliate society in the state (if such an affiliate society exists).

(c) Be a member in good standing with ACOFP ~~and AOA~~.

ARTICLE VI - BOARD OF GOVERNORS

Section 2. Composition

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

Section 6. Duties

The duties of the Board of Governors shall be:

I. To approve the granting of the designation "Fellow of the American College of Osteopathic Family Physicians (FACOFP). AND "DISTINGUISHED FELLOW OF THE AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS (FACOFP *dist.*)."

ARTICLE X - DEPARTMENTS & COMMITTEES

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

~~Standing c~~Committee chairs ~~and committee members~~ shall be OSTEOPATHIC PHYSICIANS WHO ARE active members of this College in good standing, or academic or associate members of this College~~.~~, OR ALLOPATHIC PHYSICIANS WHO MEET THESE REQUIREMENTS AND HAVE COMPLETED OSTEOPATHIC FOCUSED EDUCATION AT RESIDENCY PROGRAMS WITH ACGME OSTEOPATHIC RECOGNITION STATUS.

COMMITTEE MEMBERS SHALL BE OSTEOPATHIC OR ALLOPATHIC PHYSICIANS WHO ARE ACTIVE MEMBERS OF THIS COLLEGE IN GOOD STANDING, OR ACADEMIC OR ASSOCIATE MEMBERS OF THIS COLLEGE.

OFFICIAL CALL • 2019 CONGRESS OF DELEGATES OF THE ACOFP

You are hereby notified that the ACOFP Congress of Delegates will convene on March 20 - 21, 2019 at the Sheraton Grand Chicago hotel in Chicago, Illinois.

Credentialing of Delegates and Alternate Delegates will take place on the afternoon of Wednesday, March 20 before the start of Session I, and Session II which will convene on the morning of Thursday, March 21. Each ACOFP Affiliate State Society shall certify the names of its Delegates and Alternate Delegates to the ACOFP Executive Director by February 15, 2019.

Any reports, resolutions, or other business for this meeting should be submitted by February 15 to Annie DeVries at annied@acofp.org so that they can be posted on the ACOFP website and available to Delegates to review in advance.

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

Rocky Mountain OPTI/Sky Ridge Medical Center

Neuromusculoskeletal Medicine + 1 Residency

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

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

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

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

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

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

John Martin Littlejohn, DO

Guide for...

READERS

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mc04.manuscriptcentral.com/ofp.

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EXAM SCHEDULE

CERTIFICATION & OCC (RECERTIFICATION)

AOBFP EST. 1972

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

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

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American College of Osteopathic Family Physicians

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William Carey University College of Osteopathic Medicine

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Osteopathic Family Physician
JOURNAL

2019 CALL FOR PAPERS

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

RESERVE A TOPIC

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

CLINICAL IMAGES

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

REVIEW ARTICLE TOPICS

- ADHD Management in Primary Care: with osteopathic component
- Disorders of Puberty: An Approach to Diagnosis and Management with an osteopathic component
- Chronic Kidney Disease: Detection and Evaluation with an osteopathic component
- Direct Primary Care: Emerging Practice Alternative with an osteopathic component
- Diagnosis and Management of Non-Melanoma Skin Cancer with an osteopathic component
- Update on Office-Based Strategies for the Management of Obesity with an osteopathic component

RESEARCH TOPICS

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

The content should include the following:

Abstract
Introduction
Methods
Results
Discussion
Conclusions
Acknowledgments

Ronald Januchowski, DO, FACOFP
Editor-in-Chief

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

acofp AMERICAN COLLEGE OF OSTEOPATHIC FAMILY PHYSICIANS

EDITOR'S MESSAGE

Our 2019 Journey Begins

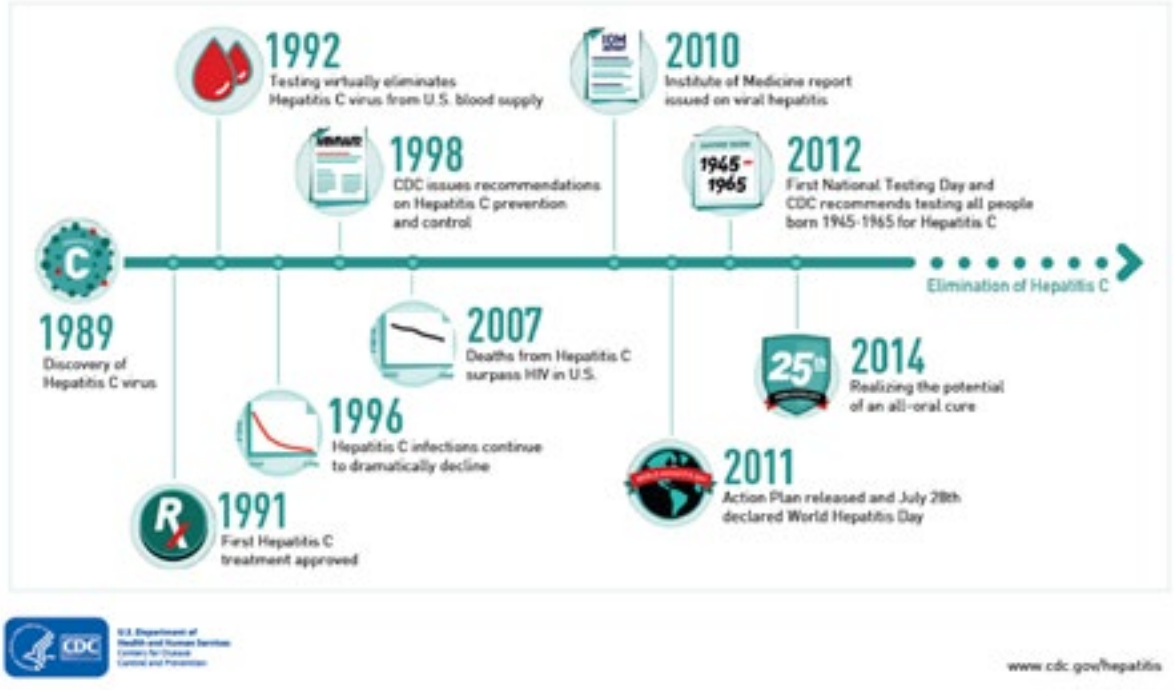
Ronald Januchowski, DO, FACOFP, Editor, Osteopathic Family Physician

Happy New Year and welcome to 2019! I hope your year is starting well and thanks for reading our first issue of the year. This issue contains excellent articles of value for the practicing physician. The lead article on Hepatitis C provides a review of a chronic disease process that has undergone an incredible journey from the discovery of the causative agent a mere 30 years ago in 1989 to now being one of the few curable chronic diseases in humans. Third in the hepatitis virus discovery process (behind Hepatitis B in 1967 and Hepatitis A in 1973), the medical progress associated with this virus can be seen as a shining star in the medical scientific community. This bench work scientific progress has directly translated to *Osteopathic Family Physicians* being able to provide improved care to patients. This is one disease that many practicing physicians can pull out the phrase "when I was in medical school..." referring to the strides taken in diagnosis and treatment.

Related to the lead article, *Chronic Abdominal Pain: Tips for the Primary Care Provider* addresses the wide differential diagnoses seen with this common patient presentation. The additional two review articles address common dermatologic concerns seen in the office. While MRSA is always a worry when seeing a patient with a skin infection, the *Skin and Soft Tissues* article reviews other diagnoses that may be seen. *Treat the Whole Not Just the Whole: Holistic Wound Care Approach* provides information on care of more complex skin infections.

Thanks for reading and have a wonderful, prosperous 2019!

Hepatitis C: 30 Years Since Discovery



LETTER TO EDITOR

Six Generations: Physicians Need to Realize What is Valuable Before it is Lost

To the Editor:

"*Hi, Doctor Kamajian! I finally got health insurance that I can use to come to see you with my son.*"

I looked at the chart and realized it had been three years since I had seen her very familiar face. So, before the exam, we chatted and got reacquainted. It is remarkable what family doctors remember about their patients. This is not an unusual conversation.

Patient: *I have a new job. I took three years off to take care of my son.*

Dr. Kamajian: *So you aren't working at the pet store anymore?*

Patient: *Oh no, I left that after he was born. You know my grandmother died...she loved sharing her music with you.*

Dr. Kamajian: *How many years ago was that....three already?*

And so the conversation goes. We talked about her mom, her grandparents, her great-grandparents, and her two older children. I have been the doctor for all six generations.

"*You know,*" she says, "*My son is only five, but he is writing poetry too, just like my great-grandmother.*"

I excuse myself and walk out of the room and come back with an autographed book of poems written by her great-grandmother (who was born in 1890). Her great-grandmother's message to me on the inside flap of her book of poems simply read, "*To the doctor who keeps my hands and mind still able to write poems.*"

My patient looks at the book of poems and tears up. "*You know I was only four when she died. I can still remember how she looked and her voice. I wish I had gotten to know her better. I knew she wrote but have never seen any of her poems. What can you tell me about my great-grandmother and great-grandfather?*" So I tell her a story her great-grandmother had told me about attending live theater in London before World War II. I can still remember her great-grandmother saying "*anyone could afford live theater even during the depression. London has changed so much.*" Her great-grandmother had died in 1994. She would have been shocked at the London of today we both commented. I gave her the book of poetry and she asked, "*When I come back the next time I will bring all of my children. Please tell us stories about both of my great-grandparents.*" Oh, the stories I could tell, but that would be breaking the doctor-patient relationship, even this many years later.

My patient asked, "*What story can you tell me about my grandparents?*" I told her the story of how after he retired her grandfather finally took oil painting classes and said to me "*I wish I had never been a businessman. I was a success, but I always wanted to be an artist.*" The last years of his life he painted like a madman, trying to put on canvas all that he had wanted to express his entire life. I asked her, do you have any of his artwork? She said, "*No, my aunt and cousins tossed everything after he died. The house was full of paintings and no one wanted them.*" I told her I would bring one of his paintings of a storm at sea from my home and give it to her when she comes in next time.

Over 10 minutes had passed before I started taking her medical history and doing a physical exam. I helped her with her current issues and we went to the reception area together. There she introduced me to her husband and five-year-old son. The other children were at their first day of school.

So, it goes in an osteopathic family physician's office. With time, you become part of the community's memory. You know the families. Sometimes better than even they remember. You have heard the dreams and the fears. You have taken the time to look into their eyes and listen to their voices and know like your mother knew when she looked at you when things were different - when things were not right. You have helped when people were sick of course, but you have also helped when they were down and out financially, and emotionally. You have comforted the dying and heard their last thoughts and prayers and their last fears and seen their last moment of joy.

Who are we that we have been so blessed? We are the lucky ones that got into medical school. So many of our classmates applied and never got into medical school. Now and again, I run into them. Read about them in my college alumni book. Hear about their lives. Many have earned more and have not had the sleepless nights, the stress, and the losses that an osteopathic family doctor experiences. None have had a young person walk into their office and heard the question, "Tell me more about my great-grandparents." We have had the opportunity to practice the art of medicine.

I see this beautiful profession from the long view of forty years. I listen to my students. I watch their heads buried in the EMR, rarely if ever looking up at the person who is talking to them. I see how they are rewarded by the prompts of the EMR and by the managers who manage everything. I hear the anger of physicians and know the ever-increasing significance of burn out. I know what happens when we all become employees and are told we have 15 minutes not only to see the patient but do the electronic charting or you have to finish the charts at home. I know what it feels like to have been converted from family physician to clerk typist.

Students tell me, "*I won't be shamed into feeling bad that I don't know anything about the patient other than why they came to see the doctor. I will not be shamed into feeling bad about not knowing what*

the patient looks like. I won't be shamed into feeling like I am missing something by letting a hospitalist see the patient. Continuity of care means only being able to access the EMR and read what was done. I won't be shamed when I never take a call on nights or weekends and sign out to a telemedicine corporation and the nurses at the clinic in the pharmacy down the street."

It is a shame however that they are missing so much. Will this model improve the health of the patient? Will this improve the health of the doctors? Will this improve the family life of the physicians? Will this decrease burn out?

The science is in. Burn out rates are dramatically higher with this model. What is the doctor missing that all of these changes were supposed to improve? The doctor is losing the doctor-patient relationship and has replaced it with the doctor-computer and doctor-corporation relationships. I do not think that forty years from now my younger collogues will be sharing poems and paintings and family stories when a patient walks into the room. Unless we all see what is valuable before it is lost. If we do not, we will then find ourselves like this patient's grandfather, at the end of our lives trying to do art when we have missed our forty-year opportunity to do the art of medicine.

Steven Kamajian

Steven Kamajian, DO, CMD, FACOFP

Chief Medical Officer, Westminster Free Clinic

FROM THE PRESIDENT'S DESK

Fond Memories & New Beginnings

Duane G. Koehler, DO, FACOFP *dist*.
2018 - 2019 ACOFP President

Along with the ACOFP Board of Governors and Past Presidents, I would like to recognize the important work and years of dedication of our recently-retired Executive Director, Peter Schmelzer, MBA, CAE. Pete's accomplishments include winning the American Osteopathic Association's Bob E. Jones, CAE Executive Director Award and Association Forum's John C. Thiel Distinguished Service Award in the Association Professional Category.

Pete has made a positive, lasting impression on the College and will be missed by all. He holds a special place in the hearts and minds of ACOFP Past Presidents and Board members, who enjoyed Pete's unwavering support over the years. The group wanted to join in wishing Pete a happy and healthy retirement by sharing fond memories and kind words of appreciation.

Pete has been the heart and soul of ACOFP for 18 years. His dedication and diligence kept our organization strong. He believed in our profession, our goals and our vision. Thanks Pete for all the help and dedication.

~ Robert C. DeLuca, DO, FACOFP dist.

I have always found Mr. Peter Schmelzer to be a very dependable leader as well as a talented writer who put others before himself and promoted excellence within the ACOFP Membership, the Board and the ACOFP President.

~ Paul A. Martin, DO, FACOFP dist.

Words cannot say 'thank you' enough! The support I received from Pete allowed me to serve the ACOFP to my best. Wishing Pete happiness and success in future adventures.

~ Carol L. Henwood, DO, FACOFP dist.

We have more stories than anyone wants to hear. One encounter stands out when Pete amazed us by showing his love of Tasty Kakes!

~ Kieran P. Knapp, DO, FACOFP dist.

I want to thank Peter for welcoming us into the ACOFP family. He is so nice and goes out of his way to put others at ease. He will be missed.

~ Gautam J. Desai, DO, FACOFP

Pete has always been a prepared and outstanding leader for our College. He has the answers to both big and small questions. No project has ever been too big or small for Pete!

~ Ronna D. New, DO, FACOFP

Pete is one of the most truly caring people I know, the best cat (board) herder in the business, and a trusted friend and advisor. Plus, I never had trouble finding Pete in a crowd.

~ Kevin V. de Regnier, DO, FACOFP dist.

I had an excellent working relationship with Peter Schmeltzer. Peter is a strategically focused and goal-oriented administrative leader.

~ George T. Sawabini, DO, FACOFP dist.

Pete is loyal and supportive of his colleagues and co-workers. He has mentored and supported them through thick and thin. Pete is one of the best men I have had the pleasure to know. I appreciate him for who he is more than what he has done, and to say that I love him like a brother would not be an exaggeration.

~ Ronnie B. Martin, DO, FACOFP dist.

As a friend, I valued Pete's wise counsel. He has wonderful ethics that we all appreciated and tried to emulate. He was a mentor who provided us with good judgment, positivity, stability and guidance.

~ Steven F. Rubin, DO, FACOFP dist.

Working with Pete on the ACOFP Board was a blessing and a joy – his guidance, leadership and assistance with my concerns created many memorable moments.

~ Jan D. Zieren, DO, FACOFP dist.

Pete was always there, even if in the background. His devotion to the ACOFP was always evident. He deserves special kudos for hosting our Chinese friends through working with the nternational Primary Care Educational Alliance. Pete never found a need that he could not meet.

~ Royce K. Keilers, DO, FACOFP dist.

Pete's known for his famous Indianapolis meeting once a year with the racing set and due to his height, such comments as, "how is the atmosphere up there?" and "do you shake with earthquakes?" All of which he has heard many times.

