

Guest editorial

The menopause: physiology or pathology?

Thus it is easy to prove that the wearing of tall hats and the carrying of umbrella's enlarges the chest, prolongs life, and confers comparative immunity from disease; for the statistics shew that the classes which use these articles are bigger, healthier, and live longer than the class which never dreams of possessing such things.

George Bernard Shaw: Preface to *The Doctor's Dilemma* (1906).

In a woman's life there are two milestones, both related with menstruation and both to be considered as a point of transition. The first milestone is the start of menstruation around the 12th year. This event – the menarche – marks the transition from childhood to adulthood and is characterized by the onset of the menstrual cycle. The second milestone is the cessation of menstruation around the 52nd year. This event – the menopause – marks the transition from the fertile years to a life phase characterized by a relative hormonal rest and stability, which shows a certain similarity with the life period preceding the first menstruation.

Both transitions – which in a way are each other's mirror image – are to be considered as natural processes, which does not mean that their course is always uneventful. Every transition means an adaptation to a new situation, and adaptation processes can sometimes be turbulent before a new balance is achieved. The transition period around the *first* menstruation is, for example, sometimes accompanied by temporary physical and psychic imbalance, and the same can hold true for the transition period around the *last* menstruation.

All the same, and despite the fact that the majority of women go through menopause with minimal or no complaints [1], this period of life is still popularly associated with ill-health. As Ballinger points out: “Negative expectations of the menopause and the conviction that it presages a marked deterioration in mental health still persists. It is a tribute to the power of culturally determined attitudes, media pressure and the promotion of oestrogen sales that this menopause myth persists, despite all the evidence to the contrary” [2].

Interest in the menopause and the postmenopausal years has boomed over the last three decades. There is probably no other health topic that has received clinical and scientific attention from such a diversity of disciplines, including gynecology, endocrinology, cardiology, orthopedics, rheumatology, urology, dermatology, psychiatry, psychology, epidemiology, sociology and anthropology. According to Medline, publications on the (post)menopause have increased from 80 in 1965 to 800 in 1995. It seems as if menopause has become the central health issue of the aging woman.

In a typical bio-medical approach, the temporal *association* of phenomena, complaints and diseases (also occurring at younger ages and in men) with the peri- and postmenopausal years, has readily evolved into their *attribution* to the hormonal changes surrounding the menopause, and eventually, under the flag of *causality*, into the construction of a “menopausal syndrome” and the definition of the (post)menopause as a deficiency disease [3] or a form of endocrinopathy [4]. The logic consequence

of this concept has been that hormonal replacement therapy (HRT) is advocated for the treatment and prevention of complaints and diseases allegedly caused by the hormonal deficiency.

A frequently heard argument in the physiology versus pathology debate in relation to postmenopausal status is that, as a consequence of the increase in life expectancy over the past centuries, we are nowadays confronted with a new phenomenon: women are living long past their originally normal life span. In this view a postmenopausal life period of 30 years constitutes an unnatural consequence of improved socio-economic status and medical care, calling for new approaches. Although the theory seems attractive, its validity may, at least in part, be questioned. Over the past 150 years, the average life expectancy of women has doubled from 40 to 80 years. These data relate to life expectancy *at birth*; interestingly enough, life expectancy at the age of 65 has only increased four years for women and has remained unchanged for men over the same period [5]. The explanation seems simple: the increase in life expectancy is largely due to a reduction of mortality causes before the age of 65. From this it may be obvious that surviving the menopause for a long period of time is far from being a new phenomenon, although it is also clear that the total proportion of women reaching old age has substantially increased.

Although data on changes in the age of menopause over the past centuries have been conflicting [6], there seems to be enough circumstantial evidence to allow the conclusion that there is a relationship between age at menopause and socio-economic and health status, and that in western countries age at menopause has shown a moderate average increase of four years (from 47 to 51) over the last hundred years [7]. This would nicely parallel the earlier mentioned increase in “postmenopausal” life expectancy, and support the theory that ovarian aging, as reflected by age at natural menopause, might be correlated to the aging process in general, and that “postmenopausal” morbidity and mortality is not due to menopause itself, but rather to the relation of menopause to human development and aging [8,9]. This view seems to be substantiated by a recent study on twins which provides convincing evidence for the importance of genetic factors in determining age at menopause [10].

Hence the basic question remains: are phenomena and diseases occurring during the peri- and postmenopausal years related to the accompanying estrogen depletion, and is, therefore, the menopause to be considered as a pathogenetic life event with all the corresponding “devastating effects of oestrogen deficiency” [11]? Or is the menopause just one of the expressions of aging, and are these phenomena and diseases only for a small part related to estrogen depletion, and mainly a consequence of aging and, like in men, of the genetic, lifestyle and risk factors that influence this aging process and the concomitant morbidity and mortality? In my opinion, there seems to be more evidence for the latter perspective, if only because the vast majority of women, despite long term “postmenopausal estrogen deficiency” are healthier and live longer than their male counterparts.

