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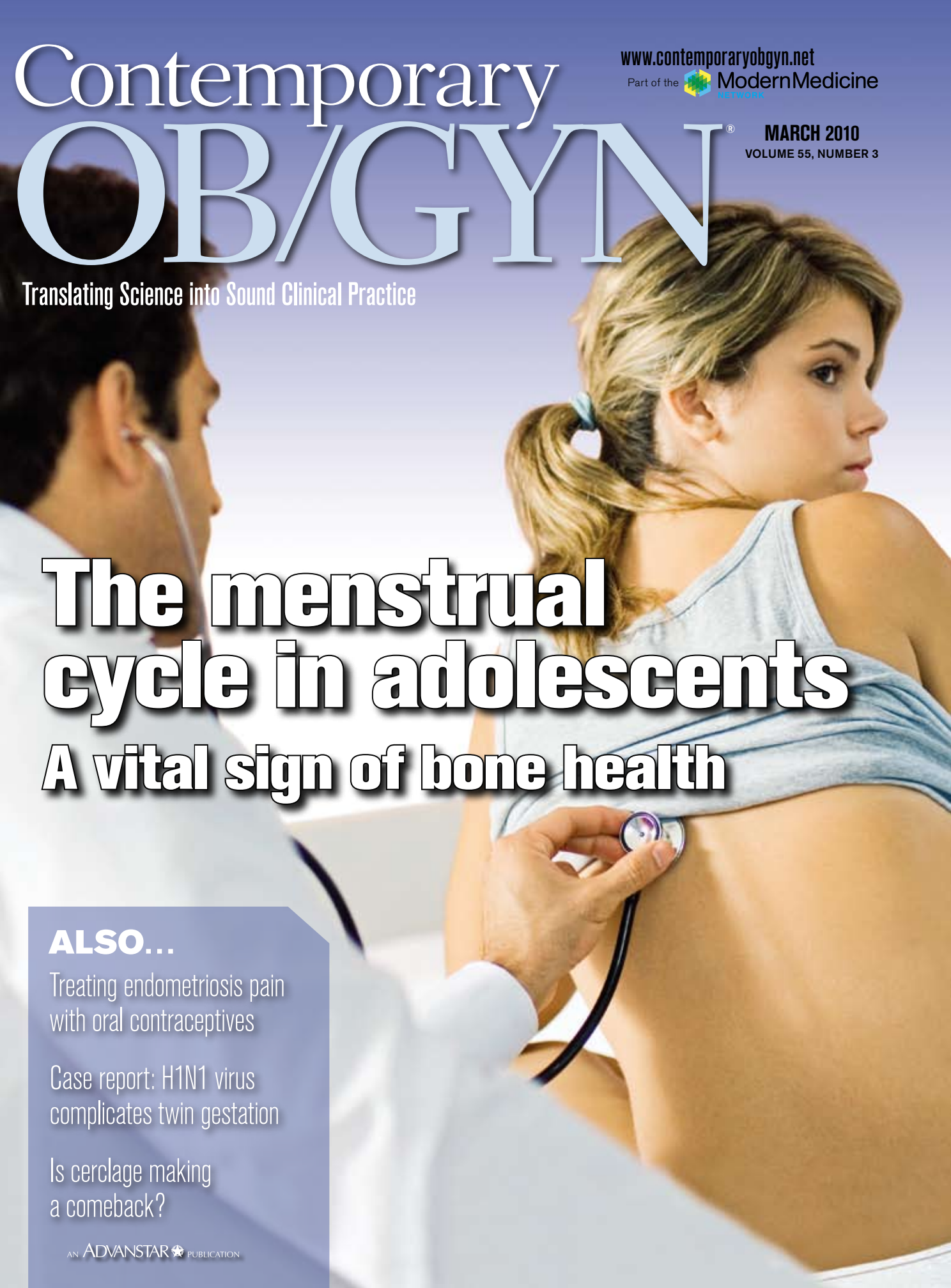

