# ACOOG

## American College of Osteopathic Obstetricians and Gynecologists

"The American College of Osteopathic Obstetricians and Gynecologists is committed to women's health through the Osteopathic and holistic practice of obstetrics and gynecology.

Year of 2023 Summer Edition

Inside This Issue



# President's Message

Mark LeDuc, DO, FACOOG, (Dist.)

To My ACOOG Family,

I hope this message finds you all well.

It remains a great honor to represent ACOOG as your President.

I would like to take this opportunity, to thank Dr. Catherine Bernardini for her impeccable leadership and the positive influence that she has provided for our college. She has become not only an incredible mentor, for me but an even better friend during our involvement with ACOOG and AOBOG. Also, I need to thank Dr. Michael Geria for his continued guidance and leadership of ACOOG as the Executive Vice President/ CEO. Dr. Geria and President-Elect Bill Bradford, DO, will strongly represent ACOOG at the AOA's Annual Business/ House of Delegates Meeting in Chicago in July.

It was great to see the College together again in San Diego. The weather wasn't always perfect, but the environment in the conference center, with all the smiles, was beautiful. A special thanks goes to the conference chairs, Shania Seibles, DO, JD, and Jennifer Caruso, DO, for a terrific educational program.

As I sit here and try to put some ink on the paper, I am casually staring outside. Here in the Midwest, the seasons are changing. The snow has nearly melted. We have temperatures in the low 80's and in the same day, we experience rain and then snow. The constant ebb and flow of the seasons is much like our lives.

As providers of women's healthcare, our days are often like the changing weather and seasons. We are experiencing an interesting time. The last three years have been difficult for all of us, navigating COVID as well as the changing social and political landscape of our specialty.

Even with this ever-changing landscape, the one constant that we can rely on is family and friends. ACOOG is family. We have all negotiated the rigors of medical education and the treacherous learning curve of residency. This is truly a bond that cannot be taken from us. Within every family, there are quarrels and disagreements. I am reminded by my wife that most misunderstandings are due to a lack of communication. I would like to stress that, as ACOOG members, we may view some things differently than others. However, I can assure each and everyone of you that ACOOG will continue to be guided by our mission (which identifies our organization's purpose), our vision (aspirational goals for the success of our members), our values (guiding principles) and goals

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*President's Message*

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(strategies to achieve our goals). If there is ever a concern that we may be deviating from our guiding principles, please feel free to contact me directly!

As I stated in my presidential address, during these difficult times, we need each other. I can promise you that ACOOG will continue to be our mooring buoy, and that it will provide a strong and steadfast anchor no matter how rough the waves may become.
I hope that all of you have a great summer. I look forward to seeing as many of our members as possible at the Fall Conference from Sept. 28-Oct. 1, 2023, in Atlanta, GA.

Sincerely,

Mark M. LeDuc, DO, FACOOG (Dist)
ACOOG President, 2023-2024

# Vice President's Message
## from the Executive's Desk

Michael J. Geria, DO, FACOOG, (Dist.)

Summer is here!

COVID is nearly behind us and things are sort of getting back to normal. The Annual Meeting in San Diego was a great success. One very important thing that we have learned is that distance really does make the heart grow fonder and that even though we were physically apart, COVID could not weaken the bonds that unite us as members of this college. Our annual conference in San Diego, California was certainly very special. As I always do in these messages, I will extend many thanks to the program chairs for this year's annual meeting. Shania Seibles, DO, FACOOG, and Jennifer Caruso, DO, FACOOG, prepared an outstanding curriculum for this year's annual conference. I also extend an extra thank you to Cecilia Banga, DO, FACOOG and her outstanding Continuing Medical Education Committee (CME). I would like to recognize the ACOOG staff. Their dedication and skills during this past year have been outstanding. The ACOOG continues to be committed to providing the highest quality CME and is proud to have maintained ACCME accreditation.

Once again, thank you to our incredible staff, Jimmie Evans, Andy Crim, Martha Prud'homme, Nnamdi Ibegbu and Beth Roach. We are truly fortunate to have this exceptional group of individuals as part of our organization and I always take this opportunity to recognize them and thank them. Congratulations to our new president, Mark LeDuc, DO, FACOOG(Dist) and our newest member of the Executive Committee, Vice President Ashley Hood, DO, FACOOG(Dist).

Congratulations go out to all our graduating resident members and especially to those residents who have served on ACOOG committees, Kimberly Agbo, DO, Government Affairs Committee, Nathan Fairbourn, DO, Resident Representative to the Board of Trustees, Antoinette Kitch, DO, History and Traditions Committee, Seth Minton, DO, Membership and Promotions Committee, and Amanda Mirmanesh, DO, Continuing Medical Education Committee. Thank you for your service to the college, and again, congratulations. I am sure that they will stay involved in our organization. We wish all the best in their future endeavors for all our graduating residents.

