

When HRT is not possible

M. Neves-e-Castro

INTRODUCTION

Hormone Replacement Therapy (HRT) has been one of the more convincing approaches to add quality and years to the life of postmenopausal women.

The concept of HRT is open to discussion. (1)

After the onset of menopause many women complain of disturbing symptoms that may adversely affect their quality of life. Vasomotor symptoms (hot flushes and flashes), irritability, depressive mood, insomnia, sexual dysfunctions, bone and joint pains, weight gain, etc, are among those that more often cause discomfort and determine that a woman seeks medical support.

Alternatively, it is well established that after the menopause there is a clear increase in the risk for cardiovascular diseases and osteoporosis.

Both the often incapacitating symptoms and the risk for diseases later in life are accepted to be mainly due to the pronounced fall in circulating estrogens that are characteristic of the primary ovarian failure, a landmark of the physiologic menopause, in middle age women. Treatment with estrogens is effective in the relief of most symptoms and in the favorable modification of the incoming above mentioned risk factors.

Hormones have since long been considered by many women either as wonder drugs or very dangerous

medications that may be related to cancer, hirsutism, weight gain, etc.

Conversely, there are a few absolute and relative medical contraindications that may prevent the use of HRT by some women.

However, in the majority of cases, HRT may be not possible because it is not wanted by the women who are negatively affected by the bad news that are often inaccurately transmitted by the media.

Unfortunately, in many cases, bad news is good news and that is what sells best. The symptomatology of menopausal women is not universal.

In a number of studies, among several ethnic and cultural groups in the world, it was found that there are "important differences in women's experiences of symptoms and their responses to them, reflecting

cultural influences on explanatory models of menopause, lifeways, and in turn, biology" ... "Their lifeways, including exercise and nutritional intake, affect symptom experiences and symptom distress". (2) Filipino American midlife women consider the perimenopausal transition in a positive light as part of normal life that does not warrant concern. (3)

The 1998 North American Menopause Society Survey concluded that the majority of women viewed the menopause and midlife as the beginning of many positive changes in their lives and health. (4)

Thus, some women may not feel the

need for HRT, whereas others may not want to take it.

In a recent study involving 3.000 women > 50 years old, 1.350 were not on HRT. Of those, 82% were menopausal out of which only 21 % had been treated with HRT in the past. The reason for not taking HRT included the following: 49% no longer had menopausal symptoms, 45% did not want to take HRT, 33% were not offered it by their doctors, 28% were afraid to use it. (5) Therefore, HRT is sometimes not possible either because women do not feel the need, or because they are afraid. Often this is due to lack of information for which health providers are responsible.

OBJECTIVES

Assuming that, no matter why, HRT is either not possible or not wanted, which are the goals of the attending physician and what can be offered to a menopausal women who seeks support?

Basically, with or without HRT, there are always three fundamental objectives:

- a) relief of symptoms
- b) maintenance and improvement of health
- c) prevention (primary or secondary) of diseases

The assessment of health is far more difficult than the diagnosis of disease. However, WHO has given a definition of health that can be very useful as a guide line: "Health is a condition of physical, mental and social wellbeing and not only the absence of disease". Thus, the attending physician must adopt a holistic vision of the middle age woman who comes to him for support. He must be concerned and involved in all the aspects that define health. If he is a gynecologist

he should be aware of the etymology of this word of Greek origin (gyneka = woman / logos = science). Gynecology in its broader dimension means the science or the knowledge about women, and not only the treatment of the diseases of the reproductive track. May be one should invent another designation (hybrid from Latin and Greek) like feminology or holistic feminology to better define the role of a modern gynecologist. As a matter of fact, if he is only a good specialist, with an average knowledge of internal medicine and little time or talent to establish a good empathic relationship with a human being, he is certainly not a good gynecologist. Middle age women do not routinely visit a cardiologist or a rheumatologist, but they go regularly to their gynecologists for a routine pelvic examination, a Pap Smear, a mammography, etc. It is the responsibility of the modern gynecologist to take advantage of this opportunity to do the necessary screenings to identify risks (cardiovascular, osteoporosis, cancer, etc) and to attempt to modify them to the extent of his capacities and possibilities.

THE WOMAN

She may be defined as:

- a) a menopausal women – if one considers that the shut down of ovarian function and the consequent hypoestrogenism is the key problem, or as
- b) a middle age woman – in whom natural aging is already playing a role, both from a biological and a psychological perspective.

