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Oral contraceptives and breakthrough bleeding: What patients need to know

Managing expectations is as important as adjusting formulations

Practice recommendations

- Lack of adherence is a common cause of breakthrough bleeding. Focus counseling on ensuring that patients understand and can follow pill-taking instructions before switching pills or method (**A**).
- If breakthrough bleeding extends beyond 4 cycles and a woman wish to continue using oral contraceptives, consider switching to a pill with a higher ethinyl estradiol (EE):progestin ratio, either by increasing the EE dose or decreasing the relative progestin dose (**C**).
- Breakthrough bleeding may be due to progestin type; switching from an estrane to a gonane may reduce it (**C**).
- Women who have breakthrough bleeding after having well-controlled menstrual cycles on oral contraceptives should be assessed for for causes not related to their birth control pills, such as pregnancy, cervicitis, smoking, or interactions with medications (**A**).

In 1982, more than 20% of women surveyed in a nationally representative sample had discontinued oral contraceptives (OCs) on their own or at the recommendation of their physician due to bleeding or spotting.[1] Sadly, the percentage today has not decreased much.

Understandable concern, embarrassment, and annoyance lead these women to abandon OCs.[1,2] What they often don't know, though, is that breakthrough bleeding generally is greatest in the first 3 to 4 months after starting OCs,[3] and it steadily declines and stabilizes by the end of the fourth cycle.[4] Timely counsel could enable many of these women to cope with the bleeding and stick with an effective contraceptive method. Additional incentives are noncontraceptive benefits of OCs: improved menstrual regularity and decreased menstrual blood loss, dysmenorrhea, and risk of ovarian and endometrial cancer.

Women who discontinue OCs on their own switch to less effective methods of birth control or use no method.[1,2] Consequences may be unexpected pregnancies and increased abortion rates.[5] With patients who are using OCs, it would be appropriate to ask periodically whether they are satisfied with OC use.

In this review we discuss the mechanisms and management of breakthrough bleeding in women taking OCs, and provide tips for counseling that may help decrease the risk of discontinuation due to menstrual abnormalities in the initial months of use.

Breakthrough bleeding in this review refers to either unplanned spotting or

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bleeding, regardless of requirement for protection—unless defined otherwise by a specific study under discussion.

4 factors contribute to breakthrough bleeding

Breakthrough bleeding may be due to any the following factors: 1) physiologic effects of OCs on the endometrium, 2) OC-related parameters, including dose, formulation, and regimen, 3) patient behavior, including compliance, using concomitant medications, and smoking, and 4) benign or malignant pathology.

OCs and the endometrium: Estrogen-progestin balance significant

Progestin and estrogen in combination OCs have profound effects on the endometrium, which, though not contributing to contraception, do lead to a predictable pattern of bleeding or such problems as breakthrough bleeding or lack of withdrawal bleed.

Normally, estrogen causes the endometrium to proliferate. Progesterone stabilizes the growing uterine lining. Since the introduction of OCs in 1960, the trend in formulation has been to use the least amount of hormone necessary to inhibit ovulation. Given that the progestin is primarily responsible for the contraceptive efficacy of OCs, the risk of pregnancy is not altered with decreases in the estrogen component. However, significantly lowering the estrogen in OCs may account for breakthrough bleeding. Unplanned bleeding, though, is not dependent solely on the estrogen component as variations in the progestin can contribute to breakthrough bleeding.[7]

Most OC users in the US take low-dose formulations, so designated because the estrogen component is <50 µg. This level of estrogen in combination with a progestin provides excellent contraceptive efficacy, but may be insufficient to sustain endometrial integrity in some women.[8] Studies that have compared OCs containing 20 µg ethinyl estradiol (EE) with those containing 30 µg or 35 µg EE have not been very useful for judging breakthrough bleeding rates because the products often also vary in the phasing and type of progestin. Some studies show more breakthrough bleeding with 20 µg EE pills,[9–11] but others show equal or improved cycle control with the lower EE dose.

Estrogen-progestin balance is more important than absolute level of estrogen. Endrikat et al[12] conducted a study to compare two 20 µg EE pills containing different progestins, and to compare 2 levonorgestrel-based formulations with differing EE amounts. An OC of 20 µg EE/100 µg levonorgestrel was compared with a preparation of 20 µg EE/500 mg norethisterone. A 30 µg EE/150 mg levonorgestrel pill was used as a standard reference preparation.

