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# Use of Rapid Diagnostic Tests for Diagnosis of Malaria in the United States

**April Bobenchik, Robyn Shimizu-Cohen, Romney M. Humphries**

Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California, USA

In the September issue of this journal, performance of BinaxNOW for the diagnosis of malaria in a major U.S. academic medical center was reported (1). Herein, we report performance of this test in a second large academic medical center in the United States. BinaxNOW was introduced at our institution as a component of routine blood parasite examination along with thick- and thin-blood-smear microscopy in January 2011. From 2007 to 2011, BinaxNOW was also selectively performed on specimens that were positive for malaria by microscopy as part of laboratory verification studies. In total, 251 parasite blood exams from 244 patients were performed. Of these, 239 (95.2%) were negative by microscopy. The remaining 12 positive specimens included 4 *Plasmodium falciparum* isolates, 5 *Plasmodium vivax* isolates, and 3 *Plasmodium malariae* isolates, with corresponding parasitemias of <0.01% to 0.5%. BinaxNOW resulted in 9 positive results. Three false-negative BinaxNOW results were obtained, all in patients with *P. malariae* infection and parasitemia of <0.1%. One false-positive BinaxNOW result was obtained in a 17-month-old child with 2 weeks of recurrent fevers and travel history to a region where malaria is endemic 1 year prior to symptoms. The clinical index of suspicion for malaria in this case was low. All discrepant results were confirmed by repeat testing using BinaxNOW and reevaluation of blood smears. The overall sensitivity, specificity, positive predictive value, and negative predictive value for BinaxNOW were found to be 72.7%, 96.8%, 88.8%, and 98.8%, respectively (Table 1). When patients with *P. malariae* infection or <0.1% parasitemia, neither of which are covered by BinaxNOW FDA performance claims, were removed from analysis, sensitivity improved to 100%.

**TABLE 1** Performance of BinaxNOW for 251 blood specimens evaluated for malaria at a large academic hospital laboratory between 2007 and 2012[a]

| Performance measure | Overall performance (%) (95% CI) | Performance for FDA-approved claims only (%) (95% CI)[b] |
|---|---|---|
| Sensitivity | 72.7 (39.3–92.7) | 100 (59.8–100.0) |
| Specificity | 99.6 (97.3–99.9) | 99.6 (97.3–99.9) |
| Positive predictive value | 88.9 (50.7–99.4) | 88.9 (50.7–99.4) |
| Negative predictive value | 96.4 (93.1–98.2) | 100 (98.0–100.0) |

[a] CI, confidence interval.
[b] *P. falciparum* and *P. vivax* with >0.1% parasitemia.

Based on the results of our study, our laboratory uses BinaxNOW as an adjunct to thin- and thick-smear microscopy, primarily to aid with species identification when only early trophozoites are observed by microscopy and to provide a rapid preliminary positive result identifying *P. falciparum* from non-*falciparum Plasmodium* species. A rapid identification of *P. falciparum* is critical in cases of severe malaria, which necessitate prompt treatment. In particular, intravenous artesunate has recently been made available by the Centers for Disease Control and Prevention for this indication under an investigational new drug protocol (http://www.cdc.gov/malaria/diagnosis_treatment/artesunate.html).

Performance data for BinaxNOW indicate that this test cannot replace microscopy, as we and others have observed both false-negative and false-positive results (2–5). Clinical ramifications of reporting false-negative results are of most pressing concern, in particular because many patients seen in the United States with *P. falciparum* malaria will have low-level parasitemia that is below the limit of detection of BinaxNOW. False-negative results may also be obtained at high-level parasitemia due to the prozone phenomenon or possibly a mutation in histidine-rich protein 2 (HRP-2) antigen detected by the test (1, 5).

It is unquestionable that maintaining expertise in malaria diagnostics at the hospital level in the United States is challenging due to regulatory and budget considerations and the fact that laboratories may encounter only 0 to 2 cases of malaria per year. As such, the promise of a rapid, low-complexity test that can replace labor-intensive microscopy techniques is highly attractive. However, current technologies have not yet achieved a sensitivity and specificity to allow the laboratory to discontinue microscopy. Only 17% of laboratories in the United States use rapid diagnostic tests such as BinaxNOW (2), the majority in conjunction with microscopy. We urge laboratories that are considering implementation of this test to ensure that capacity for microscopy diagnostics is maintained. Nevertheless, the implementation of the rapid diagnostic test can be very useful in providing physicians with quick preliminary results, allowing for appropriate clinical management of the patient.

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Address correspondence to Romney M. Humphries, rhumphries@mednet.ucla.edu.



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