ENDOCRINES IN THEORY AND PRACTICE

This article is one of a series on Endocrinology contributed by invitation

THE MENOPAUSE

BY

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The menopause is a period of variable duration through which women pass naturally some time between the ages of 45 and 55. For about 15 per cent. of women it is symptomless: in the remainder the severity of the symptoms varies; they may be so mild as to render treatment unnecessary or so severe as to lead to profound mental disturbances. Surgical removal of the ovaries in younger women or destruction of ovarian function by deep x rays or radium brings about an artificial menopause which is usually attended by similar but relatively more severe symptoms.

The great variety of changes which may take place can be grouped conveniently under the following headings:

Vasomotor Changes

The tendency to vasomotor instability is shown by the most characteristic menopausal manifestation—hot flushes. In these attacks dilatation of the vessels of the skin is accompanied by sweating and discomfort due to a sensation of heat and suffocation, which after a few minutes gives way to cold shivers. The hot flush is painfully obvious to those around the patient and consequently causes her some embarrassment. Flushes may appear without warning at any time of day or night, frequently awakening the patient, but they are especially prone to follow circumstances giving rise to emotional stress or excitement. Their frequency varies greatly in different patients, and they may occur only once or twice a week or twenty or thirty times a day.

Cardiovascular Symptoms

Though no organic cardiac lesion is associated with the menopause, symptoms such as palpitations and precordial pain may be experienced. The blood pressure is sometimes found to be raised, and it has been suggested, on inadequate experimental grounds, that this may be due to the excessive activity of the anterior pituitary basophil cells or of the adrenal cortex. Ovarian deficiency, both in earlier life and at the time of the menopause, is often associated with acrocyanosis, and in some cases ovarian replacement therapy has led to improvement in the circulation to the extremities.

Arthritis

Pains in the joints, backache, and fibrositis are all common complaints, and a menopausal type of arthritis is described which is due to chronic hypertrophic synovitis and usually affects the knees.

Emotional Instability

Practically every menopausal woman becomes aware of a certain mental clumsiness, an inability to cope with the ordinary problems of daily life, and a tendency to "give in." The realization of her shortcomings is worrying, and she readily becomes depressed. Emotional instability is well defined, and the patient reacts to trivial situations with rather surprising attacks of laughter or

tears. She is subject to rapid and frequent changes of mood: at one moment she will be unbearably irritable, at the next pathetically contrite. There may be marked changes in personality and severe attacks of mental depression, sometimes lasting for days, during which the patient may become suicidal. A condition of hypochondriasis, which is particularly distressing to those around her, may develop out of the complicated syndrome, even in the milder cases, and persist for the remainder of the patient's life.

Headaches and giddiness are common and appear early. Migraine is frequently aggravated or induced, but is sometimes amenable to treatment with ovarian extracts.

Endocrine Changes

Owing to the delicate interdependence of the components of the endocrine system the functional failure of one gland is likely to affect all the others. A common example is the gradual masculinization which may take place. The breasts atrophy, hair appears on the chin and upper lip, and the features assume a male appearance. This virilism is probably due to a compensatory overactivity of the adrenal cortex. Thyroid function frequently diminishes and signs of hypothyroidism are common. Skeletal changes suggestive of acromegaly may occur and provide evidence of the disturbance of pituitary secretion. There are some who believe that the obesity which commonly develops is endocrine in origin and remark on the "girdle" type of distribution, which suggests that the pituitary may be responsible.

The essential feature of the syndrome is of course amenorrhoea, which may appear quite suddenly or after some months of menstrual irregularity. Other characteristics of the gradual ovarian failure are the atrophy of the breasts, uterus, and external genitalia. Sexual desire usually wanes, particularly when the menopause has been surgically induced, but may remain unchanged.

Methods of Treatment

General.—Assistance can be rendered by the members of the patient's household. Her husband and her relatives should be told that she is passing through a difficult phase of life and that they should therefore be tolerant and sympathetic in their dealings with her. She should be shielded as much as possible from domestic worries, and sometimes a holiday away from her household duties is beneficial, though it may be harmful if she is a woman of forceful personality who will worry over the conduct of her home in her absence. She should be encouraged to pursue any hobby which will prevent her from becoming introspective about her condition. She may suffer from a secret fear that her symptoms are due to cancer, and it is wise for her doctor to reassure her specifically on this point. Bromides and valerian are popular and sometimes efficacious. Thyroid extract is of value only in those cases in which there is clinical evidence of hypothyroidism.

