Age and 'Straintranscending' Immunity to

*Plasmodium falciparum*

J. Kevin Baird

*Department of Parasitology US Naval Medical Research Unit 2, jakarta, jkevinbaird@yahoo.com*

Follow this and additional works at: [http://digitalcommons.unl.edu/publichealthresources](http://digitalcommons.unl.edu/publichealthresources)
Age and 'Strain-transcending' Immunity to Plasmodium falciparum

Roberts et al. cited work from this laboratory, which to them suggested that ‘... immunity can develop after relatively few (certainly less than 10) episodes of clinical malaria’. Although this statement appears largely true to the cited work, it is important to point out that the supporting evidence applied to adults but not to children. In our studies of people with limited histories of exposure to endemic malaria, children remained susceptible to frequent and high-grade parasitemia after several years, whereas adults apparently developed protection. These findings were confirmed with additional studies. A paradigm for the relationship between antigenic variation and the development of clinical immunity to falciparum malaria must ultimately account for this important difference between children and adults.

The thoughtful exchange between Roberts et al.1 and Gupta and Day2 was especially relevant in this regard. In the original description of antigenic variation by malaria parasites, Brown and Brown3 recorded in Plasmodium knowlesi what they described as ‘the simultaneous occurrence of two levels of immunity, one specific for each relapse variant, and the other transcending antigenic variation...’. They cited work suggesting that ‘... the young of some hosts may be constitutionally incapable of developing a generalized [strain-transcending] immunity...’. Brown and Brown3 wondered whether childhood susceptibility to infection was due to a lack of experience with antigenic variation (relative to adults) or to a constitutional inability to respond appropriately to endemic infection pressure. That question burns today and bears directly upon the arguments raised by Roberts et al.1 and Gupta and Day2.

In considering the issue of an immune response which may transcend antigenic variation, some important papers seemed neglected. In addition to the work of Brown and Brown3, Digg's et al.4 reported dramatic therapeutic effects of purified adult African IgG against Asian isolates of P. falciparum in Aotus monkeys. This was also true when adult African IgG was injected into Thai patients ill with P. falciparum5. The clinical studies of malariotherapy of syphilis patients also offer evidence of strain-transcending immunity. The work and review by Jeffery6 is instructive; patients with immunity to homologous strains of P. falciparum usually showed markedly attenuated susceptibility to heterologous strains from widely separated geographic regions. It may be essential to recognize that all of the clinical studies exploiting the practice of malaria therapy used adult humans. Those findings cannot be extrapolated to children. The rate of development of clinical immunity to homologous and heterologous strains of parasites may be dramatically different in children. The existence of a 'strain-transcending' immune response might be reconciled with data from adults but not from children.

References
1 Roberts, D.J. et al. (1994) Parasitology Today 10, 64
5 Brown, K.N. and Brown, L.N. (1965) Nature 208, 1286–1288

J. Kevin Baird
Department of Parasitology
US Naval Medical Research Unit 2, Jakarta
Box 3, American Embassy
APD AP 96520-8132, USA

Reply

Baird proposes that the rate of development of clinical immunity to malaria may be very different in children compared with adults. He cites his own data from Irian Jaya1,2, reporting age-related differences in malariometric indices in Javanese transmigrants and Melanesians to support this hypothesis. The data presented by Baird et al.1,2 show in some, but not all, slide-positivity studies that Javanese adults experience fewer parasitic episodes of Plasmodium falciparum than do children from the same geographic origin. Data are reported for the first two years of residence of the Javanese migrants in a holoendemic malaria area of Irian Jaya. The Javanese are believed to have no previous history of exposure to malaria before arriving in Irian Jaya. This may be a valid conclusion, but the reader of these papers has to take this on faith, as malaria prevalence figures given for the Javanese islands are only from 1980. As there appear to be subjects in the study population up to 60 years of age, it would be interesting to know the malaria-transmission conditions that these older individuals were exposed to in Java. Frequently, data are pooled for all subjects >15 years to define an adult age class for comparison with children aged 2–5 years. This assumes that all subjects >15 years have the same history of exposure to malaria. Is this the case? Small sample sizes for individual villages also require data to be pooled to observe the differences in parasitemia rates between adults and children2. This is valid if there are no significant inter-village differences in malaria transmission. Given the above concerns, the observed age-specific differences in parasitic rates are justified if there are no age-specific differences in either exposure to transmission or antimalarial usage for the Javanese population.

While these studies report interesting findings, they do not directly address the issue in question, i.e. the age-specific rate of development of clinical or anti-disease immunity. They report age-specific differences in the prevalence of parasitemia but not clinical episodes of the Javanese study population. In the design and discussion of these studies, Baird et al. do not draw any distinction between anti-disease immunity and anti-infection immunity which clearly develop at quite different rates (see review by Gupta and Day5) and persist for different periods4. Given this distinction, we believe that the data of Baird et al. attempt to address the question of the age dependence of the development of infection-blocking rather than anti-disease immunity. Consequently, they are only relevant to the current discussion if variant surface antigens are the target of both types of immunity. Epidemiological data from other areas do not support Baird's hypothesis. For example, clinical data from areas of low endemicity show little age dependence in the distribution of clinical cases. Similarly, a study of epidemic malaria in Madagascar has shown that all age classes except those previously exposed to malaria were equally susceptible to disease6. We therefore do not believe that there is sufficient, well-defined clinical data to propose that an age-dependent difference in the rate of acquisition of immunity that protects against malariadisease.

Baird also raises the issue of the importance of strain-transcending immunity in controlling disease. Our interpretation of the induced experimental evidence is that it is strain-specific rather than strain-transcending immunity that protects against disease. Jeffery's review7, in fact, states ‘... in all homologous species re-inoculations, there were significant modifications of the infections, which were enhanced if both exposures were to the same strain. Variable results were seen after re-inoculation of patients with heterologous species.’

Similar points are made by Boyd8 and Hackett9, among others. We believe that, in areas of high endemicity, strain-transcending immunity plays an important role in the eventual development of immunity against infection, but not against disease. For a more detailed discussion of these issues, see Gupta and Day5.