Dysfunctional Uterine Bleeding and Prior Life Stress

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Dysfunctional uterine bleeding (DUB) that occurs between menarche and menopause is often described but poorly understood. Relatively few studies have tried to associate DUB with life change and stress. In this present case-control study, questionnaires measuring life change events and self-scored life stress were administered to 26 patients with DUB and 31 controls. The participants were matched for age, gravidity, and contraceptive use. The participants were all aged between 18 and 35 years, and none were perimenopausal.

A statistically significant relationship was found between DUB and recent prior life changes and experienced stress from those changes. In particular, personal-social and health stresses showed the widest differences between the patients with DUB and controls. These findings persisted when statistical corrections were made for use of various contraception devices. This study may help to focus on a more specific cause of DUB. In addition, it may assist the family physician in diagnosing and treating this condition.

Dysfunctional uterine bleeding (DUB) with its various synonyms (eg, functional uterine bleeding) is an often seen but poorly understood entity. It is usually defined as abnormal menstrual bleeding in which organic lesions cannot be detected by ordinary means.[1,2] Examples of DUB include problems of menstrual irregularity and bleeding difficulties (ranging from menorrhagia to secondary amenorrhea) in the absence of organic disease or pregnancy. DUB is commonly seen during the extremes of the fertile period—menarche and menopause. At these times it is often easily explained in terms of hormonal disequilibrium. The cause of DUB between those extremes, however, is usually not known.

The case has been made for a psychoemotional cause of DUB. Secondary amenorrhea has been found to be related to the stress of being an inmate during war[3,4] and to stresses such as entering college or awaiting execution.[5-7] Other researchers found secondary amenorrhea and dysmenorrhea more common in certain psychiatric patients.[8-11] More recent stress-related research has used the social readjustment scale[12] to relate life changes to illness[13,14] as well as the Schedule of Recent Experiences,[15] which uses self-scored stress value estimates for experienced life changes. Using these new stress questionnaires, some researchers have found relationships between stress scores or life changes and dysmenorrhea.[16,17]

Table 1. Number, Age, Gravidity, and Contraception Uses of Participants

| | Total Number | Mean Age (yr) | Gravidity (Mean) | Contraception Use | | |
				Oral Contraceptives	IUD	Other/None
Study group	26	25.1	(0.5)	6	4	16
Control group	31	25.4	(0.5)	10	1	20

$\chi^2 = 2.83$, 2 *df*, P = .24

Little, if any, research has taken a comprehensive look at DUB, examining its relationship to prior life changes and stress. Pepitone-Arreola-Rockwell et al[18] carefully defined DUB as six possible symptom or sign complexes of irregularity or secondary amenorrhea and tried to relate it to job stress only, but they failed to find a significant relationship.

Siegel et al[17] looked at the relationship between the accumulation of life changes (especially "negative" ones) and menstrual irregularity. No significant relationship was found. These studies and others[6,10,11,17,18] used retrospective records of self-recording to determine the diagnosis of DUB. In addition, several critics[19-21] have reported that very few studies in this area have had good objective diagnostic criteria for DUB. The research in this area has also been criticized for having poor or no controls.[19] It has also been suggested that self-scoring of stress by the participant instead of the total count of life change events might more accurately take into account other important mediating variables, such as support systems, dimensions of various life events, and coping mechanisms of the participants.

There are several studies linking some forms of dysfunctional uterine bleeding to extreme examples of stress. In addition, an inorganic menstrual symptom such as dysmenorrhea has been shown to be related to life changes and life stress. Based on these studies it seems reasonable to assume that there is a relationship between stress and DUB. Anecdotal evidence from the investigator's clinical practice also supports this hypothesis.

However, there are no well-controlled studies of this hypothesis. The present study examines the relationship between carefully defined DUB (diagnosed prospectively) and recent life changes and self-scored stress scores of those changes that are experienced.

Methods

The study was done at the Family Practice Unit of Memorial University in St. John's, Newfoundland, Canada. The unit comprises 7 faculty and 3 to 4 residents at any one time. Approximately 22,000 patients are seen per year.

The participants were all those women aged 18 to 35 years who were attended by three of the faculty physicians at the Family Practice Unit and who came in for a regular checkup or suffered from dysfunctional uterine bleeding. The patients were asked to participate in a study looking at life changes. They were told that many of the women in the clinic were being included in this study.

The study (experimental) group consisted of those 26 participants newly diagnosed as suffering from dysfunctional uterine bleeding as defined below. The control group consisted of 31 participants seen consecutively by the same three physicians during the same time period for regular checkups and diagnosed as being well with no menstrual problems. The two groups were statistically matched for age, gravidity, and contraceptive use; no significant differences were found for these three indices (Table 1).

A version of the Recent Life Changes Questionnaire, tested many times for validity and reliability by others,[15] was used. The questionnaire yielded a count of all experienced life changes for the previous year. In addition, subjective self-scores of stress for each life change experienced by the participant were calculated (stress score of 1 to 100 for each life change). Self-scored stress scores were calculated for the same 12-month period.

