Which OC would you choose?
Test your skills with these 3 cases

In selecting the optimal oral contraceptive for your patient, your experience and the patient’s preference should be your guide.

Like most family physicians, you’ve probably prescribed oral contraceptive pills (OCPs) for countless patients. But are you up to date on the intricacies of dosage and hormone formulations, biphasic and triphasic pills, and non-traditional dosing schedules that allow patients to extend the frequency of—or even avoid—scheduled withdrawal bleeds?

Use the 3 patient scenarios that follow to test your knowledge of today’s OCPs and the text and tables that follow to fill in any details you may be missing. We’ll discuss the best approach for each patient at the end of this article.

CASE 1 ➤ Mandy, age 33, comes in asking for OCPs. She is newly married and would like to start a family in 2 or 3 years. The patient—a smoker—previously used a transdermal contraceptive patch.

CASE 2 ➤ Julie, age 18, recently became sexually active and would like to start taking OCPs. She will be spending much of the coming year abroad, Julie explains, and would really like to take “the pill that keeps you from getting your period.” Other than acne, which she is treating with a topical benzyl peroxide/antibiotic combination, Julie has no health problems—and no medical coverage.

CASE 3 ➤ Sandra, age 41, has taken OCPs in the past, but was taken off them after she was hit by a car and sustained a pelvic fracture 2 years ago. A mother of 4, Sandra delivered twins 6 weeks ago. She would like to take OCPs again, but wonders whether the hormones would interfere with nursing.

Is your patient a candidate for an OCP?
Before you prescribe OCPs for these women, or for any patient, there are a number of things to consider. First and
foremost, does the patient have any contraindications to hormonal contraceptives related to the risk of adverse vascular events?

**Absolute contraindications.** Oral contraceptives are contraindicated (TABLE 1) in women older than 35 years who smoke and in women who have uncontrolled hypertension, a past history of venous or arterial vascular complications or a family history of thrombosis, diabetes with end-organ damage, migraine headaches with focal neurologic symptoms, or a history of breast cancer or liver disease.1,2 (A venous thromboembolism [VTE] that occurred in a clinical setting with a clear initiating risk factor—a fractured femur secondary to trauma complicated by a VTE, for example—is not an absolute contraindication to OCP therapy, particularly if it occurred years ago. Such patients may use OCPs if other contraceptive methods are not acceptable.1)

**Relative contraindications.** Pregnancy is a relative contraindication, as no prescriber would intentionally give a contraceptive medication to a woman known to be pregnant. It is important to note, though, that no harm has been associated with inadvertent use of OCPs during pregnancy.3

Obesity is also a relative contraindication. There is evidence that obese women (body mass index >30 kg/m²) have a higher failure rate with OCPs compared with women who are not overweight. The American College of Obstetricians and Gynecologists (ACOG) recommends nonhormonal contraception for obese patients due to the reduced efficacy of hormonal contraception and increased risk of VTE based on case-control studies.5 An obese patient should not, however, be precluded from using OCPs if her only other option is to use a less effective contraceptive.

Lupus was previously considered a relative contraindication, but recent studies did not find any exacerbation of stable lupus with OCPs.4

**Compliance.** In determining whether a patient is a candidate for oral contraceptives, you should also discuss the need for daily compliance, the moderate effectiveness of OCPs (which have a 7% failure rate with typical use6), and the importance of refilling the prescription in a timely manner. If the patient indicates that she has trouble following a daily routine, you may want to discuss other contraceptive options.

### TABLE 1

**Contraindications to oral contraceptives**

<table>
<thead>
<tr>
<th>Absolute</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal or family history of DVT or PE</td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
</tr>
<tr>
<td>Smoker &gt;35 years of age</td>
</tr>
<tr>
<td>Migraine with aura</td>
</tr>
<tr>
<td>Diabetes mellitus with end-organ damage</td>
</tr>
<tr>
<td>History of breast cancer</td>
</tr>
<tr>
<td>Liver disease</td>
</tr>
<tr>
<td>Relative</td>
</tr>
<tr>
<td>Pregnancy</td>
</tr>
<tr>
<td>History of DVT/PE from a known cause that is no longer present (eg, healed lower extremity fracture)</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
</tbody>
</table>

DVT, deep vein thrombosis; PE, pulmonary embolism.

Women with a BMI >30 have a higher failure rate with OCPs compared with women who are not overweight.

