

CONTINUING MEDICAL EDUCATION

The Treatment of Climacteric Symptoms

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SUMMARY

Background: Peri- and postmenopausal women commonly suffer from climacteric symptoms. In this article, we provide information to help physicians recognize climacteric symptoms and treat them appropriately.

Methods: The information presented here is based on a selective search of the literature for pertinent articles that appeared from 2008 to early 2011, including the German S3 guideline on hormone therapy (HT) during and after menopause, which was published in 2009.

Results: Perimenopausal women often suffer from climacteric symptoms. Typically, women undergoing menopause complain of heat waves and vaginal dryness. According to randomized controlled trials as well as national and international guidelines, HT is the most effective treatment for vasomotor symptoms and also improves vulvovaginal atrophy; for the latter indication, HT is preferably administered locally. Vaginal estrogen therapy lowers the frequency of recurrent urinary tract infections. However, HT is associated with an increased risk for a number of diseases, including stroke, thromboembolic events, gallbladder diseases, and breast cancer. Alternative treatments for climacteric symptoms have little or no efficacy.

Conclusion: HT should only be used to treat climacteric symptoms after extensive patient education about its benefits and risks. Participatory decision-making is desirable. The generalized use of HT by all women with climacteric symptoms cannot be recommended.

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Peri- and postmenopausal women often seek medical help, and climacteric symptoms are their most common reason for doing so. These symptoms are due to changes in ovarian function during the menopause. The transition from full ovarian function in the premenopausal period to a complete lack of ovarian estrogen synthesis in the postmenopausal period is, fundamentally, a normal aspect of human physiology, but specific disturbances or diseases may develop as a result of diminished estrogen synthesis. Moreover, the peri- and postmenopausal periods are marked by psychosocial and other age-related changes that can also cause certain physical symptoms. A rational approach to climacteric symptoms *per se* requires a well-founded knowledge of the specific physiological and pathophysiological changes affecting women at this time in their lives. A number of treatments are available; a commonly used one is peri- and postmenopausal hormone therapy (HT) with sex steroids. There has been a search for alternative treatments, particularly in recent years. In this review, we will discuss the main types of climacteric symptoms and their treatment. We will direct our attention primarily to HT, as it is clearly the most effective treatment available today.

Learning objectives

Readers of this article should gain knowledge of the following aspects of the treatment of climacteric symptoms:

- the recognition of climacteric symptoms,
- the effects of hormone therapy on them,
- the risks of hormone therapy, and
- alternative treatments.

Methods

This review is based on a selective search in PubMed for articles published from 2008 to 2011 that contained the key words “climacteric symptoms.”

Climacteric symptoms

There are a number of ways to treat climacteric symptoms. Hormone therapy with sex steroids is a common form of treatment in the peri- and postmenopausal periods.

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“menopausal symptoms,” “menopausal hormone therapy,” and “hormone replacement therapy.”

The retrieved publications are discussed in the text of this article if they contain information that is relevant to the topic of the article, as defined above. The state of scientific knowledge based on publications up to 2008 has already been taken into account in the creation of the German S3 guideline on hormone therapy (HT) in the peri- and postmenopausal periods (1, 2, e1).

This systematic search and assessment of scientific evidence was performed in relation to climacteric symptoms, quality of life, urogenital symptoms, the musculoskeletal apparatus, bone metabolism, cardiovascular diseases, other diseases and aging processes, CNS diseases, cancer, premature ovarian failure, and alternative treatments.

A detailed description of the manner of testing and assessing the scientific evidence can be found in the methods report accompanying the S3 guideline. The guideline contains position statements that were issued on the basis of an evaluation of the evidence followed by a consensus-building process. These statements, in turn, provided the basis for the clinical recommendations that were derived from them.