In both cases she may suffer from a lack of estrogens and from aging. Biological age and chronological age run in parallel. She may complain of somatic and of psychic symptoms. For practical purposes one must accept that there is a biological syndrome and a psychological syndrome that affect these women. The purpose of the anti-aging interventions is to dissociate the biological age from the chronological age (6) and thus to compress morbidity as late as possible in the life time (7). Adding life to the years and years to life is the target to hit. That is to say longer life but with greater quality.

The biological syndrome

Estrogens have profound effects in almost every organ and tissue of the body. Be it through genomic (a and b receptors) or non genomic mechanisms the fact is that estrogen deprivation may cause dysfunctions and that treatment with estrogens may have corrective effects.

With aging and lack of estrogens it is almost a universal phenomenon the development of insulin resistance, increase in blood pressure, changes in lipid metabolism, a decrease in immune function, and increase in stored fat. These are the major factors for the high cardiovascular morbidity from which women were protected until the onset of menopause.

Insulin resistance (with hiperinsulinemia) seems to be one of the major factors of aging. It has profound impact on other hormonal systems, in particular eicosanoids, considered to be the molecular foundation of aging (6). Insulin causes the production of more “bad”

(vasoconstrictor) than “good” (vasodilator) eicosanoids. Insulin increases also the fat stores in the body.

Besides hyperinsulinemia there is also an excess in free radicals and cortisol, both with dangerous effects in the aging process.

According to Sears (6) excessive insulin, excess in glucose, excess in free radicals and excess in cortisol cause increased caloric consumption, increased DNA turnover, increased AGE's formation (advanced glycosylated end products), neural death in some areas of the brain and an imbalance in eicosanoid synthesis, considered to be the molecular nature of chronic diseases. From the above it can already be inferred that nutrition, exercise and life style are closely related to these problems, as shall be discuss later.

The lack of estrogens, lower amounts of Vitamin D, lack of exercise, poor calcium intake are some of the factors that contribute to osteopenia and osteoporosis.

Therefore, osteoclasts become more active (due to increased PTH secretion resulting from a lesser negative feedback of calcium) and osteoblasts are not stimulated by the low levels of estrogens and androgens.

These woman seek help mostly because of:

- a) weight gain
- b) different body fat distribution
- c) increased appetite
- d) asthenia, tiredness
- e) pain in the bones and joints
- f) precordial pressure
- g) hypertension
- h) dyspareunia (dry vagina)
- i) stress incontinence
- j) breast tenderness (in early menopause)

Which are the markers of good health? (6) (8) (9)

- a) fasting insulin levels less than 10 uU/mL
 - b) fasting glucose / insulin ratio (mg/dl: uU /mL) greater than 4.5
 - c) glycosylated hemoglobin less than 5%
 - d) fasting triglycerides less than 140 mg/dL
 - e) low total cholesterol (less than 200 mg/dL)
 - f) LDL less than 130 mg/dl and HDL greater than 50 mg/dL
 - g) Triglycerides/HDL ratio less than 2
 - h) Total cholesterol/HDL less than 4.5
 - i) BMI (Body Mass Index) 20 – 25 Kg/m²
 - j) Body fat less than 22%
 - k) Blood pressure: diastolic less than 90 mm Hg and systolic less than 140 mm Hg
 - l) Bone mineral density: T above – 1.0 SD
- B) The psychic and neurovegetative syndromes

- vasomotor symptoms (hot flushes and flashes)
- insomnia
- irritability
- depressive mood
- frigidity
- headaches and migraine
- poor memory

These symptoms are not necessarily estrogen related, other than the hot flushes and flashes. However, since the brain is a target for estrogens that act via several neurotransmitters, it is likely that its lower levels after the menopause may have an impact on mood, sleep, memory. Since in industrialised countries the menopause has for many women (and men, too) a negative

connotation, being considered the beginning of the end, the lack of femininity, etc., it is conceivable that menopausal women consider themselves very insecure (feelings of jealousy, need of reaffirmation, etc). The unhappiness they may feel needs compensatory gratifications (food, sweets, etc). The “empty nest” syndrome does not help them to reformulate their life styles; they do not feel any interest in life, they became inactive and do not want to make exercises, and they may often feel miserable. Estrogens act also on the arterial wall and stimulate the synthesis of nitrous oxide (NO) by the endothelium. NO is a potent vasodilator. The lack of NO may cause vasospasm and cause headaches and migraine.

STRATEGIES

It is obvious that despite the fact that HRT is very important to help in the maintenance of health, the prevention of diseases and the relief of symptoms, there are many other possibilities, other than the use of hormones, to help those women who cannot or do not want to take HRT.