The procedure was a case-control format. During an office visit with a potential participant (study or control), the attending physician noted the woman's birthdate, physician, chart number, presence and duration of DUB, gravidity (number of pregnancies), uses of specific contraception methods, and a detailed history (on a checklist) of the form(s) of DUB detected. The list of symptoms and reported signs was derived from Kistner[1] and included all forms of irregularity or secondary amenorrhea collectively known as dysfunctional uterine bleeding.

All charts were examined three months after study entry to determine whether the diagnosis of DUB could still be made in retrospect. Three study participants were dropped from the study because an organic etiology for their DUB was subsequently detected. The study was terminated when an acceptable number of study subjects was reached. The minimum number of subjects in each group was judged to be 25 to 30 to obtain a 95 percent confidence level in the statistical analyses (*t* test).

Results

There were 26 study participants with dysfunctional uterine bleeding and 31 controls. Results of *t* tests indicated there were no significant differences between the two groups in age, gravidity, or contraceptive use (Table 1).

The number of life changes (life change events) was determined for the 12-month period prior to study entry (Table 2). The range was 3 to 34 life change events for the study group and 0 to 14 for the control group. Results of the *t* test indicated that the differences between the two groups were highly significant (P < .001).

The total stress scores for all experienced life change events were determined for the same

Table 2. Comparison of Life Change Events and Life Stress Scores (on a scale of 1 to 100) Between Groups (*t* test)				
	Life Change Events (all subjects)		Life Stress Score (all subjects)	
	Mean	SD	Mean	SD
Study group	18.4	6.7	87.4	57.5
Control group	11.6	6.1	42.1	26.5
	t = 4.02, 55 *df*, P < .001		*t* = 3.92, 55 *df*, P < .001	

12-month period (Table 2). The range was 205 to 2,800 for the study group and 3 to 1,179 for the control group. Results of the *t* test indicated that these differences were also significant (P < .001) between the groups.

The use of various contraceptives was not statistically significantly different between the groups (Table 1), but there were more oral contraceptive users in the control group and more intrauterine device (IUD) users in the study group. For this reason *t* tests were repeated three ways for life change events and stress scores: (1) dropping all IUD users from the analysis, (2) dropping all oral contraceptive users, and (3) dropping all IUD and oral contraceptive users. For each of these tests there were still significant differences between the two groups for the life change events and self-scored stress scores. P values for these six analyses were all less than or equal to .001. None of the participants was taking estrogens or other replacement hormones for menopausal symptoms.

The Recent Life Changes Questionnaire is subdivided into five areas of life change: changes in health, job, family, personal-social, and financial areas of life. For each of the five areas *t* tests were used to examine life change events and stress scores (Table 3). For self-scored stress scores there were significant differences between groups for all areas of life stress excluding the job area. For the life change events there were significant differences between the groups only for the health and personal-social areas. Stress and life change

Table 3. Comparison of the Types of Life Change Events and of the Types of Life Stress Scores

	Life Events		Stress Scores	
	Study Group (Mean Number)	Control Group (Mean Number)	Study Group (Mean Number)	Control Group (Mean Number)
Health	2.7	1.2*	120	36*
Job	2.5	2.7 (NS)	147	101 (NS)
Family	3.6	2.4 (NS)	185	89**
Personal-Social	7.4	4.2*	355	163*
Finance	1.6	1.2 (NS)	73	36**

*P < .001
**P < .05
NS = Not significant

events in the health and personal-social areas seem to be the most sensitive predictors of DUB.

Discussion

The study group with dysfunctional uterine bleeding documented significantly more life change events in the year prior to study entry than did the control group of healthy women. In addition, the study group documented that the life changes gave them more stress in that year than did the control group. All these relationships among life change, stress, and DUB were independent of contraceptive use, which may suggest another reason why some women have menstrual difficulties with either IUDs or oral contraceptives. DUB symptoms may sometimes be attributed to the life changes and stress experienced by the contraceptive user rather than to the contraceptive.

The health and personal-social types of life changes and stress scores seem to be the best predictors of dysfunctional uterine bleeding. The health differences may, however, just reflect the health stress of having DUB itself. A future prospective cohort study could examine this variable.

A potential explanation for this study's findings is that stress and significant emotional change can influence hypothalamic control in the brain by means of the cerebral cortex and limbic system.[22] Mild dysfunctions in the hypothalamic-pituitary-ovarian axis can affect production levels of estrogen, which in turn can affect release of luteinizing hormone or follicle-stimulating hormone. Significant alterations in the levels of these two hormones can affect the menstrual cycle, often causing anovulatory cycles, which are one of the most common physiological events underlying dysfunctional uterine bleeding.

