Loss of female hormones after menopause: Effects and implications

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Loss of Female Hormones after Menopause:
Effects and Implications

By

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Exhibit Design and Construction Information with Illustrations
Exhibit Design and Construction Information

The goal of my visual thesis was to create an exhibit for the lay person with the specific purpose of clarifying and elucidating the impact that the loss of female hormone production has on many organs of the body, and the implications this loss has on quality of life for the individual. I also wanted to include some simple anatomy and physiology lessons about hormone synthesis and release.

I devoted a great deal of time to choosing, discarding, rearranging, designing and redesigning my exhibit. Repeated conferences with my advisors, Professor Wabnitz and Professor Hintz were essential to the evolution of the exhibit design as well as to the practical construction details. Several meetings with Professor Thompson of the Industrial Design Department proved invaluable as well, and in a few hours I felt I had obtained a mini course in exhibit production and feasibility.

After a great deal of revision I produced five miniature panels, 4 inches wide by 7 3/4 inches high. I finally achieved a reduced scale finished product which was a faithful rendition of the proposed exhibit. Drawings, color scheme and type size and style had to be exactly right because I would be constructing the actual panels at home. I would be on my own, with no consultations with my advisors and no time to redo mistakes!

I decided to use 3/16 inch foam core board for construction of the finished panels because although it is
fragile, it is very lightweight! After some practical consideration such as measuring the cargo space of my station wagon, I decided on a finished panel size of 32 inches wide by 72 inches tall. This made the size ratio of mock up to finished piece 1 to 8. Therefore, 1 inch equaled 8 inches, 1/2 inch equaled 4 inches, etc. Then it was easy to make a grid system out of tracing paper to enlarge my small sketches to fit the finished format. I also utilized enlarged xeroxed reproductions of pre-existing drawings of the brain and vertebral column and tailored them to my use - a big time saver!

To prepare the 3/16 inch foam board to accept paint without warping, I brushed on three coats of Minwax clear satin finish polyurethane on the right sides of the background and cut out pieces of foam core board, allowing drying time between layers. I didn't find it necessary to apply polyurethane to the undersides, as long as I did not paint them. After the polyurethane dried, I used Mantrose Haeuser ready patch spackling to finish all visible edges, and sanded them smooth after the spackling had dried. Then I was ready to paint all pieces. I used regular flat latex wall paint. It was inexpensive and afforded me a huge color selection. I did find that even after I had carefully selected my colors from the custom mix color cards it was necessary to ask for small quantities of the base colors in the mixes, as machine blended colors can vary from the sample, and correction was needed. I also used acrylic paints for some details.
I needed to reproduce several photographs in a greatly enlarged dot pattern, which required that a negative be made of my small photographs and a screen be used to produce the desired effect. In dealing with production printers it was necessary to be extremely specific about the finished product desired, even to the degree of counting the dots per inch of the reproduction, and what type of paper would be used. I learned to take nothing for granted!

I used several brands of instant type, and I would recommend planning well in advance exactly how many sheets of what type of lettering are needed, because some brands of type provide more of a specific letter than others. There is also a big price difference between instant lettering brands.

As construction evolved, I used Elmers school glue to bond the components of each panel together. After applying the glue, I stacked heavy books on the panel to hold the pieces together for several hours at least, and overnight if possible. I attempted to complete each part of a panel before I glued the portions of that panel together. This took careful planning, especially in reference to applying the type correctly, but it was worth it because it was much easier to work on small pieces and then assemble them as a final step.

It was exciting to complete each step in the building process and finally realize the goal I had worked for so long to achieve!
Loss of Female Hormones after Menopause:
Effects and Implications
In fact the role of women and the attitudes toward them have changed more in the past hundred years than in the previous thousand. ¹

Changes – change of status, change of expectation, change of life – women today are pioneers. The female student, the young mother, the mature woman, and the elderly woman of today are truly innovators, living in a time of revolutionary upheaval, where there are no comforting traditions of expectations and roles. They are unquestionably breaking new ground.

For the student selecting courses and considering vocations there is the realization that her choice will be a life long career. In all probability it will not be preparation for a stop gap job until marriage and motherhood intervene; it will not be just a supplement to her husband's income; nor will it be an "insurance policy" in case of widowhood. It will be for life. The young mother of today no longer leaves the job world. Chances are that she will remain in the workforce until retirement age. The mature woman faces the challenge of making health decisions at menopause which will help insure that her longer life expectancy will be productively used and enjoyed. The elderly woman is faced with her own set of choices. Never before has medical technology created so many options for advanced life support treatment. There may well be life and

death choices which will be hers alone to make.

Women today must feel akin to the explorers of old, setting out to discover new worlds with very few stars to guide them! There is no authoritative evidence to count on - no "bible" to live by. They are bombarded with a bewildering array of conflicting advice. One expert proclaims that day care will encourage sociability and independence in her child; another insists that a mother must remain at home with her baby for at least the first three years, or that child could be irreparably damaged. Medical studies provide evidence that ingestion of large amounts of calcium will prevent osteoporosis in postmenopausal women. Then contrasting information is publicized stressing that replacement estrogen must be given to prevent that bone thinning disease. Coronary artery bypass surgery is promoted to prevent heart attacks. Then further studies proclaim that in most cases medication can produce the same results. Many consumer advocate organizations are questioning the appropriateness of employing artificial life support systems, including tube feeding to prolong life at any cost, while other groups caution that selective use of advanced technology sends us down the slippery slope towards euthanasia.