It is beyond of the scope of this chapter to go through all the steps that are applicable to all women who are in this phase of their lives. Instead, reference will be made to a number of interventions that are usually omitted despite their proven efficacy as anti-ageing, anti-cardiovascular diseases, anti-osteoporosis and even anti-cancer. The following topics deserve far greater attention than they have had so far. As a matter of fact it is easier and less time consuming to prescribe pills than to persuade a woman to change her life-style,

nutrition, etc.

Time to listen

The most important single measure is to have time to listen and to talk. Many of the problems faced by these women can be solved or greatly alleviated if the attending physician believes that he is capable of understanding, supporting and give, sometimes for the first time, the information those women are lacking. If a woman is properly informed about the physiology of this change in her life, and that most other women do have similar complains, then the mystery starts fading out and doors can be opened to establish a positive dialogue. Sometimes if one explains to them the meaning of some clinical trials they may understand what is a benefit / risk analysis, or a relative risk, and eventually change their minds.

But, assuming that HRT is out of question what should be the next step?

Physical activity

It is well established that a well planned physical exercise has very positive effects in mood and in the sense of well being (due i.a. to the release of beta endorphins by the brain). It helps to develop motivation. It contributes to weight loss, to muscle strength, to a better cardiovascular function, and it helps the bone and joint function. And it decreases stress, too. Women who took part in moderate exercise, as little as once a week, were 24% less likely to die prematurely than women who did not exercise. Women who took part in vigorous exercise (jogging, swimming, etc) more than four times

a week had 43% lower risk of premature death. (10)
(see nutrition and weight control)

Anti-Stress

The attending physician, with time (!) is often in a better position than a psychotherapist to give the support and advise that may help to decrease psychic stress and distress. Explaining how the central and autonomic nervous systems and the adrenal glands may cause vasospasm (headaches, migraine, hypertension), increase cortisol secretion (with all the metabolic consequences) and make one feel unhappy, is one first steps to help that women to look into herself, in the mirror, to start equating her problems and may be solving some of them. Stress is a major risk for coronary heart disease. If needed the attending physician should not refrain from complementing his mild psychotherapy with mild tranquillisers or antidepressants. It is expected that he knows how to manipulate these psychopharmacological medicines and that he also is capable of identifying mental disorders that should be treated by another specialist.

Vasomotor Symptoms

Sometimes they are intense and require treatment. Antidopaminergics (veralipride) and a 2 blockers (clonidine) have been used with some success. However, even when HRT is not possible, an injection of 150 mg medroxyprogesterone acetate is more effective. The side effect to be considered is on mood.

Insomnia

No problem to prescribe mild sedatives and hypnogens.

Headaches and migraine

If acetilsalicylic acid is well tolerated, for short periods, it is acceptable since it also has antiaggregating effects, preventing atheromatous plaque formation. Otherwise, other mild analgesics are to be recommended. Ergot derivatives should be used with caution. A balanced diet may help. Smoking should be proscribed, since it causes vasoconstriction.

Dyspareunia, frigidity

Only later in the menopause is the vaginal epithelium atrophic enough to cause dyspareunia. In the majority of cases, in the early menopause, dyspareunia is psychogenic and due to perineal muscle spasm. The same with frigidity and anorgasmia that are seldom hormone related. Lubricant jellies are effective. Even when HRT is not possible there is no reason to avoid estrogen vaginal suppositories or creams. When possible it is advisable to have a joint conversation with the partner to demystify the problem and to propose some techniques that may be less traumatic and more gratifying.

Nutrition and Weight Control

There is a significant association between younger age at menopause and higher risk of coronary heart disease among women who experienced natural menopause and never used hormone therapy. (11) Therefore, particular attention must be paid to this group of women

particularly if they are obese. Obesity is a significant independent predictor of cardiovascular disease. (12)

Aerobic exercise plays an important role in preventing obesity in most persons. Genetic factors do not predispose to obesity as it is sometimes accepted. In a study conducted in 970 healthy female twins (mean age 55.5 years) it was concluded that physical activity is the strongest independent predictor of total-body fat and central abdominal fat, far greater than other environmental factors. (13)

