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FOR CLINICIANS WHO PROVIDE CARE FOR WOMEN

What are the options for providing contraception to perimenopausal women?

► DEBORAH E. IKHENA, MD, AND JULIA V. JOHNSON, MD

Perimenopause—the years approaching menopause—presents many challenges to women. This time has been labeled as the *menopausal transition* by an NIH panel, which defined it as:

...the time of an increase in follicle-stimulating hormone and increased variability in cycle length, 2 skipped menstrual cycles with 60 or more days of amenorrhea (absence of menstruation), or both.¹

For many women, that transition is associated with anovulatory effects (menorrhagia, irregular menses) and hypoestrogenic effects (vasomotor symptoms) (FIGURE, PAGE S3).

Women might be aware that their fertility declines markedly during perimenopause, but they might not realize

that the risk of unintended pregnancy remains—and that it is therefore critical for them to consider contraceptive options during this time. Likewise, clinicians must consider the risks posed by contraceptives in perimenopause and the risks presented by pregnancy to mother and fetus.

In addition, women might not appreciate the potential benefit of hormonal contraceptives for alleviating perimenopausal symptoms.

This article examines the risks of pregnancy during perimenopause and the risks and potential benefits of contraceptives for this population of women.

Why does contraception matter during this time?

Fecundity is diminished in perimenopausal women. An observational study suggested that the mean age of last birth was 45.7 years (range, 45 to 49 years), and that most women are infertile during the perimenopausal years.² Nevertheless, unplanned pregnancy is a relevant concern in this age group.

Unintended pregnancy. Data from a national survey of family growth show that 17.9% of all pregnancies in women older than 35 years

were unplanned.³ Regrettably, the prevalence of unintended pregnancy in older women that is related to non-use of contraception is high—suggesting that older women are not aware of the risk of unwanted pregnancy during their perimenopausal years.⁴ Stud-

Key points about contraception during perimenopause

- It is critical for you to discuss contraception with your perimenopausal patients: Although women in the menopausal transition have decreased fecundity, they are at risk of pregnancy until menopause.
- All contraceptive methods are reasonable to consider during this time—although the increased risk of venous thromboembolism and cardiovascular disease among older women must be factored in when considering combined hormonal contraception.
- Consider the noncontraceptive benefits of hormonal contraception for women who have perimenopausal menorrhagia, irregular menses, or vasomotor symptoms.
- It is important for your patients to have a good understanding of **1)** the risk associated with these methods of contraception and **2)** the benefit of preventing unwanted pregnancy.

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Is there a time for a woman to stop contraception?

"Can I finally stop my birth control pills now?"

I think most of us have heard this question from our perimenopausal patients. Because women often continue taking an oral contraceptive into their 40s, they have questions about the utility of continuing to take a pill every day to prevent pregnancy. To complicate matters, these patients ask us about the potential risks of pills for women in their age group.

In this issue of *Menopausal Medicine*, Deborah E. Ikhenya, MD, and Julia V. Johnson, MD, review the evidence for the benefits and risks of various contraceptive options during the perimenopause. Certainly, pregnancy has its own set of risks for older women, but many do not consider the potential *noncontraceptive* benefits of hormonal contraception. For example:

- Vasomotor symptoms and irregular bleeding, which can begin years before the last menstrual period, are minimized with an oral contraceptive
- Bone density can be strengthened by taking an oral contraceptive
- Other contraceptive options, such as an intrauterine device, might particularly appeal to some women in this age group who have menorrhagia and are unable to take an estrogen oral contraceptive.

Providing optimal contraception and easing women through the menopausal transition are the best care we can offer to our perimenopausal patients.