~Martin J. Porcelli, DO, PhD, MHPE, FACOFP

Pete always kept a level head, in public, and was always there for anyone who needed him.

~ Kenneth A. Heiles, DO, FACOFP dist.

Peter was respected and admired by his staff who were inspired to go that extra mile when needed. We all shined a little brighter in front of our membership and other organizations because of Peter's leadership. We are all proud to say we served with him at ACOFP. Thank you, Pete, for a great ride.

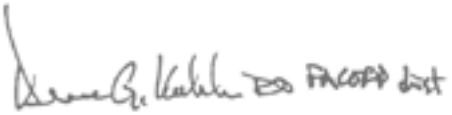
~ Thomas N. Told, DO, FACOFP dist.

Pete has done an amazing job of guiding the actions of the Board, of offering counsel to Presidents and even shared his victory dance when the Cubs won the World Series. Thanks for securing the foundation of the ACOFP. Wishing the best for you in retirement.

~ Duane G. Koehler, DO, FACOFP dist.

As we ring in the new year, we look forward to exciting things to come with our new Executive Director, Bob Moore, MA, CAE. Moore brings the outstanding experience and knowledge that can successfully guide ACOFP through a changing landscape while ensuring that it remains a leading voice for osteopathic family medicine nationwide.

Happy New Year to all!



Duane G. Koehler, DO, FACOFP *dist*.
2018 - 2019 ACOFP President

REVIEW ARTICLE

Hepatitis C – Screening, Diagnosis, Management & Treatment

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KEYWORDS:

Disease Prevention and Wellness

Hepatitis C

Infectious Disease

Jaundice

Transaminitis

Abstract: Hepatitis C virus (HCV) infection is a major cause of chronic liver disease, hepatocellular carcinoma and cirrhosis with at least 185 million people infected worldwide, causing 399,000 deaths annually. HCV is transmitted through blood or body fluids. Transmission most commonly occurs through sharing of injection drug, occupational exposure through needlestick injuries in healthcare settings, and birth to an HCV infected mother. There are seven known genotypes of HCV, 1a, 1b, 2, 3, 4, 5, and 6, with the most common genotypes in the U.S. being 1a, 1b, 2, and 3, which comprise approximately 97% of all U.S. HCV infections. Risks for disease progression include baseline liver histology, age, ethnicity, gender, alcohol use, comorbidities and immune response. There are multiple screening recommendations currently in place, some of which are based on risk factors, with others based on legislation. The screening test of choice is the anti-Hepatitis C virus antibody, with a confirmatory HCV RNA PCR with genotyping. Once the diagnosis is made, assessing the level of fibrosis and/or cirrhosis is an important step in determining the pathway to treatment. There are multiple new options for treatment with improved efficacy and less side effects. Patient being treated for HCV should be monitored and assessed for compliance with therapy and adverse effects, including new or worsening psychiatric illness and screened for alcohol and substance abuse. Several studies have shown the long-term outcomes with the above treatments reducing morbidity and mortality. A summary of key clinical recommendations can be found in *Table 1*.

INTRODUCTION AND BACKGROUND

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease, hepatocellular carcinoma and cirrhosis worldwide.[1] The World Health Organization reports that there are at least 185 million persons worldwide with the infection, causing 399,000 deaths annually.[1] In 2014, the Center for Disease Control reported 20,000 deaths in which HCV infection was a factor in the US.[2] Globally, 71 million people have chronic HCV infection, while in the United States, an estimated 2.7-3.9 million individuals are chronically infected with HCV.[2] In 2015, there were an estimated 34,000 new HCV infections in the US, a 2.9-fold increase from 2010.[2]

The burden of HCV infection in the United States is expected to increase as the large number of individuals infected in the 1960's and 1970's are tested due to new guidelines and legislation.[3] The CDC also predicts an increased burden in younger populations with the current opioid epidemic.[2] In 2013, the total cost of HCV infection in the United States was estimated at $6.5 billion.[4] Chronic HCV infection leads to significantly more lost days of work, decreased productivity, and increased health care costs.[5] Chronic HCV infection is also the leading indication for liver transplant in the US.[2]

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PATHOPHYSIOLOGY

There are seven known genotypes of HCV, 1a, 1b, 2, 3, 4, 5, and 6. The most common genotypes in the United States, comprising approximately 97% of all US HCV infections, are 1a, 1b, 2, and 3.6 The mechanism of hepatocyte damage induced by HCV infection is not completely understood but may involve direct cell injury and a local immune-mediated mechanism that causes a chronic inflammatory state.[7,8] Acute HCV infection progresses to chronic infection (detectable virus after 6 months) in 75% to 85% of cases and clears spontaneously in 15% to 25% of patients.[2] Of those originally infected, 60-70% will develop chronic liver disease (stable chronic infection and/or development of hepatic fibrosis), 5-20% will develop cirrhosis over a period of 20-30 years, 1-5% will die of a HCV infection-related complication and 1-3% will develop hepatocellular carcinoma.[2]

RISKS FOR DISEASE PROGRESSION

Risks for disease progression include abnormal baseline liver histology, age, ethnicity, gender, alcohol use, comorbidities and cellular immune response. Patients with HIV, Hepatitis B, diabetes[13], obesity[14] and Vitamin D deficiency (<10ng/ml)[15] are associated with faster progression to fibrosis. Male gender and HCV infection after age 40-55 are also associated with faster progression to fibrosis.[10, 11] Patients with less inflammation and less hepatic fat on histology or by non-invasive evaluation are at lower risk for progression to cirrhosis.[9] Progression in African American patients appears to be slower.[12]

TABLE 1:

Summary of key clinical recommendations

RECOMMENDATION	EVIDENCE RATING	REFERENCES
Patients at high risk for acquisition of HCV should be screened periodically, and those born between 1945-1965 should be screened once.	B	16, 18
Initial screening should be performed with qualitative HCV antibody test	C	1, 18
Confirmation of positive screen should be performed with quantitative HCV RNA viral load by PCR with genotyping prior to starting treatment	A	1, 16
All patients with chronic HCV infection being evaluated for treatment should be assessed for degree of fibrosis and cirrhosis	C	1, 16
All patients with chronic HCV infection should be considered for treatment based on genotype, degree of fibrosis, prior treatment, comorbidities and potential adverse effects.	C	1, 16
All patients undergoing treatment should be screened for alcohol use, illicit drug use and new/worsening psychiatric disorders at every visit	C	1, 16
Immunization for Hepatitis A and B is recommended for susceptible patients with HCV infection	C	16

MODES OF TRANSMISSION & RISK FACTORS FOR TRANSMISSION

HCV is a blood borne virus and predominantly transmitted through blood or body fluids.[1,16] It is most commonly transmitted through sharing of injection equipment associated with injection drug abuse, needlestick injuries in the healthcare setting, and birth to an HCV infected mother.[2] In the US, transmission via blood, blood products or organ transplantation was once the most common mode of transmission, however, with the onset of blood screening in 1992, this is now exceptionally rare.[2] The CDC reports that the chances of HCV infection through blood products is now less than 1 per 2 million units transfused. Other less efficient modes of transmission include sex with an HCV infected partner and sharing of personal effects (razors, toothbrushes, etc.). However, sexual practices where there is a chance of blood-to-blood contact increase the possibility of transmission.[17]

Intravenous drug use is the most important risk factor for HCV infection, accounting for approximately 60% of acute infections in the United States.6 Recent surveys by the CDC revealed that approximately 33% of those with history of IVDA age 18-30 are infected and 70-80% of older individuals with history of IVDA are infected.[2] A summary of risk factors is shown in *Table 2*.

TABLE 2:

Summary of risk factors for transmission of Hepatitis C

Higher Risk of Transmission	Lower Risk of Transmission
• IV Drug Abuse • Blood transfusion before 1992	• Birth to a HCV + mother • History of chronic hemodialysis • History of needlestick or mucosal exposure • Incarceration • HIV+ men who have sex with men • Organ transplant prior to 1992 • Persistently elevated ALT • Recipient of clotting factor concentrate before 1987 • Sex with a HCV+ partner • Sexual contact where blood/ blood contact may occur • History of intranasal illicit drug use • Tattoos from an unregulated establishment

SYMPTOMS & TIMING OF INFECTION

Symptoms will vary between patients and typically only occur in acute infections. Most are not likely to prompt a medical visit as they can be mild, vague and are typically self-limited. Another consideration is that a large number of patients now acquiring acute Hepatitis C are IV drug users and symptoms can mimic opiate withdrawal. Patients in this population are frequently uninsured or underinsured, which is another barrier to presentation for care. Distrust of the medical profession can also exist in these patients. Symptoms include fever, fatigue, dark urine, clay-colored stool, abdominal pain, loss of appetite, nausea, vomiting, joint pain and jaundice.[2] Approximately 20-30% will have experienced fatigue, abdominal pain, loss of appetite or jaundice. The range in which patients experience symptoms from time of infection is 2-24 weeks; however, most symptoms occur between 4-12 weeks of infection.[2] Because of the nature of these symptoms, the fact that they can mimic other more common diseases like gastroenteritis, influenza, etc., it is difficult to diagnose acute Hepatitis C.

SCREENING

Screening has long been a standard with blood product donation and collection since its implementation in 1992, however, routine screening in other healthcare settings has undergone recent changes. Recommendations from several professional organizations and governing bodies are below.

The CDC recommends screening for people born between 1945-1965, anyone who has ever injected illegal drugs (even if it is only once), recipients of clotting factor concentrates made before 1987, recipients of blood or organ transplants before 1992, patients who have ever received long term hemodialysis, patients with known exposures to HCV, all patients with HIV infection, patients with signs of symptoms of liver disease and children born to HCV positive mothers.[2] The CDC notes routine testing is of uncertain need in recipients of certain tissues (corneal, musculoskeletal, skin, ova or sperm), non-injecting illegal drug users, those with tattoo or body piercing, persons with history of multiple sexual partners or sexually transmitted infections, or long term steady sex partners of HCV positive persons.[2] The CDC recommends against routine testing in the following populations when they are without risk factors: Healthcare care, emergency medical and public safety workers, pregnant women, household (nonsexual) contacts of HCV positive patients, and the general population.[2]

The USPSTF recommends screening patients at high risk (those with any risk factors in table above) and also those born from 1945-1965. This grade B recommendation was published in 2013 and the USPSTF is currently in the process of updating this recommendation.[18]

Some states have passed laws surrounding screening for Hepatitis C. The Commonwealth of Pennsylvania passed a law in 2016 requiring any individual born between the years of 1945 and 1965 who receives health services as an inpatient or who received primary care services in an outpatient setting be offered a Hepatitis C screening test or Hepatitis C diagnostic test.[19] Other states including Connecticut, Massachusetts and New York have similar screening laws for patients in that population.

Pregnant women are a special population that requires more discussion. Without risk factors, screening is not recommended, however in certain geographic locations, especially those with high incidence of Hepatitis C, more consideration may be necessary. The CDC reported that rates of HCV infection in women of childbearing age (15-44) increased 22%, and hepatitis C testing of children age <2 increased 14%.[2] Overall births to mothers with HCV infection rose from 0.19% to 0.32% based on 2014 data. Vertical transmission to infants born to HCV-positive mothers is between 5-6%. Although these numbers are very low, screening based on individual patient history is important and should not be ignored.[20] Ultimately, having a high index of suspicion and screening patients who participate in behaviors placing them at high risk for Hepatitis C is essential. This applies to both pregnant and non-pregnant patients. Data from the National Notifiable Diseases Surveillance System compiled in a study in the Annals of Internal Medicine reported an increase in HCV infection of reproductive age women from 16,000 in 2006 to 31,000 in 2014.[21]

DIAGNOSIS

The screening test of choice is the anti-Hepatitis C antibody (sensitivity of 95%, specificity of 99%, positive likelihood ratio of 95, and negative likelihood ratio of 0.05).[16] It can detect the antibody 4-10 weeks after exposure and detect >97% of cases by 10 weeks after exposure.[2] If the result is positive, then confirmatory testing should be pursued with a Hepatitis C RNA viral load by PCR with a genotype. HCV RNA can be detected 2-3 weeks after initial infection. If the result is negative and there is significant suspicion for exposure within the previous 6 months, HCV RNA should be ordered every 4-8 weeks, or repeat antibody testing can be performed at 12 weeks. If the HCV antibody is positive, but the HCV RNA is negative, the patient is considered to not have HCV infection.[17]

In patients with a positive HCV RNA test, but negative anti-Hepatitis C antibody, an acute infection is diagnosed. Treatment is not recommended for patients with an acute infection, however the HCV RNA viral load should be monitored for 6 months to evaluate for spontaneous clearance.[17] The process of screening and potential outcomes are demonstrated in *Figure 1*.

ASSESSMENT

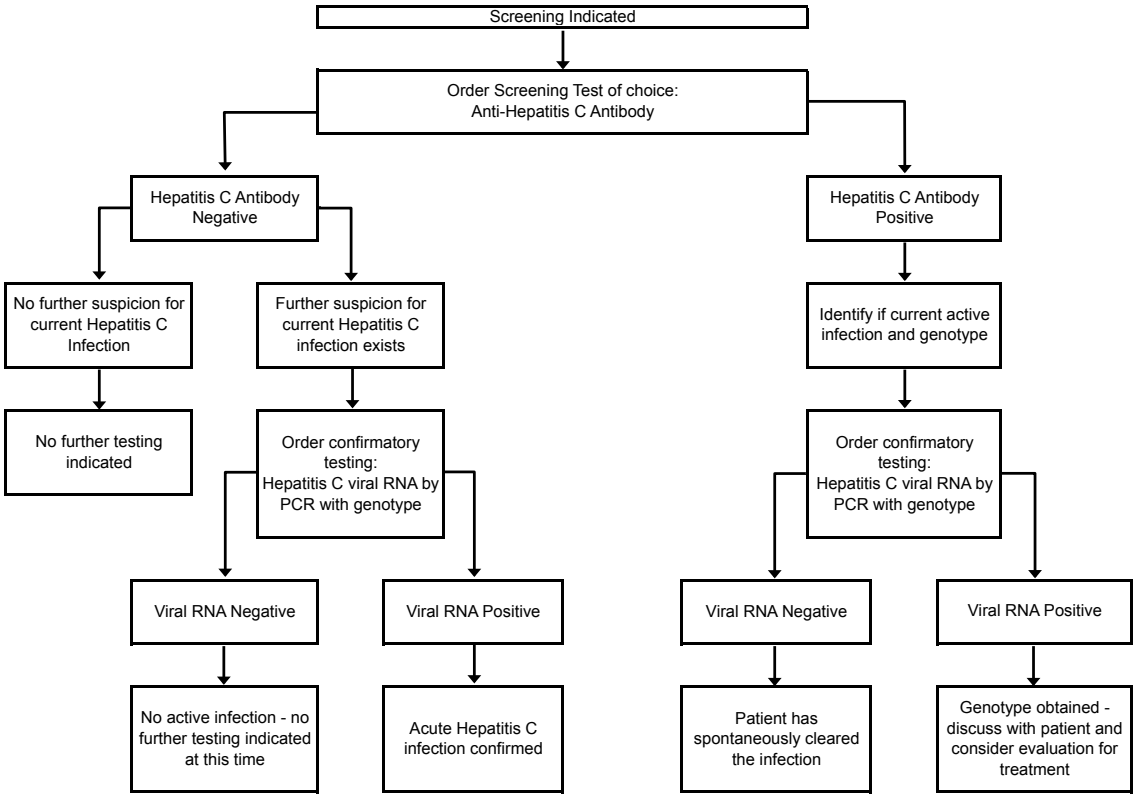
Once the diagnosis is made, assessing the level of fibrosis and/or cirrhosis is an important step in determining the pathway to treatment. The preferred method is a liver biopsy, however biomarkers can be an acceptable alternative. There are a number of different biomarkers, including several cytokines, collagens, collagenases, etc. that mirror the breakdown of hepatic extracellular matrix. These can be used in certain combinations to predict progression, however they are not widely available and there is a paucity of confirmatory and comparison studies. Because of the rapid growth of new developments in biomedicine and biotechnology, biomarkers provide interesting future options once studies are done to determine their effectiveness in predicting hepatic damage.[50] The recommendations for grading and treatment are based on the Metavir scoring system, which scores fibrosis from 0-4 points, and recommends pursuing treatment based on a score of 2 or greater.[16] Scores are assigned as follows: 0 for no cirrhosis, 1 for minimal scarring, 2 for scarring beyond areas containing blood vessels, 3 for bridging fibrosis with connections to other areas of fibrosis and 4 for cirrhosis or advanced scarring.[16] These patients should also be assessed for Hepatitis B, HIV and other conditions that can cause more rapid fibrosis as mentioned in the section entitled “risk factors for disease progression” above. Patients with HCV infection should also be immunized for Hepatitis A and B if not already fully vaccinated and have no history of infection.[16]

TREATMENT

All patients with chronic HCV infection should be considered for treatment based on genotype, degree of fibrosis, prior treatment, comorbidities and potential adverse effects.[17] The goal of treatment is to reduce all cause mortality and hepatic-associated complications. Success of treatment is evaluated by repeat measurement of HCV RNA. A sustained viral response (SVR) is defined as absence of HCV RNA on PCR testing 24 weeks after

FIGURE 1:

The process of screening and potential outcomes



completion of treatment and is associated with a 99% chance to be HCV negative in long term follow up. Factors contributing to higher rates of SVR include patients younger than 40-45,[22] genotypes 2 and 323, lower viral load[22], being treated with a statin[2,4] and African American race.[22] Factors contributing to lower rates of SVR include advanced fibrosis[22] and concurrent diabetes mellitus.[25] It should be noted that some of these align with the risk factors for disease progression, as African American patients and those diagnosed before age 40 have slower rates of progression and higher rates of SVR. In contrast patients with diabetes and other comorbidities have faster rates of progression and lower rates of SVR.

