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The relationship between stress levels and menstrual cycle regularity in students of the faculty of medicine, universitas kristen Indonesia, class of 2017

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Abstract
The menstrual cycle is the distance between the first day of menstruation and the next menstruation. One of the factors that influence the menstrual cycle is stress. Stress stimulates the hypothalamus-pituitary-adrenal cortex axis to produce cortisol hormone. Cortisol hormone causes hormonal imbalance, including the reproductive hormones that affect the menstrual cycle. This study aimed to determine the relationship between stress levels and regularity of the menstrual cycle in female students of the Faculty of Medicine, Universitas Kristen Indonesia class of 2017. It was conducted in November 2018. It was an analytic survey that used a cross-sectional design. The sampling technique used purposive sampling to get 52 respondents following the specified criteria. The technique of collecting data used questionnaires MSSQ to measure the level of stress and questionnaires to determine the menstrual cycle. The analysis of data used the Chi-square test with a significance level of 0.05. The results showed that 35 to 52 respondents who experienced mild, moderate, and severe stress have a regular menstrual cycle (67.3%). The results of the analysis data obtained a p-value of 0.006, which indicated that there is a significant relationship between the stress level with the regular menstrual cycle in the female students of the Faculty of Medicine, Universitas Kristen Indonesia class of 2017.

Keywords: stress level, menstrual cycle, stressor

Introduction
Stress is a universal phenomenon in everyday life and cannot be avoided and experienced by everyone. Stress is a term to indicate pressure or demand experienced by an individual to adapt or adjust. Adjustment is needed in undergoing life transitions, one of which is the transition in the campus environment. Stress has a broad impact on a person's life because stress can affect the endocrine system, immune system, and menstrual cycle [1].
Students in their activities can not be separated from stress. Stressors or causes of stress in students can come from their academic life, especially from external demands and expectations [2]. External demands can be sourced from coursework, study load, parental demands to succeed in college and social adjustment in the campus environment. This demand also includes the competence of lectures and the increasing complexity of increasingly difficult lecture materials. The demands of student expectations can be sourced from the ability of students to take lessons. On the other hand, academic factors also contribute to stress, for example, changes in learning styles from secondary school to higher education, lecture assignments, target achievement scores, and other academic problems.
Stress stimulates the HPA (hypothalamus-pituitary-adrenal cortex) axis, resulting in the production of the hormone cortisol, causing hormonal imbalances, including reproductive hormones and an irregular menstrual cycle [3]. According to data from Basic Health Research (Riskesdas) in 2010, women in Indonesia who experience irregular menstrual problems at the age of 17-29 years and 30-34 years are quite a lot, namely 16.4%. As for women who said they had irregular menstrual cycles due to stress and many thoughts, 5.1% [4]. Based on the description that has been described above, the authors are interested in researching "The Relationship between Stress Levels and Menstrual Cycle Regularity in Students of the Faculty of Medicine, Universitas Kristen Indonesia Class of 2017".
Based on the background stated above, the problem in this study can be formulated as follows: "Is there a relationship between stress levels and the regularity of the menstrual cycle in students of the Faculty of Medicine, Universitas Kristen Indonesia, class of 2017?" to know whether or not there is a relationship between stress levels and the regularity of the menstrual cycle in students of the Faculty of Medicine, Universitas Kristen Indonesia, class of 2017.

Literature Review
Stress is a physiological, psychological and behavioural response of humans trying to adapt and regulate both internal and external stress [5]. There is no clear definition for stress because each individual will react differently to the same stress. Stress is an unpleasant feeling and is interpreted differently from one individual to another. So, it can be concluded that stress is an individual response, either in the form of physical or psychological response, to the demands or threats faced throughout his life, which can cause changes in the individual, both physical, psychological and spiritual changes [6]. Stress is divided into two types, namely, eustress and distress. Eustress results from a response to stress that is healthy, positive and constructive (constructive). On the other hand, distress results from a response to unhealthy, negative, and destructive stress. Distress is any form of stress that exceeds the ability to cope, burdens the body, and causes physical or psychological problems.
Acute stress is a reaction to an immediate threat, commonly

known as the fight or flight response. Acute stress causes include noise, crowds, isolation, infection, and the image of a threat or memory of a dangerous (horrific) event [7]. Chronic Stress - Common causes of chronic stress include: persistently high-pressure work, long-term problems, loneliness, and constant financial worries.

