

The response of *Plasmodium falciparum* isolates to dihydrofolate reductase inhibitors (DHFRIs) was examined in Malindi, Kenya. All 20 infected children treated with pyrimethamine/sulphadoxine responded. In contrast, after treatment with pyrimethamine, parasitaemia in 9 of 14 infections failed to clear or recrudesced during the seven-day follow-up. In a 48-hour *in vitro* test, five of six isolates resistant to pyrimethamine *in vivo* had a minimal inhibitory concentration (MIC) to pyrimethamine ≥ 300 nmoles/l compared with ≤ 100 nmoles/l for the four sensitive isolates; four isolates did not grow. MIC to M-B 35769, an experimental DHFRI structurally similar to pyrimethamine were the same (six isolates) or 10-fold lower (three isolates). In the laboratory four of five isolates adapted to *in vitro* culture had the same MICs as in the field while one isolate became less responsive to both drugs. Cycloguanil (the active metabolite of proguanil) was more active *in vitro* in the laboratory than pyrimethamine or M-B 35769.