Climacteric symptoms and the quality of life

Perimenopausal women report so-called climacteric symptoms with varying frequency (1–3, e1). Some of these are clearly attributable to the reduced synthesis of sex steroids (e.g., vasomotor symptoms), while others may be of multifactorial origin (e.g., mood fluctuations). The constellation of symptoms is often designated the climacteric syndrome; there is, however, no uniform definition of this syndrome. Many cohort studies and cross-sectional studies have been performed for the purpose of characterizing climacteric symptoms (4–8, e2, e3). The ones most consistently found were hot flashes and vaginal dryness. Further symptoms such as sleep disturbances, bodily symptoms of various kinds, urinary tract symptoms, sexual problems, and mood changes were less consistently present (Box 1). The duration of hot flashes in relation to the beginning of menopause was the subject of a recently published cohort study of 436 initially premenopausal women aged 35 to 47. 90 of them developed mild hot flashes, while 259 developed moderate to severe hot flashes, and 55 had none at all. The mean duration of moderate to severe hot flashes

BOX 1

Climacteric symptoms

- **Consistently appearing symptoms**
 - vasomotor symptoms (hot flashes, diaphoresis)
 - vaginal dryness
- **Less consistently appearing symptoms**
 - sleep disturbances
 - mood changes
 - urinary tract symptoms
 - sexual problems (loss of libido, dyspareunia, other)
 - other bodily symptoms

was 10.2 years; they lasted particularly long (>11.57 years) if they had begun in the early perimenopausal period (3).

An overall assessment of the available studies provides no clear answer to the question whether women have a worse quality of life during this phase of their lives. The quality of life, however, was not uniformly defined from study to study, and women with and without vasomotor symptoms were included in the analysis. Clinical experience clearly shows that women who suffer from these symptoms to a major extent consider their quality of life to be markedly reduced. This is why they seek treatment.

Alternatives to hormone therapy

Because HT has certain risks, there has been a search for other treatments, particularly with drugs. Preparations of botanical origin are especially popular. There have been many trials on the treatment of climacteric symptoms with phyto-estrogens in the form of isoflavone from red clover or soya and *Cimicifuga racemosa*. Most of the placebo-controlled trials have failed to show any significant reduction of vasomotor symptoms (9), although some did reveal a small effect. Urogenital symptoms were not improved. In particular, nothing is known about the long-term safety of these preparations. For these reasons, phyto-estrogens and other botanical and non-hormonal alternatives to hormone therapy cannot be recommended.

Consistently present climacteric symptoms

- vasomotor symptoms (hot flashes, diaphoresis)
- vaginal dryness

Less consistent climacteric symptoms

- sleep disturbances
- mood changes
- sexual problems
- other bodily symptoms

BOX 2

Types and modes of application of hormone therapy

ET	estrogen therapy
EPT	combined estrogen-progestagen therapy
HT	hormone therapy (ET and EPT, orally and transdermally administered systemic therapy)
Vaginal ET	low-dose vaginal estrogen therapy with little or no systemic effect

A number of changes in lifestyle can, to some extent, improve mild vasomotor symptoms. This is suggested mainly by data from observational studies. Hot flashes can be reduced by low ambient temperatures. Women with a higher body-mass index were once thought to have less frequent hot flashes because of greater aromatization of androgens in adipose tissue, but recent studies have shown that they actually have more frequent hot flashes; thus, weight reduction down to a normal body weight is desirable. Non-smoking women suffer from hot flashes less commonly than smokers. Regular physical exercise, too, can improve hot flashes. Relaxation exercises have a beneficial effect on the frequency and intensity of hot flashes (e4).

Women for whom hormone therapy is contraindicated, such as women with breast cancer, are in a special situation. The selective serotonin reuptake inhibitors venlafaxine and fluoxetine have been found effective against vasomotor symptoms; on the other hand, there is no clear evidence for the effectiveness of the antihypertensive agents clonidine and methyl dopa in this context. Gabapentin, an anticonvulsant, has been found to have a beneficial effect on climacteric symptoms. The medications mentioned here as effective have not been approved for the treatment of climacteric symptoms. It would seem appropriate to use them off label, after sufficient patient education, in cases where hormone therapy is contraindicated (1, 2, e1).