Higher levels of physical activity lessen total body and abdominal fat, prevent insulin resistance, hypertension and cardiovascular diseases. This can be achieved with 2 hours of sport or 15 Km of walking per week. Weight-bearing sport of any intensity was related to lower fat deposits and greater muscle strength. Therefore, physical activity seems to be, according to this study, the strongest determinant of body fat, more than diet. It should be, together with physical activity, another leg of the tripod that supports good health and longevity. (The third leg – pharmacological intervention- will be discussed later). This does not mean, of course, that the food intake is not extremely important both quantitatively and qualitatively. One should never talk about a diet. That woman has already followed many of them and is frustrated by not achieving what she expected. What is important is to explain how the body functions. How much protein, fat and carbohydrate is needed for that particular person, with that type of energy consumption. It is mandatory to take measures, to determine the body mass index, the percentage of body

fat and to set the objectives. One must take the time to explain the nutritional value of the aliments and their content in substances that are health protective. This may be reinforced by the information of the high or low prevalence of several diseases in different areas of the world as a function of their nutrition. Many women ignore that excessive weight and a high consumption of animal fat is higher a risk for breast cancer than HRT. A high consumption of vegetables, fruits and fiber is linked with a lesser prevalence of cardiovascular events, cancer of the colon and breast. It can be stated that modern nutritional advise is very effective for the prevention of cancer and cardiovascular diseases. It is this type of information that motivates a woman to change her alimentary habits. The objective is not to start on a diet but to change and incorporate the change. This is fundamental for behaviour support.

Antioxidants

It was previously mentioned that a typical marker of aging is an increase in oxygen free radicals that damage cells. Antioxidants prevent free radicals from damaging the cells. Aging appears to be due, in good part, to the oxidants produced by mitochondria as by-products of normal metabolism. Vitamins C, E and betacarotene are good antioxidants that are contained in certain foods (fruits, vegetables). Olive oil is a powerful antioxidant, too.

Oxygen free radicals oxidise LDL cholesterol particles, that are atherogenic.

Antioxidants may prevent heart diseases, and also cancer.

(14)

Tomatoes are rich in antioxidants (lycopene and carotenoids) and do protect from coronary heart diseases and cancer. (15)

In a recent study involving 2400 Greek women it was shown that the incidence of breast cancer dropped with a higher intake of olive oil, certain vegetables and fruits. (16) Similar conclusions were reported in other studies. (17) (18)

Frequent nut consumption is associated with a reduced risk of both fatal coronary heart disease and non-fatal myocardial infarction (relative risk 0.65, 95% confidence interval 0.47 to 0.89, P for trend = 0.0009). Adjustment for intakes of dietary fats, fiber, vegetables and fruits did not alter these results derived from the Nurses` s Health Study. (19)

Phytoestrogens

Red clover and soy are particularly rich in phytoestrogens. (20) Green split peas, chicken peas and broad beans are also rich in some isoflavones (genistein, daidzein, biochamin, formononetin) that have special estrogenic effects. May be this is why traditional legume based diets used by Asiatic populations are associated with reduced heart diseases and also breast cancer.

Some commercial preparations contain these isoflavones are available and have been tested in clinical trials. (21) (22)

Isoflavones are also strong antioxidants.

Dietary fiber

Wolk et al (23) examined the association between long-term intake of total dietary fibre and the risk of CHD in women aged 37 to 64 years, followed for 10 years, without

evidence of heart disease, hypercholesterolemia or diabetes, at base line. The age-adjusted relative risk (RR) for major coronary heart disease (CHD) was 0.53 for highest quintile of total dietary fibre intake (median, 22.9 g/d) compared with women in the lowest quintile (median, 11.5 g/d). After controlling for age, cardiovascular risk factors and multivitamin supplement use the RR was 0.77. Only cereal fiber was strongly associated with a reduced risk of CHD.

These fiber rich diets may also increase insulin sensitivity (reduce insulin resistance) and lower triglyceride levels. The recommended daily intake of fiber is 20 to 35 grams. Rich in fiber are: whole wheat bread, oatmeal, brown rice, apple (with skin), avocado, oranges, prunes, raspberries, kidney beans, etc.

Vitamins (Vit C, A and β -carotene)

Vegetables and fruits are very good sources, namely, broccoli, Brussels sprouts, chicory, tomatoes, carrots, kiwis, citrus fruits, raspberries and strawberries, watermelons and many others.

The natural micronutrients contained in food seem to be more protective than in their pure form. Deficiency of Vit B12, folic acid, B6, niacin, C, or E, or iron, or zinc appears to mimic radiation in damaging DNA by causing single and double strand breaks, oxidative lesions, or both. Micronutrient deficiency may explain, in good part, why the quarter of the North American population that eats the fewest fruits and vegetables (five portions a day is advised) has approximately double the cancer rate for most types of cancer when compared to

the quarter with the highest intake. (24)

Whole foods and fibers

Even if one takes tablets, daily, with vitamins and minerals, a balanced diet with whole foods must be a centerpiece. An orange or a glass of milk supply much more than Vit C or protein.