Treatment candidates include those who are 18 years of age or older, are able and willing to adhere to treatment, have elevated AST and ALT levels and have a Metavir score of 2 or more.[16] Treatment has traditionally been managed by specialists, however, new studies are showing that treatment success rates are similar between specialists and adequately trained primary care providers. A study published in the Annals of Internal Medicine in 2017 enrolled 600 patients and had them follow with a specialist, PCP or nurse practitioner.[26] All providers underwent the same 3 hour HCV training program. SVR overall were 85-90% and similar among all provider groups, with follow up being greatest with the PCPs (63%) and NPs (74%) compared to the specialists (56%).[26] Adverse events were similar among all groups and consistent with previous safety trials. This study suggests that HCV treatment can safely and effectively provided by appropriately trained primary care physicians and that the patients are more likely to complete follow up.

Interferon and Ribavirin were long-time mainstays of treatment, however had significant associated complications. Ribavirin has a black box warning for hemolytic anemia, can worsen cardiac disease, and has significant teratogenic effects.[47,48] The teratogenic effects are so serious that women taking the drug and who were partners of men taking the drug were required to have 2 forms of reliable contraception. Interferon caused serious adverse effects including development of life threatening neuropsychiatric, autoimmune, ischemic and infectious disorders.[49]

However, new direct acting antiviral medications, ledipasvir, sofosbuvir, glecaprivir, pibrentasvir, velpatisvir, and voxilaprivir have been approved for the treatment of Hepatitis C. These new agents are used in combination with one another and are all oral agents. They have excellent cure rates, lower side effect profiles and increased ease of use. However, there is significant cost associated with these newer regimens. As these medications are oral tablets and are taken daily, compliance is much easier to attain. In addition, side effect profiles are significantly better than previous medications, as the major side effects are nausea, headache and fatigue. Once the medication is prescribed, the patient takes it daily as prescribed and follows up for monitoring as below. A comprehensive list of approved medication combination pills as of January 2018 is shown in *Table 3*. A summary of the most common side effects of these medications is found in *Table 4*.

TABLE 3:

Approved medication combination pills as of January 2018

MEDICATION & ADMINISTRATION	GENOTYPE	PATIENT SELECTION & TREATMENT LENGTH	SUSTAINED VIRAL RESPONSE (SVR)	ESTIMATED COST
Ledipasvir-sofosbuvir (1 oral tab daily)	1	TNP[27,28,29] : 8 weeks if viral load <6 million and no cirrhosis, 12 weeks if viral load > 6 million and/or cirrhosis TEP[30]: 12 weeks	>95% 95%	**$37,800 per 4 weeks**
	4	TNP, TEP[41,42]: 12 weeks	95%	
	5	TNP, TEP[42]: 12 weeks	95% (N=41)	
	6	TNP, TEP[42]: 12 weeks	96% (N=25)	
Sofosbuvir-Velpatasvir (1 oral tab daily)	1	TNP[31,32,33]: 12 weeks regardless of cirrhosis TEP[31,32,33]: 12 weeks regardless of cirrhosis	98-99% 98-99%	**$29,900 per 4 weeks**
	2	TNP[31,36]: 12 weeks regardless of cirrhosis TEP[31,36]: 12 weeks regardless of cirrhosis	98-99% 97%	
	3	TNP[31,36]: 12 weeks regardless of cirrhosis TEP[31,36]: 12 weeks regardless of cirrhosis	98% (93% if cirrhosis) 91% (89% if cirrhosis)	
	4	TNP, TEP[31]: 12 weeks regardless of cirrhosis	100% (N=116)	
	5	TNP, TEP[31]: 12 weeks regardless of cirrhosis	97% (N=35)	
	6	TNP, TEP[31]: 12 weeks regardless of cirrhosis	100% (N=41)	
Glecaprevir-pibrentasvir (3 oral tabs once daily)	1	TNP[34,35]: 8 weeks without cirrhosis, 12 weeks with cirrhosis TEP[34,35]: same as TNP	99% 99%	**$15,840 per 4 weeks**
	2	TNP[34,37,38]: 8 weeks without cirrhosis, 12 weeks with cirrhosis TEP[34,37,38]: same as TNP	98% Limited Data	
	3	TNP[39]: 8 weeks without cirrhosis, 12 weeks with cirrhosis TEP[40]: regardless of cirrhosis	95% 98% 96%	
	4	TNP, TEP[34,37]: 8 weeks without cirrhosis, 12 weeks with cirrhosis	93% (N=46) 99% (N=16)	
	5	TNP, TEP[34,37]: 8 weeks without cirrhosis, 12 weeks with cirrhosis	93% (N=27 total) 99%	
	6	TNP, TEP[34,37]: 8 weeks without cirrhosis, 12 weeks with cirrhosis	100% (N=30 total) 100%	
Sofosbuvir-velpatasivr-voxilaprevir (1 tab daily)	1-6	TEP with previous failure[43]: 12 weeks	98%	**$29000 per 4 weeks**

MONITORING & FOLLOW UP

Patients being treated for HCV should be monitored and assessed for compliance with therapy and adverse effects, including new or worsening psychiatric illness, and screened for alcohol and substance abuse at every visit.[1,16] CBC, CMP, HIV, Hepatitis B status and pregnancy test (when appropriate) should be monitored initially and at week 4. HCV RNA viral load is recommended at week 4 of treatment and also at 12 and 24 weeks after treatment.[17] Patients with resolved or inactive Hepatitis B are at risk for reactivation during treatment, which also requires consideration for screening/monitoring. Some experts have suggested monitoring HBV DNA levels during treatment, as increases in HBV DNA are the most likely finding of reactivation. If this were indicated, monitoring at weeks 4, 12, and 24 with other lab work would be reasonable. The risk of Hepatitis B reactivation and treatment should be discussed with patients on an individual basis.[44]

LONG TERM OUTCOMES

Several studies have shown the long term outcomes with treatments discussed above are reducing morbidity and mortality. A prospective study published in *Gastroenterology* followed 1323 patients with cirrhosis for complications after treatment, which included direct antivirals as they became available and also previous interferon therapy. 5 year survival was 88.6%, with 50.5% achieving SVR. Achieving SVR lowered mortality (HR 0.27), lowered hepatic decompensation (HR 0.26) and lowered rates of hepatocellular carcinoma (HR 0.29).[45]

Another study examining over 3004 patients from multiple countries, using phase 3 clinical trial data has shown that only 12 out of 3004 patients had detectable levels of HCV RNA at 24 weeks, after having SVR at 12 weeks. Seven were found to be a result of reinfection, with only 5 being the result of relapse (medication failure). This data shows that if SVR is achieved with the direct-acting antivirals, long term SVR is very likely to be achieved without relapse.[46]

AUTHOR DISCLOSURES:
No relevant financial affiliations

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TABLE 4:

A summary of the most common side effects

	ADVERSE REACTIONS	CONTRAINDICATIONS
All Medications	Headache (11-31%) Fatigue (10-18%) Nausea (6-13%)	
Ledipasvir-Sofosbuvir	Weakness (11-31%) Myalgia (9%)	None
Sofosbuvir-Velpatasvir	Increased Lipase (>3x Upper Limit of Normal) (5-7%)	None
Glecaprevir-Pibrentasvir	Diarrhea (7%)	Coadministration of rifampin or atazanavir in Child's-Pugh Class C liver disease
Sofosbuvir-Velpatasvir-Voxilaprevir	Diarrhea (14%) Weakness (5%) Increased bilirubin (4-13%)	Coadministration of rifampin

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REVIEW ARTICLE

Chronic Abdominal Pain: Tips for the Primary Care Provider

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Osteopathic Manipulative Medicine

ABSTRACT: Chronic abdominal pain (CAP) has become a common diagnosis in the primary care setting. It is characterized by intermittent abdominal pain lasting for at least six months. The list of causes in the differential diagnosis is extensive. The costs associated with diagnostic workup is a expensive burden to healthcare. Management of CAP is determined by the etiology. This manuscript reviews the causes of CAP, diagnostic workup, osteopathic considerations, special populations experiencing CAP, and management.

INTRODUCTION

Chronic abdominal pain (CAP) is defined as a continuous or intermittent abdominal discomfort lasting for at least six months.[1, 2, 3] CAP is common in the primary care setting and is caused by a variety of abnormalities ranging from organic to functional. Managing CAP can be challenging, due to a broad differential diagnosis and sometimes extensive and negative workup.[2] This condition is commonly associated with significant healthcare costs, largely because it is so often misdiagnosed and many primary care practitioners are unfamiliar with how to approach diagnosis in a cost effective manner.[4] Patients complaining of CAP may present with long standing symptoms or an exacerbation of an already existing problem. Evaluation of CAP requires detailed history taking, awareness of alarm symptoms, thorough physical exam and its correlation to pattern recognition for a variety of diseases, psychosocial assessment consideration, and diagnostic investigation.[5] This initial evaluation approach will aid the primary care physician's ability to narrow down the differential diagnoses and drive further diagnostic testing when appropriate. Management of CAP includes, lifestyle modifications, discontinuation of offending agents, medical management, injections, osteopathic techniques, and referral to a specialist if surgery is required.

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EPIDEMIOLOGY

The prevalence of CAP is uncertain. However current data propose that the incidence of CAP is 22.9 per 1000 person-years.[6] Abdominal pain was reported in 25% of the adult population during cross-sectional surveys. There appears to be no substantial difference in prevalence among different age groups, ethnicities, and geographic regions.[6] Although there are studies that suggest that women are more likely to report abdominal pain than men. The lack of statistical data to support precision in the reported epidemiology of CAP could be accounted for in the varied interpretation of symptoms.

PSYCHOSOCIAL

Historically, there has been well-documented correlation between somatic complaints and psychosocial conditions. It has been estimated that nearly two thirds of patients with depression present to primary care with somatic dysfunction.[7] In regards to CAP there has been a well recognized association between CAP presentation and a history of PTSD, abuse, somatization, anxiety, and depression.[8, 9, 10] Timely consideration of psychosocial factors can help primary care providers determine appropriate testing and management plans. Discussing family dynamics, screening for new life stressors, such as caring for a sick loved one, financial hardships, birth of new child, etc. may help with establishing a correlation between the onset of CAP symptoms and mood changes. Ultimately, this can substantially decrease healthcare costs by minimizing unnecessary investigation and redirect care plans to managing underlying psychosocial condition with talk therapy intervention and/or medication if appropriate, which will likely result in resolution of patients CAP. [2, 7]

CLINICAL PRESENTATION

Careful history taking is critical in guiding the initial evaluation. General information to gather during this initial history taking include symptom onset, duration, location, diffuse vs. non-specific, quality and severity of pain, exacerbating factors, and alleviating factors. Associated signs and symptoms are paramount in narrowing the differential diagnosis. The localization of chronic abdominal pain is a common hurdle for patients to articulate to healthcare providers. This ultimately makes it harder for primary care physicians to sort through a multitude of possible differential diagnoses. Classification by organ system, as seen in *Table 1*, should be considered when patients present for CAP. Keeping this categorization in mind may assist in directing questions during patient encounters.

The alarm symptoms , as seen in *Table 1*, from the history are cause for concern: Fever, unexplained weight loss, loss of appetite, pain that awakens the patient during the night, hematemesis, hematochezia, hematuria, severe vomiting, severe diarrhea, anemia, Jaundice, swelling of abdomen or legs, and difficulty swallowing.[3,11,12] Tachycardia, Tachypnea, and hypotension are considered urgent, and require immediate attention.[2] The emergence of new symptoms or any physiologic change in the description of pain should prompt the physician to consider an acute on chronic condition.[2] For example, immediate severe pain can be suggestive of an acute bile duct obstruction by a stone, perforation of a hollow organ (duodenal ulcer), gastroparesis in a diabetic patient or a catastrophic ischemic condition (acute mesenteric anemia).[13] These conditions have serious outcomes and require immediate evaluation and intervention.[2]

PHYSICAL EXAM

Patients presenting with CAP should have a thorough physical exam including vital signs, abdominal exam, and osteopathic structural exam. In patients with suspected psychogenic abdominal pain, it is important to perform the abdominal examination while the patient is distracted. Systemic examination that may provide useful clues to diagnosis include: lack of moist mucous membranes (dehydration), conjunctival pallor (anemia), icteric sclera (hepatobiliary disease), sunken eyes, prominent clavicles, and temporal wasting (significant weight loss).[2] The location of pain will help guide the primary care physician's examination and thought process for further evaluation, see *Figure 1, Page 22*.