Overall, the 30 µg EE preparation showed a lower cumulative incidence of breakthrough bleeding compared with the 20 µg EE/100 µg levonorgestrel and 20 µg EE/500 µg norethisterone pills over 13 cycles (1.0% vs 4.1% vs 11.7%, respectively). However, the 20 µg EE/500 µg norethisterone pills consistently had higher breakthrough bleeding rates than the 20 µg EE/100 µg levonorgestrel pill. This suggests that, although the higher EE component

How is irregular bleeding defined?

For the purpose of performing studies, unplanned bleeding is classified by the World Health Organization into 2 categories: 1) breakthrough bleeding, which requires sanitary protection, and 2) spotting, which does not require sanitary protection.[6] Despite this formal classification, trials have varied in their terminology and method of recording menstrual irregularities, making comparisons between studies difficult. In addition, there is wide variation among women in tolerance to bleeding abnormalities, perceptions of heavy vs light bleeding, as well as the need for protection.[3]

Nevertheless, menstrual abnormalities are consistently cited as a common reason for discontinuing OCs. A prospective US study of 1657 women performed in the 1990s reported that 37% of OC users had stopped taking OCs by 6 months after starting a new prescription because of side effects.[2] Irregular bleeding was the most common cause; cited by 12% of women, followed by nausea, weight gain, and mood changes, which ranged from 5% to 7%.

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Low-level estrogen in combination with a progestin is excellent for contraception but may not sustain endometrial integrity in some women

TABLE 1

Available OCs by formulation and regimen

TRADE NAME	GENERIC NAME(S)	ESTROGEN (DOSE)	PROGESTIN (DOSE)
MONOPHASIC			
Alesse, Levlite	Aviane, Lessina	Ethinyl estradiol (20 µg)	Levonorgestrel (0.1 mg)
Mircette	Kariva	Ethinyl estradiol (20 µg x 21 days + 10 mg x 5 days during placebo week)	Desogestrel (0.15 mg)
Loestrin FE	Microgestin FE 1/20, June FE 1/20	Ethinyl estradiol (20 µg)	Norethindrone acetate (1 mg)
Yaz		Ethinyl estradiol (20 µg)	Drospirinone (3 mg)
Levlen, Nordette	Levora, Portia	Ethinyl estradiol (30 µg)	Levonorgestrel (0.15 mg)
Lo/Ovral	Low-ogestrel, Cryselle	Ethinyl estradiol (30 µg)	Norgestrel (0.3 mg)
Desogen, Ortho-cept	Apri	Ethinyl estradiol (30 µg)	Desogestrel (0.15 mg)
Loestrin 21 1/5/30	Microgestin, Junel Fe	Ethinyl estradiol (30 µg)	Norethindrone acetate (1.5 mg)
Yasmin		Ethinyl estradiol (30 µg)	Drospirinone (3 mg)
Ovcon 35		Ethinyl estradiol (35 µg)	Norethindrone (0.4 mg)
Ortho-Cyclen	Mononesessa, Sprintec	Ethinyl estradiol (35 µg)	Norgestimate (0.25 mg)
Brevicon, Modicon	Nortrel, Necon 0.5/35	Ethinyl estradiol (35 µg)	Norethindrone (0.5 mg)
Demulen 1/35	Zovia 1/35	Ethinyl estradiol (35 µg)	Ethynodiol diacetate (1 mg)
Ortho-Novum 1/35, Norinyl 1+35	Necon 1/35, Nortrel	Ethinyl estradiol (35 µg)	Norethindrone (1 mg)
Ortho-Novum 1/50	Necon 1/50	Ethinyl estradiol (50 µg)	Norethindrone (1 mg)
Ovral	Ogestrel	Ethinyl estradiol (50 µg)	Norgestrel (0.5 mg)
Ovcon 50		Ethinyl estradiol (50 µg)	Norethindrone (1 mg)
Demulen 1/50	Zovia 1/50	Ethinyl estradiol (50 µg)	Ethynodiol diacetate (1 mg)
Norinyl 1/50		Mestranol (50 mcg)	Norethindrone (1 mg)
BIPHASIC			
Ortho-Novum 10/11, Jenest	Necon 10/11, Nelova 10/11	Ethinyl estradiol (35 µg)	Norethindrone (0.5 mg x 10 days, 1 mg x 11 days)
TRIPHASIC			
Ortho Tri-Cyclen Lo		Ethinyl estradiol (25 µg)	Norgestimate (0.18 mg x 7 days, 0.215 mg x 7 days, 0.25 mg x 7 days)
Cyclessa	Velivet	Ethinyl estradiol (25 µg)	Desogestrel (0.1 mg x 7 days, 0.125 x 7 days, 0.15 mg x 7 days)
Triphasil, Tri-Levlen	Trivora, Enpresse	Ethinyl estradiol (30 µg x 6 days, 40 µg x 5 days, 30 µg x 10 days)	Levonorgestrel (0.05 mg x 6 days, 0.075 mg x 5 days, 0.125 mg x 10 days)
Tri-Norinyl		Ethinyl estradiol (35 µg)	Norethindrone (0.5 mg x 7 days, 1 mg x 9 days, 0.5 mg x 5 days)
Ortho Tri-Cyclen	Tri-Sprintec TriNessa*	Ethinyl estradiol (35 µg)	Norgestimate (0.18 mg x 7 days, 0.215 mg x 7 days, 0.25 mg x 7 days)
Ortho-Novum 7/7/7	Nortrel 7/7/7, Necon 7/7/7	Ethinyl estradiol (35 µg)	Norethindrone (0.5 mg x 7 days, 0.75 mg x 7 days, 1 mg x 7 days)
Estrostep FE		Ethinyl estradiol (20 µg x 5 days, 30 µg x 7 days, 35 µg x 9 days)	Norethindrone acetate (1 mg)
EXTENDED CYCLE			
Seasonale		Ethinyl estradiol (30 µg x 84 days followed by 7 placebo pills)	Levonorgestrel (0.15 mg)
Seasonique		Ethinyl estradiol (30 µg x 84 days followed by 10 µg x 7 days)	Levonorgestrel (0.15 mg)

