Continuing Medical Education

Medical Eligibility for Contraception in Women at Increased Risk

Thomas Römer

Summary

Background: Most women of child-bearing age want a safe method of contraception. Numerous methods are available, with different modes of application. In situations involving particular risks, the selection of the right method poses a special challenge.

Methods: Contraceptive methods for use in various situations with increased risk are presented in the light of a selective review of the literature, including the relevant current guidelines.

Results: The current recommendations of the World Health Organization (WHO) can be used to determine whether any particular contraceptive method is applicable. In particular, the use of combined hormonal contraceptives may be contraindicated in the presence of certain risk factors, especially when there is an elevated risk of thromboembolism. Situations of increased risk include a genetic predisposition to thrombophilia, diabetes mellitus, age over 35, and nicotine abuse. Careful attention to the choice of an appropriate contraceptive agent is also necessary for women with hypertension, hepatic tumors, headache (including migraine), and epilepsy. For such patients, good alternatives include the use of a gestagen (=progesterone) single-agent preparation, an intrauterine device, or a pessary.

Conclusion: Meticulous history-taking and clinical examination are important components of contraceptive counseling that enable the identification of all potential risk factors. In situations of increased risk, decisions must be taken individually. Depending on the nature of the patient's underlying illness, interdisciplinary collaboration may be advisable. Even in situations of increased risk, an appropriated risk-benefit analysis should make it possible to find a suitable contraceptive method for any woman who needs one.

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Many different methods of contraception are now available in Germany. Most of them are hormone-based, including the commonly used combined oral contraceptives (1, e1–e3).

Vaginal rings and transdermal contraceptive patches are less commonly used. Further alternatives include gestagen (=progesterone) single-drug preparations, with various modes of administration: oral ingestion (desogestrel single-agent pills), depot injection (medroxyprogesterone acetate in depot form), or subdermal implantation (etonogestrel) (e1, e2).

A copper-based intrauterine device can also be used for contraception. Such devices consist of a copper spiral, possibly supplemented by a silver or gold component or a copper chain or ball.

Further intrauterine contraceptives include four types of levonorgestrel intrauterine systems (LNG-IUS) that are available for administration in various doses.

Contraception

Many different methods of contraception are now available in Germany. Most of them are hormone-based, including the commonly used combined oral contraceptives.

Intrauterine contraceptive methods

Further intrauterine contraceptives include levonorgestrel intrauterine systems (LNG-IUS), which are available for administration in various doses.

The German Federal Center for Health Education *(Bundeszentrale für gesundheitliche Aufklärung)* carried out a survey on contraception in December 2018. The 705 women who were interviewed (aged 18 to 49) used one or more methods of contraception (e4):

- oral contraceptives, 47%
- condoms, 46%
- intrauterine contraceptive methods, 10%
- male sterilization, 3%
- calendar method, 3%
- female sterilization, 2%
- temperature method, 2%
- vaginal ring/NuvaRing, 2%
- three-month injection, 1%

Method

For the literature search in Medline, a selection of citations was made that are relevant to central Europe and have been incorporated into the corresponding guidelines. As hardly any randomized and controlled trials are available on the subject, the included publications consisted mainly of observational studies and meta-analyses of observational studies. Current guidelines and WHO recommendations were considered as well. The special aspects of post-coital contraception ("morning-after pills") are beyond the scope of this article.

Learning objectives

This article is intended to acquaint the reader with

- the fundamentals of contraceptive selection,
- the findings on history and physical examination that suggest the presence of special risk factors with relevance to the choice of a contraceptive method,
- the rational use of the various available methods of contraception in special situations of increased risk, and the appropriate counseling of patients in these situations.

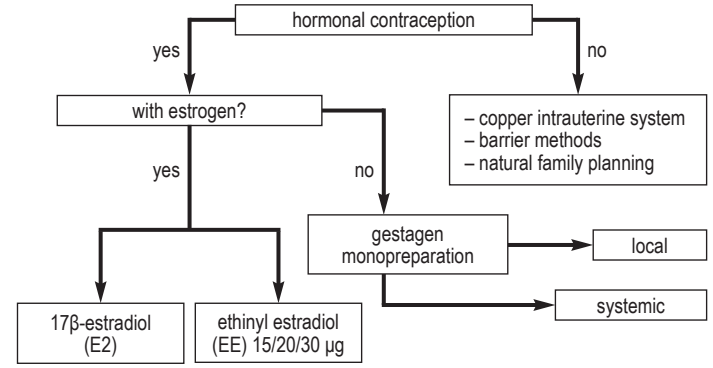
The fundamentals of contraceptive selection

The patient's wishes should be the main initial consideration in the choice of a contraceptive method. The most important aspect is the length of time over which the patient desires contraception.

Patients should be counseled about the various types of long-term contraception, i.e., contraceptive methods that are effective and reversible and do not require daily application: for example, gestagen implants or copper or hormone spirals. Such methods were, at one time, mainly used by women over age 35 who did not want to have any more children. But women are now older on the average when they bear their first child (2017: 29 years and 10 months), and the period of time in which they want contraception before their first pregnancy has become correspondingly longer (e5). As a result, long-term contraception (intrauterine methods, gestagen implants and injections) has become a more commonly used option in younger patients. Depot medroxyprogesterone acetate (MPA) is not suitable for this purpose, because ovulation may not return for up to nine months after it is discontinued (e1).

If risk factors are present, then not only the patient's wishes, but also the medical aspects of the various contraceptive methods need to be considered. There may be an absolute or relative contraindication to the use of hormonal or other contraceptive methods. A directed family history is important, for example, with respect to thromboembolic events in the patient's near relatives. As a matter of routine practice, even women with a positive family history can take hormonal contraceptives according to the current state of the scientific evidence, as long as the specific aspects of the individual risk situation are known to the physician and are taken into account (1). If a decision is taken in favor of a hormonal method,

FIGURE



Contraceptive options (algorithm for the choice of method)
E2, estradiol; EE, ethinyl estradiol

The fundamentals of decision-making

The patient's wishes should be the main initial consideration in the choice of a contraceptive method. The most important aspect is the length of time over which the patient desires contraception.

Long-term contraception

Long-term contraception was, at one time, mainly used by women over age 35 who did not want to have any more children. Because women are now older on the average when they bear their first child, long-term contraception has become a more common option for younger women as well.

