To the Editor:

Recently Gordeuk et al. have observed a drastic increase of the rate of parasite clearance in patients with asymptomatic *Plasmodium falciparum* infection. They suggested that this may be partially caused by limitation of iron by chelation, although they argued that this may not be the only mechanism limiting growth of *P. falciparum*. Previous studies have shown elevated levels of neopterin in urine of patients infected with *P. falciparum*. Neopterin is produced on stimulation with interferon-γ (IFN-γ) by human monocytes/macrophages and therefore has been established as a clinically useful marker for monitoring cellular immune activation in vivo. Most recently, an investigation demonstrated that elevated neopterin levels in malaria patients are closely correlated with enhancement of endogenous IFN-γ levels. It was shown in vitro that IFN-γ is able to inhibit the development of plasmodia by an L-arginine dependent effector mechanism.

Recent data of our group showed that even low intracellular concentrations of low molecular weight iron (25 μmol/L) drastically reduce the efficiency of IFN-γ signal in myelomonocytic cells with characteristics of macrophages. This effect, not caused by increased cytotoxicity toward these cells, can be referred to direct interference of iron with the IFN-γ signal. The inhibitory effect of iron was fully reversed when iron was concomitantly administrated with equimolar concentrations of desferrioxamine, while desferrioxamine alone was even able to enhance the efficiency of the IFN-γ signal. From this point of view it may be reasonable that iron chelation therapy of malaria with desferrioxamine may also influence the immunostate of the patients. IFN-γ is known to initiate a lot of cytotoxic effects toward invading microorganisms. In addition, Lane et al. described that treatment of macrophages with desferrioxamine and IFN-γ inhibited the intracellular growth of *Histoplasma capsulatum*. They suggested that iron deprivation may be one base for the IFN-γ induced antihistoplasma effect of macrophages.

We conclude that the decrease of *P. falciparum* after administration of desferrioxamine may not only be referred to growth inhibition of parasites by limitation of iron availability but may in part also be caused by modulation of immunologic progress such as enhancement of IFN-γ-induced antimicrobial cytotoxicity by the drug.

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REFERENCES


RESPONSE

We agree that the mechanism of the antimalarial effect of desferrioxamine B in vivo remains to be determined, and thank Weiss et al for their idea that iron chelation may increase immune clearance of plasmodia by enhancing the effect of interferon-γ on cells of the mononuclear-phagocyte system.

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Therapy of Plasmodium falciparum parasitemia with desferrioxamine [letter; comment]

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