* Corrections were made to this chart following its publication in print.

in the 30 µg pill was important when comparing 2 formulations with the same progestin, the difference in progestins of the two 20 µg EE pills was most likely responsible for the differing rates of breakthrough bleeding.

This study highlights the ability to achieve greater cycle control by titrating the EE component of an OC in a balanced ratio with the same progestin, but suggests that the absolute quantity of EE in a given pill may be less important than maintaining a balance between the 2 hormones or less important than the impact of different progestins on breakthrough bleeding rates.

The delicate balance between estrogen and progesterone supplementation required for contraception may also lead to progestin-induced decidualization and endometrial atrophy, which can result in asynchronous, erratic bleeding.[7,13] This has been primarily studied in long-acting progestin-only contraceptives such as implants. Alterations in angiogenic factors[14] may play a role. Hysteroscopic studies have shown abnormalities in superficial endometrial blood vessels in terms of size, proliferation, and fragility in women using Norplant.[13,15,16] Abnormalities in endothelial cells and extracellular matrix proteins,[17] tissue factor,[18] and endometrial lymphoid cells[19] may contribute to breakthrough bleeding in progestin-dominant environments.

Available OC formulations, doses, and regimens

More than 30 formulations of combination OCs are available in the US, with different doses and types of estrogen and progestin (**TABLE 1**).[20] Approved OCs have been studied in clinical trials to assess contraceptive efficacy and cycle control; however, comparisons between studies regarding bleeding phenomena are impaired by inconsistent terminology.[3]

While some studies describe breakthrough bleeding and spotting according to their recognized definitions, others simply refer to intermenstrual bleeding or use spotting to refer to any unexpected bleeding. In addition, cycle control studies of OC users frequently do not account for the effects of missed pills, use of concomitant medications, or smoking. The percentage of women who experience breakthrough bleeding in a given cycle varies widely even in different trials of the same formulation.

Pay attention to progestin level. Conventional wisdom holds that OCs with the lowest doses of EE (≤20 µg) are associated with more breakthrough bleeding.[11] However, even moderately low doses of either EE or progestin can increase the incidence of breakthrough bleeding. For example, when 3 pills with the same estrogen and progestin (50 µg EE /100 µg norethindrone; 35 µg EE/100 µg norethindrone; and 35 µg EE/50 µg norethindrone) were compared in 192 women over 8 cycles, the pill containing the lowest amount of norethindrone (35 µg EE/50 µg norethisterone) caused the highest rates of breakthrough bleeding (decreasing to approximately 50% by cycle 8 as compared with 35% in the 35 µg EE/100 µg norethindrone pill and 25% in the 50 µg EE /100 µg norethindrone pill).[21]

In addition, the number of intermenstrual bleeding days plateaued more slowly as the amount of both hormones in the OC formulations decreased. This underscores the importance of the relative proportions of estrogen and progestin contained in combination OCs and its impact on breakthrough bleeding.