How can women come to terms with the challenge of making these new decisions? More and more in our better educated, more consumer oriented and self accentuated society, we will face the reality of becoming our own experts and the realization of
shouldering the burden of responsibility for the decisions we make. After all, we can almost always cite at least one scientific source somewhere to back up whatever position we wish to take!

Consequently, in this thesis it is not sufficient to solely present the facts on the effects of female hormone loss at menopause as we currently know them. There is a plethora of information already available on that subject. We must also explore the larger questions of what we will do with this information. What are our individual risks and benefits? How can we work with our doctors as partners to obtain the most accurate monitoring, and if needed, treatment for our hormone loss before damage is done?

In the very near future we will become an older society. It has been predicted that by the year 2030 the median age for Americans will be 42 and the median age at death will be 84 - both 11 years higher than present day figures. Since our worker pool will be aging, the trend toward early retirement will be reversed, and we will be on the job longer. We cannot afford to be robbed of our good health by diseases such as athrosclerosis or osteoporosis. We will be needed longer at our posts to pay into entitlement programs, plus there will not be enough younger replacement workers available to allow us to retire until later.

These trends have ramifications for ourselves as well as

2 "Face of a Nation Growing Older," Democrat and Chronicle, 12 December 1987, Sec. 3, p. 7
society. In order to understand and incorporate the basic findings about hormone loss and confidently become information gatherers, synthesizers, and utilizers we must assume a new role, that of equal partner with our physician in assessing our present health state, our future health risks, and what choices we will make at the menopause time of life.

Since woman's life expectancy has jumped from a median age of 44 years in 1887 to 79 years in 1987 and the average age of menopause, 51, has remained virtually the same during that time period, it is easy to see that we now can count on spending about one-third of our lives in a state of female hormone deficiency. If or until evolution "catches up" it is our responsibility to conscientiously monitor our own health status including degree of hormone loss and how it is affecting the organs of our body. We cannot afford any unpleasant "surprises" such as a broken hip or vertebral crush fractures that could have been prevented.

Gone are the days when the doctor's word was law - not even to be questioned. Your life is the only one you have. It is up to you to protect it and keep it healthy. Assertively researching and sharing in the decision making burden with our doctor is a new role for most women (and most doctors, too!). In order to come to terms with our new responsibilities and have confidence that we are equal to the task it is essential that we

3 Lewis Miller, The Life You Save (New York: William Morrow and Co., Inc. 1979), p. 21
interpret our past - what has happened in this short one hundred years. Our place in society has evolved so rapidly in such a quick timespan than we need to understand where we have come from in order to overcome our hesitancy about where we are going.
Prior to the late nineteenth century, fewer than 30% of females reached the menopausal age of 51 years, today, nearly 90% of women in the United States will experience menopause -- 4

That nineteenth century female remained in the home - her sanctuary, and also her isolation. Unless dire economic necessity drove her out into the workplace, a woman's life consisted of housework and family care.

In her book, Woman's Proper Place, Sheila Rothman identifies four major shifts in definition of woman's place from the post Civil War era to the present. Until 1900 the concept of virtuous womanhood prevailed. Women gradually emerged from the home, not to work, but to participate in womens groups such as the Women's Christian Temperance Union (WCTU) and the Young Woman's Christian Organization (YMCA). These groups initiated social reforms and attempted to impose middle class morals on lower classes - primarily immigrants. This stage led into the concept of educated motherhood and the idea of university training for young women. Public programs aimed at promoting the health and welfare of women and children were beginning to replace private charities, so women graduated to the next level of development - woman as wife-companion, which was to begin in the early 1920's and last through the 1950's, when the final concept, woman as person evolved.


The evolution of woman's maturation from virtuous womanhood to woman as person advanced as a steady progression. Certainly there were many women employed outside the home in 1900, but working was still only legitimate for a brief time before marriage. It was essentially a temporary state - certainly not a career!

Technology had freed the housewife from some of the backbreaking labor involved in running a home and family, but did not free her from the commitments and obligations of the home. Now woman had time to caretake and nurture outside the home. She expanded her skills into the community with the origin of the reform movement. Women's clubs were the school of the married woman. They were a mutual improvement society as well as an opportunity to bring about social improvement. Thus began organized female fellowship. This antidote to the isolation suffered by their mothers evolved into a powerful network of Mothers' Clubs - the National Congress of Mothers which later became the Parent Teachers Organization. Reform groups became the vehicle for woman's suffrage since the right to vote was won, not necessarily for equality, but to give women the power to effectively influence legislation for the improvement of child labor laws and other family reforms.

Educated motherhood became a way of integrating the concept of university education with the future expectation of motherhood. The number of women enrolled in colleges rose

6 Ibid., p. 65
dramatically after Mathew Vassar proved that a college education was not detrimental to a young girl's constitution. He devised a regimen of structured physical activity interspersed with study to counter warnings that excess mental strain would damage women's health. Vassar and other women's colleges did provide education for women, but did not encourage them to enter the business or professional worlds. The number of college educated women climbed from 85,000 in 1900 to 250,000 by 1920, but women still represented only 10% of physicians and 2% of lawyers. Coeds were offered a wide choice of social science courses, such as Bryn Mawr's "Charities and Corrections." Many undergraduates worked in settlement houses during vacations.

Women's social service coalitions were conducive in pushing through the passage of the Sheppard-Towner Act by congress in 1921. This, the first federally funded health care program for women and children, was implemented by women physicians, public health nurses, and social workers to provide prenatal care and well baby checkups. This act was instrumental in targeting the need for preventive medicine, which was soon recognized by physicians as a service that should come under their own professional auspices. By 1930 Sheppard-Towner was repealed and the General Practitioner had shifted his practice from the sickroom to the office to provide this care.