Symptoms that indicate stress are: Physical symptoms in the form of fatigue, insomnia, headaches, muscle stiffness and tension, especially in the neck or nape, shoulders and lower back, palpitations, chest pain, shortness of breath, shaking, hands and feet feel cold, face feels hot, sweats cold and menstruation is disturbed. Mental symptoms are in the form of reduced concentration and memory, indecision, confusion and loss of sense of humour. Emotional symptoms can include anxiety, depression, hopelessness, irritability, fear, frustration, sudden crying, feeling helpless, withdrawal from society, and avoiding previously enjoyed activities [8]. Behavioural symptoms can include restlessness, nail-biting, changes in eating patterns, screaming, swearing, even throwing things or hitting.

Stress levels are divided into three categories: a) Normal Stress - Normal stress is faced regularly and naturally. As in situations: fatigue after doing the task, fear of not passing the exam; b) Light Stress - Light stress is a stressor regularly faced that can last a few minutes or hours. This stressor can cause symptoms, including frequent dry lips, difficulty breathing (often gasping for air), feeling weak, sweating excessively when the temperature is not hot and not after activity, fear for no apparent reason, tremors in the hands and feeling very relieved when the situation ends; c) Moderate Stress - Moderate stress occurs longer than light stress and light stress. The duration ranges from a matter of hours to several days, for example, disputes with friends. This stressor causes symptoms such as irritability, difficulty resting due to anxiety, facing disturbances in what is being done, irritability, restlessness; d) Severe Stress - Severe stress is a chronic situation that occurs within a few weeks years. Symptoms that are usually experienced are unable to feel positive feelings, feel no longer being strong enough to do an activity, feel there is nothing to look forward to in the future, sad and depressed, hopeless, lose interest in everything, feel worthless as a human being. Thinking that life is useless [8], and e) Very Severe Stress - Very severe stress has a higher level than severe stress. The time of occurrence is from several months to an indefinite time limit. A person with very severe stress has no motivation to live and tends to give up. Usually, a person with this level of stress is identified as having major depression [9].

The cause of stress or stressor is any situation or event that causes changes in a person's life (which disrupts balance or homeostasis), so that person must make adaptations or adjustments to overcome them. Stressors are classified into two, namely internal stressors and external stressors. Internal stressors cause stress that comes from within the individual, and external stressors are the causes of stress outside the individual [10]. Stressors are divided into three: a) Physical stressors are stressors or sources of stress from a person's physical. As in the example of a state of infection or pain felt by the body; b) Psychological stressor, which means the source of stress comes from a person's psychological state. For example, fear, worry, anxiety, anger, loneliness, and others; c) Socio-cultural stressors, meaning that stressors come from the culture or culture that is the background of a person's life. For example, divorce, disputes, unemployment and others [11].

Physical or emotional stress activates the amygdala, part of the limbic system associated with the brain's emotional component. Emotional responses that arise are restrained by input from higher centres in the forebrain. Neurological responses from the amygdala are transmitted and stimulate hormonal responses from the hypothalamus. The hypothalamus will release the hormone CRF (corticotropic releasing factor), which stimulates the pituitary to release another hormone, namely ACTH (adrenocorticotropic hormone), into the blood. ACTH instead stimulates the adrenal glands to produce cortisol [12].

Simultaneously, the hypothalamus acts directly on the autonomic system to stimulate an immediate stress response. The autonomic system itself is needed in maintaining the balance of the body. The autonomic system is divided into two, namely the sympathetic and parasympathetic systems. The sympathetic system is responsible for the presence of stimulation or stress. Reactions arise in the form of increased heart rate, rapid breathing, decreased gastrointestinal activity. While the parasympathetic system makes the body return to a resting state by decreasing heart rate, slowing breathing, increasing gastrointestinal activity.

In assessing stress, the Medical Student Stressor Questionnaire (MSSQ) instrument can be used. This questionnaire consists of 40 questions that cause stress to medical students, divided into two parts, namely part A, which consists of items 1-20 and part B, which consists of items 21-40. MSSQ is measured using a scale of 1 to 4 (1 equals to causes light stress, 2 equals to causes moderate stress, 3 equals to causes severe stress, and 4 equals to causes very severe stress) [13].