Dietary fibers are important for digestion. Soluble fiber (in most fruits, certain beans and grains, some vegetables) may help prevent heart diseases and diabetes.

Insoluble fibers, found in most vegetables, some fruits and breakfast cereals, can prevent constipation and colon cancer.

A diet high in fruits and vegetables reduces the risk of cancer, heart diseases and stroke.

High intake of whole-grain products is linked to reduced mortality among older women by 15% compared to non users. (25)

Fish

The more fish one eats the less coronary artery disease one has. Salmon, tuna fish and sardines are particularly rich in Omega 3 polyunsaturated fatty acids. Eating these fishes can reduce triglycerides and cholesterol because of their content in Omega 3 fatty acids. The American Heart Association recommends eating fish two or three times a week.

It is of interest to note that a reduction in total or saturated fat intake, or cholesterol intake is significantly associated with a reduction in area of breast density on mammography. A dense breast tissue is a risk for breast cancer i.a. because it may occult minor atypical lesions. (26)

MORE SPECIFIC INTERVENTIONS

Again the targets for primary and secondary prevention will be the cardiovascular system and the bones. Cancer is not the women's big killer. They live and suffer with their heart, and it is ultimately the heart that will kill most of them!

- What to do to prevent coronary heart disease (CHD)?
- What to do to decrease insulin-resistance?
- What to do in cases of resistant obesity?
- What to do to prevent osteoporosis?

Coronary heart disease (CHD)

Reducing cholesterol and blood pressure as well as smoke cessation are effective strategies to prevent cardiovascular diseases.

There are many convincing coronary primary prevention trials, all showing that either with diet or with lipid lowering agents (cholestyramine, gemfibrozil, nicotinic acid, simvastatin, pravastatin, pravachol) there was a decrease in mortality due to CHD. Unfortunately, these trials were conducted only in men. It is hoped that the same conclusions may apply to women, what seems to be the case at least with the statins(27) (28)

There are some new preventive strategies that include the liberal use of antioxidants, the use of angiotensin converting enzyme inhibitors (ACEI) and homocystein lowering. (29)

Cholesterol lowering by pharmacological means prevents atherosclerotic plaque progression and has been shown to reduce both fatal and nonfatal coronary events in

patients with or without CHD. Simvastatin for secondary prevention and lovastatin for primary prevention have a very favourable cost-effectiveness profile. (30)

Vitamin E seems to be a good choice in doses of 200 mg / day although the final proof in terms of death reductions is not yet known since the ongoing trials have not yet been reported. (31)

Vitamin E besides being a powerful antioxidant (inhibits the oxidation of LDL-cholesterol) has also a biological anti-inflammatory effect that contributes to the prevention of fatty plaque formation on the arterial wall. Recent studies suggest that plaque formation is an inflammatory process.

Of greater interest seem to be the ACEI's that are anti-proliferative, improve endothelium function, may act as antioxidants, decrease platelet aggregation and enhance fibrinolysis.

Homocysteine, an amino-acid, can experimentally induce vascular damage. It was demonstrated that there is a linear independent relation between homocystein concentration and cardiovascular risk. (32)

Low circulating concentrations of folic acid, vitamins B-6 and B-12 increase the risk of cardiovascular disease and cause a rise in homocysteinemia. Administration of folic acid and those vitamins rapidly decreases the levels of homocysteine. Clinical trials are underway to determine if these strategies are cardioprotective. It has been suggested that even people with normal levels of homocysteine might benefit from its reduction. Elderly patients taking vitamin B-6 supplements of 100-200 mg / day showed a 73% reduction in the risk of angina and myocardial infarction with an average increase

in lifespan of eight years. (33) In the Nurse's Health Study it was found that the intake of folate and vitamin B-6 above the current recommended dietary allowance may be important in the primary prevention of CHD among women. (34) The understanding of coronary artery disease risk and atherogenesis has changed very much in recent years. It is the unstable soft plaque, that cannot be seen in angiography, that is prone to rupture and result in infarction. There are also important changes in vascular reactivity that result from diet. Most infarctions occur in patients who have normal total cholesterol levels. At risk patients can be identified using the ratio total cholesterol / HDL, and triglycerides / HDL. Primary prevention trials demonstrate that coronary artery disease risk can be lowered dramatically, with diet and drug therapy. (35)

Insulin-resistance

A fasting glucose / insulin (G:I) ratio (mg/dL: uU/mL) less than 4.5 is the single best screening measure for detecting insulin-resistance. (36) Strong physical activity and a properly balanced diet are the best initial approaches. The so called insulin sensitizers can be used, with caution, as if these women had a type 2 Diabetes. For this purpose biguanides (like metformin) have been widely used. A new class of compounds, the glitazones (37), was recently introduced in the market; they may have some liver toxicity.