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A vital sign of bone health

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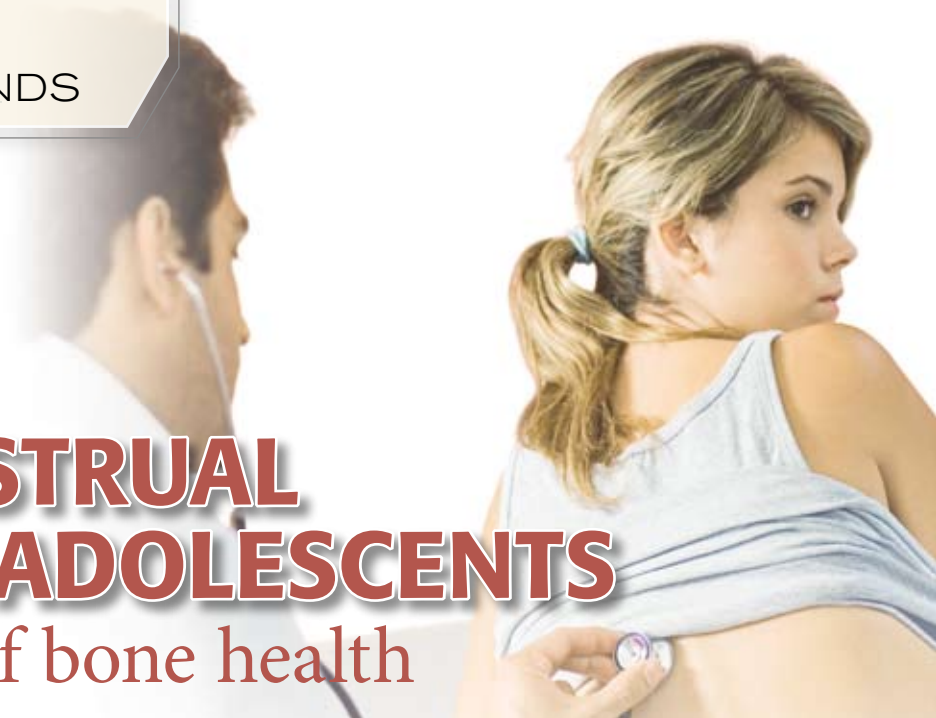

THE MENSTRUAL CYCLE IN ADOLESCENTS

A vital sign of bone health

Menstrual regularity in adolescent girls provides valuable clues about current and future bone integrity. This article explains the importance of using this often-overlooked health factor to help your patients achieve and maintain optimum lifelong skeletal health.

BY **LAWRENCE M NELSON, MD**

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Menstruation is a Jekyll-and-Hyde phenomenon, depending on cultural context.[1] As Hamlet says: "There is nothing either good or bad, but thinking makes it so." Many anthropologic accounts stress the importance of menarche as a sign of a girl's transition into womanhood, physical maturity, and fertility, and something to be celebrated. Some American Indian cultures mark the first menses with an elaborate celebration, such as the Apache Sunrise Dance. Such rituals are a positive and enabling social force. For these American Indian tribes, the first menstrual cycle places the girl in an empowered state in which she can influence the well-being of others.[2] In some cultures, however, including in the United States, menstruation is viewed as a nuisance and a source of physical and psychological problems. Research suggests that girls in the United States are not knowledgeable about menstruation and that their expectations regarding it are negatively biased.[3]

Transition into womanhood is accompanied by remarkable skeletal growth. The teen years are a critical time for building bone; peak volumetric bone mineral density and bone size are almost fully attained during late adolescence.[4] It has been said that osteoporosis is a pediatric disease with geriatric consequences.[5] Bone density can be compared to a bank account: We need to take care of it when we are young so it is there to take care of us in our old age.

Bone health presents an opportunity to say something positive about menstruation and give the menstrual cycle due respect. In studying girls and young women with primary ovarian insufficiency, it has become clear that the menstrual cycle is a marker of general health.[6] According to published data, more than 50% of women with primary ovarian insufficiency (also known as premature menopause or premature ovarian failure) saw 3 or more different clinicians before somebody took the condition seriously and performed

laboratory testing to make a diagnosis.[7] Also, many women delayed seeking evaluation, and most did not consider missing menstrual periods as a significant problem. The cost for a delay in diagnosis of an estrogen-deficient state is reduced bone mineral density.[8]

In this regard, the menstrual cycle can be considered a vital sign of bone health. Teenage girls have an early warning sign of estrogen deficiency: the menstrual cycle. Regular menses are a sign that the ovaries are working normally in their endocrine capacity as a source of estradiol. Estradiol, the major natural human estrogen, plays a critical role in building bone mass. Remarkably, this is true even for men. Men lacking the estradiol alpha receptor or the ability to synthesize estradiol because of aromatase deficiency develop osteoporosis in spite of having normal serum testosterone levels.[9] Thus, estradiol is important to achieving peak bone mass for both men and women.