The MSSQ consists of six dimensions based on the causes of stress in medical students [14], namely Academic Related Stressors (ARS), Intrapersonal and Interpersonal Related Stressors (IRS), Teaching and Learning Related Stressors (TLRs), Social Related Stressors (SRS), Drive and Desire Related Stressors. (DRS), and Group Activities Related Stressors (GARS). The stress level score will be obtained by adding the total score in parts A and B then dividing by the number of questions per stress dimension. Calculation of stress, in general, can be done by adding up the total value of parts A and B from each dimension and divided by a total of 40 question items. Furthermore, the score results from the stress assessment that have been known are interpreted according to the results below [15].

0 – 1 = light stress
1,01- 2 = moderate stress
2,01- 3 = Severe stress
3,01- 4 = very severe stress

Menstruation is periodic and cyclic bleeding from the uterus accompanied by desquamation of the endometrium [10]. Menstruation is periodic bleeding from the uterus that begins about 14 days after ovulation periodically due to the shedding of the uterine endometrial lining [12]. The menstrual cycle is from the first day of menstruation until the arrival of the next menstrual period. The occurrence of a regular menstrual cycle is a sign that a woman's reproductive organs are functioning correctly [16].

The menstrual cycle in normal women ranges from 21-35 days with an average cycle duration of 28 days [1]. Each month menstruation lasts about 3-7 days. After the fifth day of the menstrual cycle, the endometrium begins to grow and

thicken in preparation for a possible pregnancy. The endometrium sloughs off if fertilization does not occur, and the next cycle occurs.

During the menstrual phase, the superficial and middle endometrial layers are shed, but the deep basal layer of the endometrium is preserved. On average, this phase lasts for five days (range 3-7 days). At the beginning of the menstrual phase, the estrogen levels, progesterone, LH (Luteinizing Hormone) decrease or at their lowest levels, while the cycle and levels of FSH (Follicle Stimulating Hormone) are just beginning to increase.

Proliferative Phase - In the proliferative phase, the repair process occurs after the endometrium sheds during menstruation. The proliferative phase is rapid growth that lasts from day 5 to day 14 of the menstrual cycle. The endometrial surface ultimately returns to normal about four days or before the bleeding stops. In this phase, the endometrium grows to a thickness of ± 3.5 mm, which will end at ovulation. In the proliferative phase, there is an increase in the hormone estrogen level [17].

Recreational or Luteal Phase - The secretory phase lasts from the day of ovulation until about three days before the next menstrual period. Generally, women will be more sensitive in the post-ovulatory phase because the reproductive hormones (FSH, LH, estrogen and progesterone) have increased.

Ischemic or Premenstrual Phase - If fertilization and implantation do not occur, the corpus luteum, which secretes estrogen and progesterone, shrinks. As the levels of estrogen and progesterone rapidly decrease, the spiral arteries spasm so that the blood supply to the endometrium is cut off, and necrosis occurs. The functional layer separates from the basal layer, and menstrual bleeding begins [18].

Hormones that Control the Menstrual Cycle - Follicular maturation and ovulation are controlled by the hypothalamus-pituitary ovarian axis. The hypothalamus controls the cycle, but the hypothalamus can be affected by higher stimuli in the brain, such as anxiety and stress. The hypothalamus stimulates the pituitary gland by secreting gonadotropin-releasing hormone (GnRH) [19]. GnRH secretion regulates the synthesis and release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH).

Follicle-stimulating hormone (FSH) is a glycoprotein hormone that stimulates follicle maturation during the follicular phase of the menstrual cycle. FSH also helps LH stimulate the secretion of steroid hormones, especially estrogen, by the granulosa cells of mature follicles. LH also includes glycoproteins. LH participates in steroidogenesis in follicles and plays a vital role in ovulation. Progesterone production by the corpus luteum is also influenced by LH.

