Correspondence

Studies on Severe Malaria are Still Possible and Essential

To the Editor—We were very interested in the recent editorial by Shanks [1], which asserted that clinical studies on severe malaria may no longer be possible. Two main reasons were outlined. The first, that any such study should include support equivalent to that provided by most intensive care units (ICUs),[Q2] is far from universally agreed. Most countries in which malaria is endemic manage patients with severe malaria in the absence of an ICU. The challenge is to design research aimed at cost-effectively improving case fatality rates and morbidity in settings where most of the disease occurs; that is evidently not in Western travelers returning home from a tropical holiday. Relevant topics include, for instance, optimizing antimalarial and fluid therapy, timing of enteral feeding in comatose but nonintubated patients, and affordable adjunctive therapies. In general, the results of a trial performed in a highly sophisticated setting cannot be directly translated to the developing world. The requirement for high-level ICU facilities could even be interpreted as derogatory for brilliant clinical researchers who happen to be based in developing countries that lack these facilities.

The large South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT) [Q3] trial [2] was the first trial involving adult severe malaria to show an important impact on mortality, with a 34.7% reduction in favor of artesunate over quinine. Recruitment was in general medical units across Asia, with very few patients reaching an ICU. Another large trial with a similar design (the African Quinine Artesunate Malaria Trial [AQUAMAT] trial) is now underway involving African children[3] and is recruiting in 8 countries. A large multinational fluid trial is also ongoing. We agree that the number of mortality–end point trials involving malaria is limited by the available research capacity, but we do not think that the planned RTS-S[Q4] vaccine trial “will fully occupy most of the research capacity of Sub-Saharan Africa for at least 3 years” [1].[Q5] Also, if ICU care were a prerequisite for research on severe diseases in developing countries, neither SEAQUAMAT nor AQUAMAT would have been possible.

The second proposed threat to severe malaria research in the editorial is the reduction of malaria incidence attributable to successful control measures in countries such as Vietnam and Thailand. However, there are still an estimated 1 million deaths annually [3] from severe malaria, and malaria elimination in many countries where malaria is endemic is unlikely to happen in the near future. There will remain a large number of potentially avoidable deaths while we await malaria elimination. This would be compounded if containment of the recently confirmed artemisinin-resistant parasites in Western Cambodia were to fail [4, 5]. Moreover, if malaria elimination campaigns conducted in high-transmission settings are successful, then the falling incidence of malaria will result in diminished population immunity among adults and older children with a possible increase in severe disease in this group [6, 7]. It is all the more important to continue to improve our understanding and management of severe malaria. Collaborative efforts in sufficiently powered multinational, multicenter trials will remain necessary to provide definite answers to important research questions aimed at improving the still unacceptably high malaria-attributable mortality.

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