Medical student education remains a top priority for our organization. The National Student Society (NSS) of the ACOOG continues to grow. The VPROF program is still active, albeit virtual. Even though it is virtual, it still attracts many

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*Vice President's Message*

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student members to the educational offerings. This past fall, we welcomed the new officers to the NSS, NSS-ACOOG President Zoe Beausoleil, OMS-4 PCOM, NSS-ACOOG Vice-President, Priya Thakur, OMS-3 KCU, and NSS-ACOOG Secretary-Treasurer, Kaitlyn Stenberg, OMS-4 RVU.

Women's reproductive health continues to be at the forefront, and as obstetricians and gynecologists, we must provide the highest quality of care possible to our patients. The ACOOG stands committed to our mission, vision, and values. Our organization remains healthy and dynamic because of you, the members, and the volunteers.

Have a wonderful and safe summer. Take care of your families, yourselves, and each other. I look forward to seeing all of you in the fall.

Sincerely,

Michael J. Geria, DO, MS, FACOOG(Dist)
Chief Executive Officer

# CME Article

## DKA in Pregnancy

**CME Credit Available**

This activity offers
0.75 Category 1-B AOA
0.75 *AMA PRA Category 1 Credits*™

**About**

Diabetic ketoacidosis (DKA) is a life-threatening condition that impacts 5-10% of pregnancies in patients with pre-existing type 1 diabetes. Importantly, clinicians must also recognize that DKA can also affect pregnancies in patients with type 2 diabetes or, in rare cases, gestational diabetes.

**Faculty**

Melisa Lott, DO

Dr. Lott is a board-certified Maternal-Fetal Medicine Physician and Obstetrician-Gynecologist with an extensive background in medical education, research, and clinical practice. She currently serves as an Adjunct Faculty at Midwestern University Illinois, and Maternal-Fetal Medicine Physician at Access TeleCare and Advocate Medical Group. Notably, Dr. Lott founded and directed the Center for Excellence for Diabetes Care in Pregnancy at Advocate Lutheran General Hospital. She completed her Doctor of Osteopathic Medicine at Midwestern University and further specialized in Maternal-Fetal Medicine through a fellowship at Geisinger Health System.

Dr. Lott has also made significant contributions to medical literature, with several published research articles, and has shared her expertise through numerous invited lectures and teaching activities. Her dedication to patient care is underscored by her impressive range of procedural skills, from general obstetrics to complex fetal interventions.

**Learning Objectives**

Those participating in this activity will receive information that should allow them to:

1. Evaluate and diagnose DKA in pregnancy
2. Apply appropriate treatment protocols for DKA in pregnancy

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3. Monitor DKA recovery and post-treatment status

**Conflict of Interest Disclosures**

ACOOG requires each planner and presenter to identify all conflicts of interest, and mitigates risk of bias using a series of strategies for relevant conflicts. Unless otherwise noted below, the ACOOG, ACOOG staff and planners for this activity have no relevant financial relationships to disclose.

Dr. Lott has no relevant relationships with ineligible companies to disclose.

**Release & Review Date:**

This activity is valid between June 1, 2023 and December 31, 2023.

**System Requirements**

An internet connected device (computer or mobile device) with high speed access is required. It is designed to work on most popular web browsers. JavaScript and cookies should be enabled in your browser in order for the activity to properly work. If you're experiencing technical issues, please update your browser, and clear your browsing history, cookies, and cache. This often solves most common technical issues.

**Requirements for Successful Completion**

To successfully complete this activity, participants must:

1. Complete the pre-test
2. Read the text-based content
3. Pass the post-test (70% or greater)
4. Complete the activity evaluation
5. Claim credit

A certificate will be immediately available.

**Commercial Support**

This activity is not commercially supported.

**CME Accreditation**

The American College of Osteopathic Obstetricians and Gynecologists is accredited by the American Osteopathic Association to provide osteopathic continuing medical education for physicians.

The American College of Osteopathic Obstetricians and Gynecologists is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

**CME Credit Designation**

The American College of Osteopathic Obstetricians and Gynecologists designates this program for a maximum of 0.75 AOA Category 1-B credits and will report CME and specialty credits commensurate with the extent of the physician's participation in this activity.

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The American College of Osteopathic Obstetricians and Gynecologists designates this enduring activity for a maximum of 0.75 *AMA PRA Category 1 Credits*™*.*

Physicians should only claim credit commensurate with the extent of their participation in the activity.

**ACOG Cognate Credit(s)**

The American College of Osteopathic Obstetricians and Gynecologists designates this activity for Category 1 College Cognate Credits. Maximum Cognates are equal to the number of maximum *AMA PRA Category 1 Credits™*. A reciprocity agreement with the AMA exists that allows AMA PRA Category 1 CreditsTM to be equivalent to ACOG Cognate Credits.

**NPs, PAs & CNMs**

The American Academy of Nurse Practitioners Certification Board (AANPCB) recognizes activities approved for Category 1-A credit through the American Osteopathic Association and Category *1 AMA PRA Category 1 Credits*™ as providing advanced practice CE content hours for applicants seeking renewal through continuing education credit.

