given (one 6150 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 27-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 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 postabortal and postpartum courses were uneventful.

There is evidence that APC resistance in symptom-free women might contribute to midtrimester fetal loss.[2] 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[3] after previous fetal loss.

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SIR—Data from the EPCOT study[1] show an increased risk of fetal loss in women with thrombophilia, especially in those with antithrombin deficiency or combined defects. For carriers of factor V Leiden no evidence of an excess risk of miscarriage was found and data on the risk of stillbirth were inconclusive. However, no separate analysis of women with homozygous or heterozygous factor V Leiden was undertaken.

We have investigated 27 women homozygous for the factor V Leiden mutations (median age 36 years, range 21–60). Some were enrolled in the EPCOT study. 26 women had had at least one venous thromboembolic event (VTE); all had the factor V Leiden mutation, which was detected during laboratory evaluation, one woman was symptom-free and her factor V Leiden status was discovered by chance. A standardised questionnaire was completed by personal interview at the participating centres with particular emphasis on obstetric history. Miscarriage was defined as fetal loss before and including the 28th week of gestation, and stillbirth was defined as intrauterine death after the 28th week of gestation. 18 women had been pregnant at least once (median=2, range 1–6) and had in total 42 pregnancies. In two of the pregnancies thromboprophylaxis was carried out. Seven (17%) pregnancies ended in miscarriage (three) or stillbirth (four), and nine (21%) in termination. One miscarriage and three stillbirths, but none of the terminations, were followed by deep vein thrombosis (DVT); in one woman DVT was combined with pulmonary embolism. In two of 24 successful pregnancies without thromboprophylaxis DVT occurred during pregnancy and one woman had DVT after delivery.

We conclude that the risk of stillbirth in women homozygous for factor V Leiden (10%) is greater than that in healthy women, who have a prevalence of stillbirth of about 1%.[1,2] The risk of miscarriage was not increased. More than half the fetal losses were followed by VTE. The prevalence of VTE during pregnancy and after delivery in pregnancies with successful outcome was moderately increased, but lower than in women with heterozygous deficiency of antithrombin protein C, or protein S, who have a pregnancy-associated frequency of VTE of 15–51%.[3] Thromboprophylaxis could be considered during pregnancy in women homozygous for factor V Leiden to reduce the increased risk of stillbirth and VTE.

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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 sporozoitic 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