Many who discuss the Equal Rights Amendment struggle of

Ibid., p. 103
the 1970s do not realize that this amendment was first bitterly debated in the 1920s. The National Woman's Party pushed vigorously for full social and economic equality for women, but other factions of the suffrage coalition demanded protective legislation for the female worker. Those for protection prevailed, which was one factor in the tendency for women to remain in certain occupations such as teaching and office work.

As social reforms became more and more under government control, women entered a new era and assumed a new role, that of wife-companion. The revolutionary idea that woman's primary concern should not be mother to her child but fascinating partner to her husband was reflected in magazines, films of the day and the rise of the cosmetic industry. Woman now had to assume responsibility for keeping romance alive in marriage (a notion as modern as Marabel Morgan's The Total Woman.) "She still remained as home, but she moved from the nursery to the bedroom." At the college level, sorority house living superceded the settlement house dorm. One sorority objective was to train its members to be ideal wives and hostesses (another idea that persisted well into the 1950s, as the author can attest to!) This new wife-companion was not a reformer, she was more private, more self oriented. She was also interested in sex.

To Margaret Sanger, the concept of birth control (in the form of a diaphragm) was a panacea for all the problems of the

8 Ibid., p. 177
lower classes. She urged women's organizations to strive for the legalization of birth control devices as they had striven for suffrage, but she was unsuccessful in her endeavor. Many reformers would not publicly support birth control. They believed a woman's role "...was not to emulate the bestial male but to curb and refine him" - through lofty womanhood, not contraceptives!

Just as well baby care came under the sole auspices of doctors in the defeat of the Sheppard-Towner Act, so the original concept of the trained lay person or nurse dispensing birth control devices and information was unsuccessful and the duly licensed physician became the only one legally able to prescribe birth control (disease control). The middle class wife-companion eagerly adopted birth control devices, but because of the lack of public health clinic distribution, the lower classes were slow to benefit from contraceptives - the very people Margaret Sanger had targeted to help.

The ongoing development of the wife-companion was interrupted by the depression and World War II. The federal government began to fund day care centers in the 1930s - not to free women for careers, but to employ out of work teachers. Day care was still considered a last resort. This concept continued through World War II, even though women were going to work in unprecedented numbers. On one hand the government pleaded with women to contribute to the war effort through jobs, popular

9 Ibid., p. 198
opinion and literature of the day still frowned upon working mothers and chastised them for "parking" their children in day care centers.

After the war, men quickly replaced women in manufacturing jobs. "The war was not so much a transforming experience as an interruption, after which women returned to pursue an inherited role."  

Now the post war building boom produced new suburbs and new isolation for women. Between 1950 and 1960, the population in 225 major cities rose 8.7% and their suburbs, 47%. These new "bedroom communities" created a ghetto for women. Suburbia became fertile ground for Betty Friedan's classic story based on her 1942 Smith classmates as seen 15 years after graduation. "Is this all?" was the plaintive question asked by those for whom living through husband and children was not enough. That empty feeling would persist until woman was able to choose a satisfying career for herself.

Time saving household helpers such as freezers, dishwashers, dryers, no frost refrigerators, garbage disposals, self cleaning ovens, and no wax floors cut housework to a minimum. These advances combined with many other factors, not the lease of which was Enovid, the new "miracle" birth control

10 Ibid., p. 224
pill, culminated in the woman as person revoltion of the 1960s.

This liberated woman derived unexpected benefits from the civil rights movement. The drive for school desegregation instigated a major reevaluation of children's learning patterns, which would alter learning concepts for women and lead to the realization that social expectations were often self fulfilling prophecies.

Even as Betty Friedan was writing, more and more women were entering the labor force to find that satisfying career, and the composition of that labor force was undergoing a fundamental change - it was composed of married women with children. In 1948, mothers of preschool children made up 10% of all women workers; by 1974 1 out of every 3 mothers of preschoolers were at work.

Other factors, such as an all time low of 1.8 children per family, soaring divorce rates and revision of divorce laws encouraged women's headlong rush into the world of work. "Even infants were increasingly likely to have working mothers. As of 1985, nearly half of all women...who had a child in the preceeding 12 months were in the labor force."

When we consider that in 1890 a tiny minority of 4.6% of

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12 Rothman, Woman's Proper Place, p. 229
13 Ibid., p. 249
married women worked in the labor force compared to a majority of 56.1% in 1987 with all indications that this growth trend will continue, we realize that we must maximize woman's ability to participate fully in her work and fulfill her potential to be a healthy, independent and responsible contributor to society well past the menopausal age.

Consistent with these goals, the woman of today must reformulate her relationship with her health care professional to enter into an equal partnership, keep her own organized set of personal medical records (as there may be no all inclusive central file on her in this age of mobility and specialists), and take responsibility for keeping current on all routine tests such as pap smears and mammograms. All this will enable her and her clinician to search out the best health care plan for her as an individual, with the long term goal of preventing disability or any other roadblock to vigorous well being now and in the future.


Osteoporosis

Menopause is a natural event, but doctors in the United States developed, and some still perpetuate, the medical myth that menopausal women suffer a crisis of a "deficiency disease" for which treatment is needed.\(^{17}\)

The medical infirmities resulting from estrogen deprivation take a high toll among postmenopausal women. Nearly 200,000 hip fractures occur annually in this group, resulting in 15,000 deaths and a high morbidity rate.\(^{18}\)

These are but two of the many divergent opinions offered to us by experts in various health related fields. In conjunction with our role of informed consumers, we need to explore the nature of estrogen and progesterone loss and how it will affect us in the years ahead.

