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THE PREMENSTRUAL TENSION SYNDROME AND ITS TREATMENT

BY

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Premenstrual tension is a syndrome occurring during the second half of the menstrual cycle and consisting of a number of mental and physical symptoms. The syndrome is composed of marked general tension and irritability, together with one or more of the following symptoms: anxiety, depression, bloated abdominal feelings, swelling of subcutaneous tissues, nausea, fatigue, painful swelling of the breasts, headaches, dizziness, and palpitations. Less frequently there may be increased sex desire, excessive thirst, increased appetite, and hypersomnia. The symptoms usually start about seven to fourteen days before menstruation and pass off soon after the onset of the menses, although some patients continue to have symptoms throughout the period. The syndrome must not be confused with the premenstrual discomfort experienced by many women. The premenstrual tension syndrome may seriously interfere with work and social activities, and can be incapacitating. The condition is by no means as uncommon as suggested in some reports.

Literature

The aetiology of the condition is still obscure. Frank (1931), who introduced the term "premenstrual tension," considered it to be due to excess of circulating oestrogen. Israel (1938) believed the syndrome not to be due to excess oestrogen itself, but rather to the action of unantagonized oestrogen resulting from faulty luteinization. Gillman (1942) and Hamblen (1945), in contrast, implicate progesterone as the responsible hormone. Convincing evidence in support of the hypothesis of faulty luteinization permitting the action of unantagonized oestrogen as the primary cause of premenstrual tension is, however, given by Morton (1950).

Water retention is postulated by Greenhill and Freed (1941) as the immediate cause of premenstrual tension symptoms. Hoffman (1944) considered that an unstable nervous system was an important factor, and a number of authors have expressed the opinion that the condition seems to be more frequent in unstable women.

Rees (1953), in a psychosomatic study of 145 subjects, including normal and psychiatric patients, found that marked premenstrual tension could exist in normal women of stable personality and that many severely neurotic women were free from it. In neurotic patients with premenstrual tension

there was a positive correlation between degree of premenstrual tension and degree of personality instability and severity of neurosis. Rees, while in general supporting the theory that the condition was primarily physiogenic and due to changes resulting from defective progesterone secretion, stressed that the syndrome was of complex causation in which personality and constitutional and emotional factors operate in addition to the primary physiogenic changes.

There is now considerable evidence to suggest that the bodily changes of the premenstrual tension syndrome are primarily due to a lack of progesterone, which allows the unopposed action of oestrogens during the second half of the menstrual cycle. It is known that oestrogens cause sodium and water retention. Hydration is a common feature of the premenstrual tension state, and many patients put on from 2 to 9 lb. (0.45 to 4.1 kg.) in weight during the premenstrual phase and lose a corresponding amount with the diuresis following the onset of the menses. Oestrogens stimulate growth of the epithelia of the breast, vagina, and endometrium, and this together with hydration may account for painful swelling of the breasts. Hypoglycaemia and hyperinsulism have been noted to occur during premenstrual tension states (Billig and Spaulding, 1947; Morton, 1950) and may be the cause of increased appetite and fatigue noted in some patients. These changes in the internal environment cause a number of specific symptoms and also may result in autonomic lability, causing such symptoms as palpitations and dizziness. The patient's reaction to these changes can be influenced by such factors as personality type and stability, emotions, attitudes, and degree of autonomic instability.

The treatment of premenstrual tension can therefore be directed at different aetiological levels. (1) Psychotherapy, including explanation and re-education to improve attitudes, relieve symptoms, and minimize degree of incapacity. (2) Dehydration by means of diuretics to relieve symptoms due to hydration and possibly to facilitate elimination of the noxious agent. (3) Administration of progestogens to compensate for any lack of progesterone and to antagonize action of oestrogens. (4) Administration of androgens to antagonize action of oestrogens as suggested by Greenblatt (1940), Geist (1941), and Freed (1945).

Gonadotrophins are generally considered to be ineffective (Bowes, 1950), and as oestrogens tend to intensify symptoms (Morton, 1950) they are contraindicated.

