The Fate of the Nontreated Postmenopausal Woman: A Plea for the Maintenance of Adequate Estrogen from Puberty to the Grave

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The unpalatable truth must be faced that all postmenopausal women are castrates. There is a variation in degree but not in fact. Men do not live as long as the so-called weaker sex. However, they age, if free from serious disease, in a proportional manner. The pituitary-adrenal axis and thyroid are relatively intact until very old age. The gonads fade gradually, but there is no sudden shutdown. Hamburger (1) measured colorimetrically the total urinary neutral 17-ketosteroid excretion in men. He found a gradual decline with advancing years, the excretion between the ages of 30 and 90 years declining from about 15 mg. to 4 mg. per twenty-four hours. With his co-workers (2) he also determined the 24-hour urinary androgen excretion of men between 30 and 80 years of age, using the capon’s comb method. The curve showed a very gradual decline. This absence of a sudden decrease is evidence against the existence of a true male climacterium. The results of other investigators (3) agree closely. From a practical point of view, a man remains a man until the end. The situation with a woman is very different. Her ovaries become inadequate relatively early in life. She is the only mammal who cannot continue to reproduce after middle age.

The ovary of the young girl produces small but increasing amounts of estrogen for several years before puberty. This estrogen helps to control bone growth and develop body contours, but essentially the young girl is of a neuter gender. At puberty, in response to considerably larger amounts of follicle-stimulating hormone (FSH), the ovary produces increased quantities of estrogen and the girl becomes a woman. (Ovulation may not occur for two to three years.) Altered body contours, breast development and hair distribution are now distinctly apparent. The most dramatic changes are seen in the growth of the uterus, tubes and ovaries, and the maturation of the vagina. The vagina changes from a poorly distensible, thinly lined canal, susceptible to infection, to the adult form. These and other numerous changes of psyche and soma are due to the presence in the blood of steroid compounds known as estrogens. For convenience, we shall consider them under the single word estrogen. The best known are: estrone, estriol and estradiol-17β, sometimes called the “classical estrogens” because they were the first ones isolated and identified in the urine of pregnant women. Since 1953 seven compounds structurally related to them have been isolated from pregnancy urine. Recently Smith, Smith and Gavian (4) have reported 6 to 7 more new compounds.

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The pure follicular hormone is \( \beta \)-estradiol. It is metabolized to many products such as estrone, estriol and other compounds. They are excreted in the urine and to some extent in the bile. Because they all produce epithelial changes in the genital tract that are characteristic of estrus, they are called collectively estrogens. Estrogen is also produced by the adrenals and by conversion of other steroids in the liver. It is found in some foods, especially fish and hops. Without ovarian production the total amount is completely inadequate. Estrogen production under varying circumstances is shown in Figure 1.

During each month the estrogen level rises steadily and is highest before ovulation. It then drops considerably, rising during the luteal phase, and is again high before menstruation. Then a sharp drop of at least 50 per cent occurs, and this loss of estrogenic support partly accounts for the shedding of the endometrium. Studies on blood and urine have shown average monthly levels to be highest between the ages of 15 and 20 years; there is a decline to very low levels at age 60 (Table 1). This deprivation markedly impairs homeostasis. We no longer have the "whole woman"—only the "part woman."

The steep decline in estrogen excretion with the onset of the menopause is shown by the observations of Pedersen-Bjergaard and Tonnesen (5) on 360 women. That gonadal failure is dramatic was further verified in 1958 by Paulsen

![Fig. 1. Estimates of the approximate amount of estrogen produced by the nonpregnant human female under different conditions. (Courtesy of the Excerpta-Medica Foundation of Amsterdam and New York.)](image)

<table>
<thead>
<tr>
<th>Age (yrs.)</th>
<th>Total Estrogens (r.u./24 hrs.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-20</td>
<td>38.2</td>
</tr>
<tr>
<td>30-39</td>
<td>38.9</td>
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<tr>
<td>40-49</td>
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<td>10.8</td>
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<td>0.7</td>
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<tr>
<td>70-79</td>
<td>7.3</td>
</tr>
<tr>
<td>80-96</td>
<td>0.7</td>
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* Pincus, quoted by Kirk (57).
TABLE 2