The word "menopause" actually refers to a specific event -- the last menstrual period. "Perimenopause" refers to the transitional time before and shortly after this event when ovarian function and its hormone production is declining. The ovary, with its components, primordial follicles and interstitial tissue, undergoes gradual loss of the follicles, which are the usual source of estrogen and progesterone, and gain of interstitial cells, which are a probable source of androgens. From a level of about half a million ovarian follicles in


childhood, the number of follicles declines until there are few remaining at menopause.

Before menopause, the major estrogenic hormone secreted by the ovaries, estradiol, is released at a rate of 0.05 to 0.3 mg per day into the systemic circulation. After menopause, the rate of estradiol secretion (produced, not by the ovaries, but from estrone, in adipose tissue) drops to 0.005 to 0.02 mg per day. Since estrogen receptors have been identified in many tissues of the body, including hypothalamus, endometrium, and vaginal epithelium, these tissues will be directly affected by the presence or absence of steroid hormones. Although no receptors have been found in osseous tissue, the loss of estrogen has a very definite effect on bone resorption.

Bone remodeling, the cycle of resorption and formation of trabecular and cortical bone, is maintained in delicate balance. Until early adulthood both males and females produce more new bone tissue at a higher rate than is broken down. Bone mass reaches its peak at about age 30 to 35. For women after either

19 Stuart Campbell, ed., The Management of the Menopause and Postmenopausal Years (Maryland: The University Park Press, 1976), p. 15


natural or surgical menopause, trabecular bone may be lost at the rate of 5% annually, but then levels off at about age 65. By the time she is 80, a woman will have lost about half her trabecular bone, a man only 14%. At menopause the rate of cortical bone depletion increases somewhat, but does not reach a plateau at age 65. Cortical bone loss continues for the rest of life.

Osteoporosis is the consequence of bone resorption progressing at a faster rate than new formation, but that bone is essentially normal - there is just less of it. Scientists usually classify osteoporosis into two major syndromes: type I, postmenopausal osteoporosis and type II, age related bone loss that can affect both men and women.

Bone loss is most severe 5 to 6 years after menopause, and the more porous trabecular bone succumbs before the dense cortical bone. Thus, bones rich in trabecular bone and/or responsible for weight bearing are prime targets for fracture. The vertebrae, which are composed of 65% trabecular and 35% cortical bone are often the first to show signs of osteoporosis. The affected vertebrae, usually between the midthoracic and upper lumber segments, become biconcave, then collapse to form wedge fractures. The posterior vertebral height is usually maintained while the anterior portion is crushed. If several collapse, many vertebrae may compress together and cause the rib cage to tilt downward to produce kyphosis, or "dowager's

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hump." Eventually a woman can lose up to 8" of height. Vertebral fractures usually begin at about age 60. One half of all 65 year old women have detectable wedging of one or more vertebrae.

Wrist fractures of the distal radius (sometimes called Colle's fractures) are increasingly common in women over age 50, occurring 10 times more often in women than men.

Hip fractures are the most disabling and life threatening consequence of osteoporosis. The over 75 age woman (one of the fastest growing segments of our society) is more likely to sustain this injury because the upper femur contains a relatively large amount of cortical bone. Fewer than half of all women who fracture a hip regain normal function. 15% die shortly after injury and nearly 30% die within a year, not from the fracture itself, but from complications of bed rest such as pneumonia and thrombosis. Last year in the United States, 6 billion dollars were spent on the treatment of hip fractures alone. Thus osteoporosis, the most common disorder of the skeleton, is the most serious consequence of menopause.


24 Morris Notelovitz, M.D., Ph.D. and Marsha Ware, Stand Tall (Florida: Triad Publishing Co., Inc., 1982) p. 35

25 Ibid., p.36

If no estrogen receptors have been identified in osseous tissue, how then does lack of estrogens cause osteoporosis? Almost all of the body's calcium is found in the skeleton, but the small amount remaining is essential for many other operations, such as muscle contraction, blood clotting, and brain function. An elaborate regulating system allows for calcium blood level control. Vitamin D, parathyroid hormone (PTH), and calcitonin are primarily involved in this mechanism. Among other things, vitamin D increases the absorption of calcium in the intestines. High levels of estrogens stimulate the synthesis of vitamin D and increase this absorption in the intestines. One of the functions of PTH is stimulation of osteoclastic bone resorption to release stored calcium into the bloodstream. Estrogens act as inhibitors to decrease the responsiveness of bone to PTH. At this point, researchers seem to disagree about whether PTH production decreases or increases after menopause, but regardless, when estrogen levels fall, bone becomes vulnerable to even relatively low levels of PTH, and bone breakdown accelerates without the mitigating effects of estrogen. Calcitonin, a hormone mainly released by the thyroid, directly inhibits the activity of osteoclasts, and is stimulated by estrogens. More studies need to be done on calcitonin, but we do know that it decreases with age, and women with osteoporosis have less of it than women with normal bone.

27 Notelovitz, Stand Tall, p. 44-46
Plain radiography is the least sensitive method for assessing bone density. 30% of bone mass must be lost for evidence to show up on X ray. Years of routine dental X rays may be of value for showing some changes consistent with bone mineral loss. Blood and urine tests reflecting the loss of calcium and hydroxyproline may also be helpful in establishing general increase in bone resorption after menopause.

