

# Menstruation: choosing whether . . . and when

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Received 29 September 2000; accepted 13 October 2000

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## Abstract

For many women in the United States, menstruation is a major health concern because menstrual disorders and other conditions that may be aggravated during menses (e.g., migraine headaches, epilepsy) carry substantial morbidity. Women today menstruate nearly 3 times as often as in primitive societies, and evidence suggests that frequent, repetitive menstrual cycles may increase health risks. Because the conventional 21/7 combination oral contraceptive (OC) regimen provides only limited relief for women with menstrual disorders, alternative OC regimens that reduce menstrual frequency have been proposed. A new OC formulation specifically designed to decrease menstrual bleeding to 4 times per year is currently under investigation. Most women welcome less frequent menses or even amenorrhea. Women who may derive particular benefit from reduced menstrual frequency include not only those with medical conditions directly caused or aggravated by menses, but also those serving in the military, female athletes, mentally-retarded women with menstrual hygiene problems, young teens, and perimenopausal women. © 2001 Elsevier Science Inc. All rights reserved.

*Keywords:* Menstruation; Oral contraceptives; Intrauterine device; Injectable contraception; Amenorrhea

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## 1. Menstruation—monthly nuisance or major cause of morbidity?

The burden of menstruation ranges from a monthly nuisance to a major health concern of women. In the United States, menstrual disorders are the most common gynecologic complaint, affecting nearly 2.5 million women aged 18 to 50 [1]. Two-thirds of these women contact a doctor regarding menstrual problems each year, and 31% report spending a mean of 9.6 days in bed annually [1]. Among young women, primary dysmenorrhea is the most common cause of time lost from work or school [2]. The costs of menstrual disorders to US industry have been estimated to be 8% of the total wage bill, and the impact is particularly acute in industries that employ predominantly women [3]. According to Thomas and Ellertson [3], Texas Instruments noted a 25% decrease in productivity among female workers around the time of menses.

Other conditions may be aggravated during menstruation (Table 1). After dysmenorrhea, migraine headaches are the most frequent menstrual-related symptom and are thought to be related to changes in reproductive hormones [4,5].

Likewise, hormonal changes around the time of menses can contribute to aggravation of porphyria, epilepsy, and chronic pelvic pain (often due to endometriosis) [4]. Excessive menstrual volume also contributes to anemia, representing a serious problem for otherwise healthy women as well as those with pre-existing conditions such as iron-deficiency anemia and hereditary anemias [4]. As Thomas and Ellerston so succinctly put it, “There can be no other disease or condition that affects so many people on such a regular basis with consequences, at both the individual and societal level, which is not prioritized in some way by health professionals or policy makers”[3].

## 2. Is monthly menstruation necessary?

Contemporary women in Western societies who live to age 50 will experience an estimated 450 lifetime ovulations or episodes of menses, whereas women in primitive foraging (i.e., hunter-gatherer) societies who lived to experience menopause would have had only one third as many cycles (160) [6]. There is evidence to suggest that this pattern of frequent, repetitive menstrual cycles may actually increase health risks. For example, characteristics found to be protective against breast and gynecologic cancers, including late menarche, early first birth, high parity, and early meno-

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Table 1  
Conditions associated with or aggravated by menses

Dysmenorrhea	Epilepsy
Migraine	Porphyria
Chronic pelvic pain/endometriosis	

pause, which were present in hunter-gatherer women, are no longer present in women of today [6].

When the idea of hormonal contraception using a progestational agent was first suggested in the 1950s, a regimen consisting of 21 days of active drug followed by 7 drug-free days was suggested because the manufacturer of orally-active progestins was unwilling to supply them for any use that would be perceived to interfere with the normal menstrual cycle [7]. In addition, Drs. Gregory Pincus and John Rock felt that mimicking the average length of the normal menstrual cycle would make the idea of an oral contraceptive (OC) more acceptable to women, clinicians, and the church [8,9]. He and others developing OCs appreciated the fact that the monthly bleed experienced by users was not “biological” but rather induced by withdrawal of the hormones. Nevertheless, women and many health care providers continue to believe that this monthly bleeding contributes to female health despite a lack of supportive evidence [3]. In fact, a recent prospective study in 262 women currently using or starting OCs showed that nearly all hormonal symptoms were reported more frequently during the 7-day hormone-free interval than during the 21 days of active hormones [10]. Menstrual disorders, including dysmenorrhea/pelvic pain (19%), menorrhagia (15%), irregular menses (25%), and premenstrual syndrome (3%), were the reasons for OC use by most of the 158 current users in this cohort. Current OC users reported increased symptomatology during the pill-free interval (Table 2), and a similar pattern was observed in new OC users after the first cycle.