TABLE 1

Factors to be considered in the determination of the ethinyl estradiol dose in a combined oral contraceptive

Factors/symptoms	COC with ≤ 20 µg ethinyl estradiol	COC with ≥ 30 µg ethinyl estradiol
Cycle	regular	irregular
Skin lesions	no	acne
Ovarian cysts	no	yes
Other drugs (risk of interactions)	no	yes
Risk factors for thromboembolism	yes	no
Cigarette smoking	yes	no
Reliable intake of COC	yes	less reliable

COC, combined oral contraceptives

an important question is whether a method containing estrogens can be used, because many of the risks of hormonal contraceptives arise only with combined preparations. Gestagen monotherapy is often a good alternative when combination therapy is contraindicated. If there are risk factors contraindicating gestagen monotherapy as well, contraception can usually be given with a levonorgestrel intrauterine system or intrauterine spirals instead *(Figure)*. If a a combined hormonal contraceptive method is decided on, it needs to be determined which estrogen should be used. Ethinyl estradiol is the most common estrogen in combined preparations, but there are also preparations (one each) that contain estradiol and estradiol valerate. If an ethinyl estradiol preparation is used, the dose can be selected in the range of 15 to 50 µg *(Table 1)*, with 20- and 30-µg preparations being the ones most commonly used. The choice of gestagen is a further important matter. Here, the thrombogenic potential of different classes of gestagens is typically the main issue, but there are also other effects to consider, including their partial anti-androgenic and antimineralocorticoid effects. These additional therapeutic effects of oral contraceptives can play an important role. The thromboembolic effect of combined hormonal methods does not vary significantly with the method of administration (oral, patch, vaginal ring) (2, 3). For combined oral contraceptives, the thromboembolic risk (estimated incidence) lies between 5 and 12 per 10 000 women per year of application; the corresponding figures for the vaginal ring and the contraceptive patch are 7.8 and 9.7, respectively (2, e6).

It remains unclear whether hormonal contraception raises the incidence of breast cancer. A mildly increased risk, both while the patient is taking oral contraception and afterward, cannot be excluded (e3, e7, e8).

WHO recommendations on contraception

As there is no current contraception guideline in Germany (except for a recently published version for use in consultations) (e2), the current WHO recommendations are most commonly used in practice. The WHO regularly publishes recommendations for the use of contraceptive methods in particular situations, which are classified in four categories (2) *(Table 2)*. This scheme also provides a basis for clinically and medicolegally secure documentation in routine practice.

Individual decisions may, however, need to be taken in special risk situations that are not clearly reflected in the WHO recommendations. Such decisions often require interdisciplinary consultation, particularly when the patient suffers from a specific medical condition that is outside the gynecological sphere (1).

Risk situations

Age of the patient

In healthy women, age alone does not contraindicate combined hormonal contraception. If an older woman has other risk factors as well, such as obesity, hypertension, or a positive family history of thromboembolic events, then the use of combined hormonal methods should be viewed critically, and an alternative method should be used if possible, e.g., a gestagen single-drug preparation, a levonorgestrel intrauterine system, or a copper spiral (1, 4).

In the WHO guidelines *(Table 2),* a score of 2 is assigned to all combined contraceptive methods for patients aged 40, which means that their benefit is held to outweigh their risks (2). The practical implication is that, for patients aged 40 or above, further risk factors must be meticulously sought and documented (e.g., nicotine abuse, hypertension), and a different method must be chosen if necessary. In women with no further risk factors, increasing age is not an obligatory indication for a change of method. For adolescents, there is, generally speaking, no contraindication for any method of contraception, except depot MPA (e9). When a contraceptive method is prescribed for a patient under age 18, the relevant legal restrictions in Germany need to be taken into account as well. These will not be discussed here.

The WHO recommendations

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Age of the patient

In healthy women, age alone does not contraindicate combined hormonal contraception.

Obesity

The WHO defines obesity as a body-mass index (BMI) greater than 30 kg/m^2. The degree of obesity is important: grade 3 obesity, with a BMI over 40 kg/m^2, is more relevant to the choice of a contraceptive method than grade 1 obesity, with a BMI of up to 35 kg/m^2.

Obesity is considered a risk factor for the use of combined oral contraceptives both in the WHO recommendations and in the German Red Hand Letter (2, 4). The WHO recommendations assign a score of 2 (=no contraindication) to the used of combined oral contraceptives in obese women who have no further risk factors, but this is only rarely the case, and meticulous history-taking is needed to determine which further risk factors these patients have. If hypertension, hyperlipidemia, or diabetes mellitus is present, then another contraceptive method should be chosen, e.g., gestagens (1). Obese women have a tenfold elevation of the thrombotic risk under treatment with combined oral contraceptives, compared to women of normal weight who are not taking combined oral contraceptives (5). The more obese the patient, the higher the risk (up to a 24-fold elevation) (6).

In practice, however, the higher incidence of hemorrhagic disorders in obese women taking oral gestagen monotherapy can be problematic (e9). There is also discussion in the literature of a possibly higher failure rate of combined hormonal contraceptives (7, 8). Whether the efficacy of combined hormonal contraception depends on the patient's body weight or BMI is currently a matter of debate. A Cochrane analysis did not reveal any direct dependence of efficacy on BMI (e10). In a single study, the risk of pregnancy was higher (relative risk [RR], 2.49) in women with BMI greater than 25 kg/m^2 taking combined oral contraceptives containing ethinyl estradiol and norethisterone acetate (e11). For the contraceptive patch, a significantly elevated failure rate was seen in women weighing more than 90 kg (e12). The consultation edition of the guideline therefore recommends that women with grade 2 or 3 obesity should preferably be treated with a copper intrauterine pessary or with non-hormonal methods (e3).

Thromboembolism

The German Federal Institute for Drugs and Medical Devices issued a Red Hand Letter on 30 January 2014 reflecting the current recommendations of the European Drug Agency (4), mainly with regard to the use of the various types of combined hormonal contraception and the varying associated risks of thromboembolism.

TABLE 2

Categorization according to clinical assessment in the WHO recommendations on contraception, 2015 (2)

Classification in the WHO recommendations	
Category	**Clinical assessment**
1 🟢	No restriction on use of method
2 🟡	Benefit > risk
3 🔴	Risk > benefit (meticulous monitoring is needed!) – The method may be used if the patient wishes and: – the risks are thoroughly explained, understood, and accepted – no alternatives are available
4 🔴	The method should not be used: it is contraindicated because the risk to health is too high

Checklists for the documentation of risk factors can be downloaded from bfarm.de (4).