Pituitary Extracts.—There is an increasing tendency to prescribe anterior pituitary preparations. This form of therapy is based on a misunderstanding of the endocrinology of the condition. The relative activity of the ovary and pituitary is complementary, so that when ovarian

function is declining the gonadotropic activity of the anterior pituitary is excessive. That there is no deficiency of pituitary secretion at the time of the menopause is shown by the increased concentration of the follicle-stimulating factor in the urine. Furthermore, it has been pointed out that the severity of the symptoms—for example, the number of hot flushes a day—runs parallel with the curve of urinary excretion of the follicle-stimulating factor. Nor does there appear to be a reasonable basis for attempting to control the uterine haemorrhages which sometimes occur during the early stages of the menopause with gonadotropic preparations. These are designed theoretically to stimulate ovarian function, whereas the failure of ovarian function at the menopause is progressive and inevitable, so that any attempt at artificial stimulation merely exemplifies the unsound principle of “flogging the tired horse.” It is, moreover, fashionable to administer anterior pituitary preparations by mouth. For this there is no experimental justification. All animal experiments so far conducted on these substances have failed to show any effect if the material is administered in any other way than by injection. A few encouraging results of irradiation of the pituitary with the object of diminishing its gonadotropic activity have been reported, but in the majority of cases this seems an unnecessarily drastic procedure.

Ovarian Extracts.—By far the most satisfactory method of controlling the symptoms of the menopause is by the administration of oestrogenic preparations. This method of treatment produces results probably by temporarily restoring the endocrine balance until the patient has accustomed herself to the new level of endocrine activity. The ovarian extract acts both by replacing the ovarian deficiency to some extent and by damping down the excessive activity of the pituitary.

Principles of Treatment with Oestrin

Urinary Estimations.—It has already been pointed out that, owing to the compensatory overactivity of the pituitary, an excess of the follicle-stimulating factor can be demonstrated in the urine. Quantitative estimations of this principle are, however, laborious, expensive, and subject to a considerable margin of technical error. It is hoped that in the near future such estimations will be placed on a more practical basis, but at the present they are merely of rather doubtful academic interest.

Vaginal Smears.—The use of the vaginal smear technique of Papanicolaou and Shorr has proved to be of greater value. As the result of deprivation of oestrin the vaginal mucosa undergoes atrophy, and the appearance of the menopausal vaginal smear is quite characteristic. By the examination of such a smear, therefore, it is possible to identify those cases in which the symptoms are associated with ovarian deficiency. In the first group oestrin therapy usually produces satisfactory results; in the second group it is without effect. Furthermore, it is fortunate that the human vagina is a delicate indicator of oestrogenic influence, for one is enabled to estimate the correct dose of ovarian extract for each individual patient by determining the amount necessary to induce an oestrous type of smear. This applies only to the more common and milder symptoms, which are gradually coming under control by the time an oestrous smear has been produced. This is of importance, for the object of the treatment is not completely to replace the ovarian activity of preclimacteric life, nor entirely to counteract the excessive activity of the pituitary, but to accustom the patient gradually to the new level of endocrine balance.

The Psychological Factor.—A preliminary course should be given exactly resembling the intended regime of oestrin therapy with regard to mode of administration—whether by mouth or by injection, colour of the tablets, appearance of the solution for injection, etc.—but differing from it in that the material administered is inert. For this purpose “dummy” tablets of oestrin or a solution of sterile olive oil may be employed. This procedure serves to differentiate the more fanciful complaints, which tend to disappear, from the genuine symptoms of ovarian deficiency or gonadotropic excess which persist at the conclusion of such a course.

Hot Flushes as an Indicator.—The hot flush is the most clearly defined of the subjective symptoms, and is therefore a valuable indicator of progress. The patient should be instructed to keep a note of the daily number of hot flushes both during the preliminary period of “control” treatment and later when active oestrogenic compounds are being administered. One should aim not at complete elimination of the hot flushes but at reducing them to one or two every day or every other day, since, as has already been pointed out, the object of the treatment is not to postpone the menopause artificially by giving large doses of oestrin, but to alleviate the symptoms sufficiently to allow the patient to accustom herself as comfortably as possible to the new level of endocrine balance.