Stress from health problems may have shown up as a good predictor of DUB because many illnesses and medications used to treat those illnesses can affect the hypothalamic-pituitary-ovarian axis. A more detailed collection of data on the participants' health history would have to be done to clarify whether the illnesses or the stress from these illnesses were the crucial variables involved. Personal-social types of stress were also shown to be good predictors of DUB. A possible explanation is that this particular group of stresses (changes and stresses of social activities, friendships, accidents, major personal decisions, and education) may affect a woman (and her endocrine system) more directly because personal-social life changes usually provide the most intimate stresses of life.

Research that attempts to find relationships between stress and disease is open to problems of validity and bias. The problem of internal validity

to address in this study is whether the differences found between the two groups of participants are due only to the presence or absence of DUB and not to some other confounding variable(s). The participants in this study were self-selected and did not necessarily represent a random sample. In particular, the control group comprised women who decided to see their physician for a checkup. Such women may come from less stressful backgrounds and perhaps DUB illness in itself may account for much of the perceived stress documented in this study. In addition, there may be a recall bias because the participants were asked to recall events that occurred up to 12 months prior to study entry. Self-selection bias and recall bias could be minimized by repeating the study as a long-term prospective cohort study of asymptomatic women using daily log diaries of stressful events and menstrual difficulties. Such a study would be able to examine whether stress preceded the onset of DUB.

The problem of external validity to address in this study is whether the findings can be expanded to the general population. This study did not examine certain demographic data of the population such as socioeconomic status. A future study as described above would have to include such data.

Another potential bias is the ascertainment bias of whether a participant has a valid diagnosis of DUB. One way to minimize this bias would be to consult a "blind" gynecologist for a diagnosis on all participants. Unfortunately DUB is a diagnosis of exclusion of other organic disease, and no standard investigations are available to validate the diagnosis of DUB.

The personal-social and health stress elements of the questionnaire were so critical in this study that they should be looked at more closely in a future cohort study to discover the best predictors of DUB so that ways of preventing this problem may become available.

Conclusions

A statistically significant relationship was found between dysfunctional uterine bleeding and recent prior life changes and experienced stress from those changes. In particular, personal-social and health stresses showed the widest differences between the DUB sufferers and controls. These find-

ings were independent of contraception use, even though there were more IUD users among the DUB sufferers and more oral contraceptive users among the controls. This study may thus help focus on a more specific cause of DUB.

References

1. Kistner RW: Gynecology Principles and Practice. Chicago, Year Book, 1971
2. Chamberlain G: Dysfunctional uterine bleeding. Clin Obstet Gynecol 8:93, 1981
3. Whitacre F, Barrera B: War amenorrhea. JAMA 124:399, 1944
4. Sydenham A: Amenorrhea at Stanley Camp, Hong Kong, during internment. Br Med J 2:159, 1946
5. Drew FL: The epidemiology of secondary amenorrhea. J Chronic Dis 14:396, 1961
6. Osofsky HF, Fisher S: Psychological correlates of the development of amenorrhea in a stress situation. Psychosom Med 29:15, 1967
7. Singh K: Menstrual disorders in college students. Am J Obstet Gynecol 140:299, 1981
8. Kelly K, Daniels GE, Poe J, et al: Psychological correlations with secondary amenorrhea. Psychosom Med 16:129, 1954
9. Gregory B: The menstrual cycle and its disorders in psychiatric patients. J Psychosom Res 2:199, 1957
10. Diamond SB, Rubinstein AA, Dunner DL, Fiere RR: Menstrual problems in women with primary affective illness. Compr Psychiatry 17:541, 1976
11. Coppen A: The prevalence of menstrual disorders in psychiatric patients. Br J Psychiatry 3:155, 1965
12. Holmes TH, Rahe RH: The social readjustment rating scale. J Psychosom Res 11:213, 1967
13. Theorell T, Rahe RH: Psychosocial factors and sudden cardiac death: A pilot study. J Psychosom Res 15:19, 1971
14. Perlman LV, Ferguson S, Bergum K, et al: Precipitation of congestive heart failure: Social and emotional factors. Ann Intern Med 75:1, 1975
15. Rahe CDR: Epidemiological studies of life change and illness. Int J Psychiatry Med 6:133, 1975
16. Wentz AC: Abnormal uterine bleeding. Primary Care 3:9, 1976
17. Siegel JM, Johnson JH, Sarason IG: Life changes and menstrual discomfort. J Human Stress 5:41, 1979
18. Pepitone-Arreola-Rockwell F, Sommer B, Sassenrath EN, et al: Job stress and health in working women. J Human Stress 7:19, 1981
19. Minter RE, Kemball CP: Life events and illness onset: A review. Psychosomatics 19:334, 1978
20. Rabkin JG, Struening EL: Life events, stress, and illness. Science 194:1013, 1976
21. Gannon L: Evidence for a psychological etiology of menstrual disorders: A critical review. Psychol Rep 48:287, 1981
22. Check JH: Emotional aspects of menstrual dysfunction. Psychosomatics 19:178, 1978

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