The National Commission on Certification of Physician Assistants (NCCPA) recognizes activities approved for Category 1-A credit through the American Osteopathic Association and *AMA PRA Category 1 Credits*™ as Regular Category 1 CME for national certification maintenance.

The Certificate Maintenance Program of the American Midwifery Certification Board accepts *AMA PRA Category 1 Credits*™ to satisfy its contact hours requirement.

All NPs, PAs, CNMs and other health professionals participating in this activity will receive a certificate of completion commensurate with the extent of their participation in the activity. ACOOG strongly recommends all non-physician health professionals check with their certification/licensing organizations to confirm credit reciprocity.

**Disclaimer**

This activity is offered by the American College of Osteopathic Obstetricians and Gynecologists (ACOOG) for educational purposes only. Every patient case is different, and physicians must rely on their medical knowledge, experience, and relationships with patients to make clinical decisions. This material is not intended to represent the best or only methods or procedures appropriate for the condition discussed; rather the material is intended to present an approach, view, statement or opinion of the authors or presenters, which may be helpful, or of interest to

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other practitioners. Physician judgment must remain central to the selection of diagnostic tests, management strategies, therapy options, and follow-up of a specific patient's medical condition.

**Grievances**

Any registrant finding evidence that the continuing medical education program presented is inappropriate with regard to facilities, materials, content, or observes any unacceptable promotion by a commercial interest in the same room as the educational activity, whether by company representative or presenter, may submit a grievance in writing to ACOOG, PO Box 17598, Fort Worth, TX 76102. Unresolved issues regarding this activity will require a formal written complaint to the AOA Division of CME, 142 East Ontario Street, Chicago, IL 60611.

**Privacy Policy**

This activity complies with ACOOG's privacy policies.

**Data Use**

Data collected as part of this activity may be analyzed as part of educational research to study the effectiveness of educational interventions on health care, population health, health care providers and others, or to identify additional needs and gaps for future interventions.

**Refunds**

Refunds are not available for this educational product.

CLAIM CME CREDIT

# DKA in Pregnancy

Diabetic ketoacidosis (DKA) is a life-threatening condition that impacts 5-10% of pregnancies in patients with pre-existing type 1 diabetes. Importantly, clinicians must also recognize that DKA can also affect pregnancies in patients with type 2 diabetes or, in rare cases, gestational diabetes.

The pathophysiology of DKA in pregnancy is unique in that the hormonal milieu of pregnancy leads to increased insulin resistance and a relative state of "accelerated starvation." While this is noted to be most evident in the third trimester, the challenges of nausea/vomiting and decreased oral intake during the first and second trimesters also can have a significant impact on blood sugars and insulin management.

*The risk factors for DKA include new-onset undiagnosed diabetes, pre-gestational type 1 diabetes, infection such as upper respiratory infection or urinary tract infection, steroids or beta-mimetics such as terbutaline.*

Presenting signs and symptoms can be challenging to elicit in the pregnant patient, as complaints such as fatigue or nausea/vomiting are common pregnancy symptoms. Diagnostic signs of DKA in pregnancy include hyperglycemia, acidosis, positive serum ketones, and often an anion gap >12. Importantly, the patient may not be as profoundly hyperglycemic as the non-pregnant patient with DKA – DKA can occur with mildly elevated blood sugars 180-200 mg/dL, and cases of euglycemic DKA have been reported.

The risk factors for DKA include new-onset undiagnosed diabetes, pre-gestational type 1 diabetes, infection such as upper respiratory infection or urinary tract infection, steroids or beta-mimetics such as terbutaline. The administration of steroids, such as antenatal corticosteroids, also lends an increased risk of DKA.

The symptoms of DKA, including nausea, vomiting, abdominal pain, and occasionally altered mental status, are like those of the non-pregnant patient. Dehydration may also lead to contractions or cramping, which may be the initial presenting symptom. The mainstay of management is aggressive IV fluid hydration, administration of insulin, correction of electrolyte abnormalities and, most importantly, identification and treatment of the underlying cause.

Initial evaluation of the gravid patient with suspected DKA involves a careful history and physical examination, assessment of vital signs, and fetal monitoring if the patient is at a viable gestation. If the patient is early in

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gestation, ultrasound or bedside Doppler to evaluate for fetal viability can be considered. Laboratory evaluation is an important component of confirming the diagnosis. The initial recommended laboratory evaluation includes a complete blood count (CBC), basic metabolic panel (BMP), serum ketones such as beta-hydroxybutyrate, urinalysis for ketones and/or evidence of infection, urine culture, and arterial blood gas. Further assessment will depend on the patient's presentation, and consideration can be given to other imaging modalities, such as a chest x-ray for suspected pneumonia. Evaluation of an insulin pump and its components for malfunction is also important, if applicable.