Obesity

In most cases it is psychogenic in its

origin. If general measures (38) (physical exercise, balanced nutrition) do not work it is essential to refer that woman to a behaviour trained psychotherapist. Two new compounds have been introduced in the market. Orlistat (39) decreases the intestinal absorption of dietary fat. Sibutramine (40) inhibits the reuptake of both serotonin and norepinephrine; it reduces food intake and increases thermogenesis, thus contributing to weight loss. Obesity, per se, is a cause of insulin resistance which, in turn, can also cause obesity. In such cases, when hyperinsulinemia is present, these cases should be managed as in insulin resistance.

Osteopenia and Osteoporosis

In a recent study (41) it was concluded that subclinical vitamin D deficiency may contribute to increased fractures. Low levels of vitamin D are associated with high levels of PTH that may cause a PTH mediated bone loss. Vitamin D and calcium therapy reduce PTH and decrease bone resorption with a consequent decrease in fractures. It is estimated that 800 I.U. of vitamin D and 1 g. elemental calcium per day are needed to reduce fractures. This is a recommendation for the primary prevention of bone loss. Fatty fish is a good source of vitamin D. Too much protein in the diet can result in increased loss of calcium in the urine; the same is true for too much sodium, caffeine and alcohol. Smoking increases the risk for osteoporosis.

If one has to complement these measures with drugs, SERM's (specific estrogen receptor modulators) like raloxifene, cannot be considered as being hormones

and may safely be used. Besides increasing bone mineral density and preventing osteoporosis, they also have a positive effect in lipid metabolism, they do not stimulate the endometrium and may even protect from breast cancer. (42) (43) Bisphosphonates (44) have a very positive effect on the bone and are used with success for the treatment of osteoporosis.

Breast Cancer

Another important information from the Nurse's Health Study suggests that folates, which are involved in DNA synthesis, may reduce breast cancer risk, particularly among women with greater alcohol consumption (at least 15 g/d of alcohol). (45) (The relative risk of breast cancer for current users of folate supplements vs. never users was RR 0.74; 95% CI, 0.59-0.93) It is known that alcohol increases breast cancer risk, too.

This study did not show any association between total folate intake and breast cancer risk among women who consumed less than 15 g/d of alcohol.

Thus, a decrease in alcohol and also in animal fat consumption seems a wise measure to decrease the risk of breast cancer, even more so if one also eats more fruits and vegetables containing isoflavones.

CONCLUDING REMARKS AND PRATICAL GUIDELINES

There seems to be little doubt that Hypocrates was right when he said 2.500 years ago "Let food be your Medicine, and let Medicine be your food". Barry Sears (7) has made a monumental contribution to the science of nutrition with a very

comprehensive and highly scientific logic approach to anti-aging. Public Health authorities are concerned with the little attention that is paid to the urgent need to change alimentary habits and life styles, as a cheap and very effective strategy to prevent many diseases. Health care providers are also not motivated to implement and reinforce such life-saving strategies. There is nowadays an abuse of drug consumption. Most people do not know, or do not believe, that many a times a proper nutrition, good physical exercise and changes in life-style can achieve more, in terms of disease prevention and health maintenance, than some tablets taken by month.

When HRT is not possible, what to do for a menopausal women?

It is unquestionable that estrogens can be of great help during the early and late postmenopausal phases of a woman's life. Nevertheless one can often achieve as much with nonhormonal medications or even without drugs. It may take longer but, in the long run, it pays.

The following suggestion and recommendations should be made to all middle age women wether or not they are on HRT:

- Start a Mediterranean diet (46) or a "zone" diet (6), eating:
 - more whole breads and cereals
 - more root vegetables, green vegetables and legumes (beans, pears, carrots, broccoli, tomatoes, etc)
 - more fish (salmon, tuna, etc)
 - more fresh fruit (apples, citrons, et)
 - replace beef with poultry
 - no butter
 - plenty of olive oil
 - some red wine

- plenty of black or green tea
- nuts
- Start a program of physical fitness, and exercise as much as possible
- Keep mentally active
- Reformulate the life-style
- Take the following nutrients (essential):
- * Vitamin A 4.000 IU/d
- * Vitamin B6 5-10 mg/d
- * Vitamin C 500-1000 mg/d
- * Vitamin D 400-800 IU/d
- * Vitamin E 200-400 IU/d
- * Folic acid 0.5-1.0 mg/d

