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THE EVOLUTION OF ENDOMETRIAL CYCLES AND MENSTRUATION

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ABSTRACT

According to a recent hypothesis, menstruation evolved to protect the uterus and oviducts from sperm-borne pathogens by dislodging infected endometrial tissue and delivering immune cells to the uterine cavity. This hypothesis predicts the following: (1) uterine pathogens should be more prevalent before menses than after menses, (2) in the life histories of females, the timing of menstruation should track pathogen burden, and (3) in primates, the copiousness of menstruation should increase with the promiscuity of the breeding system. I tested these predictions and they were not upheld by the evidence.

I propose the alternative hypothesis that the uterine endometrium is shed/resorbed whenever implantation fails because cyclical regression and renewal is energetically less costly than maintaining the endometrium in the metabolically active state required for implantation. In the regressed state, oxygen consumption (per mg protein/h) in human endometria declines nearly sevenfold. The cyclicity in endometrial oxygen consumption is one component of the whole body cyclicity in metabolic rate caused by the action of the ovarian steroids on both endometrial and nonendometrial tissue. Metabolic rate is at least 7% lower, on average, during the follicular phase than during the luteal phase in women, which signifies an estimated energy savings of 53 MJ over four cycles, or nearly six days worth of food. Thus, the menstrual cycle revs up and revs down, economizing on the energy costs of reproduction. This economy is greatest during the nonbreeding season and other periods of amenorrhea when the endometrium remains in a regressed state and ovarian cycling is absent for a prolonged period of time. Twelve months of amenorrhea save an estimated 130 MJ, or the energy required by one woman for nearly half a month. By helping females to maintain body mass, energy economy will promote female fitness in any environment in which fecundity and survivorship is constrained by the food supply. Endometrial economy may be of ancient evolutionary origin because similar reproductive structures, such as the oviducts of lizards, also regress when a fertilized egg is unlikely to be present.

Regression of the endometrium is usually accompanied by reabsorption, but in some species as much as one third of the endometrial and vascular tissue is shed as the menses. Rather than having an adaptive basis in ecology or behavior, variation in the degree of menstrual bleeding in

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primates shows a striking correlation with phylogeny. The endometrial microvasculature is designed to provide the blood supply to the endometrium and the placenta, and external bleeding appears to be a side effect of endometrial regression that arises when there is too much blood and other tissue for complete reabsorption. The copious bleeding of humans and chimps can be attributed to the large size of the uterus relative to adult female body size and to the design of the microvasculature in catarrhines.

INTRODUCTION

THE FUNCTION of menstruation is a central enigma of mammalian, and especially primate, reproductive physiology. Each cycle the uterus builds a glandular epithelium with a high secretory capacity and an elaborate microvasculature, only to reabsorb or void it with the menses if implantation does not occur. Why does the endometrium not maintain a steady state of readiness for implantation by the blastocyst? What is the selective advantage of cyclical regeneration and regression?

A recent answer proposed by Profet (1993) is that menstruation protects the uterus and oviducts from colonization by pathogens transported by sperm. According to Profet (1993), menstrual blood dislodges infected endometrial tissue and delivers immune cells to the uterine cavity to combat pathogens. Aside from brief remarks (Ravenholt 1966; Alexander 1979:167; Shaw and Roche 1985; Finn 1987; Garey 1990; Worthman et al. 1992; Haig 1993), Profet's antipathogen hypothesis is the first explanation for the evolution of a phenomenon that previously had been explained only in terms of proximate mechanisms (e.g., Baird and Michie 1985; Johnson and Everitt 1988; Ferin et al. 1993). The potential medical implications of the antipathogen hypothesis have received wide publicity in the popular media. These implications include Profet's argument that contraceptives that suppress menstruation may promote uterine infection, and her suggestion that curtailing uterine bleeding at times of infection may undermine the body's natural defenses. In view of the wide publicity generated by these clinical recommendations, it is important that the antipathogen hypothesis be rigorously tested.

In the first part of this article, I briefly summarize the cyclic changes that occur in the uterus during the menstrual cycle in Old World primates. These cyclic changes are important because, to understand menstruation, we need to examine the entire cycle of which menstruation is only the end point. In the second part, I test the following three predictions from the antipathogen hypothesis: (1) uterine pathogens are more prevalent before menses than after menses, (2) the timing of menstruation tracks pathogen burden, and (3) in primates, the copiousness of menstruation increases with the promiscuity of the breeding system (see Profet 1993:345, 370, 360). In the third part, I suggest that the functional significance of endometrial regression is metabolic economy, and that menstrual bleeding is merely a side effect that occurs when there is too much blood for complete reabsorption. I also discuss three alternative hypotheses that focus on endometrial neoplasia (Ravenholt 1966), the advertisement of fertility (Worthman et al. 1992), and endometrial decidualization (Finn 1987, 1994).

UTERINE CYCLICITY IN OLD WORLD PRIMATES

Uterine cyclicity primarily involves the endometrium (Figure 1), which is the mucosa that lines the uterine cavity. The endometrium is served by a microvascular blood supply, and has a superficial layer of columnar epithelial cells above a vascularized stroma made of connective tissue. For the reviews that provide the basis for this summary, see Ferin et al. (1993), Johnson and Everitt (1988), and Padykula (1988).

Proliferative Phase. During the latter half of the follicular phase of the ovarian cycle, estradiol stimulates DNA synthesis and mitotic activity in the endometrium. As a result, the mucosa doubles in thickness, and the tubular glands—invaginations of the epithelium that penetrate the stroma—become greatly enlarged (Figure 1).

Secretory Phase. After ovulation, the endometrium enters the secretory phase which corresponds to the luteal phase of the ovarian cycle (Figure 1). The estrogen-primed endometrium binds progesterone, which stimulates the glands to secrete a rich mixture of glycoprotein, sugars, and amino acids. Glandular

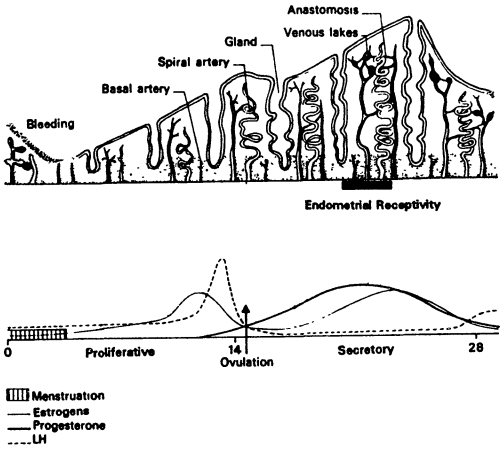


FIGURE 1. REGRESSION AND RENEWAL OF THE HUMAN ENDOMETRIUM AND ASSOCIATED STEROID HORMONE CHANGES

Note the brief period of endometrial receptivity indicated by the black bar (after Johnson M H and Everitt B J, *Essential Reproduction*, 3rd ed, Blackwell Scientific Publications, 1988).

secretion peaks in humans at the midpoint of the secretory phase, approximately seven days postovulation. If fertilization has occurred, it coincides with the time of implantation by the blastocyst. Progesterone also causes the enlargement of stromal cells and the expression of an array of genes that code for proteins believed to be important for successful implantation (Ferin et al. 1993). Within the stromal tissue, progesterone causes the microvasculature to complete its development. The superficial stromal cells surrounding the spiral arterioles enlarge and begin to differentiate into decidual cells which, after implantation, are a major source of nourishment for the embryo. The decidual tissue contains lipids, carbohydrates, nucleic acids, and proteins and has been compared to the yolk reservoir of birds' eggs (Johnson and Everitt 1988:234). Aside from nourishing the embryo, the decidua may protect it against immunologic rejection; the decidua may also protect maternal tissue against uncontrolled invasion by the trophoblast (Riddick et al. 1983:238; Haig 1993).

Menstruation. If implantation does not occur, then ovarian steroid levels fall, triggering the collapse of the elaborate microvasculature and, ultimately, the secretory epithelium. In most mammals, endometrial tissue is digested by lysosomal lytic enzymes and extracellular proteases and reabsorbed without external bleeding. In menstruating primates, however, about a third of the endometrial tissue is shed as the menses together with blood from the ruptured microvasculature (Nalbandov 1976; Johnson and Everitt 1988; Kaiserman-Abramof and Padykula 1989; Ferin et al. 1993). The first day of menstrual bleeding is customarily defined as day one of the menstrual cycle.

THE ANTIPATHOGEN HYPOTHESIS

Prediction: Uterine pathogens are more prevalent before menses than after menses.

If the function of menstruation is cyclically to destroy the pathogens that infect the endometrium, then uterine pathogens should decrease after menses. This is probably the most direct prediction from the antipathogen hypothesis but, according to Profet (1993:345), cyclical variation in endometrial pathogen load has not been studied. Hemsell et al. (1989), however, tested for an association between phase of the menstrual cycle and bacteria in the uterine endometrium in 33 asymptomatic women (age 18 to 44 years) who were normal upon pelvic examination and who had no history of pelvic infection. Twenty-four of the women were not practicing any form of contraception, and nine had an intrauterine device (IUD) (Hemsell, personal communication). None of the women in the analysis were using barrier methods of contraception or oral contraceptives. This is significant because these modes of contraception reduce the possibility of endometrial infection by preventing sperm from getting past the cervix; in the case of oral contraceptives this is achieved by alterations in the cervical mucus (Ferin et al. 1993: 189). Hemsell et al.'s conclusion is that phase of the menstrual cycle was not associated with the number of bacterial species recovered (Hemsell et al. 1989). Although Hemsell et al. (1989) provide data that are contradictory to her hypothesis, Profet (1993:344) only mentions their finding that fewer bacterial species were cultured from the endometrium than the endocervix, evidence which she uses to un-

derscore the ability of the uterus to rapidly clear bacteria.

Bollinger (1964) provides data on phase of the menstrual cycle and the presence or absence of bacteria in endometrial cultures of 173 indigent women who were free of any significant pelvic abnormalities. Bollinger does not describe contraceptive use in his sample, but pathogenic bacteria were present in 41.6% of the cultures, suggesting that contraception had not sealed off the upper reproductive tract. Approximately the same percentages of cultures were positive as negative at each phase of the menstrual cycle (day 1 to 7, 15 to 21, 22 to 28, and day 29 to 35) except for days 8 to 14 when 51 (65%) of cultures were positive and 28 (35%) were negative. Thus neither Hemsell et al. nor Bollinger found a decrease in bacteria after menses.

In both studies only one endometrial sample was collected per woman so the problem remains that differences in endometrial bacteria among women might have masked changes occurring within women over the course of the cycle. Further studies are therefore needed in which individual women are sampled repeatedly. The endometrial flora can be sampled transcervically using a cotton-tipped swab or a double lumen catheter with a brush; both are quick office procedures (Martens et al. 1989).

The prediction that uterine pathogens "are more prevalent before menses than after menses" is actually stated by Profet (1993:345) as ". . . more prevalent before menses than they are between the end of menses and the first postmenstrual copulation." Data are not available on women who were sampled after menses but before the first postmenstrual copulation. However, if a single postmenstrual copulation is enough to bring the endometrial pathogen load up to premenstrual levels, then menstruation is not an effective defense against pathogens. If menstruation is a pathogen defense, then fewer pathogens should be recovered early in the cycle, soon after menstruation, than late in the cycle because: (1) bacterial populations reduced by menstruation will have had a longer time to recover, (2) later in the cycle more acts of intercourse will have occurred since menstruation (in some cases sexual partners might also accumulate), and (3) the cervical mucus is most penetrable to sperm around ovulation, which means that it is at midcycle that sperm-borne pathogens are most likely to be transmitted (Chretien and David 1978; Wolf et al. 1978). In summary, the antipathogen hypothesis predicts that more pathogens should be recovered just before menses than earlier in the cycle, but current data do not support this prediction (Hemsell et al. 1989; Bollinger 1964).

If the immune agents in menstrual blood are effective in combating pathogens, then they should depress not only uterine but also vaginal pathogens after menses. Profet (1993: 343) states that fluctuations in vaginal bacteria counts should be small because the ". . . vagina is constantly reexposed to and colonized by bacteria in the external environment. . . ." However, the bacterial flora of the vagina is at least as similar, and in some respects more similar, to the flora of the cervix than it is to the flora of the vulva (Domingue et al. 1991). Thus, colonization of the cervix by vaginal bacteria is probably at least as prevalent as colonization of the vagina by vulvar organisms. This implication is important because cervical infections in humans may ascend to the uterine mucosa and thence to the oviducts (Mardh et al. 1981). Inert substances placed in the cervix before hysterectomy have been isolated from the endometrium during surgery (Keith et al. 1984), and the standard way to infect the uterus in laboratory animals is to infect the vagina.

To find out if menstrual blood helps rid the vagina of pathogens, I reviewed the data on the bacteriology of the vagina over the course of the menstrual cycle in healthy, asymptomatic women. On the basis of a qualitative study of cultures obtained serially from 89 women at four-day intervals, Mehta (1982) concluded that stage of the menstrual cycle was not correlated with the prevalence of aerobic or anaerobic bacteria. Furthermore, bacterial growth in premenopausal and menopausal women did not differ qualitatively from that found in menstruating women. In a quantitative study of ten women who were sampled at weekly intervals, Wilks and Tabaqchali (1987) replicated the finding that there are no major changes in the vaginal bacterial flora during the menstrual cycle. Some minor changes were found and these imply, if anything, that

pathogen burden is lowest just prior to menses. Specifically, the mean number of species isolated per specimen decreased significantly ($p < 0.05$) from a mean of 4.6 in the first week after menses to 2.9 in the fourth week after menses. A low pathogen burden prior to menses was also reported by Bartlett et al. (1977) who quantified the bacteria in 35 samples of vaginal secretions taken serially from five women at intervals of three to five days. They found no significant differences in the concentrations of anaerobic bacteria over the menstrual cycle, but concentrations of aerobic bacteria were 100-fold higher ($p \leqslant 0.05$) in the first week after the onset of menses than in the week before. Johnson et al. (1985) obtained serial vaginal cultures from 34 women over the menstrual cycle. They recovered a mean of 4.8 aerobic species during menses compared with 3.5 in the intermenstrual cultures ($p < 0.0005$) and 5.6 anaerobic species during menses compared with 4.10 in the intermenstrual cultures ($p < 0.05$). A quantitative analysis showed no significant difference in the total number of bacteria in the menstrual and intermenstrual cultures (Johnson et al. 1985). In summary, menstrual blood does not cleanse the vagina of pathogens.

Phase of the menstrual cycle is correlated with the prevalence of sexually transmitted organisms—but not in the direction predicted by the antipathogen hypothesis. For example, as Profet (1993:347, 365) herself reports, numerous studies demonstrate that *Neisseria gonorrhoeae*—a major cause of infections of the endometrium (endometritis) and oviducts (salpingitis)—is more prevalent in endocervical cultures obtained during and shortly after menses (e.g., Johnson et al. 1969; Holmes et al. 1971; James and Swanson 1978; McCormack et al. 1982; Sweet et al. 1986). In a study of women (N = 42) with acute gonococcal infection, the onset of salpingitis occurred one week after the onset of menses in 55% and two weeks after the onset of menses in 81% of the women (Sweet et al. 1986). Exogenous iron promotes the growth and virulence of *N. gonorrhoeae* (Payne and Finkelstein 1978), which may explain the association between *N. gonorrhoeae* and menstrual bleeding.