## IV Hydration

Once DKA is diagnosed, aggressive treatment with IV hydration and insulin are paramount. Careful attention to electrolytes is necessary, as hypokalemia may occur if potassium is not provided in IV fluids and monitored closely. IV hydration with isotonic solution 0.9% normal saline (NS) is recommended, and over the course of resuscitation, the pregnant person may require up to 6-10 liters of fluid over 24 hours. Initial management begins with an IV bolus of 1 L 0.9NS within the first hour. For the three subsequent hours, administer 500 mL/hour. For the next 24 hours, or until the patient is out of DKA, whichever is later, give 0.45% NS at 250mL/hr until 80% of the total body water deficit is corrected while blood glucose is >200 mg/dL. A transition to dextrose-containing fluid such as D5NS or D5 0.45%NS once blood sugars fall below 200 mg/dL will allow for adequate insulin resuscitation. Often, potassium chloride will be added to IV fluids as well.

## Insulin administration and electrolyte balance

First, check electrolytes and verify potassium is at or above 3.3 mEq/L before administering insulin. If the patient is severely hypokalemic (<3.3 mEq/L), replete with IV potassium prior to starting insulin. Insulin drip with regular insulin should be initiated, and the patient should be given 0.2-0.4 units/kg IV as a loading dose. After the loading dose is complete, then continue at 2-10 units per hour until bicarbonate normalizes and anion gap is closed. If the blood glucose does not fall by 20% within the first two hours, then consider doubling the insulin infusion rate. Titration of the insulin depends on hourly glucose checks while monitoring for a steady decrease in blood glucose. Potassium should be maintained between 4-5 mEq/L throughout treatment and the addition of supplemental potassium chloride in IV fluids is essential throughout resuscitation, unless the initial potassium is >5 mEq/L in which it can be omitted until the value falls below 5 mEq/L. Phosphate repletion can be considered if the patient has altered mental status.

## Laboratory monitoring throughout treatment

Frequent assessment of improvement

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of hyperglycemia, ketonemia, and electrolyte balance is paramount to the management of DKA during pregnancy. Monitoring serum glucose, ketones and electrolytes every 1-2 hours is recommended. If the blood glucose does not decrease by 20% within the first two hours, consider doubling the insulin IV infusion rate. Once the blood glucose reaches 200 mg/dL, switch IV fluids from 0.9% NS to D5 0.45%NS and aim to maintain blood glucose 100-150 mg/dL (ACOG). Insulin drip should be continued until acidosis resolves; and the anion gap is closed x2 blood draws. Prior to discontinuing the insulin drip, the patient should be administered subcutaneous insulin such as an intermediate or long-acting insulin.

## Fetal monitoring through treatment

If the fetus is at a viable gestational age, continuous fetal monitoring should be undertaken. It is important to remember that while the pregnant person is acidotic during DKA, the fetus will also be acidotic and the fetal heart rate tracing will demonstrate acidosis. Notably, there may be absent to minimal variability and recurrent late decelerations. While this fetal heart rate tracing can seem ominous, it is imperative to treat the pregnant person first and correct the DKA. As DKA is treated the pregnant patient's pH will rise, and thus the fetal heart rate tracing will improve. Certainly, clinical judgment regarding patient status and other risk factors will play a role in the decision to deliver. It is important to refrain from delivery for recurrent late decelerations in a patient with proven DKA, as the neonatal outcomes are poor. Fetal mortality can be as high as 10%, even with aggressive management of DKA.

Delivery secondary to DKA alone is rarely indicated; therefore, the administration of antenatal corticosteroids is not necessary as the fetal status will improve as the gravid patient is adequately resuscitated. Furthermore, administration of steroids during acute DKA will worsen patient status and make blood sugars more challenging to control, leading to prolongation of DKA. In the pre-viable patient, intermittent assessment of fetal heart tones can help alleviate patient worry and anxiety about fetal wellbeing.

## Post-DKA monitoring

After a patient is adequately resuscitated and DKA has resolved, post-treatment monitoring is typically inpatient for 24-48 hours to ensure s maternal status and that DKA does not occur again. This also allows for optimization of insulin regimen. Identification of the trigger for DKA is essential to ensuring DKA does not recur during the pregnancy. For the newly diagnosed diabetic patient, insulin teaching and diabetic education with close outpatient monitoring of control of blood glucose and overall health literacy can prevent recurrence of DKA. The remainder of the pregnancy will progress as usual for the diabetic patient including a level II anatomy ultrasound, fetal echocardiogram, serial growth ultrasounds and antenatal testing in the third trimester. Frequent