Sulak [11] recently commented that the conventional 21/7 combination OC regimen provides only limited relief for women with menstrual disorders, and that they would benefit by extending the duration of active hormone, perhaps over several cycles, and also shortening the hormone-

free interval to 4 or 5 days. This and other innovative approaches to OC use are feasible in today’s culture in which OC users have access to sensitive urine pregnancy tests and, therefore, do not rely on the occurrence of monthly cycles to reassure them that they are not pregnant.

### 3. Clinical experience with reducing menstrual frequency

As early as 1977, Loudon and colleagues studied the acceptability of an OC regimen that reduced menstrual frequency to once every 3 months [8]. A total of 196 women took a combination OC consisting of 50  $\mu$ g ethinyl estradiol (EE) and 2.5 mg lynestrenol for 84 days followed by 6 pill-free days. The regimen provided good cycle control; only 8.5% (17) of the 196 women reported breakthrough bleeding in the first cycle, which was related to missed tablets in 6, and 24% (47) reported spotting. The frequency of breakthrough bleeding and/or spotting decreased with each successive 3-month cycle, and none of the 107 women who completed the trial experienced breakthrough bleeding after 9 months of use. Ninety-one percent of the study participants who completed the trial refused to revert to a monthly OC regimen when given the option, preferring to continue the trimonthly regimen. In view of the high dosage of estrogen and progestin used in this older OC formulation, it is not surprising that breast discomfort and weight gain were the main side effects; nonetheless, these occurred no more often than in women on a conventional (21/7) OC regimen.

More recently, a trimonthly regimen in which women took a combination OC consisting of 30  $\mu$ g EE and 0.15 mg levonorgestrel (Nordette/Wyeth) for 84 days followed by a 7-day placebo period was investigated [12]. Of 203 women enrolled, 133 completed 13 weeks, 90 completed 26 weeks, 65 completed 39 weeks, and 59 completed 52 weeks. Although disappointed by the low completion rate (~30%), the Australian investigators noted that young women often change their contraceptive method. The main reason for discontinuing the trimonthly regimen was breakthrough bleeding, which was cited by 51% of 144 women, followed by breast tenderness (21.5%) and headaches (21.5%). Breakthrough bleeding also was experienced by 71% (42) of the 59 women who completed the study, with 14% (6) indicating that this symptom only occurred when they missed pills or took them late. Although women using this monophasic 30  $\mu$ g EE trimonthly 84/7 regimen receive an annual total dose of estrogen and progestin 23% greater than with a conventional 21/7 formulation, this still is substantially less estrogen than that consumed annually by a woman using a 50  $\mu$ g EE OC. Neither of the aforementioned trials examined the impact of reducing menstrual frequency on problems such as dysmenorrhea, migraines, and menorrhagia that occur in some patients during the pill-free period.

Table 2  
Symptoms reported by current OC users during the hormone-free interval [10]

Symptom	Percent of users reporting (n = 158)	
	7 days no hormone	21 days hormone
Pelvic pain	70% <sup>a</sup>	21%
Headaches	70% <sup>a</sup>	53%
Use of pain medication	69% <sup>a</sup>	43%
Bloating or swelling	58% <sup>a</sup>	19%
Breast tenderness	38% <sup>a</sup>	16%

<sup>a</sup> Statistically significant increase compared to hormone-free days,  $p < 0.001$ .