The Red Hand Letter states at the outset that the risk of venous thromboembolism is low for all types of low-dose combined oral contraceptive (ethinyl estradiol content <50 µg). Evidence does suggest, however, that the venous thromboembolic risk may depend on the type of gestagen contained in the preparation. According to current evidence, the gestagens levonorgestrel, norethisterone, and norgestimate are associated with the lowest risk among combined oral contraceptives. The estimated incidence (per 10 000 women per year) is 2 for women who are not pregnant and do not use contraception; for levonorgestrel, 5–7; for dienogest, 8–11; for gestodene, desogestrel, and drospirenone, 9–12, and for etonogestrel and norelgestromin, 6–12. Adequate data are not yet available for chlormadinone acetate and nomegestrol acetate in combination *(Table 3)* (e5). The risk of thrombosis is significantly lower for combined preparations with 20 µg ethinyl estradiol and levonorgestrel than for combinations with 30 µg ethinyl estradiol and other gestagens (9). In a study of nearly 5 million women aged 15 to 49 who took combined oral contraceptives for at least one year, the relative risk of pulmonary embolism with the use of combined oral contraceptives containing 20 µg ethinyl estradiol and levonorgestrel was 0.74 (95% confidence interval [0.59; 0.91]) compared to a combination of 30–40 µg ethinyl estradiol and levonorgestrel. For a combination of

Obesity

Obese women have a tenfold elevation of the thrombotic risk under treatment with combined oral contraceptives, compared to women of normal weight who are not taking combined oral contraceptives.

Gestagens (progesterones)

According to current evidence, the gestagens levonorgestrel, norethisterone, and norgestimate are associated with the lowest risk among combined oral contraceptives.

TABLE 3

The risk of venous thromboembolism associated with various types of combined oral contraceptive[*1] (Red Hand Letter, December 2018)

Gestagen	Relative risk (compared to levonorgestrel)	Estimated incidence per 10 000 patient-years
Non-pregnant non-users	–	2
Levonorgestrel	Reference	5–7
Norgestimate/norethisterone	1.0	5–7
Dienogest	1.6	8–11
Gestodene/desogestrel/ drospirenone	1.5–2.0	9–12
Etonogestrel/norelgestromin	1.0–2.0	6–12
Chlormadinone acetate / nomegestrol acetate (E2)	yet to be confirmed[*2]	yet to be confirmed[*2]

E2, estradiol

[*1] Red Hand Letter on combined hormonal contraceptives – updated for dienogest/ethinyl estradiol, December 2018

[*2] Further studies are in progress to provide adequate data on the risks associated with these preparations.

20 µg ethinyl estradiol with gestodene, the adjusted RR was 1.96 [1.47; 2.6], compared to ethinyl estradiol 20 µg and levonorgestrel (9). Current studies (INAS score) show, however, that the tetraphasic combination of estradiol valerate and dienogest is associated with a similarly low thromboembolic risk (10, 11); this information has been incorporated in the summary of product characteristics (e13). The Red Hand Letter makes it clear that the risk of venous thromboembolism is elevated in women who use a combined oral contraceptive—especially in the first year, but also upon restarting contraception after an interruption of four or more weeks (4). The risk factors must be meticulously assessed before any first prescription of oral contraceptives, and on every follow-up appointment.

The risk increases with age, particularly in patients with nicotine abuse, diabetes mellitus, hypertension, obesity, or thrombophilia, as well as after trauma or immobilization (7, 12). The risk is also elevated during pregnancy and the puerperium (7, 12). In healthy women, the risk of venous thromboembolism is 4–5 per 10 000 person-years, and twice as high when a combined oral contraceptive is used (13). The risk is highest in the first year of contraceptive use (odds ratio [OR]: 7.0), and somewhat lower after five years (OR: 3.1), compared to women who do not take contraception (13, 14). Some studies have shown a somewhat higher risk in the first year among women taking oral contraceptives that contain drospirenone (hazard ratio [HR]: 1.77) (13, 14). The incremental risk does not subside completely in subsequent years of use (13). A recent meta-analysis concerning preparations with 30 µg of ethinyl estradiol confirms that the risk is higher with combined preparations that contain certain second- and third-generation gestagens, compared to levonorgestrel combined preparations (RR: 1.5–2.0) (15). Smoking is the single most important risk factor; the factor V Leiden mutation, which is not uncommon, is a further one (16). The risk of thrombosis in women with the factor V Leiden mutation who take oral contraceptives is likewise influenced by the particular gestagen contained in the preparation (16). Another relevant risk factor is a family history of thromboembolism in a first-degree relative (WHO category 2) *(Table 4)* (2). Combined oral contraceptives can also unmask previously undetected thrombophilic states. If a woman taking a combined oral contraceptive sustains a thromboembolic event, the contraceptive must be discontinued at once (1, 2). The used of an injected gestagen (MPA) is associated with a higher risk of thrombosis than the application of an intrauterine system containing levonorgestrel (17). Two studies have shown an elevated risk of thromboembolism in healthy women taking depot MPA (e14).

Combined oral contraceptives are contraindicated in women with acute thromboembolism, as are the vaginal ring and the transdermal contraceptive patch. Estrogen-free antiovulatory drugs and depot gestagens are likewise contraindicated in the setting of acute thromboembolism. Alternative contraceptive methods include barrier methods, an intrauterine pessary, or, possibly, levonorgestrel-containing intrauterine systems, although no pertinent study data are available. One the patient has recovered from the acute thromboembolic event, an oral gestagen monopreparation can be used (2). The WHO, in its recommendations, states that the use of combined oral contraceptives is contraindicated in women who have sustained a thrombosis even if they are simultaneously anticoagulated, but recent data show no elevated risk of recurrent thrombosis under anticoagulation (18). There is no indication for the screening of all patients for thrombophilia before prescribing a combined oral contraceptive. Patients should, however, be screened if there is a positive personal or family history of a thromboembolic event.

Risk of thrombosis

Smoking is the single most important risk factor; the factor V Leiden mutation, which is not uncommon, is a further one. The risk of thrombosis in women with the factor V Leiden mutation who take oral contraceptives is likewise influenced by the particular gestagen contained in the preparation.

Contraindication: thromboembolism

Combined oral contraceptives are contraindicated in women with acute thromboembolism, as are the vaginal ring and the transdermal contraceptive patch.

Diabetes mellitus

For women who do not have diabetes, there are no relevant differences between the available hormonal contraceptive drugs (19). Diabetes, in and of itself, does not contraindicate the use of combined oral contraceptives, as long as the patient has no vascular disease or other diabetic sequelae (20). Combined oral contraceptives that have a residual androgenic effect should be used with the utmost caution, and this also holds for depot gestagens (20). Combined oral contraceptives can thus be used by women with uncomplicated diabetes (WHO group 2), but further risk factors must be examined in this situation as well.

Depot MPA should be used with caution in this situation, as type 2 diabetes is more likely to become clinically manifest when depot MPA is used; nonetheless, despite this study (e15), a history of gestational diabetes does not imply any restriction on the type of contraceptive that may be used (WHO group 1).