Substances used for hormone therapy

In non-hysterectomized women, combined estrogen-gestagen therapy (EPT) must be administered instead

of estrogen therapy alone (ET) in order not to elevate the risk of endometrial hyperplasia and endometrial carcinoma. Both oral and transdermal preparations of EPT are available (Box 2); natural progesterone can also be administered vaginally. Either progesterone derivatives or norethisterone derivatives (C-21 or C-19 steroids, respectively) can be used; these may have different partial effects, and one or the other can be chosen for use accordingly. Combined estrogen-gestagen therapy is administered either sequentially, with at least ten days of gestagen administration per month, or continually in combination. A seven-day hormone-free interval (as in oral contraceptive therapy) is no longer recommended, as it often leads to a worsening of symptoms.

Various estrogens are used to treat climacteric symptoms. Estradiol, estradiol valerate, estriol, estriol succinate, and conjugated or esterized estrogens are available in various preparations (Box 2). Systemic administration can be by the oral, transdermal, intranasal, or intramuscular route. For urogenital symptoms, estradiol is given as a vaginal tablet, ring, or cream; estriol is also given in these ways for this indication. Estradiol can be given transdermally (as a plaster or gel) in dosages from 0.25 to 0.1 mg/day. For the vaginal application of estradiol, there are vaginal tablets containing 0.025 mg/day, vaginal rings containing 0.075 mg/day, and creams containing 0.1 mg/day. The daily dose of estriol administered vaginally ranges from 0.02 to 0.5 mg/day. When estradiol is given orally, the bioavailability of the steroid is only 5%, because of a first-pass effect; on the other hand, when it is given transdermally, it is nearly 100% bioavailable. This is why the usual doses vary depending on the route of administration. Drugs are very well absorbed when given vaginally. Conjugated estrogens contain a mixture of 10 different types of estrogen; their main components are estrone, equiline, 17 β -dehydroequiline, and 17 β -estradiol. After the oral administration of 2 mg of estradiol, serum levels of ca. 40–80 pg/mL are measured (10); similar levels are reached when 0.05 mg are given in the form of a plaster, or 3 mg in the form of a gel. It should be borne in mind that the vaginal administration of estrogens also gives rise to measurable serum concentrations. For example, when 0.5 mg of estriol is given vaginally, a serum estriol concentration of up to 100 pg/mL can be measured (e5). Thus, vaginally administered estrogens can have systemic effects.

Alternatives to hormone therapy

- aiming for normal body weight
- smoking cessation
- regular physical exercise
- relaxation exercises

Estrogens for the treatment of climacteric symptoms

- estradiol
- estradiol valerate
- estriol
- estriol succinate

Tibolone, a norethinodrel derivative with estrogenic, androgenic, and gestagenic properties, is also used to treat climacteric symptoms (1, 2, e1). Before any hormone therapy is started, the indication should be carefully considered; the patient should be evaluated with extensive history-taking and physical examination, including a gynecological examination. Only in this way can the physician detect certain contraindications and health risks that might arise if HT were to be initiated (*Table*).

The effect of hormone therapy on climacteric symptoms

Many placebo-controlled, double-blind trials have shown that HT relieves vasomotor symptoms. It lowers the frequency of hot flashes by about 75%. Estrogens have been found to be effective, sometimes in combination with gestagens and tibolone. The reported side effects include breast tenderness, uterine bleeding, hemorrhage, arthralgia, emotional changes (irritability, loss of motivation, depression, other), and, less commonly, nausea, vomiting, headache, weight changes, rash, and pruritus (relative risk, 1.41; 95% confidence interval, 1.00–1.99) (7). The risks of other important clinical endpoints are mentioned in other subsections of this review. The efficacy of HT is rated as high in a position statement of the North American Menopause Society, published in 2010 and closely following the German S3 guideline in updated form. Estrogen therapy (ET) with or without the additional administration of gestagens is stated to be the most effective treatment for perimenopausal vasomotor symptoms. The latter are the main indication for HT (11).