Sulak and colleagues conducted a prospective analysis of 50 OC users who experienced menstrual-related problems during the pill-free interval [13]. Patients continued to use the same low-dose (less than 50  $\mu\text{g}$  estrogen) monophasic combination OC that they were using at the start of the trial. Thirty-seven patients (74%) were stabilized on an extended regimen of 6 to 12 consecutive weeks of active tablets followed by a 7-day pill-free interval, and 16 patients (26%) either discontinued OC use or went back to the standard 21/7 regimen before being stabilized. Reasons commonly cited for discontinuing the extended OC regimen were breakthrough bleeding or spotting (8 women) and headaches (6 women). Among those stabilized, 16 used a 12-week (84/7) regimen, 13 used a 9-week (63/7) regimen, and 8 used a 6-week (42/7) regimen. Although patients were not required to keep menstrual calendars, a delay in onset and a decrease in severity of menstrual-related complaints were reported by all 37 women who extended the use of active OCs. Ten stabilized patients discontinued the extended regimen, but only 2 did so because of side effects. These 10 women completed from 6 to 17 months of extended OC use (average duration 11 months). The 27 women continuing extended OC use at the time of the report had completed 12 to 23 months of use (average duration 17.2 months). No method-related side effects were reported by 14 of the 27 women, and 10 had occasional spotting which they viewed as unimportant. One woman reported many days of breakthrough spotting but continued the extended regimen because of the relief from migraines previously experienced during pill-free intervals. Other minor reported side effects such as breast tenderness (2 women), bloating (2 women), and headache (1 woman) also were tolerated because of the relief of menstrual complaints provided by extended OC use.

### 3.1. Acceptability

Most of the women who participated in these clinical trials of extended continuous active tablet OC use welcomed infrequent menses [8,12,13]. In the earliest trial using the 50  $\mu\text{g}$  EE OC, all 196 participants completed a questionnaire regarding their perceptions of the trimonthly regimen. Favorable features cited by those continuing and those discontinuing the extended regimen included infrequent periods (82%), fewer menstrual problems (20%), and easier pill-taking (19%) [8]. Even 46% of the 89 women who discontinued the study said they would be willing to try a trimonthly regimen again, using a lower-dose OC. Additionally, in the study with a 30  $\mu\text{g}$  EE OC, few study participants expressed concern regarding deferral of withdrawal bleeding [12].

Women's attitudes toward changes in menstrual bleeding patterns caused by OCs and hormone replacement therapy were assessed in a 1996 telephone survey of Dutch women [14]. Only the findings pertaining to use of OC regimens by adolescents (ages 15–19;  $n = 323$ ), reproductive-age

Table 3  
Preferred frequency of menstrual bleeding if manipulated by oral contraceptives (expressed as percentage of respondents) [14]

	OC age category (years)		
	15–19	25–34	45–49
Number responding	321	324	319
Once a month	26.2	33.3	28.8
Once every 3 months	38.3	25.0	21.3
Once every 6 months	7.8	6.8	4.4
Once a year	4.0	3.4	6.6
Never	21.8	25.0	26.3
Not inclined to use OC	1.9	6.5	12.5
$\chi^2$ (4 df)	21.1	13.3	
p-value	0.001	0.02	

women (ages 25–34;  $n = 326$ ), and perimenopausal women (ages 45–49,  $n = 325$ ) will be discussed here. With regard to preferred changes in current menstrual bleeding characteristics, adolescents indicated a desire for less painful and shorter menstrual bleeding significantly more often than reproductive-age women ( $p < 0.001$ ), and significantly more perimenopausal women preferred amenorrhea than those of reproductive age ( $p < 0.001$ ). Women in all three age groups expressed a preference for decreasing the frequency of bleeding to less than once a month or completely eliminating menses. When asked what bleeding frequency they would prefer if manipulated by OCs, less than once a month or never was selected by 72% of those aged 15 to 19, 60% of those aged 25 to 34, and 59% of those aged 45 to 49 (Table 3). All age groups had a negative view of unexpected bleeding and heavier flow; a positive view of amenorrhea was noted with increasing age. Among current or prior OC users, 69% of those aged 15 to 19 and 63% of those aged 25 to 34 reported having used OCs to postpone menstrual bleeding. As noted by the Dutch investigators, the preferences of women for infrequent or no menstrual bleeding contrasts with the usual OC (21/7) regimen designed to mimic monthly menstruation. Moreover, when OC users experience amenorrhea, clinicians often change the formulation to one more likely to produce monthly withdrawal bleeding.

