Rapid HIV-1 Testing During Labor
A Multicenter Study

Marc Bulterys, MD, PhD
Denise J. Jamieson, MD, MPH
Mary Jo O’Sullivan, MD
Mardge H. Cohen, MD
Robert Maupin, MD
Steven Nesheim, MD
Mayris P. Webber, DrPH
Russell Van Dyke, MD
Jeffrey Wiener
Bernard M. Branson, MD
for the Mother-Infant Rapid Intervention At Delivery (MIRIAD) Study Group

THE CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC) ESTIMATES THAT BETWEEN 280 AND 370 INFANTS ARE BORN INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) ANNUALLY IN THE UNITED STATES DESPITE RECOMMENDATIONS FOR UNIVERSAL PRENATAL HIV SCREENING AND WIDE USE OF ANTIRETROVIRAL DRUGS IN PREGNANT HIV-INFECTED WOMEN.1-14 PERINATALLY ACQUIRED HIV INFECTIONS MAY RESULT FROM MISSED OPPORTUNITIES FOR PREVENTION, SUCH AS INADEQUATE PREGNATAL CARE.6,7 IDEALLY, ALL PREGNANT WOMEN SHOULD RECEIVE EARLY PRENATAL CARE WITH VOLUNTARY HIV TESTING. HOWEVER, FOR THOSE WHO DO NOT, RAPID TESTING DURING LABOR COULD PROVIDE HIV-INFECTED WOMEN WITH IMMEDIATE ACCESS TO ANTIRETROVIRAL PROPHYLAXIS.15,16

We sought to determine the feasibility of rapid HIV testing during labor, assess barriers to HIV testing, and facilitate comprehensive care for HIV-infected mothers and their infants. A US Food and Drug Administration treatment investigational device exemption permitted the use of a rapid test before its approval in November 2002.8,9 This test yields HIV results in 20 minutes, making it ideally suited for point-of-care use. This report describes the experience of performing rapid HIV testing during labor and the factors associated with acceptance of rapid testing.

METHODS

The CDC funded 16 hospitals in 6 US cities (Atlanta, Ga; Baton Rouge, La; Chicago, Ill; Miami, Fla; New Orleans, La; and New York, NY) to participate in the MIRIAD (Mother-Infant Rapid Intervention At Delivery) study, which offered HIV counseling, voluntary rapid testing, and, if indicated, antiretroviral prophylaxis to women with undocumented HIV status late in pregnancy. Counseling, voluntary rapid testing, and antiretroviral prophylaxis (as well as study enrollment) were offered by la-

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Rapid HIV Testing During Labor

Blood was collected for both rapid testing and enzyme immunoassay (EIA) and, when indicated, Western blot confirmation testing. Laboratory technicians and labor and delivery staff performed rapid test proficiency panels for quality assurance. The EIA, and if needed, Western blot testing, was performed immediately following rapid HIV testing in the MIRIAD protocol. Nine institutions used the Abbott HIV-1/HIV-2 EIA (Abbott Laboratories, Abbott Park, Ill) and the Genetic Systems HIV-1 Western blot (Bioread Laboratories, Hercules, Calif); 7 institutions used the Genetic Systems HIV-1/HIV-2 Peptide EIA (BioRad Laboratories) and 4 of these used the Genetic Systems HIV-1 Western blot (BioRad Laboratories) and 3 used the Cambridge Biotech HIV-1 Western blot (Calypte Biomedical, Rockville, Md). In all institutions, initially reactive EIAs and rapid tests were repeated in duplicate; specimens with repeatedly reactive EIA or rapid tests were tested using Western blot. Women identified as HIV-positive by the OraQuick Rapid HIV-1 Antibody Test (OraSure Technologies Inc, Bethlehem, Pa) or EIA, and those with discordant rapid test and EIA/Western blot results were followed up together with their infant for at least 6 months. The infants were tested using HIV DNA polymerase chain reaction (PCR) at less than 48 hours, 2 weeks, 6 weeks, and 3 months, and if having an indeterminate status, at 6 months.