**Which OCP? A look at the choices**

In determining which OCP to prescribe for a particular patient, there are a number of issues to consider:

- What estrogen dosage and progestin formulation should be used for this patient?
- Should the patient be placed on a monophasic, biphasic, triphasic, or quadraphasic pill?
- How frequently does she want to menstruate?
- Has she taken OCPs before, either for primary contraception or for another condition that the pill is frequently prescribed for, such as dysmenorrhea or premenstrual syndrome? If she has taken OCPs, did she experience any significant adverse effects?

Most commonly prescribed OCPs are a combination of an estrogen and progestosterone. Progestin-only OCPs are also available, but are used less frequently than combination pills because they must be taken within a
smaller window of time each day to maintain their effectiveness.

**Pill formulations**

Combination OCPs typically contain the estrogen ethinyl estradiol (EE) or its precursor, mestranol, which is metabolized into EE, and one of the 9 progestins available in the United States.6,7 (An OC approved in May 2010 contains a new estrogen, estradiol valerate [EV], and dienogest, a novel progestin.)

Categorized according to when they were approved or introduced, progestins include:
- norethindrone, norethindrone acetate (first generation)
- norgestrel, levonorgestrel, ethynodiol diacetate (second generation)
- norgestimate, desogestrel (third generation)
- drospirenone, dienogest (other).6,7

Each progestin differs in its affinity to progesterone, estrogen, and androgen receptors and, therefore, each has a slightly different physiologic effect. The first-generation progestins norethindrone and norethindrone acetate have a shorter half-life compared with those introduced later. While some studies have shown that third-generation progestins have a greater risk of VTE compared with first- and second-generation formulations, others have not found that to be the case. Two recent studies, conducted in the Netherlands and Denmark, did find an increased risk of VTE associated with the third-generation progestin desogestrel.8,9

Drospirenone, one of the more recently approved progestins, should be used with caution in any patient who may be at increased risk of hyperkalemia because of its spironolactone-like effects.10 Overall, however, there is little evidence to help guide initial OCP selection based on patient characteristics.

**Dosing considerations**

Estrogen dosages range from 10 to 50 mcg EE (and from 1 to 3 mg EV); progesterone dosage is ≤1 mg, with the exception of dienogest (2-3 mg). (Pills with higher doses of estrogen were available in the 1960s and 1970s, but were phased out because they carried a greater risk of vascular complications.) Your goal should be to select the lowest effective dosage of estrogen to minimize the risk of adverse effects.

There is a tradeoff, however: The lowest dose pills (10-20 mcg EE) have an increased risk of irregular bleeding, although they also have a reduced risk of minor adverse effects (eg, breast tenderness and headache, among other premenstrual symptoms).11 And, for women who are not meticulously compliant, low-dose pills are associated with a greater failure rate compared with OCPs with higher doses of EE.10

Other than the reduction of premenopausal symptoms, the advantages of pills with a lower dose of estrogen remain largely theoretical. The most serious adverse effects associated with estrogen—deep vein thrombosis (DVT) and pulmonary embolism—may not be significantly different between the lower or higher dose pills, although 2 recent studies found a reduced risk of VTE with lower estrogen doses.8,9

The original OCPs were monophasic, with each active pill having the same amount of estrogen and progesterone. Biphasic pills generally increase in progesterone dose, typically containing one dose for the first 10 days of the pill pack and an increased dose for the next 11 days.

Triphasic pills, designed to mimic the endogenous fluctuation of estrogen and progesterone during the menstrual cycle, have 3 levels of hormones in the active pills. Typically, the progesterone dose is lowest for the first 7 days and then increases on Day 8 and again on Day 15, while the estrogen dose remains constant. In some triphasic formulations, however, the estrogen dose increases and then is reduced in the last 7 days of active pills. (Natazia, the EV/dienogest OCP approved last year, is quadraphasic, featuring 2 different dosages of EV-only pills and 2 different dosages of estrogen/progestin pills.)7

There is no evidence of any advantage of triphasic pills over monophasic pills in terms of effectiveness, bleeding patterns, or discontinuation rates,12 but there is some evidence that biphasic pills result in more adverse effects.13

**Frequency of withdrawal bleeds**

Traditional OCPs have 21 active pills and 7 days of placebos. Women taking them have a menstrual cycle every 4 weeks during the
Extended and continuous dosing regimens have benefits for women with endometriosis, dysmenorrhea, and chronic pelvic pain.

Placebo days. Patients can choose to have less frequent periods or avoid a menstrual cycle altogether either by taking one of the name-brand OCPs designed for extended or continuous dosing (Table 2) or by skipping the placebo pills in a traditional OCP regimen and starting the next pill pack immediately after taking the final active pill of the previous pack.