Dosage of Oestrin

With this object in view it is obviously desirable to start with relatively small doses; the administration of large doses from the beginning in order to enhance one's reputation with the patient by procuring miraculous and immediate results is to be deprecated. In the milder cases it is well to begin by giving 1,000 international units daily by mouth. There is usually a latent period before an effect is established, and one should consequently persist in this dose for at least a fortnight. At the end of this time evidence of progress or otherwise should be sought from the records of frequency of hot flushes and from the microscopical examination of the vaginal smear, and with the aid of these indicators the dose should be cautiously raised until the correct level is established. From this plateau one should equally cautiously descend. The symptoms can usually be kept under control by oral administration, but some of the more serious manifestations, such as severe attacks of mental depression, may require relatively high doses by injection. Such injections should be administered twice weekly and intramuscularly. There are certain disadvantages of high-dosage therapy. The patient may complain of unpleasant moliminal symptoms, or she may actually experience a “period,” which is in fact an oestrin-withdrawal bleeding, some days after the cessation of the course of treatment. Unless previously warned of this possibility she is apt to be alarmed and to lose confidence in her medical attendant. High-dosage therapy should never be continuous, but always intermittent; otherwise it may cause tenderness and swelling of the breasts, cystic endometrial hypoplasia, or deleterious effects from prolonged inhibition of the pituitary.

The beneficial results of successful oestrin therapy include, apart from the relief of symptoms, the development of a feeling of well-being, and in some cases a return of sex desire.

Sequels of the Menopause

There are certain late sequels which may follow a symptomless menopause and occur as late as six or seven years after the cessation of the menses. These are directly

due to ovarian deficiency, and remarkably satisfactory results have followed treatment with oestrin. To one group belong the conditions resulting from the lack of ovarian stimulus to the external genitalia, such as atrophic senile vaginitis and ulceration, pruritus and kraurosis vulvae, associated with dyspareunia as the result of the shrunken and tender introitus, and, according to some authorities, leucoplakia vulvae. Another group consists of a number of skin lesions, which are gradually becoming recognized as being associated with the menopause. One example is a patchy keratosis which is typically confined to the palms of the hands and the soles of the feet, and which appears to benefit from oestrin therapy.

"NIGHTMARE'S NEST"

LONDON SEEN AS AN INFERNO

It is commonly held that the habit of understating one's case is peculiarly a British, even an English, monopoly. If it is primarily, as some contend, an affectation or a piece of illogical hypocrisy, it is so extraordinarily effective that it has become almost part and parcel of the English method of conducting controversy. But it does not appeal to everybody, and conspicuously not to Mr. Robert Sinclair, whose savage attack on London, Londoners, and London government, entitled *Metropolitan Man*,¹ overstates so grossly and unfairly what might (or might not) have been a good case, if it had been put with moderation, that it is bound to have an effect exactly opposite to that which its author may be assumed to have desired—that is, the general uplift of our social conditions. After 323 pages packed with choice and savage invective against London and everything connected with it, including politicians of all parties, he concludes with a note to the reader in which he claims that his book is "not intended to be a vehicle of opinion," that his presentation of statistics is "common-sense arithmetic," and that his virtue lies in the disinterment from Blue Books and similar publications of guaranteed "facts."

The sensationalism and the violence of Mr. Sinclair's criticisms, the long list of sources (given at the end of the book) from which his statistics have been derived, and the implied failure of preventive medicine to remedy the dreadful state of public health in London will probably lead thoughtful laymen to ask members of the medical profession whether Mr. Sinclair is right or wrong, or perhaps how far he is right and how far he is wrong. It is therefore advisable that some critical examination of the statistics presented should be made in order that doctors may be able to assist the layman on such points. It is not enough to say that Mr. Sinclair is a sensation-mongering pessimist, deliberately shutting his eyes to everything that is good, ignoring purposely (as he himself confesses, on page 20, that he does) the great and steady improvements of the last two or three generations, and twisting facts and statistics to suit his preconceived ideas and prejudices. It is necessary to see where and how he has erred in arriving at conclusions which to anyone who knows London are so obviously fantastic.