To determine factors associated with acceptance of HIV testing, odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using unconditional logistic regression, adjusting for study site and other covariates. Reported ORs should not be misinterpreted as relative risks. Sensitivity, specificity, and positive and negative predictive values were determined using the EIA/Western blot algorithm as the gold standard. For each of these measures, CIs were estimated using exact binomial methods. Median turnaround times were compared using the Wilcoxon rank-sum test. We used SAS statistical software version 8 (SAS Institute Inc, Cary, NC) and S-Plus version 6.1 (Seattle, Wash). All P values reported are 2-sided and P ≤ .05 was considered statistically significant.

RESULTS

Between November 16, 2001, and November 15, 2003, there were 91707 visits to the labor and delivery units of the 16 participating hospitals and 7381 women (8% of all visits recorded) were eligible for rapid HIV testing. Of these, 1637 women (22%) were not approached for rapid HIV testing for reasons that included no staff member being available or verification for HIV testing during pregnancy still pending. Every attempt was made to have continuous labor and delivery coverage but some hospitals were less successful (implementation issues are being addressed in separate analyses). The remaining 5744 women were offered rapid HIV testing.

Data on frequency of visiting the units were not collected and some women may have visited the units more than once. Written informed consent for both rapid testing and study participation was obtained from 4849 (84%) women.

Thirty-four women tested HIV-1 positive with both rapid test and EIA, and all were confirmed by Western blot (prevalence = 7/1000). There were 4 false-positive and no false-negative rapid test results. All 4 patients presented in active labor and were given antiretroviral prophylaxis, which was stopped when clinicians were notified that the rapid test result was false-negative. Sensitivity of the rapid test was 100% (95% CI, 90%-100%) and specificity was 99.9% (95% CI, 99.78%-99.98%). Negative predictive value was 100%; positive predictive value was 99% (95% CI, 97%-97%). The EIA had 11 false-positive results: 5 in women with an indeterminate Western blot result (usually a single p24 band) and 6 others with negative Western blot results. All 11 women had negative rapid test results. No false-negative EIA results were identified. The specificity of EIA was estimated to be 99.8% (95% CI, 99.6%-99.9%); positive predictive value was 76% (95% CI, 61%-87%).

In analyses adjusted for study site, acceptance of HIV testing during labor was associated with younger age, Hispanic ethnicity, gestation of less than 32 weeks, time of admission, and no prenatal care (Table 1). In multivariate analysis, black as well as Hispanic women were more likely than white women to accept testing. Younger age, gestation less than 32 weeks, and no prenatal care also remained significant (Table 1). Hospital admission between 4 PM and midnight was associated with lower HIV test acceptance (adjusted odds ratio [AOR], 0.7; 95% CI, 0.5-0.9); acceptance was lowest on Friday nights (P = .001).

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infected infants had a vaginal delivery. The infant who was DNA-PCR negative at birth but positive by 6 weeks was delivered vaginally. Of the 32 infants, 27 were followed up for 6 months. Many of the women have started highly active antiretroviral therapy for their own health (follow-up of women testing positive is continuing and being addressed in separate analyses). Of the 34 HIV-infected women identified, 30 were black, of whom 21 (70%) were born in the United States and 9 (30%) were immigrants from Africa and the Caribbean. Regarding test performance with non-clade B HIV-1, there was 100% sensitivity in use of the rapid test with whole blood and no indication in the MIRIAD study that specificity was decreased in African women.

**COMMENT**

We found that rapid HIV testing yielded accurate and timely results to women in labor and that implementing rapid testing was acceptable and feasible. Overall test acceptance was nearly 85%. Lower
acceptance during evening shifts may be explained in part by fewer available personnel. Informed consent was obtained not only for rapid HIV testing but also for participation in a research study.