POWER POINTS

Peak volumetric bone mineral density and bone size are almost fully attained during late adolescence.

Regular menses are a sign that the ovaries are working normally as a source of estradiol, which plays a critical role in building bone mass.

Women who had the onset of menstrual irregularity before the age of 20 years were nearly 3 times as likely to have bone mineral density below normal for their age compared to women who had onset after age 20.

The goal of this article is 2-fold: 1) to advocate for a more aggressive approach to the evaluation of amenorrhea; and 2) to appeal for a comprehensive approach to the management of hypogonadism to optimize bone health and reduce the risk of osteoporosis in later years. To care appropriately for adolescents with hypogonadism, the clinician needs to make the diagnosis in a timely manner, inform the patient (and the parents/guardians, in the case of a minor) of the diagnosis with due care, determine the cause of the condition, and manage the potential emotional and physical sequelae (Table 1).[10]

The view that anything goes with regard to menstrual cycle regularity during adolescence is an unfortunate misconception that is a major contributor to the delay in diagnosis of hypogonadism in this population. Longitudinal studies of the menstrual cycle in normal girls have demonstrated unequivocally that, even during the first year after menarche, it is statistically unusual for a girl to have more than 90 days between menses.[10-12] Therefore, evaluation is indicated for cycle intervals of more than 90 days.

A complete discussion of the evaluation and management of delayed puberty and primary amenorrhea is well beyond the scope of this article. The focus here is on the evaluation

TABLE 1 Appropriate care for adolescent girls with hypogonadism

Make the diagnosis
▪ Think of the menstrual cycle as a vital sign ▪ Evaluate abnormalities by the following criteria—avoid "anything goes" perspective in teens – Menses absent 90 days – Menses not started by age 15 – No signs of puberty by age 13 – Menses not started within 3 years of thelarche
Inform patient and parents as appropriate
▪ Adolescence encompasses a broad spectrum of emotional maturity ▪ The diagnosis affects both parent and child ▪ The family is an emotional unit
Manage the condition
▪ Emotional health ▪ Genetic health ▪ Physical health ▪ Family planning

American Academy of Pediatrics Committee on Adolescence, et al.[10]

"It has been said that osteoporosis is a pediatric disease with geriatric consequences. Bone density can be compared to a bank account: We need to take care of it when we are young so it is there to take care of us in our old age."

TABLE 2 Important aspects in the evaluation of an adolescent with secondary amenorrhea after pregnancy is ruled out

Questions to ask
▪ Is this the earliest manifestation of a decline in general health?
▪ Is there excessive exercise?
▪ Is there inadequate caloric intake?
▪ Is there excessive emotional stress?
▪ Has there been prior radiation or chemotherapy?
▪ Is there galactorrhea, headache, or visual disturbance?
▪ Are there signs of androgen excess?
Initial tests to run[a]
▪ Prolactin
▪ FSH
▪ TSH
Major mechanisms to consider[a]
▪ Polycystic ovary syndrome
▪ Hypothalamic amenorrhea
▪ Hyperprolactinemia
▪ Primary ovarian insufficiency

Abbreviations: FSH, follicle-stimulating hormone; TSH, thyroid-stimulating hormone.

[a]Information from Practice Committee of the American Society for Reproductive Medicine.[13]

TABLE 3 Significant modifiable factors that increase the risk for bone density below the expected normal range for age in young women with estrogen deficiency

▪ >1-year delay in diagnosis of the estrogen deficiency
▪ Low serum vitamin D levels (<32 ng/mL)
▪ Estrogen replacement nonadherence
▪ Low daily calcium intake (<1,000 mg)
▪ Lack of regular exercise

Data from Popat VB, et al.[8]

of secondary amenorrhea in the adolescent, meaning that the girl has completed normal pubertal development and has experienced at least 1 menses.