Cynthia K. Sites, MD

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FIGURE
The STRAW+10 staging system

Stage	Menarche			FMP (0)						
Stage	-5	-4	-3b	-3a	-2	-1	+1a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSAL			
	Early	Peak	Late		Early	Late	Early			Late
					<i>Perimenopause</i>					
Duration	Variable				Variable	1-3 years	2 years (1 + 1)	3-6 years	Remaining lifespan	
PRINCIPAL CRITERIA										
Menstrual cycle	Variable to regular	Regular	Regular	Subtle changes in flow/length	Variable length; persistent ≥7-day difference in length of consecutive cycles	Interval of amenorrhea of ≥60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑Variable* Low Low	↑>25 IU/L** Low Low	↑Variable Low Low		Stabilizes Very low Very low	
Antral follicle count			Low	Low	Low	Low	Very low	Very low		
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms <i>Likely</i>	Vasomotor symptoms <i>Most likely</i>			Increasing symptoms of urogenital atrophy
<p>*Blood draw on cycle days 2-5. **Approximate expected level based on assays using current international pituitary standard. ↑ = elevated</p> <p>Source: Harlow SD, Gass M, Hall JE, et al; STRAW +10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop +10: addressing the unfinished agenda of staging reproductive aging. <i>Fertil Steril.</i> 2012;97(4):843-851. Used with permission.</p>										

ies also show that, although the rate of abortion among women older than 35 is generally lower than it is among younger women, women older than 35 were the only group that exhibited an increased frequency of abortion between 1998 and 2008.⁵

In short, although fecundity is reduced during perimenopause, women at this age continue to be at risk of pregnancy until menopause, and they should be counseled to use a form of contraception until the end of menses.

Maternal and fetal risks. It is also critical for perimenopausal women to be aware of the maternal and fetal risks of unplanned pregnancy. Women who are older than 50 at delivery have an increased risk of diabetes, hypertension, and hospitalization⁶; it has been

strongly advised⁷ that women be aware of these obstetrical risks and undergo close surveillance when they become pregnant at an older age.

The risk of fetal anomalies in older women is well recognized; in turn, this increases the risk of spontaneous abortion, with 75% of pregnancies resulting in early loss for women older than 45.⁸ Advanced maternal age is associated with high risk of a trisomy conceptus and an increased risk of congenital anomalies and gene disorders. Sadly, the rate of fetal deaths appears to be elevated for all infants born to older women.⁹

Considering the risks that unintended pregnancy presents to older women and their baby, clinicians must discuss contraceptive choices with perimenopausal women. The diminished fecundity of this population shouldn't give false reassurance that they will not become pregnant. It's fortunate for these women that they have many suitable, effective contraceptive options.

What are the contraceptive options?

According to the World Health Organization (WHO), no contraceptive option is contraindicated based on age alone. As a result, both hormonal and nonhormonal methods are available for use during perimenopause.¹⁰ This means that clinicians need to individualize the choice of birth control to the patient's situation.

Hormonal contraceptive options

Combined hormonal contraceptives. Combined oral contraceptives (COC) have been used widely for birth control in the United States since being approved by the Food and Drug Administration in 1960. This form of contraception has been extensively studied, and its risks and benefits are

well known. With an efficacy rate of 92% to 98% (ie, typical vs perfect use), COCs are a highly effective form of birth control.¹¹ In addition, the hormonal components of COCs can alleviate such perimenopausal complaints as vasomotor symptoms and oligo-ovulatory bleeding.

Discussion of the use of COCs in perimenopausal women does raise concern about the risk of venous thromboembolism (VTE), stroke, myocardial infarction, and breast and cervical cancer.

Venous thromboembolism. Combined oral contraceptives have been associated with an increased risk of VTE in all age groups. This risk further increases with age, making the problem a key concern for perimenopausal women. The absolute risk of VTE with a COC in this group is still very low, however—18 events for every 100,000 women.¹²

A woman is at highest risk of VTE if she is a first-time user of a COC or has any of several other risk factors, including obesity, smoking, immobility, and a family history of VTE. The World Health Organization specifically recommends that:

- A woman smoker who is older than 35 years and who smokes fewer than 15 cigarettes a day should take a COC only if no other method is available to her
- A COC is completely contraindicated in a woman who smokes more than 15 cigarettes a day.¹⁰ Providers must consider these factors when weighing the use of a COC for a perimenopausal woman.

Myocardial infarction. The risk of myocardial infarction (MI) increases with age, with an exponential increase after 35 years. A meta-analysis by Khader and colleagues showed that, among current COC users older than 35, the odds ratio (OR) for MI,

compared to that of COC nonusers, is 2.15.¹³ It is also important to note that, despite this risk, the annual risk of death from MI attributable to COC is 22 for every 1 million users in the 40- to 44-year-old group.¹²

Other cardiovascular risk factors. Smoking, diabetes, obesity, and hypertension also factor in to the risk equation, significantly increasing a woman's risk of an MI while she is taking a COC.

