Am. J. Trop. Med. Hyg., 71(1), 2004, p. 1

LETTERS TO THE EDITOR

Dear Sir:

Scott and others[1] report that their results with B6 mice and *Plasmodium yoelii* 17X "suggest that chronic tuberculosis worsens in the presence of an acute malarial infection." Several old studies with *Macaca mulatta* on the reciprocal interaction may be of interest here. First, Coggeshall and Kumm[2] made the intriguing claim that, "It has been repeatedly observed that tuberculosis has an inhibitory effect on the course of *P. knowlesi* infection in monkeys," although their own results seemed to involve just one unexpected, concurrently-infected survivor. Singh and others[3] found peak and mean *P. knowlesi* parasitemia were dramatically decreased by concurrent tuberculosis, but all 15 experimental and 10 control animals died quickly; with *P. inui*, three concurrently infected animals died within days versus months in five controls. Bazaz-Malik[4] reported increased survivorship, with these two species and *P. cynomolgi*. Finally, in this journal, Freund and others[5] summarized the results of their famous malaria-vaccine adjuvant studies: "Killed *P. knowlesi* parasites emulsified in paraffin oil containing killed tubercle bacilli protect rhesus monkeys against fatal infection with *P. knowlesi*. … No satisfactory substitutes were found for killed tubercle bacilli."

REFERENCES

1. Scott CP, Kumar N, Bishai WR, Manabe YC, 2004. Short report: modification of *Mycobacterium tuberculosis* infection by *Plasmodium* in the murine model. *Am J Trop Med Hyg 70:* 144–148.
2. Coggeshall LT, Kumm HW, 1938. Effect of repeated superinfection upon the potency of immune serum of monkeys harboring chronic infections of *Plasmodium knowlesi. J Exp Med 68:* 17–27.
3. Singh JP, Ray AP, Nair CP, 1956. Relationship of tuberculosis on the course and intensity of plasmodial infections in *M. mulatta. Indian J Malariol 10:* 3–10.
4. Bazaz-Malik G, 1973. Increased resistance to malaria after *Mycobacterium tuberculosis* infection. *Indian J Med Res 61:* 1014–1024.
5. Freund J, Thomson KJ, Sommer HE, Walter AW, Pisani TM, 1948. Immunization of monkeys against malaria by means of killed parasites with adjuvants. *Am J Trop Med 28:* 1–22.

F. E. McKenzie, PhD
Fogarty International Center
National Institutes of Health
Bethesda, MD 20892
Telephone: 302-496-2147
Fax: 301-496-8496
E-mail: mckenzel@mail.nih.gov

Dear Sir:

We appreciate the comments of Dr. McKenzie. We are also interested in the other side of the coin; the effect of tuberculosis infection on the course of malaria. In our published series of experiments, there was a suggestion that peak parasitemia occurred slightly earlier in co-infected mice, although the gross pathologic appearance of the co-infected organs showed more hemozoin pigmentation suggesting a higher organ burden of parasites.[1] In addition to the data cited by Dr. McKenzie in non-human primates,[2,3] results of bacille Calmette-Guérin (BCG) vaccination experiments in mice have shown that BCG vaccination 30 days prior to lethal *P. yoelii* intraperitoneal challenge can favorably modulate the course of lethal rodent *Plasmodium* infection to survival.[4,5] We have also seen increased survival in mice aerosol-infected with *M. tuberculosis* 14 days prior to lethal *P. yoelii* challenge (Manabe YC and others, unpublished data). Modulating the timing of co-infection and understanding its impact on the pathogenesis of both diseases may provide important insights into human infection given the high prevalence of tuberculosis in areas where malaria incidence is also high.

REFERENCES

1. Scott CP, Kumar N, Bishai WR, Manabe YC, 2004. Short report: modification of *Mycobacterium tuberculosis* infection by *Plasmodium* in the murine model. *Am J Trop Med Hyg 70:* 144–148.
2. Bazaz-Malik G, 1973. Increased resistance to malaria after *Mycobacterium tuberculosis* infection. *Indian J Med Res 61:* 1014–1024.
3. Singh JA, Ray P, Nair CP, 1956. Relationship of tuberculosis on the course and intensity of plasmodial infections in *M. mulatta. Indian J Malariol 10:* 3–10.
4. Matsumoto S, Yukitake H, Kanbara H, Yamada H, Kitamura A, Yamada T, 2000. *Mycobacterium bovis* bacillus Calmette-Guerin induces protective immunity against infection by *Plasmodium yoelii* at blood-stage depending on shifting immunity toward Th1 type and inducing protective IgG2a after the parasite infection. *Vaccine 19:* 779–787.
5. Matsumoto SH, Yukitake H, Kanbara H, Yamada T, 1999. Long-lasting protective immunity against rodent malaria parasite infection at the blood stage by recombinant BCG secreting merozoite surface protein-1. *Vaccine 18:* 832–834.

Yukari C. Manabe, MD
Center for Tuberculosis Research
Johns Hopkins School of Medicine
Baltimore, MD 21231-1002
Telephone: 410-614-6600
Fax: 410-614-8173
E-mail: ymanabe@jhmi.edu

Cherise P. Scott, MPH
Nirbhay Kumar, PhD
Department of Molecular Immunology and Microbiology
Johns Hopkins Bloomberg School of Public Health
Baltimore, MD 21205
Telephone: 410-955-7177
E-mails: chscott@jhsph.edu and nkumar@jhsph.edu