Data on the relationship between *Chlamydia trachomatis* and the menstrual cycle are less clear cut. According to Sweet et al. (1986), *C. trachomatis* varies with the menstrual cycle in the same way as *N. gonorrhoeae*. In a sample of 28 women with chlamydial infections, the onset of acute salpingitis occurred one week after the onset of menses in 57% and two weeks after the onset in 82% of the women. Rosenthal and Landefeld (1990), however, found that women sampled late in the menstrual cycle had slightly more chlamydial infections than women sampled earlier. Specifically, 13% of 86 women sampled on days 22 to 35 of the menstrual cycle had chlamydial infections, compared to only 1.6% of the 252 women sampled on cycle days 1 to 21. Although the sample sizes of infected women were small (11 and 4, respectively), the results were significant ($p < 0.001$). An earlier study found no relationship between phase of the menstrual cycle and chlamydial infection (Tait et al. 1980). Mardh et al. (1981) and Ingerslev et al. (1982) conclude that cyclical shedding of the endometrium is inadequate for ridding the mucosa of *N. gonorrhoeae* and *C. trachomatis* because these organisms infect the endometrial crypts, which are deep in the mucosa and are not shed.

The concentration of *Trichomonas vaginalis*, a protozoan parasite of the human urogenital system, has also been charted in relation to the menstrual cycle. Specifically, Demes et al. (1988) reported that in 21 of 30 patients the concentration of parasites in vaginal washes was reduced by a mean of 68% (range 7% to 100%) during menstruation compared with extramenstrually. However, the beneficial effect of menstruation was transient and pertained primarily to the first two days of bleeding. During the final days of bleeding, and immediately afterwards, parasite numbers rebounded to premenstrual levels. Thus menstruation had no sustainable impact.

If the function of menstruation is pathogen defense, then rates of organism recovery upon culture should be lower after menses. This prediction was directly refuted by the serial cultures of vaginal bacteria which show that if menstruation has any effect at all, it is to promote bacterial growth. In the case of infections of *N. gonorrhoeae*, menstruation is clearly exacerbatory. Current data provide no evidence for an association between phase of the menstrual cycle and endometrial bacteria.

The relationship between chlamydial infection and the menstrual cycle remains ambiguous, while the menstrual decline in *T. vaginalis* attenuates even before the cessation of bleeding. In conclusion, data presently available do not support the argument that menstruation has a role in controlling the microbial flora of any part of the female reproductive system (uterus, oviducts, cervix, vagina).

On the contrary, menstruation may aggravate the growth of microbial flora because blood is an excellent culture medium for bacteria (Johnson et al. 1985; Eschenbach 1976). It contains not only iron, but also amino acids, proteins, and sugars that are needed for bacterial growth. Serum is therefore the most common nutrient in cell culture media. Mucosal and cutaneous barriers ordinarily exclude microorganisms from the blood vessels, but when these barriers are breached, infectious organisms enter the bloodstream (Campos et al. 1994). Circulating antibodies and other proteins usually destroy bacteria, but as soon as the blood leaves the vessels these immune defenses are overwhelmed (see Bollinger 1964; Masur and Fauci 1991:465; Campos et al. 1994). The potential for blood to worsen infections was demonstrated by Weinstein et al. (1974) who reported that when fresh blood was added to a bacterial inoculum introduced into the pelvic region of rats, mortality was higher than in control rats who received the inoculum alone. *Staphylococcus aureus*, the organism associated with Toxic Shock Syndrome (TSS), becomes more virulent when the iron in its culture medium is enhanced (Payne and Finkelstein 1978). Because blood is a source of exogenous iron, it is not surprising that in a study of women with TSS, 75% of cases involved some form of bleeding. Fifty-five per cent involved menstrual bleeding and 25% involved bleeding from surgical or nonsurgical wounds (Reingold 1991).

Prediction: Menstruation tracks pathogen burden. Profet suggests that there is an adaptive fit between the problem (pathogen defense) and the proposed mechanism by which the problem is solved (menstruation). If there is an adaptive fit, then the timing of menses in the life histories of females should correlate with pathogen burden. Menstruation should be either: (1) a facultative phenomenon occurring in response to pathogen load or (2) linked to some other phenomenon that is a good predictor of pathogen load. The first of these possibilities need scarcely be refuted. Rather than being a facultative event, menstruation is tied to the ovarian cycle: it happens at the end of the luteal phase in response to progesterone or estradiol withdrawal (Nalbandov 1976:140; Ferin et al. 1993:67). Profet (1993:370–371) emphasizes the second possibility: "The timing of menstruation indicates that it is designed to occur in response to sperm-borne pathogens. Menstruation tracks sexual activity. . . . Since copulation in mammals is usually tied to ovarian cyclicity, and since copulation entails the transmission of some pathogens to the uterus, ovarian cyclicity and menstruation should be inextricably linked."

Humans, however, do not fit this argument because sexual activity may be present, but menstruation is absent during pregnancy, postpartum amenorrhea, and the postmenopausal years (Clarke 1994; Finn 1994; Strassmann 1994). Menstruation is relatively copious in humans, which makes this contradiction particularly problematic. To resolve this discrepancy, Profet proposes that ancestral hunter-gatherers may have abstained from sexual intercourse during middle and late pregnancy, during lactation, and after menopause. To evaluate the possibility of such pervasive abstinence, it is helpful to consider data on preindustrial societies. In a majority of societies, intercourse during pregnancy is reported during the first two trimesters and people resume sexual relations prior to the end of postpartum amenorrhea (Nag 1983). For example, among the Dogon of Mali, the postpartum abstinence taboo is generally respected for only a month or two while the median duration of postpartum amenorrhea is twenty months. The frequency of sexual intercourse appears to decline with marital duration (Goldman et al. 1987), but it does not cease abruptly at menopause (Leidy 1993). Thus, in both modern and preindustrial societies, menstruation does not track sexual activity and is therefore unlikely to have evolved as a defense against sperm-borne pathogens.

Profet suggests that menstruation is adaptively designed for a role complementary to

that of the cervical mucus which helps bar sperm passage during times of infecundity. Cervical mucus does show steroid-dependent changes that help to keep sperm out of the upper reproductive tract except during the six or seven days around ovulation in cycling women (Chretien and David 1978; Wolf et al. 1978). Cervical secretions also help occlude the cervical canal during at least the first seven months of pregnancy and during menopause, usually creating a highly effective barrier to sperm (Chretien 1978). Vigil et al. (1991) reported that the cervix is a less reliable barrier to sperm passage during lactational infertility. He tested sperm migration in cervical mucus collected from fully breast-feeding, amenorrhoeic women at 30, 60, 90, 120, 150, and 180 days postpartum. Although sperm migration was not as effective as in periovulatory samples (it occurred in 39% of the postpartum cervical mucus samples and 100% of periovulatory samples), some samples from each interval did allow sperm migration, and there was no significant change with time postpartum. These results suggest that although some sperm do get past the cervix, this organ plays a major role in regulating the access of microorganisms to the uterine cavity (Chretien 1978; Chretien and David 1978). As numerous gynecologists have noted, however, menstrual bleeding dissipates the cervical mucus—which makes it easier, not harder, for sperm-borne pathogens to ascend to the uterus (Eschenbach 1976).

Menstruation occurs during cycling, and is absent during pregnancy and amenorrhea, but it is doubtful that this timing is due to complementarity with the cervical mucus. In a later section of this article, I provide evidence for an alternative reason why menstrual bleeding is associated with cycling. In brief, the microvasculature that bleeds during menstruation also provides the blood supply to the placenta in the event of pregnancy. During menopause and amenorrhea there is no possibility of implantation and at these times only a rudimentary microvasculature is present; thus, it is not surprising that it does not bleed. In claiming an adaptive fit between pathogen defense and menstruation, Profet (1993:370) states: "Periodic bleeding of the reproductive tract occurs asymmetrically between the sexes because these vectors [sperm-borne pathogens] are transmitted unidirectionally." A simple, alternative reason why males do not menstruate is that they do not have the endometrial microvasculature that is required for implantation and pregnancy.

Profet's claim for an adaptive fit between pathogen defense and menstruation, is also challenged by the rarity of menstruation (among healthy women of reproductive age) in the absence of contraception. For example, Dogon women (N = 39) aged 20 through 34 years had a median of only two menses each during a two-year period. They spent 15% of the time in menstrual cycling, 29% of the time pregnant, and 56% in postpartum amenorrhea (Strassmann 1992). These data are not subject to reporting bias because they are based on women's visits to menstrual huts and are corroborated by hormonal data (Strassmann 1996). Assuming that menstruation was also a rare event over human evolutionary history, then it is doubtful that it evolved as a defense against pathogens (Clarke 1994; Strassmann 1994).

According to Profet (1993:335, 348–350), other forms of normal uterine bleeding, including implantation bleeding, postpartum bleeding, and proestrous bleeding, also serve an antipathogen function. However, she does not consider alternative explanations for these phenomena. Implantation bleeding is usually regarded as a side effect of invasive implantation that occurs when a conceptus penetrates the uterine epithelium and pervades the underlying stroma. In humans it leads to the erosion of blood vessel walls and hence, bleeding (Johnson and Everitt 1988). Implantation bleeding is a one-time occurrence (Ferin et al. 1993) that cannot protect against pathogens transmitted later in pregnancy. Thus, the argument that it is a consequence of invasive implantation appears sufficient to account for it.

Postpartum bleeding is caused by the tearing of maternal tissue upon parturition and is inevitable when the placenta forms an intimate connection between fetal and maternal tissues (Nalbandov 1976:256). It is also a one-time event and is unlikely to protect against pathogens introduced during lactational amenorrhea. Furthermore, postpartum bleeding is associated with an increase in bacteria that appear to thrive on the nutrients in blood, lo-

chia, and necrotic tissue (Johnson et al. 1985). Severe cases of postpartum infection are known as puerperal sepsis (Wood 1995).

Profet's view that proestrous bleeding defends against sperm-borne pathogens has already been aptly critiqued (Finn 1994; Clarke 1994). In particular, Finn notes that proestrus bleeding in dogs occurs prior to copulation. Hence, it could only rid the uterus of bacteria from the prior estrus, an event which probably took place several months earlier. Rather than delaying the attack on sperm-borne pathogens for several months, it is more plausible that selection has fashioned another, more expeditious, means of protecting the uterus: namely, the mucosal immune system.

In summary, proestrus, postpartum, and implantation bleeding are unlikely to have a role in pathogen defense. Menstruation in humans is a rare event that dissipates the cervical mucus and does not track sexual activity—a conclusion that directly contradicts the argument that there is an adaptive fit between the problem (pathogen defense) and the proposed solution (menstruation).

Prediction: The copiousness of menstruation increases with the promiscuity of the breeding system.

According to Profet, the degree of menstruation should increase with the sexually transmitted pathogen load. She suggests that pathogen load varies with the breeding system in order of descending risk, as follows: multimale breeding systems, polyandry, breeding systems of solitary mammals, harems, and monogamy (Profet 1993:354–355). To help evaluate this prediction she provides an appendix with data from a literature review on the duration and amount of menstrual flow, female body mass, and breeding system in primates and a few other mammals. She does not analyze the data statistically because in her view the studies did not employ "systematic methodology," comment on menstruation only "incidentally," did not use "objective" measures of menstrual blood loss, and are "incomparable." Furthermore, she states, "... data on uterine bleeding are lacking in most species of wild mammal" (Profet 1993:360). In spite of these limitations in the data, she concludes that the following results provide "considerable support" for the antipathogen hypothesis: (1) humans and chimps have more profuse menses than gorillas and orangutans, (2) a black gibbon (*Hylobates concolor*) (N = 1 individual) had more profuse menses than members of two other species of gibbon, and (3) five species of New World monkeys in the family Cebidae had "slight" menses while two species had "covert" menses (Profet 1993:360–361, 384). Profet requires three variables to explain these results: breeding system, overall body size, and presence or absence of continuous sexual receptivity. She concludes: "Although the nonhuman menstruation data currently available are sparse, they support the antipathogen hypothesis" (Profet 1993:361).

This conclusion is tenuous in view of the anecdotal nature of the evidence. To better evaluate the prediction, a quantitative test is needed with a reasonably large sample size of species. This test will require accurate data on variation in the degree of menstrual bleeding within and between species. Although such data are difficult to gather and may be unavailable for a long time, it is possible to demonstrate that Profet's conclusion is not warranted by the data now in hand.

For this demonstration, I used data on menstrual flow in primates from reviews by Profet (1993:384–386) and Hrdy and Whitten (1986: 372–378). As shown in the appendix, these two sources are in close agreement on most species. Where minor discrepancies occur I assigned priority to Hrdy and Whitten (1986) because their characterizations were "blind" with respect to the hypotheses in question. By combining data from these two sources I was able to increase the sample size: Profet largely omits the prosimians while Hrdy and Whitten's review lacks data on most species of New World monkeys. I used Harcourt (1991) for data on breeding system (see appendix). He classifies primates into two groups: those in which females typically mate with only one male per cycle (promiscuity = low), and those in which females typically mate with more than one male per cycle (promiscuity = high). When Harcourt (1991) regressed testis mass (g) against body mass (kg) (both Log_{10}), he showed that the genera in the high promiscuity group were above or on the regression line, and the genera in the low promiscuity group were below the regression line. This result im-

TABLE 1
Promiscuity of the breeding system and copiousness of menstruation

	Absent/Covert	Slight	Overt
Low Promiscuity	*Varecia*	*Theropithecus*	*Erythrocebus*
	Callithrix	*Pongo*	*Papio*
	Aotus	*Gorilla*	*Presbytis*
			Hylobates
			Homo
High Promiscuity	*Galago*	*Alouatta*	*Macaca*
	Saguinus	*Ateles*	*Papio*
	Saimiri	*Lagothrix*	*Pan*
		Cebus	
		Cercocebus	
		Cercopithecus	
		Macaca	
		Colobus	

Fisher's Exact Probability Test, Two-Tail, $p = 0.31$, N = 25. If the polymorphic genera *Macaca* and *Papio* are excluded, then $p = 0.21$, N = 21. Data on promiscuity are from Harcourt (1991). Data on menstruation are from Hrdy and Whitten (1986) and Profet (1993).

plies that his classification is sound. When promiscuity is high, the ratio of testis mass to body mass should increase on account of sperm competition (Short 1979; Harcourt 1991).