Though many cases present with a benign physical examination, clinical findings that require urgent attention include: rebound abdominal tenderness, guarding or tenderness to palpation. Rectal exam should be considered in patients presenting with rectal bleeding or discharge. The presence of occult blood in stools may provide clues to gastrointestinal cancer, bowel inflammation, or peptic ulcer disease.[13] In women with pelvic or lower abdominal pain, a pelvic exam may help determine whether the pain arises from the abdominal wall or is gynecologic in origin. If found during examination, costovertebral angle tenderness is suggestive of renal pathology. Diminished peripheral pulses and abdominal tenderness in the setting of vascular compromise is suggestive of mesenteric ischemia.[2, 14]

TABLE 1:

Chronic Abdominal Pain: Differential Diagnosis

PULMONARY
Cystic Fibrosis

GASTROINTESTINAL
Gastroesophageal Reflux
Esophageal Cancer
Hernias (ventral, hiatal)
Chronic Gastritis
Gastric Cancer
Gastroparesis
Functional Dyspepsia
Peptic Ulcer Disease
Chronic Cholecystitis
Chronic Cholelithiasis
Cholangiocarcinoma
Chronic Hepatitis
Hepatocellular Cancer
Chronic Pancreatitis
Pancreatic Cancer
Celiac Disease
Irritable Bowel Syndrome
Lactase Deficiency/Intolerance
Crohn's Disease
Ulcerative Colitis
Colorectal Cancer
Chronic Mesenteric Ischemia
Post-Surgical Abdominal Adhesions
Chronic Abdominal Wall Pain
Narcotic Bowel Syndrome
Abdominal Migraine
Subacute Intestinal Obstruction

GENITOURINARY
Nephrolithiasis

GYNECOLOGIC
Ovarian Cyst
Ovarian Cancer
Sequelae of Pelvic Inflammatory Disease
Leiomyoma
Endometriosis

HEMATOLOGIC
Sickle Cell Anemia

PSYCHOLOGICAL
Psychiatric Disorders

MISCELLANEOUS CAUSES
Functional Abdominal Pain Syndrome
Referred Pain from
Extra-Abdominal Organ
Drug/Medication Induced

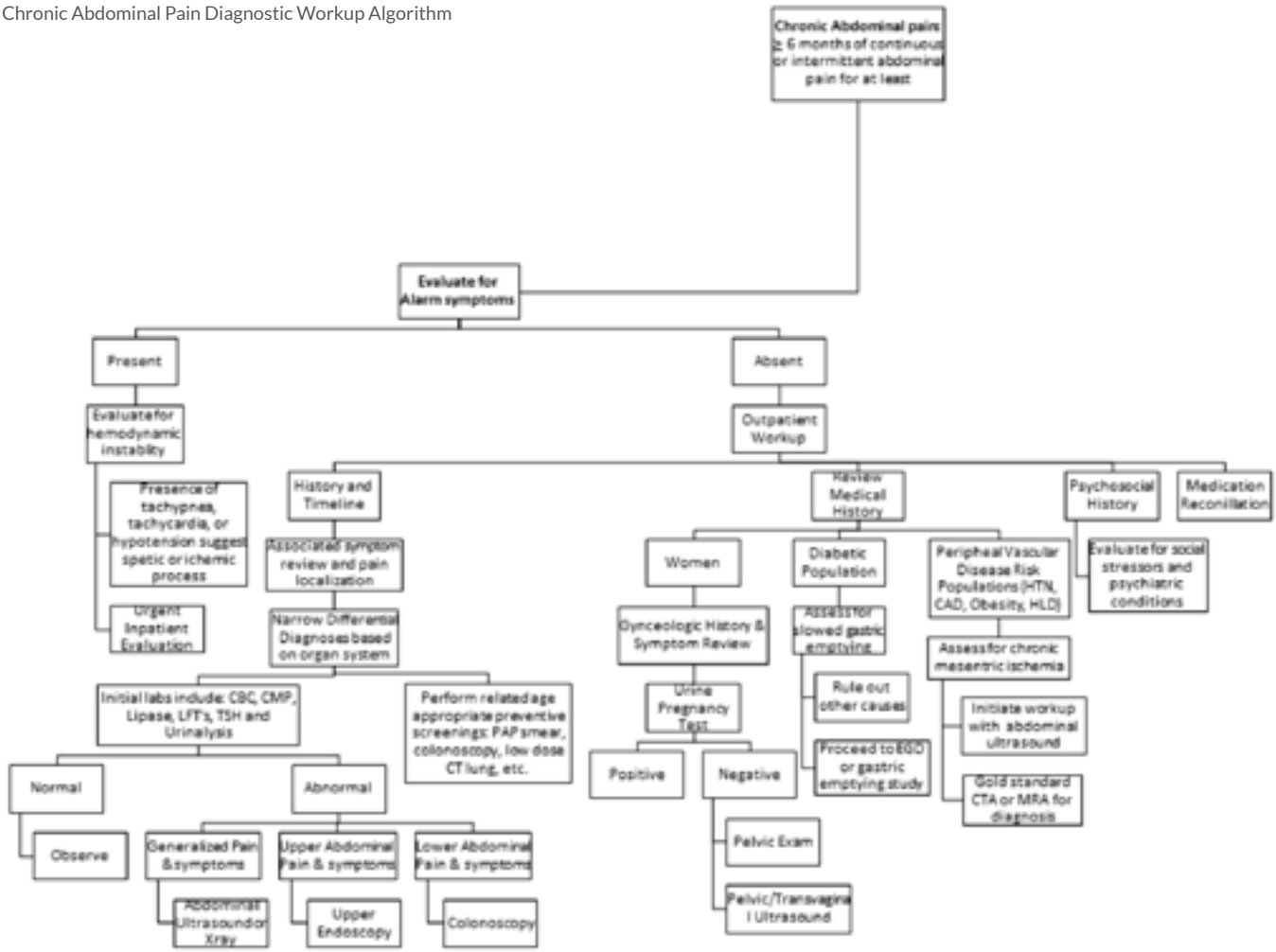
NEUROLOGIC
Abdominal cutaneous nerve entrapment syndrome
Centrally Mediated Abdominal Pain Syndrome
Herpes Zoster
Chronic Narcotic Use

One specialized maneuver associated with abdominal pain and possible cause is the carnett's sign. The patient lies supine, tenses their abdominal wall and lifts their head off the table. A positive sign (increased or unchanged tenderness) is suggestive of abdominal wall/ somatic pain. A negative sign (decreased pain) is suggestive of intra-abdominal/ visceral pain.[2, 15, 16] Several studies have demonstrated that a combination of history, physical and positive Carnett's sign is a reliable predictor of chronic abdominal wall pain.[16] A key feature of chronic abdominal wall pain is that patients are able to isolate the pain to a specific point/location unlike, many other conditions that have a generalized abdominal pain presentation.

The etiology of chronic abdominal pain may be visceral, psychological or mechanical. An osteopathic structural exam should be included. Additional Information contributing to the diagnose may be found through palpation of regions of the autonomic innervation in particular as outlined in *Figure 1, Page 22*.[17]

FIGURE 1:

Chronic Abdominal Pain Diagnostic Workup Algorithm



DIAGNOSTIC WORKUP

A thorough workup of labs and appropriate imaging will support or refute the diagnosis. Begin by determining if there are any alarm symptoms to warrant immediate inpatient evaluation. If alarm symptoms are absent, proceed to the outpatient workup, refer to *Figure 1*. The following lab measurements are recommended for initial work up of patients with CAP: urinalysis, complete metabolic panel, complete blood count, thyroid function tests, lipase, amylase, and liver function tests. All women of reproductive age should undergo urine or serum pregnancy testing prior to any diagnostic imaging.

Diagnostic imaging in the setting of CAP is often overused and approached erratically. One reliable starting tool for the primary care physician is an abdominal ultrasound. Abdominal ultrasound is a sensitive, non-invasive, cost effective test that can be used to help diagnose the cause of abdominal pain. For pain located in the lower abdomen and pelvic regions, a pelvic and/or transvaginal ultrasound can also be useful in determining whether the pain is abdominal or gynecologic in nature.[2, 18] While the abdominal CT is also a useful tool in the diagnostic workup, it is extremely costly to the healthcare system. In 2012-13, Mendelson et al. reported that there were over 330, 000 abdominal CT scan related Medicare services at a cost of $146 million.[3] Once initial testing has been performed, there are more specific tests to be considered based on clinical findings. Upper GI causes should be evaluated via EGD, and lower GI causes evaluated via colonoscopy.

Diagnostic imaging is not often indicated in the evaluation CAP.[3] Thus it is important to make enlightened cost effective decisions about ordering radiographic studies. Ultimately, it is the primary care physician's duty to determine which modalities are most appropriate, to form a diagnosis, and subsequently develop a plan for management.

MANAGEMENT

The etiology of a patient's CAP can be from any organ system, making it extremely difficult to have a single specific treatment algorithm. In general for all patients, management should be, etiology specific and can include a combination of lifestyle modifications, medical therapies, OMT, surgical interventions, and alternative modalities.

TABLE 2:

SYSTEM	AUTONOMIC		FOCUSED OSTEOPATHIC STRUCUTRAL EXAM	SOMATIC DYSFUNCTIONS TO CONSIDER	POSSIBLE TREATMENT
	PARASYMPATHETIC	SYMPATHETIC			
Psychological	• Increased tone = constricts pupil, significantly increased secretions of nasal, lacrimal, and submandibular glands. • Facial (CN VII), glossopharyngeal (CN IX) — cranial dysfunction • Vagus nerve CN X exits the jugular foramen (comprised of occiput and temporal bones) • Somatic Dysfunctions of occipito-atlantoid joint (OA), atlanto-axial joint (AA), C2 Compression of occipitomastoid sutures	• Increased tone = vasoconstriction and slight secretions of nasal, lacrimal, and submandibular glands, increased blood flow to skeletal muscle • Somatic Dysfunction of T1–T5	Head Cervical Thoracic Upper Extremity Abdomen	1. Any cranial or facial bone somatic dysfunction 2. Cranial venous sinous restrictions 3. Any cervical dysfunction 4. Temporomandibular joint dysfunction — medial pterygoid, posterior digastric m uscles, and glossal muscles; hyoid muscles; and fascial estrictions 5. Muscle hypertonicity and tenderness associated with body habitus in response to anxiety/stress a. Scalene (all) b.Trapezius c. Rectus Capitus Posterior d. Levator scapulae e. Sternocleidomastoid (SCM) 6. Celiac ganglion restriction 7. Thoracic somatic dysfunctions	1. Cranial manipulation 2. Venuos sinous drainage 3. Counterstrain (CS), muscle energy (ME) 4. Direct inhibition (DIR) 5. Myofascial release (MFR), CS, ME, High Velocity, Low Amplitude (HVLA) 6. MFR 7. Myofascial release (MFR), CS, ME, High Velocity, Low Amplitude (HVLA)
Pulmonary	• Increased volume of secretions and relative bronchiole constriction • Vagus nerve CN X exits the jugular foramen (comprised of occiput and temporal bones • Somatic Dysfunctions of occipito-atlantoid joint (OA), atlanto-axial joint (AA), C2 • Compression of occipitomastoid (OM) sutures	• Increased tone • Vasoconstriction and slight secretions of nasal, lacrimal, and submandibular glands, increased blood flow to skeletal muscle • Decreased secretions and bronchiole dilation • Somatic Dysfunctions of T1–T7	Head Cervical Thoracic Rib Upper Extremity Abdomen	1. OM restriction 2. Anterior cervical and sternal fascial restrictions 3. Cervical somatic dysfunction 4. Muscle hypertonicity and tenderness a. Sternocleidomastoid b. Serratus Anterior c. Respiratory diaphragm 5. Inhalation or exhalation rib dysfunctions 6. Thoracic somatic dysfunctions Thoracolumbar dysfunction (diaphragm attachment)	1. V-spread, MFR 2. MFR 3. Myofascial release (MFR), CS, ME, High Velocity, Low Amplitude (HVLA) 4. Counterstrain (CS), muscle energy (ME) 5. ME, Balanced ligamentous tension (BLT) 6. Myofascial release (MFR), CS, ME, High Velocity, Low Amplitude (HVLA)
Gastrointestinal	• Increased tone = increased acid secretion and increased peristalsis • Vagus nerve CN X exits the jugular foramen (comprised of occiput and temporal bones) • Somatic Dysfunctions of occipito-atlantoid joint (OA) , atlanto-axial joint (AA), C2 • Compression of occipitomastoid sutures • Pelvic splanchnics—S2–S4 • Sacroiliac dysfunctions	• Increased tone = increased acid secretion and increased peristalsis • Vagus nerve CN X exits the jugular foramen (comprised of occiput and temporal bones) • Somatic Dysfunctions of occipito-atlantoid joint (OA) , atlanto-axial joint (AA), C2 • Compression of occipitomastoid sutures • Pelvic splanchnics—S2–S4 • Sacroiliac dysfunctions	Head Cervical Thoracic Rib Upper Extremity Abdomen Innominate Sacrum	1. OM restriction 2. Anterior cervical and sternal fascial restrictions 3. Muscle hypertonicity and tenderness a. Serratus Anterior b. Respiratory diaphragm 4. Lower ribs 6-10 Inhalation or exhalation rib dysfunctions (diaphragm attachment) 5. Thoracic somatic dysfunctions Thoracolumbar dysfunction (diaphragm attachment) 6. Mesenteric restriction Innominate dysfunctions 7. Sacral dysfunctions 8. Muscle hypertonicity and tenderness of pelvic floor muscles	1. V Spread MFR 2. MFR 3. CS, ME 4. ME, BLT 5. MFR, CS, ME, HVLA 6. Meseneric lift
Genitourinary/ Gynecological	• Increased tone = increased bladder contraction • Vagus nerve CN X exits the jugular foramen (comprised of occiput and temporal bones) – Somatic Dysfunctions of occipito-atlantoid joint (OA) , atlanto-axial joint (AA), C2 – Compression of occipitomastoid sutures • Pelvic splanchnics—S2–S4 – Sacroiliac dysfunctions	• Increased tone = increased bladder contraction • Vagus nerve CN X exits the jugular foramen (comprised of occiput and temporal bones) – Somatic Dysfunctions of occipito-atlantoid joint (OA) , atlanto-axial joint (AA), C2 – Compression of occipitomastoid sutures • Pelvic splanchnics—S2–S4 – Sacroiliac dysfunctions	Head Cervical Thoracic Rib Upper Extremity Abdomen Innominate Sacrum	1. OM restriction 2. Anterior cervical and sternal fascial restrictions 3. Muscle hypertonicity and tenderness a. Serratus Anterior b. Respiratory diaphragm 4. Lower ribs 6-10 Inhalation or exhalation rib dysfunctions (diaphragm attachment) 5. Thoracic somatic dysfunctions Thoracolumbar dysfunction (diaphragm attachment) 6. Innominate dysfunctions 7. Sacral dysfunctions 8. Muscle hypertonicity and tenderness of pelvic floor muscles	1. V Spread MFR 2. MFR 3. CS, ME 4. ME, BLT 5. MFR, CS, ME, HVLA 6. ME, ART 7. ME, ART 8. DIR

Lifestyle modifications

Prior to proceeding to specific investigations, a low cost strategy in the treatment of CAP is lifestyle and dietary modifications. This can be particularly helpful for chronic abdominal pain thought to be secondary to GERD, lactose Intolerance, Peptic Ulcer Disease, Gastroparesis, and chronic mesenteric ischemia. Simply limiting certain foods that trigger pain symptoms, modifying diet to smaller frequent meals, and/or changing to semi-solid or liquid form foods can be prove to be effective.

Other lifestyle modifications for consideration include smoking cessation and cutting down alcohol intake. Patient's with CAP who are smokers should be counseled on the impact of smoking to the digestive system which include increased risk for GERD, peptic ulcer disease, increased risk of gallstones and cancers originating from the GI tract.[19] Quitting smoking will reverse some of these effects on the digestive system as well as relieve CAP symptoms. In regards to alcohol consumption, high amounts have been linked to delayed gastric emptying, which can also lead to CAP. Referral to a rehab program can beneficial to such patients.

Medications

CAP can also have iatrogenic causes such as medication induced. There are several drugs that can cause delay in gastric emptying which leads to nausea and abdominal discomfort symptoms. Therefore it is crucial that an extensive review of medications be completed before starting on any potential treatment for CAP. Medications that should prompt concern as possible etiology for CAP are listed in *Table 3* by drug class.[20] In regards to medication for treating chronic abdominal pain, this simply lies on the determined etiology.

Surgical interventions

When considering surgical interventions for CAP, the etiology and its severity will dedicate the available surgical options. Surgical treatment can include open surgical repair via transaortic endarterectomy or retrograde bypass grafting as seen in chronic mesenteric ischemia. Also some conditions can be mediated via the surgical insertion of a stimulation device, such as in gastroparesis.[21, 22]

A less invasive surgical technique to consider are trigger point injections for the abdominal wall, especially in patients with chronic abdominal wall pain (CAWP). Ultrasound guided injections of a long acting anesthetic can provide decent relief with minimal complications. Since this isn't a common technique for primary care doctors to perform, once the diagnosis is made and trigger point injection is being considered, it suggested that patients be referred to an gastroenterologist or physical medicine and rehabilitation physician for this procedure.[23]

OSTEOPATHIC MANIPULATIVE TREATMENT (OMT)

The goals of an osteopathic structural exam and subsequent OMT is fourfold; to address viscero-somatic and somato-visceral reflexes that can contribute to and maintain disease, to remove impediments to lymphatic flow, to disrupt psychosomatic reflexes that maintain pain cycles and to remove somatic causes of pain and disease. To accomplish this the autonomic innervation to the diseased system(s) as well as the lymphatic and surrounding musculoskeletal components should be addressed. The sympathetic innervation to all organs are housed in the prevertebral ganglion of the abdomen and in the sympathetic chain ganglion with sits anterior to the rib heads and transverse processes of the thoracic spine. All parasympathetic innervation comes from the vagus nerve that exits the jugular foramen with ganglion anterior to C1-2 and the pelvic splanchnics that arise from the sacrum. Addressing the various diaphragms of the body that may impede lymphatic vessels is a focused approach to improving lymphatic movement. In the case of CAP, the most prevalent are the respiratory diaphragm and the pelvic floor muscles. A correlation of systems to the body regions, potential somatic dysfunctions and treatments is outlined in *Table 2, Page 23*[17]

Alternative Techniques

Alternative techniques are good management options in patients who have a negative diagnostic workup for CAP or those who have a terminal condition (i.e.. colon cancer) where pain management options are limited. First step in such patients, is to revisit psychosocial assessment to rule out underlying disorders. If psychosocial screening is negative, consider focusing on mind-body therapies. This has been studied in conditions like irritable bowel syndrome. Brain gut interactions are increasingly recognized in the pathogenesis of IBS.[24] Thus, hypnotherapy and CBT are logical therapeutic choices, and enough evidence exists to consider their use in appropriate patients with IBS.[24] The goal of cognitive therapies is to assist patients in regaining control over their pain symptoms allowing them to maintain functional lives. Other modalities such as acupuncture can be an option for some patients, although there is insufficient evidence to support its benefits.