The effect of hormone therapy on the quality of life

Only a very small number of randomized, placebo-controlled trials have addressed this issue, yielding inconsistent findings. It should be pointed out that the quality of life was not defined uniformly. No improvement in the quality of life was found in the WHI study, yet smaller-scale placebo-controlled trials that were conducted over relatively short times did, in fact, reveal that HT improved the quality of life. The consensus paper of the North American Menopause Society takes the position that it is unclear whether HT improves the health-related quality of life of asymptomatic women (11).

The effect of hormone therapy on climacteric symptoms

Many placebo-controlled, double-blind trials of HT in symptomatic women have clearly revealed an effect on vasomotor symptoms.

TABLE	
The risks of perimenopausal hormone therapy ^{*1}	
Endpoint	Absolute risk
Thromboembolic events	ET: +6 events/10 000 women/year (21 [HT] vs. 15 events [placebo])
	EPT: +18 events/10 000 women/year (35 [HT] vs. 17 events [placebo])
Any biliary disease	ET: +31 events/10 000 women/year (78 [HT] vs. 47 events [placebo])
	EPT: +20 events/10 000 women/year (55 [HT] vs. 35 events [placebo])
Breast cancer	ET: -7 events/10 000 women/year (26 [HT] vs. 33 events [placebo]) (ns)
	EPT: +8 events/10 000 women/year (38 [HT] vs. 30 events [placebo])
Stroke	ET (any stroke): +12 events/10 000 women/year (44 [HT] vs. 32 events [placebo])
	EPT (ischemic stroke): +8 events/10 000 women/year (26 [HT] vs. 18 events [placebo])

^{*1} Published data from the available studies in which absolute risk figures are given for the four endpoints in the left column of the table. These risks may be independent of the duration of therapy and the time of its initiation in relation to the age of menopause (see text; adapted from [2]). HT, hormone therapy; ET, estrogen therapy; EPT, estrogen-gestagen therapy; ns, not significant.

Urinary incontinence

A meta-analysis of 50 small-scale trials led to the conclusion that ET can partially or completely relieve urinary incontinence, particularly when an overactive bladder is the cause.

Vulvovaginal atrophy

Meta-analyses have led to the conclusion that HT by any route of administration improves the signs and symptoms of vaginal atrophy (12, e6). Low-dose, local ET is just as effective as systemic ET. If symptomatic vaginal atrophy is the only indication for treatment, local vaginal ET should be given. This is the recommendation of both the German S3 guideline and the position paper of the North American Menopause Society (1, 2, 11, e1, e7).

Urinary incontinence

The various types of urinary incontinence have many different causes. Urinary incontinence can take one of two main forms: an overactive bladder, or stress incontinence. A meta-analysis of 50 small-scale trials led to the conclusion that ET can partly or completely relieve urinary incontinence, particularly when due to an overactive bladder (13). Two randomized trials, HERS and WHI, revealed that oral HT makes urinary incontinence worse (14, 15). Transdermal or vaginal estrogen application improved incontinence to a not necessarily significant extent. Thus, oral HT should not be prescribed for the treatment of urinary incontinence; in cases of bladder overactivity, vaginal ET can be considered, in view of its favorable risk/benefit profile. The current state of the evidence is judged similarly in the position paper of the North American Menopause Society, in which it is stated that local ET can improve urge incontinence in patients with vaginal atrophy; on the other hand, its efficacy against stress incontinence is debated. It should be mentioned that various types of incontinence can be treated with non-hormonal medications, physical therapy, and operations whose efficacy is well documented (1, 2, 11, e1, e8).

