

## **CARDIOVASCULAR RISK AND THE RETURN TO FERTILITY ASSOCIATED WITH ORAL AND INTRAUTERINE HORMONAL CONTRACEPTION**

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The development of hormonal contraception was one of the great medical and social revolutions of the 20th Century.

Combined oral contraceptives (COCs) as well as the hormone containing intrauterine system (IUS) are the most widely used forms of hormonal contraception today. Both are among the most safe and effective forms of birth control available worldwide.

One of the primary considerations in the development of new hormonal contraceptives is to achieve reliable contraception at dosages that are expected to be associated with low frequencies of undesired side effects without sacrificing good cycle control.

While hormonal contraception is very safe, nevertheless, it is also important to note that COCs slightly increase the risk for rare cardiovascular events, such as venous thromboembolism (VTE) and arterial thromboembolic events (ATE) (Crosignani et al. 1999). These cardiovascular outcomes are very rare in typical COC user populations and the risk associated with COC use is lower than the risk associated with pregnancy and delivery. Therefore, despite the slightly higher VTE and ATE risk, the public health risk benefit balance of COC use remains overwhelmingly positive for the vast majority of COC users

The slight increase in VTE risk during COC use is thought to be mainly related to dose of ethinylestradiol (EE) contained in the preparation. The most recently well-conducted, large, prospective, comparative, cohort studies suggest that the risk for deep vein thrombosis and pulmonary embolism is similar for all low EE dosed COCs (Dinger et al 2007). The risk for VTE increases approximately 2-fold during COC use, which is - however - much lower than the approximate 6-fold increase in VTE risk seen during pregnancy and delivery. Potential COC users with a personal and/or family history of VTE, who are obese (BMI >35) and/or are over 40 years old have a several fold higher risk compared to COC users who are young and not overweight. Therefore, contraceptive decision making should always be based on a careful benefit/risk assessment that considers the individual woman's needs.

Overall the risk for ATE, such as myocardial infarction (MI) and stroke, is extremely low in typical COC users. By far the most important independent risk factor for stroke and MI among COC users is cigarette smoking (WHO 1997, Croft et al 1989). According to Croft et al, the relative risk for both stroke and MI is higher among current COC users with a history of hypertension than in normotensive women. Use of low dose COCs is thought to increase the risk of MI by approximately 2-fold among users even after controlling for cardiovascular risk factors (such as smoking, hypertension, and obesity) (Tanis 2001). In contrast, the evidence for an increase in stroke in users of modern low dose COCs is considered to be more controversial (Chan 2004). Recent data from Asia substantiate a higher risk for hemorrhagic stroke in older, hypertensive Chinese COC users (Ying APCOC, 2007). The risk of stroke and MI in COC users is age related, rarely occurring in nonsmoking, nondiabetic, non-hypertensive women under the age of 35 (WHO 1998). COCs that contain progestins that do not have a negative effect on blood pressure should be considered.

Hormonal contraception users are sometimes worried if the therapy will have a negative effect on their return to fertility once they stop therapy to become pregnant. Time to conception was investigated in 2,064 participants of the European Active Surveillance Study on Oral Contraceptives, who stopped COC use to become pregnant. The results from this prospective cohort study on COC use suggest that past COC use does not negatively impact conception rates (Cronin, ACOG 2007). The conceptions rates in past COC users were comparable to the rates reported in literature for non COC users planning pregnancy. Also long term past COC use did not negatively affect conception rates. Similar results have also been found for hormone containing IUSs.

Overall, hormonal contraceptives are among the most safe, effective and easily reversible forms of contraception available today. Individual risk factors must be carefully weighed when prescribing these medications as they are typically used by healthy, young women, who often plan to become pregnant during their lifetime. It is important that prescribing physicians are familiar with the most recent benefit and risk literature to ensure that patients receive the best care that suits their individual needs. Both oral contraceptives as well as the hormone containing IUS are highly effective and very safe options for fertility control methods for the vast majority of users. For potential users with high risk factors for cardiovascular outcomes many methods can be considered safe to use. Ultimately the individual contraceptive choice must be based on both the risks but also on the benefits each option offers.