SPECIAL POPULATIONS

Since chronic abdominal pain is common in primary care, there are certain patient populations who when presented with CAP, require close attention. These include diabetics, individuals with peripheral vascular disease, narcotic users, and women.

TABLE 3:

Medications Known to Impair Gastric Emptying

CARDIAC MEDICATIONS
Beta-Blockers
Calcium Channel Blockers

PAIN MEDICATIONS
Narcotics
NSAIDS

GI MEDICATIONS
Aluminum-containing antacids
Ondansetron
Proton Pump Inhibitors
Sucralfate

ANTICHOLINERGICS
Atropine
Atrovent
Bentyl
Lomotil

ANTIPSYCHOTICS/ANTIDEPRESSANTS
Lithium
Phenothiazines
Tricyclic Antidepressants
SSRI Antidepressants

OTHER/MISCELLANEOUS
Clonidine
Cyclosporine
Diphenhydramine
Levodopa
Nicotine
Progesterone

Diabetics

Gastroparesis is the most common GI complication of diabetes. 5% of Type 1 diabetics and 1% of Type 2 diabetics will experience gastroparesis.[20] Gastroparesis is the delayed emptying of food from the upper GI tract in the absence of mechanical obstruction.[20, 25] This is due to hypermobility associated with hyperglycemia. Patients with uncontrolled blood glucose levels presenting with CAP, complaints of early satiety, postprandial fullness, bloating, or vomiting undigested food should be evaluated for gastroparesis and treated accordingly.

Peripheral Vascular Disease

Conditions that predispose patients to atherosclerosis such as peripheral vascular disease (PVD) have been linked to the development of chronic mesenteric ischemia, which was first described as "abdominal angina" in 1918.[21,26] Although, seen as rare disorder, chronic mesenteric ischemia is life threatening, and increased prevalence in women.[14] In addition, with increasing populations of obesity, hypertension, diabetes, and hypercholesterolemia, this is a disorder that should not be overlooked, especially in patients over the age of 60 with known tobacco use history and/or the presence of cardiovascular risk factors. Typical presentation includes postprandial abdominal pain, weight loss usually secondary food phobia, malnutrition, and possible abdominal bruit on physical exam.[2,21] The abdominal pain classically starts 15 to 30 minutes after a meal and typically lasts for 30 minutes.[14] Diagnosis is confirmed via CT angiography.[20]

In conditions such as chronic mesenteric ischemia, surgical considerations are used with the goal of restoring blood flow to the mesenteric vessels.

Chronic Narcotic Users

Review of past medical history such as co morbidities as well as medication use can also aid in gauging the cause of the abdominal pain. For example, CAP occurring in the setting of chronic narcotic use, with or without escalating doses is known as narcotic bowel syndrome (NBS).[2] It is well known that opiates impact gastrointestinal and biliary motility and secretion. These changes described as opioid bowel dysfunction classically present as bloating, nausea, constipation, and abdominal pain.[27,28,29] In NBS, the abdominal pain is characterized as chronic or intermittent colicky pain that worsens when the narcotic effect wears down. The danger with this phenomenon is providers tend to increase the dose of the patients narcotic medication.[30] Initially this may appear to be helpful, however, pain-free periods get shorter and there is an enhancement of pain sensation and decreased gastrointestinal motility, leading to more NBS symptoms, and subsequently aggravate CAP symptoms.[30] Treatment of NBS has been described via a biopsychosocial approach, which involves withdrawal of narcotic, treatment of immediate withdrawal side effects, addressing underlying psychological conditions, and using other modalities to achieve pain control.

Women

When evaluating women with CAP, it is certainly important to consider pain originating from abdominal viscera as well as pain referred from an extra abdominal source, especially within the pelvis.[2] Chronic pelvic pain (CPP) can often be confused by patients as chronic abdominal pain. It is important to understand that CPP has its own lists of possible differentials, which include, interstitial cystitis, endometriosis, adhesions, urethral syndrome, changes or dysfunction of the pelvic muscles. Thus, including reproductive and gynecologic history in the history of present illness (HPI) is vital to initiating the next step for diagnosis and management.[2] Red flag findings of concern in women include postcoital bleeding, postmenopausal bleeding or onset of pain, unexplained weight loss, pelvic mass, and hematuria which may indicate systemic disease and warrant prompt follow up.[18,31]

SUMMARY

Chronic abdominal pain (CAP) is common chief complaint to primary care with its work up leading to a high cost burden to the healthcare system. A systematic approach to determining the etiology of CAP is vital to diagnosis and management. In patients with CAP, the presence of alarm symptoms require immediate attention. Since evaluating for the cause of CAP can be challenging and costly. Always conduct a psychosocial assessment prior to extensive workup as CAP is a common somatic complaint in patients with mood disorders. Then start with basic initial serum tests and the least invasive imaging in the diagnostic workup first. Management requires a thorough evaluation and is dictated by etiology. Treatment options include lifestyle modifications, medical therapies, surgical procedures, and alternative therapies. It benefits the primary care provider to be aware of special populations when evaluating patients for chronic abdominal pain complaints.

Key Points:

- Chronic abdominal pain typically lasts six months or longer
- The presence of alarm symptoms require urgent evaluation
- Initial diagnostic testing includes: UA, CMP, CBC, lipase, amylase, thyroid function tests, and liver function test. These tests are performed to look for underlying causes of pain
- Additional tests and imaging are required for patients who have abnormal lab results and/or symptoms associated with a specific disorder.
- Management of CAP is multifactorial: discontinue offending agent, lifestyle changes, pharmacological therapies, surgical options, OMT, or alternative therapies.
- Special populations that would be beneficial to the primary care physician: women, diabetics, patients with PVD , chronic narcotic users and chronic abdominal wall pain patients.

AUTHOR DISCLOSURES:
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REVIEW ARTICLE

Skin & Soft Tissue Infections: It's More Than Just MRSA

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ABSTRACT: Skin and soft tissue Infections (SSTIs) encompass a broad range of pathologies and represent a significant reason for outpatient visits. It is important to distinguish between complicated and uncomplicated SSTIs, which differ in terms of its presentation, severity, and treatment options. Uncomplicated SSTIs can present as furuncles, carbuncles, cutaneous abscesses, or cellulitis, whereas complicated SSTIs are deeper, with the potential of systemic issues. Complicated SSTIs include necrotizing fasciitis, resulting in emergent surgical treatment. Imaging studies, such as plain X-rays, MRI, or CT scan, can be performed to rule out underlying issues that can alter the course of treatment. It is important to note that MRSA can cause both complicated and uncomplicated SSTIs and need to be considered as an etiology in both situations. Immunocompromised patients are a special population that requires swift identification and management, recognizing their atypical presentation and propensity for rapid decline. Successful treatment of SSTIs is crucial to diminish the likelihood of complications and hospital admissions.

INTRODUCTION

SSTIs include a wide range of diseases, from cellulitis to necrotizing fasciitis. SSTIs often involve microbial infections of the skin, subcutaneous tissue, fascia, and muscle.[1] Given the high rates of morbidity and mortality caused by SSTIs among hospitalized patients, physicians should take care to properly diagnose and treat SSTIs. Non-life threatening SSTIs can be managed in the outpatient setting, but more serious cases will require more sophisticated care.[2] Family physicians, in particular, can play an important role in the early detection and appropriate microbial management of SSTIs.

The workup of a patient with a skin infection requires a high degree of clinical vigilance, so that complicated and more serious infections may be excluded. Any patient presenting with signs of a systemic infection will require a full work up, to include blood cultures, complete blood count, creatinine phosphokinase, bicarbonate and C-reactive protein.[3] These clinical studies are necessary to exclude any systemic illness.

UNCOMPLICATED SKIN & SOFT TISSUE INFECTIONS

Uncomplicated SSTIs (uSSTIs) are a common reason for physician office visits. Determining the etiology and appropriate treatment is important to rule out the potential presence of a more serious infection. Less serious skin infections typically do not invade below the skin or subcutaneous tissue layers and respond well to outpatient antibiotic therapies. Risk factors that predispose a patient to developing a soft tissue infection include health conditions that contribute to poor tissue perfusion and venous stasis, such as obesity, diabetes mellitus, peripheral vascular disease and peripheral neuropathy. Health conditions that contribute to poor wound healing, such as a compromised immune system, inadequate nutrition and cirrhosis, can also predispose a patient to soft tissue infections.[4] Diagnosis of soft tissue infections is largely clinical. Wound and blood cultures, as well as imaging, are not indicated in patients who do not exhibit signs of systemic infection.

The common etiological agents causing these infections are strains of Staphylococcus aureus and β-hemolytic streptococcus.[5] Community Acquired Methicillin Resistant Staphylococcus aureus (CA-MRSA) is associated with a variety of uncomplicated SSTIs including, but not limited to, furuncles, carbuncles, cutaneous abscesses, and cellulitis.[6,7] Furuncles are transdermal hair follicle infections that typically present as draining, pustular or nodular lesions. Carbuncles are the result of the coalescence of furuncles. Cutaneous abscesses typically present as single or multiple fluctuant, erythematous nodules that are tender to palpation and contain purulent material. Most cutaneous abscesses are caused by staphylococcus spp., especially MRSA. The recommended treatment for uncomplicated furuncles, carbuncles, and cutaneous abscesses is incision and drainage. Wound culture is also recommended at the time of incision and drainage. Use of antibiotics for uncomplicated cutaneous abscesses caused by MRSA does not improve patient outcomes or prognosis and is not recommended. If antibiotic treatment is considered, empiric treatment for suspected CA-MRSA SSTIs in the ambulatory setting include oral trimethoprim sulfamethoxazole,

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doxycycline, and clindamycin. Cellulitis generally presents with unilateral cutaneous edema, erythema, and warmth. The purulent exudate that attends cellulitis may suggest MRSA as a cause, but the more common causes include Streptococcus spp., especially S. pyogenes. However, at this time, cases of uncomplicated purulent cellulitis do continue to warrant culture and empiric treatment for CA-MRSA.

COMPLICATED SKIN & SOFT TISSUE INFECTIONS

Skin and soft tissue infections should be considered complicated if systemic signs of illness such as fever or elevated WBC count are present, and in more severe cases, if tachycardia and hypotension are present.[8] These types of infections account for a significant percentage of the morbidity and mortality rates in this patient population. These infections are also responsible for longer hospital stays and loss of revenue for hospitals.[9] A timely diagnosis is critical in establishing a successful therapeutic intervention. Complicated soft tissue infections are defined by the presence of microbiome invasion beyond deep layers of the skin, or by an infection requiring surgical intervention.[10] These infections can be the result of burns, skin ulcerations, or poorly-healing abscesses. Soft tissue infections can also be classified as complicated in cases where the patient's ability to fight infection is compromised by various health conditions. Thus, co-morbid diseases, such as diabetes mellitus, immunodeficiency states, and arteriovenous insufficiencies, can all be contributing factors in the development of soft tissue infections that are clinically more difficult to treat. Furthermore, epidermal infections with accompanying fever, hypothermia, tachycardia, and hypotension would be highly indicative of an associated sepsis and are likely to create an infection that would be considered highly complicated.[11]

As with the case of uncomplicated soft tissue infections, the most common etiologic agents for complicated skin and soft tissue infections (cSSTIs) are gram positive microbes, such as Staphylococcus aureus and the β-Hemolytic streptococci strains (including group A, B, C and G). Strains of Staphylococcus aureus and β-Hemolytic streptococcus are capable of producing exotoxins that can result in a necrotizing infection. Necrotizing infections are medical and surgical emergencies, which require prompt treatment with aggressive surgical debridement. These infections involve fascial planes, leaving the skin intact. In these infections, a dermatological exam may reveal a mild cellulitis, but a more insidious infection is often present. Clinical exam findings can include systemic signs of infection, as well as pain that is out of proportion with clinical findings. In addition to rapid surgical debridement, intravenous antibiotics, analgesics, and electrolyte management are the standard of care for the treatment of necrotizing infections.

Imaging studies may be useful in the setting of complicated SSTIs. Plain x-rays are indicated if there is known trauma at the site of the SSTI, or may be considered if there is a preexisting chronic wound. Xrays may uncover a fracture, foreign body, or osteomyelitis. Magnetic resonance imaging (MRI) is the best choice to show the extent of corporal involvement. Soft tissue is also well visualized with computed tomography (CT), if shorter image time is warranted. Both MRI and CT are usually not necessary, but an option if needed for further evaluation.[13]

Unusual pathogens are a significant source of complicated soft tissue infections and are often overlooked in the clinical setting. Inquiring into a patient's recent history of travel, antibiotic usage, hospitalizations and exposure to animals may yield highly valuable information for purposes of determining etiologies. A list of unusual pathogens is listed in *Table 1*. Animal bites represent a common etiology of skin and soft tissue infections. Bites from felines are quite common and frequently get infected with Pasteurella Multocida and Bartonella Henselae, which are the most common pathogens in this situation. Dog bites are also commonly encountered in clinical settings but are less likely to become infected. No specific workup is necessary for animal bites in patients who are not exhibiting signs of systemic infection.

