

# Guide to Contraceptive Counseling for Women With Medical Comorbidities, Part 1

## *Combined Progestin + Estrogen Options*

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Clinicians frequently provide contraceptive counseling to women who have medical conditions that may be exacerbated by pregnancy or who have medical comorbidities that necessitate the use of potentially teratogenic medications.<sup>1</sup> Effective counseling requires up-to-date knowledge about hormonal contraceptive methods that differ in hormone dosage, cycle length, and hormone-free intervals and are delivered by oral, transdermal, transvaginal, injectable, or implantable routes. Effective counseling also requires an understanding of a woman's preferences and medical history, as well as the risks, benefits, side effects, and contraindications of each contraceptive method.

Part 1 of this review focuses on combined hormonal contraceptives (CHCs) only, with special consideration to the

use of contraception in women with medical comorbidities.

### Case Example: A Twenty-Something Migraneur

A 29-year-old woman with a history of migraines without aura asks her physician whether she should begin oral contraceptives (OCs), stating that she is willing to take a daily pill. She reports dysmenorrhea and bloating for the 3 days leading up to her menses, which she describes as "heavy" and lasting for 6 days. This patient smokes 3 cigarettes a day, and her mother was diagnosed with breast cancer at age 65 years.

### Does this patient have any contraindications to taking OCs? What side effects should you discuss with her prior to prescribing OCs?

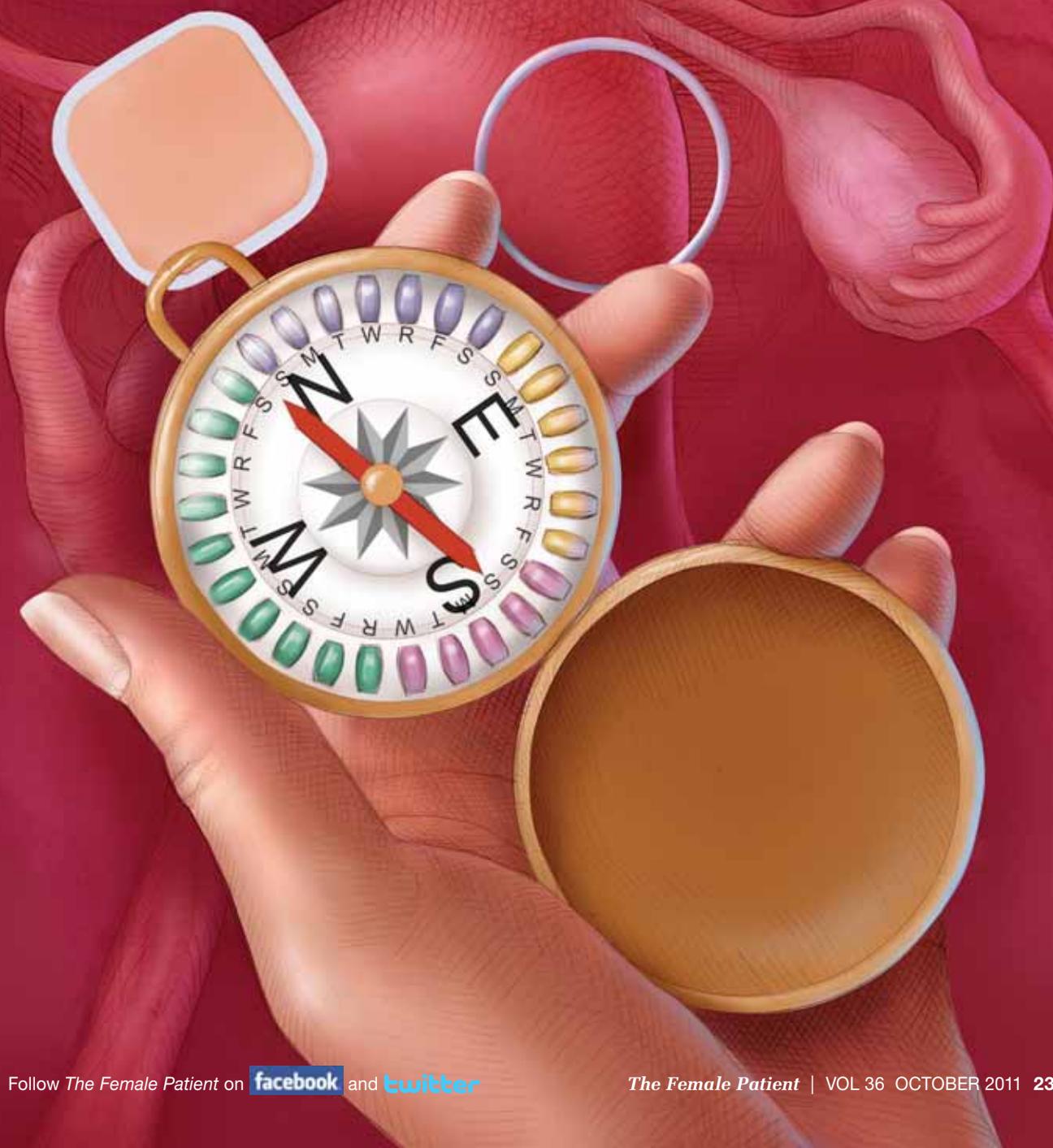
A complete medical history is important in deciding whether OCs would offer this patient benefit or substantial risk. Indeed, most contraindications to hormonal contraception can be ruled out during the history-taking. Although a pelvic examination is not necessary before prescribing hormonal contraception, a focused physical examination, including blood pressure (BP) measurement, may guide your decision.<sup>2</sup>