Stroke. The risk of stroke is also modestly increased in women taking a COC—a risk that, of course, further increases with age. A study performed by the World Health Organization showed that the estimated attributable risk for stroke ranged from 2 to 8 for every 100,000 woman-years, depending on whether the COC contained a low dose or a high dose of estrogen.¹⁴

Breast cancer. A causative relationship between COCs and breast cancer has not been demonstrated. Some studies have shown a small increase in risk of breast cancer when taking a COC; others have failed to show any association.^{12,15} The risk of breast cancer associated with the use of estrogen and progestin after menopause cannot be extrapolated to an increased risk of breast cancer for perimenopausal women. All women, however, should continue to undergo recommended breast cancer screening as established for their risk profile under current guidelines.

Cervical cancer. Use of a COC has been associated with an increase in the risk of cervical cancer, compared to the risk seen in never-users of a COC; the association strengthens with duration of use.

Moreno and colleagues observed that, after 5 years and 10 years of COC use, the odds ratio for development of cervical cancer in patients with human papillomavirus infection was 2.82 (95% confidence interval [CI], 1.46-



5.42), compared to 4.03 (95% CI, 2.09–8.02) in never users.^{12,15,16} (Of note, the incidence of cervical cancer peaks at 30 to 35 years—which, in most cases, is before the perimenopausal period.¹² A woman taking a COC should continue to be screened routinely for cervical cancer, in accordance with guidelines of the American Society for Colposcopy and Cervical Pathology.)

Protective effect against some cancers? Despite the concerns just described, use of a COC is associated with a decrease in the rates of ovarian and endometrial cancer. Collaborative data has shown that the overall relative risk of ovarian cancer declined by 20% for every 5 years of use of a COC; 15-year users had a 50% decline in risk.¹⁷ The use of a COC is protective against endometrial cancer, with about a 50% to 85% reduction in COC users.¹⁸ Although attempting to decrease the risk of ovarian and endometrial cancer isn't an indication for COCs during perimenopause, the observational data can reassure a COC user that the risk of these two cancers does not increase with the use of this contraceptive option.

Other benefits. COCs may also be beneficial in preserving bone mineral density (BMD) by providing a steady level of exogenous estrogen and progestin during a time when women experience an intermittent decrease in estrogen production. Although a relationship between BMD and use of a COC has not been clearly documented, the data trend toward demonstrating a protective effect.¹⁹

A significant benefit for COC users is regulation of menses and control of menorrhagia. Heavy, irregular menses are a common problem for perimenopausal women, and studies have demonstrated that COCs markedly lower menstrual blood loss and improve iron status²⁰—suggesting that they are

a good option for treating perimenopausal menorrhagia.²¹ In addition to managing menses, COCs are effective treatment for vasomotor symptoms for perimenopausal women.

Other combined hormonal contraceptives are also an option for perimenopausal women; these include the etonogestrel and ethinyl estradiol (EE) vaginal ring and the norelgestromin and EE transdermal system. Both have a side effect profile similar to that of COCs. Although some studies have suggested that there is an increase in the risk of VTE associated with transdermal contraception, a comparison between the norelgestromin and EE transdermal system and COCs containing 35 µg of EE show no difference in the rate of VTE.²²

In some patients, these methods offer a greater likelihood of compliance than COCs and, therefore, a higher rate of efficacy with typical use. The compliance advantage arises from the fact that the etonogestrel and EE vaginal ring can remain in place for 3 weeks, and the norelgestromin and EE transdermal system for 1 week, before it is necessary to remove them.

Overall, combined hormonal contraception is a good option during perimenopause. Therapy has to be individualized, however, based on risk factor profile and the patient's preferences. In addition, the noncontraceptive advantages of COCs are recognized and may, for some women, offer an advantage over other forms of contraception.

Progestin-only contraceptives

Progestin-only pills are 92% to 98% effective in preventing unplanned pregnancy. They are a useful option for patients in whom a combined oral contraceptive is contraindicated, but who want an oral form of birth control.

Progestin-only birth control pills have not been associated with

an increased risk of VTE, myocardial infarction, or stroke—although research on this association is limited.