New assessment methods such as single-photon absorptiometry (SPA), which compares the bone mineral content of the patient's radius (95% cortical bone) with the bone mineral content from a standard sex and age graph, and dual-photon absorptiometry (DPA), which directly measures mineral content of hip and the first through fourth lumber vertebrae (65% trabecular bone), are much more sensitive to bone loss than plain X ray. Quantitative CT scanning, which obtains a cross sectional view of the vertebral body is an accurate indicator of osteoporotic change. Obviously, DPA and CT scanning are more valuable tools than SPA for evaluating postmenopausal osteoporosis.

Hopefully in the near future lower cost, greater availability and lower radiation dosage will make these techniques as routine as mammography has become today to provide initial screening and long term follow-up of patients.

28 Kaplan, M.D., Clinical Symposia, p. 23


30 Kaplan, M.D., Clinical Symposia, p. 24
It is beyond the scope of this paper to examine and advise therapies for the prevention and control of postmenopausal osteoporosis. At this time, although replacement estrogen is clearly an effective bone loss treatment, contraindications and future implications make this therapeutic strategy a highly individual decision to be made after much investigation and deliberation by the patient-doctor partnership.

However, certain osteoporosis risk factors have been defined as guidelines for all women today:

. Caucasian or oriental background--Black women, with their heavier bone mass, rarely develop osteoporosis
. Fair skin, light eyes and hair--Bone mass seems to be directly related to amount of skin pigment
. Slender build--Women weighing under 120 pounds
. History of cigarette smoking and alcohol intake
. Never pregnant
. Never taken birth control pills
. Little weight bearing exercise
. History of taking steroids
. Early menopause, either natural or surgical
. Diet--Low calcium consumption.

Diet seems to be one of the most important factors in preventing postmenopausal osteoporosis. The best guard against this bone thinning disease is to take steps to build the greatest possible bone mass early in life. Many young girls are at

31 Budoff, M.D., No More Hot Flashes, p. 54
greater risk than even before for future osteoporosis because they are chronic dieters. Johns Hopkins studies on bone mineral density of young women in their twenties have shown decreases of 10 to 20% below normal density for that age, which will give them a head start on osteoporosis when they enter menopause.

Thus calcium may have its greatest effect at an age when a woman is least likely to be compliant with calcium supplementation--that is, during the stage of bone growth and the early adult years, when most people are not particularly concerned about a disorder that may not affect them until they are 65 to 75 years old. 33

32 Sue Miller, "Women are feeling age in their bones," Times Union, 12 February 1987, sec. C, p. 5

Target Tissue Response to Hormone Loss

The menopause has a significant complicating factor in that the aging process must also be considered when evaluating the effect of estrogens on host tissues----Aging begins at the moment of conception and continues throughout life. However, the aging process is usually referred to [as] the period of life in which our bodies can no longer maintain the equilibrium and literally begin to "wear out." 34

Since a woman faces menopause at a point in her life when she must also face the incidence of degenerative disease as well as changing family situations, it is important to try to differentiate between which derangements are due to aging and which are clearly the result of steroid hormone loss. Since estrogen receptors have been identified in many tissues such as hypothalamus, vaginal epithelium and uterine endometrium, these tissues are named target tissues. We can document their response to the presence or absence of steroid hormones by structure and function alternation. "Target tissues are defined as tissues characterized by the presence of highly specific protein receptor molecules within the cells that are able to bind firmly to the specific circulating steroid." 35

"Estrogen receptors are found in the cytoplasm of estrogen sensitive tissues and function by selective high

34 Buchsbaum, ed., The Menopause, p. 9

35 Utian, Menopause in Modern Perspective, p. 48

affinity binding of steroid hormones to begin this process of transforming molecular events into psysiologic responses." (underlining mine)

The vaginal epethelium is highly responsive to estrogen depletion. Premenopausal vaginal epithelium contains approximately 30 cell layers. After menopause there is a failure of production of glycogen containing superficial cells and epithelium may thin to as few as 6 fragile cells deep as epithelial maturation decreases. Vaginal pH increases to a range of between 6.0 and 8.0 which tends to allow unusual bacteria to replace the normal bacteria present. The vagina also becomes narrower, shorter, and bereft of rugae. The estrogen deprived vagina can easily become irritated and bleed, a condition known as atrophic vaginitis.

The distal urethra is affected by the same changes as those of the vagina. This is reasonable because embryologically, the lower urinary tract and reproductive tract have a similar origin. When estrogen deficiency converts the distal urethra to an inelastic, easily inflamed tube--a condition called atrophic urethritis, stricture formation may develop. Estrogen receptors have been identified in the urethra and in the trigone of the

37 Buchsbaum, ed., The Menopause, p. 67
38 Budoff, M.D., p. 32
39 Buchsbaum, ed., The Menopause, p. 133
The bladder's transitional epithelium also exhibits the same response to ovarian hormones as the vaginal epithelium.

The postmenopausal cervix shows epithelial atrophy with a flattened superficial epithelial layer. The endocervical glandular tissue becomes less active and less and less mucus is produced. The atrophic changes resulting from estrogen depletion also cause a predominance of parabasal cells, and the cervix shrinks so that the external opening is nearly flush with the shortened vaginal walls.

The body of the uterus responds to estrogen loss by becoming smaller and the walls thinner. Uterine weight can go from the normal 120 grams before menopause to as little as 25 to 30 grams in advanced age. Both estrogen and progesterone receptors are present in the uterine endometrium, and estrogen depletion affects both the endometrium and the myometrium layers. The columnar epithelium of the endometrial glands flattens to cuboidal epithelium and there is little secretion. These glands begin to intermingle with the underlying muscular fibers. The myometrial fibers atrophy and the smooth muscle takes on a more cellular appearance.