In Table 1, I tabulate the degree of promiscuity (low, high) against the degree of menstruation (absent/covert, slight, overt). Following Profet's (1993:359) definitions, menstruation is covert when blood is not externally detectable, slight when blood is externally detectable, and overt when blood is externally obvious. The results of the tabulation provide no evidence for an association between promiscuity and the copiousness of menstruation in primates (Fisher's Exact Probability Test, Two-Tail, $p = 0.31$, N = 25). Five genera with low promiscuity have overt menses and three genera with high promiscuity have overt menses. Three genera with low promiscuity and three genera with high promiscuity have covert menses. Macaques (*Macaca*) have a multi-male breeding system and high promiscuity, but some species have slight menses and others have overt menses. Baboons (*Papio*) have overt menstruation regardless of whether promiscuity is high or low in a particular species. *Macaca* and *Papio* each occur in two cells of the table because these genera are dimorphic with respect to menstruation, but if they are omitted altogether the results remain nonsignificant (Fisher's Exact Probability Test, Two-Tail, $p = 0.21$, N = 21). The absence of a relationship between promiscuity and menstruation calls into question the "preliminary but illuminating" results and "considerable support" for the antipathogen hypothesis that Profet derives from an analysis of three subsamples of this data set (*Hominoidea*, N = 4 species; *Hylobatidae*, N = 3 species; *Cebidae*, N = 7 species). Moreover, these results falsify Profet's claim that no taxa are anomalous with respect to the predictions of the antipathogen hypothesis.

The foregoing tabular analysis treats different genera as independent data points and does not take into consideration the phylogenetic histories of the different genera. This approach can be criticized for failure to control for the confounding influence of phylogeny (Pagel and Harvey 1988; Harvey and Purvis 1991; Maddison 1994). I therefore repeated the analysis using a phylogenetic method which identified independent instances of evolutionary change in the two characters: menstruation and promiscuity. The goal of this analysis was to find out whether copious menstruation was more likely to evolve in the presence of high promiscuity.

The first step in this analysis was to identify an appropriate phylogenetic tree for the primates. I used the suprageneric phylogeny of Fleagle (1988) with modifications in the Papi-

onini from Disotell (1994) and in the Cheirogaleidae from Yoder (1994). I then used the computer program MacClade 3 (Maddison and Maddison 1992) to map menstruation and promiscuity onto the phylogeny in a fashion that was parsimonious (i.e., minimized the number of transitions required to generate the character states observed in extant primates). The results are shown in Figures 2 and 3.

To find out whether copious menstruation was more likely to evolve in the presence of high promiscuity, I used Maddison's (1990) concentrated changes test. This test determines whether phylogenetic changes in the dependent variable (e.g., gains or losses in menstruation) are more or less concentrated in the presence of a particular character state for the independent variable (e.g., high promiscuity). The key advantage of this test is that it takes into account the phylogenetic distribution of both the dependent and the independent variables. When the concentrated changes test is run in MacClade, the program calculates the number of different ways of having the observed number of gains and losses in the dependent variable, in the branches with a particular character state for the independent variable, given the observed number of gains and losses of the dependent variable over the entire tree. MacClade also calculates the number of different ways there are to have the observed number of gains and losses in the dependent variable over the entire tree, without regard to the character state for the independent variable. The ratio of the two numbers is the probability (under the random model) of obtaining the observed number of transitions in the dependent variable on the designated branches (Maddison 1990; Maddison and Maddison 1992:307).

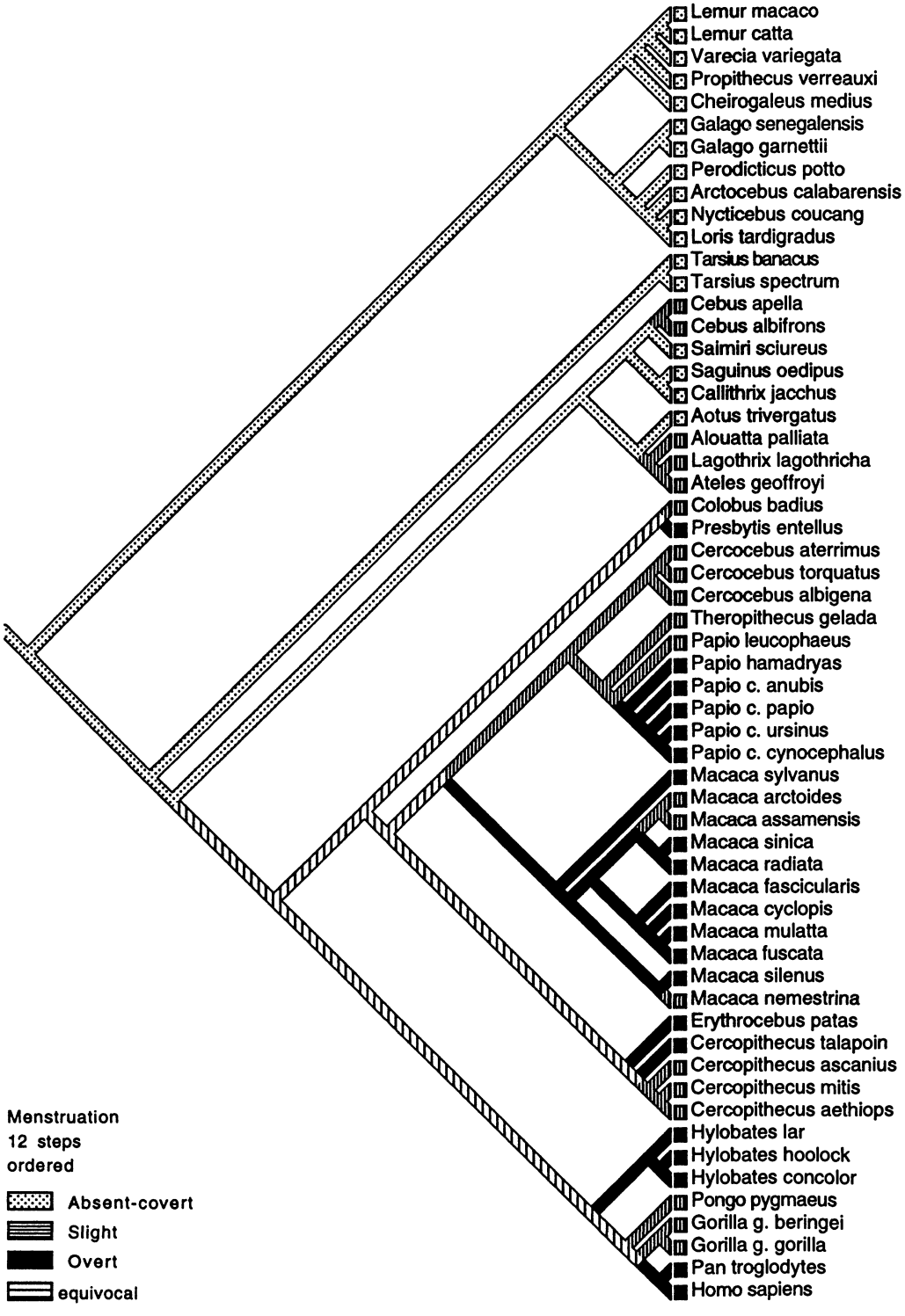
Because the concentrated changes test requires binary data, I categorized menstruation as: absent/covert/slight versus overt (Figure 4). Under this categorization scheme, there are two ways to interpret the character state transitions: (a) either overt menstruation was gained at least seven times and was lost at least two times, or (b) overt menstruation was gained at least two times and was lost at least seven times. The results of the concentrated changes test are shown in Table 2. If we assume possibility (a), then in the presence of low promiscuity, overt menstruation was gained at least four times ($p < 0.01$); in the presence of high promiscuity, overt menstruation was gained at least two times and was lost at least two times ($p < 0.01$). If we assume possibility (b), then gains and losses in menstruation were not correlated with promiscuity (p values ranged from 0.13 to 0.22).

I then categorized menstruation as absent/covert versus slight/overt (Figure 5). Under this categorization scheme, there were at least three independent transitions to slight/overt menstruation and no reversals to absent/covert menstruation. The transitions to slight/overt menstruation occurred in the presence of high promiscuity, but this association was not significant (p values ranged from 0.31 to 0.49) (Table 2). In summary, regardless of how menstruation is dichotomized, the results of the concentrated changes test do not suggest that high promiscuity was a predisposing factor for the evolution of copious menstruation.

This conclusion is not contingent on the resolution of the subgeneric polytomies (multiple nodes) in the phylogeny. The concentrated changes test cannot be applied to polytomous trees; therefore I resolved the phylogeny so that the branching was dichotomous. The sub-

FIGURE 2. PHYLOGENY OF THE PRIMATES SHOWING THE DISTRIBUTION OF THE TRICHOTOMOUS CHARACTER MENSTRUATION (ABSENT/COVERT, SLIGHT, OVERT) AMONG EXTANT TAXA AND THE INFERRED ANCESTRAL STATES IN EACH LINEAGE

Suprageneric relationships in the tree are based on Fleagle (1988) with modifications in the Papionini from Disotell (1994) and Yoder (1994). Subgeneric relationships are in some cases not well established, but have been arbitrarily resolved in order to perform the concentrated changes test (see text). Data on menstrual copiousness are from Hrdy and Whitten (1986) and Profet (1993) (see appendix). A minimum of twelve evolutionary steps are required to account for the distribution of menstrual copiousness among extant taxa.


Lemur macaco
Lemur catta
Varecia variegata
Propithecus verreauxi
Cheirogaleus medius
Galago senegalensis
Galago garnettii
Perodicticus potto
Arctocebus calabarensis
Nycticebus coucang
Loris tardigradus
Tarsius banacus
Tarsius spectrum
Cebus apella
Cebus albifrons
Saimiri sciureus
Saguinus oedipus
Callithrix jacchus
Aotus trivergatus
Alouatta palliata
Lagothrix lagothricha
Ateles geoffroyi
Colobus badius
Presbytis entellus
Cercocebus aterrimus
Cercocebus torquatus
Cercocebus albigena
Theropithecus gelada
Papio leucophaeus
Papio hamadryas
Papio c. anubis
Papio c. papio
Papio c. ursinus
Papio c. cynocephalus
Macaca sylvanus
Macaca arctoides
Macaca assamensis
Macaca sinica
Macaca radiata
Macaca fascicularis
Macaca cyclopis
Macaca mulatta
Macaca fuscata
Macaca silenus
Macaca nemestrina
Erythrocebus patas
Cercopithecus talapoin
Cercopithecus ascanius
Cercopithecus mitis
Cercopithecus aethiops
Hylobates lar
Hylobates hoolock
Hylobates concolor
Pongo pygmaeus
Gorilla g. beringei
Gorilla g. gorilla
Pan troglodytes
Homo sapiens
Menstruation
12 steps
ordered
Absent-covert
Slight
Overt
equivocal

generic polytomies are heavily debated, but alternative resolutions did not alter the conclusion. The character states for some branches could not be resolved; therefore I assigned these equivocal branches all to one character state or all to another. These alternative decision rules also did not affect the conclusion.

In summary, I tested three predictions from the antipathogen hypothesis and the results are as follows: (1) microbes (including pathogenic species) in the reproductive system of human females do not appear to decrease after menses, (2) the timing of menses in the life histories of females does not imply an adaptive fit between the problem (sperm-borne pathogens) and the proposed solution (menstruation), and (3) copious menstruation was not more likely to evolve in the presence of high promiscuity. Thus, none of the three predictions of the antipathogen hypothesis were supported.

MENSTRUAL BLEEDING AS A SIDE EFFECT OF ENDOMETRIAL REGRESSION

According to the classical interpretation of menstrual bleeding in primates, the endometrial arterioles that bleed during menses did not evolve primarily for that purpose. These arterioles emanate from arteries in the uterine myometrium and form part of an endometrial microvasculature that services the endometrial tissue by nourishing it and providing for respiratory exchange. During the menstrual cycle, the superficial lining of the endometrium, the transient functionalis, proliferates in preparation for implantation. The microvasculature grows in concert so that no cell is too far from its vascular support. Thus, the first function of the endometrial arterioles is to provide the blood supply for the endometrium. If implantation occurs, then the endometrial arterioles assume a second important function: they become the conduits through which the maternal blood reaches the placenta (Kaiserman-Abramof and Padykula 1989). In humans, there is one artery for each placental chamber (Blum 1986:293).

If implantation does not occur, then the endometrium actually erodes and its injured vasculature bleeds into the uterine cavity (Christiaens et al. 1985; Shaw and Roche 1985). Bleeding is stopped by the occlusion of vessels with haemostatic plugs and by vasoconstriction (van Eijkeren et al. 1991). Blood and other cellular debris must be either reabsorbed or shed, otherwise the uterine cavity would eventually be occluded (Shaw and Roche 1985). The low coagulability of menstrual blood can be explained as a mechanism to clear it from the endometrium (Shaw and Roche 1985; Rybo et al. 1985). Blood and necrotic tissue provide nutrients for bacterial growth, so it would be particularly disadvantageous for them to accumulate.

The chief difference between this interpretation of menstrual bleeding and that of Profet is that she regards pathogens as ". . . the main selection pressure that shaped the machinery of menstruation" (Profet 1993:371). Her discussion of the "machinery of menstruation" focuses on the endometrial arteries and arterioles—especially those with a spiral configuration (Profet 1993:339–340). If these vessels are primarily designed for menstruation, however, then their role as conduits of blood for the endometrium and the placenta might be misconstrued as secondary or incidental. Here I will present three lines of evidence that suggest that it is menstrual bleeding that is incidental, and that the endometrial microvasculature is primarily designed to provide the blood supply for the endometrium and the placenta.

First, if the endometrial arteries were primarily designed to bleed so as to defend against pathogens, then one would expect them to belong to a larger class of arteries that protect the entire reproductive tract by bleeding during menstruation. In particular, the vagina and cervix should bleed because they have a much

FIGURE 3. DISTRIBUTION OF HIGH AND LOW PROMISCUITY IN EXTANT TAXA AND THE INFERRED ANCESTRAL STATES FOR THIS CHARACTER IN EACH LINEAGE USING THE SAME PHYLOGENY AS IN FIGURE 2

Data on female promiscuity are from Harcourt (1991). A minimum of nine evolutionary steps are required.


Lemur macaco
Lemur catta
Varecia variegata
Propithecus verreauxi
Cheirogaleus medius
Galago senegalensis
Galago garnettii
Perodicticus potto
Arctocebus calabarensis
Nycticebus coucang
Loris tardigradus
Tarsius banacus
Tarsius spectrum
Cebus apella
Cebus albifrons
Saimiri sciureus
Saguinus oedipus
Callithrix jacchus
Aotus trivergatus
Alouatta palliata
Lagothrix lagothricha
Ateles geoffroyi
Colobus badius
Presbytis entellus
Cercocebus aterrimus
Cercocebus torquatus
Cercocebus albigena
Theropithecus gelada
Papio leucophaeus
Papio hamadryas
Papio c. anubis
Papio c. papio
Papio c. ursinus
Papio c. cynocephalus
Macaca sylvanus
Macaca arctoides
Macaca assamensis
Macaca sinica
Macaca radiata
Macaca fascicularis
Macaca cyclopis
Macaca mulatta
Macaca fuscata
Macaca silenus
Macaca nemestrina
Erythrocebus patas
Cercopithecus talapoin
Cercopithecus ascanius
Cercopithecus mitis
Cercopithecus aethiops
Hylobates lar
Hylobates hoolock
Hylobates concolor
Pongo pygmaeus
Gorilla g. beringei
Gorilla g. gorilla
Pan troglodytes
Homo sapiens
Promiscuity
9 steps
ordered
Low
High
equivocal

higher pathogen load than the endometrium (Nelson and Nichols 1986; Hemsell et al. 1989). Bleeding would destroy organisms that might ascend to the uterus and oviducts. However, the vagina and cervix do not bleed. A likely reason is that they do not need to vascularize to support a secretory epithelium that will be the site of implantation and they do not need to provide the arterial blood supply for the placenta. In the Transvaal elephant shrew (*Elephantulus myurus*), menstruation is overt but is restricted to the menstrual polyp, the small area of the uterus that is the site of implantation (van der Horst 1941, 1955). The restriction of menstruation to the site of implantation cannot be explained by the antipathogen hypothesis. Pathogens that were removed from the polyp by menstruation would soon recolonize it from other areas of the uterus.