### 3.2. New products undergoing clinical investigation

A multicenter, phase III investigation of an OC formulation (Seasonale) specifically designed to decrease menstrual bleeding to 4 times per year is currently in progress. A monophasic combination of EE and levonorgestrel provided in a single trimonthly pill pack, this OC is taken continuously for 84 days followed by 7 placebo days. Dedicated packaging should make innovative use of OCs much simpler for women and their clinicians.

Another potential advantage of a dedicated 84/7 OC

Table 4

Conditions for which reduced menstrual frequency or amenorrhea may have therapeutic benefit

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Menorrhagia
Associated with uterine leiomyoma/adenomyosis
Associated with inherited bleeding disorders
von Willebrand's disease
Hemophilia
Factor XI deficiency
Associated with acquired bleeding disorders
Chronic anticoagulation
Thrombocytopenia
Dysmenorrhea (primary or acquired)
Endometriosis/chronic pelvic pain
Premenstrual syndrome
Anemia

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regimen may be greater contraceptive efficacy. Unintended pregnancies often occur because of confusion about when to start the next pill pack or forgetting to start it at the correct time [15,16]. Thus, because the trimonthly regimen decreases the stop and start cycle from 13 to 4 times a year, it could decrease the number of unintended pregnancies in long-term OC users.

#### 4. Benefits of reduced menstrual frequency/amenorrhea for women with medical conditions

Decreasing the frequency of menstrual bleeding or inducing amenorrhea can provide relief for a number of conditions directly caused by menses (see Tables 1 and 4). For example, because combination OCs reduce menstrual blood loss in women with normal menses as well as in those with menorrhagia, they are used as first-line therapy for dysmenorrhea and menorrhagia in women with uterine fibroids [17]. By reducing menstrual blood loss, the frequency of anemia can be reduced as well. Women with inherited bleeding disorders, particularly von Willebrand's disease, frequently suffer from menorrhagia. Investigators in the United Kingdom found that the incidences of menorrhagia were 74%, 57%, and 59%, respectively, in patients with von Willebrand's disease, carriers of hemophilia, and patients with factor XI deficiency, compared to 29% in a control group [18]. Quality of life for these patients is substantially impaired by menorrhagia. In a recent survey of women with inherited bleeding disorders, 39% reported reducing work and other activities during menstruation, 47% felt less productive, and 40% found that work required extra effort [18]. Moderate, severe, or very severe dysmenorrhea was an additional problem for 51% of these women. Clinical evidence indicates that use of combination OCs in the standard 21/7 regimen can reduce menorrhagia in women with von Willebrand's disease [19]. Clearly, such patients could benefit from either less frequent menses or amenorrhea through extended use of OCs.

Table 5

Potential benefits of OC use for sportswomen with menstrual disturbances [22]

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Reduction in premenstrual symptoms
Less menstrual blood loss
Ability to control timing of cycle
Lower risk of musculoskeletal injury
Increased bone density (particularly in athletes with baseline hypopostrogenism)

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Menstrual disorders including dysmenorrhea, menorrhagia, irregular menses, and premenstrual syndrome are reported by women who experience spontaneous ovulatory menses as well as by OC users who experience monthly bleeding due to exogenous hormone withdrawal. In the latter group, there is growing evidence that the symptoms experienced during the pill-free interval can be substantially reduced by extending the use of active OC tablets [13]. Women with endometriosis, which appears to be caused by, and is clearly aggravated by menstruation, are often treated medically with drugs that inhibit ovulation and menstruation. Obstetrician/gynecologists have for decades used extended OC regimens in the treatment of endometriosis [20]. With regard to other conditions aggravated during menses, less frequent menses or amenorrhea with extended OC use might minimize cyclical exacerbation in some patients with migraines or seizure disorders.