40 Utian, M.D., Ph.D., Menopause in Modern Perspective, p. 55
41 Buchsbaum, ed., The Menopause, p. 14
42 Utian, M.D., Ph.D., Menopause in Modern Perspective, p. 54
43 Buchsbaum, ed., The Menopause, p. 14
The fallopian tubes also contain estrogen receptors and are subject to the same changes as the uterus—epithelial and muscular atrophy.

The inexorable process of atrophy continues when we discuss another target tissue for estrogen and progesterone stimulation—the breast. The breast undergoes cyclic changes during the reproductive years. Estrogen, among other hormones, determines duct development, while progesterone influences the glandular proliferation and fluid retention which occurs during the second half of the menstrual cycle. After menopause, the glandular substance of the breast atrophies, and adipose tissue tends to be replaced by fibrous tissue. "Indeed, atrophy of the breasts becomes obvious as soon as six months after removal of functional ovaries from premenopausal women." The skin of the breasts atrophies at a different rate than the tissues underneath, so the breasts develop a flattened appearance.

Certainly, estrogen receptors have been identified in skin, but considering every major body organ, skin becomes the best example of the difficulties apparent in differentiating

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44 Ibid.
45 Utian, M.D., Ph.D., *Menopause in Modern Perspective*, p. 58
46 Ibid.
47 Buchsbaum, ed., *The Menopause*, p. 17
specific hormonal target tissue responses from general aging and environmental factors, such as sun exposure.

Estrogens have been found to be actively bound and metabolized in all skin components. The epidermis becomes thinner after menopause. There is also a progressive decrease in scalp and body hair follicles. Sebaceous and sweat gland function becomes reduced. These factors result in dry, easily traumatized skin. The dermis also becomes thinner, with less resilience and pliability of the skin. Skin pigmentation and hypopigmentation may also be hormone related. Alteration of functions such as degree of water retention, number of mitoses, extent of perfusion and carbohydrate metabolism all lead to the fact that postmenopausal hormone skin changes contribute to skin aging and add to its effect.

48 Utian, M.D., Ph.D., Menopause in Modern Perspective, p. 56
49 Ibid.
50 Buchsbaum, ed., The Menopause, p. 19
"...in a woman with normal ovulatory menses the hormones and the autonomic hypothalamic center functions...are at equilibrium to form a functional entity. As soon as the menstrual pattern begins to deviate from the norm, a disturbance of endocrine function may be expected to exist. This will be most pronounced after cessation of the menses but in most cases nature will eventually restore a balance between the two functional systems..." 

During a woman's reproductive years, pituitary gonadotropin production and release is controlled by two centers in the hypothalamus. The tonic center controls production of follicle stimulating hormone (FSH) and luteinizing hormone (LH), while the cyclic center controls release of these hormones. The centers are influenced by the ovarian hormones estradiol, estrone and pregnesterone. Depending on how these steroid hormones occupy receptor sites in the hypothalamus dictates positive or negative feedback. This will be shown as either an increase or decrease in gonadotropin releasing hormone (GnRH) production.

At the time of menopause, this delicate mechanism changes, but the basic cycle is still in effect. After menopause however, this altered continuity disappears.

Even as early as 10 years before menopause, a gradual increase in plasma levels of FSH can be detected. Later, there is a concurrent increase in plasma LH levels. These changes are

51 Stuart Campbell, ed., The Management of the Menopausal and Postmenopausal Years, p. 17

52 Utian, M.D., Ph.D., Menopause in Modern Perspective, p. 35

53 Ibid.
probably brought about by small decreases in estradiol production. Several theories have been proposed, but another possible explanation for the premenopausal increase in FSH production is the possibility that the ovaries respond less and less to gonadotropin stimulation. After menopause, plasma levels of both FSH and LH are quite high. Compared to the premenopausal state, FSH levels can be 14 times as high and LH levels 3 times as high. Both these gonadotropins reach their highest level about 3 years after menopause.

When interviewing postmenopausal women, the author found that hot flashes (or flushes) were the most common complaint these women reported. Since most women in this age group today are employed outside the home, there is no opportunity to cope during working hours by a quick shower and change of clothes--strategies their nonworking counterparts might use. Studies have shown that as many as 85% of women who go through menopause experience hot flashes, and as many as 45% still have hot flashes 5 to 10 years later.

As mentioned earlier, receptors for both estrogens and progestins are found within the anterior hypothalamus. It is now clear that hot flashes occur together with pulsatile release of LH. The pathogenesis of a hot flash seems to be that the anterior hypothalamus responds to lack of estrogens with

54 Ibid., p. 36
pulsatile release of GnRH, causing pulsatile release of LH. Thermoregulatory centers, also located in the anterior hypothalamus are affected by the pulsatile GnRH and LH, and reset the central body thermostat downward to lower temperature. The body then adjusts to this new low set point by activating means of heat dissipation such as blood vessel dilation and perspiration--the hot flash.

Depression, irritability, insomnia, anxiety, and decreased recent memory are all common menopausal complaints--part of the menopausal syndrome.