Second, if the endometrium bleeds so as to defend against pathogens, then it is the only tissue in the entire body that evolved this defense. In other tissues the blood is always maintained within the vessels even during times of acute infection. For example, when the eye contracts conjunctivitis, the capillaries vasodilate, which brings increased quantities of immune agents to the area through enhanced blood flow. Only these agents actually leave the vessels; the erythrocytes remain inside. The lungs are exposed to numerous airborne pathogens such as *Pneumoccocus*, but bleeding is not part of the alveolar defense. Similarly, the digestive tract does not bleed adaptively in response to gastrointestinal pathogens, although it sometimes does bleed pathologically. According to Profet (1993:348), the uterus bleeds ". . . because it is the only truly internal organ that is regularly exposed to vectors of disease." She regards the lungs and gut as ". . . essentially extensions of external organs, because they function to filter substances directly from the external environment." She also states that only the uterus functions episodically and can afford "time out." These speculations on why only the uterus bleeds do not contradict the fact that no other mammalian tissue fights pathogens by bleeding.

Third, although many animals have internal fertilization (e.g., reptiles, birds, insects), no other class in the animal kingdom bleeds from the reproductive system to fight pathogens (Finn 1994; Strassmann 1994). Some of these animals store sperm for long periods of time and have evolved spermathecae specifically for this purpose. Evidently, if pathogen defense is the function of menstrual bleeding, then it is peculiar that menstruation is found only in mammals. If, however, menstrual bleeding is a consequence of endometrial vascularization in preparation for implantation, then the reason for its exclusive occurrence in mammals is obvious.

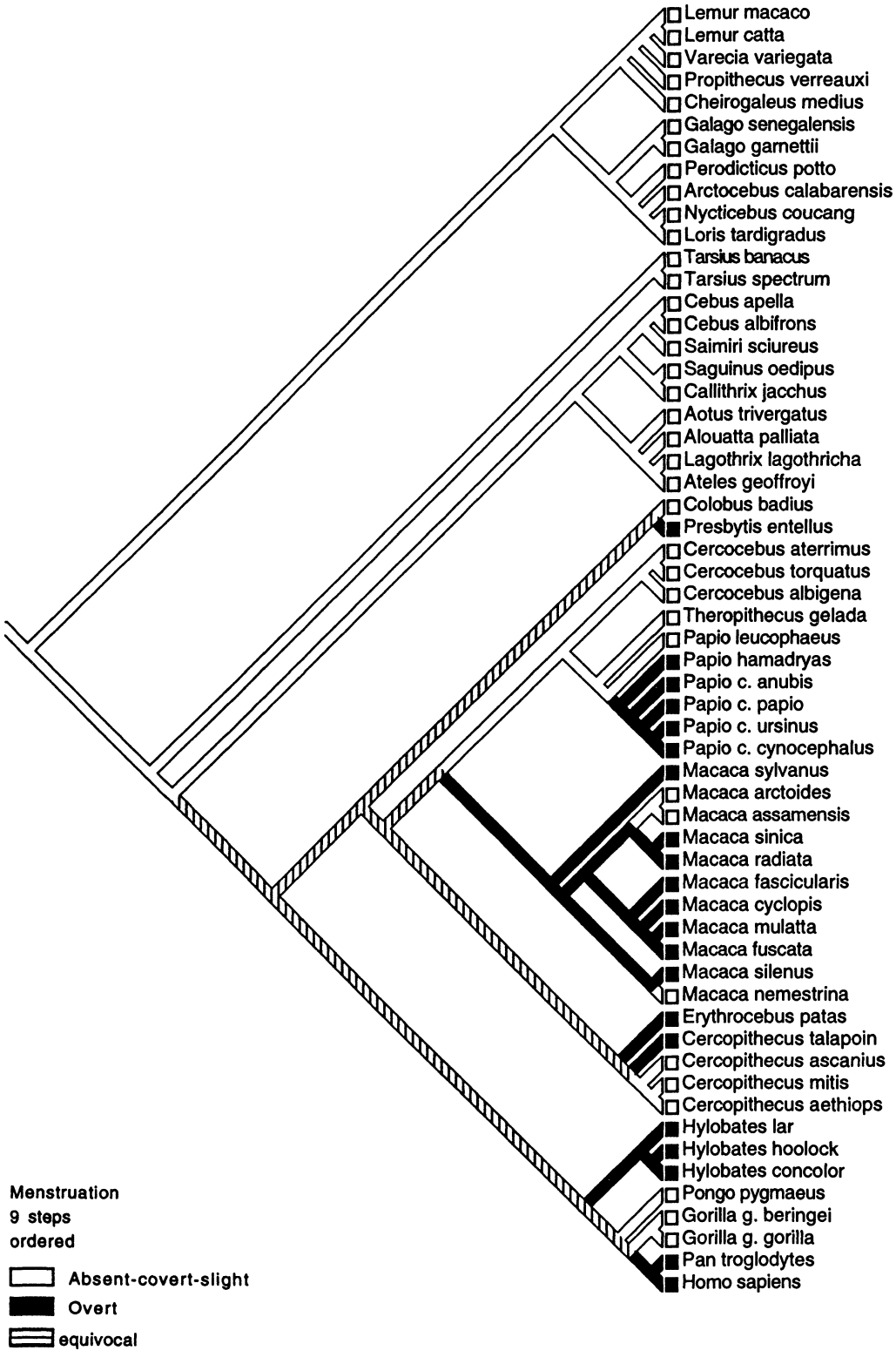
DISTRIBUTION OF MENSTRUAL BLEEDING IN MAMMALS

Although menstrual bleeding is unique to mammals, it has only been reported in a minority of species. Profet (1993:335) nonetheless predicts that menstrual bleeding is universal, or nearly so, because all mammals have internal fertilization and share the problem of sperm-borne pathogens. However, menstrual bleeding is not normal in rats and mice although these animals have the best studied mammalian reproductive systems. Many sources on comparative reproductive physiology report that menstrual bleeding accompanies endometrial regression only in primates—especially humans, apes, and Old World monkeys —and not in other mammals (e.g., Nalbandov 1976; Blum 1986; Johnson and Everitt 1988). The same opinion seems to prevail among anatomists who study the endometrium. For example, Padykula (1980) concludes that in most mammals endometrial regression is accomplished through a "bloodless" catabolism.

These generalizations probably overlook a few exceptions, and Profet (1993:382–386) lists those she could identify in an appendix.

FIGURE 4. SAME AS FIGURE 1 EXCEPT THE CHARACTER, MENSTRUAL COPIOUSNESS, WAS DICHOTOMIZED AS ABSENT/COVERT/SLIGHT VERSUS OVERT

A minimum of nine evolutionary steps were required by this phylogeny.


Lemur macaco
Lemur catta
Varecia variegata
Propithecus verreauxi
Cheirogaleus medius
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Loris tardigradus
Tarsius banacus
Tarsius spectrum
Cebus apella
Cebus albifrons
Saimiri sciureus
Saguinus oedipus
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Aotus trivergatus
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Ateles geoffroyi
Colobus badius
Presbytis entellus
Cercocebus aterrimus
Cercocebus torquatus
Cercocebus albigena
Theropithecus gelada
Papio leucophaeus
Papio hamadryas
Papio c. anubis
Papio c. papio
Papio c. ursinus
Papio c. cynocephalus
Macaca sylvanus
Macaca arctoides
Macaca assamensis
Macaca sinica
Macaca radiata
Macaca fascicularis
Macaca cyclopis
Macaca mulatta
Macaca fuscata
Macaca silenus
Macaca nemestrina
Erythrocebus patas
Cercopithecus talapoin
Cercopithecus ascanius
Cercopithecus mitis
Cercopithecus aethiops
Hylobates lar
Hylobates hoolock
Hylobates concolor
Pongo pygmaeus
Gorilla g. beringei
Gorilla g. gorilla
Pan troglodytes
Homo sapiens
Menstruation
9 steps
ordered
Absent-covert-slight
Overt
equivocal

TABLE 2

Number of gains and losses in menstrual copiousness in the presence of high and low promiscuity

	(absent/covert + slight) to (overt)				(absent/covert) to (slight + overt)
	7 gains 2 losses*		2 gains 7 losses*		3 gains
Low Promiscuity	4 gains	($p < 0.01$)	2 losses	(NS)	
High Promiscuity	2 gains + 2 losses	($p < 0.01$)	1 gain + 5 losses	(NS)	3 gains (NS)

* One gain occurred on a branch for which the character state for promiscuity was equivocal. For simplicity, this gain is not included in the table.

Her list includes 48 primates plus the following nonprimates: the marsupial cat (*Dasyurus viverrinus*); the northern coyote (*Canis latrans*); four species of bat (*Carollia perspicillata, Desmodus rotundus, Glossophaga soricina, Molossus ater*); the Malayan flying lemur (*Cynocephalus variegatus*); ten species of insectivores in the genera *Elephantulus, Erinaceus, Tana,* and *Tupaia*; and the African elephant (*Loxodonta africana*). The data for *Canis* and *Loxodonta,* however, are dubious because they are based on single individuals.

If the customary definition of menstruation is broadened to include the microscopic presence of small numbers of erythrocytes in the uterine cavity upon progesterone withdrawal, then more species can probably be added to the list of covert menstruators. Species with overt menstruation, by contrast, should rarely have been overlooked if they have been observed in captivity. In Profet's table, all the overt menstruators are catarrhines (Old World monkeys, apes, humans) and shrews, which is consistent with the usual assertion that menstruation is largely a primate phenomenon. But what about the variation in the degree of bleeding within the primates?

MENSTRUAL BLEEDING IN PRIMATES: A PHYLOGENETIC APPROACH

As shown in Figure 2, and more dramatically in Figure 5, the degree of menstrual bleeding in primates relates to phylogeny: prosimians have absent or covert menses; New World monkeys (platyrrhines) have covert or slight menses; and Old World monkeys, apes, and humans (catarrhines) have slight or overt menses. This result is also shown in Table 3 and is highly significant (Fisher's Exact Probability Test, Two-Tail, $p << 0.001$). Thus phylogeny is a useful predictor of the degree of menstrual bleeding in primates. To understand the basis for this correlation, I examined the following aspects of anatomy and physiology: endometrial microvasculature, placentation, endometrial thickness and depth of shedding, body mass, litter mass, and the ratio of litter mass to body mass.

Endometrial microvasculature. Because it is the endometrial microvasculature that bleeds during menstruation, differences in this vasculature may explain the variation in bleeding across primates. Blood loss should depend on the number of endometrial vessels and their resistance to blood flow, which will in turn depend on the length and radius of the vessels (Folkow and Neil 1971), and how long they are unconstricted after they are injured during endometiral regression. These features of the endometrial microvasculature of primates have not been systematically measured across species. They may, however, correlate with the presence of spiral arterioles. Kaiser (1947a,b) conducted histological studies of primate endometria, and concluded that catarrhines (*Macaca, Papio, Hylobates, Pan,* and *Homo*) have spiral arterioles and gross external bleeding, and platyrrhines (*Alouatta, Ateles,* and *Cebus*)

FIGURE 5. SAME AS FIGURE 1 EXCEPT THE CHARACTER, MENSTRUAL COPIOUSNESS, WAS DICHOTOMIZED AS ABSENT/COVERT VERSUS SLIGHT/OVERT

A minimum of three evolutionary steps are required by this phylogeny.


Lemur macaco
Lemur catta
Varecia variegata
Propithecus verreauxi
Cheirogaleus medius
Galago senegalensis
Galago garnettii
Perodicticus potto
Arctocebus calabarensis
Nycticebus coucang
Loris tardigradus
Tarsius banacus
Tarsius spectrum
Cebus apella
Cebus albifrons
Saimiri sciureus
Saguinus oedipus
Callithrix jacchus
Aotus trivergatus
Alouatta palliata
Lagothrix lagothricha
Ateles geoffroyi
Colobus badius
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Theropithecus gelada
Papio leucophaeus
Papio hamadryas
Papio c. anubis
Papio c. papio
Papio c. ursinus
Papio c. cynocephalus
Macaca sylvanus
Macaca arctoides
Macaca assamensis
Macaca sinica
Macaca radiata
Macaca fascicularis
Macaca cyclopis
Macaca mulatta
Macaca fuscata
Macaca silenus
Macaca nemestrina
Erythrocebus patas
Cercopithecus talapoin
Cercopithecus ascanius
Cercopithecus mitis
Cercopithecus aethiops
Hylobates lar
Hylobates hoolock
Hylobates concolor
Pongo pygmaeus
Gorilla g. beringei
Gorilla g. gorilla
Pan troglodytes
Homo sapiens
Menstruation
3 steps
ordered
Absent-covert
Slight-overt
equivocal

TABLE 3
Phylogeny and copiousness of menstruation

	Absent/Covert	Slight	Overt
PROSIMIANS			
Lemuroidea	*Cheirogaleus* (0.2 kg) *Propithecus* (3.5 kg) *Lemur* (2.5 kg) *Varecia* (3.1 kg)		
Lorisoidea	*Galago* (0.2 kg) *Arctocebus* (0.3 kg) *Perodicticus* (1.1 kg) *Nycticebus* (1.2 kg) *Loris* (0.3 kg)		
Tarsioidea	*Tarsius* (0.2 kg)		
NEW WORLD MONKEYS			
Ceboidea	*Callithrix* (0.3 kg) *Saguinus* (0.5 kg) *Saimiri* (0.6 kg) *Aotus* (1.0 kg)	*Alouatta* (5.7 kg) *Ateles* (5.8 kg) *Lagothrix* (5.8 kg) *Cebus* (2.4 kg)	
OLD WORLD MONKEYS			
Cercopithecoidea		*Cercocebus* (6.0 kg) *Cercopithecus* (3.6 kg) *Macaca* (7.9 kg) *Papio* (10.0 kg) *Theropithecus* (13.6 kg) *Colobus* (5.8 kg)	*Cercopithecus* (1.1 kg) *Erythrocebus* (5.6 kg) *Macaca* (5.5 kg) *Papio* (9.4 kg) *Presbytis* (11.4 kg)
APES and HUMANS			
Hominoidea		*Pongo* (37.0 kg) *Gorilla* (93.0 kg)	*Hylobates* (5.9 kg) *Pan* (31.1 kg) *Homo* (40.1 kg)

Numbers in parentheses refer to female body weight. Fisher's Exact Probability Test, Two-Tail, $p = 0.0000008$, N = 34. If the polymorphic genera *Cercopithecus, Macaca,* and *Papio* are excluded, then $p = 0.00001$. Data are from Smuts et al. (1986, phylogeny), Hrdy and Whitten (1986, menstruation), Profet (1993, menstruation), and Harvey et al. (1986, female body size).

have relatively straight arterioles and only microscopic bleeding. To understand the differences in the design of the endometrial microvasculature among primates, further studies are needed on the role of the microvasculature in providing the blood supply to the placenta. The copious menstrual bleeding of catarrhines is probably not adaptive, but is instead a side effect of the design of the microvasculature for its major function: nourishing the tissue that supports implantation and, ultimately, the fetus itself. As a result of this design, catarrhines appear to have too much blood for efficient reabsorbtion, and copious bleeding is the consequence.

