

# BEST PRACTICES IN: Addressing Misperceptions Related to Unscheduled Bleeding in Women Taking Combined Oral Contraceptives: Counseling Is the Key

This supplement is the second of three on oral contraception. The content is based on the proceedings of an experts' roundtable held on November 4, 2010, in Miami, Florida, with panelists:

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- Mandy Gittler, MD
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- Versie Johnson-Mallard, PhD, RN.

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## Introduction

*Breakthrough bleeding, unscheduled bleeding, withdrawal bleeding, a pill period*—these are all terms used by health care providers to describe the nonmenstrual bleeding that may occur among women taking oral contraceptives (OCs). During this experts' roundtable discussion, Dr Mandy Gittler said that, to women, "bleeding is bleeding." Unscheduled bleeding is a common, unpredictable event among OC users, as well as an often-misunderstood source of dissatisfaction with an OC regimen. The inconvenience of OC-related bleeding and the misbelief that bleeding is an indication of poor efficacy are frequent causes of OC discontinuation, said Dr Gittler. Therefore, when prescribing OCs, health care providers must discuss the possibility of OC-related bleeding with women; establish realistic expectations about if, when, and why bleeding may occur; and assure women that bleeding is not related to efficacy. With such counseling and education, long-term adherence may improve, she said.

## Defining OC-Related Bleeding

Nonmenstrual bleeding occurs in more than 20% of women taking OCs regardless of the product or duration of the cycle.<sup>1,2</sup> The frequency is variable and decreases over time. During the first 90 days of treatment, the number of bleeding or spotting days ranges from 10 to 24.<sup>2</sup> This decreases to 7.5 to 15 days by the fourth 90-day cycle.<sup>2</sup> But what, asked Dr Gittler, defines an OC-related bleed, and is the incidence of bleeding different with different products and regimens?

As the US Food and Drug Administration does not require bleeding data for drug approval (only efficacy and safety data), collection of bleeding data across trials has been inconsistent. "Given the way bleeding data are reported, it is very difficult to compare one study to the next to the next," commented Dr Christopher Estes, who also participated in this portion of the roundtable. In clinical trials, said Dr Estes, bleeding has been inconsistently defined and data variably collected.<sup>3</sup> "Studies may exclude cycles from being counted for any reason...missed pills, missed follow-up, missed diary entries..." he explained.

Consequently, comparing bleeding data across trials and products is difficult, he continued. The World Health Organization (WHO) has attempted to standardize definitions of bleeding patterns (Table 1)<sup>3</sup>; however, some categories, such as vaginal bleeding that does not require sanitary protection, may be irrelevant to women. As data are often patient reported, reliable data collection can be challenging, explained Dr Gittler.

**Table 1. World Health Organization Definitions of Menstrual Bleeding Patterns**

Term	Definition
Bleeding	Vaginal blood loss requiring the use of sanitary protection such as pads or tampons
Spotting	Vaginal blood loss not necessitating sanitary protection
Bleeding day	A day on which bleeding is reported
Bleeding or spotting episodes	Any consecutive set of $\geq 1$ bleeding and/or spotting days bounded at each end by bleeding-free days <ul style="list-style-type: none"> <li>• Either consecutive or separated by only 1 bleeding-free day</li> <li>• Bleeding-free day: no record of bleeding or spotting</li> </ul>
Bleeding or spotting segment	The sum of a bleeding or spotting episode and immediately following bleeding-free intervals

Adapted from Mishell DR Jr et al.<sup>3</sup>

Recent calls for standardization of bleeding terminology have recommended the following<sup>3</sup>:

- Adoption of the concepts of "scheduled" versus "unscheduled" bleeding (ie, bleeding that occurs during a hormone-free interval [HFI] versus that occurring during active treatment)
- Replacing the terms *periods* or *menses* with the concept of *withdrawal bleeds*
- Abandoning the term *breakthrough* as a descriptor because it does not indicate when in a cycle that bleeding occurs
- Introducing reporting of amenorrhea.

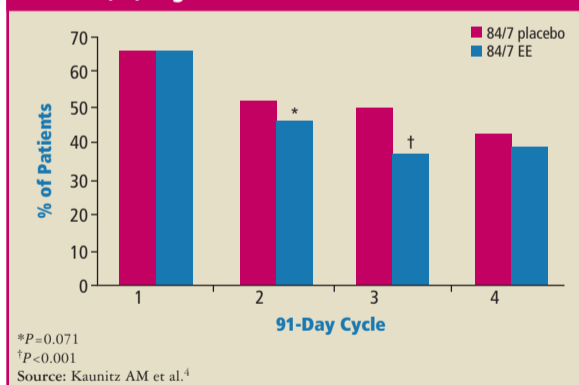
"Of course, women will continue to refer to any bleeding as a period," added Dr Estes.

