nationally agreed upon. This case illustrates another potential pitfall in melioidosis serodiagnosis. Most isolates express a conserved LPS antigen, which allows use of a single reference strain for determination of anti-LPS antibodies (8). However, because some strains express different LPS antigens, serologic tests must be performed with the patient's own strain.

This case illustrates potential pitfalls in diagnosing melioidosis, which requires clinical and laboratory awareness and knowledge of its geographic distribution. LPS-based serologic assays should use a range of isolates representative of known LPS types.

Andrew J. Brent,* Philippa C. Matthews,* David A. Dance,† Tyrone L. Pitt,‡ and Rupert Handy§

*John Radcliffe Hospital, Headley Way, Headington, Oxford, United Kingdom; †Health Protection Agency (South West), Plymouth, Devon, United Kingdom; ‡Laboratory of HealthCare Associated Infection, London, United Kingdom; and §Heatherwood and Wexham Park Hospitals, Wexham, Slough, United Kingdom

References

1. Dance DA, Smith MD, Aucken HM, Pitt TL. Imported melioidosis in England and Wales. Lancet. 1999;353:208.
2. John TJ, Jesudason MV, Lalitha MK, Ganesh A, Mohandas V, Cherian T, et al. Melioidosis in India: the tip of the iceberg? Indian J Med Res. 1996;103:62–5.
3. John TJ. Melioidosis, the mimicker of maladies. Indian J Med Res. 2004;119:vi–viii.
4. Currie BJ, Jacups SP. Intensity of rainfall and severity of melioidosis, Australia. Emerg Infect Dis. 2003;9:1538–42.
5. Jesudason MV, Anbarasu A, John TJ. Septicaemic melioidosis in a tertiary care hospital in south India. Indian J Med Res. 2003;117:119–21.
6. Dance DAB. Melioidosis: the tip of the iceberg? Clin Microbiol Rev. 1991;4:52–60.
7. Novak RT, Glass MB, Gee JE, Gal D, Mayo MJ, Currie BJ, et al. Development and evaluation of a real-time PCR assay targeting the type III secretion system of *Burkholderia pseudomallei*. J Clin Microbiol. 2006;44:85–90.
8. Pitt TL, Aucken H, Dance DA. Homogeneity of lipopolysaccharide antigens in *Pseudomonas pseudomallei*. J Infect. 1992;25:139–46.

Address for correspondence: Andrew J. Brent, Nuffield Department of Infectious Diseases & Microbiology, John Radcliffe Hospital, Headington, Oxford, United Kingdom OX3 9DU; email: dr.a.brent@ gmail.com

Subclinical *Plasmodium falciparum* Infection and HIV-1 Viral Load

To the Editor: Studies indicate that *Plasmodium falciparum* infection increases HIV replication in adults (1,2). Although malaria-related illness and death are more common in children, and HIV-1 generally progresses faster in children than in adults (3,4), to our knowledge the effect of intermittent malaria on HIV-1 viral load has not been directly explored in children. To investigate this issue, we monitored HIV-positive infants from a 1996–2001 birth cohort study in Kisumu, Kenya, a *P. falciparum*–holoendemic area.

Study design and methods have been described elsewhere (5,6). Twenty-four children that were perinatally infected with HIV were included in this substudy. During monthly visits during the child's first 2 years of life, malaria and HIV incidence were recorded (5,6). Both children with malaria-positive blood smears and those with fever but no smear result available were treated with sulfadoxine-pyrimethamine according to national guidelines. At the time of this substudy, none of the study participants were taking antiretroviral drugs.

HIV and malaria diagnoses were determined by using standard methods (5–7). To reduce the chance of including infants infected through breast-feeding, perinatal infection was defined as ≥ 2 consecutive HIV-positive tests, with the first positive PCR result by 4 months of age (7). The so-called baseline viral load was the premalaria value measured 1 month before the first observation in the analysis. To be included in the analysis, follow-up visits had to have data available on the current and previous months' viral load and malaria status and occur at roughly monthly intervals at ≥ 4 months of age.

Malaria parasites were found at 53 of 146 visits in the month before viral load measurement, although at 89% of visits in which children were malaria-positive, the children's samples had <1,000 parasites/µL, and in only 13% of visits in which children had parasitemia did they also have fever (8). Median number of observations per child was 7 (range 2–18). No significant demographic or clinical differences were found between HIV-positive children in this substudy and those enrolled in the full cohort (data not shown).

Clinical and demographic variables were evaluated in univariate repeated measures analysis to determine associations with log-transformed HIV-1 viral load. Age and

baseline viral load were strong predictors of current load (Table). Although not statistically significant, clearing the previous month's malaria infection was associated with a drop in viral load (Table, p = 0.09). It was not possible to distinguish between the effects of treatment versus malaria clearance because 87% of malaria infections were treated with antimalarial drugs. However, viral load increased in those incorrectly treated for malaria presumptively (Table).