In 2003, a continuous OCP with 30 mcg EE and 0.015 mg levonorgestrel (Seasonale) was approved. Its pill pack contains 84 monophasic active pills, plus 7 days of placebos. Patients taking Seasonale—which is now available in generic form—have a menstrual bleed every 3 months. A second 84/7-day OCP with a slightly different formulation (Seasonique) was approved in 2006. Patients who follow an 84/7-day regimen have been found to have outcomes that are very similar to those of women using OCPs in the traditional 21/7-day pattern in many respects, including the bleeding pattern, discontinuation rates, and satisfaction reported.

In 2007, an OCP featuring 365 active pills and no placebo pills was approved (Lybrel). The dosage of EE (20 mcg) and levonorgestrel (0.09 mg) remains constant each day of the year, with the intention that women on this regimen go an entire year without menstruating. No increase in adverse effects has been noted with the use of this OCP. Patients report improved symptomatology, but not a significant reduction in bleeding days compared with cyclic oral contraceptives. In fact, a potential downside is the possibility that women on extended or continuous dosing regimens may have more frequent unscheduled bleeding days.

Extended and continuous dosing regimens have benefits for patients with gynecologic conditions responsive to the suppression of menstruation, including endometriosis, dysmenorrhea, and chronic pelvic pain (Table 3). In fact, OCPs are often prescribed for these conditions, as well as for acne vulgaris, menorrhagia, premenstrual syndrome, and polycystic ovarian syndrome, as patients taking them have been found to have less difficulty with hormonal withdrawal side effects and no increased risk of adverse events.

The only problem with extended or continuous dosing is cost (Table 4). Brand-name OCPs designed as extended-cycle contraceptives are more expensive than generic pills. Similarly, creating a continuous-dosing cycle with a monthly OCP requires more than 13 pill packs a year, and some insurers will not cover the cost of the additional pills.

Currently, no particular OCP or dosing regimen has any evidence-based advantages or indications regarding contraceptive efficacy or bleeding patterns. Until there is ample evidence, further investigation is needed to determine which dosing regimen is optimal for each individual patient.

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### Table 2

**Traditional vs nontraditional dosing**

<table>
<thead>
<tr>
<th>Oral contraceptive</th>
<th>Combination pills (No.)</th>
<th>Placebos (No.)</th>
<th>Other pills (No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional OCP</td>
<td>21</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Femcon Fe†</td>
<td>21</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Mircette</td>
<td>21</td>
<td>2</td>
<td>5 (10 mcg EE)</td>
</tr>
<tr>
<td>Natazia</td>
<td>22</td>
<td>2</td>
<td>2 (3 mg EV); 2 (1 mg EV)</td>
</tr>
<tr>
<td>Lo Loestrin FE</td>
<td>24</td>
<td>0</td>
<td>2 (10 mcg EE); 2 (75 mg ferrous fumarate)</td>
</tr>
<tr>
<td>Yaz</td>
<td>24</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Seasonique</td>
<td>84</td>
<td>0</td>
<td>7 (10 mcg EE)</td>
</tr>
<tr>
<td>Lybrel</td>
<td>365</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*A partial list.
†The tablets are chewable mint-flavored.
EE, ethinyl estradiol; EV, estradiol valerate; OCP, oral contraceptive pill.
At press time, a study in the January 2011 issue of Obstetrics & Gynecology reported that a 24/4-day regimen had greater contraceptive efficacy compared with a 21/7-day regimen.

**Patient preferences, prescribing concerns**

In addition to considering OCP characteristics, patient-specific factors and preferences should be taken into account. Before you decide on a particular formulation, ask the patient whether she wishes to menstruate monthly, quarterly, or not at all (and explain that, even with continuous dosing, there will be some breakthrough bleeding). Patients should also be queried about any prior use of—and side effects or difficulty with—oral contraceptives.

For a patient with a history of OCP use, a pill that was previously used successfully is a reasonable starting point. For OCP-naïve patients, physicians may want to prescribe the least costly pill that is compatible with the patient’s health insurer and her preference, as well as your knowledge and comfort level.

**How many pill packs to prescribe?**

Most women receive 3 pill packs at a time from the pharmacy, although some get only one at a time. Yet evidence suggests that dispensing a 12-month supply of hormonal contraceptives at one time significantly increases patient continuation and use of preventive services (Pap smear screening and chlamydia testing, for example), decreases the need for pregnancy testing, and significantly cuts health care costs. Keep in mind, however, that each pack of traditional pills contains medication for 4 weeks, while a year contains 13 4-week blocks of time. So any prescription written for 12 OCP packs will be insufficient to cover the entire year.