- * Calcium(ion) 500-1000 mg/d
- * Magnesium 250-400 mg/d
- * b- carotene 5.000 IU/d
- For the prevention of atherosclerosis (advisable):
- Lovastatin or simvastatin (for primary and secondary prevention, respectively)
- aspirin (50 – 100 mg/d)- angiotension converting enzyme inhibitors

REFERENCES:

- 1- Speroff L. It's time to stop using the word "replacement". *Maturitas* 1999 (in press)
- 2- Woods NF. Symptoms among midlife women: cultural lenses, research, and health care. Editorial. *Menopause* 1999; 6: 90-91.
- 3- Berg DA, Taylor DL. *Menopause* 1999; 6: 105-114.
- 4- Utian WH, Boggs PP. The North American Menopause Society 1998 Menopause Survey. Part I: Postmenopausal women's perception about menopause and midlife. *Menopause* 1999; 6: 122-128.
- 5- Rabin DS, Cipparrone N, Linn ES, et al. Why menopausal women do not want to take hormone replacement therapy. *Menopause* 1999; 6: 61-67.
- 6- Sears, B. *The Anti-aging zone*. New York, NY: Harper Collins Publisher Inc., 1999.
- 7- Speroff L. Women's health care in the 21st century. *Maturitas* 1999 (in press).
- 8- Notelovitz M, Tonnessen D. *The essential heart book for women*. New York: St. Martin's Griffin, 1997.
- 9- Byyny RL, Speroff L. *A clinical guide for the care of older women*. Baltimore: Williams and Wilkins, 1990.
- 10- Kushi LH, Fee RM, Fulson AR, et al. Physical activity and mortality in postmenopausal women. *JAMA* 1997; 227: 1287-1292.
- 11- Hu FB, Grodstein F, Hennekens CH, et al. *Arch Intern Med* 1999; 159: 1061-1066.
- 12- Tamaka K, Nakamishi T. Obesity as a risk factor for various diseases: necessity for lifestyle changes for healthy aging. *Appl*

- Human Sci 1996; 15: 139-148.
- 13- Samaras K, Kelly PJ, Chiano MN, et al. Genetic and environmental influences on total-body and central abdominal fat: the effect of physical activity in female twins. *Ann Intern Med* 1999; 13: 873-882.
- 14- Stampfer MJ, Hennekens CH, Manson JE, et al. Vitamin E consumption and the risk of coronary disease in women. *N Engl J Med* 1993; 328(20): 1444-1449.
- 15- Giovannucci E. Tomatoes, tomato-based products, lycopene and cancer: review of the epidemiological literature. *J Natl Cancer Inst* 1999; 91: 317-331.
- 16- Trichopoulou A, Katsouyanni K, Stuver S, et al. Consumption of olive oil and specific food groups in relation to cancer in Greece. *J Natl Cancer Inst* 1995; 87: 110-116.
- 17- Block G, Patterson B, Subar A. Fruit, vegetables and cancer prevention: a review of epidemiological evidence. *Nutr Cancer* 1992; 18: 1-29.
- 18- Tavani A, La Vecchia C. Fruit and vegetable consumption and cancer risk in a Mediterranean population. *Am J Clin Nutr* 1995; 61 (Supp) 1374S-1377S.
- 19- Hu FB, Stampfer MJ, Manson JE, et al. Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. *BMJ* 1998; 317:1341-1345.
- 20- Reinil K, Block G. Phytoestrogen content of foods- a compendium of literature values. *Nutr Cancer* 1996; 26: 123-148.
- 21- Nachtigall L, Fenichel R, Lagregal L, et al. The effects of isoflavone derived from red clover on vasomotor symptoms, endometrial thickness and reproductive hormone concentrations in menopausal women – Poster 2-59- The 81st Hormonal Meeting of the Endocrine Society, USA- 1999.
- 22- Washbuen S, Burke GL, Morgan T, et al. Effect of soy protein supplement on serum lipoproteins, blood pressure, and menopausal symptoms in perimenopausal women. *Menopause* 1999; 6: 7-13.
- 23- Wolk A, Manson JE, Stampfer MS, et al. Long-term intake of dietary fiber and decreased risk of coronary heart disease among women. *JAMA* 1999; 281: 1998-2004.
- 24- Ames BN. Micronutrients prevent cancer and delay aging. *Toxicol Lett* 1998; 102-103: 5-18.
- 25- Jacobs DR Jr, Meyer KA, Kushi LH, et al. Is whole grain intake associated with reduced total and cause-specific death rates in older women? The Iowa Women's Health Study – *Am J Public Health* 1999; 89: 322-329.
- 26- Knight JA, Martin LJ, Greenberg CV, et al. Macronutrient intake and change in mammography density at menopause: results from a randomised trial. *Cancer Epidemiol Biomarkers Prev* 1999; 8: 123-128.
- 27- Williamson DR, Pharand C. Statins in the prevention of coronary heart disease. *Pharmacotherapy* 1998; 18: 242-254.
- 28- Downs JR, Clerfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels. *JAMA* 1998; 279: 1615-1622
- 29- Lonn EM, Yusuf S. Emerging approaches in preventing cardiovascular disease. *BMJ* 1999; 318: 1337-1341.
- 30- Hay JN, Yu WM, Ashraf T. Pharmacoeconomics of lipid-lowering agents for primary and secondary prevention of coronary artery disease. *Pharmacoeconomics*