CHCs can be used safely in women who have a range of medical conditions.

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Providing effective contraceptive counseling to reproductive-aged women requires an understanding of the risks and benefits of each method, consideration of patient preferences, and—most importantly in women with a comorbid condition(s)—attention to personal medical history.



These conditions include patients who have well-controlled hypertension; uncomplicated diabetes; various connective tissue disorders such as rheumatoid arthritis and systemic lupus erythematosus without antiphospholipid antibodies; and uncomplicated liver disease.<sup>3,4</sup> Current guidelines suggest that women who have migraines without aura, such as the patient presented here, can safely take OCs if they are younger than age 35 years and have no contraindications to use.<sup>3,4</sup> This patient smokes 3 cigarettes a

smokers older than age 35 years also should not be prescribed OCs because of the increased cardiovascular risk.<sup>6,8,9</sup>

OCs are contraindicated in several other groups of women. These include diabetic patients with end-organ damage; a personal history of breast cancer or estrogen-dependent tumor; unexplained vaginal bleeding; active liver disease; a history of a thromboembolic disorder; or prior venous thromboembolism (VTE).<sup>3,4</sup> OCs are also contraindicated in women who are breast-feeding within 6 weeks of delivery.<sup>3,4</sup>

OCs may be prescribed to certain other groups of women, but they must be prescribed with caution. For example, CHCs have been shown to elevate systolic and diastolic BP by about 8 and 6 mm Hg, respectively<sup>10</sup>; therefore, caution should be used when initiating OCs in women who already have elevated BP, especially women older than age 35 years. Guidelines from both WHO and ACOG suggest that the risks of OCs outweigh the benefits if BP is uncontrolled.<sup>3,4</sup>

ACOG recommends that the use of OCs in women with diabetes be limited to nonsmoking women younger than age 35 years, who are otherwise healthy and show no evidence of hypertension, nephropathy, retinopathy, or other vascular disease.<sup>3</sup> Women with mild hyperlipidemia who do not have other cardiovascular risk factors can be prescribed OCs if their low-density lipoprotein cholesterol is less than 160 mg/dL.<sup>3</sup>

The side effects of OCs should be discussed with patients considering OC use. The most common side effects include nausea, headaches, breast tenderness, and breakthrough bleeding. A more serious, but less common, side effect of OC use includes a 4-fold increase in the relative risk of VTE compared to women who do not use OCs; this risk may be higher in obese women.<sup>8</sup> Certain third-generation progestins (eg, desogestrel) and the fourth generation progestin drospirenone may further increase VTE risk compared to other progestins.<sup>11-15</sup> This increase is lower, however, than the risk of VTE as-

### FOCUSPOINT

***Women with mild hyperlipidemia who do not have other cardiovascular risk factors can be prescribed OCs if their low-density lipoprotein cholesterol is less than 160 mg/dL.<sup>3</sup>***

day, however, and she should be counseled to stop smoking.

A family history of breast cancer, as in the case of this patient, is not a contraindication to prescribing OCs.<sup>5</sup> According to the American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 73, a family history of BRCA1 or BRCA2 mutations should not preclude OC use.<sup>3</sup>

Most contraindications to OCs are due to the estrogen component. Whereas the estrogen schedule may differ depending on the CHC delivery method (oral, transdermal, intravaginal), the risks and benefits are generally believed to be similar to that of OCs and are grouped together in the World Health Organization's (WHO) updated *Medical Eligibility Criteria for Contraceptive Use*.<sup>4</sup>

Clearly, there are women for whom OCs should not be prescribed.<sup>3,4</sup> These include women who have a history of migraines with aura due to the increased risk of stroke.<sup>6,7</sup> Women with uncontrolled hypertension or who are

sociated with pregnancy, and the absolute risk of VTE among OC users remains small. It is also important to counsel patients that OCs do not offer protection against sexually transmitted infections.