The selection of a contraceptive for a diabetic woman is a more complex matter if vascular disease or other diabetic sequelae are present. Diabetic nephropathy, neuropathy, or retinopathy is designated in the WHO recommendations as a relative or absolute contraindication to the use of combined oral contraceptives (WHO group 3 or 4). The same holds for women who have had diabetes for more than 20 years: because of the longstanding disease, microvascular damage is assumed to be present. On the other hand, there is no restriction on the use of gestagens (with the exception of depot MPA), intrauterine pessaries, or intrauterine systems (21).

Planned surgery or immobilization

In theory, planned elective surgery increases the risk of thromboembolism, but this depends practically on the duration and complexity of the procedure and, above all, on the subsequent period of immobilization. It is, therefore, recommended—both in the WHO recommendations (WHO group 4) (2) and in the German Red Hand Letter (4)—that combined hormonal contraceptives should be discontinued before planned major surgery, especially if a long period of immobilization is needed thereafter. Before major surgery without prolonged immobilization (e.g., many gynecological procedures), combined oral contraceptives are assigned to WHO group 2; for relatively minor surgery without immobilization (e.g., most gynecological operations, which are usually performed endoscopically or transvaginally), they are assigned to EHO group 1 and thus do not need to be temporarily discontinued (22). If discontinuation is indicated, as, for example, before a major orthopedic procedure, then this should be done at least four weeks before surgery, or, better, six weeks before surgery (23). Acutely discontinuing oral contraceptives before emergency surgery would presumably have no effect. Combined hormonal contraceptives that have been discontinued before an elective operation should not be restarted until two weeks after full mobilization *(Table 5)* (1, 4).

There are no restrictions on the use of gestagen monotherapies, intrauterine pessaries, and intrauterine systems (WHO 1). It must be borne in mind that any restart, after surgery, of temporarily discontinued combined hormonal contraception is associated with an elevated risk of thromboembolism (4). The question whether contraceptives really need to be discontinued for surgery should therefore be critically examined for each individual patient, as this is less often the case than is commonly assumed.

Smoking (nicotine abuse)

Smoking is one of the main risk factors for thromboembolism, and the deleterious effect is even greater in women who smoke and also use combined oral contraceptives: the relative risk is 1.3 [1.0; 1.6] in women who smoke 1–10 cigarettes per day, and 1.9 [1.4; 2.7] in those who smoke more than 20 cigarettes per day (13). Smoking combined with other positive risk factors puts the patient at special risk. For example, a woman over age 35 who smokes fewer than 15 cigarettes per day and uses a combined oral contraceptive is assigned to WHO group 3, i.e., patients of

TABLE 4

WHO recommendations* 2015 – venous thromboembolism and risk factors

Risk	COC	Contraceptive patch	Vaginal ring	POP	Copper spiral	Levonorgestrel spiral
History of VTE	4	4	4	2	1	2
Acute VTE	4	4	4	3	1	3
VTE under treatment with anticoagulant drug	4	4	4	2	1	2
Positive family history (first-degree relative)	2	2	2	1	1	1

COC, combined oral contraceptives; POP, progesterone-only pill; VTE, venous thromboembolism
* 1, no restriction on use of method; 2, benefit > risk; 3, risk > benefit;
4, the method should not be used because the risk to health is too high.

Diabtes mellitus is generally not a contraindication

Diabetes, in and of itself, does not contraindicate the use of combined oral contraceptives, as long as the patient has no vascular disease or other diabetic sequelae.

Risk factor: smoking

It is urgently recommended that patients should be informed about this eliminable risk factor and motivated to lessen their nicotine consumption or to quit smoking entirely.

TABLE 5

WHO recommendations 2015*—venous thromboembolism and immobilization, modified from (2)

Risk	COC	Contraceptive patch	Vaginal ring	POP	Copper spiral	Levonorgestrel spiral
Major surgery						
– prolonged immobilization	4	4	4	2	1	2
– no prolonged immobilization	2	2	2	1	1	1
Minor surgery						
– no immobilization	1	1	1	1	1	1

COC, combined oral contraceptives; POP, progesterone-only pill.
* 1, no restriction on use of method; 2, benefit > risk; 3, risk > benefit; 4, the method should not be used because the risk to health is too high.

TABLE 6

WHO recommendations 2015*—age and smoking, modified from (2)

Risk	COC	Patch/ring	POP	3-monthly injection	Gestagen implant	Copper spiral	Levonorgestrel spiral
Age <35	2	2	1	1	1	1	1
Age >35							
<15 cigarettes/d	3	3	1	1	1	1	1
>15 cigarettes/d	4	4	1	1	1	1	1

COC, combined oral contraceptives; POP, progesterone-only pill.
* 1, no restriction on use of method; 2, benefit > risk; 3, risk > benefit; 4, the method should not be used because the risk to health is too high.

this type should, in general, not be given combined oral contraceptives (2). Women over age 35 who smoke 15 cigarettes a day and use a combined oral contraceptive are assigned to WHO group 4 *(Table 6)*. There is no restriction, however, on gestagen monotherapy or the use of levonorgestrel-containing intrauterine systems and intrauterine pessaries (2). The longer the duration of smoking and the greater the number of cigarettes smoked per day, the higher the associated mortality (24). Combined oral contraceptives also elevate the risk of myocardial infarction in women who smoke by a factor between 2 (e16) and 10 (e17). It is, therefore, urgently recommended that patients should be informed about this eliminable risk factor and motivated to lessen their nicotine consumption or to quit smoking entirely. On the other hand, combined hormonal contraceptives are not contraindicated for otherwise healthy women under age 30 who smoke. Smoking also has other effects: it alters the metabolism of ethinyl estradiol, because cytochrome P450 induction accelerates the hepatic metabolism of the drug (e18). This is presumably the reason for the frequent occurrence of additional hemorrhages in smokers (e19). Nicotine metabolism is also accelerated by the intake of combined oral contraceptives, which can thus reinforce nicotine dependence (25). There is no evidence to date regarding the putative effect of electrocigarettes on cardiovascular risk in women who take combined oral contraceptives (26). Smoking must be asked about, documented, and assessed as a risk factor for thrombosis, not only in initial history-taking before contraceptive treatment is begun, but in the subsequent annual check-ups as well.

Hypertension

Hypertension is, likewise, a relative or absolute contraindication to the use of combined oral contraceptives. Even a woman with well-controlled hypertension is assigned to WHO group 3 (relative contraindication) (2). There is no restriction on the use of gestagens. In the case of hypertension with blood pressure values above 160/100 mm Hg, combined oral

Smoking alters metabolism

Smoking alters the metabolism of ethinyl estradiol, because cytochrome P450 induction accelerates the hepatic metabolism of the drug. This is presumably the reason for the frequent occurrence of additional hemorrhages in smokers.