Based on the feasibility of rapid testing demonstrated in MIRIAD, the CDC now recommends routine rapid HIV testing using an opt-out approach (ie, a woman is informed that HIV testing will be routinely done during labor if her HIV status is unknown but she may decline testing). Each woman should be informed that a preliminary positive rapid test result means that she is likely HIV infected but that this result will need to be confirmed. If her rapid test result is positive, she should be notified that antiretroviral drugs will be offered to her and to her newborn. If her rapid test result is negative, she should be notified that she is almost certainly not HIV infected. One practical approach to implementing routine rapid testing would be for each hospital to put in place standing orders to immediately inform any woman in labor whose HIV status is unknown that she will be tested unless she declines.

The rationale for focusing on women in labor is that there is a brief window of opportunity for interventions to decrease HIV transmission to the newborn. This rationale is related to the pharmacokinetics of the antiretroviral drugs used for prophylaxis. In decision analysis modeling, rapid HIV testing during labor is cost-saving to the medical system. Our study demonstrates that, in general, results are timely and that antiretroviral prophylaxis can be provided promptly to HIV-infected women and their infants. In addition, we have previously shown that point-of-care rapid testing has the potential to save valuable time compared with sending specimens to the laboratory.

Appropriate training of staff and quality assurance processes are essential to ensure accurate rapid HIV test results. Despite high test performance, there were still instances in which preliminary HIV-1 screening tests (rapid test or EIA) yielded false-positive results. The decision to recommend antiretroviral prophylaxis on the basis of an unconfirmed test result will continue to require clinical judgment and knowledge about HIV prevalence and the performance characteristics of each test. Although EIA has been the mainstay of HIV screening, the rapid test demonstrated a higher positive predictive value in the present study.

Several study caveats should be considered. First, clinical interventions were not standardized but left up to individual practitioners following US Public Health Service guidelines. Second, the total number of encounters recorded included some women who visited the labor and delivery unit more than once. Therefore, the percentage of eligibility reported in this study (8%) is likely an underestimate of the true proportion of women with undocumented HIV status. Third, our findings about acceptance rates and the informed consent process may not directly translate to a nonresearch setting. Fourth, the utility of the program is in part contingent on accurate and accessible documentation of the HIV status to avoid redundancy of effort.

The MIRIAD findings are important both in the United States and internationally. In many settings, including in the developing world, pregnant women with unknown HIV status are often seen by clinicians for the first time during labor. Rapid testing during labor can enable pregnant women with undocumented HIV status to learn their HIV infection status so they can

### Table 2. Multivariate Analysis of Factors Associated With Receipt of Rapid HIV Test Results After Instead of Before Delivery in 4073 Women in Active Labor*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariate No./ Total (%)</th>
<th>Adjusted Odds Ratio (95% CI)†</th>
<th>( \chi^2 ) P Value for Test of Overall Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time between arrival and delivery, h (hours)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>723/856 (84.5)</td>
<td>34.5 (24.9-47.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3-5</td>
<td>349/696 (50.1)</td>
<td>5.2 (4.0-6.9)</td>
<td></td>
</tr>
<tr>
<td>6-8</td>
<td>179/506 (35.4)</td>
<td>2.2 (1.6-3.0)</td>
<td></td>
</tr>
<tr>
<td>9-12</td>
<td>146/474 (30.8)</td>
<td>2.0 (1.5-2.7)</td>
<td></td>
</tr>
<tr>
<td>&gt;12</td>
<td>206/1124 (18.3)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Time between blood collection and patient notification, min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤90</td>
<td>1021/2624 (39.8)</td>
<td>1.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;90</td>
<td>766/1437 (53.3)</td>
<td>2.2 (1.8-2.6)</td>
<td></td>
</tr>
<tr>
<td>Prenatal care visits, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-5</td>
<td>780/1738 (44.9)</td>
<td>1.0</td>
<td>.002</td>
</tr>
<tr>
<td>&gt;5</td>
<td>623/1217 (51.2)</td>
<td>1.4 (1.1-1.7)</td>
<td></td>
</tr>
<tr>
<td>Time of admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midnight-8 AM</td>
<td>717/1403 (51.1)</td>
<td>1.9 (1.5-2.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>8 AM-4 PM</td>
<td>614/1645 (37.3)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>4 PM-midnight</td>
<td>461/1024 (45.0)</td>
<td>2.3 (1.8-3.0)</td>
<td></td>
</tr>
<tr>
<td>Administration on weekend:‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>622/1263 (49.3)</td>
<td>1.6 (1.3-2.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No</td>
<td>1171/2810 (41.7)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Duration of gestation, wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;32</td>
<td>97/359 (27.0)</td>
<td>1.0</td>
<td>.002</td>
</tr>
<tr>
<td>32-36</td>
<td>254/675 (37.6)</td>
<td>1.2 (0.8-1.9)</td>
<td></td>
</tr>
<tr>
<td>≥36</td>
<td>1336/2809 (47.6)</td>
<td>1.7 (1.2-2.6)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

