Editorial

Intermittent Preventive Treatment for Malaria in Sub-Saharan African: A Halfway Technology or a Critical Intervention?

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In what was a highly influential but is now, sadly, largely forgotten essay, the eminent medical scholar Lewis Thomas distinguished halfway technologies from high technologies. He noted that while halfway technologies are simultaneously sophisticated and primitive, they are carried out after the fact, and they are “the kind of thing that one must continue to do until there is a genuine understanding of the mechanisms involved in disease.”

The notion of halfway technologies seems to apply fully to intermittent preventive therapy (as well as bednets) for malaria. On the other hand, Thomas characterized high technologies as “the most decisive technology of modern medicine,” which in the context of malaria aims at the holy grail of a highly effective vaccine. Yet because we lack precise knowledge of mechanisms of anti-malarial immunity in humans, the silver bullet of the long-promised malaria vaccine remains elusive. This lesson applies fully today to the global context of malaria. We know that malaria causes poverty; that poverty causes malaria. It is generally agreed that until a vaccine remains elusive. This lesson applies fully today to the global context of malaria. We know that malaria causes poverty; that poverty causes malaria. It is generally agreed that until a highly efficacious and deployable vaccine to eradicate malaria comes down to cost effectiveness arguments and subjective value judgments about where to deploy scarce resources amid concerns about selecting for drug resistant parasites.

Drugs for IPT must fulfill a number of criteria. Safety is paramount, given the long duration of treatment and the large scale of the intervention, and, indeed, serious adverse effects appear to be uncommon on a population basis. The pharmacokinetics of the active components of optimal IPT drug combinations must be long enough to clear parasites while impairing the formation of resistance-bearing gametocytes and preventing the emergence of de novo resistance. Clinical trials have been interpreted as indicating a range of efficacy from “very” to none. A recent pooled analysis of 6 randomized, placebo-controlled
clinical trials of sulfadoxine-pyrimethamine showed an overall protective efficacy of ~30% against episodes of clinical, symptomatic malaria, 38% against hospital admission associated with malaria parasitemia and 21% against anemia. In this pooled analysis, SP-based IPTi did not significantly reduce mortality. Some have taken these conclusions as evidence that the SP-based IPTi did not significantly reduce mortality, and that the WHO call for IPT based on SP seems to be less than fully justified. Additional commentary has made the point that the combination with an artemisinin compound is often lag behind the demonstration of drug resistance. We can hope that SP-sensitive \textit{P. falciparum} might eventually return to regions where there might have been a “drug holiday” such as happened with chloroquine in Malawi. However, given the ease with which \textit{P. falciparum} becomes resistant to anti-folates drugs, the fixation of triple mutants within local parasite populations in Africa with no obvious loss of fitness, and the widespread use of anti-folates in HIV/AIDS in Africa, the lifespan of SP for any use in malaria, including IPT, is likely coming to an end. New drugs will have to be developed for this indication, as part of ongoing halfway technologies that will ameliorate but not eliminate malaria.

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