Smokers over age 35

According to the WHO recommendations, women over age 35 who smoke more than 15 cigarettes a day should not take oral contraceptives.

TABLE 7

Antiepileptic drugs and their effect on enzyme induction and contraceptive reliability

Enzyme induction	Drugs	Contraceptive reliability
Marked	barbiturates, carbamazepine, felbamate, oxcarbazepine, phenytoin, primidone, clonazepam, topiramate	not reliable
Reciprocal interaction	lamotrigine (dose must be raised; EE induces metabolism of lamotrigine and lamotrigine induces metabolism of LNG)	beware of possible effect
None	valproic acid, gabapentin, levetiracetam, tiagabine, vigabatrin, zonisamide, pregabalin	fully reliable

EE, ethinyl estradiol; LNG, levornogestrel; LTG, lamotrigine

contraceptives are absolutely contraindicated (WHO group 4). A history of gestational hypertension places the patient in WHO group 2 with respect to the use of combined oral contraceptives. These patients at elevated risk need more frequent follow-up than usual: they should have their first follow-up appointment three months after the initiation of treatment, and subsequent ones at six-month intervals. If combined oral contraceptive treatment has been decided upon for a patient with medically well-controlled hypertension, the estrogen component should be at the lowest possible dose (i.e., a 20 µg ethinyl estradiol preparation can be used, or, alternatively, an estradiol preparation). It is very important that the blood pressure should be measured regularly (as a rule, annually), both before and during the use of combined oral contraceptives (1). The blood pressure can change when a combined oral contraceptive is given, even in a patient whose hypertension was previously well controlled with medication. If other risk factors besides hypertension are present as well, such as obesity or smoking, then combined oral contraceptives are contraindicated, because of the increased risk of arterial thromboembolic events (27). The risk of venous thromboembolism is not increased (27). The is no restriction on the use of any other type of contraceptive method. For the risk situation in patients with hepatic tumors, see the *eBox*.

Headache, including migraine

Migraine is markedly more common in women than in men (prevalence, 18% vs. 6%). Headache in general, and migraine in particular, are thus common problematic situations in women seeking a suitable method of contraception. The spectrum of headache disorders and the range of severity are very wide, and, in any patient with chronic headache, the precise classification of the disorder is important (1, 31). If the patient suffers from headaches that are timed to the menstrual cycle, are not of migrainous quality, and are not preceded by an aura, a combined oral contraceptive can help. In such situations, combined oral contraceptives are best taken in a long cycle or over the long term (32, 33). Gestagen monotherapy also improves headaches of this type (31, 32). If the administration of combined oral contraceptives fails to relieve the headache, then another cause should be sought (1, 4).

The situation is different, and more problematic, if the patient suffers from migraine. Women under age 35 with migraine headaches without an aura can take combined oral contraceptives (WHO group 2 or 3) (2). In contrast, for patients who have migraine with aura, all combined hormonal contraceptives are absolutely contraindicated (WHO group 4), because they lead to a sixfold elevation of the risk of stroke (34). For patients with persistently occurring migraine with aura, gestagen monotherapy is relatively contraindicated as well (WHO group 3), and this also applies to levonorgestrel-containing intrauterine systems. If there are any further risk factors, combined hormonal contraceptives should be avoided because of the elevated risk of thromboembolism (1). The differential diagnosis of migraine with and without aura, and of headache of other types, can be ia difficult matter, and the treating neurologist should be consulted before oral contraceptives are prescribed. This is advisable for yet another reason, namely, because the neurological guidelines are less restrictive than the gynecological ones with respect to the use of combined oral contraceptives in patients with migraine (1).

Hypertension

Hypertension is, likewise, a relative or absolute contraindication to the use of combined oral contraceptives. Even a woman with well-controlled hypertension is assigned to WHO group 3 (relative contraindication).

Migraine

Women under age 35 with migraine headaches without an aura can take combined oral contraceptives; however, for patients who have migraine with aura, all combined hormonal contraceptives are absolutely contraindicated.

Epilepsy

In women with epilepsy, seizures tend to occur more frequently during menstruation. This clearly implies that cyclical hormone changes affect the probability of having an epileptic seizure. According to the WHO criteria, in women with epilepsy who desire contraception, the benefit of contraception outweighs the risks no matter what type of contraceptive method is used (WHO group 1). None of the numerous studies that have been conducted on this matter have shown any increase in the prevalence of epilepsy from the use of combined oral contraceptives (35–38), nor has any change in the frequency of seizures been demonstrated (38). Contraceptive drugs can interact pharmacologically with antiepileptic drugs in undesired ways (36, 37), with highly variable effects on hepatic metabolism and enzyme induction. For example, enzyme-inducing antiepileptic drugs such as carbamazepine can partially or totally counteract the contraceptive effect of combined oral contraceptives *(Table 7)* (36, 37). Lamotrigine stimulates the metabolism of ethinyl estradiol; therefore, the dose of lamotrigine must be adjusted (39). Antiepileptic drugs can also lessen the effect of all orally and parenterally administered gestagen monopreparations. There is no general contraindication of combined oral contraceptives. On the contrary, in women with epilepsy, combined oral contraceptives can even lower the frequency of seizures, particularly those that tend to occur premenstrually, if they are given over the long term (i.e., continuous, uninterrupted intake of combined oral contraceptives) or in a long cycle (application with a reduced number of intervals in which no contraceptives are taken—only 2–4 such intervals per year) (40). Possible interactions with antiepileptic drugs must be bone in mind (36). In case of a marked interaction, a levonorgestrel-containing intrauterine system or a copper spiral may need to be considered as an alternative (35). To lessen potential interactions, a temporally staggered administration of antiepileptic drugs and combined oral contraceptives is generally advisable (1), but this does not always guarantee a secure contraceptive effect. The information contained in the package inserts of the antiepileptic and contraceptive drugs must be heeded in all such cases.

Overview

In situations of increased risk, especially problematic constellations need to be taken account that arise not just from the patient's underlying disease, but also from the ensuing sequelae, e.g., vascular damage. On the other hand, it is often precisely in such situations of increased risk that secure contraception is medically indicated, as an undesired pregnancy in a patient of this type would increase the risk of further adverse effects on health. The physician should focus attention on the patient's personal wishes and, especially, on the clinical history, with repeated questioning about risk factors not only when a combined oral contraceptive is initially prescribed, but also at each follow-up appointment. If the patient's living circumstances change (age, additional risk factors, obesity, smoking, new onset of diabetes mellitus or migraine), the contraceptive method must be accordingly modified to ensure that the patient has secure contraception with an acceptably low risk to her health. Contraceptive counseling in such situations is a demanding task calling for special attention in gynecological practice.