After adjusting for age and baseline viral load, we assessed $\log_{10}$ HIV viral load in relation to malaria clearance, persistence, absence, or new infection using a repeated measures model with autoregressive covariance structure. No differences were statistically significant, although clearing an infection versus no malaria had a 0.22 log viral load decrease (Table, p = 0.10). When 15 malaria episodes with malaria-free visits 1 month before and after the episode were compared, mean difference (signed-rank test) in viral load "before" and "after" malaria was not significant.

Our findings suggest that low-density malaria infection may not dramatically affect plasma HIV-1 levels in infants. This finding is similar to results of studies of perinatally HIV-infected children in which, although viral loads were unavailable, number of malaria episodes did not significantly affect development of AIDS-related symptoms (9,10). While clinical malaria leads to at least short-term HIV viral load increases in adults (1,2), the effect of subclinical malaria is unclear, and even less is known about coinfection in children. Children usually have higher baseline viral loads than adults; thus, the relative effect of malaria on viral load may not be as great. To reduce the impact of passively transferred maternal antibodies, analyses were done on visits after the child was 4 months old. However, lack of fully acquired antimalarial immunity may have led to

different HIV/malaria interactions than seen in adults.

Viral load increased in infants that were incorrectly treated presumptively (due to fever) for malaria (Table). Most of these children were found to have other infections. Fever in malaria-endemic areas is often assumed to be malaria-related, but delay in treatment of nonmalarial infections may be harmful in HIV-infected children

Our assessment was limited in size and duration. Furthermore, in attempting to provide optimal patient care

through conducting monthly surveillance and encouraging mothers to bring children in during febrile episodes, ability to assess the effect of high-density malaria was diminished because parasitemia levels never reached clinically significant levels. Finally, because malaria was diagnosed by microscopy, rather than PCR, some subclinical malaria infections may have been misclassified as malaria-negative.

Although we found no evidence of an association between subclinical,

Table. Associations with log HIV-1 viral load in infants*

Factor	No.†	Predicted beta (SE)	p value
Baseline viral load			
Log viral load per mL	146	**0.65 (0.09)**	**<0.01**
Documented fever			
Temperature ≥37°C	23	–0.02 (0.11)	0.85
Previous visit documented fever			
Temperature ≥37°C	18	0.07 (0.14)	0.62
Vaccination within 2 weeks of visit			
Yes	15	0.14 (0.14)	0.34
Vaccination within 2 weeks of previous visit			
Yes	18	0.09 (0.12)	0.46
Pneumonia			
Present	22	0.01 (0.13)	0.93
Anemia			
Hemoglobin <8 g/dL	25	–0.25 (0.16)	0.15
Anemia during previous visit			
Hemoglobin <8 g/dL	27	0.01 (0.13)	0.95
Antimalarial drugs received at or since previous visit			
Antimalarial drugs given	59	0.02 (0.10)	0.84
Malaria status current visit			
Parasitemia positive	39	–0.07 (0.10)	0.05
Malaria status previous visit			
Parasitemia positive	53	–0.14 (0.09)	0.14
Malaria status and antimalarial drug use received at or since previous visit			**<0.01**
Treated parasitemia	46	–0.11 (0.09)	0.25
Did not treat parasitemia	7	–0.002 (0.17)	0.99
Treated, no parasitemia	13	**0.28 (0.10)**	**<0.01**
Did not treat, no parasitemia	80	Reference	
Malaria dynamics (previous vs. current visit)			0.36
Cleared infection‡ (+ –)	29	–0.20 (0.11)	0.09
Reinfection/persistence (+ +)	24	–0.16 (0.15)	0.28
New infection (– +)	15	–0.18 (0.14)	0.20
No malaria‡ (– –)	78	Reference	
Age, mo			
4–9	73	**–0.39 (0.13)**	**<0.01**
10–24	73	Reference	

*Statistically significant associations (p<0.05) are indicated in **boldface**.
†Total sample size was 146 follow-up visits. Number of visits with the indicated characteristic are listed. Sample size was 145 for pneumonia and anemia and 144 for anemia during previous visit.
‡After multiple comparisons (Tukey-Kramer) between groups in a model of the effect of malaria on log HIV viral load adjusted for age and baseline viral load, no statistically significant differences were found, although clearing an infection versus no malaria had a p value of 0.10.

low-density malaria and infant HIV-1 viral load, the consequences of high-density or clinical malaria need to be explored. If clinical malaria in infants increases HIV-1 viral load as it does in adults (*1,2*), our study underscores dual benefits of malaria treatment in the context of HIV: 1) keeping malaria in check, and 2) preventing an increase in HIV viral load. Ethical issues prevent prospective studies to assess the impact of coinfection early in life, but alternatives include using animal models or stored specimens.