Present Investigation

The following therapeutic methods have been studied in a group of 30 patients suffering from severe premenstrual tension: psychotherapy; dehydration therapy using ammonium chloride; administration of progestogens, including progesterone by injection and ethisterone by mouth; and administration of androgens in the form of methyltestosterone by mouth. The patients have been observed for from six months to four years, giving a total of 207 cycles.

The assessment of premenstrual tension was made from data obtained during clinical interview and from special daily records of symptoms. Detailed instructions were given to patients regarding the daily recording of symptoms, so that scoring was, so far as possible, kept standardized. The day-to-day records were kept for some months before starting treatment, and the data so provided permitted a detailed assessment of the premenstrual tension and provided a baseline for measuring the effects of treatment.

Clinical Data.—The age distribution of the group was 15-24 years, 8%; 25-34, 56%; 35-44, 36%. Most patients had developed premenstrual tension before 35 and about one-fifth before the age of 20. Two developed premenstrual tension after childbirth, and three just before the menopause. 80% of the group were married. The mean age of menarche was 14.7 years and the frequency distribution of menarchal ages was similar to that described by Ellis (1947) for normal British women. The symptoms of premenstrual

tension usually started about seven to ten days before the period and usually cleared up soon after the onset of menstrual flow, but in some patients they occasionally continued throughout the menses. The symptomatology of the group was as follows: tension, 100%; irritability, 100%; depression, 80%; emotional lability, 80%; anxiety, 73%; swelling of fingers or legs, 73%; painful swelling of breasts, 63%; fatigue, 63%; headaches, 63%; insomnia, 40%; pruritus, 40%; palpitations, 40%; nausea, 37%; marked thirst, 20%.

Results

Psychotherapy

Premenstrual tension was not found to be amenable to psychotherapy alone. Psychotherapy of a simple kind can help the patient in understanding the condition and can improve her attitude and reaction to it. The tense, anxious, striving obsessional type of woman feels greatly frustrated by the interference with physical, mental, and social well-being caused by the premenstrual tension state. She may tend to force herself to keep up the tempo of her work and life in spite of her symptoms. This tends to lead to greater frustration and increase in tension. In this type of patient an understanding of the nature of the condition and the fact that there is an underlying physiological basis for her symptoms can help, together with the advice to modify the demands she makes on herself in relation to her premenstrual symptoms. The person who, on the other hand, is hypochondriacal or very dependent may allow the premenstrual tension state to interfere unnecessarily with her work and social activities. Again explanation, and re-education with the aim of producing a more salutary attitude to her symptoms, can be helpful.

Sixteen patients of the group were attending the psychiatric clinic for treatment of neurosis in addition to premenstrual symptoms. In all these the onset of premenstrual tension antedated the onset of neurosis. Some of them recovered from their neurosis without any significant improvement in premenstrual tension symptoms; conversely, some patients showed improvement in premenstrual tension with hormonal therapy without change in the coexisting neurosis. These facts indicate that premenstrual tension cannot be regarded as being primarily a neurosis.

Suggestion is not thought to play an important part in the condition. Most of the patients develop premenstrual symptoms without realizing the relationship to the menstrual cycle. Exhibition of inert tablets given as a control to hormone therapy produced no significant improvement.

Dehydration Therapy

Dehydration treatment was applied by giving enteric-coated tablets of ammonium chloride in 7½-15-gr. (0.5-1-g.) doses three times a day for twelve days before the period, with restriction of sodium intake. This was found to be effective in preventing the development of swelling of the fingers, legs, face, and other parts of the body. It was also successful in removing these if they had already developed.

The majority of patients reported that they felt more comfortable and had relief of the following symptoms in particular: bloated feeling in abdomen, heavy feelings in head, swelling of subcutaneous tissues and tightness of skin, general pruritus, and pruritus vulvae.