Similarly, a large comprehensive study in 1991 women compared 7 different formulations of combination OCs containing different dose combinations of EE and norgestimate—20/250, 50/250, 35/125, 20/60, 50/60, 30/90, 25/125.[25] Total intermenstrual bleeding was more frequent at lower doses of either estrogen or progestin. However, as long as a similar estrogen-progestin ratio was maintained, bleeding rates were considered acceptable (approximately 10% of days per cycle with bleeding). The authors also noted that in the low-dose range of OCs, small changes in the absolute amount of either EE or norgestimate might result in noticeable changes in bleeding.

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Regardless of the type of progestin or amount of estrogen, breakthrough bleeding generally decreases with successive cycles

TABLE 2

Progestins used in oral contraceptive formulations

ESTRANES	GONANES	SPIROLACTONES
Norethindrone	Norgestrel	Drospirinone
Norethindrone acetate	Levonorgestrel	
Ethynodiol diacetate	Norgestimate	
	Gestodene	
	Desogestrel	

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Though women may experience more breakthrough bleeding on extended-cycle regimens, the number of planned and unplanned bleeding days may still decrease

Type of progestin may affect breakthrough bleeding. All combination OCs contain either EE or mestranol. However, a variety of progestins have come into use. The 2 most common contraceptive progestins are derived from 19-nortestosterone, and are classified as gonanes or estranes (**TABLE 2**).[22]

Estranes include norethindrone and its derivatives, norethindrone acetate and ethinyodiol diacetate. *Gonanes* include levonorgestrel, norgestrel, desogestrel, gestodene, and norgestimate.

Each progestin differs in half-life, estrogenic, progestogenic, and androgenic properties, and these variations may explain differing rates of breakthrough bleeding among formulations.[4] As shown by Endrikat et al,[12] pills with the same quantity of EE but different progestins can have marked differences in breakthrough bleeding rates.

Although gonanes have greater progestational activity, no trial has determined which progestin has the best bleeding profile. A recent Cochrane review comparing different progestins did find that, compared with pills containing levonorgestrel, those containing gestodene may be associated with less intermenstrual bleeding.[23]

Regardless of the progestin used or the quantity of EE, breakthrough bleeding generally decreases with each successive cycle. One study that compared 2 combination OCs composed of EE/norgestimate and EE/norgestrel demonstrated bleeding rates of 11.3% and 10.6% during the first 6 cycles, that decreased to 5.1% and 6.3% in Cycles 13 to 24, respectively.[24] Additionally, all women using OCs can experience some cycles without a withdrawal bleed—a menstrual abnormality that may be concerning to those who desire a menstrual period as confirmation that they are not pregnant.

Comparing regimens. OC regimens are available as biphasic, triphasic, extended-cycle, and continuous use. Women using extended-cycle contraceptives may experience more breakthrough bleeding than those using a standard 28-day pill. However, in a 3-month cycle, there are only 7 days of planned bleeding. This is in contrast to 28-day cycles during 3 months in which there are 21 days of planned bleeding.

Though women on extended-cycle regimens may initially experience more breakthrough bleeding than women using 28-day regimens, the total number of planned and unplanned bleeding days may still decrease. Women using a 3-month cycle OC (30 µg EE/150 µg levonorgestrel) experienced more unscheduled bleeding than women using a standard 28-day cycle OC of the same formulation and dose.[26] The number of bleeding days decreased with each cycle. Another study examined continuous OC use (20 µg EE/100 µg levonorgestrel) over a period of 1 year, and reported a decreasing number of bleeding days over time.[27] In the case of continuous use, all bleeding is unscheduled, and any bleeding is considered breakthrough bleeding.

Multiphasic OC regimens were developed with the intention of decreasing breakthrough bleeding by mimicking the rising and falling pattern of estrogen and progesterone in the normal menstrual cycle.[28] After the introduction of the biphasic pill, an increase in breakthrough bleeding was noted, which led to the development of the triphasic pill.[29] Though the multiphasic hypothesis is physiologically plausible, recent reviews of the literature have found the evidence for its efficacy too limited and methodologically flawed to draw any definitive conclusions about a decrease in breakthrough bleeding.[30,31]

Patient behavior contributing to breakthrough bleeding

Skipping a pill is a common cause of breakthrough bleeding.[5] Compliance with any OC regimen is crucial to achieving a regular and predictable bleeding pattern. Of 6676 women surveyed retrospectively, 19% reported missing 1 or more pills per cycle, and 10% reported missing 2 or more pills per cycle.[32] Prospective studies have found even higher rates of inconsistent use.