1999; 15: 47-74.

31- Devaraj S, Jialal I. Alpha-tocopherol 2 decreases interleukin 1 beta release from activated human monocytes by inhibition of 5-lipoxygenase. *Arterioscler Thromb Vasc Biol* (United States) 1999; 19: 1125-1133.

32- Boushey CJ, Beresford SAA, Omenn GS, et al. A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. Probable benefits of increasing folic acid intakes. *JAMA* 1995; 274: 1049-1057.

33- Ellis JM, McKully KS. Prevention of myocardial infarction by vitamin B6. *Res Comm Mol Pathol Pharmacol* 1995; 89: 208-220.

34- Rimm EB, Willett WC, Hu FB, et al. Folate and vitamin B6 from diet and supplements in relation to risk of coronary heart diseases among women. *JAMA* 1998; 279: 359-364.

35- Castelli WP. The new pathophysiology of coronary artery disease. *Am J Cardiol* 1998; 82: 60T-65T.

36- Legro RS, Finegood D, Dunaif A. A fasting glucose to insulin ratio is a useful measure of insulin sensitivity in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 1998; 83: 2694-2698.

37- Nolan JJ, Ludvik B, Beerdsen P, et al. Improvement in glucose tolerance and insulin resistance in obese subjects treated with troglitazone. *N Engl J Med* 1994; 331: 1188-1193.

38- Anderson DA, Wadden TA. Treating the obese patient. Suggestions for primary care practice. *Arch Fam Med* 1999; 8:

156-167.

39- Sjöström L, Rissanen A, Andersen T, et al. Controlled trial of Orlistat for weight loss and prevention of weight regain in obese patients. *Lancet* 1998; 352: 167-172.

40- Bray GA, Blackburn GL, Ferguson JM et al. Sibutramine produces dose-related weight loss. *Obesity Res* 1999; 7: 189-198.

41- LeBoff MS, Kohlmeier L, Hurwitz S, et al. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA* 1999; 281: 1505-1511.

42- Delmas P, Bjarnason NH, Mitlak BH, et al. Effects of raloxifene on bone mineral density, serum cholesterol concentrations, and uterine endometrium in postmenopausal women. *N Engl J Med* 1997; 337: 1641-1647.

43- Walsh BW, Kuller LH, Wild RA, et al. Effects of raloxifene on serum lipids and coagulation in healthy post-menopausal women. *JAMA* 1998; 279: 1445-1450.

44- Ensrud K, Black DM, Palermo L, et al. Treatment with alendronate prevents fractures in women at highest risk: results from the Fracture Intervention Trial. *Arch Int Med* 1997; 157: 2617-2624.

45- Zhang S, Hunter DJ, Hankinson SE, et al. A prospective study of folate intake and the risk of breast cancer. *JAMA* 1999; 281: 1632-1637.

46- Greenwood S. The Mediterranean diet: acceptable and effective for Americans? *Menopause Management (NAMS)* 1999; 8: 16-19.

Suggested reading

- Notelovitz M, Tonnessen D.
Menopause and Midlife Health. New
York: St. Martin's Press, 1993.-
Menopause and the Heart, edited by

Manuel Neves-e-Castro, M.
Brkhäuser, T.B. Clarkson and P.
Collins, New York / London: The
Parthenon Publishing Group, 1999.

Web sites

Mayo Clinic
<http://www.mayo.health.org/>
(women´s health and diets)

Tufts University
<http://www.navigator.tufts.edu/>
(excellent for nutrition)