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Contraception For Women at Elevated Risk for Thromboembolic Disease

Combined Oral Contraceptives (COCs) elevates the risk of venous thromboembolism (VTE). This is due to the oestrogen's tendency to increase hepatic production of fibrinogen and other clotting factors. For this reason, women with an increased VTE risk are **not** appropriate candidates for COCs. It is worth recognizing, however, that pregnancy elevates VTE risk substantially more than use of COCs does.

Progestin-only methods, including minipills, intramuscular medroxyprogesterone (Depo-Provera), and the progestin-releasing IUD (Mirena), do not elevate VTE risk. Unfortunately, package labelling for the Norgestrel minipill and for Depo-Provera inappropriately lists prior history of VTE as a contraindication. **Drug Company Warning**: *Thrombo-embolic Disorders:* Should the patient experience pulmonary embolism, cerebrovascular disease or retinal thrombosis while receiving Depo-Provera, the drug should not be readministered. **BNF recommendations**: Progestin-only contraceptives may offer a suitable alternative when oestrogens are contra-indicated including those patients with venous thrombosis or a past history or predisposition to venous thrombosis. The BNF rather than company recommendations should be followed.

Interaction of Hormonal Contraceptive and Antiepileptics

This depends on the effect of Antiepileptics on Cytochrome P450 Liver Enzymes:

* Antiepileptics that inhibit or have no effect on this enzyme system (e.g. **Gabapentin, Lamotrigine, Levetiracetam, Tiagabine, Valproate**) do not affect the efficacy of hormonal contraception.
* Antiepileptics that induce this enzyme system (e.g. **Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin, Primidone, Topiramate**) may decrease the concentration of biologically active hormone by increasing their metabolism and therefore reduce efficacy of hormonal contraception. Standard COCs contain only the minimal dosage of hormone required to inhibit ovulation. Even small increases in metabolism may lead to contraceptive failure. A 6% per year failure rate of oral contraceptives in women taking these Antiepileptics has been reported. In order to provide acceptable contraceptive efficacy, women taking cytochrome P450-inducing Antiepileptics must receive at least 50 µg of the oestrogen component. Long-term progesterone-only contraceptive systems, such as subdermal levonorgestrel, are also prone to failure because of increased steroid metabolism. Depo-Provera has not been evaluated for efficacy in women receiving this group of Antiepileptics. For effective contraception the use of a barrier contraceptive should be advised for all women receiving hepatic enzyme-inducing Antiepileptics.

Increased Ectopic Pregnancy Risk with Emergency Contraception

Levonelle is licensed for contraception up to 72 hours after unprotected sex. It prevented 95% of pregnancies when taken within the first 24 hours, this fell to 85% on the second day and as low as 58% on the third day. **Pregnancies occur in women taking it are more likely to be ectopic.** The Committee on Safety of Medicines has advised that women should seek treatment as early as possible after unprotected sex, and be told that the treatment can fail: "Women who do not experience a normal period after using Levonelle should be followed up so that pregnancy can be excluded". "The possibility of an ectopic pregnancy should be considered, particularly in women with a previous ectopic pregnancy, Fallopian tube surgery or pelvic inflammatory disease".