Acknowledgments

Kimberly C. Brouwer,*
Lisa B. Mirel,* Chunfu Yang,*
Renu B. Lal,*
Margarette S. Kolczak,*
Anne M. Van Eijk,† John Ayisi,†
Juliana A. Otieno,‡
Bernard L. Nahlen,*§
Richard Steketee,* Ya Ping Shi,*†
and Altaf A. Lal*

*Centers for Disease Control and Prevention, Atlanta, Georgia, USA; †Kenya Medical Research Institute, Kisumu, Kenya; ‡New Nyanza Provincial General Hospital, Kisumu, Kenya; and §World Health Organization, Geneva, Switzerland

References

1. Hoffman IF, Jere CS, Taylor TE, Munthali P, Dyer JR, Wirima JJ, et al. The effect of *Plasmodium falciparum* malaria on HIV-1 RNA blood plasma concentration. AIDS. 1999;13:487–94.
2. Kublin JG, Patnaik P, Jere CS, Miller WC, Hoffman IF, Chimbiya N, et al. Effect of *Plasmodium falciparum* malaria on concentration of HIV-1-RNA in the blood of adults in rural Malawi: a prospective cohort study. Lancet. 2005;365:233–40.
3. Rogers MF, Thomas PA, Starcher ET, Noa MC, Bush TJ, Jaffe HW. Acquired immunodeficiency syndrome in children: report of the Centers for Disease Control National Surveillance, 1982 to 1985. Pediatrics. 1987;79:1008–14.
4. Pizzo PA, Wilfert CM. Markers and determinants of disease progression in children with HIV infection. The Pediatric AIDS Siena Workshop II. J Acquir Immune Defic Syndr Hum Retrovirol. 1995;8:30–44.
5. Ayisi JG, van Eijk AM, ter Kuile FO, Kolczak MS, Otieno JA, Misore AO, et al. Risk factors for HIV infection among asymptomatic pregnant women attending an antenatal clinic in western Kenya. Int J STD AIDS. 2000;11:393–401.
6. Ayisi JG, van Eijk AM, Newman RD, ter Kuile FO, Shi YP, Yang C, et al. Maternal malaria infection and perinatal HIV transmission, western Kenya. Emerg Infect Dis. 2004;10:643–52.
7. Yang C, Li M, Newman RD, Shi YP, Ayisi J, van Eijk AM, et al. Genetic diversity of HIV-1 in western Kenya: subtype-specific differences in mother-to-child transmission. AIDS. 2003;17:1667–74.
8. Bloland PB, Boriga DA, Ruebush TK, McCormick JB, Roberts JM, Oloo AJ, et al. Longitudinal cohort study of the epidemiology of malaria infections in an area of intense malaria transmission II. Descriptive epidemiology of malaria infection and disease among children. Am J Trop Med Hyg. 1999;60:641–8.
9. Greenberg AE, Nsa W, Ryder RW, Medi M, Nzeza M, Kitadi N, et al. *Plasmodium falciparum* malaria and perinatally acquired human immunodeficiency virus type 1 infection in Kinshasa, Zaire. A prospective, longitudinal cohort study of 587 children. N Engl J Med. 1991;325:105–9.
10. Kalyesubula I, Musoke-Mudido P, Marum L, Bagenda D, Aceng E, Ndugwa C, et al. Effects of malaria infection in human immunodeficiency virus type 1-infected Ugandan children. Pediatr Infect Dis J. 1997;16:876–81.

Address for correspondence: Kimberly C. Brouwer, Division of International Health and Cross-Cultural Medicine, Department of Family and Preventive Medicine, School of Medicine, University of California, San Diego, 9500 Gilman Dr, MC 0622, La Jolla, CA 93093-0622, USA; email: kbrouwer@ucsd.edu

African Tickbite Fever in Travelers, Swaziland

To the Editor: African tickbite fever (ATBF), which is caused by *Rickettsia africae*, is well documented in travelers to southern Africa (*1–3*) and transmitted by ungulate ticks of the genus *Amblyomma*. Positive serologic results were reported in 9% of patients (*1*) and 11% of travelers (*4*) from southern Africa. We report an outbreak of ATBF with an attack rate of 100% among 12 Dutch travelers to Swaziland.

The 12 travelers (9 male and 3 female) visited Mkhaya Game Reserve in Swaziland in May 2003 for several days. Upon retuning to the Netherlands, they consulted our clinic for assessment for fever, malaise, and skin eruptions. Epidemiologic and clinical data were obtained after the patients provided informed consent. All symptomatic patients were treated before serum samples were collected.

Acute-phase and convalescence-phase serum samples were obtained from 8 patients at 3 and 9 weeks, respectively, after symptoms were reported. Only convalescent-phase serum samples were obtained from the other 4 patients. Serologic assays were conducted for screening and confirmation in Rotterdam, the Netherlands (Department of Virology, Erasmus University Hospital) and Marseille, France (Unité des Rickettsies, Faculté de Médecine, Université de la Mediterranée), respectively.

In Rotterdam, immunofluorescence assays for immunoglobulin G (IgG) and IgM against *R. conorii*, *R. typhi*, and *R. rickettsii* were performed with multiwell slides on which antigens were fixed (Panbio Inc., Columbia, MD, USA). Serum samples with fluorescent rickettsiae at dilutions ≥1:32 were considered positive.