Placentation. Kleine (1931:470) associated the occurrence of menstruation in anthropoids with hemochorial villous placentation, which means that the trophoblast and chorioallantoic villi are in immediate contact with maternal blood. This is a promising lead, but Kleine did not explain why we should expect species with hemochorial villous placentation to menstruate. With the possible exception of the family Hyaenidae (aardwolves and hyenas), hemochorial villous placentation is found only in catarrhines (Mossman 1987), which is consistent with a possible relationship between this type of placentation and copious menstruation. However, the nonprimate mammals that menstruate have hemochorial labyrinthine or endotheliochorial labyrin-

thine placentation (Mossman 1987; Profet 1993:336). Clearly placentation type is a crude way of capturing the enormous degree of placental variation, so it would be desirable for a comparative zoologist to investigate this matter further. Probably the relevant factor is not placentation type per se, but rather the design of the endometrial arterioles that service the placenta.

Endometrial thickness and depth of shedding. Differences in endometrial thickness may contribute to the amount of blood and other tissue shed with the menses. This argument is supported by the observation that platyrrhines have relatively thin endometria and scant bleeding, whereas catarrhines have relatively thick endometria and copious bleeding (Kaiser 1947b). In no primate is the endometrium entirely shed with the menses. Instead, part is shed (the transient functionalis) and part is reabsorbed (the germinal basalis). In many catarrhines, the upper third of the microvasculature and the surrounding stromal and glandular tissue is shed (Kaiserman-Abrahmof and Padykula 1989), but across primates the differences in the depth of shedding have not been well characterized (Padykula 1980). It is not clear how these differences relate to implantation and placentation, but whatever their origin, they are likely to contribute to differences in the degree of bleeding.

Body mass. The blood supply to the uterus should increase with the size of the uterus. For a given depth of endometrial shedding (e.g., one-third of the endometrium), one might therefore expect a larger endometrial volume to result in more copious bleeding. Data on endometrial volume in most primates are unavailable, but female body mass might be a good proxy variable. Does female body mass contribute to the correlation between degree of bleeding and phylogeny? I addressed this question by testing for an association between degree of bleeding and body mass after controlling for phylogeny. To control for phylogeny, I used phylogenetically independent contrasts in the MacIntosh program, Comparative Analysis by Independent Contrasts (CAIC) (Purvis and Rambaut 1994). A contrast is diagramed as a path linking two or more species in a phylogenetic tree. Contrasts whose paths do not intersect at any point are phylogenetically independent (Burt 1989; Purvis and Rambaut 1994). The CAIC program extracts a set of independent contrasts from a phylogeny; the contrasts can then be tested for a consistent association between changes in the dependent and independent variables.

I tested the null hypothesis that the evolution of menstruation in primates is unrelated to the evolution of body mass. This null hypothesis predicts that half of the contrasts in the continuous variable, body mass, should be positive and half negative, and the mean value of the contrasts should be zero. Under the alternative hypothesis that the evolution of copious menstruation is correlated with the evolution of higher body mass, one expects a significant bias towards positive values for the contrasts, and the mean of the contrasts should be significantly greater than zero. I used the primate phylogeny shown in Figures 2 through 5 and assumed that each branch in the phylogeny is the same length. Body mass data are from Harvey et al. (1986) and were log transformed to comply with the assumptions of the model (Purvis and Rambaut 1994).

The results are shown in Table 4. When menstruation is dichotomized as absent/covert versus slight/overt, then only three independent contrasts are possible, all of which are positive, but the sample size is too small to draw any firm conclusions (sign test, two-tailed, $p = 0.25$). When menstruation is dichotomized as absent/covert/slight versus overt, then three of nine contrasts are positive and six are negative (sign test, two-tailed, $p = 0.51$), which means we cannot reject the null hypothesis of no correlation between the evolution of menstruation and the evolution of body mass. In summary, this analysis does not support Profet's (1993:357) statements that "Mammalian body size should influence the likelihood and degree of menstruation. . . ." and that large mammals ". . . can afford to menstruate a larger volume of blood relative to body size."

If one compares the body mass and taxonomic status for extant genera in Table 3, then the results of the analysis of independent contrasts make intuitive sense. All the prosimians have absent or covert menses regardless of body size which ranges from 0.2 kg to 3.5 kg.

TABLE 4

Phylogenetically independent contrasts between high and low menstruators with respect to body mass, litter mass, and the ratio of litter mass to body mass

Continuous Variable	Menstruation*	Σ Species	Σ Contrasts	Mean	SD	Sign	Sign test two-tailed p
log body mass	1 v. 2 + 3	52	3	0.345	0.08	+++	NS
log body mass	1 + 2 v. 3	52	9	−0.063	0.162	−+−−−−+−+	NS
log litter mass	1 v. 2 + 3	38	3	0.205	0.146	+++	NS
log litter mass	1 + 2 v. 3	38	6	−0.042	0.115	−+−−+−	NS
log (litter mass/ body mass)	1 v. 2 + 3	38	3	−0.135	0.092	−−−	NS
log (litter mass/ body mass)	1 + 2 v. 3	38	6	0.11	0.054	++++++	0.03

* 1 = absent/covert; 2 = slight; 3 = overt

The catarrhines with overt menstruation tend to be no larger than those with slight menstruation (for example, in Table 3 see *Cercopithecus, Macaca, Papio,* and the hominoids). New World monkeys are the only taxon in which the genera with large body size also appear to have more copious menstruation (slight instead of covert). However, menstruation in most New World monkeys was coded only by Profet—not by Hrdy and Whitten—and the coding was not "blind" to the possibility of a body size effect. Moreover, three of the four genera of New World monkeys that Profet coded as having "slight" menstruation are elsewhere (Kaiser 1947b) reported to have only microscopic bleeding (i.e., covert menses). In the mammals as a whole, body size is not a good predictor of the copiousness of menstruation because many large mammals have never been reported to menstruate, so if they bleed at all it is probably covert. Thus, current data do not support the argument that the degree of menstrual bleeding increases with female body size, independent of phylogeny.

Litter mass. Average litter mass (from Harvey et al. 1986) might be a better proxy variable for uterine volume than adult female body mass. However, when the method of independent contrasts was used to control for phylogeny, it was not possible to reject the null hypothesis that the evolution of litter mass was unrelated to the evolution of menstruation (Table 4). Regardless of how menstruation was dichotomized, the results were nonsignificant (sign test, two-tailed, $p = 0.25$ and $p = 0.41$).

Litter mass/body mass. If two species have the same size uterus and equal volumes of menstrual blood loss, but one species has a much larger body mass, then its menses may be less visible to human observers. It might be reported to have slight menses while the smaller species is reported to have overt menses, even though blood loss is the same. Another possibility is that the larger species also has a larger vagina and actually reabsorbs the menstrual blood more completely. Both of these possibilities predict that the species reported to have overt menstruation have a higher ratio of litter mass to body mass. I tested this prediction using phylogentically independent contrasts (Table 4). When menstruation is dichotomized as absent/covert/slight versus overt, then all six contrasts are positive (sign test, two-tailed, $p = 0.03$), which supports the prediction that the evolution of "overt" menstruation correlated with the evolution of higher ratios of litter mass to body mass. If we assume that the assumptions of the t-test are satisfied (which appears to be true within the limits of the small sample size available to evaluate this issue), then the power of the test can be increased ($t = 5.01$, 5 df, two-tailed $p < 0.005$).

The six independent contrasts in the above analysis are all within the catarrhine clade because, in primates, only catarrhines have overt menstruation. It is convenient that this analysis is confined to the catarrhines because all catarrhines have spiral arterioles, and this confounding variable is thereby controlled for. The results suggest that in species that have spiral arterioles, bleeding is overt if the ratio of

litter mass to body mass is high, and bleeding is slight if this ratio is low. For example, in the hominoid clade (which generated two of the six contrasts), the ratio of litter mass to body mass is higher in *Homo sapiens* (0.06 to 0.08) and in *Pan troglodytes* (0.06), than in *Pongo pygmaeus* (0.05) and *Gorilla gorilla* (0.02). Note that *H. sapiens* and *P. troglodytes* have overt menstruation, whereas *P. pygmaeus* and *G. gorilla* have slight menstruation.

When menstruation is dichotomized as absent/covert versus slight/overt, then only three contrasts are obtained, all of which are negative. This result is in the opposite direction from the prediction, but is nonsignificant (sign test, two-tailed, $p = 0.25$). Caution is required here because of the small sample size involved. Moreover, two of the three contrasts involve New World monkeys and, as stated previously, the coding in this clade is questionable. However, perhaps the ratio of litter mass to body mass is not useful for distinguishing absent/covert versus slight/overt bleeding because this distinction depends on the presence or absence of spiral arterioles.

In summary, to explore the basis for the correlation between degree of menstrual bleeding and phylogeny, I considered the following aspects of anatomy and physiology: endometrial microvasculature, placentation, endometrial thickness and depth of shedding, body mass, litter mass, and the ratio of litter mass to body mass. These variables are interrelated and several may be important simultaneously. A new finding of particular interest is that the ratio of litter mass to body mass distinguished the catarrhines with slight menstruation from the catarrhines with overt menstruation. Catarrhines with higher ratios of litter mass to body mass reabsorb the menstrual blood less completely, or in these species blood loss may simply be more noticeable. These results are consistent with the hypothesis that menstrual bleeding is a functionless side effect of endometrial regression.

If menstrual bleeding were functional, one might expect differences in the degree of bleeding among primates to relate to differences in ecology and behavior. However, primates that have the same degree of bleeding (see appendix), vary markedly from each other with respect to ecology (e.g., habitat types, diet) and behavior (e.g., nocturnal/diurnal, mating system, solitary/social) (see Smuts et al. 1986). Furthermore, species belonging to different superfamilies may resemble each other in terms of major features of ecology and behavior, but it does not follow that they are similar in regard to menstrual bleeding. Therefore, it appears unlikely that ecological and behavioral differences can explain the variation in menstrual bleeding among primates. If a candidate difference emerges, however, it should be quantitatively tested using the methods employed above.

INTRASPECIFIC VARIATION IN BLEEDING

To evaluate the hypothesis that menstrual bleeding is a functionless side effect of endometrial regression, it would be helpful to understand not only interspecific but also intraspecific variation in bleeding. In women, blood loss increases with parity, which can be attributed to increased uterine size and vascularity with successive births (Cole et al. 1971; Woessner and Brewer 1963; Rybo and Hallberg 1966). Increased blood loss in taller women and in women whose previous children had a relatively high birthweight, can also be explained by uterine size and blood flow (Cole et al. 1971). Depth of endometrial shedding can influence menstrual blood losses. Shedding is more profound in some women than in others and, in a given woman, some areas of the endometrium are reabsorbed without shedding (Shaw and Roche 1985). Age (15 to 45 years) does not correlate with blood loss until the perimenopause (age 50) when confounding variables such as uterine fibroids cannot be excluded (Shaw and Roche 1985). Overall, the within-woman variation in blood loss is significantly less than the between-women variation. This result applies to the population as a whole and to dizygotic twins, but not to monozygotic twins, implying a heritable component to blood loss (Rybo et al. 1985). Although a great deal remains to be learned about the causes of intraspecific variation in menstrual bleeding, current data—in particular, the increase in blood flow with parity, maternal height, and birthweight —are compatible with the hypothesis that menstrual bleeding is merely a by-product of endometrial regression.

THE FUNCTION OF ENDOMETRIAL REGRESSION

Although menstrual bleeding occurs in only some taxa, cyclical endometrial regression and renewal is universal in mammals (Nalbandov 1976; Padykula 1980; Johnson and Everitt 1988; cf. Profet 1993). In all species, endometrial cyclicity is linked to ovarian cyclicity and reflects changes in steroid hormones over time. Due to the close coordination between the endometrium and the ovaries, the endometrium is able to sustain implantation by the blastocyst only for the brief period during which a blastocyst is actually present and available to implant (Figure 1). In humans, the duration of endometrial receptivity is probably about three days per cycle (Ferin et al. 1993). Selection to extend endometrial receptivity beyond this time should be nonexistent because in the absence of a blastocyst higher rates of implantation would not result.

Following birth, both the ovaries and the endometrium enter a prolonged period of quiescence before cycling again resumes. During this postpartum interval, the endometrium remains in a regressed state and menstruation is absent. What prevents the endometrium from becoming active during the postpartum interval? A possible answer is that maintenance of the elaborate secretory endometrium that is able to sustain implantation is a significant energy expense that is spared until ovarian cycling resumes. Upon the resumption of cycling, the endometrium builds up again because the blastocyst cannot implant successfully in denuded tissue. But why does the endometrium cyclically regress after each failure of implantation, instead of being maintained throughout episodes of ovarian cycling?

COST OF MENSTRUAL BLEEDING

According to Profet, endometrial regression at the end of each ovarian cycle is a nutritional expense and must have an adaptive advantage to offset the costs. In support of her argument, she states that some women lose enough blood to significantly decrease their iron stores. However, the mean blood loss in healthy West European women is about 40 ml, and only 9% to 14% of women lose more than 80 ml; the threshold for iron deficiency in women who cycle repeatedly (Christiaens et al. 1985). In populations that do not practice contraception, menstruation is a relatively rare event among women of reproductive age (Short 1976; Strassmann 1992). Menstruation must have been similarly rare over human evolutionary history, and the iron lost through menses trivial relative to dietary intake. Anemia would have been especially unlikely among hunter-gatherers whose diets contained significant quantities of meat.

The protein lost in menstrual blood and tissue can be measured from its nitrogen content (1 g of nitrogen = 6.25 g protein). In a study of sixteen menses in six women, nitrogen loss per menstruation ranged from 0.43 g to 2.5 g and the requirement for nitrogen intake over the entire menstrual cycle averaged 73 $\pm$ 20 mg/kg (Calloway and Kurzer 1982). In a 55 kg woman, the nitrogen lost during menses should therefore comprise 0.01% to 0.06% of the required intake. Clearly, the protein lost during menses is negligible relative to the required protein intake over one cycle. Menstrual protein loss is also minor compared to fecal protein loss over one cycle (Finn 1994). In the six subjects, fecal protein loss was 0.746 + 0.325 g/day and crude digestibility was about 87% (Calloway and Kurzer 1982).