Epilepsy

None of the numerous studies on this matter have shown any increase in the prevalence of epilepsy from the use of combined oral contraceptives, nor has any change in the frequency of seizures been demonstrated.

Conflict of interest statement

Prof. Römer has served as a paid consultant for Bayer and Gedeon Richter. He has received reimbursement of congress participation fees from Bayer, as well as travel and accommodation expenses from Aristo Pharma, Exelitis, Dr. Kode, and Hexal. He has recieved lecture honoraria from Bayer, Exeltis, Hexal AG, and Aristo Pharma.

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References

1. Römer T, Göretzlehner G: Kontrazeption mit OC in 238 Problemsituationen. 3rd edition, Berlin: De Gruyter 2017; 3–320.
2. WHO: Medical eligibility criteria for contraceptive use. 5th ed, Geneva, WHO, 2015.www.who.int/reproductivehealth/publications/family_planning/Ex-Summ-MEC-5/en/ (last accessed on 23 September 2019).
3. Lidegaard O, Nielsen LH, Skovlund CW, Lokkegaard E. Venous thrombosis in users of non-oral hormonal contraception: follow-up study, Denmark 2001–10. BMJ 2012; 344: e2990.
4. Bundesinstitut für Arzneimittel und Medizinprodukte: Rote-Hand-Brief zur kombinierten hormonalen Kontrazeptiva. www.bfarm.de/SharedDocs/Risikoinformationen/Pharmakovigilanz/DE/RHB/2014/rhb-khk.html (last accessed on 23 September 2019)
5. Pomp ER, le Cessie S, Rosendaal FR, Doggen CJ: Risk of venous thrombosis: obesity and ist joint effect with oral contraceptive use and prothrombotic mutations. Br J Haematol 2007; 139: 289–96.
6. Horton LG, Simmons KB, Curtis KM: Combined hormonal contraceptive use among obese women and risk for cardiovascular events: a systematic review. Contraception 2016; 94: 590–604.
7. Dinger J, Minh TD, Buttmann N, Bardenheuer K: Effectivenes of oral contraceptive pills in a large U.S. Cohort comparing progesterone and regimen. Obstet Gynecol 2011; 117: 33–40.
8. Brunner Huber LR, Hogue CJ, Stein AD, Drews C, Ziemann M: Body mass index and risk for oral contraceptive failure: a case-cohort study in South Carolina. Ann Epidemiol 2006; 16: 637–43.
9. Will A, Dalichampt M, Raguideau F, et al.: Low dose oestrogen combined oral contraception and risk of pulmonary embolism, stroke and myocardial infarction in five million French women: cohort study. BMJ 2016; 353: i2002.
10. Dinger J, Do Minh T, Heinemann K: Impact of estrogen type on cardiovascular safety of combined oral contraceptives. Contraception 2016; 94: 328–39.
11. Heinemann K, Dinger J, Minh TD, Franke C: Cardiovascular safety among users of different combined oral contraceptives – final results from the INAS-SCORE study. Contraception 2017; 96: 292–3.
12. Pomp ER, Lenselink AM, Rosendaal FR, Doggen CJM: Pregnancy, the postpartum period and prothrombotic defects: risk of venous thrombosis in the MEGA study. J Thromb Haemost 2008; 6: 632–7.
13. Lidegaard Ø, Edstrom B, Kreiner S: Oral contraceptives and venous thrombo-embolism: a five-year national case-control study. Contraception 2002; 65: 187–96.
14. Sidney S, Cheetham TC, Connell FA, et al.: Recent combined hormonal contraceptives (CHCs) and the risk of thromboembolism and other cardiovascular events in new users. Contraception 2013; 87: 93–100.

15. Dragoman MV, Tepper NK, Fu R, Curtis KM, Chou R, Gaffield ME: A systematic review and meta-analysis of venous thrombosis risk among users of combined oral contraception. Int J Gynaecol Obstet 2018; 141: 287–94.
16. Hugon-Rodin J, Horellou MH, Conard J, Gompel A, Plu-Bureau G: Type of combined contraceptives, Factor V Leiden mutation and risk of venous thromboembolism. Thromb Haemost 2018; 118: 922–8.
17. Van Hylckama Vlieg A, Helmerhorst FM, Rosendaal FR: The risk of deep venous thrombosis associated with injectable depot-medroxyprogesterone acetate contraceptives or a levonorgestrel intrauterine device. Arterioscler Thromb Vasc Biol 2010; 30: 2297–300.
18. Martinelli I, Lensing AW, Middeldorp S, et al.: Recurrent venous thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use. Blood 2016; 127: 1417–25.
19. Lopez LM, Grimes DA, Schulz KF: Steroidal contraceptives: effect on carbohydrate metabolism in women without diabetes mellitus. Cochrane Database Syst Rev 2014; 2014: CD006133.
20. Shawe J, Mulnier H, Nicholls P, Lawrenson R: Use of hormonal contraceptive methods by women with diabetes. Prim Care Diabetes 2008; 2: 195–9.
21. Visser J, Snel M, Van Vliet HA: Hormonal versus non-hormonal contraceptives in women with diabetes mellitus type 1 and 2. Cochrane Database Syst Rev 2006; 4: CD003990.
22. Oakes J, Hahn PM, Lilicrap D, Reid RL: A survey of recommendations by gynecologists in Canada regarding oral contraceptive use in the perioperative period. Am J Obstet Gynecol 2002; 187: 1539–43.
23. ACOG Practice Bulletin: Use of hormonal contraception in women with coexisting medical conditions. Obstet Gynecol 2006; 73: 1453–72.
24. Vessey M, Yeates D, Flynn S: Factors affecting mortality in a large corhort study with special reference to oral contraceptive use. Contraception 2010; 73: 221–9.
25. McClave AK, Hogue CJ, Brunner Huber LR, Ehrlich AC: Cigarette smoking women of reproductive age who use oral contraceptives: results from the 2002 and 2004 behavioral risk factor surveillance systems. Womens Health Issues 2010; 20: 380–5.
26. Riley HE, Berry-Bibee E, England LJ, Jamieson DJ, Marchbanks PA, Curtis KM: Hormonal contraception among electronic cigarette users and cardiovascular risk: a systematic review. Contraception 2016; 93: 190–208.
27. Curtis KM, Mohllajee AP, Martins SL, Peterson HB: Combined oral contraceptive use among women with hypertension: a systematic review. Contraception 2006; 73: 179–88.
28. Kapp N, Curtis KM: Hormonal contraceptive use among women with liver tumors: a systematic review. Contraception 2009; 80: 387–90.
29. Mathieu D, Kobeiter H, Maison P: Oral contraceptive use and focal nodular hyperplasia of the liver. Gastroenterol 2000; 118: 560–4.
30. Maheshwari S, Sarraj A, Kramer J, El-Serag HB: Oral contraception and the risk of hepatocellular carcinoma. J Hepatol 2007; 47: 506–13.
31. Tepper NK, Whiteman MK, Zapata LB, Marchbanks PA, Curtis KM: Safety of hormonal contraceptives among women with migraine: a systematic review. Contraception 2016; 94: 630–40.
32. Ahrendt HJ, Kleinschmidt S, Kropf S, Kose D: Präventive Wirkung hormoneller Kontrazeptiva bei menstrueller Migräne. Frauenarzt 2007; 48: 1186–92.
33. Machado RB, Pereira AP, Coelho GP, Neri L, Martins L, Luminoso D: Epidemiological and clinical aspects of migraine in users of combined oral contraceptives. Contraception 2010; 81: 202–8.
34. Champaloux SW, Tepper NK, Monsour M, et al.: Use of combined hormonal contraceptives among women with migraines and risk of ischemic stroke. Am J Obstet Gynecol 2017; 216: 489e1–489e7.
35. Burakgazi E, Harden C, Kelly JJ: Contraception for women with epilepsy. Rev Neurol Dis 2009; 6: 62–7.
36. Schwenkhagen A, Schaudig K, Rabe T, Stodiech SR: Kontrazeption bei Frauen mit Epilepsie. Gynäkologe 2012; 45: 723–31.
37. Wang H, Bos JHJ, de Jong-van den Berg LTW: Co-prescription of antiepileptic drugs and contraceptives. Contraception 2012; 85: 28–31.
38. Beier CP, Garcia Rodriguez LA, Saez ME, Gaist D, Gonzales-Perez A: Hormonal contraception is not associated with increased risk for seizures in the general population: results from a cohort study using The Health Improvement Network. Eur J Clin Pharmacol 2018; 74: 1175–80.
39. Legro RS, Pauli JG, Kunselman AR, et al.: Effects of continuous versus cyclicyl oral contraception: a randomized controlled trial. Clin Endocrinol Metab 2008; 93: 420–9.
40. Harden CL, Leppik I: Optimizing therapy of seizures in women who use oral contraceptives. Neurology 2006; 76: 56–8.