When an electronic device was used to monitor pill ingestion, up to 81% of women were found to miss at least 1 pill per cycle and up to 51% missed 3 or more pills per cycle.[33]

Other side effects also adversely affect adherence. For example, women experiencing nausea may skip pills, which leads to breakthrough bleeding and, ultimately, discontinuation.[34] Patients need to understand the impact of skipping pills. Women who report irregular bleeding are 1.6 to 1.7 times more likely as those not reporting this side effect to miss 2 or more pills per cycle.[5] Even 1 missed pill can increase the risk of bleeding irregularities.[35]

Failure to take the pill at the same time every day, as well as poor comprehension of pill-taking instructions, are other strong predictors of inconsistent use and breakthrough bleeding.[32]

Taking some prescription and over-the-counter medications, as well as herbal supplements, may interfere with the activity of OCs to alter bleeding patterns and contraceptive efficacy.[36] Medications that induce the cytochrome P-450 system (CYP450) in the liver increase the metabolism of OCs. Anticonvulsants, the antituberculosis agent rifampin, and antifungals such as griseofulvin, can increase the clearance of steroid hormones and thus lead to breakthrough bleeding. The herbal supplement St. John's Wort, commonly used for mild to moderate depression, is associated with CYP450 induction. It has been shown to increase the incidence of breakthrough bleeding and probably ovulation in women taking OCs.[37]

Smoking is associated with such anti-estrogenic effects as early menopause, osteoporosis, and menstrual abnormalities.[38] These effects may be related to the induction of hepatic estrogen and progesterone metabolism by cigarette smoking.[39,40]

Before receiving OCs, women are made aware of the relationship between smoking, OCs, and an increased risk of myocardial infarction, stroke, and venous thromboembolism.[41] They should also understand that the anti-estrogenic effect of smoking may lower estrogen levels and lead to breakthrough bleeding, even in women who are reliable pill-takers.[42,43]

Smoking appears to have a dose-response relationship with breakthrough bleeding. Increasing levels of smoking have been associated with an increased risk of spotting or bleeding in each cycle.[44] The difference in cycle control between smokers and nonsmokers appears to be more pronounced with each cycle. Smokers demonstrate a 30% elevation in the risk of bleeding irregularities compared with nonsmokers in the first cycle of use, which rises to an 86% increased risk by the sixth cycle.

Reports conflict regarding the relationship between smoking and contraceptive efficacy, suggesting that confounding factors like compliance may be more important than the antihormonal effect of cigarettes.[45] Nevertheless, women who smoke should be informed of this potential complicating factor to OC use and as yet another reason to encourage smoking cessation.

Pathologic causes of breakthrough bleeding

When a woman experiences difficult cycle control after the first 3 to 4 months of OC use, consider the possibility of benign and malignant growths, including endometrial polyps, submucous myomas, and cervical or endometrial cancer.[46] Additionally, contraceptive failure must always be a consideration and that what appears to be breakthrough bleeding may actually

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Skipping pills, smoking, and taking certain medications and herbal supplements are common causes of breakthrough bleeding

TABLE 3

What to review with patients who are starting a combination OC

- Breakthrough bleeding in the initial months after starting OCs is common
- Breakthrough bleeding, if experienced, usually diminishes over the first 3 months of OC use and abates by the 4th cycle
- Skipping even one pill can result in breakthrough bleeding
- Avoidance of breakthrough bleeding can be aided by taking your pill at the same time every day; you may find it helpful to make pill-taking part of another daily routine such as tooth brushing
- Tell me about other medications you are taking, including over-the-counter preparations or herbal supplements
- If you smoke, the chances of breakthrough bleeding are increased
- If bleeding continues beyond the 4th cycle, there are diagnostic tests available to explore possible underlying causes
- If bleeding continues without adequate explanation and despite adherence to the regimen, we can try switching you to a different formulation to see if that helps

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Women should be told that bleeding is common, and usually declines after 3 or 4 months

represent bleeding in early pregnancy.

Cervicitis is an important but largely unrecognized source of unplanned bleeding in women using OCs. Causative organisms include chlamydia, gonorrhea, and trichomonas.[22] Intermenstrual bleeding in women previously well controlled on OCs is particularly suggestive of asymptomatic chlamydia cervicitis.