The idea that menstruation is nutritionally costly also does not fit data on nonhuman mammals. In a majority of species endometrial regression involves either no bleeding or covert bleeding (see above). In covert menstruators all of the endometrial tissue is reabsorbed and detection of erythrocytes in the uterine cavity requires microscopic examination.

COST OF MAINTAINING THE ENDOMETRIUM

The nutritional cost of menstruation itself is trivial, but what about the cost of not menstruating? The elaborate secretory endometrium that is able to sustain implantation is temporally restricted in its utility, so the question arises: Is it more costly to maintain the endometrium when it is not needed, or to regenerate it each cycle? I propose that the energetic costs of maintenance exceed the energetic costs of renewal and that this disparity has a role in endometrial cyclicity. This hypothesis is suggested by the following well-known aspects of the luteal phase: (1) in-

creased metabolic activity in the endometrium including glandular secretion of glycoprotein, sugars, and amino acids; (2) increased uterine mass relative to the follicular phase; and (3) a progesterone induced rise in basal body temperature of 0.2 to 0.8°C (Landau 1973; Ferin et al. 1993).

METABOLIC RATE AND FOOD INTAKE DURING CYCLING

To evaluate the above hypothesis, I reviewed the literature on energy expenditure and the menstrual cycle (Table 5). Soloman et al. (1982) is the earliest study conducted under controlled conditions using appropriate statistical methodology, therefore I will disregard the older literature. Soloman et al. (1982) analysed the relationship between basal metabolic rate (BMR) and the menstrual cycle in six women who were confined to a metabolic unit under carefully controlled conditions for 92 days. In five subjects BMR decreased from the onset of menses until approximately one week before ovulation and then increased until the beginning of menses. The average difference in BMR from nadir to zenith was 1503 kJ/day which, according to Prentice and Whitehead (1987), is an amplitude of up to 10% (note: one kJ equals 0.24 kcal). Bisdee et al. (1989) studied eight women who were confined to a metabolic ward for one menstrual cycle. The mean metabolic rate during sleep increased by 412 kJ/d from the late follicular to the late luteal phase, a change of 7.1% ($p < 0.001$). Meijer et al. (1992) measured metabolic rate during sleep in sixteen women who spent two nights in a respiration chamber in opposite phases of the menstrual cycle. Metabolic rate increased by a mean of 446 kJ/day, which is a difference of 7.7% from the follicular to the luteal phase ($p < 0.001$). Webb (1986) measured 24-h energy expenditure by direct calorimetry in ten women over the menstrual cycle. Mean 24-h expenditure increased by 613 kJ/day or 8.7% from the follicular to the luteal phase ($p < 0.00002$).

Ferraro et al. (1992) found no significant differences in energy expenditure (adjusted for body composition, age, and activity levels) in 28 postmenopausal women and 30 follicular-phase women who spent 23 hours in a respiration chamber. After pooling these women to form a "nonluteal" group (N = 58), they were compared with 12 luteal phase women. Basal metabolic rate, metabolic rate during sleep, and 24-hour energy expenditure were higher in the luteal phase by 833 ± 222 kJ/d ($p < 0.001$), 452 ± 176 kJ/d ($p < 0.02$), and 444 ± 163 kJ/d ($p < 0.01$), respectively. In summary, the expectation that metabolic energy expenditure is higher in the luteal than in the follicular phase was strongly supported (Table 5).

Future research should attempt to quantify the uterine and nonuterine components of cyclical variation in metabolic rate through comparison of hysterectomized and nonhysterectomized women. If the ovaries are left intact, then hysterectomy should not alter the secretion of ovarian steroids, and it should be possible to measure the collective metabolic effects of steroids on nonuterine targets. Through such a controlled study, one could assess the fraction of the luteal phase increase in metabolic energy expenditure that is due to changes in the endometrium and other uterine tissues.

Data on the relationship between metabolic rate and the estrous cycles of nonhuman mammals are surprisingly scarce and this is another area in which further research is needed. Several studies, however, report increased food consumption during the luteal phase in primates such as rhesus macaques (Czaja 1978) and chacma baboons (Billboard and Busse 1983). Rats treated with progesterone increase their food intake so long as they have been pretreated with estradiol, which increases the concentration of progestin receptors (Shimizu and Bray 1993; Guyard et al. 1991). Increased food intake also occurs during the luteal phase in humans, when progesterone levels are high. For example, voluntary food intake in eight free-living women was 2110 kJ/day higher ($p < 0.0004$), on average, during the ten days before menses compared with the ten days after menses (Dalvit 1981) (Table 5). Food intake in these eight women was an average of 2076 kJ/day ($p < 0.008$) higher during the ten premenstrual days in a second cycle (Dalvit 1981). Similarly, Manocha et al. (1986) found a mean increase of 1325 kJ/day ($p < 0.05$) and 1275 kJ/day ($p <$

TABLE 5

Change in energy metabolism (kJ/d) over the menstrual cycle

Source	Energy Measure ($\bar{X} \pm SD$)	Follicular Phase (kJ/d)	Luteal Phase (kJ/d)	Follicular to Luteal Increase (kJ/d)	N (women)	*p* value
Soloman et al. 1982	Metabolic rate (Basal)	5033 ± 578 (entire cycle)		1503	6	$p < 0.05$
Bisdee et al. 1989	Metabolic rate (Sleep)	5775 ± 368	6187 ± 562	412	8	$p < 0.001$
Bisdee et al. 1989	24-h energy expen.	10910 ± 605	11164 ± 832	254	8	NS
Meijer et al. 1992	Metabolic rate (Sleep)	5789 ± 619	6235 ± 648	446	16	$p < 0.001$
Webb 1986	24-h energy expen.	7051 ± 1017	7664 ± 1172	613	10	$p < 0.00002$
Ferraro et al. 1992	Metabolic rate (Basal)	6423 ± 1315 (entire cycle)		833 ± 222	70	$p < 0.001$
Ferraro et al. 1992	Metabolic rate (Sleep)	5937 ± 1047 (entire cycle)		452 ± 176	70	$p < 0.02$
Ferraro et al. 1992	24-h energy expen.	8164 ± 1474 (entire cycle)		444 ± 163	70	$p < 0.01$
Dalvit 1981	Food intake	5991 ± 1264	8101 ± 1562	2110	8	$p < 0.0004$
Dalvit 1981	Food intake	6067 ± 1336	8143 ± 1470	2076	8	$p < 0.008$
Manocha et al. 1986	Food intake	5440 ± 1215	6765 ± 1150	1325	11	$p < 0.05$
Manocha et al. 1986	Food intake	5440 ± 1065	6715 ± 1130	1275	11	$p < 0.01$
Gong et al. 1989[1]	Food intake	7674 ± 611	8541 ± 653	867	7	$p < 0.05$
Pliner and Fleming 1983	Food intake	7492 ± 2687	8427 ± 2229	935	33	$p < 0.05$
Tarasuk and Beaton 1991	Food intake	7628	8005	377	14	$p < 0.05$
Johnson et al. 1994	Food intake	7157 ± 1763[2]	7843 ± 1863	686	26	$p < 0.05$

Note: 1 kJ = 0.24 kcal. [1]Calculated from data in Gong et al. (1989, Table 3); [2]Value for follicular/ovulatory phase.

0.01) from the ten days after menses to the ten days before menses in eleven women whose intake was monitored for two cycles. Gong et al. (1989) reported that voluntary food intake by seven women over one menstrual cycle was 867 kJ/d greater during the luteal phase than during the follicular phase and 1185 kJ/d greater during the luteal phase than during the periovulatory phase ($p < 0.05$). Pliner and Fleming (1983) reported that consumption increased by a mean of 935 kJ/d ($p < 0.05$) from the follicular to the luteal phase in 22 of 33 subjects. Tarasuk and Beaton (1991) found an increase in mean food intake of only 377 kJ/d ($p < 0.05$) in 14 subjects, but they suggest that their results may have been dampened by the wider age range in their sample or inaccurate reporting of the onset of menses. Finally, Johnson et al. (1994) reported that energy intake increased by a mean of 686 kJ/d ($p < 0.05$) from the follicular/ovulatory to the luteal phase in 26 subjects (Table 5).

SIGNIFICANCE OF THE WHOLE BODY ENERGY SAVINGS

Cycling. It is helpful to compare the magnitude of the increase in daily energy expenditure during the luteal phase to the average daily energy requirement over the entire cycle. Age, physical activity, body size, and other factors contribute to the average daily energy requirement (NRC 1989), so a single value cannot represent the requirement for all women. Therefore, I calculated the significance of the cyclical change in energy metabolism for women of a given energy requirement, 9.2 MJ/d (2,200 kcal/d). In particular, I asked: How substantial is the energy savings of the follicular phase over four cycles? Energy Savings = (Σ cycles) · (Σ follicular days per cycle) · (luteal to follicular difference in energy metabolism). The World Health Organization (WHO 1982) reported a mean of 15.7 ± 0.57 days for the follicular phase with a range of 11 to 25 days and a mean of 12.8 ± 0.72 days for the luteal phase with a range of 8 to 19 days. Given a 16 day follicular phase, and a luteal increase in BMR of 833 kJ/d (Ferraro et al. 1992), then over four cycles the savings is 53.3 MJ. Assuming a daily energy requirement of 9.2 MJ/d, this translates into 5.8 days worth of food.

Over human evolutionary history, an energy savings worth nearly six days of food over four months could have been advantageous for fertility and survivorship during times of food stress. The idea that fertility is related to the food supply was noted by Darwin (1898) and extended to humans in pioneering work by Frisch (e.g., 1978). Numerous physiological studies have demonstrated that energy availability constrains reproductive functioning in humans (for reviews see Warren 1983; Ellison et al. 1993) and other mammals (for review see Wade and Schneider 1991). In demographic studies of human populations the effects of chronic malnutrition on fertility can be small and difficult to measure (Wood 1995:522–529), but even a positive selection coefficient of 1% signifies an important fitness advantage over the long term (Fischer 1958; Trivers 1985). In many human populations adequate nutrition is a persistent problem, so we should expect ongoing selection for the ability to resist the hunger season with fat deposits. Furthermore, epidemiological data suggest that both acute and chronic malnutrition are associated with an elevated risk of mortality (Pelletier et al. 1993). A metabolism that slows down during part of the menstrual cycle should help women to maintain body mass. Thus, the coupling of female reproductive cycling to metabolic cycling is unlikely to be fortuitous. The menstrual/ovarian cycle revs up and revs down, economizing on the energy costs of reproduction.

Amenorrhea. The magnitude of the metabolic economy achieved by foregoing the luteal phase is especially great during amenorrhea; a time when women are likely to be nutritionally stressed and/or lactating. To appreciate the magnitude of the savings, consider a woman who has 13 luteal days per month when she is cycling and who expends 833 kJ/d more energy during the luteal phase. If she foregoes the higher energy cost of the luteal phase during amenorrhea, then over 12 months she saves 130 MJ according to the following equation: Energy Savings = (Σ months) · (Σ luteal days per month) · (luteal to follicular difference in energy metabolism). If her mean daily energy requirement is 9.2 MJ/day, then she saves 14 days worth of food annually. This value would be higher in

women with a lower daily energy requirement and lower in women for whom the luteal phase is less costly relative to the follicular phase. For example, if a woman expends only an additional 446 kJ/d during the luteal phase [as reported by Meijer et al. (1992) for sleeping metabolic rate], then she saves about 70 MJ or eight days worth of food.

Ferraro et al. (1992) estimated that the loss of periodic luteal phase increases in metabolic rate reduces the annual metabolic rate of postmenopausal females by ~15,000 to 20,000 kcal which is 63 to 84 MJ. They suggested that this energy savings may contribute to postmenopausal weight gains. Ferraro et al. do not explain how they arrived at their estimate, so it is unclear why it is lower than my own calculation of 130 MJ based on their data. Refining the estimate of the cost of the luteal phase is a worthwhile task for the future. We should also try to calculate a value for the energy savings of amenorrhea that does not equate amenorrhea with the follicular phase. The follicular phase is energetically cheaper in kJ/d than the luteal phase, but amenorrhea is energetically even cheaper. Finally, although metabolic rate is higher on average during the luteal phase than during the follicular phase, ambiguity remains in regard to the cycle day(s) of peak metabolic expenditure.

Although the energy spared by amenorrhea is not yet precisely quantifiable, it is already widely recognized that amenorrhea is adaptive because it spares energy (Warren 1983; Myerson et al. 1991; Bonen 1994). Empirical support for this argument includes evidence that oxygen consumption at rest is lower in amenorrheic women than in eumenorrheic women (Graham et al. 1989). Moreover, despite similar caloric intake, resting metabolic rate is significantly lower in amenorrheic high mileage runners than in eumenorrheic high mileage runners (4667 ± 184 kJ/d versus 5559 ± 239 kJ/d), and the latter is significantly lower than resting metabolic rate in sedentary women (6166+184 kJ/d) (Myerson et al. 1991). A shortage of metabolic fuels is sufficient to cause amenorrhea in menstruating primates (including women) and anestrus (cessation of cycling) in laboratory and domestic animals (Wade and Schneider 1992). Amenorrhea is adaptive not only because it spares energy, but also because it allows reproductive effort to be postponed to more favorable conditions (Frisch 1978; Van der Walt et al. 1978; Ellison 1990; cf. Wood 1995:523–529).

ENERGY SAVINGS AND THE ENDOMETRIUM

The proximate mechanisms that generate the relationship between the menstrual cycle and metabolic rate involve the ovarian steroids estradiol and progesterone. Receptor concentrations for these hormones are particulary high in reproductive organs including the uterus, ovary, and mammaries, as well as the hypothalamic pituitary unit (Ferin et al. 1993). The action of the ovarian steriods on all the target tissues is responsible for the luteal phase increase in metabolic rate. Although the increase in metabolism in any single tissue may be small, the combined effect of the ovarian steroids on all the target tissues is substantial. The role of the endometrium has been particularly well studied. In animals as disparate as rats and humans, it has been shown that the ovarian hormones stimulate endometrial metabolism (Roberts and Szego 1953; Clark and Yochim 1971; Wynn and Jollie 1989:314). It would be interesting to know how the metabolic effects of the ovarian steroids are partitioned between the endometrium and other uterine and nonuterine tissues, but data on this topic are lacking. To assess the role of the endometrium, it is therefore useful to consider data on endometrial oxygen uptake over the course of the menstrual cycle.

