

CHAPTER 1

The Menstrual Cycle

SEVERAL KEY POINTS ON MENSTRUAL PHYSIOLOGY:

- **What initiates menses (and the next cycle)** is atrophy of the corpus luteum from the current cycle, leading to a fall in serum estrogen (E) and progesterone (P) levels. Without hormonal support, the endometrium sloughs. This drop in hormonal levels is also detected by the hypothalamus and pituitary, and FSH levels increase to stimulate follicles for the next cycle (see Figures 1.1 and 1.2).
- **Anovulation in women NOT on birth control pills usually leads to amenorrhea or to irregular bleeding.** Although cycles in women on pills are anovulatory, they are usually regular because the hormones in pills stimulate and support the endometrium. When the placebo pills are taken, the drop in circulating hormone levels causes withdrawal bleeding. Progestins in pills protect the endometrium from endometrial hyperplasia and cancer. The absence of progesterone in anovulatory women not on pills places these women at risk for endometrial hyperplasia and cancer. ←
- **The two-cell, two gonadotrophin theory:** LH-stimulated *theca* cells comprise the outer cell layer surrounding the follicle and produce androgens (testosterone and androstenedione). These androgens diffuse toward the inner layer *granulosa* cells where they are converted into estradiol (E₂) by FSH-stimulated aromatase (see Figure 1.3).
- In a developing follicle, **low androgen levels** not only serve as the substrate for FSH-induced aromatization, but also stimulate aromatase activity. On the other hand, **high levels of androgens** (an “androgen-rich” environment) lead to inhibition of aromatase activity and to follicular atresia.
- Each woman is born with 1-2 million follicles, most of which undergo atresia before puberty. Hundreds of thousands of other follicles are lost in the preantral stage during the reproductive years. Only about 18-20 follicles each month are recruited by rising FSH levels. Of those 18-20 follicles, usually only one dominant follicle ovulates.
- FSH levels drop 4-5 days before ovulation as a result of negative feedback from FSH-stimulated production of E₂ and inhibin B. The dominant follicle “escapes” the effects of falling FSH levels before ovulation, because it has more granulosa cells, more FSH receptors on each of its granulosa cells, and increased blood flow. Cut off from adequate FSH stimulation, the other follicles undergo atresia.
- Once the other follicles are out of the picture, leaving only the dominant follicle, total production of E₂ and inhibin drops, FSH levels rise again. This induces an outpouring of E₂ from the dominant follicle. When E₂ production is sustained at sufficient levels (about 200) for more than 50 hours, negative feedback of E₂ on LH reverses to positive feedback. The LH surge occurs, and an oocyte is extruded.
- From the remaining cells, the corpus luteum is formed. Some granulosa cells continue to produce E₂ and inhibin but many join the outer layers of theca cells to produce progesterone (P) and activin. Inhibin selectively suppresses FSH, not LH. The highest levels of inhibin are during the mid-luteal phase, causing FSH levels to be the lowest in the mid-luteal phase. At the end of the cycle (10-14 days after ovulation) if the corpus luteum is not rescued by HCG produced by the implanted trophoblast, the corpus luteum will undergo programmed atresia. Falling E₂, P, and inhibin levels induce the release of FSH to initiate another cycle.

Figure 1.1 Menstrual cycle events - Idealized 28 Day Cycle

[Hatcher RA, et al. *Contraceptive Technology*. 16th ed. New York: Irvington, 1994:41]

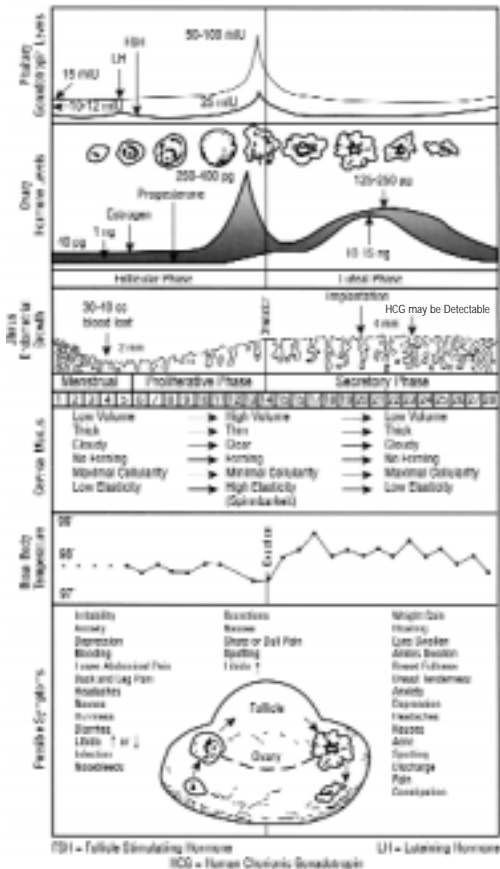
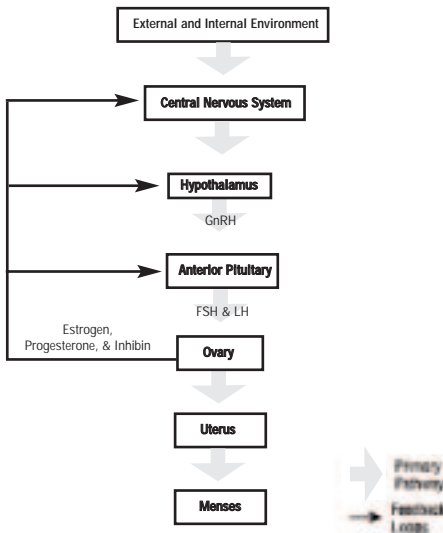