There is increasing concern about the medicalisation of the third age of women. The postmenopausal phase of life is depicted as potential pathogenetic and (long term) hormone treatment is advocated for the prevention of a variety of diseases such as cardiovascular disease, osteoporotic fractures and, recently, even Alzheimer’s disease.

It should be kept in mind that the results of studies showing a reduced risk for these diseases by HRT are influenced by population bias [12]. It has become clear that the hormone users in these studies differ from the non-users with respect to health promotion and disease prevention measures. These biases of self-selection could explain some or even all of the differences in outcome observed. Moreover the findings usually are based on relative risk (RR) figures, which tell us little about the actual risk reduction for the individual patient. For a better insight in the dangers involved in confusing relative risk with individual risk, one should read Murphy’s book *Honest Medicine*. He summarizes his

chapter on *Numbers behind the medical "facts"* as follows [13]: "Medical science is very subjective. It is based on statistics, which do not provide clear-cut, black-white answers. Statistics are based on probabilities and on an arbitrary threshold. Statistically significant medical findings may or may not be clinically significant. Medical journals and the media typically report a study's statistical significance, not its clinical significance."

Murphy goes on to consider a hypothetical study in which the effect of aspirin on the risk of heart attack is evaluated. It appears that ten out of 1000 volunteers who took one aspirin a day had a heart attack during the five years of study, while twenty of the 1000 volunteers who took a placebo did so. How will the medical journals and the media, and – for that matter – the drug companies report this difference to emphasize the importance of this finding? They will most likely report the *relative* risk reduction of 50% instead of the actual *individual* risk reduction of 1%. So it appears that scientific, journalistic and commercial interests dictate the public presentation of epidemiological research results.

The doubt one can have as to the clinical significance of epidemiological research is exemplified by the famous study of Grady et al. [14], who published an extensive and thorough review on the prevention of disease and the prolongation of life by HRT. Depending on how you read their findings, the results of their calculations could in fact be interpreted as a plea against long term postmenopausal hormone therapy. Assuming that HRT indeed reduces the relative risk for cardiovascular disease and osteoporosis (of which there is still no convincing proof) they have computed from all available epidemiological studies that for estrogen therapy alone the relative risk of coronary heart disease is 0.65, for stroke 0.96, for hip fracture 0.75 and for breast cancer 1.25. When progestogen is added the figures remain essentially unchanged for stroke and osteoporosis but they are higher for coronary disease (0.65–0.80) and breast cancer (1.25–2.00). Translated into overall life probability figures estrogen use alone would prolong life for an average of 0.9 years and estrogen + progestogen for 0.1–1.0 years (consequent upon the assumed adverse effect of progestogens and the assumed decrease in relative risk of coronary heart disease). The authors conclude that "hormone therapy should probably be recommended for women who have had a hysterectomy".

One wonders whether we can speak about a major break-through in preventive medicine when on basis of a not yet proved assumption healthy women are subjected to long term hormone "therapy" in order to prolong their lives with an average of one year at the most. As said before, women are already healthier and live longer than men. Moreover very little is known about the possible adverse medical–ecological consequences of such preventive treatment. It might be that women survive a fatal heart attack only to have a stroke. Not to speak of medical (and drug) dependence, side effects, vaginal bleeding, increased hysterectomy rates (to avoid the unpleasant necessity of prescribing additional progestogens), and increased diagnostic procedures (D&C, mammography) needed for the early diagnosis of diseases that might be in part caused by the preventive measures.

The biomedical approach to the (post)menopause is consistently characterized by numerous industry-sponsored congresses and symposia, the conclusions of which are subsequently conveyed to women through the mass media. A recent example of the latter is the cover story of *Time* (June 26, 1995) with the following headline: "Menopause is unnecessary. Thanks to hormone therapy [women] may look forward to prolonged well-being and extended youth."

Concerns about these developments and about the underestimation of the consequences and potential risks of long term hormone treatment led the University of Leiden, The Netherlands, to organize a symposium on "The menopausal transition: a different view", which took place in June 1997. An account of the proceedings by Barbara Mintzes appears in this issue of the Journal. The full papers

presented at the symposium have already been published in the *Journal of Psychosomatic Obstetrics and Gynecology* [15]. It is sincerely hoped that they will serve as an “eye opener” for all those interested in the bio-psycho-social health of women in their third age, and that the views expressed will eventually lead to a more balanced information on this topic to the public.

The attribution of complaints and/or diseases to the hormonal changes accompanying or following the menopausal transition is not supported by consistent scientific data, whether one considers mood changes, aging processes (osteoporosis and skin thinning) or disease (cardiovascular, Alzheimer and bone fractures). The use of the terms menopausal and postmenopausal in this respect wrongly singles out women as potentially ill (mentally and physically) by the mere fact that they reach the age of the menopause; it has to be considered as an inappropriate, sexist and agist medical misnomer.

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