NOTABLE CONSIDERATIONS ON MRSA

Methicillin-resistant Staphylococcus aureus (MRSA) has become an increasingly common cause of SSTIs in both outpatient and inpatient settings and has become associated with high morbidity and mortality rates.[14,15] The continuing rise of MRSA cases in ambulatory settings has been attributed to the widespread emergence of community-associated (CA-MRSA) strains. Traditionally, risk factors for MRSA SSTIs included nasal colonization, previous MRSA infection, recent antibiotic therapy, hospitalization, and intravenous drug use;[16] CA-MRSA is, however, frequently isolated from SSTIs in individuals who lack these traditional risk factors.[17] Favorable patient outcome following an SSTI from MRSA depends on early diagnosis by a physician, followed promptly by appropriate management.[18]

NOTABLE CONSIDERATIONS ON IMMUNOCOMPROMISED PATIENTS

A patient population that requires additional surveillance includes patients who are immunocompromised. This includes, but is not limited to, patients who are receiving immunosuppressant medication, radiation therapy, corticosteroids, chemotherapy, and those who are infected with HIV/AIDS Immunocompromised patients require extra vigilance from the clinician in order to facilitate prompt management and to identify appropriate

TABLE 1:

Unusual Pathogens [30,31]

BITES (ANIMAL)	Bacteroides, Bartonella henselae, Capnocytophaga canimorsus, Eikenella corrodens, Pasteurella multocida, Peptostreptococcus, S. aureus, Streptobacillus moniliformis;
FOLLICULITIS	Candida, dermatophytes, Pseudomonas aeruginosa, S. aureus
CLOSTRIDIAL MYONECROSIS	C. perfringens, C. septicum

pharmaceuticals for unusual and diverse microorganisms. For such patients, infections can quickly become life-threatening and are challenging to treat solely through antimicrobial therapy.[19] Common opportunistic organisms causing SSTIs in immunocompromised patients include drug resistant gram negative bacteria such as Pseudomonas species, anaerobes such as Clostridium species, and fungi such as Cryptococcus species. While cultures may not be indicated in most healthy patients, they are useful for immunocompromised patients who are at risk for sepsis, cellulitis, lymphangitis, and recurrent persistent abscesses.[20] It is important to note that immunocompromised patients will not exhibit the classic symptoms of SSTIs, owing to their diminished immune system's response. For this reason, diagnostic tests should be completed in a timely fashion to investigate the microbial landscape for susceptibility testing and to determine the appropriate pharmaceutical therapy.[21] This is a crucial step especially considering that many microorganisms may be acquired in the hospital and are strongly resistant to common antimicrobial drugs. Consequently, empiric treatment in immunocompromised patients may prove problematic, if not downright difficult. [22] What may appear as a deceptively simple skin infection in an immunocompromised patient can quickly progress to systemic infection or, even worse, to necrotizing fasciitis. This accelerated progression is due to the immunocompromised patient's weakened immune capacity, which reduces the patient's ability to stave off an infection that begins in the skin or soft tissues.[23] An important sign of a systemic infection is pain that is out of proportion to the presenting SSTI, and such a sign should prompt extensive investigation into the underlying cause. Other signs of systemic complications include bacteremia, leukocytosis, and fever.[24] Even if the original bacterial SSTI is resolved, it can return with a concurrent secondary fungal infection.[25] When managing SSTIs in immunocompromised patients, antibiotic therapy should encompass both gram positive and gram negative bacteria, using agents such as higher generation cephalosporins or imipenum. Patients allergic to penicillin-based medications can receive fluoroquinolones. When considering MRSA in the immunocompromised patient, the clinician may utilize vancomycin, clindamycin, or daptomycin, as appropriate and depending on the patient. The use of such antibiotics to treat MRSA-associated carbuncles and furuncles is recommended for immunocompromised patients and for infections with associated septic phlebitis or concomitant systemic inflammatory response syndrome.[26,27] Fungi can be managed with amphotericins, triazoles, or echinocandins.[28,29]

DIFFERENTIAL DIAGNOSIS

There are other lesions and conditions that can mimic both uncomplicated and complicated SSTIs. This includes, but is not limited to, herpes zoster, acne, deep vein thrombosis (DVT), gout, contact dermatitis, autoimmune etiologies, allergic dermatitis, and venous stasis.

TREATMENT

The treatment of skin and soft tissue infections will vary depending on local patterns of antibiotic resistance and sensitivity, as determined by local health officials. See *Table 2* for the management of common SSTIs.

CONCLUSION

The increasing prevalence of SSTIs requires primary care clinicians to be well versed in the inpatient and outpatient management of these diseases. When appropriate, surgical referrals may be needed in order to effectively treat SSTIs and minimize further complications. If antimicrobial therapy is determined to be the appropriate treatment, the patient's health status and condition should be considered to increase the likelihood of a successful outcome. Symptoms such as fever, tachycardia, hypotension, or any other indications of systemic infection should prompt investigation of the underlying cause.

AUTHOR DISCLOSURES:
No relevant financial affiliations

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TABLE 2:

Management of Common SSTIs [30]

MANIFESTATION	COMMON ETIOLOGY	MANAGEMENT OPTIONS	COMMENTS
Nonpurulent SSTIs			
Cellulitis	β-hemolytic streptococci, polymicrobial	Oral penicillin, amoxicillin, cephalexin, clindamycin	A 5 day course is recommended for uncomplicated cases
Erysipelas	β-hemolytic streptococci	Oral cefazolin, ceftriaxone, penicillin, amoxicillin	If indistinguishable from purulent cellulitis, cefazolin is preferred due to coverage for S. aureus for 7-10 days
Folliculitis	S. aureus	Topical clindamycin, mupirocin	Recurrent cases require systemic treatment with cephalexin or dicloxacillin for up to 4-6 weeks
Impetigo	S. pyogenes, Staphylococcus spp.	Topical mupirocin, retapamulin. Oral dicloxacillin, cephalexin, penicillin	Oral penicillin is preferred for cases of isolated streptococci impetigo 7-10 days
Necrotizing Infection	Mixed anaerobic bacteria, S. pyogenes	Surgical tissue debridement, empiric broad-spectrum antibiotics such as clindamycin plus vancomycin plus meropenem	Hyperbaric oxygen is used in necrotizing fasciitis
Purulent SSTIs			
Carbuncle/Furuncle	MSSA producing PVL, MRSA	Incision and drainage with addition of oral TMP-SMX, doxycycline, clindamycin	Oral antibiotics are required only for complicated cases
Cellulitis	CA-MRSA	Oral clindamycin, doxycycline, TMP-SMX	Additional coverage for streptococci is warranted in addition to MRSA coverage for 7-14 days
Cutaneous Abscess	MSSA producing PVL, MRSA	Incision and drainage	Addition of antibiotics for coverage of MRSA is indicated in immunocompromised patients or patients with systemic inflammatory response syndrome for 7-14 days

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Treat the Whole Not Just the Hole: Holistic Wound Care Approach

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ABSTRACT: The key to successful wound care lies in the provider's ability to accurately identify etiology of the wounds and recognize factors that may contribute to their chronicity. Some of the most commonly encountered and clinically significant barriers include macro- or micro-angiopathic diseases, infection, protein-energy malnutrition, smoking, and metabolic disorders. In this article, we evaluate a case of chronic non-healing wounds in a patient with hypothyroidism, Factor V Leiden mutation, and obstructive sleep apnea. Attention is drawn to the impact of these comorbid conditions on integrity and regeneration of soft tissues, both from pathophysiological and histological aspects.

INTRODUCTION

Long-standing wounds are crippling physically, psychologically, and emotionally. Understanding biochemistry of healing and factors that facilitate or impede this process is essential. Chronic wounds often regain their positive healing trajectory when etiology and contributing factors are correctly identified and adequately managed.[1]

CASE PRESENTATION

44-year-old male with history of morbid obesity, peripheral vascular disease, lymphedema, and multiple episodes of bilateral lower extremity (b/l LE) cellulitis came to our clinic for a second opinion. His chief complaint was chronic non-healing b/l LE wounds that started twelve years prior after a trip-related DVT. Patient reported having profuse drainage, malodor, swelling and pain in both legs. His independence, lifestyle, and ability to work were greatly affected. Review of systems revealed weight gain, lack of energy, and tiredness.

Surgeries included bilateral hip arthroplasties due to congenital hips dysplasia, right foot trans-metatarsal amputation due to invasive infection, and has right lower extremity vein stripping in 1994. He is married and has one daughter; denied tobacco, alcohol, or illicit drugs use. His family history revealed an unknown hypercoagulable disorder in this mother.

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WOUND CARE TREATMENT

Due to lymphedema and chronic venous insufficiency, the main stem of his treatment was compression therapy with multi-layer compression wraps and pneumatic compression devise. Adding energy-based modalities, such as ultraviolet C light, electrical stimulation, and high-frequency megahertz ultrasound did not show robust changes. Due to his chronic lymphorrhea and high propensity to soft tissue infection, we used antimicrobial absorptive dressings. Sharp debridements were employed on as needed basis. Bioengineered skin substitute, such as Apligraf, was utilized twice. Although complete wound closure was not achieved, we were able to control his pain, profuse drainage, and malodor.

PATIENT EVALUATION

Detailed history, thorough physical exam, differential diagnoses, and appropriate work up are critical components of the initial evaluation. Our patient had mentioned significant weight gain, lack of energy, and tiredness, which prompted further testing and laboratory work up and revealed an elevated thyroid stimulating hormone (TSH) level, Factor V Leiden deficiency and obstructive sleep apnea.

WOUNDS AND HYPOTHYROIDISM

Prevalence of hypothyroidism, both overt and subclinical, is up to 9.5% of the general population as reported in the prevalence studies.[2,3] Hypothyroidism is associated with hyperlipidemia,[4] cardiovascular disease,[5] and depression;[6] however, it has also been shown by numerous studies to have direct[7-24] and indirect effect on wound healing.[25-28] The impairment of cutaneous wound healing has been demonstrated in hypothyroid states, induced by anti-thyroid drugs,[16,17] thyroid radiation,[12] or surgical ablation.[11]

Hypo-functional thyroid gland directly interferes with fibroblast utility[10,11] prolongs the proliferative phase of healing and alters the quality of collagen, forming thinner and smaller collagen fibers.[12,13,15] Since collagen is the only protein in the body containing hydroxyproline in significant amounts, hydroxyproline became the focus of many studies since the 1960s. It is released with collagen degradation and is excreted in urine.[29] Excretion of hydroxyproline is greatly reduced in hypothyroidism and may be corrected by hormone replacement therapy, thereby normalizing collagen metabolism.[30]

In order to analyze the relationship between hypothyroidism and wound healing, Natori et al. induced a state of severe hypothyroidism in rats and then assayed the levels of hydroxyproline and pro-collagen peptide.[11] He was able to demonstrate significantly decreased levels of type IV collagen and hydroxyproline throughout the inflammatory phase extending to the proliferative phase of healing. These findings suggest that low levels of thyroid hormone cause disturbance in the tissues' metabolic activity and lead to down regulation of collagen production through multiple phases of healing.

At the molecular level, thyroid hormone can act directly on cutaneous tissues by binding to the thyroid hormone receptor.[9, 24] Immunohistochemical localization and quantitative polymerase chain reaction have shown all three thyroid hormone binding receptor isoforms to be expressed in the skin.[31,32] As Safer et al. described it, thyroid hormone receptors have been detected in a variety of cells: epidermal keratinocytes, skin fibroblasts, hair outer root sheath, dermal papilla, fibrous sheath of the hair follicle, arrector pili muscle cells, sebaceous glands, vascular endothelial cells, smooth muscle cells, and Schwann cells.[9]

Saner et al. described a decreased serum zinc level in patients with hypothyroidism.[33] Another study demonstrated positive effect of thyroid hormone replacement therapy with addition of supplemental zinc on wound healing in hypothyroid rats.[17] However, Ekmektzoglou et al., pointed out that zinc, most likely, does not have a direct effect on the amount of collagen synthesis, but rather affects more directly the cross-linking of formed collagen and therefore influences the tensile strength of the wound.[8]

Hypothyroidism is treated systemically by oral administration of levothyroxine. There are multiple works describing topical application of the thyroid hormone analog TRIAC (triiodothyroacetic acid) to the wounds in vivo. Findings show accelerated epidermal proliferation, dermal thickening, hair growth, and even reversal of the dermal atrophy associated with corticosteroids.[20,24,34,35] Topical triiodothyronine has been shown to stimulate growth of both epidermal keratinocytes and dermal fibroblasts; however is dependent on the presence of systemic triiodothyronine.[20]

Indirectly, thyroid dysfunction is associated with recalcitrance of wounds by markedly altering cardiovascular and renal function, leading to fluid retention. Villabona et al. were able to show not only decreased myocardial contractility, cardiac output, and oxygen consumption, but also an increased peripheral resistance as direct effects of hypothyroidism.[25] It was also pointed out that transcapillary escape of albumin into the extravascular space may add to the development of edema.[25,28] Effects of hypothyroidism extend to decrease renal blood flow, glomerular filtration, and solute-free water excretion.[27] Patients with advanced primary hypothyroidism may be hyponatremic and fail to suppress plasma arginine vasopressin with an acute water load.[26] Luckily, the adverse effects of hypothyroidism might be reversed, and the symptoms relieved with the substitutive therapy.

WOUNDS AND HYPERCOAGULABLE STATE

While initially having positive healing trajectory, our patient had a setback when he developed an acute deep vein thrombosis (DVT) in the right lower extremity. Anticoagulation therapy was started, and further work up revealed Factor V Leiden mutation. This hypercoagulable state shed light onto his high recurrence rate despite adequate compression and aggressive wound care.

Hypercoagulable disorders may cause ulcerations, either indirectly because of deep venous thrombosis, or directly by thrombus formation in small arteries, arterioles, capillaries, or venules.[36-38] In fact, Factor V Leiden mutation is associated with increased prevalence of venous leg ulcers.[39,40]

Gaber et al., within a 2-year period examined 100 consecutive patients with leg ulcers for Factor V Leiden mutation. His investigation showed 36% prevalence rate of Factor V Leiden mutation in patients with post-thrombotic leg ulcers.[41] Later, Hafner et al. confirmed these findings in his study of 73 consecutive patients with venous ulcers. He concluded that in post-thrombotic ulcers, the prevalence of the Factor V mutation was 38%. Even patients with non-post-thrombotic venous ulcers showed a moderately elevated prevalence (16%) of Factor V Leiden mutation.[42]

Factor V is a protein of the coagulation system, sometimes referred to as proaccelerin or prothrombin accelerator. In contrast to most other coagulation factors, it is not enzymatically active but functions as a cofactor. Deficiency leads to predisposition for hemorrhage, while some mutations (most notably Factor V Leiden) predisposes for thrombosis.[43]

Factor V Leiden is named after the city Leiden in Netherlands, where it was first identified in 1994 by Bertina et al.[44] Factor V Leiden thrombophilia is characterized by a poor anticoagulant response to activated protein C (APC) and an increased risk for venous thromboembolism (VTE).[45,46] DVT is the most common VTE, with the legs being the most common site.[45]

During healthy coagulation cascade, prothrombin is converted to thrombin, which in turn activates factors V and VII that further accelerate the cascade to form a blood clot. The coagulation process is normally controlled by circulating antithrombin III, and locally by thrombomodulin, an endothelial receptor that binds thrombin. The thrombin-thrombomodulin complex activates protein C, which subsequently inactivates factor V, thereby inhibiting blood clod formation. However, the mutant form of Factor V, Factor V Leiden, is resistant to inactivation by protein C (APC-resistant) and further induces the coagulation cascade. Consequently, the local protection mechanism against thrombosis is not functioning adequately[46,47] (*See Figure 1)*.

After initiation of anticoagulation therapy with Warfarin we noticed marked improvement in the healing rate of our patient. Nevertheless, we observed inverse relationship between the sizes of his ulcers and INR. Occasional sub-therapeutic INR levels (<1.5) have led to further setbacks in his management. Most likely due to microvascular thrombi formation during inadequate

anticoagulation causing local hypoxemia and subsequent volumetric wounds enlargement. Despite the fact that there are no published reports on the relationship of sub-therapeutic INR level and the size of the venous ulcers, convincing clinical data demonstrates the benefit of anticoagulation in prevention of VTE due to Factor V Leiden mutation.[48]

WOUNDS AND OBSTRUCTIVE SLEEP APNEA

The state of wound oxygenation is a key determinant of healing outcomes. Intermittent hypoxia (IH) or periodic exposure to hypoxia interrupted by return to normoxia or less hypoxic conditions occurs in many different diseases, including sleep-disordered breathing manifested as recurrent apneas.[1] Based on the experimental studies conducted by Prabhakar el al., chronic intermittent hypoxia (CIH) leads to accumulation of reactive oxygen species (ROS) and activation of ROS dependent responses, such as altered carotid body function; elevated blood pressure; enhanced release of transmitters and neurotrophic factors; altered sleep and cognitive behavior; and activation of second-messenger pathways and transcriptional factors.[49]

Moreover, obstructive sleep apnea (OSA) directly affects vascular endothelium by promoting inflammatory and oxidative stress while decreasing nitric oxide availability and repair capacity.[50-52] Vasoconstriction is another cause of local tissue hypoxia that leads to the chronicity of wounds in people with OSA. This is due to endothelin, a potent vasoconstrictor that increases within several hours of untreated OSA,[53,54] likely due to hypoxia.[55]

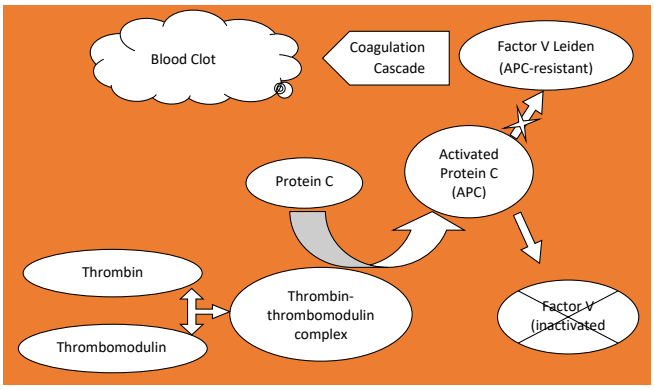
Another interesting fact is the correlation of bilateral lower extremities edema with OSA. Hudgel et al. conducted a three-year investigative research with fifteen patients. All subjects were obese with bilateral pitting leg edema, whose echocardiogram demonstrated pulmonary hypertension only. Despite the small sample size, they were able to trace a correlation between OSA, pulmonary hypertension, and edema. Several possible mechanisms that might lead to edema have been proposed:

- Nocturnal hypoxia activates neuroendocrine system (renin-angiotensin-aldosterone system) and leads to salt and water retention[52,56-58]
- Increased venous and lymphatic hydrostatic pressure due to obesity contributes to swelling
- Secondary pulmonary hypertension caused by intermittent apneic episodes transmits to peripheral venous and lymphatic systems and contributes to edema
- ntermittent right ventricular failure as a result of acute elevations in pulmonary artery pressure during episodes of sleep-associated hypoxia[56]

One of the main treatment criteria of OSA with continuous positive airway pressure (CPAP) is respiratory disturbance index of 5 to 30 events per hour. This should be accompanied by symptoms of excessive daytime sleepiness, impaired cognition, mood disorders, insomnia, or documented cardiovascular diseases: hypertension, ischemic heart disease, or stroke.[59] However, if OSA causes fluid retention and vasoconstriction, then it may be appropriate to expand the indications for treating OSA in patients with accompanying symptoms such as bilateral lower extremity edema, venous stasis ulcers, lymphedema, stasis dermatitis, and cellulitis.[57]

FIGURE 1:

Coagulation Cascade



Chandan Sen conducted sleep screening of 105 patients with chronic wounds and found 51% of them to either have or be at high risk for OSA.[1] Patt et al. carried-out home sleep studies on 50 consecutive patients with unselected chronic lower extremity wounds using an apnea-hypopnea index of 15 events per hour. The results of this study showed the prevalence of OSA to be 57% in patients with wounds.[60]

Much to our surprise, after the initiation of CPAP therapy, pitting edema in our patient had gone down and improvement in ulcer healing was noticed thereafter. Undoubtedly, OSA contributed to the bilateral leg edema and the chronicity of his ulcers. Upon review of the literature, one possible explanation of CPAP benefit in lowering edema in patients with OSA is its effect on aldosterone level. Saarelainen et al. was able to demonstrate that aldosterone and 24-hour mean heart rates decreased during CPAP treatment. Their data also suggested that OSA causes disturbances in blood volume homeostasis which can be corrected by CPAP.[61]

DISCUSSION

Our patient is one of many with chronic, recalcitrant, non-healing wounds. Even though the majority of ulcers are venous, arterial, diabetic, or of mixed etiology, less common conditions should not be missed. This patient is unique and difficult, as the chronicity of his ulcers was perpetuated by multiple problems: morbid obesity, chronic venous insufficiency, lymphedema, hypothyroidism, Factor V Leiden mutation, and OSA.

Despite the prevalence of OSA, by one estimate 1 to 5%[62], the majority of patients with OSA remain undiagnosed. In fact, up to 5% of adults in Western countries are likely to have undiagnosed OSA syndrome, and hence be candidates for treatment.[63] Moreover, approximately one-third of patients with OSA have leg edema at the time of the diagnosis confirmation by polysomnography.[64] Appropriate index of suspicion may aid clinicians to diagnose OSA. Even without traditional signs and symptoms, physical examination findings, such as unexplained pedal edema, recurrent “cellulitis”, and chronic non-healing skin ulcers may facilitate the diagnosis and improve rates of detection of OSA.

Clinical signs of hypercoagulable state, such as repeated thrombophlebitis or unexplained thrombosis, in view of a positive family history of blood clots, are an indication for screening for clotting disorders. Initial laboratory screening tests usually include coagulation profile (PT/PTT/INR), Factor V Leiden mutation, Factor II (prothrombin) mutation, antithrombin III, proteins C and S, lupus anticoagulant, and anticardiolipin.[47]

Finally, consider hypothyroidism as a contributing factor to uncontrolled edema. If this complex metabolic disease treated properly and in a timely fashion, one could reverse the tissue damage, facilitate healing, and improve patient's functional capacity.

AUTHOR DISCLOSURES:
No relevant financial affiliations

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BRIEF REPORT

Myasthenia Gravis

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KEYWORDS:

Acetylocholine

Lipoprotein receptor-related protein

Muscle Specific Kinase

Myasthenia Crisis

Myasthenia Gravis

Myasthenia gravis is an autoimmune disorder affecting 36,000 – 60,000 Americans. This article reviews the incidence, presentation, immune system markers and various treatment options for this illness. Family physicians must be aware of this disorder as they may be the first health professional contact for patients experiencing symptoms.

INTRODUCTION

Myasthenia Gravis (MG) is a neuromuscular autoimmune disorder characterized by muscle weakness and fatigability. It often presents with the ocular manifestations of ptosis and diplopia, however, it can include difficulty swallowing, generalized muscle fatigability, and respiratory muscle weakness. The disorder is caused by autoantibodies that target the neuromuscular junction, specifically at the acetylcholine receptor or related molecules described below. The prevalence of MG is 14 – 20 per 100,000 population in the US with approximately 36,000 – 60,000 total cases at any given time. Formerly it occurred twice as often in women, in whom the peak onset is during childbearing years. Men have a peak onset at age 70 and with the increase in late onset MG, men are now affected more often, usually after age 50. The symptoms can range from ocular weakness, to mild generalized symptoms and to severe symptoms leading to respiratory failure requiring intubation and mechanical ventilation *(Myasthenia Crisis)*.[1]

In 2010, Carr et al estimated an annual incidence of 9.4 cases per million person years from a variety of international studies.[2] The current incidence in the United states in not available in the literature. The antibody most commonly present in MG targets the acetylcholine receptor (anti-AChR) which approaches 100% specificity for the disease and occurs in 80% of MG patients.[3] Antibodies to muscle specific kinase (MuSK) are present in 4% of patients– including 40% of those with generalized MG. Another 2% have antibodies to lipoprotein receptor-related protein 4 (LRP4).[4] Most authors consider patients without AChR antibody seronegative, while others refer to patients without antibodies to AChr, Musk or LRP4 as seronegative. Patients with generalized Myasthenia Gravis are more likely to have MuSK or AChR. Some patients may have other less common antibodies (titin, agrin, striated muscle).[5,6,7] Positive antibody tests in patients with symptoms of MG are diagnostic. This variation in antibodies creates a dilemma in diagnosis and prognosis, given the additional variability in presentation and outcomes. Presently studies are being undertaken to discover if treatment should be tailored to the identified antibody type.

Myasthenia Crisis is a severe form of the illness in which respiratory muscles are affected, leading to periods of decompensation requiring respiratory support including intubation and mechanical ventilation or noninvasive ventilatory support to avoid intubation.[8] Myasthenia Crisis usually occurs in patients with generalized MG within the first two years following diagnosis. Patients with Myasthenia Crisis may have frequent admissions to the intensive care unit and have a poorer quality of life (QOL) score.[10,11,12]

The Myasthenia Gravis Foundation of America MGFA clinical classification for MG identifies patient characteristics as follows:

DIAGNOSIS

Myasthenia Gravis most often presents with symptoms of diplopia, from extraocular muscle weakness, and ptosis. Therefore, the physician must have a level of familiarity with the disease and clinical suspicion to diagnose the patient. Patients with these ocular findings without other causes should raise the suspicion of MG. Many patients complain only of muscle fatigue, a complaint with which physicians are commonly confronted. Finding an etiology becomes more difficult in the MG patient due to the intermittent nature of symptoms and findings, making a detailed patient history the most important aspect of the encounter. The hallmark of the disease is patient reports of intermittent weakness and fatigue of voluntary muscles, which become worse with activity. Periods

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TABLE 1:

MGFA Clinical Classifications[13,14]

Class I	– Any ocular weakness – May have weakness of eye closure – All other muscle strength is normal
Class II	– Mild weakness affecting other than ocular muscles – May also have ocular muscle weakness of any severity
Class IIa	– Mild weakness predominantly affecting limb, axial muscles, or both – May also have lesser involvement of oropharyngeal weakness
Class IIb	– Mild weakness predominantly affecting oropharyngeal respiratory, muscles or both – May also have lesser or equal involvement of limb, axial muscles or both
Class III	– Moderate weakness affecting other than ocular muscles – May also have ocular muscle weakness of any severity
Class IIIa	– Moderate weakness predominantly affecting limb, axial muscles, or both – May also have lesser involvement of oropharyngeal muscles
Class IIIb	– Moderate weakness predominantly affecting oropharyngeal, respiratory muscle or both – May also have lesser or equal involvement of limb, axial muscle or both
Class IV	– Severe weakness affecting other than ocular muscles – May also have ocular muscle weakness of any severity
Class IVa	– Severe weakness predominantly affecting limb and/or axial muscles
Class IVb	– Severe weakness predominantly affecting oropharyngeal, respiratory muscles or both – May also have lesser or equal involvement of limb, axial muscles or both
Class V	– Defined by intubation, with or without mechanical ventilation, except when employed during routine post-operative management. The use of a feeding tube without intubation places the patient in class IVb

of exacerbation followed by remissions are common. Additional symptoms, although less common, may include facial paresis, dysphonia, and neck weakness. The weakness is not associated with sensory abnormalities, resulting in a normal sensory exam. Patients with more advanced disease can have bulbar symptoms (difficulty swallowing, dysarthria, slurred speech) or generalized symptoms (extremity and respiratory muscle weakness) on presentation. A patient with findings of fatigability and any of these symptoms should be tested for MG.[15,16] The differential diagnosis in patients presenting with these findings includes amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS) and myasthenic syndromes; Lambert-Eaton Syndrome and toxic and drug induced myasthenic syndromes from botulism, Penicillamine, chloroquine, hydroxychloroquine.[17]

Although, not studied in a large cohort, case reports suggest the "ice pack test" may help with the diagnosis. This test is easily performed in the office and is accomplished by placing an ice pack over an affected eye for 2 minutes.[18] Improvement in the ptosis suggests a diagnosis of myasthenia gravis. This test has limited utility in diagnosing MG, since patients may not have ptosis at the office visit.

Laboratory testing is the primary method of diagnosing MG. Over 80% of MG patients have antibodies to the Acetylcholine receptor at the neuromuscular junction and a positive AChR Binding Antibody test. Additionally, 30% of generalized MG patients and 95% of MG patients with thymoma test positive for muscle specific tyrosine kinase antibodies (MuSK).[19] Finding these antibodies in the presence of symptoms of fatigability provides a diagnosis. Patients without AChR or MuSK antibodies (double seronegative) create a more difficult diagnostic challenge. Recently Lipoprotein receptor – related protein 4 (LRP4) was shown to be positive in a subset of seronegative patients.[20] Single-fiber Electromyography (SFEM) and Repetitive Nerve Stimulation (RNS) provide additional diagnostic options.[21] Clinically, the use of edrophonium hydrochloride, the "Tensilon Test", through its ability to briefly alleviate symptoms in patients with MG can lead to the diagnosis. Patients with antibodies to Acetylcholine receptors should be screened for thymoma, although there is a recent case report of thymoma occurring in a patient without this antibody. *Figure 1* represents the diagnostic workup for MG.

TREATMENT

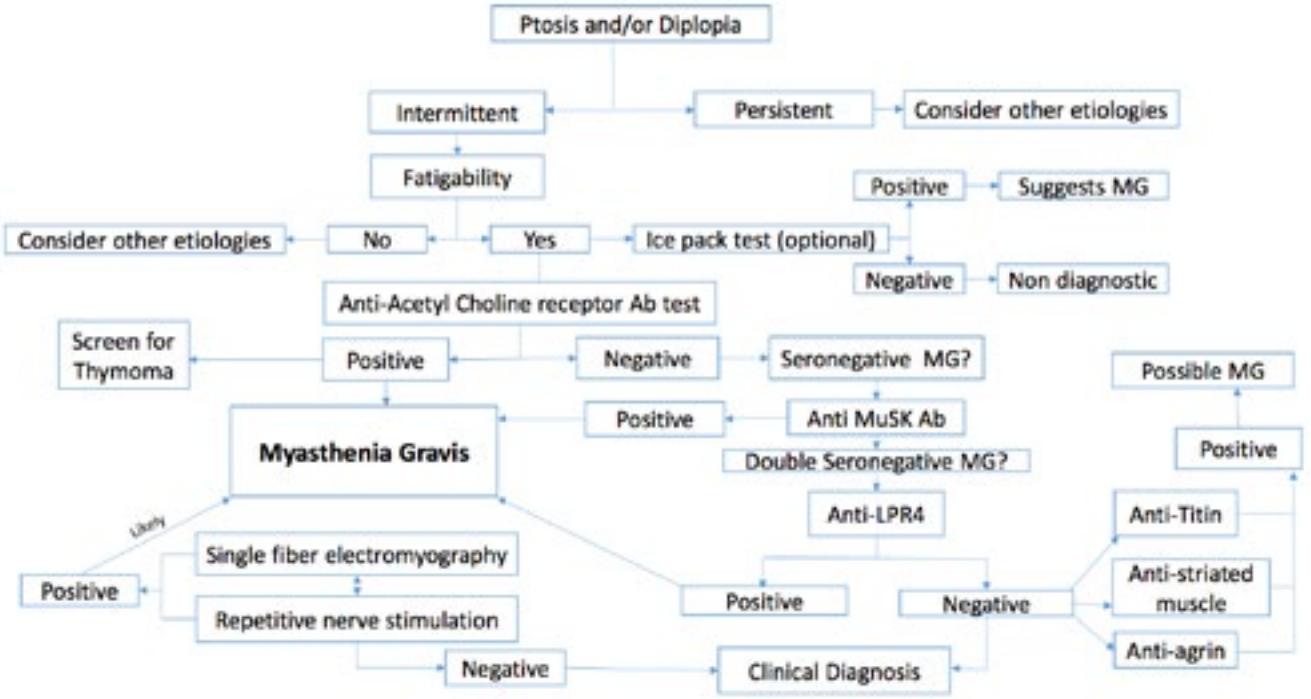
Once diagnosed, treatment depends on severity of symptoms and response to standard regimens. Most patients are initially started on acetylcholinesterase inhibitors, and /or corticosteroids to control symptoms.[23] Patients with persistent debilitating symptoms require long-term immunosuppressive agents, such as azathioprine, cyclosporine,[24,25] tacrolimus,[26,27] Methotrexate,[28] or mycophenolate mofetil,[29] all of which have been investigated with varying results. Still others with generalized refractory MG, particularly those with Myasthenia Crisis, may require cyclophosphamide,[30] rituximab,[31] and eculizumab,[32] and intravenous IVIg or plasma exchange (PLEX) for maintenance or crisis.[33,34] Select patients may also undergo thymectomy.[35,36] More recently, the use of autologous stem cell transplantation has been reported with some success, although the precise mechanism by which this alters the course of MG is unknown.[37,38,39,40] Various treatments for MG are listed in *Table 2*.

CONCLUSION

Because of the low prevalence of MG, large double blind studies of these treatments are lacking. Additionally, criteria for positive outcomes are variable.[41] Much of the guideline information is the result of studies with small cohorts and is based on expert opinion. Therefore, the treatment of the patient with myasthenia gravis requires the input of experts in the field. Often, the family physician will be the first contact for the patient and can play an integral role in the initial diagnostic workup for this disease. This is of importance since these patients often have a delay in diagnosis.

FIGURE 1:

Diagnosis of Myasthenia Gravis



The specialty centers available to patients, particularly helpful for those with generalized and refractory myasthenia gravis, are often far from the patient's home. Frequent exacerbations can be physically and emotionally debilitating for the patient and require expedited office and hospital care. The family physician should participate in team-based care of these patients, which often includes input from neurology, pulmonology, respiratory therapy, physical therapy, and behavioral health. As the patient's primary provider of health care, the family physician can be a source of emotional support and provide prompt treatment of acute events resulting from MG. Additionally, the family physician must ensure that, like other major diagnoses, an MG diagnosis does not result in neglect of routine and preventive medical care.