Recurrent urinary tract infection

Estrogens have direct proliferative effects on the urethral and vesical epithelium. Further effects include a buildup of the vaginal epithelium and reconstitution of the vaginal flora, resulting in a lower frequency of colpitis. In small-scale trials, vaginal ET significantly reduced the frequency of urinary tract infections (16). On the other hand, oral HT has no protective effect of this kind. Vaginal estrogen is recommended for the treatment of recurrent urinary tract infections both by the North American Menopause Society and in the German S3 guideline (1, 2, 11, e1). The relative risk is reduced by 36% to 75% (16).

Recurrent urinary tract infections

Vaginal estrogen treatment is recommended for recurrent urinary tract infections both by the German S3 guideline and by the North American Menopause Society.

Risk/benefit assessment

All the above makes clear that HT can be an effective method of treating climacteric symptoms. The decision whether or not to give oral or parenteral HT depends in large measure on the individual patient's state of health. Perimenopausal women generally have fewer comorbidities than older, postmenopausal women. Meticulous history-taking is needed in any case before the treatment is initiated. Sex steroids can affect the risk of developing certain diseases. A thorough understanding of these risks is important, as they depend not only on the patient's health profile, but also on the particular hormonal regimen used (ET, EPT) and on the duration of administration. Some risks are much greater than others. All patients should be adequately informed about the risks of their treatment.

Osteoporosis

HT has been found to lower the incidence of fractures both in observational studies and in randomized, controlled clinical trials (17–19, e9). The clinical fracture rate is lowered, as is that of so-called osteoporosis-associated fractures. In general, however, the prevention and treatment of osteoporosis is not an issue for women seeking treatment for climacteric symptoms (1, 2, e1). Although EPT is an effective means of preventing osteoporosis, it cannot be recommended as a first-line therapy except in rare cases, in view of its unfavorable risk/benefit profile. The risks of ET, on the other hand, are commensurate with its benefits (e10).

Cardiovascular diseases

Coronary heart disease

The WHI study revealed a mild elevation of the risk of cardiovascular events among women receiving HT. This was a surprising finding, as a protective effect had been expected in view of the biological effects of estrogens on lipoproteins and arterial vessels. The median age of the subjects in the WHI study was 60; one cannot, therefore, extrapolate the finding to healthy women around age 50 who are treated with estrogens (alone or in combination with gestagens) for climacteric symptoms. There is no evidence that such women have a significantly elevated risk of coronary heart disease. Indeed, there is evidence that, when ET is initiated early (after hysterectomy), it may actually lower the cardiovascular risk (20, 21).

Risk/benefit assessment

The individual patient's state of health is a very important consideration with respect to the indication for HT. Perimenopausal women generally have fewer comorbidities than elderly postmenopausal women.

Stroke

Randomized, controlled trials and meta-analyses of observational studies have revealed that ET and EPT elevate the risk of stroke. In the WHI, the relative risk was 1.39 for ET and 1.44 for EPT, while the absolute risk was +12 events per 10 000 women per year for ET, and +8 for EPT (Table). Tibolone roughly doubles the risk of stroke. Perimenopausal women have a low risk of stroke in any case but should be informed of the risk before ET or EPT is begun, in view of the seriousness of the condition.

Venous thromboembolism

The risk of venous thromboembolism is elevated in the first year of treatment to a greater extent than in later years; thus, special care should be exercised here. The absolute elevation of risk is +6 events per 10 000 women per year under ET, and +17 under EPT (Table).

Biliary diseases

HT elevates the risk of biliary diseases. The risk is already elevated in the initial phase of treatment, particularly in overweight patients or those with a history of biliary disease (1, 2, e1).

Diseases of the central nervous system

Cognition

Meta-analyses have shown that neither ET nor EPT prevents the decline of cognitive functions in older, postmenopausal women. The putative cognitive effects of HT in younger postmenopausal and perimenopausal women are currently debated.

Dementia

Continuous combined HT elevates the risk of dementia in women over age 65. This fact, however, appears to be of little relevance for the decision whether to treat climacteric symptoms with HT (1, 2, e1).