**Perinent Data Regarding Distorted Endocrine Integrity in Aging Women**

1. The pituitary gland is remarkably stable from ages 20 through 80. Its gross weight and cytology are relatively constant (38, 59).
2. The thyroid is well maintained, with only a very slow decline in the serum concentration of organic iodine. There is also a gradual but very slow decline with age in the oxygen consumption calculated per sq. m. of body surface. The concentration of circulating thyroid hormone is probably not altered by age (60, 61).
3. Laboratory data show that there is no alteration in 11-oxysteroid levels with advancing years. Injections of adrenaline affect the eosinophil count in the same manner as in the very young. There is no evidence that age substantially impairs the adrenal glands (62, 63).
4. The parathyroid glands are very resistant to changes associated with aging (64).
5. Pancreatic function shows a high degree of correlation with the changes of age. (In 50 per cent of older people the glucose tolerance curve is of the diabetic type.) (27, 65).
6. The average urinary estrogen excretion of regularly menstruating women is 2.29 µg. per 24 hours; that of postmenopausal women is only \(\frac{1}{3}\) of this amount—0.35 µg. per 24 hours (6).

*et al.* (6). They found the average 24-hour urinary estrogen excretion of regularly menstruating women to be 2.29 µg., whereas that of 51 postmenopausal women was only 0.35 µg. Stoll (7) studied 516 apparently normal women who were two years or more past the menopause and found that in only 18.2 per cent did the vaginal smears indicate estrogen; 50 per cent had androgenic smears, and 27 per cent atrophic smears; in 4.5 per cent the status was undetermined.

Apparently 10 to 15 per cent of women have a fairly good level of estrogen until even age 60 (8) but a rapid decline then occurs. The other 85 to 90 per cent of women become castrates earlier and must continue to live in this state. Many live for a longer period without active ovaries than with them. It is in this rapid failure of gonadal function that women differ markedly from men. They do not age proportionately; the aging process is distorted (Table 2).

Masters (9) considers the ovaries to be the Achilles heel of the woman's body. The aging ovary appears phylogenetically unable to respond to even very high levels of FSH. Morphologically it becomes small and hard, and is often a source of amazement to the medical neophyte. Microscopically, all ova disappear within two to three years after the menopause. There is loss of fluid and dense fibrosis of the stroma. Other elements of the genital tract can be rejuvenated—but not the ovary, even in the slightest degree.

**SERIOUS CONSEQUENCES OF A DRASTIC DECLINE IN BODY ESTROGEN**

The consequences of estrogen lack are primarily medical rather than gynecologic. They are of special interest to the internist, general practitioner, geriatrician and orthopedist.

**Negative nitrogen balance**

Estrogen favors improvement in cell permeability (10). It is concerned with such factors as micronutrients, cardiovascular and other enzymes (11), glucose, electrolytes and water balance (12). It is essential for anabolism and nitrogen
Retention (13). Loss of estrogen results in a negative nitrogen balance, with its multiple consequences. All muscle cells, particularly the voluntary ones, lose their strength. The remaining cells are smaller and there is much replacement with fibrous tissue, associated with weakness and stiffening of muscles and ligaments. Thus, to the muscle weakness of physiologic aging is added the loss of weight and energy due to estrogen deprivation. Every effort should be made to change this negative nitrogen balance to a positive one.

Hypercholesteremia

During the menstrual cycle, circulating cholesterol and beta-lipoprotein levels fall when the estrogen concentration rises, and rise when the estrogen concentration falls (14). Administration of estrogen lowers elevated serum lipid levels (15). Coronary atherosclerosis is 10 to 40 times more common in young men than in young women (16). This premenopausal protection is not present in bilaterally oophorectomized women (17). Coronary lesions in chickens, induced by high cholesterol feedings, can be reversed by administration of estrogen (18). Women gradually lose their favorable protected status after the menopause; thus the incidence of coronary heart disease associated with hypercholesteremia becomes comparable with that for men of a similar age. Estrogen can change abnormal concentrations of cholesterol (even in men) to a more favorable level, and decrease the amount of coronary insufficiency and atherosclerosis (15, 19, 20). Recent controlled studies show that the lives of men and women with previous coronary atherosclerosis can be significantly lengthened by estrogen administration (15, 20). There seem to be compelling reasons why the beneficial protective effect of estrogen should be continued postmenopausally.

