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Risk factors for severe malaria: importance of careful study design: a reply

The study by KORAM *et al.* (1995: *Transactions*, 89, 151-154) failed to demonstrate the role of socio-economic factors as major determinants for severe malaria in Gambian children and this led the authors to conclude that improving knowledge of the recognition and management of malaria and improving treatment facilities may not be particularly effective in reducing the incidence of severe disease in The Gambia. In a letter published in the previous issue (1999: *Transactions*, 93, 679), BENNETT and colleagues (the authors of the Gambian study) suggest again that socio-economic factors have no influence on severe malaria, a point that we consider is not only wrong but also potentially dangerous since it may contribute to discourage medical teams and health workers. In their letter, Bennet *et al.* criticize the methodology of the Brazzaville study (CARME *et al.*, 1994: *American Journal of Tropical Medicine and Hygiene*, 50, 131-136) the results of which indicated an influence of socio-economic factors on the occurrence of cerebral malaria. We refute the claims that the method of selection of the control group led to false findings. In contrast to Bennett *et al.*'s affirmation, the expected family size under the null hypothesis of no effect of family size on the risk of severe malaria is higher for cases than for controls (4.8 versus 4.0; $P < 0.05$) when using the observed numbers of Brazzavillian children for each family. Thus the significant differences are not an artefact of the study design. Moreover, the statistical unit was the family and not the child, both for controls and cases (all selected children with cerebral malaria belonged to different families). Because of the spacing between births (~3 years in Brazzaville), a woman could not have more than 1 or 2 children at high risk of severe malaria (aged 1-5 years) at any moment. Matching controls with cases by number of children in the family is not a correct approach because this would eliminate as a potential risk factor the size of the family and reduce the impact of any variable that is correlated with it.

The study of LUCKNER *et al.* (1998: *Transactions*, 92, 478-481) in Lambaréné (Gabon) found no influence of socio-economic factors on the severity of disease. We agree with the authors that the most probable explanation is the high socio-cultural homogeneity of this forest population of Central Africa. By contrast, we believe that the results of the study of Koram *et al.* in The Gambia are open to doubt. According to GREENWOOD *et al.* (1987: *Transactions*, 81, 478-486) in their study on mortality and morbidity from malaria among children in a rural area of that country, 23 (92%) of the 25 reported deaths of children who had probably died from malaria occurred at home and only 2 (8%) in a dispensary; no child died in hospital. Indeed in The Gambia, as in Senegal and in most other countries of the Sudan and Sahel regions of West Africa, many illiterate families consider that severe neurological signs and symptoms (e.g., coma and seizures) are within the competence of traditional medicine. Most cases of severe malaria are treated by *marabouts*, not doctors or nurses. This does not apply to simple malaria attacks since families generally consider cases of fever alone much better treated with modern drugs in nearby dispensaries. For this reason, we believe that there are important biases in the study of Koram *et al.* where severe malaria cases were enrolled in hospitals and mild malaria cases (controls) in dispensaries. Children from families with the best education and socio-economic status were much more likely to be hospitalized than children from other families. This may mask substantial differences in the incidence of severe malaria related to socio-economic factors.

To conclude we agree with Bennett and collaborators on the following point: these difficulties demonstrate the importance of a careful case-control study design!

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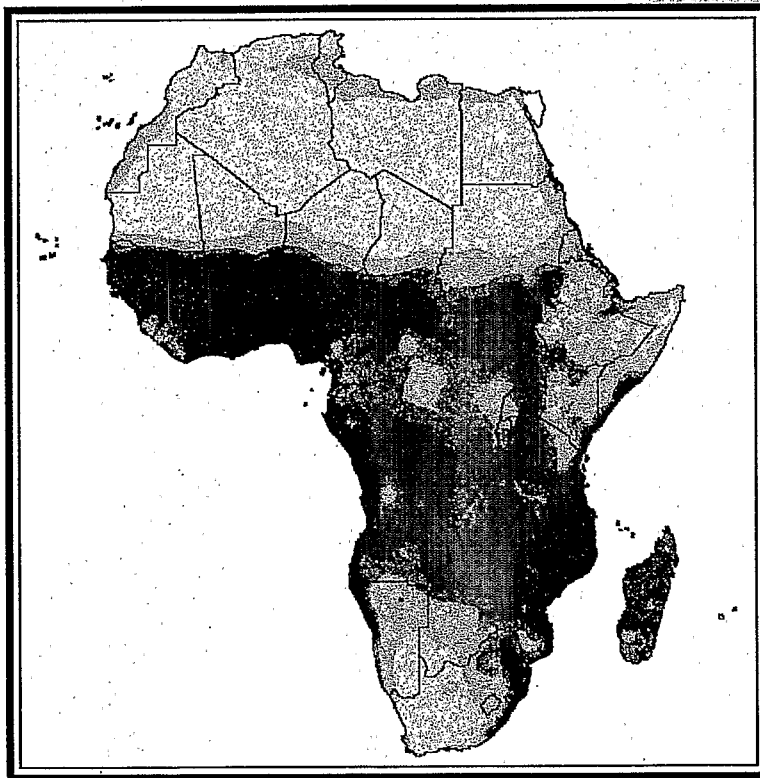
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