Cancer

Breast cancer

EPT elevates the risk of breast cancer from the sixth year of treatment onward. Newer analyses of the WHI data have revealed that EPT administered early in the postmenopausal period can also elevate the risk of breast cancer within the first five years of treatment (e11). In one study of ET, the risk of breast cancer was actually found to be lower after a mean duration of treatment of 5.9 years (21), but meta-analyses of randomized, controlled trials and observational studies

have revealed an increased risk with more than 5 years of treatment (e12). These meta-analyses also confirmed the risk-increasing effect of EPT and showed it to be markedly higher than that of ET. It can be concluded that ET must be given for a much longer time than EPT to elevate the risk of breast cancer. The significant lowering of the breast-cancer risk by ET in the WHI study is of unclear meaning (21). In summary, for women in the climacteric period who seek hormonal therapy of less than five years' duration for their climacteric symptoms, an elevated risk of breast cancer is either not a consideration at all (ET), or not a major one (EPT).

Endometrial cancer

ET increases the risk of endometrial cancer in postmenopausal, non-hysterectomized women. This increase is large compared to the low-to-moderate increase in breast cancer risk. In women who have been under ET for more than three years, the relative risk of endometrial cancer is raised as much as fivefold; after ten years, as much as tenfold (19, e13, e14). When climacteric symptoms are treated with an appropriately constituted EPT, i.e., one in which gestagens are given at least ten days per month, the risk of endometrial cancer is not elevated.

Ovarian cancer

A meta-analysis of a large amount of study data revealed that HT raises the relative risk of ovarian cancer to 1.24. ET elevates the risk more than EPT does, and the risk is not elevated at all if the treatment is given for less than five years. HT for more than ten years has been found to raise the relative risk to 1.21 (e15). On the other hand, an observational study that was conducted on a very large scale showed an increase of relative risk to 1.38 after a median follow-up of eight years. It is estimated that it takes one year of HT in 8300 women to produce one additional case of ovarian cancer (22).

Colorectal cancer

Meta-analyses of observational studies have shown that the risk of colorectal cancer is about 20% lower in women who have undergone HT (23). In the WHI study, a significant lowering of the risk was found only in association with EPT; in most observational studies, however, both ET and EPT lowered the risk. Recent data from the European Prospective Investigation into

Cardiovascular diseases

The WHI revealed that HT mildly elevates the risk of cardiovascular events.

Breast cancer

EPT raises the risk of breast cancer. An elevated risk has been demonstrated only after five or more years of EPT.

Cancer and Nutrition (EPIC) study have led to a renewal of debate on the subject: in this study, which was carried out on nearly 140 000 postmenopausal women, neither ET nor EPT had any significant effect on the risk of colorectal cancer (24).

HT after cancer

HT should not be given in the aftermath of any type of hormone-dependent malignant disease. As pointed out in the German S3 guideline, an analysis of the available evidence reveals, for example, that HT elevates the risk of recurrence in women who have been treated for breast cancer. The risk of recurrence of endometrial, ovarian, and colorectal cancer has not been adequately studied, and nothing can be said about other types of cancer in view of the lack of data. Thus, HT is contraindicated after breast cancer; after other types of cancer, particularly those that are hormone-dependent, decisions must be made on an individual basis. The main considerations here are factors such as hormone dependency, the risk of recurrence, and the scientific understanding of the oncogenic effect of HT (1, 2, e1).

Overview

HT is the most effective means of treating climacteric symptoms. It can be recommended for the treatment of bothersome vasomotor symptoms and associated disturbances. Local ET is suitable for the treatment of vulvovaginal atrophy and recurrent urinary tract infections. Before HT is begun, the patient must be adequately informed of the risks and benefits, so that she can decide whether her climacteric symptoms are disturbing enough to warrant treatment with HT. Treatments other than HT are less effective or ineffective.

Conflict of interest statement

Prof. Ortmann is a paid consultant for Dr. Wolff Pharma and receives research support from medinova.

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Endometrial carcinoma

ET raises the risk of endometrial carcinoma in post-menopausal, non-hysterectomized women.