**What are the noncontraceptive benefits of OCs from which this patient may benefit?**

Patients may experience several benefits from OC use in addition to pregnancy prevention.<sup>16</sup> In the case of this patient, OCs may reduce dysmenorrhea and menorrhagia, and offer improved cycle control and regularity. OCs are often first-line treatment for women with dysfunctional uterine bleeding. Diminished intensity and duration of menses also reduces iron-deficiency anemia.

Women with polycystic ovary syndrome (PCOS) may receive particular benefits from OCs, such as improve-

ralocorticoid activity that may result in less weight gain and less water retention, and may also offer even greater reduction in acne and hirsutism.<sup>17</sup> OCs also have demonstrated significant risk reduction for endometriosis, ovulatory pain, ovarian cysts, benign breast disease, premenstrual syndrome, premenstrual dysphoric disorder (PMDD),<sup>16,17</sup> and ovarian and endometrial cancers.<sup>18,19</sup>

**Based on this patient's symptoms and contraceptive needs, would you choose an extended-cycle or conventional OC? What are the options and how do they differ?**

It is important to discuss a patient's preferences for menstrual frequency, as well as her tolerance for scheduled and unscheduled bleeding. A patient's response to these issues will help to decide which OC will best fit her needs.

Traditional OC regimens include 21 days of hormones, followed by a 7-day, hormone-free interval (HFI), which can result in hormone withdrawal symptoms in women who are sensitive to fluctuating hormone levels. With extended-cycle regimens, the HFI is shortened or eliminated to manage common menstrual symptoms (eg, headaches, tiredness, bloating, excessive bleeding, menstrual pain) more effectively, as well as improve OC compliance.<sup>17,20-32</sup>

Women with hormone withdrawal symptoms or severe dysmenorrhea may benefit from fewer periods a year and shorter HFIs. Examples of extended-cycle OCs that offer relief from both withdrawal symptoms and dysmenorrhea include Seasonique® (150 mcg levonorgestrel [LNG]/30 mcg ethinyl estradiol [EE] and 10 mcg EE; no HFI) (Teva Women's Health, Inc) and

ment in acne and hirsutism, as well as regulation of menses. These effects are secondary to the elevation in sex hormone-binding globulin, which reduces circulating free testosterone and ameliorates many androgenic effects.

OCs containing the progestin drospirenone have antiandrogen and antimin-

**TABLE. Hormonal Contraception: Combination Estrogen-Progestin Options**

	COCs <sup>a</sup>	Ortho Evra <sup>®</sup>	NuvaRing <sup>®</sup>
<b>Duration</b>	Daily pill	Weekly application	Monthly insertion
<b>Reversibility</b>	Immediate	Immediate	Immediate
<b>Cost</b>	\$20-\$60/month	~\$50/month	~\$50/month
<b>Side effects<sup>b</sup></b>	Spotting, nausea	Dysmenorrhea, site reaction, patch falling off	Vaginal discharge, discomfort
<b>Consider in<sup>c</sup></b>	PCOS, cycle control, dysmenorrhea	Unable to take daily pill	Unable to take daily pill, obese patients

<sup>a</sup> \$60 = extended cycle contraceptives; Seasonale<sup>®</sup>/Seasonique<sup>®</sup>; Yaz<sup>®</sup> (drospirenone and ethinyl estradiol) (Bayer HealthCare Pharmaceuticals Inc); newer oral contraceptives.

<sup>b</sup> Note: For all combination methods, major side effects include venous thromboembolism, stroke, myocardial infarction.

<sup>c</sup> Note: For all combination methods, must have no contraindication to estrogen use.

Abbreviation: COCs, combined oral contraceptives; PCOS, polycystic ovary syndrome.