Tuberculosis in the Metropolis

No better illustration can be selected, perhaps, than his treatment of the tuberculosis figures for London. Everyone knows that for sixty years past tuberculosis has been a steadily declining disease, and that its control is in fact one of the "high spots" of preventive medicine. Readers of *Metropolitan Man* might well conclude that the exact contrary is the case; for Mr. Sinclair, out of the masses of statistics at his disposal, picks out for

his sole quotation the (indisputable) fact that in 1930 there was a definite and considerable increase in the mortality rate from tuberculosis amongst females in the 15 to 25 years age group, and makes great play with this regrettable and unexplained occurrence. It is therefore a matter of public interest and public concern to state quite definitely that since 1930 the rates of this particular group have declined, as in all other groups they have been for fifty or sixty years declining, and to put down in black and white the broad facts about tuberculosis as a whole. The death rate in London from tuberculosis—all forms, not pulmonary tuberculosis alone—has been as follows:

1891-1895, yearly average per 1,000 living,	2.63
1896-1900 " " " "	2.44
1901-1905 " " " "	2.15
1906-1910 " " " "	1.87
1911-1915 " " " "	1.78
1916-1920 " " " "	1.77
1921-1925 " " " "	1.20
1926-1927 " " " "	1.06
1933 " " " "	0.93
1934 " " " "	0.87
1935 " " " "	0.79

But not a line or a word of Mr. Sinclair's would lead any reader to suspect that progress on this astonishing scale has been and is being achieved by the people he spends his time in abusing. As for his particular age and sex group, the L.C.C. reports show that in 1930 there were 1,229 notifications—the deaths are not given separately every year—and that in 1934 there were in the same group 1,060 notifications; in 1935 967 notifications; and in 1936, 931 notifications. In connexion with tuberculosis in children he has bitter and burning words to say about the maiming and crippling brought about by the surgical forms of the disease; but he does not tell his readers that whereas fifteen years ago the distribution of Lord Mayor Treloar's Christmas hampers for cripples involved picking and choosing among the applicants, nowadays there are not enough cripples to go round; nor does he quote the figures that he might have got from one of the actual documents which (in this connexion) he quotes—namely, that tuberculosis in children caused 10,637 deaths in England in 1914 and 6,053 in 1924.

More "Common-sense Arithmetic"

When Mr. Sinclair ventures on prophecy he is, of course, less amenable to criticism—anyone can prophesy, and no one can say for many years whether the prophecy is right or wrong. In London there were in 1935 575 cases of suicide: Mr. Sinclair's handling of this figure is to commit himself to the statement, emphasized in bold type on the dust wrapper, that "ninety thousand future suicides are walking the streets of London to-day." It is not unfair to say that if his prophetic powers are on a par with this "common-sense arithmetic" no one need pay much attention to his anticipations. Elsewhere he proceeds to examine maternal mortality, which he says has "grown worse" in the last twelve years: here, too, it is profitable to study the actual London figures, which are as follows: 1924, 3.08 per thousand births; 1925, 3.19; 1926, 3.35; 1927, 2.91; 1928, 3.59; 1929, 3.61; 1930, 3.33; 1931, 3.81; 1932, 2.99; 1933, 3.66; 1934, 2.80; 1935, 2.58 (the lowest on record).^{*} He further names four Continental countries where the figures are stated to be lower; but he does not say whether, as in London, the statistics include deaths from abortion, which very heavily weight the figures in this country.

On the nutrition of school children his presentation is equally untrustworthy. He says that fewer than 1 in 6 of London children "appear to be adequately nourished," and that 5.7 per cent. are definitely undernourished. This is an interpretation of the Board of Education reports which in our judgement distorts the facts and the truth. The actual number of really and incontrovertibly under-

^{*} The provisional approximate figure for 1936, supplied by courtesy of the M.O.H. for London, is 2.03.

¹ *Metropolitan Man. The Future of the English.* By Robert Sinclair. (Pp. 365. 10s. 6d. net.) London: G. Allen and Unwin. 1937.