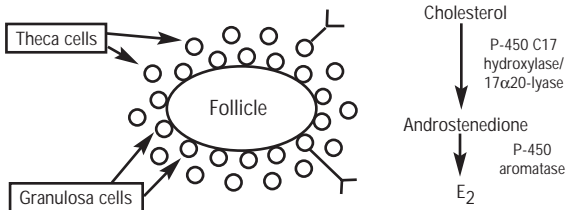
Figure 1.2 Regulation of the menstrual cycle

[Hatcher RA, et al. *Contraceptive Technology*. 16th ed. New York: Irvington, 1994:40]



Primary hormone pathways (—) in the reproductive system are modulated by both negative and positive feedback loops (---). Prostaglandins, secreted by the ovary and by uterine endometrial cells, also play a role in ovulation, and may modulate hypothalamic function as well.

Figure 1.3 The Two-cell, two gonadotrophin theory



➔ ***Is Menstruation Obsolete? Who Needs a Period?***

What is "natural" — 50, 150, or 450 menstrual periods in a woman's lifetime?

In prehistoric times women had 50 menstrual cycles or less. In Colonial America, when women were having an average of 8 babies and nursing each baby for 2-3 years, women averaged 150 menstrual periods per lifetime. Currently in America women average 450-480 menstrual cycles per lifetime. [Segal, 2001]

Some women find regular menses reassuring, positive, "natural" or important evidence that they are still capable of reproducing. Other women, who regularly experience extremely painful menses, menses heavy enough to cause anemia, severe cyclic migraine, depression, premenstrual symptoms, or breast tenderness, would be happier having no periods at all.

Clinicians must know how the menstrual cycle changes caused by a specific contraceptive may affect a patient coming to them for contraceptive advice. Close to half of all visits to gynecology clinicians are for difficulties women experience at the time of their menses. [Segal, 2001] Women with undesirable symptoms associated with their menses may benefit from contraceptives that alter the likelihood of ovulation, the amount of blood lost each month, or the extent of menstrual cramping and pain. In some instances, women may benefit from contraceptives that completely eliminate monthly periods.

Unfortunately, few women are aware of the noncontraceptive benefits caused by contraceptives and tend to have exaggerated perceptions of the negative effects of contraceptives. This has been well documented in a study of the knowledge of educated women of oral contraceptives. [Peipert 1993]

Clearly some women choose contraceptives to gain relief from symptoms related to their menstrual cycle. Others discontinue them due to undesirable effects on the pattern of their menses. In the pages ahead, the advantages and disadvantages of each contraceptive related to the menstrual cycle are described. Given the importance of the menstrual cycle to women, the sections on the effects of contraceptives on menses are very important.

➔ A provocative book by Coutinho and Segal raises the question: ***Is Menstruation Obsolete?*** [Coutinho, 1999] These two individuals played pivotal roles in the research leading to the approval of a number of our current contraceptives. The absence of menses is a particularly important issue for clinicians to be able to discuss with women considering taking birth control pills continuously (no 7-day hormone-free interval), or thinking of using Depo-Provera or the Mirena intrauterine contraceptive that may eliminate periods completely. Here are two comments on their book:

➔ Kate Miller, MPH, of the University of Pennsylvania states: ***One of the difficulties of regular menstruation is the usual assembly of monthly symptoms - cramps, headache, fatigue, irritability - which are often dismissed as part of "the curse" that women must simply endure. Since women tolerate these symptoms so regularly, they may not automatically include them in the "risks" of monthly menstruation. Again, the reader is encouraged to recognize what may have previously gone unnoticed: that this monthly discomfort is simply not obligatory. In fact, it can be a startling exercise for a woman to imagine her life without the hassles and ailments of regular menstruation. This is a message whose time has come.***

➔ Faye Wattleton, formerly president of the Planned Parenthood Federation of America, said ***Is Menstruation Obsolete? challenges the Holy Grail of one of the most intimate aspects of a woman's body and life experience. This unprecedented scientific analysis of the health and social consequences and role-defining power of menstruation is certain to trigger consternation and, hopefully, thoughtful consideration. Let the debate begin.***