Although estrogen replacement therapy has been shown to be helpful in alleviating these symptoms in many women, there is a great deal of controversy about this subject. In The Menopause, edited by Buchsbaum, two different hypotheses are proposed by the same researcher. In her chapter "The Climacteric," she states that "aging and decreased estrogen levels may alter dopamine-norepinephrine metabolism in the brain sufficiently to result in an instability of the autonomic nervous system." She also mentions the role of prostaglandins, which are present in high concentrations in the hypothalamus, with the speculation that norepinephrine or prostaglandin could produce vasospasm and result in the menopausal irritability, depression, and memory loss. She further relates that it is difficult to

56 Ibid., p. 1286

57 Buchsbaum, ed., The Menopause, p. 27
distinguish between hormone deprivation and the normal aging process.

In another chapter, "Estrogen Replacement Therapy," the same writer states that mental status does improve with ERT, but it does so indirectly, by removing the irritants of night sweats and insomnia, and the fact that estrogens do change sleep patterns by shortening the time required to fall asleep and increasing the length of REM sleep.

In her book, *No More Hot Flashes*, Dr. Budoff discusses a study by M. Aylward in which ERT lifted menopausal depression, possibly by increasing the availability of free tryptophan, which is converted to other substances utilized by the brain. In *Management of the Menopause and Postmenopausal Years*, Jaszmann also mentions that in his studies estrogen also increased the level of free tryptophan.

Research into steroid hormone influence on brain cells continues. Studies delineating the identification and importance of neurons that concentrate estradiol in parts of the brain such as the medial preoptic area, medial nucleus of the amygdala, and

58 Ibid.
59 Ibid., p. 81-2
60 Budoff, M.D., *No More Hot Flashes*, 41
61 Campbell, ed., *Management of the Menopause and Postmenopausal Years*, p. 39
ventromedial and arcuate nuclei of the hypothalamus--the most dense collections of estrogen concentrating cells, have been carried out on fish, birds, reptiles and mammals, primarily rodents. Regions of the hypothalamus and limbic system just mentioned have long been known to project into the midbrain, but until recently it has not been known exactly which cell bodies sent axons to particular midbrain regions.

The brain has been found to contain receptors for all types of steroid hormones. These receptor sites, as mentioned before, are not distributed evenly, but occupy specific areas in the brain. Because of this, research into these particular areas of the brain is particularly valuable and may answer many questions about estrogen loss related depression at menopause and hypotheses about sex differences in hormone action on the brain.


63 Ibid., p. 229


65 Ibid., p. 813
"Men were designed for short, nasty, brutal lives," says Dr. Estelle Ramey of Georgetown University Medical School, "Women are designed for long, miserable ones." One explanation lies in evolution. Nature gives females a hormonal edge during the reproductive years, when more women than men are needed to perpetuate the species. Estrogen helps a woman's liver prevent the accumulation of cholesterol and makes her blood vessels more resilient to stress. Men are designed to protect women: the possibility for injury may be one reason his blood clots faster than hers — and why he has a greater risk of an early heart attack. But the female edge disappears with menopause. When estrogen production stops, she becomes prone to heart disease and the crippling wasting of bones known as osteoporosis.

Ischemic heart disease is the number one cause of death for both men and women in the United States. Although breast cancer claimed the lives of 36,000 women in 1982, cardiovascular disease was the cause of death for 355,000 women in this country.

For some time it has been observed that estrogens exert a protective effect on lipid and lipoprotein metabolism. Premature menopause has been associated with increased incidence and early development of ischemic heart disease. The rise in plasma cholesterol occurs after either surgical or natural


68 Chris Anne Raymond, Ph.D., "Hormone Replacement: Gynecologists Consider the Heart of the Matter," *Journal of the American Medical Society*, 258, no. 12 (Sept. 25, 1987), p. 1573
menopause.

"The plasma concentrations of certain cholesterol carriers, such as high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol are strong and consistent predictors of the risk of ischemic heart disease." High levels of HDL seem to be protective, while high levels of LDL appear to increase heart disease risk.

However, most research on heart disease has been conducted on men, and several studies utilizing women subjects have had seemingly contradictory findings, so a definitive conclusion has certainly not been reached.

One large piece of research, the Framingham Heart Study examined "...the effect of estrogen use on morbidity from cardiovascular disease in 1234 postmenopausal women, aged 50 to 83 years...", and concluded that "No benefits from estrogen use were observed in the study group; in particular, mortality from all causes and from cardiovascular disease did not differ for

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69 Whitehead and Fraser, "Controversies concerning safety of ERT," p. 1317

70 Ibid.

71 Ibid.

estrogen users and non users."

After this study's publication in The New England Journal of Medicine, a flurry of letters appeared in the same journal rebutting the study's conclusion because it did not conform to the rigorous criteria of a double blind randomized trial and claiming it was flawed and could not be definitive about the effects of estrogen use on cardiovascular disease. In fact there was a barrage of letters written to the editor, each with different explanations and conclusions about the Framingham and other related studies on estrogen and cardiovascular disease.

In the Journal of the American Medical Association's "Medical News and Perspectives," debate continued as Lila E. Nachtigall, M.D., associate professor of obstetrics and gynecology at New York University School of Medicine predicted that "the risk of cardiovascular disease will soon become an indication for estrogen replacement therapy." However, in the same article, Robert Schlant, M.D., Chairman of the American Heart Association's Clinical Cardiology committee was quoted as stating that "we do not have any clinical data from a good, controlled group to say that [a long term] homonal replacement therapy is of definite value. [for the reduction of

73
Ibid.

74
Estrogen has been found to increase levels of the "good" HDL and decrease levels of the "bad" LDL, but the problem is that progestins, normally given along with estrogen in E.R.T., have been shown to lower HDL levels by 15%, which is equivalent to the increase brought on by the estrogen.