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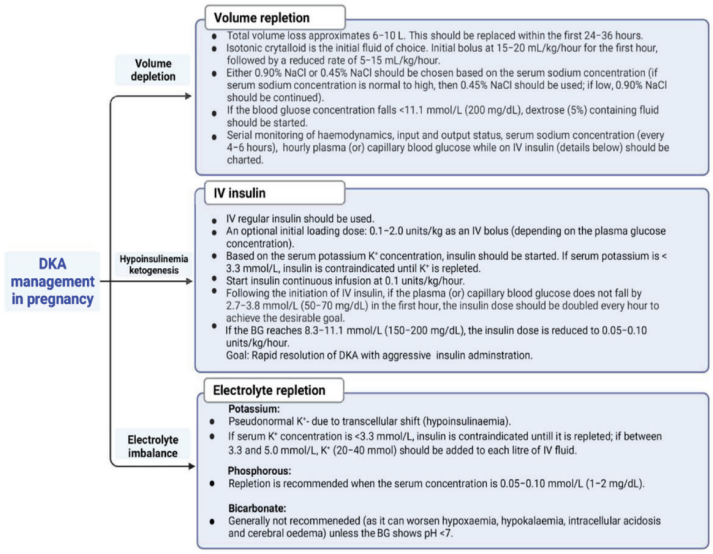
blood glucose monitoring and coordination of care with the patient's physician responsible for managing diabetes (such as Maternal-Fetal Medicine or Endocrinologist) to maintain tight control throughout pregnancy will optimize outcomes.

Figure 2: Management of diabetic ketoacidosis during pregnancy.




BG: blood gas; DKA: diabetic ketoacidosis; K+: potassium; IV: intravenous; NaCl; sodium chloride.

*Used with permission*

Maheswaran Dhanasekaran, Sneha Mohan, Aoife M Egan. EMJ Diabet. 2022; DOI/10.33590/emjdiabet/10194487. https://doi.org/10.33590/emjdiabet/10194487.

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# 2023-2024 Board of Trustees

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## *2023-2024 Board of Trustee*

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*2021-2022*

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# 90th Annual Conference Highlights

## Recognizing the new President of ACOOG . . .

March 26-31, 2023
Manchester Grand Hyatt- San Diego, CA

Incoming President Dr. Mark LeDuc.

*Welcome to all new Fellows of the ACOOG 2023-2024 as well as congratulations to all recipients who received an award this year at the conference banquet held this year at the La Quinta Resort.*

**Outstanding Resident of The Year**
Joseph Bush, DO, LT
Presence St Francis Hospital
Evanston, IL

**New Fellows – Front Row from left:** Kathryn Kauffman, Melisa Lott, Sarah Spencer, Nnenna Maduforo, Jessica Green, Erica Zaworski, Harika Kantamneni.
**Back Row from left:** Maeve Gleason, Jacquelyn MacIntosh, Katie Bieber, Andrew Felman, Elizabeth Kermis, Stacia Dzikunu, Jennifer Enos, Taraly Sowby, Sheena Favor-Williams.

**Honorary Membership Award:** presented to Mary Cameron Tallman by Carolyn Quist, DO

**MEFACOOG Distinguished Lecture Award** to Charles Lockwood, MD by Mark LeDuc, DO

**Distinguished Service Award** presented to Octavia Cannon, DO by Thomas Dardarian, DO

Dr. Mark LeDuc's swearing in of the new President to Dr. Marydonna M. Ravasio

**ACOOG Mentor of the YearAward** presented to Teresa A. Hubka, DO by Marydonna M. Ravasio, DO

**17 Years of Dedicated Service Award** presented to Valerie Bakies Lile, CAE by Mark LeDuc, DO

**90th Annual Conference Program Chairs** Shania J. Seibles, DO, JD, Marydonna M. Ravasio, DO and Jennifer Caruso, DO

**MEFACOOG Commendation Service Award** presented to Octavia Cannon, DO by Thomas Dardarian, DO

**Sages of ACOOG Unity Lecture Award** presented to Ronald J. Librizzi, DO by Mark LeDuc, DO

# Welcome to New ACOOG Members

## Regular/Senior Members

**Senior Members are in Bold*

**Amber Allen, DO, FACOOG**
**Ajaykumar Amin, DO, FACOOG**
**Melissa Bibicoff, DO, FACOOG**
**Paula Bilica, DO, FACOOG**
**Emily Broomell, DO, FACOOG**
**Natalie Bulock, DO, FACOOG**
Joseph Bush, DO
**Jerome Frazier, DO, FACOOG**
**Christina Lam, DO, FACOOG**
**Regina Lovette, DO, FACOOG**
Lena Nguyen, DO
Rebekah Sessoms, DO
**Taralyn Sowby, DO, FACOOG**
**Todd Stalnaker, DO, FACOOG**
**Russell Stanley, DO, FACOOG**
**Maia Uli, DO, FACOOG**
**Jay Williamson, DO, FACOOG**
**Marcietta Wilson-Coleman, DO, FACOOG**

## Life Members

Thomas Alderson, DO, FACOOG (Dist)
Manuel Ballas, DO
Michele Cherry, DO
Gloria Jue, DO
Johnette Maehren, DO
Susan Peck, DO