The earliest studies of endometrial metabolism over the menstrual cycle employed the Warburg method, which gave conflicting results (e.g., Raab 1929; Stuermer and Stein 1952; Hagerman and Villee 1953). More recently, Okagaki and Richart (1970) measured endometrial oxygen consumption in vitro (N = 43), using an oxygen electrode, a more sensitive technique. Oxygen uptake was at a nadir in the early proliferative phase (0.646 ± 0.226 μl/mg of dry mass/h), increased during the late proliferative phase (0.880 μl/mg of dry mass/h; SE not indicated), reached a zenith in the early secretory phase (1.387 μl/mg of dry mass/h; SE not indicated), and declined in the late secretory phase (1.332 ± 0.112 μl/mg of dry mass/h). The increase in oxygen consumption from the proliferative to the se-

cretory phase was statistically significant ($p < 0.01$). This cyclic change in oxygen consumption by human endometria parallels the cyclic change in oxidizing enzymes found by previous authors (Steuermer and Stein 1952; McKay et al. 1956).

Price et al. (1981) reported that Okagaki and Richart (1970) probably underestimated endometrial oxygen uptake because they used minced endometrial tissue: a procedure that reduced oxygen uptake by more than 30% ($p < 0.01$). Price et al. therefore used an oxygen electrode to measure the in vitro oxygen consumption of intact endometrial strips. Oxygen consumption (μl oxygen/mg protein/h) was lowest in the early proliferative stage, increased almost sevenfold until around ovulation, and declined nearly threefold during the secretory phase (Figure 4a in air phase in Price et al. 1981). Although Price et al. reported an ovulatory peak in oxygen consumption, their data do not appear adequate to distinguish between an ovulatory and early secretory peak because they did not have data on the timing of ovulation. As noted by these investigators, ovulation is not histologically observable in the endometrium until 24 to 36 hours after it takes place, and some of the "ovulatory" endometrial strips may have been misclassified. Nonetheless, the study by Price et al. shows an almost sevenfold increase in oxygen consumption during the proliferative phase, which implies a nearly sevenfold energy savings (per mg protein/h) for the endometrium in the regressed state. Moreover, since endometrial oxygen consumption is greater during the ovulatory/luteal phase than during the proliferative phase, rebuilding the endometrium after it has regressed is cheaper than maintaining it. Profet emphasized the nutritional content of the menstrual flow. However, according to the data on oxygen consumption, it is cheaper to lose blood and other tissue during menstruation, than to waste additional energy by providing the metabolic support required to sustain this tissue when it is not needed.

The evidence that regressed endometria consume less oxygen corroborates the results of earlier studies that employed the Warburg method. For example, Abe (1961) reported that oxygen uptake is higher in normal uteri than in amenorrheic uteri, and Hagerman and Villee (1953) reported that oxygen consumption was depressed in endometrial samples from menopausal women. Hackl (1968) compared oxygen uptake in 42 endometrial biopsies from control women and 32 biopsies from women on combination oral contraceptives. The endometria from the oral contraceptive users were less well developed and consumed only about half as much oxygen (Hackl 1968, 1973).

To evaluate the significance of endometrial regression, one should consider what might happen if the endometrium did not regress upon the failure of implantation. During episodes of amenorrhea cause by negative energy balance or stress, the endometrium would remain primed for long periods before ovulation resumed. Clearly, maintenance of the endometrium in the absence of ovulation would be a waste of energy.

ENDOMETRIAL BLOOD FLOW

Blood flow to the uterus varies over wide limits and is influenced in a major way by ovarian steroid hormones during both cycling and pregnancy (Finn and Porter 1975; Greiss and Rose 1989). Variation in uterine blood flow provides an indirect measure of variation in endometrial oxygen consumption in species for which direct measures are unavailable. In ewes, cows, and sows, uterine blood flow peaked with the onset of estrus and was associated with a high estrogen:progesterone ratio in systemic blood (Greiss and Rose 1989). In rabbits, however, the blood content of the whole uterus was twofold higher under progesterone domination than under estrogen domination (Kao and Gams 1961). In rats, the combined action of estrogen and progesterone is known to stimulate endometrial vascularization, blood flow, and oxygen consumption (Mitchell and Yochim 1968). Under the influence of estrogen and progesterone, the postovulatory primate endometrium experiences a rapid growth of the coiled arterioles and other components of an increasingly differentiated microvasculature (Kaiserman-Abramof and Padykula 1989). In humans, the diameter of the endometrial arterioles increased from 28 μ in the proliferative phase to 45.5 μ in the secretory phase, implying a concomitant increase in blood flow (Salvatore 1968).

This result was confirmed by doppler ultrasound studies of the uterine artery, which showed that blood flow to the uterus increased with rising levels of plasma estradiol and progesterone (Goswamy and Steptoe 1988).

OTHER EXAMPLES OF METABOLIC ECONOMY

The hypothesis that the capacity to adjust the quantity of metabolically active tissue is an adaptation for saving energy is new with respect to endometrial regression during cycling, but is implicit in explanations for changes in tissue mass elsewhere in the mammalian body.

Lactation. During lactation, breast tissue mass increases by about 500 g (Hytten and Leitch 1971). This increase is temporary and the regression of mammary tissue after lactation presumably spares energy. From estimates of the increase in metabolically active mammary tissue and the cost of milk synthesis during lactation, Prentice and Whitehead (1987) calculate that BMR should theoretically increase above the nonpregnant, nonlactating state by 12%, 10%, and 9% at 0 to 6, 6 to 12, and 12 to 24 months postpartum. More recent research has evaluated these theoretical estimates with empirical data from longitudinal studies. Specifically, Goldberg et al. (1991) measured the BMR of each of 10 lactating British women at 36 weeks of gestation, after 4, 8, and 12 weeks of lactation, and in the nonpregnant and nonlactating (NPNL) state at 3 months postweaning. At 36 weeks gestation, BMR was an average of 24.8 ± 8.3% higher than in the NPNL state ($p < 0.001$). Throughout lactation, however, BMR remained surprisingly constant and was not significantly different from the NPNL value. Goldberg et al. calculated the metabolic costs of milk synthesis to be 445 kJ/d in their study population; this cost should lead to a concomitant increase in BMR above the NPNL state. The lack of elevation in BMR during lactation implies the suppression of one or more components of maternal metabolism. One possibility is that maternal maintenance metabolism (e.g., protein turnover) might be suppressed in lactating women and, although potentially detrimental to long-term health, such suppression may be an adaptation for meeting the immediate energy demands of reproduction (Prentice and Whitehead 1987; Goldberg et al. 1991). Thus, if endometrial regression evolved to lower energy costs and balance the energy budget, it is not greatly different from either the adaptive lowering of BMR that occurs during lactation, or the regression of mammary tissue after lactation.

Pregnancy. Theoretical estimates of oxygen consumption by the fetus and associated tissues suggest that BMR should increase in the four quarters of pregnancy by an average of 3%, 7%, 11%, and 17% above the prepregnant value (Hytten and Leitch 1971; see also Prentice and Whitehead 1987). At term the predicted increase is 22% which is only triple the conservative estimate that BMR increases by 7% from the follicular to the luteal phase of the menstrual cycle.

Actual measures of BMR show that there is substantial interindividual variation in response to pregnancy. For example, in a study of twelve British women, six subjects showed an immediate and progressive increase in BMR in line with the predicted increases, but the other six subjects experienced an initial decrease in BMR—or a negligible increase—which was not followed by a substantial increase until late in pregnancy (Goldberg et al. 1993). The group mean (±SD) change in BMR over the NPNL state was 2.8 ± 6.7% at 12 weeks, 9.5 ± 11.2% at 24 weeks, and 24.9 ± 11.8% at 36 weeks ($p < 0.001$). At 36 weeks the increase in BMR in the 12 women ranged from 10% to 50%.

Poppitt et al. (1993) tested the hypothesis that energy sparing decreases in BMR may enable women to maintain the positive energy balances needed to protect fetuses from growth retardation when maternal energy intake is low. Their subjects were twenty chronically undernourished Gambian women. Six showed steady increases in BMR from conception onward that were in line with the predicted increases, while the other fourteen showed a significant decline in BMR during early gestation. The cumulative maintenance expenditure of the twenty Gambian women was well below that of well-nourished Western women, and enabled a savings of 345 kJ/d during pregnancy. This savings may have been accomplished through significant reductions in maternal metabolism. The change in BMR

per kg of lean body mass ranged from −15.4% to +17.1% at 36 weeks gestation. The best predictors of a woman's metabolic response to pregnancy were her gain in mass, lean body mass, and fat mass during pregnancy, rather than her nutritional status before pregnancy (Poppitt et al. 1993). Although the mechanisms that limit increases in BMR during lactation and pregnancy are not yet understood, it is evident that selection has acted on BMR, preventing increases that might lead to negative energy balances and reproductive failure.

Food Stress. Energy sparing reductions in BMR are also caused by food restriction in the absence of pregnancy or lactation (Henry 1992). In a study of humans who were semistarved for 168 days, basal metabolic rate dropped 85% from 6510 kJ/d to 953 kJ/d (Keys et al. 1950). Anorexia nervosa is associated with a 19% to 39% reduction in basal metabolic rate (Forbes et al. 1984). For example, in a study of six patients, BMR was 4170 kJ/d compared with 5520 kJ/d in six control subjects matched for age and height (Casper et al. 1991). Resting metabolic rate (per kilogram of lean body mass) was 13.8 % lower in chronically undernourished Indian laborers than in sedentary controls (Shetty 1984).

ENERGY SPARING MECHANISMS IN OTHER VERTEBRATES

Metabolism is also suppressed during energy restriction in hibernating mammals (Hochachka and Guppy 1987:100) and is often accompanied by gonadal regression (see Wade and Schneider 1992) and atrophy of the mucosal lining of the small intestine (Carey 1990). Absence of food also causes energy sparing reductions in intestinal mucosal mass in nonhibernating vertebrates such as rats (Carey 1990; McBurney 1993). Mucosal up regulation and down regulation is particularly dramatic in the Burmese python (*Python molurus*), a species that saves considerable energy by not maintaining a functional intestinal mucosa during the long periods of fasting between meals (Secor and Diamond 1995).

Seasonal breeding is a strategy for keeping the energy costs of reproductions in check because it concentrates these costs in the season(s) when reproductive success is most likely and curtails these costs at other times. In seasonal breeders, the gonads commonly regress in the nonbreeding season in both males and females (Nalbandov 1976). For example, the mean ovary mass in starlings is about 8 mg in early winter, but just prior to the onset of egg laying in mid-April, the mean ovary mass increases to 220 mg (Witschi 1956:34). This is nearly a thirtyfold increase beyond the ovary mass in the inactive season. Moreover, yolk is synthesized for maturing oocytes only a few days before ovulation and no yolk is synthesized in the nonbreeding season (Follett 1984). The cessation of vitellogenesis is an obvious energy economy because a laying female requires 20% to 70% more energy than at other times (King 1973). Selection to spare energy via seasonal reproduction in birds is directly comparable to selection to spare energy via metabolic cycling in women.

The origin of endometrial regression as an energy sparing mechanism may predate the evolution of the mammals because comparable energy sparing processes occur in other vertebrates. The uterus of viviparous mammals probably evolved from the glandular region of the oviduct of oviparous species (Mossman 1987:98). Furthermore, the uterine endometrium in mammals is similar to the epithelium of the oviducts in extant reptiles. Both are secretory linings that transfer nutrients from mother to embryo. Outside the breeding season, reptilian oviducts are thin and straight but, as vitellogenesis begins in the ovarian follicles, the oviducts undergo a dramatic increase in mass due to hypertrophy of the epithelium and associated glands. The growth of the oviducts is associated with an increase in biochemical activity (Licht 1984:231). Thus reptilian oviducts change in mass in relation to the ovarian cycle in a fashion that is comparable to the changes in the mammalian endometrium. Both structures have secretory activity only when a fertilized ovum or embryo is likely to be present. If this similarity between mammals and reptiles reflects homology not analogy, then endometrial regression is of ancient origin. I suggest that a major selective pressure for both the origin and continued maintenance of oviducal/endometrial cyclicity is energy limitation. This hypothesis is compatible with a substantial body of data, but what about alternative hypotheses other than that of Profet?

MENSTRUATION AS A DEFENSE AGAINST NEOPLASM

Ravenholt (1966) observed that endometrial regression rids the uterus of endometrial neoplasia, which raises the question: could menstruation have evolved for this purpose? Rapid cellular reproduction leads to neoplasia by increasing the chances that unrepaired DNA lesions will be replicated. Malignant neoplasia are not a problem with adult neurons because neurons do not reproduce, but it is a relatively common occurrence in mitotically active tissue such as skin, breasts, and bones. The uterus might be prone to neoplasms if mutated cells were not cyclically deleted (Ravenholt 1966), because estrogen stimulates mitotic proliferation of the endometrium.

If endometrial regression did not occur at the end of the luteal phase, however, then there would be no need for the extensive mitotic proliferation of the follicular phase. In the absence of mitotic proliferation during the follicular phase, there would be no problem of neoplasia. Moreover, if mitotic proliferation during the follicular phase is somehow indispensable, then we need not invoke neoplasia to explain regression at the end of the luteal phase. Successive rounds of mitotic proliferation would eventually fill the uterine cavity and prevent implantation and pregnancy. Endometrial regression would then be a necessity.

MENSTRUATION AS A SIGNAL OF FERTILITY

Worthman et al. (1992) propose that copious menstruation evolved in humans as a signal of potential fertility. In particular, they suggest that it has the advantage of disclosing female reproductive status without giving away the exact timing of ovulation. Previous empirical data support the argument that menstruation reveals female reproductive status (cycling, pregnant, amenorrheic), and that menstrual taboos can be imposed on females to force them to signal their menses (Strassmann 1990, 1992). However, the idea that copious menstruation itself evolved as a signal does not yet have empirical support. In an earlier article (Strassmann 1992) I argued against this possibility, but since it has not been tested with data on primates, I will do so here.

If copious menstruation evolved as a signal of female reproductive status, then it should be present in humans because ovulation is concealed and it should be absent in species with conspicuous sexual swellings. This prediction is based on the expectations that: (1) if ovulation is concealed, then information about the timing of menses is potentially more useful, and (2) if estrus is already advertised by swellings, then menstruation cannot add further information. To evaluate this prediction, I tabulated data on menstrual flow (from Hrdy and Whitten 1986, and Profet 1993) against data on visual cues of female receptivity (from Hrdy and Whitten 1986).

As shown in Table 6, there is no apparent relationship between the copiousness of menstruation and the presence of sexual swellings (Fisher's Exact Probability Test, Two-Tail, $p = 0.15$, $N = 33$). In contradiction to the prediction, several species in the genera *Macaca, Cercopithecus, Papio,* and *Pan* have overt menses despite the presence of obvious swellings. Chimpanzees (*Pan*) are particularly at odds with the hypothesis of Worthman et al. because they have unusually profuse menses, yet they also have dramatic sexual swellings. Therefore, copious menstruation in chimpanzees must have evolved for a reason other than advertisement of fertility. Although it could be argued that menstruation in humans is a different phenomenon from menstruation in chimps, this possibility is weak because humans and chimps share a recent common ancestor and menstruate through similar, if not identical, mechanisms.

