methods for documenting subclinical menstrual disturbances are presented. Next, 3 general mechanisms are outlined whereby vegetarianism, considered at the broadest level, could affect the menstrual cycle. These mechanisms include energy imbalances associated with body-weight disturbances or exercise, psychosocial and cognitive factors, and specific dietary components. Finally, results of studies that have compared menstrual cycle characteristics of vegetarian and nonvegetarian women are described.

THE MENSTRUAL CYCLE

The female human menstrual cycle represents a complex interplay of hormones (12). During menstrual flow, the onset of which is used to define the first day of the cycle, circulating concentrations of both estradiol and progesterone are low. These low concentrations allow gonadotropin-releasing hormone (GnRH) from the hypothalamus to stimulate release of low concentrations of both follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior lobe of the pituitary gland. FSH stimulates the growth of a number of ovarian follicles, which begin to mature and secrete estrogen. Estrogen concentrations rise gradually during the follicular phase of the cycle and cause thickening of the endometrial lining of the uterus. The increasing estrogen concentrations inhibit FSH secretion, and all but the most mature of the developing follicles undergo atresia. This dominant follicle produces large amounts of estrogen, which in turn appear to stimulate a surge in LH. The LH peak has ≥ 3 functions: it inhibits estrogen production by follicular cells, initiates changes that result in the rupture of the dominant follicle and release of the ovum (ovulation), and brings about transformation of the ruptured follicle into the corpus luteum, resulting in the synthesis of both estrogen and progesterone during the luteal phase of the cycle. If fertilization does not occur, estrogen and progesterone concentrations begin to fall and the corpus luteum undergoes luteolysis 10-16 d after its formation. The decline in ovarian hormones results in the shed-

Vegetarianism and menstrual cycle disturbances: is there an association?1-3

Susan I Barr

ABSTRACT The question of whether menstrual disturbances are more common in vegetarian than in nonvegetarian women is complex. Disturbances of the cycle may be clinical (ie, amenorrhea or oligomenorrhea) or subclinical (ie, normal-length cycles with anovulation or a short or defective luteal phase). Detection of the latter requires that the menstrual cycle be monitored, but may help prevent recruitment bias in studies comparing vegetarians with nonvegetarians because vegetarians with menstrual disturbances may be more likely to volunteer for a study on menstrual disturbances and vegetarianism. Three general mechanisms that could contribute to menstrual disturbances that may differ between vegetarians and nonvegetarians include energy imbalances associated with body-weight disturbances or exercise, psychosocial and cognitive factors, and dietary components. Evidence for each of these mechanisms is reviewed and studies comparing menstrual function between vegetarians and nonvegetarians are described in this article. Although results from several cross-sectional studies suggest that clinical menstrual disturbances may be more common in vegetarians, a prospective study that controlled for many potential confounders found that subclinical disturbances were less common in weight-stable, healthy vegetarian women. Because the sample studied may not be representative of all vegetarian women, however, these results cannot be generalized. Population studies are needed to draw definitive conclusions. Am J Clin Nutr 1999; 70(suppl):549S-54S.

KEY WORDS Vegetarians, menstrual cycle, menstrual disorders, amenorrhea, oligomenorrhea, luteal phase, luteal-phase defects, anovulation, anorexia nervosa, obesity, body weight, dietary restraint, women

INTRODUCTION

It is frequently suggested that vegetarianism is associated with menstrual disturbances (1-6). If so, potential health consequences could include reduced fertility, loss of bone mineral density, and increased risk of osteoporosis (7, 8). However, in most cases the studies that drew this inference were not designed to examine this question directly or failed to consider confounding factors; therefore, the results may not be helpful.

As background for this examination, the normal ovulatory

menstrual cycle is described. Because cycle disturbances progress

from subclinical to clinical (9-11), any effect of vegetarianism on

the cycle would first be evident at subclinical levels. Accordingly,

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ding of the thickened endometrium as menstrual flow, beginning the next cycle. The characteristics of the cycle are such that it averages 28 d in length, with a normal range of 21-35 d.

