to our hospital with congestive heart failure. She had a 7.0 French dual-lumen Hickman catheter through which she had been receiving regular blood transfusions and iron chelation treatment with deferoxamine. The heart failure was controlled with diuretics and digoxin. Three days after admission, she complained of fever and chills and was treated empirically with vancomycin and ceftazidime. No obvious focus of infection was identified, and blood counts showed only neutrophilia (14.0×10^9 cells/L). *Nocardia asteroides* was isolated from blood samples drawn simultaneously from both lumens of the catheter and a peripheral vein. Because of lack of response, treatment was changed to meropenem (100 mg/kg/day iv for 3 weeks). The signs and symptoms of infection subsided promptly and results of subsequent blood cultures were negative. The catheter was retained.

Nocardia bacteremia complicating the use of a central venous device is a rare clinical event. Whether the indwelling catheter should be removed immediately deserves further discussion. In the case we described in our previous report [2], which was cited by Kontoyiannis et al. [1], we managed to clear the infection while the Hickman catheter was left in situ. In their table 1, Kontoyiannis et al. [1] incorrectly reported that the catheter was removed; in fact, the catheter was only removed 6 months later, when the patient no longer required it. However, our successful experience of retaining the central venous catheter in catheter-associated nocardiosis may be different from others' experiences. Both our patients were suffering from thalassemia and were not receiving chemotherapy at the time of infection. The patients described by Kontonyiannis et al. [1] and Miron et al. [3] had malignant diseases and were receiving cytotoxics and radiotherapy (table 1). Hence, we agree with Kontoyiannis et al. that patients with catheter-associated nocardiosis should be carefully evaluated. Removal of the catheter is not absolutely indicated but should be seriously considered when the patient is receiving immunosuppressive therapy.

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Subacute Malaria Due to *Plasmodium falciparum* and the Role of Polymerase Chain Reaction

Sir—We read with interest the article by Klement et al. [1] and would like to comment on some issues raised in their paper. We disagree with the conclusion that, for the 4 patients the authors observed, "the diagnosis of malaria could easily have been missed because the clinical signs were uncommon" ([1], p. e1). It is, in fact, well-known that for all subjects who have recently returned from areas of endemicity, regardless of whether they received prophylaxis, clinicians should always suspect malaria and perform the appropriate diagnostic tests until this diagnosis is either confirmed or definitively ruled out. An insidious presentation and "atypical" symptoms, such as intermittent low-grade fever, lumbosacral muscle pain, fatigue, malaise, and nonspecific gastrointestinal discomfort, as well as afebrile cases, have been described elsewhere in patients with malaria who had received chemoprophylaxis [2–4].

Furthermore, in 2 of the 4 patients described by Klement et al. [1], intermittent or low-grade fever was associated with thrombocytopenia and elevated liver enzyme levels, which is highly suggestive of malaria. In fact, thrombocytopenia, although it is not pathognomonic, is a quite frequent and early feature of malaria that is found in at least 50%–70% of patients [5]. In a case-control study performed to identify signs and symptoms that predict malaria infection in febrile patients who had recently traveled to a area where malaria is endemic, Svenson et al. [6] found that a low platelet count had the strongest association with the disease.

Moreover, the statement that "chloroquine-proguanil prophylaxis is not always effective in countries with a low rate of chloroquine resistance" ([1], p. e1) is not new, since a lower efficacy (70%) of this combination compared with mefloquine was reported among travelers to East Africa in 1993 [7]. We do not know whether Senegal should be considered an area with a low rate of chloroquine resistance; however, according to the advice issued by both the World Health Organization and the Centers for Disease Control and Prevention, the drug of choice for malaria prophylaxis in nonimmune travelers to this country is mefloquine [8–9].

Finally, we agree with Klement et al. [1] that PCR may be the best tool to reveal subpatent parasitemia in cases similar to those they described. With respect to this point, from June 1996 through August 1999 we conducted a prospective study to evaluate the use of PCR for the diagnosis of malaria in patients who presented to the emergency department of L. Sacco Hospital in Milan, Italy, after returning from areas where malaria is endemic and experiencing symptoms suggestive of the disease. We used a nested PCR protocol targeted to a fragment of the small subunit ribosomal RNA gene of *Plasmodium* species that infect humans, as described by Snounou et al. [10]. Blood film results (both thin and thick smears) indicated that 47 (40.8%) of 115 patients were infected with malaria parasites. Among the

Table 1. Utility of PCR for the diagnosis of malaria in 4 paradigmatic cases in Italian patients.

Patient	Age in years, sex	Countries visited (length of stay)	Prophylaxis	Symptoms	Malaria test results	
					Microscopy	PCR
1	57, M	Kenya (1 week)	Chloroquine, proguanil[a]	Low fever 7 days after return (treated with acitaminophen); high fever (39°C) and chills on day 30	Negative from day 7 to day 10; positive for *Plasmodium falciparum* on day 30 (0.5% parasitemia)	Positive for *P. falciparum* on day 9 (untreated)
2	26, M	Tanzania and Kenya (3 days)	None	Fever (38°C), headache, asthenia, and mild thrombocytopenia 30 days after return	Negative at onset and then for 3 days;[b] positive for *Plasmodium malariae* on day 9	Positive for *P. malariae* on day 6
3	50, F	Central Africa (8 months)	None	High fever (39°C) and chills 7 days after return; self-treatment with sulfadoxine/pyrimethamine	Negative on day 1 after self-treatment[c]	Positive for *P. falciparum* on day 1 after self-treatment
4	34, M	Cape Verde, Gambia, and Senegal (30 days)	Mefloquine	Low fever, headache, and mild thrombocytopenia 8 months after return	Negative for 2 days after onset; positive for *Plasmodium vivax* on day 3	Positive for *Plasmodium ovale* on day 2

[a] Prophylaxis stopped on return to Italy.
[b] Results of a MalaQuick test (ICT-malaria P.f.; Standby Diagnostics) were negative.
[c] Results of a MalaQuick test (ICT-malaria P.f.; Standby Diagnostics) were positive.

47 patients with acute malaria, parasite morphology showed that 29 (61.7%) were infected with *Plasmodium falciparum*, 11 (23.4%) with *Plasmodium vivax*, 4 (8.5%) with *Plasmodium ovale*, 2 (4.2%) with *Plasmodium malariae*, and 1 with both *P. falciparum* and *P. malariae*. PCR analysis confirmed the diagnosis of malaria in all cases that were initially diagnosed by microscopy. A discordant diagnosis at the species level between microscopy and PCR was registered in 2 cases in which *P. ovale* was initially misdiagnosed by microscopy as *P. vivax*.

The use of PCR was particularly useful for the 4 cases presented in Table 1. These cases highlight the clinical situations in which molecular amplification may aid in the diagnosis of malaria: subpatent parasitemia associated with chemoprophylaxis (patient 1); malaria infection with *Plasmodia* characterized by low levels of parasitemia, such as *P. malariae* infection (patient 2); diagnosis of malaria that is confirmed during the convalescent period (patient 3); and diagnosis of mixed infections unrecognized at onset with reappearance of symptoms due to hypnozoite (patient 4). However, because PCR has a high cost and a high turnaround time compared with microscopy performed by well-trained personnel, the use of PCR for the routine diagnosis of malaria in Western countries is not advisable and should be limited to selected cases.

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