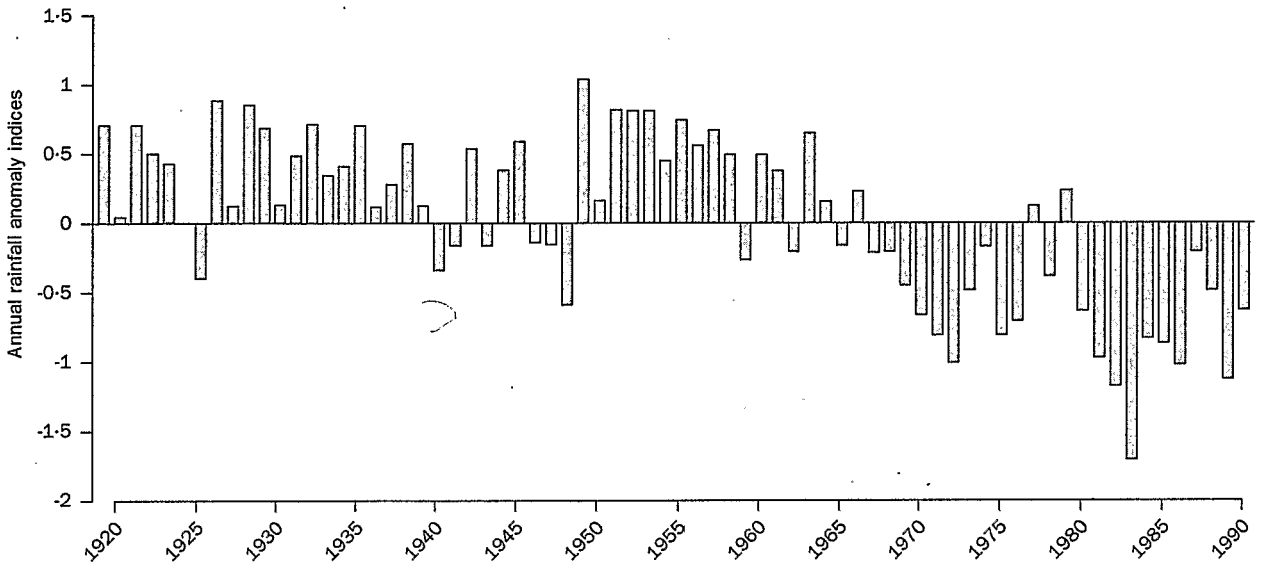

Figure: **Annual rainfall anomaly indices* in the Sahel**
*Anomaly indices calculated with respect to mean 1931–90 rainfall.[5]

vectors until 1971. Since then it has not been recorded.[2] At the same time malaria indices decreased sharply in all study sites. In the Niayes, the parasite index of children under 9 years dropped from 50% to 8%.[1] In 1991–92, only four malaria cases were observed in a cohort of 100 children in an area where case incidence was 340 per 1000 population in 1967.[3] Therefore, the parasite prevalence fell by 84% and the case incidence by more than 82%. Malaria prevalence along the Niger River was around 69% in 1969 and only 23% in 1994. In Zinder, prevalence dropped from 89% (1922)[4] to 32% (1994). Along Lake Chad, the prevalence was 40% in 1967. Now the lake has retreated by more than 100 km to the south and no longer reaches the Niger Republic. The parasite prevalence in the same area is now only 7%.

The sharp decrease of malaria indices is most likely a consequence of the disappearance of the vector *An funestus*, itself due to environmental changes (drought and human activities).

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Malodorous wounds

SIR—Mills and colleagues report (Nov 9, p 1282)[1] a man who pricked his finger and smelled putrid for 5 years. Clostridia were isolated repeatedly and could not be eradicated by prolonged courses of antibiotics despite very good in-vitro susceptibilities.

A 58-year-old woman presented to the Department of Internal Medicine at Karl Franzens University with a 35×15 cm large skin ulcer beneath the right axilla which developed over a 4-year period after lung surgery. The ulcer was very malodorous, and anaerobic grampositive rods were isolated (*Eubacterium lentum* and *Clostridium* spp). Despite repeated antibiotic treatment the ulcer did not decrease in size, odour did not diminish, and anaerobic bacteria persisted. Multiple repeated stains for acid-fast bacteria and mycobacterial cultures were negative. Finally, after five repeated biopsies the histological work-up revealed granulomas consistent with tuberculosis. Acid-fast bacilli were not seen. The ulcer healed promptly under tuberculostatic triple therapy. We have also reported another patient with salmonella sepsis recurring eight times despite prolonged treatment with different antibiotic regimens that were highly active in vitro.[2] Salmonellae were eradicated with unusually high doses of intravenous ceftriaxone plus ciprofloxacin after the eighth recurrence of sepsis. Finally tuberculosis of the liver was diagnosed by PCR and histological work-up of biopsy material, and the patient recovered fully with appropriate triple therapy.

In both our cases the main bacteria isolated caused superinfections and persisted after antibiotic treatment despite high sensitivity in-vitro. Tuberculosis was the underlying disease in both patients, possibly leading to an immunological so-called blind spot for other bacteria.[3] Because of the non-suppurative inflammation Mills and colleagues report (which did not subside with a broad spectrum of commonly used antibiotics), the chronic course of the disease, and the fact that atypical mycobacteria can be frequently isolated from chickens,[4] mycobacterial infection should be considered in their patient. For the management of the patient we suggest examination of biopsy specimens for granulomas, and even in the absence of granulomas[5] antimycobacterial therapy seems indicated.

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