CYCLE DISTURBANCES AND ASSESSMENT METHODS

The normal ovulatory cycle described above does not occur without fail between menarche and menopause. Deviations are more common during the periods after menarche and preceding menopause (13), but alterations in cycle length, cycle characteristics, or both can occur at any age in response to physiologic or psychosocial stressors. Disorders of cycle length include secondary amenorrhea (absence of flow for ≥ 6 mo in a nonpregnant woman) and oligomenorrhea (irregular cycles of 36-180 d). Disturbances of cycle characteristics include anovulation, which frequently occurs in women with oligomenorrhea but may also occur in women with cycles of normal length, and luteal phase disturbances, which include short luteal-phase cycles (cycles in which the luteal phase lasts <10 d) and luteal-phase defects such that the length of the luteal phase is normal but progesterone secretion is subnormal. Amenorrhea and oligomenorrhea are apparent to women because of the absence or irregularity of menstrual flow. However, because they occur within cycles of normal length, anovulatory, normallength cycles and cycles with short luteal phase or luteal-phase defects are not readily apparent. Whereas it is often assumed that a normal-length cycle reflects normal ovulatory function, this is not the case. Instead, the cycle must be assessed by measuring hormone concentrations or by using methods such as endometrial biopsy, ultrasound, and analysis of basal body temperature (BBT).

A cycle can be assumed to be ovulatory if estrogen and progesterone concentrations are above baseline (day 1 of the cycle) in a single blood or saliva sample obtained between days 18 and 22 (the midluteal phase of an average-length cycle). More frequent samples, however, are needed to establish luteal-phase length and adequacy, and days 18-22 may precede ovulation in cycles of greaterthan-average length. Assay of LH in urine samples collected at midcycle (days 12-16 in a typical cycle) detects probable ovulation, because an LH surge is a necessary prerequisite. In the absence of a LH peak by day 16, continued testing is needed to detect a delayed LH peak. Because cellular characteristics of the endometrium change across the cycle, histomorphometric examination of endometrial biopsy specimens can be used to indicate the cycle phase and to characterize cycles as ovulatory or anovulatory. Establishing that ovulation has occurred can also be done by using ultrasound visualization of the ovary to confirm the presence of the corpus luteum. Finally, because the hypothalamus responds thermally to progesterone, the average BBT in the luteal phase of the cycle is ≈ 0.3 °C higher on average than in the follicular phase. Computer analysis of daily BBT records allows the characterization of cycles as ovulatory or anovulatory and the estimation of the luteal-phase length of ovulatory cycles (14).

MECHANISMS FOR DIFFERENCES IN MENSTRUAL DISTURBANCES BETWEEN VEGETARIANS AND NONVEGETARIANS

Establishing whether menstrual disturbances are or are not more common among vegetarians is a complex undertaking. At least 3 general mechanisms—energy imbalances associated with body weight disturbances or exercise, psychosocial and cognitive factors, and components of the diet—acting singly or in combination could differ systematically between vegetarian and nonvegetarian women and thereby contribute to possible differences in their menstrual cycle.

Energy imbalance

Inadequate energy availability

It is well established that starvation and emaciation are almost invariably associated with amenorrhea, the most profound disturbance of the menstrual cycle. In anorexia nervosa, amenorrhea and failure to maintain a body weight within 15% of that expected are both diagnostic criteria (15). However, extreme weight loss is not a prerequisite for menstrual cycle disturbances because dieting can induce missed cycles before substantial weight loss occurs (16, 17). Even a very short-term (ie, 4-d) acute energy shortage can interfere with LH pulsatility and thereby affect cycle function (18).

Vegetarians are often leaner and lighter than nonvegetarians (19-21); however, the extent to which differences in body weight contribute to menstrual differences between vegetarians and nonvegetarians is unclear. The issue of body weight is complex, particularly in North American women. Most women report desired weights that are lower than their current weights (22, 23); however, negative publicity associated with dieting and eating disorders may prevent some normal-weight women from admitting to others their desire for weight loss. Instead, while adopting dietary practices that lead to weight loss-their desired outcome-they may report modifying their diets because they want to "eat well." The extent to which this is associated with adopting a vegetarian diet is not known. Nevertheless, it is not unreasonable to suggest that it does happen. Evidence is provided by studies exploring motivations for becoming vegetarian: "health reasons," including the belief that a vegetarian diet will contribute to weight loss, are commonly cited (24-26). Other supportive evidence comes from studies in women with anorexia nervosa. Among consecutive patients with anorexia nervosa in 2 studies, the prevalence of vegetarianism (red meat avoidance) was 45% (1) and 54% (27). In the latter study, however, vegetarianism preceded the onset of anorexia nervosa in only 6% of the patients, suggesting that many individuals at risk for developing anorexia may adopt a vegetarian diet as a means of limiting the amount of food eaten. In other words, for these women, vegetarianism appeared to be a consequence rather than a cause of the eating disorder and associated menstrual disturbances.