Hypertension

Recent experimental data strongly suggest a connection between the development of hypertension and the decline of ovarian function. Stamler (21) cites the following supporting evidence: hypertension is more common in young men than in young women but after 40 the reverse is true; estrogens induce acute vasodilation in rabbits, rats and men; estrogens inhibit experimentally produced hypertension induced by adrenal corticosteroids in both cockerels and hens.

Davis, Jones and Jarolim (22) recently reported on their study of long-term estrogen substitution and atherosclerosis. They found that the incidence of abnormal electrocardiograms was lower for hormonally treated castrates than for untreated women, whether naturally postmenopausal or oophorectomized. Also, when ten or more years had elapsed since the menopause or operation, the incidence of hypertension was lower in the treated women. These authors concluded: "The sporadic administration of estrogens for the relief of menopausal symptoms is widely used. Their long-term administration is important in the retardation of atrophic changes in the reproductive organs and throughout the body. Their most important role, however, may be their use to retard atherosclerosis and its serious sequelae. This area of prophylactic therapy must be explored more widely in the hope that women may retain good health in their advancing years."
Osteoporosis

This insidious, often overlooked, and sometimes crippling disease is the eventual fate of practically all women past 50 years of age (23). The previously mentioned nitrogen deficiency results in a decreased production of bone matrix, which is protein in nature. The osteoblastic cells are under direct estrogen control. The more estrogen, the more osteoblastic activity. Osteoclasts, however, are not affected by estrogen. So not only is there less matrix due to lack of protein and impaired osteoblastic activity, but there is excessive destruction due to the continuous osteoclastic activity. Usually a deficiency of calcium and phosphorus is observed because lack of estrogen also causes a negative balance of these minerals and excess amounts are found in the urine. Even when sufficient amounts of calcium and phosphorus are present, there is not sufficient matrix in which they can be deposited. The bones are lighter, thinner and contain less calcium. However, more than 40 per cent of calcium must be lost before the lack can be demonstrated clearly on x-ray films. Such bones break or collapse more easily, and the broken hips of elderly women are largely due to this condition. Fractures of the wrists, humerus and ribs after mild trauma are frequently seen. There is a progressive loss of height (1 to 5 inches) which may be accompanied or caused by compression and fracturing of individual vertebrae (24). The vertebral changes are clearly shown by x-ray examination. Of particular interest is the dorsal kyphosis (dowager’s hump, Fig. 2) which results from the preceding

![Figure 2](image.jpg)

**Fig. 2.** Woman showing some of the stigmata of “Nature’s defeminization.” The general stiffness of muscles and ligaments, the “dowager’s hump” and the “negativistic” expression are part of a picture usually attributed to age alone. Some of these women exhibit signs and symptoms similar to those in the early stages of Parkinson’s disease. They exist rather than live.
degenerative changes plus weak, stiff ligaments. Almost all estrogen-deficient women after age 50 show this defect. It is one of the earlier signs of osteoporosis. Low backache is the most common symptom, and 90 per cent of cases respond remarkably in a few weeks to large doses of estrogen. Reversal of the bone changes is difficult to show roentgenographically, as the deposition of additional bone matrix must reach at least 40 per cent before it is demonstrable. Neurologic symptoms are not common. Treatment of older women by estrogen and androgen should be considered. Younger women should have estrogen only. Certainly prevention is much easier than cure.

Menopausal arthropathies

The etiology of these disorders and their accompanying arthralgias is not satisfactorily understood, but it is important to remember that Heberden’s nodes are found ten times more often in females than in males, and that the shoulder-arm syndrome is a prominent feature of the postmenopausal state. Jeffcoate (25) has written that “whilst the ordinary methods of treatment should not be omitted in such cases, oestrogenic hormone therapy is most useful and the results are often dramatic.” Cohen and his associates (26) conclude “that this form of treatment has a definite place in the treatment of such cases of atrophic arthritis.”

Impairment of carbohydrate metabolism

Estrogen helps to mobilize and distribute glucose by acting upon two carbohydrate enzymes, hexokinase and glucokinase. Somewhat like insulin, it stimulates both energy production and glycogen deposit. A deficiency of estrogen is bound to have unfavorable effects on the individual cell. These effects are subtle and difficult to evaluate. The lack of an inhibiting estrogenic influence on the pituitary probably accounts for the increased incidence of diabetes at the time of the menopause (27). Clinically, estrogen is employed to provide added protection in postmenopausal diabetes (28).