As with all continuous hormonal contraceptives, progestin-only pills often cause irregular bleeding; in fact, menstrual cycle disruption is one of the most common reasons that women discontinue this type of contraception.²³ For most women, this disruption manifests as an increase in the number of days of light bleeding, but is not associated with greater overall blood loss or an increase in the risk of anemia.

Other progestins available in the United States for contraception include depot medroxyprogesterone acetate (DMPA) injection (Depo-Provera) and the implantable etonogestrel-releasing device (Implanon). Both options are feasible for perimenopausal women and have been associated with a high level of compliance. Studies of DMPA show an association between DMPA and a decrease in BMD; the effect is reversible, however, and does not result in a significant change in BMD after menopause.¹⁹

Levonorgestrel containing intrauterine system (LNG-IUS)

This system (Mirena) works by releasing 20 µg of levonorgestrel a day. It is reported to be 99% effective for as long as 5 years. As with all intrauterine devices, placement of this system during an active pelvic infection increases the risk of advanced infection; placement in such women should be delayed for 3 months after treatment of documented gonorrheal or chlamydial infection.

The LNG-IUS has *not* been associated with a decrease in BMD in women of reproductive age. It provides the additional benefit of inducing amenorrhea in about 50% of women who use it, which may be a desirable side effect for perimenopausal women who

have heavy or bothersome anovulatory bleeding.²⁴ This contraceptive may be effective for women with perimenopausal menorrhagia.

Nonhormonal contraceptive options

The rhythm method of contraception is 75% effective with typical use. The unpredictable ovulation pattern during the menopausal transition, however, makes this method even less effective in this age group. Consequently, the rhythm method is an unreliable method of birth control in the perimenopausal period. Ovulation predictor kits can be used in an attempt to time ovulation, but this technology can be costly and time-consuming for an oligo-ovulatory woman.

Barrier methods—condoms, cervical caps, and the diaphragm—can be considered in a perimenopausal woman who does not want to take a hormonal contraceptive. In recent years, the cervical cap and the diaphragm have become less popular choices for birth control; in fact, the cervical cap is no longer sold in the United States.

On the other hand, male condoms are widely accepted and, of course, available, and offer the additional advantage of protection against sexually transmitted infection. You should strongly encourage any woman at risk of a sexually transmitted infection to have her partner use a condom even if she is using another form of contraception.

Female condoms, which also provide the additional advantage of protection against STIs, are also available commercially—but are not as widely accepted, or as easy to use, as a male condom.

Copper-containing intrauterine device (IUD). The copper IUD works by continuously releasing copper ions into the intrauterine cavity. This

is a highly effective contraceptive, approved by the FDA for as long as 10 years of continuous use.

A common reason that women discontinue using an IUD is menorrhagia,²⁵ which can be a particular concern for perimenopausal women. However, an IUD might be a feasible option during perimenopause as a bridge to menopause.

The recommendation for perimenopausal women is that the IUD be removed after 1 year without menses. The provider should ensure that the patient has had the device removed so that it is not retained for a prolonged time after menopause.²⁶

Sterilization. Permanent sterilization is a reasonable option for a perimenopausal woman, either as tubal ligation or occlusion for her or vasectomy for her partner.

The route of tubal sterilization that you undertake depends on several variables, including the history and the woman's preference. Options are laparoscopic bilateral tubal ligation or transcervical approaches with tubal occlusion. Either method offers effective contraception. Always consider the risk of the surgery or procedure when counseling women about sterilization. ■

References

1. NIH State-of-the-Science Panel. National Institutes of Health State-of-the-Science Conference Statement: Management of Menopause-Related Symptoms. *Ann Intern Med.* 2005;142(12 part 1):1003-1013.
2. Laufer N, Simon A, Samueloff A, et al. Successful spontaneous pregnancies in women older than 45 years. *Fertil Steril.* 2004;81(5):1328-1332.
3. Henshaw SK. Unintended pregnancy in the United States. *Fam Plann Perspect.* 1998;30(1):24-29, 46.
4. Wu J, Meldrum S, Dozier A, et al. Contraceptive non-use among US women at risk for unplanned pregnancy. *Contraception.* 2008;78(4):284-289.
5. Pazol K, Zane SB, Parker WY, et al; Centers for Disease Control and Prevention (CDC). Abortion surveillance—United States, 2008. *MMWR Surveill Summ.* 2011;60(15):1-41.
6. Simchen MJ, Yinon Y, Moran O, et al. Pregnancy outcome after age 50. *Obstet Gynecol.* 2006;108(5):1084-1088.
7. Sauer MV, Paulson RJ, Lobo RA. Pregnancy in women 50 or more years of age: outcomes of 22 con-

