

FAST FACTS

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*All You Need to
Keep up to
Speed*

Menopause

Second edition

by David H Barlow and Barry G Wren

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HEALTH PRESS

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Declaration of Independence

This book is as balanced and as practical as we can make it. Ideas for improvement are always welcome: feedback@fastfacts.com



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Glossary

CEE: conjugated equine estrogen

CT: computed tomography

DXA: dual-energy X-ray absorption

EDRF: endothelial-derived relaxing factor

EPT: estrogen plus progestogen

FAI: free androgen index

FSH: follicle-stimulating hormone

HABITS: Hormone Replacement Therapy After Breast Cancer – Is It Safe?

HDL: high-density lipoprotein

HERS: Heart and Estrogen/Progestin Replacement Study

HT: hormone therapy (also called HRT)

HRT: hormone replacement therapy (also called HT)

LDL: low-density lipoprotein

MORE: Multiple Outcomes of Raloxifene Evaluation

NO: nitric oxide

SHBG: sex-hormone-binding globulin

SERM: selective estrogen-receptor modulator

SSRI: selective serotonin-reuptake inhibitor

STEAR: selective tissue estrogenic activity regulators

WHI: Women's Health Initiative

A note on terminology: We have used American spelling and terminology throughout this book. With respect to vasomotor symptoms, 'flashing' and 'hot flashes', as they are called in North America, are known in many parts of the English-speaking world as 'flushing' and 'hot flushes'.

Introduction

This concise handbook provides an overview of menopausal and postmenopausal health issues and their management. We have attempted to include a wide and relevant range of topics from our perspective as clinicians in women's postreproductive healthcare.

When discussing health topics, it is all too easy to focus on 'ill health' issues, as these tend to be the greatest concern for those seeking advice. It is therefore important to emphasize at the outset that, for a large number of women, the menopause is free of unpleasant symptoms, or relatively so. Many postmenopausal women will not experience osteoporosis, or the other problems discussed here, in later life and will lead active lives without using hormone therapy (HT). However, these diseases and other related conditions do have a major impact on the quality of life of some older women.

Common diseases in the elderly female population such as osteoporosis, cardiovascular disease, cerebrovascular disease and Alzheimer's disease pose a substantial financial burden on health resources, and knowledge about the effects, or lack of effects, of HT on these conditions has recently been considerably expanded. The potential impact of HT on both individual quality of life and overall healthcare costs is, therefore, an important issue beyond the usual boundaries of traditional 'women's healthcare'. The aims of this book are to increase understanding of the physiological and psychological effects of the menopause and, ultimately, to contribute to effective management.

Female reproductive maturity is characterized by monthly cycles of ovarian follicular development. The cycles govern a woman's circulating hormone levels and provide eggs for potential conception. The menopause is the inevitable consequence of the exhaustion of the supply of ovarian follicles, and can be regarded as a physiological form of ovarian failure.

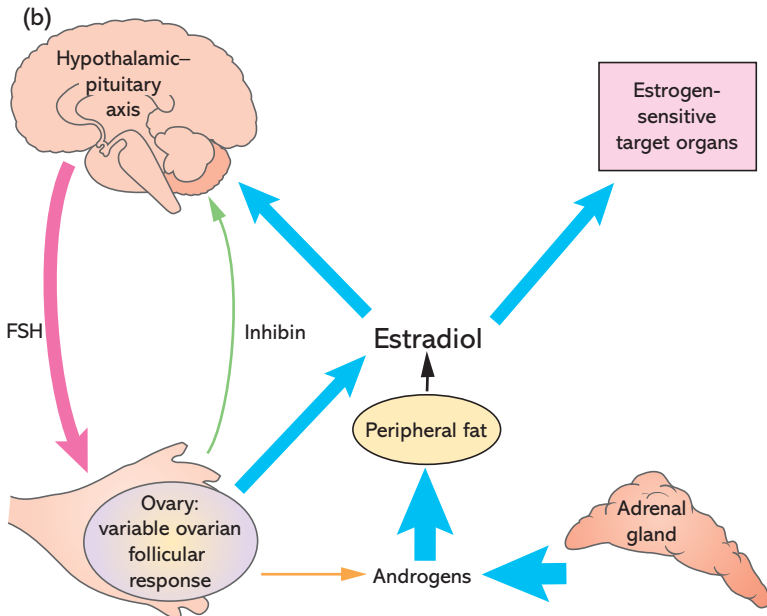
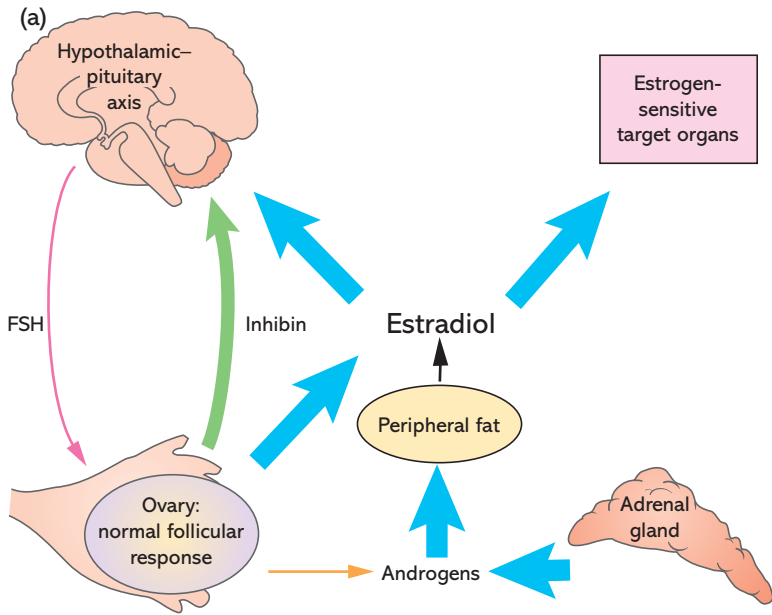
Stages

