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Combined Hormonal Contraception and Thrombophilia Screening in Patients with a Family History of Thrombosis

A clinical guideline recommended

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Background

There are 3 types of combined hormonal contraception (CHC) licensed for use in the UK; the combined oral contraceptive pill (COC), the combined transdermal patch (CTP) and the combined vaginal ring (CVR). Data for venous thromboembolic (VTE) risk associated with the CTP and CVR are limited and conflicting and for the purposes of this guideline, the three methods will be assessed together under the term CHC.

The United Kingdom Medical Eligibility Criteria (UKMEC) classification of CHC use in the presence of VTE is as follows:

Risk factors	UK Medical Eligibility Criteria
Personal history of VTE (idiopathic or provoked)	UKMEC 4 (completely contraindicated)
Family history VTE in first degree relative < 45 years	UKMEC 3 (risks likely to outweigh benefits)
Family history VTE in first degree relative > 45 years	UKMEC 2 (benefits likely to outweigh risks)

All women requesting CHC should have a careful medical history taken documenting personal and family history of VTE in order to identify those women in whom CHC use represents an unacceptable risk (UKMEC 4) or where the risks are likely to outweigh the benefits (UKMEC 3). Women should be informed about the health risks associated with use of CHC and with regard to VTE, advised that the use of CHC is associated with an increased risk of VTE, but that the absolute risk of VTE for an individual CHC user remains very small.

Baseline risk of VTE associated with non-use and CHC use over the course of 1 year

	Risk of VTE per 10,000 healthy women
Non-contraceptive users and not pregnant	2 - 5
CHC containing ethinylestradiol plus levenorgestrel, norgestimate or norethisterone	5 - 7
CHC containing ethinylestradiol plus gestodene, desogestrel, drospirenone	9 - 12
CHC containing etonorgestrel (ring), and norelgestromin (patch)	6 - 12
Pregnancy	29
Immediate post partum period	300 - 400

There appears to be synergism between risk factors for VTE and in particular obesity. Whilst age and raised BMI (>30kg/m^2) are independent risk factors for VTE, none of these factors on their own limit a woman's suitability to use CHCs. However, if multiple risk factors exist, these should be taken into account.

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Thrombophilia screening

Heritable thrombophilia describes an inherited tendency for VTE. Testing for heritable thrombophilia does not typically predict recurrence in unselected patients. In a large cohort study, testing for inherited thrombophilia did not reduce VTE recurrence. Moreover, in affected asymptomatic relatives followed prospectively, there is a low risk of VTE.

Thrombophilia testing is expensive and time-consuming. Indiscriminate testing can result in uncertainty about the practicalities of dealing with positive results. Positive results may cause unjustified concern to an individual and their families whereas a negative result may provide false reassurance. It is important, therefore, that if screening is considered, it is targeted appropriately and only performed when the results will have a direct impact on clinical management.

Thrombophilia screening and CHC use

Screening for inherited thrombophilia in women requesting CHC with no known family history of thrombophilia is considered to be neither cost effective nor necessary.

Screening women with a first-degree relative who has a hereditary thrombophilia is of uncertain benefit and studies evaluating the cost-effectiveness are of generally low quality. One limitation of these studies is that they consider only 1 year of COC use rather than the longer durations that reflect many women's use. Furthermore, they do not take into account other situations that increase VTE risk – pregnancy, surgery, air travel – for which knowing thrombophilia status could be beneficial. Due to the lack of high-quality evidence, the Faculty of Sexual & Reproductive Healthcare (FSRH) CHC Guidance advises that a woman with a first-degree relative who has an inherited thrombophilia can be counselled that a negative thrombophilia screen does not necessarily exclude thrombophilia (particularly if the relative has had a VTE event) and therefore a contraceptive method other than CHC, that is not associated with increased VTE risk, should be considered. If no other method is acceptable, specialist opinion should be obtained.

Recommendations

1. Women should be considered at higher risk of VTE than the general population if they have a first degree relative with a history of:
    - Venous thrombosis under age 45.
    - Arterial thrombosis under age 30.
    - Known family thrombophilic defect.
2. Such women should be advised to consider contraception other than CHC. If alternative methods are unacceptable or if they have been tried and found to have unacceptable side effects, thrombophilia screening *may* provide further information on the risks of VTE. If another risk factor for VTE is present, such as BMI>30, CHC is completely contraindicated.
3. Women with a negative thrombophilia test must still be considered at increased risk of VTE as many thrombophilic abnormalities remain undetectable by current techniques – thus, the benefits of thrombophilia

screening in these women are not clear-cut and this should be understood by the patient and clinician prior to testing. A discussion with a Consultant Haematologist concerning the value of thrombophilia testing in these circumstances should be considered.

4. It may take about 1 month for results to become available. Current tests look for inherited abnormalities in anti-thrombin 3, protein C, protein S, factor V Leiden and prothrombin gene mutations. The lupus anticoagulant / anticardiolipin antibodies are acquired thrombophilic defects but should also be checked (as part of their global thrombophilia risk).

5. A careful risk-benefit analysis considering medical and family history, individual risk factors and test results, must be made for all patients, particularly if an abnormality is found at screening. This should include advice from a Consultant Haematologist and a Consultant in Sexual & Reproductive Health. If a compound defect or anti-thrombin deficiency or lupus antibodies are found CHC should not be prescribed. The clinical history of the affected relative is important and caution should be exercised if the VTE was apparently unprovoked or linked with the use of CHC or with pregnancy.

6. If COC is prescribed it should be a low dose brand (20-30 µg ethinylestradiol) containing either levonorgestrel or norethisterone as the progestogen component.

   Rigevidon/Levest/Ovranette/Microgynon/Maexeni/Elevin.

   Loestrin 30/Loestrin20.

   Logynon/Triregol.

7. Risk of VTE is highest in the months immediately after initiation of CHC or when restarting after a break of at least 1 month. The risk then reduces over the first year of use and remains stable thereafter. Frequent stopping and starting of CHC is therefore discouraged. For women using CHC for more than 1 year who subsequently develop a significant family history of VTE, there may be less benefit from thrombophilia screening.

8. CHC should be stopped 6 weeks before screening as it affects protein C and S levels.

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This guideline was originally produced in co-operation with Dr K Nash (Sexual and Reproductive Health) and Dr H Lyall, Consultant Haematologist.

This guideline has been updated by Dr C Schunmann (Consultant in Sexual and Reproductive Health) and Dr H Lyall (Consultant Haematologist).

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