Lybrel® (90 mcg LNG/20 mcg EE; no HFI) (Pfizer, Inc).<sup>\*</sup> Lybrel is the first FDA-approved OC in which active pills are taken 365 days a year. Because there are no placebo pills or HFI, Lybrel is an option for women who do not want scheduled monthly periods. The safety and efficacy of Lybrel are similar to that of other OCs, and women can expect rapid return to fertility after its discontinuation.<sup>33,34</sup>

It remains unknown whether the additional weeks of hormone exposure increase the risk of VTE in extended-cycle users. However, a systematic review of extended-cycle versus traditional 28-day cycle OCs found similar efficacy and safety, and no difference in patient adherence.<sup>35</sup> Health care providers should educate patients on the benefits and potential risks of extended-cycle contraception and inquire as to preference for monthly menses. If the patient in this case example seeks fewer periods per year, we would prescribe an extended-cycle OC.

When prescribing an OC, another thing to consider is its progestin component and how it may help combat specific menstrual or premenstrual symptoms. OCs containing drospirenone, a synthetic progestin chemically related to spironolactone, may cause less weight gain and reduced water retention, and may also offer greater decrease in acne, hirsutism, and PMDD compared to traditional OCs.<sup>17,27,29,34</sup>

### **What if the patient is interested in receiving the benefits of a combined hormonal method but is unwilling to take a daily pill?**

If a patient has difficulty remembering to take a daily OC, 2 other delivery options are available: the OrthoEvra® transdermal contraceptive system (6,000 mcg norelgestromin [NRGM]/750 mcg EE, releasing 150 mcg NRGM/20 mcg EE per 24 hours) (Janssen Ortho, LLC) and the NuvaRing® vaginal ring (11,700 mcg etonogestrel [ETG]/2,700 mcg EE, releasing 120 mcg ETG/15 mcg EE per 24 hours) (Organon, a subsidiary of Merck & Co, Inc).

Although the patch is an effective contraceptive method, studies have shown decreased effectiveness in obese women (>90 kg).<sup>35</sup> The side effects, cardiovascular risks, and contraindications of the patch are similar to other CHCs,<sup>3,4</sup> except for the risk of VTE. Whereas retrospective studies to assess the risk of contraceptive patch-associated VTE provided conflicting data, at least 2 studies showed an approximate 2-fold increase in risk compared to women taking OCs.<sup>36-38</sup> These studies warranted the FDA-mandated update to the Ortho Evra label to reflect the higher risk of VTE.<sup>39</sup> Of note, VTE risk with the Ortho Evra patch is lower than VTE risk during pregnancy.<sup>40</sup>

NuvaRing is a soft, plastic ring that is inserted vaginally for 3 weeks. The HFI is a ring-free week. The vaginal ring contains enough hormones to be effective for 4 to 5 weeks. Therefore, some women may choose to use a ring for 4 weeks before having an HFI. Each ring releases about half the level of hormones as the average OC without affecting efficacy. This may be particularly beneficial for women who are intolerant of the side effects of traditional OCs.

Unlike the contraceptive patch, weight does not affect the efficacy of the vaginal ring. Nearly all women find the ring easy to insert and remove and found tolerability to be comparable to that of OCs.<sup>41,42</sup> The large majority of partners of vaginal ring users rarely felt the ring during intercourse.<sup>42</sup> The vaginal ring has similar side effects, cardiovascular risks, and contraindications as other CHCs,<sup>4</sup> with the only unique side effect being a possible increase in leukorrhea.<sup>41,42</sup> If the ring falls out (2.5% of women experience 1 event/year), patients can be counseled to rinse and replace it, without change in efficacy.<sup>41</sup>

### **Conclusion**

A comprehensive, up-to-date knowledge of currently available CHC options is essential for all health care providers car-

<sup>\*</sup>Please note that these products represent only a couple of examples of the extended cycle OCs currently available.

ing for reproductive-aged women. Careful consideration and history-taking is especially important in women with medical comorbidities to determine if any contraindications to CHC use exist and which method and mode of delivery is appropriate for the individual patient.

Traditional OCs have a long track record of safety, acceptability, and efficacy, with well-described contraceptive and noncontraceptive benefits. Extended-cycle CHCs offer similar safety and efficacy, and may also reduce unwanted symptoms (eg, headaches, bloating, mood changes) by preventing endogenous estradiol production with shorter HFIs.

Discussing a patient's preferences for menstrual frequency, as well as her tolerance for scheduled and unscheduled bleeding, is important in deciding whether a traditional or extended-cycle OC will best fit her needs. The contraceptive patch and vaginal ring are CHC options if a woman cannot take a daily pill but seeks the benefits of a CHC. A brief summary of CHCs is provided in the Table.

This is part 1 of a 2-part article. In the November 2011 issue, part 2 will focus on available progestin-only contraceptive options in women with medical comorbidities.

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