Disorders in the Menstrual Cycle - The menstrual cycle in normal women ranges from 21-35 days, with the average cycle duration being 28 days. Menstrual disorders in the form of abnormal uterine bleeding occur in 9-14% of women of reproductive age (between menarche and menopause) and have a significant impact on quality of life and financial burden [1]. Abnormal uterine bleeding in adolescents to women in the perimenopausal phase is broadly divided into two categories. They are anovulatory and ovulatory. Anovulatory bleeding is characterized by irregular or infrequent menstruation, accompanied by light to very severe bleeding. Forms of menstrual disorders with anovulatory bleeding include amenorrhea (no menstruation for more than three cycles or 90 days), oligomenorrhea (menstruation at intervals of more than 35 days), and metrorrhagia (irregular intervals with severe bleeding for more than seven days). Anovulatory pattern and ovulatory bleeding occur at regular intervals (every 24 to 35 days) but with a large blood volume or duration of more than seven days [1].

Amenorrhea is when menstruation stops or does not occur during the fertile period or when menstruation should occur regularly. Amenorrhoea can be divided into two types, namely primary amenorrhea and secondary amenorrhea. Primary amenorrhea is a term used for women who start menstruating late. Usually, a woman will experience her first menstruation around the age of 10 to 16 years. If he is 16 years old and has not menstruated, this is called primary amenorrhea. A person who starts menstruating late can be caused by several things, including hormonal disorders, physical health problems or mental and emotional stress problems [20].

Secondary amenorrhea is the cessation of menstruation for at least three consecutive months, even though someone has experienced menstruation before. Secondary amenorrhea can be caused by low levels of gonadotropin-releasing hormone (GnRH = Gonadotropin-Releasing Hormone), a hormone produced by the hypothalamus one of whose functions is to regulate the menstrual cycle. In addition, stress conditions and ovarian cysts can also cause amenorrhea [21].

Polymenorrhea is a menstrual cycle disorder that causes women to experience menstruation many times in a month; it can be two or three times or even more. Typically, the menstrual cycle lasts for 21-35 days, with about 3-7 days. Women who experience polymenorrhea have menstrual cycles shorter than 21 days with a regular pattern, and the amount of bleeding is relatively the same or more than usual. Polymenorrhea can be caused by an imbalance of the hormonal system in the hypothalamic-pituitary-ovarian axis. This hormonal imbalance can cause interference with the ovulation process (release of eggs) or shorten the time needed for a regular menstrual cycle to occur so that more frequent menstruation is obtained [4].

Oligomenorrhea - Oligomenorrhea is when the menstrual cycle extends more than 35 days while bleeding remains the same. Women who experience oligomenorrhea will experience menstruation that is less frequent than usual. Oligomenorrhea usually occurs as a result of hormonal imbalance in the hypothalamic-pituitary-ovarian axis. These hormonal disorders cause the length of the normal menstrual cycle to lengthen so that menstruation becomes less frequent. Oligomenorrhea often occurs in the first 3-5 years after menstruation or several years before menopause. Oligomenorrhea that occurs at that time is a normal variation [22].

Menorrhagia– Menorrhagia is the medical term for excessive menstrual bleeding. The average woman loses about 30-40 ml of blood during about 5-7 days of menstruation in one normal menstrual cycle. If the bleeding is more than seven days (more than 80 ml), it is categorized as menorrhagia or severe menstruation. Menstruation is considered severe if someone has to change pads every hour or every few hours in a row. Other symptoms of excessive menstruation can include nighttime bleeding that makes someone wake up to change pads, large blood clots during menstruation, menstruation lasting more than seven days,

and in severe cases, menstruation can interfere with sleep and daily activities [23]. Many things can cause menorrhagia, including hormonal imbalance, the presence of uterine fibroid tumours, cervical polyps, endometrial polyps, pelvic inflammation, or worse, cervical cancer or endometrial cancer.

Relationship of Stress Levels with Menstrual Cycle - Stress often creates an irregular menstrual cycle. It happens because stress as a stimulus to the nervous system is transmitted to the central nervous system, namely the limbic system, through nerve transmission. The autonomic nerves will be forwarded to the hormonal (endocrine) glands to secrete neurohormonal secretions to the pituitary through the frontal system to secrete gonadotropins in the form of FSH. Follicle Stimulating Hormone) Furthermore, LH (Luteinizing Hormone) hormones are influenced by RH (Realizing Hormone), which is channelled from the hypothalamus to the pituitary. RH release is strongly influenced by the feedback mechanism of estrogen to the hypothalamus so that it will affect the menstrual process [24]. Disorders of menstrual patterns involve integrative regulatory mechanisms that affect biochemical and cellular processes throughout the body, including the brain and psychology.