## Affiliate Members

Janye Osegueda
Michele Stegmaier
Paige Cross

## In Memoriam

Terry Badzinski, DO, FACOOG
Bernard Billman, DO, FACOOG (Dist)
Saul Jeck, DO, FACOOG (Dist)
Richard Markwood, DO, FACOOG (Dist)
Howard Saul, DO, FACOOG (Dist)
Thomas Zima, DO, FACOOG

# CME: Guest Article

## *Expanding the Horizons of Vasomotor Symptom Management*

**CME Credit Available**

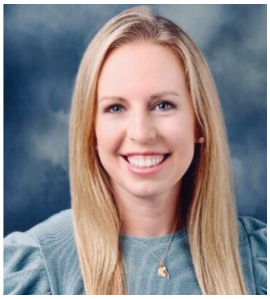
This activity offers
1 Category 1-B AOA
1 *AMA PRA Category 1 Credits*™

**About**

Vasomotor symptoms (VMS) are some of the most bothersome presentations associated with menopause. They occur in up to 80% of women and can persist, on average, for an entire decade. Hot flushes, also known as hot flashes, are often the most distressing symptom of menopause and represent the most frequent reason women seek medical care during this transitional period in their lives. VMS cause so much disruption in women's lives that studies have demonstrated women can accurately recall the frequency, severity, and specific impact on their lives several years after menopausal symptoms have subsided. The FDA recently approved the first of a new class of drugs to address VMS - the first advance in this areas in decades.

**Faculty**

Diana Okuniewski, DO, FACOOG



Dr. Okuniewski is a Board-Certified OB/GYN who received a B.A. in Biology from Kalamazoo College in Kalamazoo, MI, and Medical Degree from Michigan State University College of Osteopathic Medicine in East Lansing, MI. She completed an internship and residency in Obstetrics and Gynecology at Ingham Regional Medical Center in Lansing, MI. Dr. Okuniewski is licensed in Michigan, Ohio, and Rhode Island, and provides on-site leadership as the Site Director of Hospitalists.

Dr. Okuniewski serves on the CME Committee for the American College of Osteopathic Obstetricians and Gynecologists and is a frequent presenter and contributer to CME activities.

**Learning Objectives**

Those participating in this activity will receive information that should allow them to:

1. Assess and identify the appropriate candidates for hormone therapy for

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vasomotor symptoms, taking into account individual patient risk factors such as history of breast cancer, coronary heart disease, venous thromboembolic events, stroke, and liver disease.
2. Evaluate FDA-approved hormonal and non-hormonal treatments for VMS, including the risks and benefits associated with each, in order to personalize therapy for each patient.
3. Compare the effectiveness of alternative non-hormonal therapies for VMS, such as SSRIs/SNRIs, gabapentin, clonidine, and oxybutynin, with patients to involve them in shared decision-making.
4. Evaluate novel therapeutics, such as neurokinin B antagonists, for managing VMS in patients who are unable or unwilling to take hormone therapy.

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- Complete the activity evaluation
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# Expanding the Horizons of Vasomotor Symptom Management

## Introduction

Vasomotor symptoms (VMS) are some of the most bothersome presentations associated with menopause. They occur in up to 80% of women and can persist, on average, for an entire decade [1]. Hot flushes, also known as hot flashes, are often the most distressing symptom of menopause and represent the most frequent reason women seek medical care during this transitional period in their lives [2]. Night sweats are also distressing, as they can significantly disrupt sleep so that women may experience daytime fatigue and reduced energy levels which may significantly impact quality of life. VMS can range from a minor inconvenience to a severe hindrance, impacting a woman's quality of life, occupational performance, and ability to socialize comfortably [2]. VMS cause so much disruption in women's lives that studies have demonstrated women can accurately recall the frequency, severity, and specific impact on their lives several years after menopausal symptoms have subsided [3].

## Challenges in VMS Management and the Need for Alternative Treatments

The treatment of VMS has experienced a significant paradigm shift since the publication of the Women's Health Initiative (WHI) report in 2002. Before the report, hormone therapy (HT) was a mainstay in treating VMS and was widely considered safe by both physicians and patients [4]. However, the media reported the results from WHI in a such a fashion that contributed to confusion and concern among women using HT and their healthcare providers. The prevailing message was that HT posed more risks than benefits. Specifically, that the risks of increased breast cancer rates and cardiovascular concerns outweighed the advantages for women experiencing menopausal VMS [4, 5], though educated menopause experts understand this is untrue for the majority of patients, this data was not presented clearly by the media. Even now, nearly two decades later, uncertainties about VMS management persist. In a recent survey by the American College of Osteopathic Obstetricians and Gynecologists, 76% of the 126 OB/GYN respondents expressed a lack of confidence in their responses to case-based scenarios related to menopausal symptom management [6]. This lack of confidence reflects the inconsistency in the application of clinical recommendations for women in their 40s and 50s presenting with VMS [7, 8].