Ovarian carcinoma

A large-scale meta-analysis revealed that HT is associated with a relative risk of 1.24.

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The CME unit "Insect Stings: Clinical Features and Management" (Issue 13/2012) can be accessed until 11 May 2012. For issue 21/2012, we plan to offer the topic "Acute Confusional States in the Elderly".

Solutions to the CME questions in issue 9/2012:
 Horneber M et al.: Cancer-Related Fatigue.
 Solutions: 1a, 2d, 3c, 4e, 5a, 6b, 7d, 8d, 9b, 10c

Please answer the following questions to participate in our certified Continuing Medical Education program. Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1

Which of the following climacteric symptoms are consistently present?

- a) Sleep disturbances and bodily symptoms
- b) Heat waves and vaginal dryness
- c) Urinary tract symptoms and sexual problems
- d) Mood changes and sleep disturbances
- e) Bodily symptoms and mood changes

Question 2

Oral hormone therapy elevates the risk of which of the following diseases?

- a) Urticaria
- b) Thromboembolism
- c) Acne vulgaris
- d) Osteoporosis
- e) Hip dysplasia

Question 3

By what percentage does hormone therapy reduce hot flashes?

- a) 15%
- b) 35%
- c) 55%
- d) 75%
- e) 95%

Question 4

What mode of application of hormone therapy is NOT effective for the treatment of vasomotor symptoms?

- a) transdermal
- b) oral
- c) vaginal
- d) nasal
- e) intramuscular

Question 5

A perimenopausal patient asks you for information about hormone therapy and the risk of venous thromboembolism. What should you tell her?

- a) Hormone therapy lowers the risk.
- b) Estrogen monotherapy changes the risk to the same extent as combined estrogen-progestagen therapy.
- c) The risk is markedly elevated in the first year of hormone therapy.
- d) Obesity and thrombophilia have no effect on the risk of venous thromboembolism.
- e) An elevated risk has only been observed after multiple years of hormone therapy.

Question 6

Hormone therapy elevates the risk of breast cancer. For what type and duration of therapy has this been demonstrated?

- a) ET for 3 years
- b) EPT for 3 years
- c) EPT for 5 years or more
- d) ET for 1 year
- e) EPT for 1 year

Question 7

What type of hormone therapy does NOT elevate the risk of endometrial carcinoma in women who have not undergone hysterectomy?

- a) pure ET
- b) EPT with five days of gestagen administration per month
- c) EPT with twelve days of gestagen administration per quarter
- d) EPT with five days of gestagen administration per quarter
- e) EPT with twelve days of gestagen administration per month

Question 8

What should you tell patients about hormone therapy and the risk of colorectal cancer?

- a) The risk of colorectal cancer can be reduced by hormone therapy.
- b) Even a short course of hormone therapy markedly lowers the risk.
- c) If colorectal cancer is diagnosed, hormone therapy must be stopped at once.
- d) Women with a family history of colorectal cancer can take prophylactic medication along with hormone therapy.
- e) Hormone therapy elevates the risk of colorectal cancer.

Question 9

How does estrogen therapy in the perimenopausal period affect the risk of stroke?

- a) +6 events/10 000 women/year
- b) +31 events/10 000 women/year
- c) -7 events/10 000 women/year
- d) -2 events/10 000 women/year
- e) +12 events/10 000 women/year

Question 10

A patient asks you about non-hormonal treatment of hot flashes. What should you tell her about the current state of scientific knowledge on this question?

- a) Isoflavones improve urogenital symptoms.
- b) Isoflavones are just as effective as hormone therapy for the treatment of hot flashes.
- c) Alternative methods are safer than hormone therapy.
- d) Serotonin reuptake inhibitors can improve the symptoms.
- e) Selective serotonin reuptake inhibitors have been approved for the treatment of climacteric symptoms.

CONTINUING MEDICAL EDUCATION

The Treatment of Climacteric Symptoms

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