Psychic manifestations

The occurrence of depression in women not previously subject thereto, is fairly frequent at the menopause. In mild and moderately severe cases estrogen is almost a specific, improvement frequently ensuing in a matter of days (29, 30). We have also seen worthwhile results in mild and moderately severe involutional melancholia, but only rarely in the severe type. If time and circumstances permit, there is much to gain from establishing vaginal cell cornification before commencing shock therapy or other radical treatment. Dynes (31) urges that “every patient with involutional melancholia should be given a trial.”

Menopausal negativism

A large percentage of women who escape severe depression or melancholia acquire a vapid cow-like feeling called a “negative state.” It is a strange endogenous misery. The late Dr. Malleson (32) wrote extensively about it. She showed
that such people react poorly to pleasant stimuli, yet do not sink to great depths of depression. The world appears as through a grey veil, and they live as docile harmless creatures missing most of life's values. If untreated, this leads to permanent negativism. The observer must first be alerted to the possibility of such a state or it may pass unnoticed. Once aware of it, he sees it all around him—a problem of vast proportions.

Effects on skin and mucous membranes

When there is lack of estrogen the skin becomes tough, dry, scaly and inelastic. The processes of keratinization may be abnormal. At times there are complaints of pruritis and formication. Striking histologic regenerative changes in the atrophic skin of aged women may occur during estrogen therapy administered locally, systemically or by both routes. These changes include improved tissue hydration, improved blood circulation and restoration of elasticity (33, 34). Estrogen has also been reported to be effective in lesions of the mucous membranes, such as kerato-conjunctivitis sicci, atrophic rhinitis and atrophy of the buccal and gingival mucosa (34, 35).

Other endocrine disorders

The level of follicle-stimulating hormone (FSH) rises as much as 50 times the normal range (36). There is an increase in luteinizing hormone (LH) and luteotrophic hormone (LTH). The master gland, the pituitary, is influenced by certain neurosecretions released from the hypothalamus into the hypophysial portal system to aid in regulating the secretory activity of the anterior lobe cells. Whenever the pituitary gland becomes disturbed by these neurosecretions, or by lack of estrogen, or by any other factor, a complex crisis occurs since the pituitary exercises stimulatory influence on other glands such as the thyroid and the adrenals. Masters (37) believes that castration results in excessive production of thyrotropic and adrenotropic as well as gonadotropic hormone. Solez (38) suggests that the decreased activity of the gonads is associated with increased corticotropic and adrenocortical activity. He also points out that in Cushing's syndrome (with its diabetes, hypertension, arteriosclerosis, facial hirsutism, obesity and muscle weakness) the disease occurs explosively, whereas in the aging female similar changes occur over a period of decades. In the case of estrogen, the more sudden and complete the deprivation, the worse the crisis. In severe cases the endocrine system is in a state of chaos.

Imbalance of the nervous systems

The ductless glands exercise varying degrees of influence on the central or voluntary nervous system (including the hypothalamus) and the autonomic or involuntary nervous system. Although they are interrelated, the autonomic nervous system is seemingly more disturbed, for it is the nervous network which, in conjunction with the autonomic nuclei of the brain, controls the vital life processes of the organism over which there is no voluntary control.

Among physiologic activities under autonomic control are the emotions (to a
great extent) and the sense of physical and mental well-being; also the cardiac
and respiratory rhythms, the digestion of various foods, and the marvelous
chemical reactions which occur in the liver.

As a result of the functional disturbance of the ovaries and interrelated glands
and the imbalance of the nervous systems, there is a multiplicity of subjective
symptoms. Treatment of these symptoms is unsatisfactory. They should be
packaged together, to be cured by treating their common cause.

**Summary and genital changes**

Afflictions resulting from changes in these target areas can be a source of much
discomfort, unhappiness and misery.

The breasts, deprived of estrogen, become flabby and atrophic. The lack of
firmness is mostly due to atrophy of the ductal system, but the absence of
progesterone causes loss of perilobular and alveolar tissue in addition. The total
decrease in size depends upon the amount of parenchymatous tissue. The nipples
become flat and nonerecile.

