**Short Report**

Menstruation Does Not Cause Anemia: Endometrial Thickness Correlates Positively with Erythrocyte Count and Hemoglobin Concentration in Premenopausal Women

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**ABSTRACT**

Menstruation has often been cited as a risk factor for iron-deficiency anemia. This study tested whether normal, premenopausal women’s luteal endometrial thickness (ET) was associated with their red blood cell count (RBC) and hemoglobin concentrations (Hg), and therefore whether a high ET put women at risk for anemia. Endometrial thickness can be considered a reasonable proxy for menstrual blood loss in normal women. Twenty-six healthy women from the Mogielica Human Ecology Study Site in Poland, aged 20–40 years (29 ± 5.3 years, mean ± SD), were selected. Subjects’ ET was measured by transvaginal ultrasound in the luteal phase of the menstrual cycle, and their red blood cell count and hemoglobin concentrations were measured by fasting morning blood samples. Controlling for day of ET measurement, RBC and Hg were positively correlated with ET ($r^2 = 0.24, P = 0.05; r^2 = 0.25, P = 0.04$, respectively). We propose that, contrary to popular understanding, a thicker endometrium suggests greater iron reserves, rather than greater risk for anemia, in healthy women. Am. J. Hum. Biol. 18:710–713, 2006.

**Iron-deficiency anemia occurs when iron stores are low, which leads to a low red blood cell count (RBC), and adequate oxygen cannot be provided to the body’s tissues. Iron is a component of hemoglobin, the oxygen-carrying pigment in the blood. Iron can be obtained from the diet and from recycling old red blood cells. Reported risk factors for iron-deficiency anemia in women include: when menstrual blood loss exceeds 80 ml a month (Janssen et al., 1998), a long duration of menstruation, and self-reported very heavy bleeding (Milman et al., 1998).

Despite the fact that only pathological, excessive menstruation has been empirically shown to increase risk, the idea that normal menstruation is itself a risk factor for iron-deficiency anemia persists: premenopausal, menstruating women are considered at high risk for developing iron-deficiency anemia by a variety of medical, scientific, and popular sources (i.e., Beard, 2000; Coutinho, 1999; Milman et al., 1998). However, a study directly comparing menstrual blood loss and iron-deficiency anemia has not been performed. Transvaginal ultrasound is a safe, minimally invasive method for measuring endometrial thickness (ET), which is far less time-consuming and uncomfortable compared to the alkalin hematine method for estimating blood loss from used sanitary napkin collection (Hallberg and Nilsson, 1964). We propose that ET measurement provides a valid proxy for nonpathological menstrual blood loss (Clancy, 2005). The intent of this study was to test the relationship between red blood cell counts and hemoglobin (Hg) concentrations of healthy women, and their luteal ETs, in order to assess their risk for iron-deficiency anemia. In contrast to the medical literature, we hypothesize that greater concentrations of iron suggest

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greater energy availability, and should be related to a thicker endometrium. Within the normal range, greater menstrual blood loss therefore indicates a reduced risk of iron-deficiency anemia.

METHODS

Subjects

Subjects were healthy premenopausal women \( (n = 26) \) living in the Mogielica Human Ecology Study Site in Poland (Jasienska and Ellison, 2004), between ages 20–40 \((29 \pm 5.3\) years, mean \( \pm \) SD). Women were screened for any major health problems, and particularly reproductive or endocrine disorders. Subjects were not currently using hormonal contraceptives, had not been pregnant or breastfeeding for at least 6 months, and were nonsmokers. Women had an average of \( 13.7 \pm 3.3 \) years of education, mean \( \pm \) SD, and 19 of them had jobs outside the home \((73\%\)). Their mean menarcheal age was \( 14.3 \pm 1.2 \) years, mean \( \pm \) SD, and 19 subjects had children \((73\%\); \( 1.7 \pm 1.3 \) children, mean \( \pm \) SD on average). No subjects were vegetarians. Subjects were recruited over the summer of 2005 through word of mouth and home visits, as well as through the approval and help of the local doctor and priest. Subjects were monetarily compensated, and were provided with copies of their ultrasound and blood-analysis results for their own records. This article combines data on the same subjects in the same menstrual cycle from two different studies: the Yale University Human Subjects Committee approved the protocols in the endometrial function investigation, and the Jagiellonian Ethics Committee approved protocols in the blood-analysis investigation (part of a greater study on ovarian function in the Mogielica Human Ecology Study Site in Poland).

Protocol

Subjects had one fasting morning blood sample drawn by a nurse at Limanowa Hospital \((\text{Limanowa, Poland})\). All blood samples were analyzed at the Limanowa Hospital Laboratory.

