Endocrine News talks with Catherine M. Gordon, MD, chair of the task force that created the latest Clinical Practice Guideline on functional hypothalamic amenorrhea. She discusses why it was important for the Endocrine Society to release a practice guideline on this topic now and why she thinks it will impact the care patients receive in the future.
In March, the Endocrine Society issued a Clinical Practice Guideline advising healthcare providers on ways to diagnose and treat functional hypothalamic amenorrhea (FHA), a condition that develops in female athletes and women who have eating disorders, which causes them to cease menstruation.

Titled “Functional Hypothalamic Amenorrhea: An Endocrine Society Clinical Practice Guideline,” the guideline was published online and will appear in the May 2017 print issue of *The Journal of Clinical Endocrinology & Metabolism (JCEM)*.

Hypothalamic amenorrhea occurs when the hypothalamus in the brain slows or stops releasing GnRH, the hormone that controls the menstrual cycle. It often affects adolescent girls or women with low body weight, a low percentage of body fat, a very low calorie or fat intake, and emotional stress. Ballet dancers, figure skaters, runners, and others who burn more calories through exercise than they consume in their diet can be at risk for developing hypothalamic amenorrhea.

*Endocrine News* spoke with Catherine M. Gordon, MD, of Cincinnati Children’s Hospital Medical Center in Cincinnati, Ohio, and the chair of the task force that authored the guideline, to find out how the guideline will help dispel some of the myths that exist about the diagnosis and treatment of this condition, as well as the importance of a multi-disciplinary approach to treatment, which should include psychological support.

**Endocrine News:** What was the main reason for the publication of the FHA guideline — what drove the decision and why now?

**Catherine M. Gordon:** FHA is a common problem and can affect patients across the lifespan — adolescent girls, adult women, including women struggling with infertility. Unfortunately, there have been myths circulating about the diagnosis and management of this clinical problem. The most appropriate diagnostic work-up has also been questioned. Through our recommendations, we have tried to dispel these myths regarding the diagnosis and treatment of this condition, as well as the importance of a multi-disciplinary approach to treatment, which should include psychological support.

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**GUIDELINE RECOMMENDATIONS**

- Hypothalamic amenorrhea is a “diagnosis of exclusion,” which requires healthcare providers to rule out other conditions that could be interrupting the menstrual cycle.

- As part of their initial evaluation, women diagnosed with hypothalamic amenorrhea should have a series of laboratory tests to check levels of hormones including estrogen, thyroid hormones, and prolactin. The workup can help identify factors preventing menstruation.

- Hypothalamic amenorrhea patients should be evaluated for inpatient treatment if they have an abnormally slow heart rate, low blood pressure, or an electrolyte imbalance. Careful monitoring is needed in these cases because there is a high mortality rate associated with hypothalamic amenorrhea in the setting of eating disorders, particularly anorexia nervosa.

- Select patients presumed to have hypothalamic amenorrhea should undergo a brain MRI to check for damage to or abnormalities of the pituitary gland or pituitary hormone deficiencies, if they exhibit select signs or symptoms, including a history of severe or persistent headaches; persistent vomiting that is not self-induced; changes in vision, thirst, or urination not attributable to other causes; neurological signs suggesting a central nervous system abnormality; or other clinical signs or test results that suggest pituitary hormone deficiency or excess.

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**EN:** What are your hopes for the impact of the guideline on endocrine standards of care of the patient with FHA?

**CMG:** We hope that our recommendations will raise awareness about FHA and lead to thorough yet standardized work-up for these patients. We also hope that endocrinologists will embrace the concept of multidisciplinary care, with input from medical, nutrition, and mental health specialists as they care for these adolescents and young women.
**EN:** How do you expect other medical specialties to be affected by your recommendations?

**CMG:** FHA is a diagnosis that can affect an adolescent girl or adult women. Patients present to pediatric, adult, and reproductive endocrinologists for management of this problem, involving clinicians trained in pediatrics, internal medicine, and obstetrics/gynecology, respectively. Our task force included experts from many disciplines. For all specialties, our recommendations attempt to provide guidance around the appropriate evaluation for patients who present with FHA as there has been a lack of consistency in current clinical practice. FHA is a “diagnosis of exclusion” meaning that underlying anatomic or organic pathologies must first be ruled out. Our guideline attempts to provide clarity around the appropriate general, endocrine, and imaging evaluations to consider for these patients.

**EN:** What are the key take-home messages for patients in this guideline?

**CMG:** In our guidelines, we call attention to the concept of an “energy deficit” that can manifest in an adolescent girl or adult woman from restricted caloric intake, expenditure of calories through exercise, or a combination thereof. There is a misconception that FHA is seen only in the underweight patient, which is not true. Our guidelines review how the seemingly “healthy” teen can present with FHA or the normal-weight but stressed adult with infertility. We also underscore the importance of bone density screening after six months of amenorrhea as bone is one of the tissues most detrimentally affected in these patients.

On the treatment front, we underscore the importance of psychological support for both adolescents and adults and select cases where short-term transdermal estrogen therapy may be helpful if a reasonable trial of nutritional, psychological, and/or exercise modifications have not resulted in the return of menses.

Other members of the Endocrine Society task force that developed this guideline include: Kathryn E. Ackerman, MD, MPH, Boston Children’s Hospital, Massachusetts General Hospital, Boston, Mass.; Sarah L. Berga, MD, and Jay R. Kaplan, PhD, Wake Forest School of Medicine, Winston-Salem, N.C.; George Mastorakos, MD, Areteio Hospital, Athens, Greece; Madhusmita Misra, MD, MPH, Massachusetts General Hospital, Boston, Mass.; M. Hassan Murad, MD, the Mayo Clinic, Rochester, Minn.; Nanette F. Santoro, MD, University of Colorado School of Medicine, Aurora, Colo.; and Michelle P. Warren, MD, Columbia University Medical Center, New York, N.Y.

The Clinical Practice Guideline was co-sponsored by the American Society for Reproductive Medicine, European Society of Endocrinology, and the Pediatric Endocrine Society. The guideline will be published online at https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2017-0131.