Nevertheless, it has been suggested that adopting a vegetarian diet for the purpose of weight loss increases the likelihood of menstrual disturbances. In one study, normal-weight women were randomly assigned to lose weight at a rate of ≈ 1 kg/wk on either a vegetarian or a nonvegetarian diet (3). Both groups lost the same amount of weight, but only 2 of the 9 women assigned to the vegetarian diet had normal ovulatory cycles compared with 7 of the 9 women consuming the nonvegetarian diet (3). Although the authors used mood ratings to suggest that women assigned to the vegetarian diet did not experience higher stress levels, the effect on the menstrual cycle of stress associated with acute dietary change cannot be excluded in this short-term study.

Women who eat little or no meat have been reported to be more physically active than those who consume meat regularly (20), and menstrual cycle disturbances appear to be more prevalent among women who exercise (28). At first glance, these findings appear to provide additional evidence of a link between vegetarianism and menstrual disturbances. However, several prospective studies have shown that menstrual function does not change with exercise, provided that increases in activity are gradual and body weight is maintained (8, 29, 30). This suggests that adequate energy availability may be a key factor in maintaining normal hormonal function with exercise. Evidence in support of this hypothesis is provided by elegant studies of aerobic exercise and energy availability by Loucks et al (18, 31). Low energy availability, whether induced by a low-energy diet or by exercise, resulted in decreased LH pulse frequency during waking hours and increased LH pulse amplitude. When the energy cost of exercise was compensated for by increased food intake, however, exercise itself was not associated with changes in either LH pulse frequency or amplitude (31).

Obesity

Cycle disturbances are associated with obesity as well as with energy shortages. A high prevalence of obesity among amenorrheic women was reported many years ago (32), and anovulatory cycles appear to be more common in obese women (33). Weight loss in obese women results in improved ovulation (34, 35) and pregnancy (35) rates. It has been suggested that high androstenedione concentrations observed in obese women may activate the conversion of estradiol to estrone in adipose tissue (36). Estrone in turn may trigger higher LH concentrations, leading to ovarian hyperstimulation, thus increasing testosterone concentrations, resulting in anovulatory cycles (36). Because vegetarian women generally weigh less than nonvegetarian women (19–21), they would be expected to experience fewer cycle disturbances of this nature.

Psychosocial and cognitive factors

Psychosocial stressors, such as grief, travel, and moving away from home, are associated with menstrual cycle disturbances (17, 37). No studies investigating whether these events are more or less common in vegetarian women were found. One might speculate that young women who become vegetarian and face opposition from family and friends would experience increased stress, but there is no direct evidence to support this.

Cognitive factors may also be associated with the stability of the menstrual cycle. One such factor is cognitive dietary restraint, the perception that food intake is constantly being limited in an effort to control body weight (38). Menstrual differences between women with high and low restraint scores were detected in 3 studies (21, 39, 40). Schweiger et al (39) found that women with high restraint scores had significantly shorter cycle lengths, shorter luteal-phase lengths, and lower mean luteal-phase progesterone concentrations. In a group of women with a wide range of physical activity levels who were initially confirmed to ovulate normally, we found that the luteal-phase length was shorter, without alteration of cycle length, in women with high restraint scores (40). Furthermore, in our 6-mo study in vegetarian and nonvegetarian women (21), those with high restraint scores had fewer ovulatory cycles $(3.6 \pm 2.3 \text{ and } 5.0 \pm 1.4; P < 0.05)$ and shorter mean luteal-phase lengths (7.4 \pm 4.1 and 10.7 \pm 3.1 d; *P* < 0.05). In most cases, mean body mass index (BMI; in kg/m²) values did not differ (39, 40) or differed only slightly (21) between women with high and low restraint scores, suggesting that body weight per se did not explain the results. A mechanism to explain the association has not yet been established, but it is possible that stress associated with food intake in women with high restraint scores leads to increased secretion of corticotropin-releasing hormone and cortisol. Corticotropin-releasing hormone has been shown to inhibit gonadotropin secretion (41), and could thereby disturb menstrual function.