Studies have been and are being made with radioactive estrogens, such as
$17\beta$-estradiol-16-$\text{C}^{34}$ and estrone-16-$\text{C}^{34}$ sulphate, to determine among other
things whether or not estrogens quickly and completely become localized in
target organs (such as the breast) or act only by tripping an enzymatic switch
as they pass through the cells of these organs. The small amount of evidence
available favors the first concept (39).

Fat is reabsorbed from the pubic area and the vulva. The labia eventually
almost disappear. There is gradual thinning of the pubic and axillary hair. The
ovaries become very small, the tubes become thread-like, and the uterus reverts
to prepubertal size. The uterine endometrium shares in the atrophy, as does the
cervix. The vagina loses its distensibility, and becomes shorter and increasingly
friable. The mucosa becomes thin, pink and sometimes hemorrhagic, due to the
poor protective support of the blood vessels (senile vaginitis). The vaginal smear
shows the cells to be almost entirely parabasal, i.e., small rounded cells with
large active nuclei. These parabasal cells have much significance when esti­
mat ing and treating estrogen deficiency on the basis of the vaginal smear. There
is a preponderance of red blood cells, leukocytes and detritus. The pH of the
vagina is increased. Glycogen globules disappear and there are no Doderlein's
bacilli. Such a mucosa is susceptible to infection. There may be simple senile
vaginitis with its adhesions and irritating discharge or the more troublesome and
concomitant infections with trichomonads or fungi. Pruritis vulvae is common.
For centuries it had been necessarily suffered in silence. The extent of the prob­
lem is partly measured by the large sale of hydrocortisone sprays, suppositories,
ointments and allied preparations. The thickened, cracked, degenerated areas
may progress to disorders such as kraurosis, or even cancer. It is generally ac­
nowledged that the pathologic lesions and the complaints are almost entirely
the result of declining ovarian function. Estrogen cream, ointments and sup­
positories are curative. It is possible to regenerate all of the genital tissues except
the ovaries. An atrophic mucosa can be restored so that the cells exhibit adequate
cornification, in less than a month. Menstrual shedding can be revived at any age, even in the woman who has not bled for twenty or more years.

COMMENT

In the Roman Empire, life expectancy was about 23 years. There were very few old women. Life expectancy in the fourteenth century was about 33 years. At the turn of this century it had risen to 48 years, but older women did not yet constitute a problem.

For well known reasons there has been a recent and marked increase in life expectancy, so that a boy born today has an expectancy of 68.5 years and a girl 75.1 (40). The projected figures for 1970 are 70.3 and 77.8 respectively (40). The same author estimates that 86.3 per cent of white female babies born in 1970 will live past the age of 65. This indicates the magnitude of the problem. In 1975 it is expected that in the United States there will be 40 per cent more women than men (41). The civilized world is becoming full of women past age 50. Such women were once considered old. Today, however, a large part of their lives is ahead of them, for many will live into their 80's or longer. Unfortunately, although women live longer than men, a greater proportion of them are chronically incapacitated after reaching 45 years of age (42).

Most elderly women in the past looked, felt, and acted old. Stiff, frail, bent, wrinkled and apathetic, they stumbled through their remaining years. The amount and variety of suffering was great. There was little or nothing to do for their skin cancers, osteoporosis, irritating leukorrhoeas, and cracked and bleeding vulvar tissues. It was all part of being old. If left to nature it still is part of being old, but most of this suffering can now be prevented and effectively treated. Formerly these women were not an economic factor but today they are rapidly becoming an important one.

Menopausal statistics are of almost no value. They barely touch the fringe of the problem. We all know women who are palpably suffering from the menopause. They bear it bravely, adjust as best they can, and never consult a physician about it. They consider it part of their life—they don’t become statistics. The more stable the woman and the more kindly life has treated her, the less she will complain, and vice versa. Although the psychic symptoms of the menopause are essentially exaggerations of the patient's former responses, the exaggerations, or swings, can be extreme. There is ample evidence that the course of history has been changed not only by the presence of estrogen, but by its absence. The untold misery of alcoholism, drug addiction, divorce and broken homes caused by these unstable, estrogen-starved women cannot be presented in statistical form.