The influence of the brain in hormonal reactions occurs through the hypothalamic-pituitary-ovarian pathway, which includes multiple effects and feedback control mechanisms. Under stress, there is the activation of the amygdala in the limbic system. This system stimulates the release of a hormone from the hypothalamus, namely corticotropic releasing hormone (CRH). This hormone will directly inhibit the secretion of hypothalamic GnRH at its production site in the arcuate nucleus. Increased CRH will stimulate the release of adeno corticotropic hormone (ACTH) into the blood. An increase in the hormone ACTH causes an increase in blood cortisol levels. These hormones cause a decrease in GnRH levels, through which stress disrupts the menstrual cycle. From the normal menstrual cycle to oligomenorrhea, oligomenorrhea, or amenorrhea. Clinical symptoms that arise depend on the degree of suppression of GnRH. These symptoms are temporary and will usually return to normal when the stress is overcome [25].

Research Method

This research is analytical descriptive using a cross-sectional study which is a research design by measuring or observing at the same time. It is done to see the relationship between stress levels and menstrual cycle regularity in the Faculty of Medicine, Universitas Kristen Indonesia Class 2017. This research was conducted on November 9, 2018, in the Faculty of Medicine, Universitas Kristen Indonesia. The population in this study were all students of the Faculty of Medicine, Universitas Kristen Indonesia, class of 2017, totalling 110 people. The sample used in this study was taken with a non-random sampling technique, namely by purposive sampling technique based on specific considerations. The number of samples in this study was calculated using the Slovin formula so that the total sample taken from the population was 52 people. The research instrument is two sets of questionnaires. The first questionnaire contains questions about the menstrual cycle, and the second questionnaire, namely the Medical Student Stressor Questionnaire (MSSQ), contains 40 questions about quantitative measures to measure the emotional state of stress experienced by medical students. The rating scale on the MSSQ is as follows: a) Causes mild stress (1); b) Causes moderate stress (2); c) Causes severe stress (3); and d) Causes extreme stress (4). Research data were taken through the questionnaire. The data is processed through the stages of editing, coding, processing, and cleaning, where the results entered into the computer program are rechecked for errors or not. Data processing and analysis were carried out with the help of a computer using the SPSS for Windows version 24.0 program. To explain or describe the characteristics of each research variable, univariate analysis was carried out and followed by bivariate analysis.

Result and Discussion

From data collection conducted on students of the Faculty of Medicine, Universitas Kristen Indonesia, class of 2017, as many as 52 people obtained data regarding the characteristics of the respondents as follows.

Table 1: Frequency Distribution of Respondents Age Characteristics

Age	Frequency	%
18 year	13	25
19 year	29	55.8
20 year	9	17.3
21 year	1	1.9
Total	52	100

Based on table 1, it was found that 13 respondents (25%) were 18 years old, 29 respondents (55.8%) were 19 years old, nine respondents (17.3%) were 20 years old, and one respondent (1.9%) was 21 years old.

Table 2: Frequency Distribution of Respondents Menarche Age Characteristics

Menarche Age	Frequency	%
9-11 year	18	34.6
12-14 year	33	63.5
>14 year	1	1.9
Total	52	100

From table 2 above, it can be seen that from 52 respondents, 18 respondents (34.6%) experienced their first menstruation at the age of 9-11 years, 33 respondents (63.5%) at the age of 12-14 years and one person (1.9%)) respondents aged> 14 years.

Univariate Analysis - Univariate analysis is used to describe the characteristics of each research variable, which is displayed in the form of frequency distribution tables and percentages. Univariate analysis was carried out to obtain information regarding the frequency distribution of the independent variable stress level and the dependent variable, namely the regularity of the menstrual cycle. Based on the results of univariate data analysis from this study, the following results were obtained:

Table 3: Frequency Distribution of Menstrual Cycle Characteristics in the Last 3 Months

Menstrual cycle in the last three months	Frequency	%
Regular	35	67.3
Irregular	17	32.7
Total	52	100

From table 3 above, it can be seen that from 52 respondents, 35 respondents (67.3%) experienced regular menstrual cycles, and 17 respondents (32.7%) experienced irregular menstrual cycles in the last three months.

