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3 Increased fetal loss recorded. However, another factor in fetal outcome was not addressed—namely, the effect of anticoagulation during pregnancy. The investigators do not mention whether any patients received anticoagulants during pregnancy, and if they did, which anticoagulant was used? Since the index group contained individuals with symptoms it would be presumed that some would have received such anticoagulation, and that the control group of healthy individuals would not.

Oral anticoagulants and fetal loss

SIR.—The EPCOT study group (Oct 5, p 913) show a relation between fetal loss and inherited thrombophilic defects. The mechanism of impaired placental development and function would certainly be a logical mechanism for the increased fetal loss recorded. However, another factor in fetal outcome was not addressed—namely, the effect of anticoagulation during pregnancy. The investigators do not mention whether any patients received anticoagulants during pregnancy, and if they did, which anticoagulant was used? Since the index group contained individuals with symptoms it would be presumed that some would have received such anticoagulation, and that the control group of healthy individuals would not.

Oral anticoagulants seem to increase fetal and neonatal deaths, whereas heparin may not have such an effect. In a retrospective study such as EPCOT, oral anticoagulants may have been used in the past, despite reluctance to use them now. Furthermore, the individuals with the highest fetal loss (combined defects and antithrombin deficiency) in this study are those who are likely to have more pregnancy/non-pregnancy associated thrombotic problems and therefore be candidates for therapeutic or prophylactic anticoagulation during pregnancy, irrespective of whether the defects were diagnosed after the pregnancies. Finally, the increased risk, if any, is low in patients with the factor V Leiden defect; this is a recently de-ribed familial thrombophilic defect. Since decisions on anticoagulation during pregnancy take into consideration underlying thrombophilic disorders, this group is less likely to have been considered for prophylactic anticoagulants before the description of the underlying defect.

The EPCOT report has raised an important issue about fetal loss and possible therapeutic interventions to reduce this loss. Information about the possible effects of anticoagulants on the results presented would be helpful in the interpretation of the data because one can postulate that oral anticoagulation could either increase or decrease fetal loss.

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Authors’ reply

Sir—Brown and Collins raise the interesting and valid point that the increased fetal losses in women with heritable thrombophilia might be influenced by losses attributable to oral anticoagulant thromboprophylaxis during pregnancy. Our results, which concur with those reported by Sanson et al., were obtained retrospectively at enrolment into the EPCOT study. Unfortunately we do not have detailed information on the use of oral anticoagulants in the women we reported. In an attempt to address the possible role of oral anticoagulants in the observed increased fetal losses we have reanalysed our data, confirming our analysis to those 600 of 966 pregnant women who have never had a venous thrombotic event. Since this group of women are the least likely candidates for anticoagulation this approach should greatly reduce the number who receive thromboprophylaxis during pregnancy. The analysis of this group led to a small decrease in the risk estimate but we still find a 25% excess risk of fetal loss. We anticipate that the prospective data arising out of the EPCOT cohort will clarify these issues.

F R Rosendal, F E Preston

Department of Clinical Epidemiology, University Hospital Leiden, PO Box 9600, 2300 RC Leiden, Netherlands; and Royal Hallamshire Hospital, Sheffield, UK


Sir—In response to Preston and colleagues’ report of the EPCOT study, we record three patients with resistance to activated protein C (APC) who, after thrombosis, had placental abruption despite thromboprophylaxis. A 25-year-old woman presented with her first pregnancy at 6 weeks’ gestation. She had a sinus thrombosis in 1991, but there was no family history of thrombosis. APC resistance was diagnosed (APC ratio 1.61). She was kept on low-molecular-weight heparin prophylaxis during pregnancy. Since this OTC report will clarify these issues.

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given (one 0150 anti-factor Xa IU subcutaneous injection daily). Despite emergency caesarean section for placental abruption, the fetus (570 g, 30 cm) died. No fetal malformation was found. The placenta showed numerous small foci of ischaemic necrosis. A 37-year-old woman (gravida 4, para 2) was admitted for uterine bleeding at 31 weeks' gestation. She had had a deep venous thrombosis 6 years earlier after a normal delivery. The patient's sister had a stillbirth at 34 weeks. APC resistance was shown (APC ratio 1.65). The patient was kept on low-molecular-weight heparin prophylaxis (3075 anti-Xa IU, nadroparin, one subcutaneous injection daily). At admission fetal death was caused by placental abruption and pregnancy-induced hypertension were found. After the stillbirth subarachnoidal haemorrhage was shown in the baby (1500 g, 44 cm) and the placental surface was coated by blood clots. In all patients the postabortial and postpartum courses were uneventful.

There is evidence that APC resistance in symptom-free women might contribute to midtrimester fetal loss. Our three cases indicate that APC resistance in women after clinical presentation of thrombosis comprises fetal outcome more severely than in symptom-free conditions because, despite thromboprophylaxis, the resistance may result in placental abruption, and fetal death. Nevertheless, our experiences suggest that the dose of low-molecular-weight heparin recommended for thromboprophylaxis should be increased during the pregnancy of the thrombophilic patient who has had thrombosis; this may reduce the risk to the fetus, just as in those mothers with antiphospholipid antibodies who were given full-dose heparin therapy after previous fetal loss.

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**Drought and malaria retreat in the Sahel, West Africa**

*Sir—The Sahel is a belt of dry savanna lining the southern border of the Sahara. Since 1970, rainfall has decreased by nearly 30% in this region with severe droughts in 1972, 1983, and 1991–92. The impact of dryness on malaria, endemic in the Sahelian belt, has been studied in Senegal (the Niayes) and the Niger Republic (Niger Valley, Zinder, Diffa).

The Niayes are marshy areas, located in north-west Senegal. Mean annual rainfall decreased from 684 mm (1931–60) to 427 mm (1980–89), and to 259 mm (1992) (figure). The rainy season shortened from 6 to 4 months. The same was observed in Niger, where the rainfall at Niamey decreased from 640 mm (1950–69) to 457 mm (1981–90). The environment has changed drastically under the combined impact of drought and population growth. Numerous trees were cut for domestic use and stayed unreplaced due to the drought. In Niger and Senegal, marshes with emergent vegetation (cattail) were larval habitats of *Anopheles funestus,* a major malaria vector. Then, these habitats became dry even after the rainy season, although their soil retained some moisture allowing vegetable cultivation. As a consequence of environmental changes this vector almost disappeared, comparing data recorded before 1970 and after 1988. In Senegal, *An funestus* accounted for 66% of night-landing collections in 1967 with an average of 33 bites per man per night and a sporozoite index between 1·2 and 3·1%. In 1991, this mosquito was no longer captured.1 In 1995, despite heavy rains, its populations did not recover because larval habitats were not restored. In Niger, *An funestus* was also one of the main