A short documentary hosted on the Guardian website highlights some fatal cases of venous thrombosis that were associated with use of combined hormonal contraception. The programme interviews the families of young American women who have died as a result of venous thromboembolic events that occurred while they were using the combined hormonal contraceptives NuvaRing® and Yaz®. It is understood that a longer version of the documentary is in production.

The CEU considers it important to put the documentary into perspective.

**Background information**

Combined hormonal contraception (CHC) contains both estrogen (usually ethinylestradiol) and a progestogen. CHC includes combined contraceptive pills, the combined skin patch and the combined vaginal ring.

**What is venous thromboembolism?**

A venous thrombosis is a clot in a vein most often diagnosed in the leg where it may cause pain, swelling and discolouration. If the clot becomes dislodged, it can travel (embolise) through the bloodstream to a lung. This results in a pulmonary embolism, a blockage of blood vessels supplying the lung which may cause chest pain, breathlessness and sometimes coughing up blood. These events are collectively termed venous thromboembolism (VTE). Very occasionally, a clot occurs in the large veins that carry blood away from the brain. This extremely rare event is termed venous sinus thrombosis and usually presents with headache.

**How likely is a woman to have a VTE event?**

VTE is rare in a woman of reproductive age (particularly a younger woman) whether or not she uses CHC.

Women of reproductive age who are not using CHC: Amongst women of reproductive age who do not use combined hormonal contraception (CHC) the risk of VTE events is about 2 per 10,000 women each year. [1,2] During pregnancy, the VTE risk is much higher (about 29 per 10,000 women) and in the weeks immediately after pregnancy it is greater still (300-400 per 10,000 women).[1]

Women of reproductive age who are using CHC: If a woman is using CHC, her VTE risk is increased compared to non-users of CHC. It has been shown that CHC containing some types of progestogen are associated with a lower VTE risk than others. COC containing the progestogens levonorgestrel, norethisterone or norgestimate increase a woman's VTE risk to 5-7 VTE events per 10,000 women per year of use. This constitutes additional 3-5 VTE events per 10,000 users each year that are attributable to COC use. [1,2]
COC containing other progestogens (desogestrel, gestodene, drospirenone (as in Yaz), nomegestrol and dienogest), the combined transdermal patch (Evra®) and the combined vaginal ring (NuvaRing) may be associated with a slightly higher risk of VTE events, between 6-12 per 10,000 users per year.[1,2] A recent study also suggests that COCs containing the lowest doses of ethinylestradiol (20μg) may be associated with lower VTE risk than those containing higher doses of ethinylestradiol (30-40 μg).[3]

**What is the risk that a woman will die if she has a VTE event while using CHC?**

About 1% of women who suffer a VTE when taking a combined oral contraceptive (COC) die.[4] Amongst each one million women of reproductive age using CHC, between three and 10 women are estimated to die each year as a result of VTE events that are attributable to use of CHC.[2,4] To put this into perspective for every one million UK women of reproductive age, about 12 die in a traffic accident and about 55 die in an accident of any cause each year.[5,6]

A large UK cohort study found that for women aged <45 years who were currently using oral contraceptives or had used them in the last five years, the risk of death from all causes was no higher than that for women who had never used oral contraceptives.[7] This study and another large UK cohort study[8] found no association between ever use of oral contraception and long term risk of death from any cause. Both studies suggested that there could be an overall reduction in risk of death for women who had ever used compared to those who had never used oral contraception.[7,8]

**What other factors increase a woman’s risk of VTE?**

VTE risk is increased independently of contraceptive use by factors such as age, obesity and a familial tendency to blood clotting. For this reason, clinicians are advised that all women considering use of CHC are routinely asked questions about their own medical history and that of their family in order to identify contraindications to CHC use.[9,10] Women who do not have such contraindications may be offered CHC along with all other suitable, effective methods of contraception.

**What do clinicians tell women about the risk of VTE with CHC?**

When discussing contraceptive choices with women, doctors and nurses are advised to explain the risk of VTE that is associated with CHC and inform women of the possible symptoms. Faculty of Sexual and Reproductive Healthcare guidance advises that “clinicians advising women on the use of hormonal contraception should be able to convey the risk of VTE and provide information on overall risk and benefit to help women judge the level of risk acceptable to them”. [1] Routine practice is to explain to the woman that the risk of VTE is increased by CHC. She should seek urgent medical attention if she experiences pain, redness or swelling in her leg, chest pain, breathlessness or coughing up blood. It should also be explained to women considering using CHC that other effective methods of contraception (such as intrauterine contraception and progestogen only contraceptives) are routinely available that are not associated with an increased risk of VTE.
Why do women choose CHC?
Over three million women in the UK choose to use CHC for contraception. Amongst 16 to 24 year olds in the UK, half choose to use oral contraception, usually combined oral contraception.[11]

If CHC is used correctly it is more than 99% effective in preventing pregnancy.[12] Women may choose to use CHC for reasons of individual preference, or because of their experience of nuisance side effects with other contraceptive methods. For the same reasons, women may opt to use a combined pill containing a particular progestogen, or a patch or vaginal ring. Some women choose CHC for the non-contraceptive benefits including management of heavy and painful menstrual bleeding and management of acne. Additionally, COC use is associated with a reduced risk of developing or dying from ovarian or endometrial cancer in later life (a benefit which persists for several decades after stopping CHC) and the evidence suggests a decreased risk of colon cancer with recent use of COC.[10]

CEU conclusion
CHC is popular and effective. VTE associated with use of CHC is a rare event. Of these already rare events, a minority (about 1%) are fatal. The risk of VTE during use of CHC is much lower than that during pregnancy and immediately after childbirth. Women of reproductive age are much more likely to die in an accident than as a result of a VTE event that is attributable to use of CHC.

Women who are considering use of CHC need to be aware of potential risks as well as benefits. FSRH guidance helps clinicians to avoid the use of CHC in woman with additional risk factors for VTE and recommends that all women requesting contraception should be informed about alternative contraceptive methods that are not associated with an increased VTE risk. Women should be given information about and access to these contraceptive methods. The contraceptive implant (Nexplanon®), the levonorgestrel-releasing intrauterine system (Mirena®, Levosert®, Jaydessa®) and the copper IUD offer the most effective contraception without any increase in VTE risk.

Women who have been made aware of the potential risks associated with CHC and that alternative, more effective methods are readily available, may judge that the level of risk is acceptable and make a fully informed decision to use CHC.

References