#### 5. Benefits of reduced menstrual frequency/amenorrhea in specific settings or patient types

Reduced menstrual frequency or amenorrhea offers specific benefits for women serving in the military [21], for female athletes [22,23], and for women with severe mental retardation [24]. A survey of 158 freshman female Cadets at the United States Military Academy at West Point found that more than 60% reported menstrual and premenstrual symptoms that interfered with physical activities [21]. Problems changing, obtaining, and disposing of menstrual hygiene materials were experienced by 63%, 52%, and 38%, respectively, of female Cadets. These findings suggest that active-duty female military recruits may experience similar (or more severe) difficulties.

Female athletes often use OCs not only for contraception but also to protect bone health, to manipulate the menstrual cycle, and to control premenstrual symptoms [22]. A recent review of the literature found that OC use offered a number of potential benefits for sportswomen with menstrual disturbances (Table 5) [22]. In addition to these benefits, by reducing menstrual blood loss and thereby the risk of iron deficiency anemia, OC use may also have a positive impact on performance, particularly among athletes with menor-

rhagia. Others have found that female athletes who use OCs suffer fewer musculoskeletal injuries, probably as the result of experiencing less premenstrual syndrome and dysmenorrhea [23]. Nevertheless, the perception persists even among otherwise well-informed clinicians that routine use of an extended OC regimen is inadvisable [23].

For a number of years, progestin-only medications have been used to induce amenorrhea in women with severe mental retardation who suffer from menstrual hygiene problems [24,25]. In this setting, an extended OC regimen might also offer substantial benefits.

### *5.1. Reducing the burden of monthly menstruation in young teens*

A group of patients with much to benefit from less frequent menses or amenorrhea are teens. With the age of menarche in the United States continuing to decline [26], young teens more often than previously are having to cope with the pain and inconvenience of monthly menstrual cycles. Absenteeism from school and inability to participate in sports activities too frequently results.

Many clinicians currently prescribe OCs to non-sexually active young teens to regularize menses and reduce cramps; in the absence of pregnancy or gynecologic disease, a pelvic examination prior to OC initiation can be deferred [27]. In this context, we should feel comfortable counseling teen patients and their mothers regarding the benefits of innovative OC schedules that reduce menstrual frequency, thereby improving the quality of life for these young patients.

### *5.2. Reduced menstrual frequency: advantages for perimenopausal women*

The perimenopausal transition, usually impacting women in their mid 40s and older, is associated with menstrual irregularities and vasomotor symptoms. Use of combination OCs regularizes menses [28] and suppresses hot flashes [29]. However, vasomotor and other symptoms may recur during the pill-free interval in perimenopausal women using the traditional 21/7 OC schedule. For these reasons, extended use of continuous OC tablets represents an appealing therapeutic option for many healthy, nonsmoking perimenopausal women, whether or not contraception is needed.

## **6. Interventions that can induce amenorrhea**

Until the development of a variety of medical alternatives, hysterectomy was the only definitive treatment available for women with severe menorrhagia and/or dysmenorrhea associated with gynecologic disease. Developed in the 1980s, endometrial ablation represents an alternative surgical procedure that costs substantially less than hysterectomy, requires little if any hospital stay, and has a shorter

recovery period [30]. Failure can occur up to 3 years after endometrial ablation and amenorrhea is established in fewer than 50% of patients [30]. However, 85% of those considered treatment successes at 3 years are cured of menorrhagia [30].

A number of medical alternatives are now available for the treatment of menorrhagia, endometriosis, and other menstrual-related disorders (Table 6). Several of these options, including continuous or extended monophasic combination OCs, depot medroxyprogesterone acetate (DMPA), and the levonorgestrel intrauterine device (approved by the FDA in December 2000) offer cost-effective, generally well tolerated alternatives to surgery, and also provide protection against pregnancy.

A recent study in 30 patients with refractory, recurrent hypermenorrhea found the levonorgestrel IUD to be as effective as rollerball endometrial ablation in reducing bleeding over 12 to 24 months [31]. In the opinion of the investigators, the levonorgestrel IUD (where available) may replace 75% of endometrial ablations.