**Variation in number and type of placebo**

Another consideration: OCPs traditionally come in 28-day pill packs, with the last 7 pills being placebos. The number of active and placebo pills has been modified in some OCPs, in an attempt to decrease the risk of ovulation and unintended pregnancy. Because some patients develop hormonal withdrawal side effects during the period of time when they’re taking placebos, several OCP formulations have added a small amount of estrogen to some, or all, of the placebos. One variation combines both concepts, featuring 24 active pills (rather than 21, to decrease the risk of ovulation) and 4 placebo pills containing 10 mcg EE (in an attempt to prevent withdrawal effects). Other variations are available, as well.

Although these pills have a greater inhibition of the pituitary-ovarian axis, they do not have better contraceptive efficacy compared with traditional dosing. Still, OCPs with such nontraditional regimens may be considered for any patient, and prescribed for women who have had prior success with this type of OCP.

### TABLE 3

<table>
<thead>
<tr>
<th>Noncontraceptive benefits—or risks—of OCPs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefits</strong></td>
</tr>
<tr>
<td>• Reduce dysmenorrhea</td>
</tr>
<tr>
<td>• Improve endometriosis</td>
</tr>
<tr>
<td>• Improve acne</td>
</tr>
<tr>
<td>• Reduce symptoms of PMS</td>
</tr>
<tr>
<td>• Suppress ovarian and breast cyst formation</td>
</tr>
<tr>
<td>• Eliminate mittelschmerz</td>
</tr>
<tr>
<td>• Reduce risk of endometrial, ovarian, and colorectal cancers</td>
</tr>
<tr>
<td>• Increase hemoglobin concentration by reducing menstrual flow</td>
</tr>
<tr>
<td>• Lower incidence of ectopic pregnancy</td>
</tr>
<tr>
<td>• Lower incidence of benign breast disease</td>
</tr>
<tr>
<td>• Reduce risk of PID</td>
</tr>
</tbody>
</table>

CVA, cerebrovascular accident; CVD, cardiovascular disease; MI, myocardial infarction; OCPs, oral contraceptive pills; PID, pelvic inflammatory disease; PMS, premenstrual syndrome; VTE, venous thromboembolism.
Getting started: What to tell patients

For many years, combination OCPs were started on the Sunday after the onset of the next menses—a method known as conventional start. But there were 3 disadvantages to this: Patients needed to use an additional form of contraception during the first month of OCP therapy, had an increased risk of pregnancy in the first month, and often misunderstood the instructions, frequently starting the pills the Sunday after their period ended, instead of the Sunday after menstrual bleeding began.

The “first day” start came next. Patients were routinely told to begin their pills on the first day of their next menses. This was easily understood and eliminated the need for an additional form of contraception in the first month, but theoretically, a woman could get pregnant while waiting for her next menstrual cycle to start the OCPs.

To address these problems, the newest option is known as the “visit day” or “quick start.” Advise patients to start the pills on the day of their office visit, either with a sample package or by picking up the OCPs at the pharmacy on the same day. This results in better short-term continuation rates and does not disrupt menstrual bleeding patterns.

Pregnancy test. Prior to the quick start, however, women should have a documented negative pregnancy test (or receive emergency contraception if they have had unprotected intercourse in the last 72 hours). If the patient had unprotected intercourse in the prior 2 weeks, the pregnancy test should be repeated 2 weeks after she starts taking the pill.

OCP timing after a pregnancy

Women who have had a spontaneous or therapeutic abortion <20 weeks’ gestation can start taking combination OCPs immediately. A patient whose pregnancy ended >20 weeks and who is not breastfeeding can use combination OCPs, as well. Because of an increased risk of VTE during the initial postpartum period, however, women should delay the start date until >3 weeks postpartum.

Breastfeeding considerations. Some women, and some clinicians, fear that combination OCPs reduce both the quantity and quality of breast milk. In fact, low-quality evidence suggests that the pills reduce the quantity of breast milk but do not impair infant growth. Studies of OCPs and breastfeeding, although of limited quality, have failed to show specific harm to the infant.

According to ACOG, women who are nursing can begin combination OCPs >6 weeks’ postpartum if breastfeeding is well established and no other form of contraception is acceptable. To address concerns about decreased breast milk associated with combination OCPs, however, progestin-only pills are frequently recommended for nursing mothers—and can be started immediately postpartum without any effect on breast milk.