Between days 16–24 (average, \( 19.2 \pm 1.95 \) days, mean \( \pm \) SD) of their cycle, subjects underwent a transvaginal ultrasound by a gynecologist trained in ultrasonography. The first four subjects had their ultrasounds performed at Limanowa Hospital, and the other 22 at a private practice in Limanowa. All ultrasounds except one were performed by the same doctor. The sonographer calculated the endometrial double-thickness measurement on the midsagittal plane, using standard clinical methods. The cycle day (number of days before next menses) on which the ultrasound was performed significantly correlated with ET \((r = 0.39, P = 0.05)\). Consequently, this factor was used in statistical analyses to control for the relationship between cycle day and ET.

Subjects completed seven 24-hr recall dietary questionnaires over the course of one menstrual cycle. Questionnaire results were calculated using Diet 2 software (National Food and Nutrition Institute, Warsaw, Poland).

Statistical analysis

Multiple regression analyses were used to test for a relationship between ET and RBC, and ET and Hg, while controlling for the ET measurement date. This analysis was done with ET as the dependent variable, and also repeated as a simple correlation without controlling for measurement date. The StatView analysis package for PCs was used to perform all analyses. Values are expressed as mean \( \pm \) standard deviation. \( P \leq 0.05 \) was used to indicate statistical significance.

RESULTS

In multiple regressions with ET as dependent variable, ET and RBC \((r^2 = 0.24, P = 0.05)\), and ET and Hg concentrations \((r^2 = 0.25, P = 0.04)\), positively correlated. Neither RBC nor Hg correlated with age, age at menarche, years since menarche, or number of children, though a negative, statistically nonsignificant trend was seen for age and years since menarche (Table 1). However, age and endometrial thickness positively correlated when controlling for ultrasound date \((r^2 = 0.24, P = 0.04)\).

All subjects’ RBCs were within US parameters for healthy range (normal range, \( 3.8–5.5 \times 10^{6}/\mu\text{l} \); subjects’ range, \( 3.61–5.27 \times 10^{6}/\mu\text{l} \)). Subjects’ Hg concentrations were within US parameters for healthy range, except for one value above and one below (normal range, \( 12.0–15.2 \text{ g/dl} \); subjects’ range, \( 11.1–15.5 \text{ gm/dl} \)). Simple regressions between age and RBC \((P = 0.13, r = -0.31)\), and age and Hg \((P = 0.11, r = -0.33)\), suggested a negative relationship, but the relationships are not statistically significant.

DISCUSSION

From a life-history perspective, the ability of the body to transport oxygen via Hg-rich
red blood cells is a survival process that has a higher priority than reproductive function. When resources are limited and a female is not pregnant or breastfeeding, endometrial function, and therefore ET, is dependent on what energy is left over after the demands of survival. It is from this thought (that factors like oxygen transport affect reproductive factors, including ET) that we challenge the directionality of the pervasive notion that menstruation significantly affects iron stores, and is itself a risk factor for anemia. Further, if normal menstruation were a risk, one would expect an inverse correlation between ET and either RBC or Hg.

We showed that increased red blood cell and Hg reserves significantly positively correlate with increased ET (and therefore, presumably, menstrual blood loss). Endometrial thickness can be understood as a proxy for endometrial function (Clancy, 2005). Reproductive function was shown to positively correlate with increased energy availability, in the forms of nutritional status, workload, energy distribution, balance, and flux (reviewed in Ellison, 2001). This was further corroborated in work on women who came from the same rural Polish population as our subjects (Jasienska and Ellison, 1998, 2004). Menorrhagia, defined as menstrual blood loss exceeding 80 ml a month and a risk factor for iron-deficiency anemia, may be caused by factors other than a thick endometrium, such as low uterine arterial flow impedance (Hurskainen et al., 1999). Menorrhagia was shown to correlate with low iron stores (Hallberg and Rossander-Hulten, 1991; Janssen et al., 1998; Larsson et al., 1992).

Other work suggested that nongynecological factors for iron-deficiency anemia are found “even when careful evaluation by a specialist in gynecology suggests a gynecological source” (Kepczyk et al., 1999). Several studies focused on nongynecological factors for iron deficiency in premenopausal women, especially upper gastrointestinal bleeding, which can be caused by long-term aspirin use or ulcers (Annibale et al., 2003; Bini et al., 1998; Kepczyk et al., 1999). Finally, Bergstrom et al. (1995) reported that the sex difference in iron status is due to a significant increase in male adolescent iron stores, not a decrease in female iron stores. As increased testosterone levels directly increase Hg concentrations, it appears that the testosterone-induced Hg concentration increase in pubertal males explains the sex difference better than the onset of menarche in females.

These results indicate that the case is not closed on whether menstruation is inherently a risk factor for iron-deficiency anemia. Future work will examine iron-deficiency in a wider context, and other proxies of menstrual blood loss.

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LITERATURE CITED