Although effective in preventing excessive water retention and its attendant symptoms, the method was not always effective in relieving the nervous tension, irritability, depression, and anxiety. This suggests that hydration is not responsible for all the symptoms of the syndrome. This is borne out, too, by the fact that some women develop signs of hydration midway between the periods without the emotional tension that develops premenstrually, and in some patients the nervous tension disappears at the onset of the menses in spite of the fact that hydration may continue for some days afterwards.

Progesterone Treatment

Progesterone was given intramuscularly on alternate days for twelve days before the period in five patients, and was found to be effective in relieving the symptoms of premenstrual tension. In view of the practical disadvantage of a treatment involving a series of injections an extensive trial was given to the orally active preparation ethisterone. This was given to all patients in the series, and observations were made on over 100 cycles.

Ethisterone was given for twelve days before the period, starting with 5 mg. twice daily, increasing to 10 mg. twice daily if necessary. Most patients responded to a dosage of 5-10 mg. daily. In about 85% of the trials ethisterone was found to produce significant relief of premenstrual symptoms. The signs and symptoms of hydration were prevented and there was usually relief of tension, anxiety, depression, fatigue, headaches, bloated feelings, and pruritus. The pain of dysmenorrhoea was not relieved, and often the patient reported increased pain indicative of more powerful uterine contractions. Occasionally delay of a few days in the onset of the menses was noted when the patient was on ethisterone.

Androgen Treatment

Treatment with methyltestosterone has been tried in 10 patients and observations were made on 40 cycles. It was given in doses of 10 mg. daily for twelve days before the period. Marked relief of premenstrual tension symptoms was obtained, including tension, irritability, anxiety, and depression; also signs and symptoms relating to hydration were prevented. As with ethisterone, the period may be delayed and uterine contractions more painful.

The relief of symptoms of premenstrual tension with methyltestosterone seems to be as effective as that given by ethisterone.

Discussion

The complex symptomatology comprising the premenstrual tension syndrome is of multiple causation. Some of the symptoms and signs are attributable to the effects of hydration, others are due to proliferative changes in the breasts and uterus. Some are possibly due to changes in blood sugar, whereas others are manifestations of autonomic imbalance. Subjective factors, such as the patient's emotional stability, personality, and her attitudes, will also influence the intensity of the degree of incapacity resulting from various symptoms.

Our observations and therapeutic results appear to lend support to the theory that the primary cause is lack of progesterone secretion, permitting the unantagonized action of oestrogens.

Oestrogens are known to cause sodium ion and water retention and proliferative changes in the breast and endometrium, and also to cause various chemical changes in the blood, including hypoglycaemia and increased carbohydrate tolerance (Billig and Spalding, 1947; Morton, 1950). These effects would appear to explain many of the symptoms and changes associated with the premenstrual tension state.

Treatment with ammonium chloride causes diuresis and removes or prevents excessive hydration, and may also serve to aid the excretion of oestrogens or other agents that may be pathogenetic in premenstrual tension. Our evidence suggests, however, that hydration does not account for the whole of the syndrome.

Progesterone and ethisterone treatment was found to be effective in alleviating not only hydration and its symptoms but also nervous tension, irritability, depression, anxiety, etc. Progesterone promotes diuresis (Selye, 1950), and our observations with ethisterone suggest a similar effect, in contrast to the water-retaining effects of oestrogens. Testosterone also promotes diuresis (Selye, 1950) and is similar in chemical constitution to ethisterone.

Ethisterone and testosterone are both diuretic and antagonistic to oestrogen, and this would appear to be the rationale for their beneficial therapeutic effects on premenstrual tension.

The conclusion is that the simplest method of treating premenstrual tension is by means of diuretics such as ammonium chloride, and, if this is not effective, ethisterone or methyltestosterone should be tried.

Summary

The clinical features of premenstrual tension are described and the possible mode of origin of the various symptoms is discussed. Hydration, blood chemistry changes, autonomic nervous system responses, as well as psychogenic and personality factors are believed to play a part in the syndrome. A working hypothesis on which treatment was based is postulated.