Although various medical interventions may not induce complete cessation of bleeding, the reduction in menstrual flow is often perceived by patients as adequate (Table 7) [8,12,13,25,30,32–37]. Use of a conventional 21/7 low-dose, monophasic, combination OC may decrease menstrual blood loss by 40% to 50% [32,33], whereas the extended 84/6 OC regimen produced amenorrhea in all women in one study who continued use for 9 months [8].

With DMPA, the percentage of patients who become amenorrheic increases with increasing duration of use and is 50% to 70% after 1 year [25,34]. Some clinicians have suggested early re-injection of DMPA (e.g., each 8 to 10 weeks) to reduce bleeding, but a controlled cohort study found that this practice was not effective and predisposed to greater weight gain [38]. Although some experts feel that use of supplemental estrogen may accelerate the onset of amenorrhea in DMPA users, the one large, carefully controlled study conducted to date (which used very high estrogen doses for only 2 weeks) provides little supporting evidence [39]. If clinicians choose to use estrogen supplementation with DMPA, an appropriate dose would appear to be 0.9 to 1.25 mg daily of oral conjugated estrogen or its equivalent (oral or transdermal) administered continuously.

In women with idiopathic menorrhagia, high dose oral progestin (norethindrone acetate, 5 mg 3 times daily) and the levonorgestrel IUD reduced menstrual blood loss by 87% and 94%, respectively, after 3 months of use [35]. However, a desire to continue the regimen was expressed by only 22% of those using oral progestin compared to 76% of those using the levonorgestrel IUD, although there was no difference in the frequency of symptoms such as breast tenderness, headaches, nausea, and acne in the two groups. In my experience, a lower oral progestin dosage of one 5 mg tablet of norethindrone acetate daily produces amenorrhea in a substantial proportion of patients with menorrhagia, including those with uterine fibroids. However, even this

Table 6  
Medical options for the induction of amenorrhea

Features	Continuous or extended COC <sup>a</sup>	DMPA ± estrogen <sup>a</sup>	High dose oral progestin <sup>b</sup>	GnRH agonist ± estrogen add-back <sup>d</sup>	Danocrine <sup>†</sup>	LNG IUD
Dosage	≤35 µg estrogen Monophasic continuous or extended 84/7 regimen (Seasonale) <sup>c</sup>	150 mg IM every 3 mo	Norethindrone acetate (Aygestin) 5 mg; 1–3 tablets daily	Leuprolide acetate (LUPRON DEPOT) 3.75 mg monthly or 11.25 mg q 3 mo; OTHER (see note)	Danazol, 800 mg bid (optional titration to lowest dose sufficient to maintain amenorrhea)	Mirena, releases 20 µg LNG daily effective for 5 years
Medical uses	Menorrhagia, dysmenorrhea, endometriosis, anemia PMS, menstrual migraine	Same as COC	Same as COC	Same as COC	Endometriosis, menorrhagia	Menorrhagia
Contraception provided	Yes	Yes	Yes	No	No	Yes
Disadvantages	Breakthrough bleeding/spotting	Irregular bleeding/spotting	Progestin side effects (e.g., bloating, mood changes)	Loss of bone density, other hypoestrogenic side effects (unless add-back estrogen used)	Androgenic and hypoestrogenic side effects	Intermenstrual bleeding
Cost vs other	Cost-effective if use of sanitary products is high	Cost-effective	More costly than extended COC	Very expensive	Expensive	High initial cost, cost-effective with extended use

<sup>a</sup> None of the uses listed represent FDA-approved indications.

<sup>b</sup> Approved for the treatment of endometriosis.

<sup>c</sup> Seasonale is an investigational drug.

<sup>d</sup> LUPRON DEPOT approved for treatment of endometriosis and anemia (menorrhagia) in women with fibroids. Other GnRH agonists approved for treatment of endometriosis: Synarel (nafarelin acetate nasal solution 2 mg/mL), 1 spray AM and PM (alternate nostrils); Zoladex (goserelin acetate, 3.6 mg implant) monthly.

COC = combination oral contraceptive; LNG = levonorgestrel.

dose of norethindrone acetate appears to be associated with more systemic side effects than combination OCs, DMPA, or the levonorgestrel IUD, and is somewhat more costly than combination OCs or DMPA.