Using a phylogenetic approach, I tested the

FIGURE 6. DISTRIBUTION OF THE TRICHOTOMOUS CHARACTER (SEXUAL SWELLINGS) MAPPED ONTO THE SAME PRIMATE PHYLOGENY AS IN FIGURE 2

Data on sexual swellings are from Hrdy and Whitten (1986). A minimum of sixteen evolutionary steps were required to account for the distribution of sexual swellings among extant taxa.


Lemur macaco
Lemur catta
Varecia variegata
Propithecus verreauxi
Cheirogaleus medius
Galago senegalensis
Galago garnettii
Perodicticus potto
Arctocebus calabarensis
Nycticebus coucang
Loris tardigradus
Tarsius banacus
Tarsius spectrum
Cebus apella
Cebus albifrons
Saimiri sciureus
Saguinus oedipus
Callithrix jacchus
Aotus trivergatus
Alouatta palliata
Lagothrix lagothricha
Ateles geoffroyi
Colobus badius
Presbytis entellus
Cercocebus aterrimus
Cercocebus torquatus
Cercocebus albigena
Theropithecus gelada
Papio leucophaeus
Papio hamadryas
Papio c. anubis
Papio c. papio
Papio c. ursinus
Papio c. cynocephalus
Macaca sylvanus
Macaca arctoides
Macaca assamensis
Macaca sinica
Macaca radiata
Macaca fascicularis
Macaca cyclopis
Macaca mulatta
Macaca fuscata
Macaca silenus
Macaca nemestrina
Erythrocebus patas
Cercopithecus talapoin
Cercopithecus ascanius
Cercopithecus mitis
Cercopithecus aethiops
Hylobates lar
Hylobates hoolock
Hylobates concolor
Pongo pygmaeus
Gorilla g. beringei
Gorilla g. gorilla
Pan troglodytes
Homo sapiens
Sexual swellings
16 steps
ordered
Absent
Subtle
Obvious
equivocal

TABLE 6

Copiousness of menstruation and conspicuousness of sexual swellings

Menstruation	Sexual Swellings		
	Absent	**Subtle**	**Obvious**
Absent/Covert	*Saguinus*	*Cheirogaleus* *Propithecus* *Lemur* *Varecia* *Galago* *Perodicticus* *Loris* *Callithrix* *Saimiri*	*Tarsius*
Slight	*Cercopithecus* *Macaca*	*Alouatta* *Cebus* *Macaca* *Theropithecus* *Gorilla*	*Cercocebus* *Cercopithecus* *Macaca* *Papio* *Colobus*
Overt	*Macaca* *Presbytis* *Homo*	*Erythrocebus* *Macaca* *Hylobates*	*Cercopithecus* *Macaca* *Papio* *Pan*

Fisher's Exact Probability Test, Two-Tail, $p = 0.15$, N = 33. If the polymorphic genera *Cercopithecus, Macaca,* and *Papio* are excluded then $p = 0.26$, N = 22. Data on sexual swellings are from Hrdy and Whitten (1986). Data on menstruation are from Hrdy and Whitten (1986) and Profet (1993).

prediction that copious menstruation was more likely to evolve in the absence of sexual swellings. Figure 6 shows how the MacIntosh program, MacClade 3, maps sexual swellings onto the phylogeny in accordance with the principle of parsimony. Regardless of how the characters menstruation and sexual swellings are dichotomized, the concentrated changes test (Maddison 1990; Maddison and Maddison 1992) gave nonsignificant results (*p* values ranged from 0.09 to 0.83 with a median of 0.35), suggesting that the absence of sexual swellings was not a predisposing factor for the evolution of copious menstruation. Thus, whether I simply tabulated extant genera, or based the analysis on independent evolutionary events, I found no correlation between the copiousness of menstruation and the degree of sexual swellings. It therefore appears unlikely that menstruation evolved as a signal of fertility.

Menstruation and Endometrial Decidualization

Finn (1987, 1994) observes that, in women, endometrial decidualization occurs even in the absence of a blastocyst, whereas in many other mammals decidualization either does not occur at all or requires a stimulus from a blastocyst. Finn hypothesizes that this difference is the reason for menstruation in women. However, other primates also have overt menstruation even though they only undergo decidualization in the presence of a blastocyst or in response to trauma (Enders 1991; Profet 1993:336). Finn also suggests that early decidualization in menstruating species results in irreversible differentiation of the endometrium such that it must be discarded. As an explanation for endometrial regression, this argument has three drawbacks: (1) if endometrial differentiation is "irreversible" in some species, then this may be a consequence of endometrial regression (since the tissue will be destroyed anyway) rather than a cause, (2) many tissues—including gut, muscles, and breasts—regress when they are not needed even though they have merely grown and not differentiated (e.g., McBurney 1994), and (3) endometrial regression occurs in all mammals (Nalbandov 1976; Padykula 1980; Johnson and Everitt 1988) regardless of whether decidualization occurs early, late or not at all.

CONCLUSION

The endometrial cycle is coupled to the ovarian cycle. When ovarian steroid hormone levels fall, the endometrium regresses, resulting in cellular debris that must be either shed or reabsorbed. One advantage of cyclical regression that has not previously been considered is reduction in energy expenditure. When a blastocyst is unavailable for implantation, the secretory endometrium becomes a liability. If it is maintained, it requires continuous metabolic support, but if it regresses, this extra energy expense can be spared. In women, endometrial regression permits a nearly sevenfold reduction in endometrial oxygen consumption (per mg protein/h). Endometrial cyclicity is linked to the whole body cyclicity in metabolic rate caused by the action of the ovarian steroids. In women, metabolic rate is at least 7% lower, on average, during the follicular phase than during the luteal phase, which translates into an estimated energy savings of 53 MJ over four cycles. This is the equivalent of nearly six days worth of food. By helping women to maintain body mass, this economy of energy has beneficial implications for both fecundity and survivorship.

Maintenance of the endometrium in the metabolically active state required for implantation would be particularly disadvantageous during the nonbreeding season and other episodes of amenorrhea when ovulation is absent for a prolonged period of time. Twelve months of amenorrhea save an estimated 130 MJ, which would meet a woman's energy needs for nearly half a month. Endometrial regression is similar (and perhaps homologous) to the hypotrophy of reptilian oviducts in the nonbreeding season and its origins may predate the mammals. Energy sparing limitations of metabolic rate occur during lactation, pregnancy, and food stress, and are comparable to the whole body reduction in metabolic rate that occurs during menstrual cycling.

Regression of the endometrium necessarily includes the endometrial microvasculature. In most species blood from the microvasculature is entirely reabsorbed, but in Old World primates and a few other mammals, blood and other tissue that is not reabsorbed is shed with the menses. Differences in the degree of menstrual bleeding correlate with phylogeny rather than with any conspicuous differences in ecology or behavior. Relatively copious bleeding is found in catarrhines and is associated with the presence of spiral arterioles in the endometrium. The design of these arterioles probably relates to their major function, which is to provide the blood supply to the placenta. External bleeding can be interpreted as a side effect of endometrial regression and is probably caused by the presence of too much blood and other tissue for efficient reabsorption. This hypothesis can account for the increase in blood loss with parity in women, since previous pregnancies increase uterine vascularity. It also successfully predicted that catarrhines with overt menstruation have higher ratios of litter mass to body mass. Thus, the unusually profuse bleeding in humans and chimps may be due to the large size of their uteri relative to adult female body size and to the design of the microvasculature in these and other catarrhines.

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APPENDIX
Primate data

Scientific Name	Common Name	1	2	3	4	5	6	7
PROSIMIANS								
Lemuroidea								
Cheirogaleidae								
Cheirogaleus medius	Western fat-tailed dwarf lemur	None	?	1	2	0.18	0.02	?
Indriidae								
Propithecus verreauxi	White sifaka	None	?	1	2	3.50	0.11	?
Lemuridae								
Lemur catta	Ring-tailed lemur	None	?	1	2	2.50	0.11	?
Lemur macaco	Black lemur	None	?	1	2	2.50	0.10	?
Varecia variegata	Ruffed lemur	None	?	1	2	3.10	0.22	1
Lorisoidea								
Lorisidae								
Galago garnettii	Greater bushbaby	None	?	1	2	?	?	2*
Galago senegalensis	Lesser bushbaby	None	?	1	2	0.21	0.02	2
Artocebus calabarensis	Angwantibo	None	?	1	?	0.31	0.03	?
Perodicticus potto	Potto	None	?	1	2	1.08	0.05	?
Nycticebus coucang	Common slow loris	None	?	1	?	1.20	0.05	?
Loris tardigradus	Slender loris	None	covert	1	2	0.26	0.02	?
Tarsioidea								
Tarsiidae								
Tarsius spectrum	Tarsier	?	covert	1	?	0.20	0.03	?
Tarsius banacus	Tarsier	None	?	1	3	?	?	?
NEW WORLD MONKEYS								
Ceboidea								
Callitrichidae								
Callithrix jacchus	Common marmoset	Not detectable	covert	1	2	0.29	0.06	1
Saguinus oedipus	Cottontop tamarin	?	covert	1	1	0.51	0.08	2
Cebidae								
Alouatta palliata	Mantled howler	PRVE	slight	2	2	5.70	0.48	2
Ateles geoffroyi	Black-handed spider monkey	?	slight, 3-4	2	?	5.80	0.43	2
Lagothrix lagothricha	Common woolly monkey	?	slight, 3	2	?	5.80	0.45	2
Cebus albifrons	White-fronted capuchin	?	slight	2	2	2.60	0.23	?
Cebus apella	Brown capuchin	PRVE	slight, 1-8	2	?	2.10	0.25	2
Saimiri sciureus	Squirrel monkey	Never seen	covert	1	2	0.58	0.20	2
Aotus trivirgatus	Night monkey	?	covert	1	?	1.00	0.10	1
OLD WORLD MONKEYS								
Cercopithecoidea								
Cercopithecidae								
Cercocebus albigena	Gray-cheeked mangabey	NOE	slight	2	3	6.40	0.43	2
Cercocebus aterrimus	Black mangabey	?	slight/overt, 4	2	?	?	?	2*
Cercocebus torquatus	White-collared mangabey	NOE	4 days	2	3	5.50	?	2*
Cercopithecus aethiops	Vervet monkey	NOE 3.6 days	slight/covert, 5	2	3	3.56	0.31	2
Cercopithecus mitis	Blue monkey	NOE 1-4 days	slight/covert, 5	2	1	4.40	0.40	?

Appendix continued

Scientific Name	Common Name	1	2	3	4	5	6	7
Cercopithecus ascanius	Redtail monkey	NOE	?	2	1	2.90	?	?
Cercopithecus talapoin	Talapoin	OE 2-6 days	?	3	3	1.10	0.18	?
Erythrocebus patas	Patas monkey	OE 3 days	slight	3	2	5.60	?	1
Macaca sylvanus	Barbary macaque	OE 3-4 days	?	3	3	10.00	?	2*
Macaca sinica	Toque macaque	OE 1-4 days		3	1	3.40	?	2
Macaca radiata	Bonnet macaque	OE 10 days	2-7 days	3	2	3.70	0.40	2
Macaca silenus	Lion-tailed macaque	OE 2.5 days	overt, 2-2.5	3	3	5.00	?	2*
Macaca nemestrina	Pigtailed macaque	NOE	?	2	3	7.80	0.47	2
Macaca fascicularis	Crab-eating macque	OE 2-7 days	overt, 3	3	2	4.10	0.35	2
Macaca mulatta	Rhesus macaque	OE 2.6 days	overt, 4	3	2	3.00	0.48	2
Macaca arctoides	Stump-tailed macque	NOE 2-4 days	slight, 3	2	2	8.00	0.49	2
Macaca assamensis	Assamese macaque	?	slight	2	1	?	?	2*
Macaca fuscata	Japanese macque	OE 3.5 days	overt	3	2	9.10	0.50	2
Macaca cyclopis	Formosan macaque	OE 3 days	overt, 4	3	3	?	?	2*
Papio cynocephalus cynocephalus	Yellow baboon	OE 3 days	?	3	3	15.00	0.85	2
Papio cynocephalus anubis	Olive baboon	OE 3 days	?	3	3	12.00	1.10	2
Papio cynocephalus papio	Guinea baboon	OE 3 days	2-7 days	3	3	13.00	?	2
Papio cynocephalus ursinus	Chacma baboon	OE 3 days	1-7 days	3	3	16.80	?	2
Papio hamadryas	Hamadryas baboon	OE 3 days	?	3	3	9.40	?	1
Papio leucophaeus	Drill	NOE	?	2	3	10.00	?	?
Papio sphinx	Mandrill	?	1-6 days	?	3	11.50	0.60	?
Theropithecus gelada	Gelada baboon	NOE	slight	2	2	13.60	0.46	1
Colobus badius	Red colobus	NOE	?	2	3	5.80	?	2
Presbytis entellus	Gray langur	OE 2-4 days	slight/overt, 1-3	3	1	11.40	?	1
Presbytis obscura	Dusky leaf monkey	?	2-3 days	?	2	6.50	0.49	1
Rhinopithecus roxellanae	Golden snub-nosed langur	?	slight?	?	?	?	?	?
APES AND HUMANS								
Hominoidea								
Hylobatidae								
Hylobates concolor	Black gibbon	?	overt, profuse? 1-3	3	?	5.80	?	1*
Hylobates hoolock	Hoolock gibbon	?	slight/overt, 2-4	3	?	6.50	?	1*
Hylobates lar	Lar gibbon	OE 2-5 days	slight/overt, 1-3	3	2	5.30	0.41	1
Pongidae								
Pongo pygmaeus	Orangutan	NOE 3-4 days	slight	2	?	37.00	1.73	1
Pan troglodytes	Common chimpanzee	OE 3 days	overt, profuse 1-7	3	3	31.10	1.76	2
Gorilla gorilla beringei	Mountain gorilla	NOE	?	2	2	?	?	1
Gorilla gorilla gorilla	Lowland gorilla	NOE	slight/overt, 3-5	2	2	93.00	2.11	1
Hominidae								
Homo sapiens	Humans	OE 2-8 days	overt, profuse 1-7	3	1	40.10	3.30	1

Notes: 1) Menstruation as reported by Hrdy and Whitten (1986:372-378): PRVE = present, but rarely visible externally, NOE = not obvious externally, OE = obvious externally, days = duration of menstrual flow; 2) Menstruation as reported by Profet (1993:384-386): covert = blood not externally detectable, slight = blood externally detectable, overt = blood externally obvious, days = duration of menstrual flow; 3) Menstruation code used in this article: 1 = absent or covert, 2 = slight, 3 = overt; 4) Sexual swellings as reported by Hrdy and Whitten (1986:372-378): 1 = absent, 2 = subtle, 3 = obvious (in Hrdy and Whitten, species with obvious swellings have an asterisk); 5) Adult female body weight in kg as reported by Harvey et al. (1986); 6) Neonate weight in kg times litter size from Harvey et al. (1986); 7) Promiscuity of the breeding system as reported by Harcourt (1991): 1 = low (females typically mate with only one male per cycle), 2 = high (females typically mate with more than one male per cycle); * based on Harcourt's designation of the breeding system for the genus as a whole; ? = unkown.