Krettek et al[37] found that 29.2% of women who had been taking OCs for more than 3 months and presented with intermenstrual spotting had a positive test for *Chlamydia trachomatis*. By comparison, chlamydia cervicitis was found in 10.7% of matched controls taking OCs without spotting who were screened for symptoms of vaginitis or high-risk sexual behavior, and in just 6.1% of women undergoing routine screening before the initiation of contraception.

3 aspects of managing breakthrough bleeding

Managing breakthrough bleeding involves effective pretreatment and ongoing counseling, reassurance, and timely and appropriate diagnostic testing (**TABLE 3**). In some instances, pill-switching or other forms of medical management may be helpful, but these options are largely unproven.

Counseling reduces anxiety and improves satisfaction, adherence

In a recent survey, 649 Canadian women who were picking up prescriptions for OCs were asked to complete a questionnaire at the pharmacy while they waited.[48] Over one third (34.5%) reported they had not received counseling from their healthcare provider about breakthrough bleeding. Furthermore, only 28.3% of women who were counseled, and 26.1% of women who were not counseled, gave the optimal response to breakthrough bleeding as defined in this study ("continue taking pill and not call my doctor").

Lack of counseling can lead to poor method satisfaction and significant cost expenditures due to visits and phone calls by women experiencing unexpected bothersome side-effects.[5] Compared with women who reported the highest satisfaction with the care they received from their provider, those reporting the lowest scores were 1.6 to 2.2 times as likely to be dissatisfied with the pill.

Inform women that breakthrough bleeding is common in the first 3 to 4 cycles of OC use, that bleeding irregularities tend to decline with each successive cycle, and that they should not discontinue pill use without discussing their concerns with you. Remind women to keep sanitary pro-

tection with them during the first few months. The impact of poor counseling was underscored in a study of women enrolled in clinical trials of OCs, contraceptive vaginal rings, and Depo-Provera. Women taking OCs were the least likely to have been warned of menstrual irregularities and thus tended to stop using that method more often than those using a ring or Depo-Provera.[49] Of women who discontinue OCs, 47% use a less effective method and 19% use no method at all.[1]

Give specific instructions for specific regimens. Given the array of OC regimens available, make sure women know how to take them properly. This will help ensure contraceptive efficacy and cycle control. Women who do not understand pill-package instructions are up to 2.8 times more likely to miss pills, which increases the risk of breakthrough bleeding and impacts contraceptive efficacy.[5] Among women who were counseled about the consequences of missed pills, 76% reported knowing what to do in response ("use another form of birth control that month"). Of women who received no such counseling, only 48% gave the appropriate response ($P<.001$).[48] To improve adherence, advise women to establish a routine for pill-taking: taking the pill at the same time each day or linking pill ingestion with another daily activity, such as tooth brushing. Women without an established routine were 3.6 times more likely to miss 2 or more pills per cycle than women with a routine.[5]

Reassurance regarding contraceptive efficacy

Reassure users who take their pills routinely that breakthrough bleeding and contraceptive efficacy are not linked.[50] Breakthrough bleeding is not a sign that OCs are not working.[4] On the other hand, approximately 1 million unintended pregnancies in the United States each year are associated with misuse or discontinuation of OCs.[51]

When to consider diagnostic testing

For OC users who continue to experience breakthrough bleeding beyond 3 to 4 cycles, other potential causes must be ruled out using appropriate diagnostic tests. A pregnancy test, appropriate testing for cervical infection, a pregnancy test, pelvic ultrasound, Pap smear, or endometrial biopsy may be warranted depending on clinical circumstances.

Fall-back options

If breakthrough bleeding continues beyond 3 months, and other reasons including poor adherence and pathologic processes are excluded, you could consider providing estrogen or switching to a different pill, though no clinical trials support definitive recommendations.

Aside from changing from a multiphasic to a monophasic formulation, altering the progestin component is often a first step in trying to control breakthrough bleeding.[46] An OC with a gonane rather than an estrane progestin may be beneficial as this class of progestins may provide more consistent hormonal effects on the endometrium.

Choosing an OC with a higher quantity of EE may also help, particularly for women using 20 µg pills. When possible, the same progestin should be used.

You may want to start a trial of conjugated estrogen, 1.25 mg, or estradiol, 2 mg, administered for 7 days when bleeding occurs. This can be repeated if necessary; however, if breakthrough bleeding continues despite this treatment, consideration of a different pill or method should be undertaken. ■

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Women who still have bleeding after 3 or 4 cycles should have other causes ruled out: eg, pregnancy test, Pap smear, endometrial biopsy, etc

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If breakthrough bleeding continues, consider providing estrogen or switching to a different OC

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