Danocrine and gonadotropin-releasing hormone (GnRH) agonists such as leuprolide acetate (Lupron Depot<sup>®</sup>) effectively induce amenorrhea, and shrink uterine leiomyomata, but ovulation may not be universally suppressed; therefore, concomitant use of a nonhormonal contraceptive may be necessary [30]. Long-term use of these agents is limited by hypoestrogenic side effects and cost. Leuprolide acetate side effects, including breast changes, breast tenderness/pain, vaginal dryness, and loss of bone density, can be minimized by use of add-back estrogen.

GnRH agonist treatment can be useful in cancer patients who develop menorrhagia caused by chemotherapy-induced thrombocytopenia. A recent trial suggests that leuprolide acetate (7.5 mg IM monthly) is useful for the induction of amenorrhea in reproductive-age women when the first injection is given at least 28 to 39 days prior to bone marrow transplant [36]. A 3.75 mg monthly dose of leuprolide acetate used in combination with a 30 µg EE monophasic combination OC effectively treated heavy bleeding associated with thrombocytopenia in premenopausal women with

acute leukemia in another study [37]. The investigators felt that, initially, the OC is needed in combination with the GnRH agonist leuprolide acetate as the latter's onset of therapeutic effect is not as rapid as that of OCs.

## 7. Conclusions

As women become more knowledgeable about the safety, efficacy, and (for many women) desirability of the medical approaches described above, more of our patients will be choosing whether and when to bleed. When the OC was first introduced in the 1960s, many social, cultural, and religious pressures favored a regimen in which monthly withdrawal of hormones for 7 days was followed by bleeding, since this implied that the method-induced cycle was "natural." Although there is no known medical benefit to routine monthly bleeding, women continue to be prescribed the standard 21/7 OC regimen. As clinicians, our goal should be to help each woman find a contraceptive regimen and menstrual pattern that meets her individual needs. Does she wish to postpone bleeding for a particular reason—athletic competition, vacation—or prevent it altogether to relieve problems associated with menses or monthly hor-

Table 7  
Reduction in menstrual blood loss (MBL) with different medical interventions [8,12,13,25,30,32–37]

Medical intervention	Effect on MBL	Reference
Low-dose COC, 21/7	44% to 50% decrease	Larsson et al. 1992 [32]
Extended COC	40% to 100% amenorrhea <sup>a</sup>	Nilsson, Rybo. 1971 [33] Loudon et al. 1977 [8] <sup>b</sup> Kovacs et al. 1994 [12] <sup>c</sup> Sulak et al. 1997 [13] <sup>d</sup>
DMPA	50% to 73% amenorrhea @ 1 year <sup>a</sup>	Kaunitz 1996 [25]
High dose oral Norethindrone acetate	87% decrease	Kaunitz 2000 [34] Irvine et al. 1998 [35]
GnRH agonist	100%	Stabinsky et al. 1998 [30] Laufer et al. 1997 [36] Sica et al. 1996 [37]
Danocrine	100%	Stabinsky et al. 1998 [30]
Levonorgestrel IUD	94% decrease	Irvine et al. 1998 [35]

<sup>a</sup> Percentage of patients becoming amenorrheic increases with increased duration of use.

<sup>b</sup> 84 days active drug/6 pill-free days.

<sup>c</sup> 84 days active drug/7 placebo days.

<sup>d</sup> 42–84 days active drug/7 pill-free days.

COC = combination oral contraceptive; DMPA = depot medroxyprogesterone acetate.

hormone withdrawal? Therapeutic options that offer women such choices are available at present; existing low-dose monophasic OCs can be administered continuously or in an extended regimen, and the new dedicated 84/7 product under development will offer women simplified packaging and convenience. By responding to emerging patient attitudes, needs, and preferences, we have the potential to improve adherence to the regimen selected, which is likely to result in improved contraceptive efficacy compared with conventional 21/7 OC regimens. As Dr. Anita Nelson so aptly put it,

“Can we imagine how well women would take their pills if they could use them to control when (and if) they menstruated?” [40]

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