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► **Supplementary material**

For eReferences please refer to:
www.aerzteblatt-international.de/ref4519

eBox and eCase Report:
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- Participation in the CME certification program is possible only over the Internet: cme.aerzteblatt.de. This unit can be accessed until 2 February 2020. Submissions by letter, e-mail or fax cannot be considered.

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  - "Actinic Keratosis and Cutaneous Squamous Cell Carcinoma" (issue 37/2019) until 6 December 2019
  - "Benign Breast Disease in Women" (issue 33–34/2019) until 10 November 2019

- This article has been certified by the North Rhine Academy for Continuing Medical Education. Participants in the CME program can manage their CME points with their 15-digit "uniform CME number" (einheitliche Fortbildungsnummer, EFN), which is found on the CME card (8027XXXXXXXXXX). The EFN must be stated during registration on www.aerzteblatt.de ("Mein DÄ") or else entered in "Meine Daten," and the participant must agree to communication of the results.

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Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1

How long before elective major surgery requiring a long period of postoperative immobilization should combined hormonal contraceptives be discontinued?

a) 2 days
b) 1 week
c) 6 weeks
d) 2 months
e) 3 months

Question 2

If a woman is classed in WHO category 4, what does this mean in regard to contraception?

a) An individualized decision must be taken
b) The benefits and risks are of the same magnitude
c) Administration is contraindicated
d) The benefit outweighs the risk
e) The risk of thrombosis is four times as high as normal

Question 3

What method of contraception is best for a 43-year-old woman who does not want to have any more children, is a smoker, and has hypertension and a BMI of 31?

a) A copper IUD
b) Cyclical administration of a combined oral contraceptive
c) The temperature method
d) Spermicides
e) Coitus interruptus

Question 4

In obese women, by what factor does the administration of combined oral contraceptives elevate the risk of thrombosis?

a) 2
b) 4
c) 7
d) 10
e) 15

Question 5

In what period of time after the initiation of treatment with combined oral contraceptives is the thromboembolic risk highest?

a) In the first year
b) After two years
c) After five years
d) After seven years
e) After ten years

Question 6

What gestagen is associated with the lowest risk of thrombosis when used in a combined preparation together with ethinyl estradiol?

a) Gestodene
b) Desogestrel
c) Drospirenone
d) Dienogest
e) Levonorgestrel

Question 7

What preparation should be recommended for a woman with longstanding diabetes and diabetic angiopathy?

a) A combined oral contraceptive with no residual androgenic effect
b) A vaginal ring
c) A combined oral contraceptive with residual androgenic effect
d) A single-drug gestagen preparation
e) Depot MPA

Question 8

What method of contraception is advantageous for a woman who suffers from non-migrainous cycle-dependent headaches without aura?

a) The cyclical administration of combined oral contraceptives
b) The long-term administration of combined oral contraceptives
c) A copper IUD
d) Levonorgestrel intrauterine systems
e) A vaginal ring

Question 9

What antiepileptic drug has no effect on the reliability of combined oral contraceptives?

a) Carbamazepine
b) Topiramate
c) Lamotrigine
d) Primidone
e) Gabapentin

Question 10

Which of the following is a short-term contraceptive method?

a) A transdermal contraceptive patch
b) A copper IUD
c) A gestagen implant
d) A gestagen injection
e) A levonorgestrel intrauterine system

► **Participation only via Internet: cme.aerzteblatt.de**

Supplementary material to:

Medical Eligibility for Contraception in Women at Increased Risk

by Thomas Römer

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eReferences

e1. DGGG-Leitlinien. Empfängnisverhütung – Familienplanung in Deutschland ehemals S1-Leitlinie, AWMF 015/015 (Stand September 2010). www.dggg.de/fileadmin/documents/leitlinien/archiviert/federfuehrend/015015_Empf%C3%A4ngnisverhuetung/015015_2010.pdf (last accessed on 23 September 2019).

e2. Bundeszentrale für gesundheitliche Aufklärung: Verhütungsverhalten Erwachsener 2011. www.bzga.de/infomaterialien/sexualaufklaerung/verhuetungsverhalten-erwachsener-2011/ (last accessed on 23 September 2019).