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In addition to the uncertainty surrounding the HT data, another challenge faced by physicians is the discussion of non-hormonal therapeutics and complementary and alternative therapies for VMS. While current guidelines advocate for shared decision making when considering the benefits, risks, and lack of data regarding these options, many physicians feel ill-equipped to have an educated discussion about these alternatives [8]. Furthermore, there is an emerging new class of non-hormonal therapeutics that demonstrates potential in alleviating VMS and improving quality of life [9]. In order to effectively guide clinical decisions and engage patients in the shared decision-making process, physicians must be familiar with the evidence supporting all therapeutic options available, including novel therapeutics.

This article explores FDA-approved hormonal and non-hormonal treatments for VMS, including estrogens, estrogen agonists paired with agonist/antagonists, paroxetine, and a novel and promising agent, the neurokinin B antagonists.

## Hormone Therapy for Vasomotor Symptoms

Systemic hormone therapy (HT), consisting of either estrogen alone or in combination with a progestin (if a woman still has her uterus), is considered the most effective therapy for VMS related to menopause [10]. Evidence does not support the use of progestin-only medications, testosterone, or compounded bioidentical hormones in the treatment of VMS [10].

## Assessing the Risks and Benefits of Hormone Therapy

The initial step is assessing potential risks for a woman interested in HT. Non-hormonal therapies should be recommended for women where the risk may outweigh the benefit, such as those women with a history of breast cancer, coronary heart disease (CHD), previous venous thromboembolic events (VTE) or stroke, liver disease, unexplained vaginal bleeding, endometrial cancer, or those at moderate to high risk for these conditions [12]. Nonetheless, HT is safe and effective for the majority of women experiencing moderate to severe hot flashes and who have no contraindications. Women with a uterus require both estrogen and progestin, while those who have undergone a hysterectomy can receive estrogen only. Most women with mild VMS may be able to decrease VMS by introducing behavioral measures, such as lowering room temperature, using fans, dressing in layers, weight loss [11], and avoiding triggers (e.g., spicy foods and stressful situations).

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## Systemic Hormone Therapy and Its Effects

Low-dose systemic estrogen is associated with a more favorable adverse effect profile than standard doses and may reduce VMS in some women [10]. Most trials have investigated the safety of conjugated equine estrogen alone or in combination with medroxyprogesterone acetate. The WHI study demonstrated a small increased risk of breast cancer, CHD, stroke, and VTE, and a decreased risk of fractures, diabetes, lung and colon cancer after an average of 5 years of combined HT [13]. Among women receiving estrogen only, there was an increased risk of thromboembolic events but not an increased risk of cardiovascular events or breast cancer [14]. This study targeted women beyond the menopausal transition, making it difficult to apply these findings to younger women. Reanalysis of the data in women younger than 60 years and within 10 years of menopause suggests a possible cardioprotective effect of HT for this group [15]. Numerous formulations, strengths, and modes of HT delivery exist, including oral options, patches, gels, sprays, vaginal rings, intrauterine devices and injections. While all types and routes of estrogen are effective for hot flashes, transdermal preparations are associated with a lower risk of VTE and stroke compared to oral regimens [16].

## Tissue Selective Estrogen Complexes (TSECs)

Following the WHI study, an emerging class of drugs called tissue selective estrogen complexes (TSECs) was developed, these combine a selective estrogen receptor modulator (SERM) with an estrogen [17]. The conjugated estrogen 0.45 mg/bazedoxifene 20 mg combination in women with moderate to severe hot flashes reduces hot flash frequency by approximately 75% (versus 50% for placebo) [18,19]. This combination also offers endometrial protection, higher rates of amenorrhea than estrogen-progestin therapy [20,21], and lower incidences of breast pain and tenderness than combined conjugated estrogen 0.45 mg/medroxyprogesterone acetate 1.5 mg [22]. However, the risk of VTE is increased with bazedoxifene [23].

## Nonhormonal Treatment Options for Vasomotor Symptoms: SSRIs/SNRIs, Gabapentin, Clonidine, and Oxybutynin

For women with VMS who are not candidates for HT based on their risk factors or who choose not to take HT, nonhormonal medications are available. Agents found to decrease VMS in studies include SSRIs/SNRIs, gabapentin, clonidine, and oxybutynin [24,25]. Low-dose paroxetine (7.5 mg/day), an SSRI/SNRI, is the only medication from the aforementioned list approved

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by the FDA for the treatment of hot flashes and has demonstrated modest effectiveness [26,27]. It is important to note that paroxetine should be avoided in women taking tamoxifen [28]. Contraindications of SSRIs/SSNIs include prior neuroleptic syndrome, serotonin syndrome, concurrent use of monoamine oxidase inhibitors, and other medications that increase serotonin levels, such as linezolid, due to the risk of life-threatening serotonin syndrome. Patients with uncontrolled epilepsy, liver or kidney insufficiency, uncontrolled hyponatremia, poorly controlled hypertension, and concurrent use of other SSRIs or SNRIs should be closely monitored. Additionally, SSRIs and SNRIs should be used with caution in patients with known hypersensitivities or those taking other psychotropic medications. Potential risks associated with SNRIs include drug-induced liver toxicity, elevated blood pressure, risk of serotonin syndrome, suicidal thoughts or behaviors, risk of overdose, and complications during pregnancy. It's also advised to avoid alcohol consumption while on these medications due to potential exacerbation of side effects and increased risk of overdose [40].