Treatment was applied at various aetiological levels, including psychotherapy, dehydration therapy, and administration of progestogens and androgens.

Psychotherapy has an important but limited role. Dehydration therapy was found to alleviate some of the symptoms only. The most effective methods of treatment were administration of a progestogen such as ethisterone or an androgen such as methyltestosterone during the second half of the menstrual cycle.

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BRIGHT'S DISEASE

AN ATTEMPT AT A STATISTICAL ASSESSMENT OF THE CLASSIFICATION PROPOSED BY ELLIS

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[WITH SPECIAL PLATE]

In 1827 Richard Bright described the disease of the kidney to which his name is still attached. His cases included all forms of renal disease unassociated with obvious changes in the lower urinary tract, and so were composed mainly of the three main groups of chronic pyelonephritis, hypertensive nephrosclerosis, and true nephritis. The second of these was clearly separated by Allbutt (1895-6), and the last has been defined by Osler (quoted by Osman, 1939) as "bilateral, non-suppurative inflammatory disease of the kidneys." The importance and frequency of the first group as a cause of Bright's disease has only recently been recognized.

Numerous attempts have been made to subdivide these cases, but none has received general acceptance. Ellis (1942), as a result of a combined clinical and pathological investigation of "about 600" cases, "about 200" of

which were fatal, suggested that nephritis could well be separated into only two groups, which he called types I and II.

Type I nephritis is characterized by an abrupt onset with haematuria, and is often preceded by an acute infection such as a sore throat. In most adequately treated cases recovery is complete. Death may occur in the acute stage, and some cases follow a progressive course ending in death in a few months. Other cases appear to recover completely, yet after many years develop renal failure and hypertension.

Type II nephritis, on the other hand, is of insidious onset and usually presents as oedema with albuminuria. There is no history of preceding infection, and haematuria is uncommon. The course of the disease is steadily downhill, and if renal failure and hypertension supervene the oedema tends to abate. Many of these patients die from secondary infection and the remainder from hypertension or uraemia.

Ellis further suggested that the two types were not only clinically distinct but were associated with specific renal histological changes and were unrelated aetiologically. Davson and Platt (1949) supported his conclusions with the exception of the last, upon which they reserved judgment.

The present communication describes a similar investigation of a comparable group of cases, with the difference that, where possible, clinical and pathological diagnoses were made quite independently. There were two main objects. The first was to examine the lesions found in fatal Bright's disease, and the second was to see what support analysis of a further group of cases lent to Ellis's views.

Material and Method

In all, 154 cases were examined. They were those that had been indexed as Bright's disease in the necropsy records of this hospital during 1931-51. No non-fatal cases were investigated, so no comprehensive survey of the natural history of these diseases can be offered.

Twenty-seven of these cases have not been included in the analyses: 8 of them because there was a history of toxæmia of pregnancy, 2 because of industrial exposure to heavy metals; 1 was a typical case of polyarteritis nodosa, and 1 was associated with scleroderma; in the remaining 15 cases the clinical or pathological material was incomplete.

The clinical diagnoses were made on the ward records, which were examined by C. L. J., only very few of the patients being seen by either of us during life. The original necropsy reports were consulted, where necessary, only for the macroscopic observations, the histological data presented being derived from an examination of preserved material by J. B. E. At first these investigations were entirely independent, and extreme care has been exercised to avoid either diagnosis being influenced by evidence proper to the other. In all cases in which clinical and pathological diagnoses differed a re-examination was made, the only additional information at each observer's disposal then being the fact that a discrepancy had been encountered. It was rarely found possible to alter a diagnosis at this stage, and if agreement was not reached the available information was discussed and a definite decision on grouping was made. In only 9 cases (7.1%) was agreement then reached, leaving 19 cases of disagreement. All analyses, except where otherwise stated, have been based on the assumption that, wherever pathological and clinical conclusions conflicted, those drawn from the latter material were the correct ones.

Nomenclature

The classification proposed by Ellis has been used throughout, and his criteria for the diagnosis of nephritis of