Predictive value of HIV-1 DNA PCR in perinatally HIV-exposed infants born 1997-2002 in NYC

R Murphy ¹, V Peters ¹, B Gill ¹, K Dominguez ², P Thomas ¹, J Weedon ¹, KL Liu ¹, E Handelsman ³

¹ NYC Department of Health and Mental Hygiene, New York, NY; ² CDC, Atlanta, GA. ³ Kings County Medical Center, Brooklyn, NY

XVth International AIDS Conference
Bangkok, Thailand 2004
Diagnosing HIV infection in infants younger than 18 months of age requires direct virologic tests such as the HIV DNA polymerase chain reaction (PCR).

In the first weeks after birth, HIV DNA PCR has a high positive predictive value (>98%) but a lower negative predictive value.

The negative predictive value of DNA PCR is 81% in the first 7 days of life (J Pediatr 1996;129:198-207) but improves with time and within weeks of birth, a negative test is increasingly likely to indicate an uninfected child (J Inf Dis 1994;170:996-0).
The 1999 CDC guidelines for HIV case surveillance require two negative HIV DNA PCR tests, one at ≥ one month of age and the second at ≥ 4 months of age to definitively exclude HIV infection (MMWR 1999; 48 (RR-13):1-36).

Excluding HIV infection earlier could:
- improve the surveillance classification of HIV-exposed infants
- modify the need for *Pneumocystis* pneumonia prophylaxis in HIV-exposed uninfected children (MMWR 2002; 51 (RR-8):1-46)
- provide earlier reassurance for parents and clinicians.
Objective

We sought to retrospectively examine the predictive value of HIV DNA PCR in the first three months of life among HIV-exposed infants born 1997-2002 with definitively established HIV status (according to the 1999 CDC guidelines for HIV case surveillance).
Hypotheses

(1) False negative tests after 2-3 months will be uncommon and the 4 month threshold to exclude HIV infection may be an unnecessarily stringent.

(2) False positive tests will be sufficiently common to warrant repeating any positive test.
Retrospective abstraction of infant medical records at 22 NYC sites that participate in CDC’s Pediatric HIV/AIDS Surveillance and Pediatric Spectrum of HIV Disease Projects.

Positive and negative predictive values were calculated at three times: 0-42, 43-120 and >120 days.
Methods

- When only month and year of a test known, last day of month assigned.

- Inclusion criteria:
  - For uninfected infants, a test was required in each of the three time periods.
  - For infected infants, only the first positive test was used in analysis, further positives were excluded.
  - Only one unique result per time period included.
HIV-Exposed Births, 22 NYC Sites, 1997-2002
N=3,202

- **Presumptively Infected**
  - N=4 (<1%)

- **Definitively Infected**
  - N=247 (8%)

- **Presumptively Uninfected**
  - N=464 (14%)

- **Definitively Uninfected**
  - N=1,966 (61%)

- **Indeterminate HIV Status**
  - N=521 (16%)

1st DNA PCR
- 0-42 Days
  - N=113 (46%)

- 43-120 Days
  - N=58 (23%)

- >120 Days
  - N=15 (6%)

Infant Had No DNA PCR/other
- N=648 (33%)

Infant Had No DNA PCR
- N=61 (25%)

1st DNA PCR
- 0-42 Days
  - N=832 (42%)

- 43-120 Days
  - N=407 (21%)

- >120 Days
  - N=79 (4%)
**Results-1: Positive Predictive Value of 1st DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002**

*(Infants with First HIV DNA PCR at < 42 Days)*

<table>
<thead>
<tr>
<th>Age at DNA PCR</th>
<th>True Positive</th>
<th>False Positive</th>
<th>Positive Predictive Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-42 days</td>
<td>92</td>
<td>0</td>
<td>100</td>
<td>95.4-97.6</td>
</tr>
<tr>
<td>43-120 days</td>
<td>21</td>
<td>0</td>
<td>100</td>
<td>96.9-99.2</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>0</td>
<td>1</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
### Results-2: Positive Predictive Value of 1<sup>st</sup> DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002

(Infants with First HIV DNA PCR at 43-120 Days)

<table>
<thead>
<tr>
<th>Age at DNA PCR</th>
<th>True Positive</th>
<th>False Positive</th>
<th>Positive Predictive Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>43-120 days</td>
<td>58</td>
<td>1</td>
<td>98.3</td>
<td>95.0-100</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>--</td>
<td>0</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
Results-3: Positive Predictive Value of 1st DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002

- Among infected infants with 1st DNA PCR at 0-42 days:
  - 92 of 113 (81%) of infants had a positive DNA PCR by 42 days and all had a positive test by 120 days.

