

## The transition from the reproductive to the non-reproductive years of a woman's life.

by

*Manuel Neves-e-Castro, M.D.*

*Founder and Honorary President of the Portuguese Menopause Society  
Lisbon, Portugal*

This transition is like a mirror image of what happens with the initiation of the reproductive years. Thus, the menarche is preceded by an increased secretion of estrogens, which is manifested by the growth of the genital tract and breasts; it is then succeeded by the onset of menstrual cycles that are initially irregular and anovulatory. This period of time is the puberty. Conversely and similarly, as menopause approaches the menstrual cycles become irregular and often anovulatory.

The ovaries of the last premenopausal years are far from being inactive. Either because of anovulation or because of luteal insufficiencies, the predominant milieu is an absolute or relative hyperoestrogenism with great fluctuation in the secretory patterns, until amenorrhoea, lasting longer than 12 months, is established (the menopause). Then the estrogen plasma levels start decreasing with a resulting lesser stimulation of the uterus, breast and vagina.

It is during the perimenopausal years, more than after the menopause, that a number of disturbing symptoms occur with reflexes in the quality of life.

Mood swings (due to high estrogenic levels) hot flashes (due to a sudden drop of the fluctuating estrogenic secretion) dysfunctional uterine bleedings (due to unopposed and erratic estrogenic stimulation), decrease of libido, mastodynia, increase of abdominal fat, etc, these is the typical constellation of symptoms that occur in the years (up to 4 years) immediately preceding the menopause. This is a particular sensitive period of a woman's life that needs great attention and medical support.

She will be exposed to the new risks of accidental pregnancies, endometrial hyperplasia, growth of uterine miomas, breast cancer, insulin resistance (part of the metabolic syndrome), dislipidemias, hypertension, decrease in bone mass, etc.

Therefore, other than general measures (exercise, nutrition, less or no tobacco consumption, less alcohol consumption) and some helpful medication (statins, SRI's, ACEI's, diuretics, etc) the time has come to counteract this hyperestrogenic state with the cyclical administration of progestational steroids (12-13 days/month). This will

mainly protect the endometrium. Since the withdrawal bleeding presupposes the presence of estrogen induced progesterone receptors, when it does not occur anymore this means that the woman became hypoestrogenic. High FSH and LH levels with low estradiol levels will confirm this early postmenopause.

This is also the time to determine if there are risk factors for CVD, osteoporosis, breast cancer, endometrial cancer, etc.

In addition to the above mentioned general strategies and non-hormonal medications it is the moment to discuss primary and secondary prevention with hormonal treatments.

There have been many epidemiological studies (observational and clinical trials) published in the last decade that were severally misinterpreted by the medical profession, and the media, with profound negative consequences for women. None of these studies has addressed the issue of the treatment of early postmenopausal women. The consensus of the International Menopausal Society (<http://www.imsociety.org>) and the European Menopause and Andropause Society (<http://emas.obgyn.net/>) have analyzed these studies and concluded that there are no reasons for alarm or for change of the sound prescriptions habits that have been used up to now. In a recent article (Human Reproduction 2003;18(12):2512-2518), I have also critically analyzed this crisis and defined who is the “safe” woman to start a hormonal treatment.

In conclusion, and contrary to the common beliefs, this transition from the reproductive to the non-reproductive year is characterized by an erratic secretion of estrogens that results, at several levels, in a hyperestrogenic state. This has consequences in several target organs that must be protected. With the advent of the menopause, it is indicated to start early a treatment with estrogens (plus progestagens if a woman still has her uterus), if there are no contraindications. There is ample evidence, from experimental and observational studies, that this is the time for the primary prevention of CVD and osteoporosis. Estrogens, to be effective, must find a still healthy endothelium, healthy osteoblasts, healthy neurons. If these targets tissues are already damaged, (age effect) estrogens may be ineffective and even dangerous.