Dietary components

A comprehensive review of all previous research conducted on dietary components that may differ between vegetarians and nonvegetarians is beyond the scope of this article. However, considerable work has been done to explore the effects of fat and fiber (42-49), meat (50, 51), alcohol (52, 53), and other specific dietary components (54) on reproductive hormones, characteristics of the menstrual cycle, or both. Interpretation of the available data is difficult because some studies varied more than one aspect of the diet simultaneously (42, 43, 47, 49), and in studies that manipulated intakes of heterogeneous substances such as fiber, different results may have occurred depending on the source of the fiber (46). Taken together, however, the results suggest that concentrations of ovarian hormones or their metabolites may be lower at various points in the menstrual cycle in women consuming diets high in fiber, low in fat, or both (42-44, 46-49). This is consistent with cross-sectional studies reporting inverse associations between hormone concentrations and fiber intake, direct associations between hormone concentrations and fat intake (55, 56), and lower serum estrogen concentrations with faster intestinal transit (57). It also corroborates the lower estradiol and progesterone concentrations observed in women 2 y after being randomly assigned to a low-fat, high-carbohydrate diet for a study in breast cancer risk reduction (58). However, the data must be interpreted cautiously because many experimental studies were conducted over only 1 or 2 menstrual cycles (42, 43, 47-51), and other data (46) suggest that changes observed acutely may not persist over time. In addition, some subjects were free-living and others were housed in metabolic wards, which could affect the menstrual cycle differently. Finally, in many cases, menstrual cycle characteristics were not reported, and it cannot be discerned whether changes in hormone concentrations were of sufficient magnitude to lead to alterations in the cycle.

Some recent studies carefully controlled for many of the factors mentioned above. The available data, however, suggest that a simple answer may not be forthcoming regarding the effect on the menstrual cycle of components that may be present in vegetarian diets. For example, studies have been conducted to explore the effects of 2 classes of phytoestrogens, lignans and isoflavones. Phipps et al (59) studied the effects of flaxseed powder, which is high in lignan precursors, in 18 women with normal ovulatory cycles using a randomized, crossover design. Each woman followed her usual omnivorous, low-fiber diet for 3 cycles and then followed her usual diet supplemented with flaxseed powder for another 3 cycles. The last 2 cycles of each dietary period were compared. During flaxseed supplementation luteal-phase lengths were significantly longer and the ratio of progesterone to estradiol during the luteal phase was higher. Moreover, no anovulatory cycles occurred during flaxseed supplementation, but 3 anovulatory cycles occurred during the control diet period.

In contrast, Cassidy et al (60) studied the effects of isoflavones in 6 women with regular ovulatory cycles. They found that diets containing 60 g soy protein/d (with 45 mg isoflavones) significantly increased follicular-phase length compared with control diets. Subsequently, they showed that a soybean product from which the isoflavones had been extracted had no effect on the cycle (61). Thus, lignans and isoflavones, 2 different classes of phytochemicals, appeared to have different effects: flaxseed lignans increased luteal-phase length and did not affect follicular-phase length, whereas soybean isoflavones increased follicular-phase length but did not influence luteal-phase length.

That these substances were shown to have effects on the menstrual cycle when tested in isolation does not necessarily mean that they will cause net differences between the cycles of freeliving vegetarian and nonvegetarian women. For example, do intakes differ substantially between groups? And if so, how do these and other substances interact with one another? If a vegetarian had high intakes of both lignans and isoflavones, would the net effect be no apparent change in the cycle, or would both cycle phases be lengthened?

STUDIES OF MENSTRUAL CHARACTERISTICS OF VEGETARIANS AND NONVEGETARIANS

To address the questions raised in this article, free-living populations must be studied. Some of the earliest studies suggesting menstrual disturbances are more common in vegetarians than in nonvegetarians were done in athletes. In 1984, Brooks et al (2) reported on the diets of 11 amenorrheic and 15 regularly menstruating runners who had similar ages, training, and percentage body fat. Nine amenorrheic runners were vegetarians compared with only 2 regularly menstruating runners. In this study, however, vegetarian was defined by the authors as consuming <200 g meat/wk (red meat, poultry, or both). In the same year, Slavin et al (6) confirmed these findings. In a study of 173 premenopausal athletes, the prevalence of amenorrhea was 31% among the 45 vegetarians (defined as eating no red meat), 14% among the 44 women who described their diet as "high-carbohydrate, low-fat," and only 4% among the 84 who consumed a "balanced four food group" diet. These studies were important in stimulating research in this area, but their limitations must be recognized. Both relied on retrospective, self-reported data, and information on the duration of the vegetarian diet was not available.