- secutively established pregnancies from oocyte donation. *Fertil Steril.* 1995;64(1):111-115.
8. Nybo Andersen AM, Wohlfahrt J, Christens P, et al. Maternal age and fetal loss: population based register linkage study. *BMJ.* 2000;320(7251):1708-1712.
9. Reddy UM, Laughon SK, Sun L, et al. Prepregnancy risk factors for antepartum stillbirth in the United States. *Obstet Gynecol.* 2010;116(5):1119-1126.
10. World Health Organization. Medical eligibility criteria for contraceptive use, 4th ed. 2009. Available at: whqlibdoc.who.int/publications/2010/9789241563888_eng.pdf. Accessed July 13, 2012.
11. Trussell J. Contraceptive efficacy. In: Hatcher RA, Trussell J, Nelson AL, et al, eds. *Contraceptive technology.* 20th ed. New York, NY: Ardent Media; 2011:779-863.
12. Hardman SMR, Gebbie AE. Hormonal contraceptive regimens in the perimenopause. *Maturitas.* 2009;63(3):204-212.
13. Khader YF, Rice J, Lefante J, Abuieta O. Oral contraceptives use and the risk of myocardial infarction: a meta-analysis. *Contraception.* 2003;68(1):11-17.
14. Poulter NR, Chang CL. Haemorrhagic stroke, overall stroke risk, and combined oral contraceptives: results of an international, multi-centre, case-control study. *Lancet.* 1996;348(9026):505-510.
15. Kailas NA, Sifakis S, Koumanatakis E. Contraception during menopause. *Eur J Contracept Reprod Health Care.* 2005;10(1):19-25.
16. Moreno V, Bosch FX, Munoz N, et al. Effect of oral contraception on risk of cervical cancer in women with human papillomavirus infection: the IARC multicentric case-control study. *Lancet.* 2002;359(9132):1085-1092.
17. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies including 23,257 women with ovarian cancer and 87,303 controls. *Lancet.* 2008;371(9609):303-314.
18. Maxwell GL, Schildkraut JM, Calingaert B, et al. Progestin and estrogen potency of combination oral contraceptives and endometrial cancer risk. *Gynecol Oncol.* 2006;103(2):535-540.
19. Isley MM, Kaunitz AM. Update on hormonal contraception and bone density. *Rev Endocr Metab Disord.* 2011;12(2):93-106.
20. Larsson G, Milsom I, Lindstedt G, Rybo G. The influence of a low-dose combined oral contraceptive on menstrual blood loss and iron status. *Contraception.* 1992;46(4):327-334.
21. Kaunitz AM. Oral contraceptive use in perimenopause. *Am J Obstet Gynecol.* 2001;185(2 suppl):S32-S37.
22. d'Arcangues C. Management of vaginal bleeding irregularities induced by progestin-only contraceptives. *Hum Reprod.* 2000;15(3 suppl):24-29.
23. Jick S, Kaye JA, Li L, Jick H. Further results on the risk of nonfatal venous thromboembolism in users of the contraceptive transdermal patch compared to users of oral contraceptives containing norgestimate and 35 microg of ethinyl estradiol. *Contraception.* 2007;76(1):4-7.
24. Jensen JT, Nelson AL, Costales AC. Subject and clinician experience with the levonorgestrel-releasing intrauterine system. *Contraception.* 2008;77(1):22-29.
25. Rivera R, Chen-Mok M, McMullen S. Analysis of client characteristics that may affect early discontinuation of the TCU-380A IUD. *Contraception.* 1999;60(3):155-160.
26. ACOG Committee on Practice Bulletins-Gynecology. No 59. Clinical management guidelines for obstetrician-gynecologists. Intrauterine device. *Obstet Gynecol.* 2005;105(1):223-232.