AUTHOR DISCLOSURES:

No relevant financial affiliations

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TABLE 2:

TREATMENT	USE	MECHANISM	ONSET OF ACTION	ADMINISTRATION
CORTICOSTEROIDS				
Pyridostigmine Bromide	Acute and chronic treatment of Ocular and generalized MG	Increases acetylcholine at the synaptic cleft by inhibiting acetylcholinesterase	Minutes	Oral tablet, syrup IM injection
Intranasal Neostigmine			Minutes	Intranasal Spray
CORTICOSTEROIDS				
Prednisone	Initial and chronic treatment of ocular and generalized MG	Unclear mechanism in MG. Reduces leukocyte activity (recruitment, migration) and production of cytokines.	Weeks. Possible exacerbation in first 14 days	Oral
Prednisolone/ Methylpredinsolone				oral, IV
IMMUNOSUPPRESSANTS (LONG TERM)				
Azathioprine	Long term immunosuppression for generalized and refractory MG	Blocks purine synthesis in lymphocytes	3 months	Oral
Cyclosporine		Calcineurin Inhibitor	12 months	Oral
Tacrolimus		Calcineurin Inhibitor, T-cell supression	52 weeks	Oral
Mycophenolate Mofetil		Inhibits inosine monophosphate dehydrogenase in activated lymphocytes	Not superior to Placebo	Oral
Cyclophosphamide		Alkylating agent for guanine base of DNA	3 weeks to 3 months	Oral, intravenous
PLASMA EXCHANGE (PLEX)				
Plasma exchange	Generalized, severe and Myasthenia Crisis	Clears plasma of auto-antibodies	Hours to days	Procedure
INTRAVENOUS IMMUNOGLOBULIN (IVIG)				
IVIg	Generalized, severe MG and Myasthenia Crisis	Catabolizes IgG, suppresses antibody production	Hours to days	infusion
MONOCLONAL ANTIBODY				
Eculizumab (Solaris®)	Generalized refractory MG	Blocks activation of complement by binding to C5 preventing cleavage to C5a and C5b	16 weeks	IV infusion
Rituximab (Rituxan®)		Depletion of B lymphocytes	2 weeks	
THYMECTOMY				
Thymectomy	MG patients with thymus hyperplasia or suspected thymoma	Incompletely understood, but may relate to anti AChR B-Cell lymphocyte persistence in thymus	Months to years	Surgical
Stem Cell Transplant	Severe MG refractory to other treatments	Unknown	Unknown	IV Infusion

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Hyperpigmented Rash in an Obese 13-year-old Male

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A 13-year-old obese (BMI >95% for age) African American male presented with dark brown papules on the trunk that had been present for several months. The rash began on the central chest and spread to involve the upper and lower back, neck, and flanks. The patient denied pain, pruritus, and burning, and was only concerned about the pigment change. He had tried switching to a mild soap but the lesions continued to progress. Physical examination revealed dark brown warty papules coalescing into plaques circumferentially around the neck, upper and lower central back, flanks and central chest *(Figure 1)*. A potassium hydroxide (KOH) preparation was performed in the office and was negative.

QUESTION

What is the most likely diagnosis?

A. Tinea versicolor

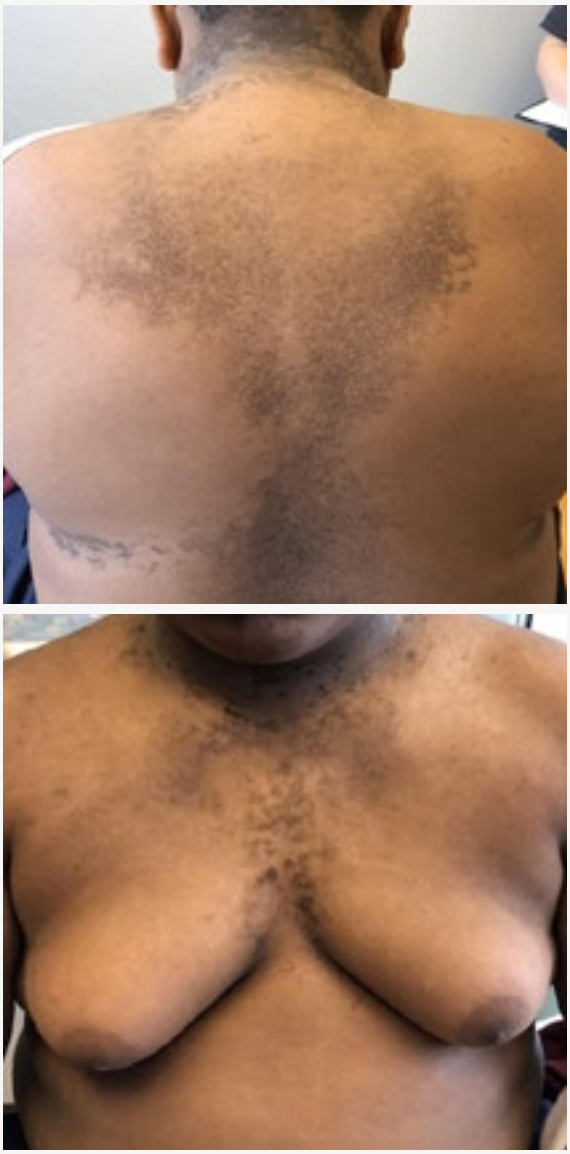
B. Acanthosis nigricans

C. Seborrheic dermatitis

D. Confluent and reticulated papillomatosis

E. Darier disease

FIGURE 1:



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ANSWER:

What is the most likely diagnosis?

Correct Answer: D) Confluent and reticulated papillomatosis

DISCUSSION

CARP is an uncommon dermatologic condition characterized by the presence of small, hyperpigmented, hyperkeratotic or verrucous papules that coalesce to form plaques with a peripheral reticulated appearance and preserved skin markings.[1,2] Onset is usually at puberty; the eruption is generally asymptomatic, begins on the neck, chest or upper back and spreads centrifugally. A KOH preparation to rule out fungus should be performed, which will be negative, and a skin biopsy can be used when the diagnosis is unclear, which will reveal papillomatosis with mild acanthosis and hyperkeratosis.[3] The differential diagnosis will often include acanthosis nigricans (AN), tinea versicolor and seborrheic dermatitis.[1]

The pathophysiology of CARP is uncertain; however, it's thought to be due to an endocrine disturbance, abnormal keratinocyte maturation, an abnormal host response to bacteria or fungi, or possibly hereditary. The leading theory is that CARP is a disorder of keratinization that results in hyperproliferation.[2] This has been supported with the histological appearance showing increased transition cell layer and lamellar granules in the stratum granulosum as well as the lack of consistently identified bacteria.[2]

Both CARP and AN appear similar, however CARP often begins in the central chest or interscapular areas and will nearly always involve the trunk; while AN favors the axilla and neck and is rarely found on the trunk.[4] Both are often observed in overweight or obese patients. Tinea versicolor is mildly pruritic and will often have a fine scale present. A positive KOH with hyphae and yeast in tinea versicolor will differentiate between the two. Seborrheic dermatitis often has an underlying red color in addition to greasy scale on top and is found in areas rich in sebaceous glands, such as the face, scalp, neck, upper chest and back.[5] Darier disease is an autosomal dominant condition exhibiting greasy brown hyperkeratotic papules in a seborrheic distribution.[6] Darier disease can be differentiated from CARP by cobblestoning of the oral mucosa, v-shaped notching or parallel red and white bands of the nails and palmoplantar pitting.[1]

Current first line treatment for CARP is minocycline 100mg BID for six weeks.[7,8] In patients who cannot take minocycline, such as those with allergies or who are pregnant, Azithromycin has been used with some success. CARP has also been shown to respond to isotretinoin, however, minocycline is still the preferred agent due to its more favorable safety profile. Topical therapies such as topical retinoids, urea, calcipotriol and tacrolimus have also been used with some success.[6]

AUTHOR DISCLOSURE:
No relevant financial affiliations

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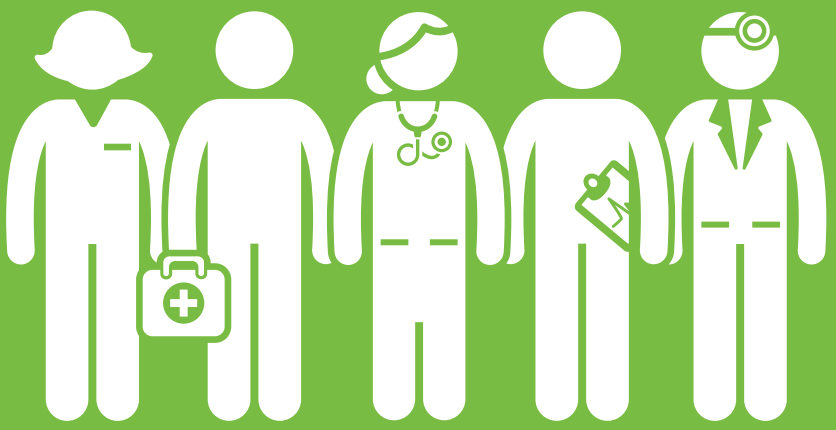
TEAMS WORK



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HOW WILL I KNOW IF I HAVE AN MRSA INFECTION?

Varsha Kishore, DO, FACOFP

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

WHAT IS MRSA?

Methicillin-Resistant Staphylococcus Aureus or MRSA is a type of bacteria (germ) that can cause a very serious and difficult to treat infection. People carry many types of bacteria in their body and on their skin. The immune system is usually able to control these bacteria, so they do no harm. About 1 in 3 people carry the Staphylococcus aureus "Staph" bacteria on their skin. In these people, the bacteria usually cause no problems. However, if they get a cut or scrape, this can serve as an opening and home for infection. Initially, most of the germs were sensitive to penicillin. In the 1950s, many infections became resistant to penicillin and methicillin (a related drug developed to treat these germs). Thus, the term methicillin-resistant Staphylococcus aureus (MRSA) was derived.

HOW DO I KNOW IF I HAVE AN MRSA INFECTION?

Many people carry MRSA on their skin without knowing it. This is called being "colonized." You can pick up the germ by touching a person who has MRSA on his or her skin, being nearby when a person with MRSA breathes, coughs, or sneezes, or by touching a table, handle, or other surface that has the germ on it.

If you get a MRSA infection, you can develop some skin problems. You might have a red, tender lump, and it might ooze pus. On the other hand, you can have a cluster of bumps that look like pimples or insect bites. If the germ is on your skin and you cut yourself or have another injury, you can become infected. If the infection gets into the blood, it can give you a fever or make you feel tired or sick.

If you are concerned about MRSA, please see your osteopathic family physician. If your physician thinks you may have MRSA, he or she can take a swab/sample from your skin and check it for bacteria. In some cases, blood tests, x-rays, and other tests might be needed as well.

MEDICAL CARE & TREATMENT OPTIONS

Your physician can give you special antibiotics to treat your infection. If you are treated with antibiotics, it is very important that you follow the directions exactly. Take all the pills you are given, even if you feel better before you finish the pills. If you do not take them all, the bacteria could come back even stronger.

In addition to antibiotics, your healthcare provider may drain the infected area by inserting a needle or making a small cut in the skin. This is done to reduce the amount of infected material (pus), which will help the tissue to heal. You should not try to drain a boil or pimple on your own because this could worsen the infection.

Bad MRSA infections are usually treated with an intravenous (IV) medication. Your doctor may continue the IV antibiotic until your condition improves.

SOURCE(S): *Red Book Online*, *Infectious Disease Society of America*, *UptoDate*

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CHRONIC ABDOMINAL PAIN

Scott Brown, DO; Alissa Cohen, DO

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

Abdominal pain is a very common concern for patients of all ages and may become chronic if your symptoms fail to improve over a period of several months. Abdominal pain can be due to many causes, including constipation, a urinary tract infection, gallbladder disease, or heartburn, among others. Abdominal pain may also be functional. Functional pain does not have a specific cause but is often related to stress or other changes in your mood. A diagnosis of functional abdominal pain generally comes after your doctor has completed testing to rule out other causes.

COMMON CAUSES OF ABDOMINAL PAIN:

Below is a list of common causes of abdominal pain organized by pain location. Note there are many other causes besides those listed, and sometimes pain may be due to a reason from a different region of the abdomen.

Common Causes of Abdominal Pain by Location

Right Upper Quadrant Liver Gallbladder	**Upper Middle Abdomen** Stomach Pancreas	**Left Upper Quadrant** Spleen Pancreas
Right Mid Back/Flank Kidney Muscles Ribs	**Belly Button/Lower Abdomen** Appendix Prostate Uterus	**Left Mid Back/Flank** Kidney Muscles Ribs
Right Lower Quadrant Appendix Ovary	**Diffuse/All Over** Small Intestine Large Intestine	**Left Lower Quadrant** Ovary Large Intestine

MONITOR YOUR SYMPTOMS:

It is important that you continue to monitor your symptoms closely and report these findings to your doctor. Many patients find journaling helpful for this. Specifically, take note of what you ate, what makes your symptoms better and worse, and look out for concerning warning signs and symptoms. These concerning symptoms include weight loss, fever, blood in your stool, vomit, or urine, a yellowing of the skin or eyes called jaundice or difficulty swallowing or going to the bathroom. If these symptoms occur, please contact your doctor's office for further recommendations.

OMT TREATMENT OPTION:

Fortunately, your Osteopathic Family Physician has received additional training to address many causes of abdominal pain with a hands-on treatment known as Osteopathic Manipulative Treatment, or "OMT." These treatment techniques are safe and generally well tolerated by patients and can help improve your symptoms along with other treatment methods. If you are interested in this treatment, please ask your doctor about whether OMT could be beneficial for your pain.

SOURCE(S): *Up to Date; DynaMed; Osteopathic Family Physician.*

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HEPATITIS C – WHAT TO LOOK FOR

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The Hepatitis C virus is a leading cause of chronic liver disease. According to the World Health Organization (WHO), there are about 71 million people with chronic hepatitis C infection. There are about 2.4 million people in the US according to the US Centers for Disease Control & Prevention.

WHO IS AT RISK FOR GETTING HEPATITIS C?

Exposure to re-used or unsterilized needles:

- Current or former needle drug users, including those who injected only once several years ago
- Prisoners
- People who have had tattoos or piercings

Exposure to poorly screened blood products:

- People who received blood transfusions, blood products or solid organ transplants before 1992

Exposure to HCV:

- People with known exposures to HCV, such as health care workers after needle sticks involving HCV-positive blood
- Chronic hemodialysis patients
- People with HIV infection
- People with sexual partners who are HCV-infected
- Children born to HCV-positive mothers

SYMPTOMS OF HEPATITIS C

Most often, an HCV infection does not have any symptoms. After exposure to HCV, it may take two weeks to 6 months for symptoms to appear.

COMPLICATIONS OF HEPATITIS C

Liver failure is known as cirrhosis and liver cancer. 15-30% of those with chronic HCV infection are at risk of developing cirrhosis within 20 years. Around the world, almost 399,000 die from cirrhosis or liver cancer.

HOW IS HEPATITIS C TRANSMITTED?

The most common way is exposure to infected blood through unsafe needles while using illicit drugs or a transfusion of unscreened blood. In the US, getting hepatitis C due to contaminated blood products has dropped due to better technology in blood screening. However, individuals born between 1945-1965 or the "Baby Boomers" is a group that could have been exposed to contaminated blood when less advanced methods were used.

The US Preventative Service Task Force (USPSTF) recommends a one-time screening for HCV infection to adults born between 1945 and 1965 and recommends screening for those at high risk for infection.

PREVENTATIVE MEASURES

There is no vaccine for hepatitis C so preventing an HCV infection depends upon reducing the risk of coming in contact with the virus. Notify your doctor if you have any risk factors for HCV exposure. Screening is one of the best ways you can help prevent long-term complications of hepatitis C.

MEDICAL CARE & TREATMENT OPTIONS

Because HCV infection often does not have symptoms, persons with HCV may not know they are infected and may live with it for several years until symptoms develop. Screening for HCV allows for early detection and treatment for hepatitis

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SOURCE(S): *U.S. Centers for Disease Control & Prevention; World Health Organization; U.S. Preventative Services Task Force; Up-to-Date*

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