Table 4: Frequency Distribution of Characteristics of Students Class of 2017 Based on Stress Levels

Stress Level	Frequency	%
Light	1	1.9
Moderate	19	36.5
Severe	29	55.8
Very Severe	3	5.8
Total	52	100

From table 4 above, it can be seen from the 52 respondents who were the research subjects, most of the respondents experienced severe stress levels, namely 29 people (55.8%) followed by moderate stress levels 19 people (36.5%), very severe stress levels three people (5.8%) and a mild stress level of 1 person (1.9%).

Table 5: Frequency Distribution of Stressors for Students Class of 2017

Stressor	Total Stressor Score
Academic Related Stressors (ARS)	1626
Intrapersonal and Interpersonal Related Stressors (IRS)	900
Teaching and Learning Related Stressors (TLRs)	721
Social Related Stressors (SRS)	664
Drive and Desire Related Stressors (DRS)	315
Group Activities Related Stressors (GARS)	391

Table 5 above explains the highest total stressor scores experienced by the 2017 Medical Faculty students. Of the 40 questions given in the questionnaire, divided into six stressor dimensions, it was found that the most significant stressor was caused by Academic Related Stressors with a total score of 1626, followed by Intrapersonal and Interpersonal. Related Stressors with a total score of 900, then Teaching and Learning Stressors with a total score of 721, Social Related Stressors with a total score of 664, Group Activities Related Stressors with a total score of 391 and Drive and Desire Related Stressors with a total score of 315.

Bivariate Analysis - Bivariate analysis was carried out on two variables that were thought to be related or correlated. Data analysis used a significant degree of significance of 0.05. The results of the chi-square analysis were compared with the p-value. If $p < 0.05$, it was statistically significant and if $p > 0.05$, it was statistically not significant. The results of the bivariate analysis of this research are as follows:

Table 6: The Relationship between Stress Levels and Menstrual Cycle Regularity

Stress Level	Menstrual Cycle				Total		P-value
	Regular		Irregular				
	F	%	F	%	F	%	
Light to Moderate	18	90	2	10	20	100	0.006
Severe to Very Severe	17	53.1	15	46.9	32	100	
Total	35	67.3	17	32.7	52	100	

Table 6 above explains that from 52 respondents, it was found that 18 people or 90% of respondents who experienced mild-moderate stress with regular menstrual cycles or 90% experienced mild-moderate stress with irregular menstrual cycles as many as two people or 10%. While the respondents who experienced severe stress levels with regular menstrual cycles were 17 people or 53.1%, those who experienced severe stress levels with irregular menstrual cycles were 15 people or 45.9%. Based on the chi-square statistical test results, the p-value = 0.006 ($p < 0.05$), meaning a significant relationship between stress levels and menstrual cycle regularity in students of the Faculty of Medicine, Universitas Kristen Indonesia, class of 2017.

The influence of the brain in hormonal reactions occurs through the hypothalamic-pituitary-ovarian pathway. In stressful situations, the amygdala in the limbic system is activated [26]. This system will stimulate the release of hormones from the hypothalamus, namely Corticotropic Releasing Hormone (CRH). The increased CRH will stimulate the release of Adrenocorticotropic Releasing Hormone (ACTH) into the blood, and the increase in ACTH levels will cause an increase in blood cortisol levels [27, 28]. These hormones, directly and indirectly, cause a decrease in GnRH so that through this mechanism, stress can affect the menstrual cycle.

Conclusion

Based on the results of the discussion of the research on the relationship between stress levels and the regularity of the menstrual cycle, it was found that: a) A total of 29 out of 52 female respondents from the Faculty of Medicine, Universitas Kristen Indonesia, class of 2017 experienced severe stress with the most stressors due to academic stressors; b) A total of 17 people from 52 respondents from the 2017 Universitas Kristen Indonesia Faculty of Medicine students experienced irregular menstrual cycles; c) There is a relationship between stress levels and the regularity of the menstrual cycle in students of the Faculty of Medicine, Universitas Kristen Indonesia class 2017. Based on the conclusions obtained, the authors hope that the 2017 Universitas Kristen Indonesia Faculty of Medicine students can manage the stressors they face to avoid harmful stress that affects them. On the menstrual cycle.

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