

irrigation in the former Punjab has increased transmission and has transformed the epidemic area into an area with more stable (endemic) malaria. Irrigation schemes have thus shifted the belt of "desert fringe" malaria with an epidemic potential to more arid regions such as the Thar desert, which has half of the rainfall of the previously epidemic Punjab.

Conditions that have resulted in epidemics in the irrigated parts of the Thar desert deserve further study. This susceptibility to epidemics suggests that transmission is not stable and limited by population immunity. Perhaps desert irrigation creates isolated foci where the absence of the parasite excludes transmission; migrating human carriers are then responsible for initiating epidemics, as has been observed in oases in Africa. Alternatively, since the 1991–92 epidemic occurred in the irrigated part of the Thar desert in absence of heavy rainfall, it may be worth investigating whether an oversupply of irrigation water led to flooding. Apart from monsoon rainfall, snow cover in the Himalays⁵ is correlated with ENSO too.

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Global burden of tropical diseases

SIR—According to the latest World Health Organisation report, of the 46·6 million worldwide deaths linked to diseases, 39 million occurred in developing countries. Of these 40% are caused by communicable diseases (eg, malaria, schistosomiasis, respiratory infections) or are due to obstetrical or perinatal causes which are rare in industrialised countries.¹ Inaccessibility or unavailability of therapeutic interventions is a major factor in global mortality: less than 40% of the population in developing countries have regular access to essential drugs.²

Consider sub-Saharan Africa (where more than 95% of needed drugs are imported): regional currency devaluation in 1994 had a rapid impact on drugs purchases (down 30–40%). One consequence has been that local needs are now being catered for by traditional medicines or counterfeit drugs. To reduce the burden of disease upon these countries' economies, an essential package of health services has been estimated to cost US\$12 per person per year.³ Most underdeveloped countries are spending less than US\$10 per capita each year. The cost of drugs is a serious impediment to equal access, especially when there is no reliable social security system.

Nearly 95% of the total expenditure on research and development by the world pharmaceutical industry is designated to drug production for the industrialised countries. Of the new molecular entities now under investigation, most (more than 100 drugs) are directed at the treatment of cancer, infection, cerebrovascular, or cardiac disease.⁴ For the major intertropical diseases there are presently less than five drugs under development or awaiting

approval for marketing. These include artesunate for malaria, and amocazine for onchocerciasis. For this category of diseases, most of the pharmaceutical efforts are concentrated either on maximising the use of existing drugs—alone (eg, albendazole, ampyroquine, liposomal amphotericin B, praziquantel) or in combination (eg, cyclin+erythromycin for malaria)—or on investigating veterinary drugs in clinical trials (eg, doramectin, triclabendazole). Moreover, 387 orphan drugs were authorised in 1994 by the US Food and Drug Administration, and less than 11 belong to the tropical medicine category.

Your editorial "Bigger companies for better drugs" (Sept 2, p 585) pointed out that "pharmaceutical companies will only develop and manufacture a drug they know they can sell". This tendency of the manufacturers to concentrate upon supplying the developed world markets may quickly lead management of tropical diseases to an impasse because of a poor pharmacopoeia. The global burden of disease will undoubtedly increase.

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Ehrlichiosis in Belgium

SIR—On July 20, a 13-year-old girl was admitted to hospital with a four-day history of fever, chills, headache, anorexia, malaise, and epigastric pain. She had spent the previous weeks in a guide camp in the Ardennes. Although she did not remember a tick bite, Lyme disease is frequently acquired in this area.¹ She had slightly enlarged neck glands and mild conjunctivitis. Body temperature was 39·0°C. Laboratory investigations revealed leucopenia ($1600 \times 10^9/L$ leucocytes), thrombocytopenia ($82\,000 \times 10^9/L$ thrombocytes), elevated AST (133 U/L), ALT (144 U/L) and bilirubin (56 $\mu\text{mol/L}$). Serum urea and creatinine were normal. In hospital, fever persisted (38·0–39·9°C) and she developed rash, icterus, and confusion. A lumbar puncture showed 5 leucocytes $10^9/L$ and negative bacterial and viral cultures. Serological tests were negative for Epstein-Barr virus, cytomegalovirus, HIV, hepatitis A, hepatitis B, and hepatitis C, toxoplasmosis, rubella, Q fever, brucellosis, *Borrelia burgdorferi*, *Leptospira*, and *Rickettsia*. She improved, became afebrile on day 11, and was discharged on day 14. Immunofluorescence antibody tests on four sequential serum samples taken during her hospital stay showed a high initial titre of 256 for *Ehrlichia chaffeensis* antigen on day 4 after onset of symptoms, that rose to 512 on day 7 and remained stable thereafter. Titres for *E. equi*, used to diagnose human granulocytic ehrlichiosis, remained negative (<64).

Ehrlichia spp, obligate intracytoplasmic gram-negative bacteria related to *Rickettsia* spp were described in 1935 as the cause of animal diseases and of sennetsu fever, a human disease confined to Japan and Malaysia. Since the first report of a case of human ehrlichiosis in the United States in 1986, two aetiological agents have been described: *E. chaffeensis*, involved in more than 400 laboratory-