DISCUSSION

Physical changes

At the time of the menopause a woman is likely to see her children leading their own lives. Her husband, at the height of his career, is preoccupied, less attentive and often not physically well. As anxiety regarding pregnancy fades,
the awaited new world of "sex without fear" may be poorly realized. She feels less useful and perhaps at times, in the way. She may have little or nothing creative to do. A common result is an anxious, irritable, unreasonable and quite frequently depressed woman. Although these factors are disturbing to most women, mental adjustment is not too difficult were it not for the physical changes. We have shown that the physical changes brought about by the abrupt decrease in estrogen and the general hormonal chaos are in addition to, and apart from, the almost imperceptible changes of chronologic aging.

There is a tendency to refer climacteric patients to the psychiatrist. This should not be done unless there is a history of premenopausal psychosis or severe neurosis, and even then these women require combined hormonal and psychiatric treatment.

Because of custom and lack of knowledge of these physical changes, their presence and importance may be overlooked even in those close to us. Yet once the veil is lifted, it is remarkable how quickly the previously uninitiated can detect these unfortunate women (Figs. 2 and 3). Our streets abound with them—walking stiffly in twos and threes, seeing little and observing less. It is not unusual to see an erect man of 75 vigorously striding along on the golf course, but never a woman of this age.

Before this moderately advanced stage is reached, the more intelligent woman instinctively knows that her loss of physical attractiveness is entirely out of proportion. She sees the marked skin changes, the disfiguring fat deposits, the

Fig. 3. Typical appearance of the desexed women found on our streets today. They pass unnoticed and, in turn, notice little.
atrophy of her breasts and the beginning disappearance of her external genitals. If married, an irritated or inadequate vagina may bring more unhappiness. All of this has a profound effect upon her psyche.

Let us reverse the situation regarding atrophy. Suppose the man of medicine noticed his own genitals gradually disappear year by year. Would he be as indifferent to genital atrophy as he now appears to be? We think not. His medicine closet would be well stocked with protective hormones.

Hormonal therapy

The hypogonadal woman of 20 or 30 years of age is not denied hormone augmentation. Fundamentally the postmenopausal hypogonadal woman of 60 or 70 years is little different—just older. Why should she be denied therapy? Who is to decide the age of denial? Substitution therapy excites no comment in thyroid, pancreatic and adrenal deficiencies. There is no age barrier.

Estrogen has been available to alleviate acute symptoms and to help during the so-called “period of adjustment.” Its prolonged unopposed use has frequently presented difficulties and problems. The recent availability of potent oral progestogens overcomes most of the objections to long-term estrogen therapy.

The vaginal smear is the only readily available and reasonably accurate method of clinically estimating estrogen levels. It is comparatively simple to adjust and improve the colpocytogram to a satisfactory standard. Symptoms persisting after a standard smear is attained are not due to estrogen deficiency. Other causes should be sought.

When correcting the cytogram 3 possibilities should be considered:

1) If the estrogen-deficient woman still menstruates regularly, an estrogen administered during the first twenty-one days of the cycle is effective. Available for hypodermic use is α-estradiol benzoate (Progynon-B); for oral administration, conjugated estrogens (Premarin).

2) If menstruation is irregular, one of the new progestogens such as medroxyprogesterone acetate (Provera) or norethynodrel (Enovid) administered from day 14 to day 25 (in addition to an estrogen) is corrective.

3) If the woman is postmenopausal, the progestogen will restart uterine bleeding in the properly primed patient. The principal object of such cyclic shedding is to prevent endometrial hyperplasia. The shedding need not necessarily be monthly.

The long-term administration of estrogen inevitably raises the following questions.

Is estrogen carcinogenic?

Although there is not a single proved case in the literature of estrogen inducing cancer in the human, several authorities in the field consider this a moot question.

1 Specific procedures for the elimination of the menopause are given in another article (43).

2 Certain concepts are briefly presented here. This question is considered in another
If estrogen be carcinogenic, malignancy of the breast should be frequently observed in pregnant women because the estrogen level rises to great heights, especially in the later months. However, breast cancer is rare in pregnancy and lactation, occurring only about 3 times per 10,000 pregnancies (45). In the few cases reported, some of the tumors may well have antedated the pregnancy.

The incidence of cancer of all sites in women shows a constant increase with age; at the same time the production of estrogen steadily declines. (High level of estrogen in youth—low incidence of cancer; low level of estrogen in old age—high incidence of cancer.) As these are irrefutable facts, it is against all logic to consider estrogen a direct cause of cancer. It is this barrier which the “dyed-in-the-wool” believer of the estrogen menace cannot explain and persistently refuses to face.