Progestin-only pills. Because progestin-only pills are taken every day with no

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**TABLE 4**

Cost of hormonal contraceptives

<table>
<thead>
<tr>
<th>Hormonal contraceptive</th>
<th>Monthly cost</th>
<th>Yearly cost (52 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination pill (brand name)</td>
<td>$23-$60</td>
<td>$299-$780</td>
</tr>
<tr>
<td>Combination pill (generic)</td>
<td>$8</td>
<td>$96</td>
</tr>
<tr>
<td>Extended-cycle pill</td>
<td>$44-$58</td>
<td>$578-$753</td>
</tr>
<tr>
<td>Progestin-only pill</td>
<td>$19-$61</td>
<td>$377-$793</td>
</tr>
<tr>
<td>Transdermal patch</td>
<td>$90</td>
<td>$1080</td>
</tr>
<tr>
<td>Transvaginal suppository</td>
<td>$77</td>
<td>$924</td>
</tr>
</tbody>
</table>

placebos, women who take them have unpredictable and irregular menstrual bleeding. In addition, patients need to know that progestin-only pills must be taken at the same time every day; even a 3-hour day-to-day variation increases the risk of contraceptive failure.20

What to do about forgotten pills?
Most women occasionally forget a pill, and it is important to tell them what to do about it (TABLE 5).28,29 Such a discussion is critical to ensure contraceptive effectiveness.

If a patient misses one or 2 pills, she may make them up, using an additional form of contraception for 7 days if she skipped 2 consecutive pills. If she misses 3 consecutive pills, advise her to start a new pill pack, use an additional form of contraception for 7 days, and consider emergency contraception (EC) if she had unprotected sex. A woman who misses 3 pills in a row also needs to be urged to consider a contraceptive method that does not depend on daily compliance29—and to consider EC if she had unprotected intercourse.

Table 5: Forgotten pill(s)? What to tell your patients

<table>
<thead>
<tr>
<th>Missed pill(s)</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>Skip the pill</td>
</tr>
<tr>
<td>Active pill &lt;24 hours (1)</td>
<td>Take the pill as soon as you remember</td>
</tr>
<tr>
<td>Active pill &gt;24 hours and &lt;48 hours (1)</td>
<td>Take the missed pill AND the scheduled pill together</td>
</tr>
<tr>
<td>Active pills (2)</td>
<td>• Take 2 pills on 2 consecutive days, then continue taking 1 pill per day</td>
</tr>
<tr>
<td></td>
<td>• Use additional contraception for 7 days</td>
</tr>
<tr>
<td></td>
<td>• Consider EC if you had intercourse when you missed pills</td>
</tr>
<tr>
<td>Active pills (≥3)</td>
<td>• Stop that pack and start a new pack</td>
</tr>
<tr>
<td></td>
<td>• Use additional contraception for 7 days</td>
</tr>
<tr>
<td></td>
<td>• Consider EC if you had intercourse when you missed pills</td>
</tr>
<tr>
<td></td>
<td>• Consider other forms of contraception that do not require daily compliance</td>
</tr>
</tbody>
</table>

EC, emergency contraception.

What would you prescribe for our 3 patients?

**CASE 1**

Mandy
You start by strongly suggesting that she stop smoking, explaining that when she reaches age 35, the oral contraceptives will be contraindicated if she continues to smoke. Because she had previously used a transdermal contraceptive patch without complications, a generic monophasic 30 to 35 mcg EE combination OCP would be a good choice. You schedule a follow-up visit in 3 months to determine how she is adjusting to the pill.
CASE 2  Julie

Julie is interested in continuous dosing but has no health insurance, so you recommend that she use a generic 21/7 combination OCP. Because of her preference for continuous dosing, however, you recommend that she start a new pack every 3 weeks, without taking any of the placebos, and tell her that this may result in improvements in her acne, as well.

CASE 3  Sandra

You reassure Sandra that combination pills have not been found to be harmful to infants, but suggest she consider a progestin-only formulation instead. You talk to her about the importance of meticulous compliance with a progestin-only OCP, which means taking her pill at the same time every day. You also explain that breakthrough bleeding is common with this type of pill, and that you can discuss a combination OCP when she is no longer nursing or if she cannot tolerate the progestin-only pill.

CORRESPONDENCE
Herbert L. Municl, Jr, MD, 1542 Tulane Avenue, Room 123, New Orleans, LA 70112; hmunicl@suhs.edu

References

Because of an increased risk of VTE during the initial postpartum period, women should delay the start date of their OCP until >3 weeks postpartum.