Three terms are used to refer to the menopause, each with a slightly different meaning:

- perimenopause
- menopause
- climacteric.

Perimenopause. The transition into the perimenopause can be relatively sudden, but it usually lasts 3–5 years. In most women, there is a noticeable decline in the quality of ovarian function. This is indicated by a change in the pattern of menstruation from regular monthly cycles to erratic menstruation with reduced or increased menstrual intervals, or both. This change is usually due to the failure of regular ovulation.

While follicular development continues, significant estrogen production is maintained. However, a rise in the level of circulating follicle-stimulating hormone (FSH) can often be detected during the perimenopause, indicating a degree of failure in feedback from the ovarian hormones (Figure 1.1). Historically, it was assumed that this reflected impaired ovarian estrogen production, but research now suggests that the rise in FSH indicates a reduction in the secretion of the ovarian follicular peptide inhibin. Therefore, the perimenopause is characterized by impaired ovarian function and elevated blood FSH (Table 1.1); there may also be reduced estrogen levels overall.



11 Risks of hormone therapy

There is an extensive debate in the medical community over the incidence of cardiovascular and neoplastic disease and the possible association with HT. These medical issues, which have been picked up by the media, have had a significant impact on acceptability for the patient and on women's continuation of estrogen or EPT. Several major observational studies published over the past few years have contributed to the debate and have caused considerable concern to both doctors and their patients. However, these studies must be carefully evaluated before the findings are accepted as being applicable to all postmenopausal women or all therapy regimens.

In contrast to these observational studies, the WHI trial has the additional validity of being a well-conducted randomized controlled trial, but it is important to emphasize that it was not designed to focus on the effects of HRT in the group of women who have commonly used HRT, namely those in the menopausal transition and in the first postmenopausal decade (say up to 60 years), often for only a few years. Instead, the study was intended to address the effects of HT taken by older postmenopausal women who might use it for an extended number of years for potential long-term health benefit (particularly cardiovascular benefit), an idea becoming popular in the USA at the time the WHI study was designed. This important difference tends to be ignored in the media attention paid to the results of the WHI study, and as a result women in the first postmenopausal decade, who have read headlines about risk, feel concerned about using HT for relief of troublesome symptoms.

Effects of estrogen and estrogen deficiency

Atherosclerosis. Until they reach menopause, women have a markedly reduced risk of atherosclerosis compared with age-matched men. Following menopause, levels of LDL cholesterol

increase. LDL cholesterol has a tendency to be deposited in the arterial intima, leading to atherosclerosis, so postmenopausal women develop atherosclerosis at a rate that parallels the rate for men. Estrogen reduces this effect.

Estrogen appears to have several effects that contribute to the prevention of atherosclerosis.

- Estrogen acts as a potent antioxidant to prevent oxidation of LDL cholesterol. Oxidized LDL is toxic to arterial endothelial cells. The toxic damage causes platelets to release a number of mitogenic factors, which make cells within the vessel wall proliferate, and also induce procoagulant activity.
- Estrogen also has a role in maintaining the integrity of the endothelium.
- In addition, estrogen has a major beneficial effect on HDL cholesterol levels.

The consequences of the hardened arterial walls of atherosclerosis include:

- increased blood pressure
- reduced peripheral blood flow
- increased arterial thrombosis
- increased cardiovascular-related mortality.

Thrombosis. The estrogen deficiency following menopause results in increased risk of thrombosis. The three main causes of thrombosis are:

- damage to the vascular endothelium, which is responsible for maintaining normal hemostasis
- stasis of circulating blood
- changes to the coagulation mechanisms, including an imbalance between the factors that favor coagulation and those that induce fibrinolysis.

Genetic defects in the hemostatic system can increase the risk of thrombosis, and it is important to distinguish these effects from that of estrogen deficiency following the menopause. Some 40–50% of women who develop a thromboembolus are subsequently found to have a congenital coagulation defect. Some women (3%) inherit an