## Differences Among OC Regimens

There are data demonstrating that 21/7 OC regimens lead to more bleeding than do extended regimens (eg, 84/7 regimens) over the long term and that continuous, extended OC regimens (eg, 84/7 regimens with ethinyl estradiol [EE] given during the HFI) may be associated with even less bleeding, said Dr Gittler.

Dr Gittler cited a cross-study analysis of two phase III trials with identical inclusion and exclusion criteria that evaluated 91-day OC regimens for 12 months. In one study, patients received 150  $\mu$ g levonorgestrel (LNG) plus 30  $\mu$ g EE for 84 days with a 7-day HFI. In the other study, patients received the same 84-day regimen plus 10  $\mu$ g EE during the HFI (the 84/7 EE regimen).<sup>4</sup> There was no difference in bleeding in the first cycle between treatments as the first 84 days of treatment were identical, but, by the end of the second cycle, there was a trend favoring the 84/7 EE regimen. The difference achieved statistical significance in the third cycle (Figure 1).<sup>4</sup>

**Figure 1. Bleeding Profiles of 84/7 Placebo and 84/7 Ethinyl Estradiol (EE) Regimens**



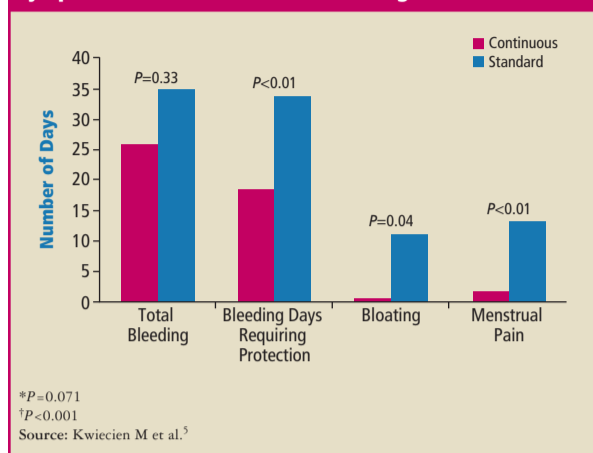
Continuous OC use may also help reduce the premenstrual-like withdrawal symptoms that women sometimes experience during the HFI. A 2003 study compared a standard 21/7 regimen of 100  $\mu$ g LNG/20  $\mu$ g EE with the same regimen given for 168 continuous days.<sup>5</sup> There was a trend toward fewer total bleeding days with the extended regimen and significantly fewer bleeding days requiring protection ( $P<0.01$ ), less bloating ( $P=0.04$ ), and less menstrual pain ( $P<0.01$ ) (Figure 2).<sup>5</sup>

## Management of OC-Related Bleeding

"The biggest bleeding management strategy is education," said Dr Gittler. The goal of education is to "help women achieve success with their birth control methods," said Dr Estes.

There are no approved methods for preventing bleeding, and there are no "treatments" for unscheduled bleeding. However, according to a 2006 study, prolonged or persistent bleeding associated with continuous OCs may be alleviated by the introduction of a 3-day HFI.<sup>6</sup> If women choose to institute a 3-day HFI to control bleeding, they must be counseled not to do so more often than every 3 weeks to ensure continued contraceptive efficacy.<sup>6</sup> If bleeding persists after an abbreviated HFI, transvaginal ultrasound may be warranted.<sup>7</sup>

**Figure 2. Continuous 168-Day Oral Contraceptive Regimen Associated With Less Bleeding/Fewer Withdrawal Symptoms Than With Standard 21/7 Regimen**



Drs Gittler and Estes outlined several key points for discussion with women. First and foremost, said Dr Gittler, women must be prepared for the possibility of unscheduled bleeding. Expecting bleeding is preferable to being surprised, she said, and she advises women starting an OC to carry sanitary protection during the first few cycles. Women must also come to understand that bleeding is not an indication of OC failure, she said. Dr Gittler explains to women that bleeding is a sign of endometrial atrophy and OC activity and that bleeding tapers when the endometrium grows "accustomed" to the OC. When prescribing an extended regimen or switching a patient from a 21/7 regimen, Dr Gittler emphasizes that monthly bleeding is not physiologically necessary and that extended regimens are associated with less bleeding and withdrawal symptoms over time.

Other factors that help facilitate patient success include consideration of costs and convenience, partner involvement, parental involvement for minors, patient access to health care providers, and regular office visits, said Dr Estes. He explained that women with knowledgeable and supportive partners (compared to those using OC in secret) are often more successful and have fewer unintended pregnancies. Likewise, supportive and knowledgeable parents/guardians usually help teenagers achieve long-term contraceptive success. Having regular access to a health care provider through e-mail or text messaging, along with in-office visits, may also help women achieve long-term success, he said.

## Conclusions

Unscheduled bleeding is a common, unpredictable and, for many women, a frustrating effect of OC use. Counseling and education are key to helping women prepare for and tolerate transient bleeding. Although women will continue to consider any vaginal bleeding to be menstrual, it is important for the medical community to develop standardized definitions and data collection methods for the creation of a reliable evidence base.

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