*Of 4073 women in active labor with information on receipt of rapid test results, 417 had missing data on time between arrival and delivery, 12 had missing data on time between blood collection and rapid test notification, 1118 had missing data on prenatal care, 1 had missing data on time of admission (and weekend), and 230 had missing data on gestational age. Overall, 1510 of 4073 women were excluded from the model due to 1 or more missing explanatory variables.

†Odds ratios were adjusted for all other variables listed as well as for study site and study year; analysis was restricted to women tested during active labor (those tested post partum were excluded). Reported odds ratios should not be misinterpreted as relative risks.

‡Weekend considered from Friday at 5 PM to Monday at 6 AM.
receive antiretroviral prophylaxis and be referred for comprehensive medical care and follow-up.

Author Affiliations: Division of HIV/AIDS Prevention, Surveillance and Epidemiology, National Center for HIV, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA (Dr Bulterys, Jamieson, and Branson and Mr Wiener); Department of Obstetrics and Gynecology, University of Miami School of Medicine, Miami, Fla (Dr O’Sullivan); Department of Medicine, Cook County Hospital, Chicago, Ill (Dr Cohen); Department of Obstetrics and Gynecology, Louisiana State University School of Medicine, New Orleans (Dr Maupin); Department of Pediatrics, Emory University School of Medicine, Atlanta, Ga (Dr Nesheim); Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY (Dr Webber); and Department of Pediatrics, Tulane University School of Medicine, New Orleans, La (Dr Van Dyke).

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Author Contributions: As principal investigator, Dr Bulterys had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Bulterys, Jamieson, O’Sullivan, Cohen, Maupin, Nesheim, Webber, Van Dyke, Bulterys. Acquisition of data: Bulterys, Jamieson, O’Sullivan, Cohen, Maupin, Nesheim, Webber. Analysis and interpretation of data: Bulterys, Jamieson, Cohen, Van Dyke, Wiener, Branson. Drafting of the manuscript: Bulterys, Jamieson, O’Sullivan, Wiener. Critical revision of the manuscript for important intellec- tual content: Bulterys, Jamieson, O’Sullivan, Cohen, Maupin, Nesheim, Webber, Van Dyke, Bulterys. Statistical analysis: Bulterys, Wiener, O’Bryant, Jolly, O’Sullivan, Cohen, Maupin, Nesheim, Webber. Administrative, technical, or material support: Bulterys, Jamieson, O’Sullivan, Cohen, Nesheim, Van Dyke, Branson.

Supervision: Bulterys, O’Sullivan, Maupin, Webber.

Mother-Infant Rapid Intervention After Delivery (MIRIAD) Study Group: Members of MIRIAD Study Group (in alphabetical order): Angela Bradley-Byers, MD, MPH, Philadelphia, PA; Andy C. Bulterys, MD, MPH, Lilian Lin, PhD, Chicago, IL; Ann Cook, RN, PhD, Charlotte, NC; Joanne David, BSN, MPH, West Palm Beach, FL; and others.

REFERENCES