- Among uninfected infants with 1st DNA PCR at 0-42 days:
  - There was only one false positive test.

- Among infected infants with 1st DNA PCR at 43-120 days:
  - All had a positive test by 120 days.

- Among uninfected infants with 1st DNA PCR at 43-120 days:
  - There was only one false positive test.
**Results-4: Negative Predictive Value of DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002**

*(Infants with First HIV DNA PCR at < 42 Days)*

<table>
<thead>
<tr>
<th>Age at DNA PCR</th>
<th>True Negative</th>
<th>False Negative</th>
<th>Negative Predictive Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-42 days</td>
<td>832</td>
<td>45*</td>
<td>94.9</td>
<td>93.9-95.8</td>
</tr>
<tr>
<td>43-120 days</td>
<td>832</td>
<td>9</td>
<td>99.0</td>
<td>98.0-99.9</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>832</td>
<td>0</td>
<td>100</td>
<td>99.0-100</td>
</tr>
</tbody>
</table>

* 21 (51%) of 45 false negative tests from 0-42 days were in the first 14 days of life.*
### Results-5: Negative Predictive Value of DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002

*(Infants with First HIV DNA PCR at 43-120 Days)*

<table>
<thead>
<tr>
<th>Age at DNA PCR</th>
<th>True Negative</th>
<th>False Negative</th>
<th>Negative Predictive Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>43-120 days</td>
<td>407</td>
<td>2</td>
<td>99.5</td>
<td>99.0-100</td>
</tr>
<tr>
<td>&gt;120 days</td>
<td>407</td>
<td>0</td>
<td>100</td>
<td>99.5-100</td>
</tr>
</tbody>
</table>
Results-6: Negative Predictive Value of DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002

■ Among infected infants with 1st DNA PCR at 0-42 days:
  – 45 of 54 (83%) false negative tests were noted in the first 42 days of life, and none were noted after 74 days.

■ Among infected infants with 1st DNA PCR at 43-120 days:
  – 2 false negative tests were noted between 49-87 days of life, and none were noted after 87 days.
Among HIV-exposed infants, a negative DNA PCR at three months of life would have been adequate to reasonably exclude infection.

Though rare, occasional false positive tests justify the current practice of obtaining two positive tests to diagnose infection.
These results may allow for the classification of HIV-exposed infants as uninfected by 3 months of age.

The guidelines governing *Pneumocystis* pneumonia prophylaxis for HIV-exposed infants until HIV infection is reasonably excluded could also be modified.

While useful as a surveillance and diagnostic tool, this finding does not alter the need to clinically follow infants classified as uninfected.
### Participating Institutions and Pediatricians at NYC Special Study Sites

- Albert Einstein Hospital (Arye Rubinstein)
- Bronx Lebanon Hospital (Saroj Bakshi)
- University Hospital of Brooklyn (Edward Handelsman)
- Harlem Hospital Center (Elaine Abrams)
- Incarnation Children’s Center (Cathy Painter)
- Jacobi Medical Center (Andrew Wiznia)
- Kings County Hospital Center (Ninad Desai)
- Montefiore Hospital (Nathan Litman)
- New York Presbyterian Hospital at New York Weill Cornell Center (Joseph Stavola)
- North Central Bronx Hospital (Jacob Abadi)
- Beth Israel Medical Center (Joanna Dobroszycki)
- Brookdale Hospital (Mahmoud Hassanein)
- Lincoln Hospital (Herman Mendez)
- Long Island College Hospital (John Belko)
- Long Island Jewish Medical Center (Vincent Bonagura)
- Metropolitan Hospital Center (Marukh Bamji)
- Mt. Sinai Medical Center (Roberto Posada)
- New York Presbyterian Hospital at Columbia Presbyterian Center (Marc Foca)
- Queens Hospital Center (Paul Zam)
- St. Luke’s/Roosevelt Hospital (Stephen Arpadi)
- St. Vincent’s Hospital (Mona Rigaud)
- Woodhull Medical and Mental Health Center (Lubin Augustine)

### Project Staff at the NYC DOHMH

- Lisa-Gaye Robinson, M.D.
- Annette Brooks
- Chere Mapson
- Sharon Browne
- Karla McFarlane
- Catrice Abner
- Myrna Beckles
- Janine Brewton
- Patricia Diggs-Herman
- Stephanie Manning
- Carol McFarlane
- Dorothy Perrier
- Samuel Sawyerr
- James Swanzy-Parker
- Rosamond Vaivao