Once pregnancy has been ruled out, clinicians need to focus on several aspects of the history (Table 2).[13] At a minimum, 3 laboratory tests need to be ordered in the evaluation of secondary amenorrhea. The majority of cases of secondary amenorrhea are caused by one of 4 major conditions: hyperprolactinemia, hypothalamic amenorrhea, primary ovarian insufficiency, and polycystic ovary syndrome. Hyperprolactinemia, hypothalamic amenorrhea, and primary ovarian insufficiency are associated with estradiol deficiency, whereas polycystic ovary syndrome is not.

Hyperprolactinemia and hypothalamic amenorrhea

Hyperprolactinemia and hypothalamic amenorrhea in many cases will respond to appropriate management, with return of normal ovarian function and remission of the estradiol deficiency. However, in the case of primary ovarian insufficiency, there are no proven therapies that will restore ovarian endocrine function. Most experts agree that physiologic estrogen and progestin replacement is reasonable in girls and young women with this condition and should be continued until they reach the age at which normal menopause occurs.[13,14]

In case-controlled studies, transdermal estradiol has a lower risk of venous thromboembolism than oral estrogen and has little effect on hemostatic factors.[15,16] The average serum estradiol level across the normal menstrual cycle is approximately 100 pg/mL.[17] A dose of 100 mcg of estradiol per day delivered by transdermal patch effectively relieves symptoms and achieves serum estradiol levels in this range.[6]

Evidence supports the use of cyclic medroxyprogesterone acetate as the preferred progestin. At a dose of 10 mg per day for 12 days each month, this regimen fully induces secretory endometrium and provides protection against endometrial cancer.[18,19] Data regarding the endometrial effects of oral micronized progesterone when given along with a full replacement dose of estrogen are not available; the available data evaluated endometrial effects at lower estrogen doses.[20]

Addressing estrogen deficiency

A recent cross-sectional study examined the risk factors associated with reduced bone density in young women with estrogen deficiency.[8] Women who had the onset of menstrual irregularity before the age of 20 years were nearly 3 times as likely to have bone mineral density below normal for their

TABLE 4 How girls can ensure healthy bones

- Correct estrogen deficiency if it exists
- Consume 1,300 mg of elemental calcium per day
- Eat foods fortified with calcium and vitamin D
- Exercise
  - Do 60 minutes of physical activity or more per day
  - Most should be moderate- or vigorous-intensity aerobic exercise
  - Perform muscle-strengthening activities at least 3 days a week

Information from US Department of Health and Human Services.[21,22]

age compared to women who had onset after age 20. Of note, approximately one-half of the patients in this study had vitamin D insufficiency and inadequate calcium intake

Researchers also found that delayed diagnosis, nonadherence to estrogen replacement therapy, and lack of regular exercise were also risk factors for reduced bone density (Table 3).[8] Taken together, these findings stress the need for early diagnosis, estrogen replacement adherence, counseling about calcium and vitamin D, and a regular weight-bearing exercise program.

The US Department of Health and Human Services recommends a calcium intake of at least 1,300 mg every day.[21] They also recommend for adolescents a minimum of 1 hour or more of moderate or vigorous aerobic physical activity every day, along with muscle-strengthening and bone-strengthening activities at least 3 days a week (Table 4).[22]

At every medical encounter involving adolescent girls, 2 questions need to be asked: 1) "When was your last menstrual period?" and 2) "Are your periods coming regularly?" The answers merit inclusion on the vital-sign line, along with temperature, pulse, respiration, and blood pressure. Abnormalities in the menstrual cycle deserve serious attention. View the menstrual cycle as a vital sign in order to make the diagnosis of estrogen deficiency in a timely manner. Inform the family and patient of the diagnosis with due care. Then provide a base for ongoing integrated and multidisciplinary care. COG

"Abnormalities in the menstrual cycle deserve serious attention. View the menstrual cycle as a vital sign in order to make the diagnosis of estrogen deficiency in a timely manner."

Online resources

www.bestbonesforever.gov/whatsbest/calcium/index.cfm

www.entrepreneur.com/tradejournals/article/205361268.html

www.health.gov/paguidelines/factsheetprof.aspx

www.nih.gov/news/radio/aug2009/20090813bonedensity.htm

www.rachelswell.org

www.womenshealth.gov/faq/menstruation.cfm

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