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Family history and risk of venous thromboembolism with oral contraception

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Collaboration is vital

EDITOR—The issue of pharmacists providing emergency contraception is controversial, as shown by the contribution by Stammers, and I am still uncertain about it.¹ Although the recent reclassification of emergency contraception can only broaden access to this useful product, I would have reservations about selling this item myself, not for any issue of conscience (which is causing great debate in the pharmacy literature in the United Kingdom) but because most British community pharmacies do not have the facilities to take a history in private. If pharmacists are going to provide this service then, as Stammers suggests, they should also be providing information about local sexual health services and advocating their use.

Contact your local sexual health centre and discuss this issue with them, and you will find that they are only too willing to help with the provision of relevant materials. This issue has the possibility to develop into yet another of those “them and us” scenarios between the medical and pharmacy professions. The time has come for everyone to work towards a common goal rather than everyone working in isolation.

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1 Stammers T Emergency contraception from pharmacists misses opportunity *BMJ* 2001;322 1245 (19 May)

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Family history is important tool

EDITOR—Cosmi et al in their article claim that family history has poor diagnostic test qualities to detect prothrombotic mutations.¹ They also indicate that overall population screening is not cost effective. Although it always was obvious that family history would never make a perfect test (of families with many cases of venous thrombosis, up to 40 or 50% have factor V Leiden²), the finding of an equal predictive value for a positive and a negative family history by Cosmi et al is surprising and might be due to the small numbers included or the type of history that was considered “positive.”

Even if family history is far from perfect as a diagnostic test for one or two mutations, the question is whether one should refrain from using it. In our original publication, we tried to emphasise the meaning of family history for the prescription of oral contraceptives, and not really as a clue for the detection of mutations.³ Apart from any prothrombotic mutation, a strongly positive family history might point to a tendency for venous thrombosis that might be taken into account clinically in the decision whether or not to use oral contraceptives.

Moreover, even the meaning of a mutation is different in the context of a positive family history: the age at first venous thrombosis with factor V Leiden is about 10 years younger in persons with a positive family history than in consecutive patients.⁴ The most important information that one would like to obtain from a family history is not a proxy test for factor V Leiden or any other mutation, but the likelihood that a woman will develop thrombosis if she uses oral contraceptives. Whether or not family history would be valuable for that purpose is the ultimate test.

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- 1 Cosmi B, Legnani C, Bernardi F, Coccheri S, Palareti G Value of family history in identifying women at risk of venous thromboembolism during oral contraception: observational study *BMJ* 2001;322 1024-5 (28 April)
- 2 Rosendaal FR Venous thrombosis a multicausal disease *Lancet* 1999;353 1167-73
- 3 Vandenbroucke JP, van der Meer FJM, Helmerhorst FM, Rosendaal FR Factor V Leiden should we screen oral contraceptive users and pregnant women? *BMJ* 1996;313 1127-30
- 4 Lensen RP, Rosendaal FR, Koster T, Allaart CF, de Ronde H, Vandenbroucke JP, et al Apparent different thrombotic tendency in patients with factor V Leiden and protein C deficiency due to selection of patients *Blood* 1996;88 4205-8

Author's reply

EDITOR—The finding of an equal predictive value of a positive and negative family history of venous thromboembolism might be because of the type of family history that was considered to be positive—that is, one first or second degree relative. However, because of the demographic changes in Italy over the past three decades, modern families are now small and many siblings are extremely rare. As a result, it would be quite difficult to find young women with two or more relatives with a history of venous thromboembolism.

Our study was prompted by the question whether clinicians can identify women at risk of venous thromboembolism during contraception only on the basis of family history. A positive personal or family history, or both, can be considered in itself a contraindication to oral contraception regardless of any thrombophilic defect. In the case of a positive history, screening for thrombophilia may be irrelevant because, even if no thrombophilic defects are found, the decision may be based only on clinical grounds. The problem can arise when clinicians obtain a negative personal or family history. We agree that family history cannot be a proxy test for any thrombophilic mutation, but it indicates the likelihood that a woman will develop thrombosis during oral contraception.

We also know that oral contraceptives may trigger thromboembolic complications in women with unrecognised thrombophilic defects. Thus women with thrombophilic defects can be considered at higher risk of developing thrombotic complications, even though the absolute risk is low. Is it necessary to search for thrombophilic defects if personal or family history is negative? Possibly not if the problem is considered from an epidemiological point of view because universal screening is not cost effective. However, women cannot be denied the knowledge and the information about the possibility of screening. We do not yet have an understanding of the biological basis of thrombotic complications during oral contraception and we have no other means of identifying women at risk of such complications. Apart from the risk of fatal pulmonary embolism, the morbidity and cost and side effects of venous thromboembolism cannot be ignored by clinicians.

Moreover, clinicians constantly face litigation, which could arise from incomplete information and the finding of a thrombophilic defect after an episode of venous thromboembolism during oral contraception.

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Author's reply to criticism of study on benzodiazepines and risk of hip fracture

EDITOR—Sgadari et al's letter¹ commented on the study that I and several others carried out to see whether benzodiazepines are associated with an increased risk of hip fracture.² We found that they are not.

In their large case-control study of 9752 patients with hip fractures compared with 38 564 controls, Sgadari et al also found no association between the use of benzodiazepines and hip fracture.³ But like us, though in different subgroups, they did find an association between certain drugs and hip fracture. They looked at the metabolic pathways involved, and it seems that in a specific subgroup of the most elderly patients these drugs may confer more risk. If this is not the result of multiple post-hoc testing it is an interesting finding, and one we did not look at.

We stated that the results we found for individual drugs might be spurious, related to multiple testing and statistical variability. But the main result is still that overall there is no increased risk of fracture associated with benzodiazepines. The risks associated with the subgroups mentioned by Sgadari et al are minuscule and apparent only because of the size of their study. This is in clear contrast with the important and constantly found dose dependent increased risk of falling, for all products, which