e3. Konsultationsfassung S3-Leitlinien. Hormonelle Empfängnisverhütung. Version 3.1 (Dezember 2017). www.dggg.de/fileadmin/documents/pressemitteilungen/2018/Gesamtdokument_Langversion_Version_3–1.pdf (last accessed on 23 September 2019).

e4. Bundeszentrale für gesundheitliche Aufklärung: Verhütungsverhalten Erwachsener 2018. www.forschung.sexualaufklaerung.de/verhuetung/verhuetungsverhalten-2018 (last accessed on 18 Oktober 2019).

e5. Statistisches Bundesamt: Geburtenziffer 2017 leicht gesunken. Pressemitteilung Nr. 420 vom 31.10.2018. www.destatis.de/DE/Presse/Pressemitteilungen/2018/10/PD18_420_122.html (last accessed on 23 September 2019).

e6. Rote Hand Brief zu kombinierten hormonellen Kontrazeptiva, Dezember 2018. www.akdae.de/Arzneimittelsicherheit/RHB/20181212.pdf (last accessed on 23 September 2019).

e7. Cibula D, Gompel A, Mueck AO: Hormonal contraception and risk of cancer. Hum Reprod 2010; 16: 631–50.

e8. Morch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard O: Contemporary hormonal contraception and the risk of breast cancer. N Engl J Med 2017; 377: 2228–39.

e9. Apter D: Contraception options: aspects unique to adolescent and young adult. Best Pract Res Clin Obstet Gynaecol 2018; 48: 115–27.

e10. Lopez LM, Grimnes DA, Chen M, et al.: Hormonal contraceptives for contraception in overweight or obese women. Cochrane Database Syst Rev. 2013.CD008452.

e11. Burkmann RT, Fisher AC, Wan GJ, Barnowski CE, LaGuardia KD: Association between efficacy and body weight or body mass index for two low-dose oral contraceptives. Contraception 2009; 79: 424–7.

e12. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW: Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril 2002; 77: 13–8.

e13. Gelbe Liste Pharmaindex: Fachinformation Qlaira. www.gelbe-liste.de/produkte/Qlaira-Filmtabletten_516019/fachinformation (last accessed on 23 September 2019).

e14. Tepper NK, Whiteman MK, Marchbanks PA, James AH, Curtis KM: Progestin-only contraception and thromboembolism: a systematic review. Contraception 2016; 94: 678–700.

e15. Xiang AH, Kawakubo M, Kjos SL, Buchanan TA: Long-acting injectable progestin contraception and risk of type 2 diabetes in Latino women with prior gestational diabetes mellitus. Diabetes Care 2006; 29: 613–7.

e16. Tanis BC, van den Bosch MA, Kemmeren JM: Oral contraceptives and the risk of myocardial infarction. N Engl J Med 2001; 345: 1787–93.

e17. Roy S: Effects of smoking on prostacyclin formation and platelet aggregation in users of oral contraceptives. Am J Obstet Gynecol 1999; 180: 364–8.

e18. Benowitz NL, Lessov-Schlaggar CN, Swan GE, Jacob P: Female sex and oral contraceptive use accelerate nicotine metabolism. Clin Pharmacol Ther 2006; 79: 480–8.

e19. Grossman MP, Nakajima ST: Menstrual cycle bleeding patterns in cigarette smokers. Contraception 2006; 73: 562–5.

e20. An N: Oral contraceptives use and liver cancer risk. A dose-response meta-analysis of observational studies. Medicine (Baltimore) 2015; 94: e1619.

eCASE REPORT

Contraception in a patient with positive risk factors

A 38-year-old woman desires hormonal contraception. She has a history of two unremarkable pregnancies and cycle-dependent migraine headaches. There is no personal or family history of thromboembolic events. On further questioning, she states that she smokes 20 cigarettes per day. Her blood pressure is 120/80 mm Hg, and her BMI is 26 (i.e., she is mildly overweight).

Fundamentals of decision-making

Her age and the fact that she smokes more than 15 cigarettes per day constitute a contraindication for all combined hormonal contraceptive methods (oral, transdermal patch, vaginal ring). She does not want to use barrier methods or sterilization. She can, therefore, be offered the following alternative options, given her desire for hormonal contraception:

- oral gestagen monotherapy
- an etonogestrel implant for three years
- depot gestagen injections every three months
- the insertion of a levonorgestrel intrauterine system (IUS) or a copper intrauterine device (IUD).

As the patient is still ambivalent about whether she will ultimately want to have more children, she does not want a long-term contraceptive method, and she therefore declines a gestagen implant or gestagen injections and likewise declines all intrauterine methods. She decides to commence treatment with a gestagen single-drug pill containing 75 µg of desogestrel. This situation is classed in WHO group 2. The patient is informed that the pill should be taken every day without interruption and with the most precise timing possible, and that interim bleeding can occur in the initial period of use.

She is also encouraged to cut down on smoking. A desogestrel monopill provides her with reliable contraception at relatively low risk. If she should subsequently decide that she does not want to bear any more children, she can be switched to a long-term contraceptive method; such methods are often associated with better patient adherence.

eBOX 1

Risk situation and risks: hepatic tumors

The types of hepatic tumor include benign lesions, such as hemangioma, adenoma, and focal nodular hyperplasia (FNH), as well as malignant ones, such as hepatocellular carcinoma and hepatoblastoma. When combined oral contraceptives are taken, hemangiomas can develop, even in adolescents (1). FNH and adenomas can arise after many years of use of combined oral contraceptives (COC); there is a positive correlation with the dose of ethinyl estradiol. The long-term use of COC has been found to be associated with an elevated risk of hepatic disease, although the evidence for this comes mainly from older studies in which the COC that were used contained 50 µg of ethinyl estradiol (1). More recent studies have shown that, in women with focal nodular hyperplasia, the use of low-dose COC does not lead to any progression or regression of the hepatic findings (28, 29). According to a meta-analysis, the evidence regarding malignant tumors, such as hepatocellular carcinoma, is mixed (30). In one review, six studies were found that showed a two- to twenty-fold elevation of the risk (30), while a further study showed no statistically significant association of combined hormonal contraception with hepatic tumors (e20).

COC and all other hormonal preparations are absolutely contraindicated in patients with hepatic hemangioma, hepatocellular adenoma, or hepatocellular carcinoma, as well as in patients with a personal or family history of these lesions. Hemangiomas and FNH reach their peak prevalence (as high as 7%) in women aged 20 to 50. In women with FNH, micropills with up to 20 µg of ethinyl estradiol can be used (WHO group 2) (2, e3). Alternatively, intrauterine contraceptive methods or gestagens can be used.