The ratio of coronary artery disease deaths in men and women differs dramatically with advancing age - at age 45 the ratio is 8 to 1, while at age 85 that ratio equalizes to 1 to 1. There are so many factors that have a major impact on the incidence of coronary deaths, such as heredity, smoking, diet, hypertension and diabetes, that it is difficult to delineate the role of estrogen as a definite factor in cardiovascular disease. Cardiovascular change is extremely difficult to separate from the aging process, since arteriosclerosis follows along with aging, so the protective nature of estrogen on coronary artery disease remains complicated and controversial.

75 Ibid.
76 Ibid., p. 1577
77 Utian, M.D., Ph.D, Menopause in Modern Perspective, p. 30
78 Ibid.
The cause-and-effect relationship between menopausal hormonal changes and target tissue effects is not always apparent because menopause is a syndrome that occurs over time---At the beginning of the climacteric---the occurrence of hot flushes, and symptoms of vaginal atrophy occur relatively close together. Later, other signs appear such as bladder symptoms and endocrine-related aspects of heart disease and osteoporosis. Thus the time discrepancy obscures the cause-and-effect relationship, as may the general aging process and even psychosocial factors. 79

And so we must succeed in separating age from illness if we are going to meet the challenge of our future years. It is not going to be enough just to survive - our goal must not be to extend old age, but to lengthen those productive middle years so that we remain valuable contributors to our families and society, and prevent ourselves from becoming emotional and financial burdens to our younger relatives.

This is indeed a tall order, but we as a population have made a start by responding to the increasing body of evidence elucidating the fact that the majority of our disabling diseases can be prevented. Eliminating smoking, exercising more and paying attention to diet are just a few examples of the results of our growing awareness of the effectiveness of prevention.


Tough choices await us along the way. Not only may we have to face the decision whether to use some of the advanced life support technology for ourselves or relatives, but we also need to be aware of what therapies exist at which hospitals - before an emergency develops. One example of this was reported in June, 1988. The two largest hospitals in Rochester, New York are divided on the type of thrombolytic drug therapy to use on patients brought to the hospital immediately after a heart attack. Rochester General Hospital uses tissue plasminogen activator (TPA), while streptokinase is the drug of the choice for Strong Memorial Hospital. This debate has ramifications for the health care consumer, and is just one of the many factors involved in selecting a hospital.

The reasonable goal of reaching that life milestone, menopause, is only a fairly recent expectation, since from 10,000 B.C. to 1640 A.D. most women could expect to live about 32 years. But it is now 1988, and we look to a future where we may expect to live a full third or more of our lives postmenopausally. Now as never before, the woman of today needs to be extremely well informed to make intelligent choices which may well affect how productive and meaningful that postmenopausal third of her life will become.


Although estrogen replacement therapy (ERT) is extremely effective in alleviating symptoms of early menopause such as hot flashes, and in preventing long term effects, such as osteoporosis, obviously a blanket endorsement of ERT should not be considered. Whatever therapy, if any, the patient and physician decide on must be carefully researched and individualized. One primary consideration is the fact that after menopause estrogen is still being converted in the adrenal glands and adipose tissue, and the amount can vary greatly from woman to woman. Normally, circulating estrogen levels are decreased in most postmenopausal women, but in some obese postmenopausal women estrogen levels may be higher than those found in other premenopausal females.

There are many obvious contraindications for ERT, but there are also some subtle implications of estrogen replacement or augmentation. Although ERT, including the addition of a progestin, has been found in most studies not to increase the risk of endometrial or breast cancer, and in some studies has actually been found to decrease those cancer risks, one must still consider that ERT may accelerate preexisting breast cancer.

83 Utian, M.D., Ph.D., Menopause in Modern Perspective, p. 31
84 Ibid.
85 Budoff, M.D., No More Hot Flashes, p. 15
especially if that cancer is the type which demonstrates estrogen receptors. Since "a single cancer cell divides on average, only once every hundred days, at that rate -- the aberrate cell may take eight years to form a pea-sized lump," a tiny cancer cell group may not be detected by mammography, but still exist in the breast. The incidence of breast cancer has been found to increase throughout a woman's lifespan, unlike cervical, endometrial or ovarian cancers, so this situation is a serious consideration in the decision to use supplemental estrogen.

This one example of the ramifications of choosing a therapy to prevent, rather than cure must, in the final analysis be the informed patient's responsibility. A recent letter to the editor of the New York Times Magazine speaks eloquently about this perspective:

> Medicine is now an interactive process between doctor and patient. The physician has the responsibility to provide the patient with a cogent explanation of his treatment and reasonable options whenever invasive care is necessary. The patient has the responsibility to integrate the treatment options and make a final, informed decision.

86 Raymond, Ph.D., "Hormone Replacement: Gynecologists Consider the Heart of the Matter," p. 1577

87 Rose, The Body in Time, p. 86


The importance of advanced decision making and the whole topic of prevention is brought into stark focus by a trip to a downtown department store. (Never mind a nursing home!) There we can see the plight of the little old lady precariously making her way with the aid of a cane, nearly bent over on her fragile bones. In the suburbs and the office one is only used to seeing the healthy young and middle aged, so a trip to the center city highlights the plight of these frail beings.

Jane Gould, director of the New York State Office of the Aging speaks of the fastest growing population group in this country - the over 85 age set, and she worries who will "---meet the needs of those with acute or chronic illnesses. Who will take care of these people?"

Studies have shown that age and illness can be separated, and that chronological age alone is not a good index of our capabilities. Therefore, with better prevention of chronic disease and earlier detection of acute illness, the answer may well be that we, the future elderly, will be taking care of ourselves.

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