Recently there has been a swing of the pendulum in the other direction. Studies, published and to be published (44, 46–56), indicate that estrogen and progesterone may be prophylactic in relation to breast and genital cancer. However, until this is further clarified, estrogen should not be administered without adequate consultation regarding the patient who has, or has had, cancer.

Cancer of the breast and genitalia appears to be a complex problem of subtle relationships between the pituitary, adrenals and gonads, with metabolic and hereditary factors prominent and a viral or other unknown causative agent in the background. Estrogen is just one of the many actors in the drama.

Androgen therapy?

It has no place in prolonged treatment of the premenopausal and menopausal patient because a relative androgenicity already exists. Increased adrenal stimulation caused by uninhibited concomitant pituitary hormones increases this androgenicity and results in such manifestations as hirsutism and voice changes. Eventually the 24-hour urinary excretion of androgen declines from a high of 18 international units at age 30 to a low of 2.6 units at age 80 (57). When androgen production is unduly low in old age, supplementation is of value, particularly for anabolic reasons.

Duration of treatment?

A beneficial estrogen level should be continued throughout life. The duration of maintenance with a progestational component will vary considerably. Such treatment should be abandoned in the uncooperative, the feeble, and the seriously ill lest it become an absurdity. An androgen preparation is substituted.

article (44). The present paper and the other 2 studies are advisable as a reference for the successful long-term administration of estrogen.

A: Ovulation—peak
B: Luteal—maximum
C: Menstrual—minimum
D: Following ovarian irradiation (premenopausal)
E: Following bilateral oophorectomy (premenopausal)
F: Following bilateral oophorectomy and adrenalectomy
G: POSTMENOPAUSAL WOMEN
H: Cortisone-treated women
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Development of tolerance?

In general, the active intelligent woman in the professions, business or the arts requires more estrogen than the woman leading a less challenging existence. A few require high dosage, as judged by the vaginal smear. Estrogen is chiefly metabolized in the liver, but the large amount utilized by highly stressed women would indicate its destruction in other areas. Progesterone requirements do not vary to any significant degree.

Interference with nature?

This point of view is frequent among the laity. It is parried by illustrating the interferences with nature as found in our civilization. Examples are numerous in medicine.

Estrogen addiction?

This is occasionally mentioned in the literature. Estrogen is so much a part of woman’s cellular metabolism that if by craving estrogen she is considered an addict, logically she is also an addict regarding such elements as water, salt and sugar.

CONCLUSIONS

Estrogen, which transforms the prepubertal girl into the mature woman, plays a cruel trick in disappearing so early in her life, since her destiny is closely intertwined with it.

In the past, so-called mental “adjustment” to the “change of life” was necessary. There was no choice. Without such adjustment, the ensuing years were hardly endurable. Today there are three choices: 1) make the best possible adjustment, 2) postpone the adjustment, or 3) avoid the necessity. Once aware of these choices, it is reasonably certain that most women will not choose either adjustment or postponement. Instead, they will elect to avoid their probable fate—hypertension, arteriosclerosis, flabby breasts, dowager’s hump, and atrophic genitals.

Three things are virtually lacking in the untreated postmenopausal woman: ova, estrogen and progesterone. Ova cannot be purchased, but the two steroids can; lifelong substitution therapy is simply a matter of “know-how.” There is great need for the reorientation of almost every man and woman in the civilized world.

REFERENCES


42. National Health Survey: Chronic ills limit mobility of 4,850,000 in U. S., New Medical Materia 2: 48 (Jan.) 1960.
43. Wilson, R. A.; Hagnstrom, H. T., and Brevetti, R. E.: Specific procedures for the eradication of the menopause. (Submitted for publication.)
56. Varga, A., and Henriksen, E.: Clinical and histopathologic evaluation of the effect
57. KIRK, J. E.: Steroid hormones and aging: a review, J. Gerontol. 6: 253-262 (July) 1951.
64. BLUMENTHAL, H. T.: Aging processes in the endocrine glands of various strains of normal mice; relationship of hypophyseal activity to aging changes in other endocrine glands, J. Gerontol. 10: 253-267 (July) 1955.