Few studies have been conducted specifically to assess whether menstrual differences are associated with vegetarian diets. The first was that of Pedersen et al (5), in which 34 vegetarian and 41 nonvegetarian premenopausal women were recruited through newsletters and newspaper advertisements. Subjects completed 3-d food records and classified their cycles over the past year as regular (11-13 menses), irregular (3-10 menses), or amenorrheic (≤ 2 menses). A higher proportion of vegetarian than nonvegetarian women reported irregular or absent cycles (26.5% and 4.9%, respectively; P < 0.01). Unfortunately, several aspects of this study make generalization of the results questionable. It is possible that a recruitment bias existed: if the study was described as assessing whether menstrual disturbances were more common among vegetarians, it is possible that vegetarian women with irregular cycles would be more likely to volunteer. Although the 2 groups did not differ in BMI, nonvegetarians had used birth control pills longer than had vegetarians $(3.0 \pm 3.4 \text{ y and } 1.4 \pm 2.2 \text{ y},$ respectively; P < 0.05). Because current use of birth control pills was not listed as an exclusion criterion, it is possible that more nonvegetarians were also currently using birth control pills. If so, this could have contributed to the observation that fewer nonvegetarians reported irregular cycles. A subsequent study by this group excluded women who had used oral contraceptives in the past 3 mo but still used retrospective, self-reported data to classify menstrual status (4). Irregular or absent cycles were reported by 4 of 27 vegetarians and none of the nonvegetarians.

When designing our study (21), we sought to avoid potential confounders. The inclusion criteria included 1) stable weight with BMI values of 18-25 (to avoid effects of weight loss and underweight), 2) age between 20 and 40 y (to avoid cycle disturbances that are more common after menarche or preceding menopause), 3) no use of oral contraceptive agents for ≥ 6 mo (to avoid the appearance of regular cycles while using these agents), 4) nulliparity (because the menstrual cycle may be more stable after childbirth), 5) exercising ≤ 7 h/wk and not a "compulsive" exerciser, 6) drinking <1 alcoholic beverage/d, and 7) cycles of normal length (to avoid the potential for a recruitment bias). Finally, to avoid possible effects of acute dietary changes, vegetarian subjects must have avoided meat, fish, and poultry for ≥ 2 y. Nonvegetarians included red meat in their diets ≥3 times/wk in addition to poultry fish. Quantitative analysis of daily BBT records kept prospectively for 6 menstrual cycles was used to classify cycles as normally ovulatory, of short luteal-phase length (<10 d), or anovulatory.

Vegetarian and nonvegetarian women were similar in age and age at menarche, but vegetarians had a lower mean BMI $(21.1 \pm 2.3 \text{ and } 22.7 \pm 1.9; P < 0.05)$. Mean cycle lengths were similar but analysis of BBT records indicated that the vegetarian women had longer luteal-phase lengths than did the nonvegetarian women (11.2 \pm 2.6 and 9.1 \pm 3.8 d; P < 0.05) and experienced fewer anovulatory cycles (4.6% and 15.1% of cycles; P < 0.01). Thus, in this highly selected sample, menstrual disturbances were less common in vegetarians. Dietary differences between groups did not appear to explain this finding. There was no significant difference in fat intake, and although fiber intake was higher in the vegetarians, this difference was confined to vegans: fiber intakes of lactoovovegetarians and nonvegetarians were similar (24). Data on intakes of substances such as lignans and isoflavones were not available, but the vegetarian women studied were not frequent users of flaxseed or soy products. Although effects of unmeasured dietary differences cannot be excluded, the finding that cognitive dietary restraint levels were significantly lower among the vegetarian women we studied may have contributed to our findings.

Although these results suggest that vegetarianism per se is not associated with increased menstrual cycle disturbances, they cannot be generalized to the entire population of women who identify themselves as vegetarian. Instead, they are limited to long-term, weight-stable vegetarians with normal BMIs. We do not know to what extent these women reflect free-living vegetarian women, nor for that matter do we know to what extent the nonvegetarian women who were studied reflect free-living nonvegetarians.

SUMMARY

It appears that there is no single answer to the question posed in the title, "Vegetarianism and menstrual cycle disturbances: is there an association?" Several general mechanisms have been identified that have the potential to affect the menstrual cycle, which may differ between vegetarians and nonvegetarians. For any individual woman, vegetarian or not, one or more of these mechanisms may influence the characteristics of her menstrual cycle, and it is their net interaction that is important ultimately. Although healthy, weight-stable, vegetarian women consuming self-selected diets did not experience more menstrual disturbances than did healthy, weight-stable nonvegetarians, population studies are needed to address the question at the broadest level.

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