Reported adverse effects of paroxetine include nausea, dizziness, dry mouth, nervousness, constipation, somnolence, sweating, and sexual dysfunction. These side effects typically resolve over time. Current evidence indicates that SSRIs/SNRIs appear to be less effective than HT for treating VMS; however, drawing conclusions is difficult due to limited studies with direct comparisons to estrogen [10].

## Alternative Therapies

Other alternatives that need further study or have not been found to be beneficial in treating VMS are black cohosh, ginseng, St. John's wort, phytoestrogens, vitamins, acupuncture, reflexology, and ginkgo biloba. There are currently insufficient data to support the use of any of the aforementioned remedies for menopausal VMS [10]. It is estimated that between 50 to 75 percent of postmenopausal women use complementary and alternative therapies for the management of menopausal VMS [34]. Safety and efficacy are not well established for most, but some studies do show benefit. However, most studies are small and short in duration, so the data may not be robust. Furthermore, as placebos have been found to reduce hot flashes in up to 50 percent of patients, carefully controlled, randomized trials are necessary to demonstrate the true efficacy of specific agents [35,36].

## Novel Treatment Options for Vasomotor Symptoms: Neurokinin 3 Receptor Antagonists

The thermoregulatory center in the brain is present within the

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hypothalamus and has neurons that are stimulated by neurokinin B (NKB) and are inhibited by estrogen. After menopause, estrogen declines and NKB signaling is increased. It has been proposed that this results in vasomotor symptoms [29,30,31]. Antagonists of NKB at its receptor, Neurokinin 3, (NK3R), have been studied as an alternative to HT for management of hot flashes, an approach that appears to be promising. These antagonists could be another viable option for women who cannot take estrogen or choose not to. One NK3R, fezolinetant, is FDA approved [39] and one, elinzanetant, is currently investigational at time of publication.

Studies that have already been published, suggest that NK3Rs appear to be ideally suited in safety, efficacy and effectiveness for VMS treatment in women who cannot tolerate or are reluctant to take HT.

A 52-week, Phase 3 study called A 52-week, Phase 3 study called SKYLIGHT 2, found that fezolinetant significantly reduced the frequency and severity of hot flashes associated with menopause throughout the entire duration of the study. The study found that doses of both 30mg and 45mg were associated with a statistically significant reduction in the frequency and severity of hot flashes. Moreover, fezolinetant also reduced sleep disturbances [37]. Another clinical trial of fezolinetant showed that after 12 weeks of use, it reduced hot-flush frequency by about 60% in women experiencing moderate or severe hot flushes, compared with a 45% reduction in those who received a placebo. Participants also reported that the drug reduced the severity of their hot flashes and improved the quality of their sleep [38].

In yet another trial of NK3R antagonists, 80 postmenopausal women with moderate to severe hot flashes were randomly assigned to receive fezolinetant (90 mg orally twice daily) or placebo for 12 weeks. Results showed the antagonist reduced the frequency of hot flashes by 93%, while placebo reduced VMS by 46%. However, an increase in ALT was more frequent with fezolinetant (5 subjects, 11.9 percent) than placebo (1 subject, 2.3 percent). The increases in ALT and AST were mild, transient, and did not exceed three times the upper limit of normal. None of the ALT and/or AST abnormalities was considered clinically significant except for one occurrence in the placebo group [32,33].

The first of this new class of NK3R-based drugs, fezolinetant, was approved by the Food and Drug Administration in May 2023 [39]. NK3Rs have the potential to be life-changing for many women and their physicians. According to Janet Maynard, M.D., M.H.S., director of the FDA's Office of Rare Diseases, Pediatrics, Urologic and Reproductive

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Medicine, in the FDA's Center for Drug Evaluation and Research, "Hot flashes as a result of menopause can be a serious physical burden on women and impact their quality of life. The introduction of a new molecule to treat moderate to severe menopausal hot flashes will provide an additional safe and effective treatment option for women [39]." A new alternative for VMS without the stigma that hormone therapy carries will truly be innovative in women's health and will alleviate unnecessary suffering.

## Conclusion

As we continue to advance our understanding of vasomotor symptoms and their impact on women's lives, it is essential for physicians to stay informed about the latest developments and treatment options. Our commitment to evidence-based practice and adherence to established guidelines is crucial in ensuring the highest quality of care for our patients. As new therapies emerge and our understanding of VMS management evolves, we must remain adaptable and open to integrating these novel approaches into our clinical practice. By fostering a collaborative, patient-centered approach to VMS management, we can empower women to make informed decisions about their health, ultimately enhancing their quality of life during and beyond the menopausal transition.

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