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

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Background – 1

- 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).*

Background – 2

- 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.

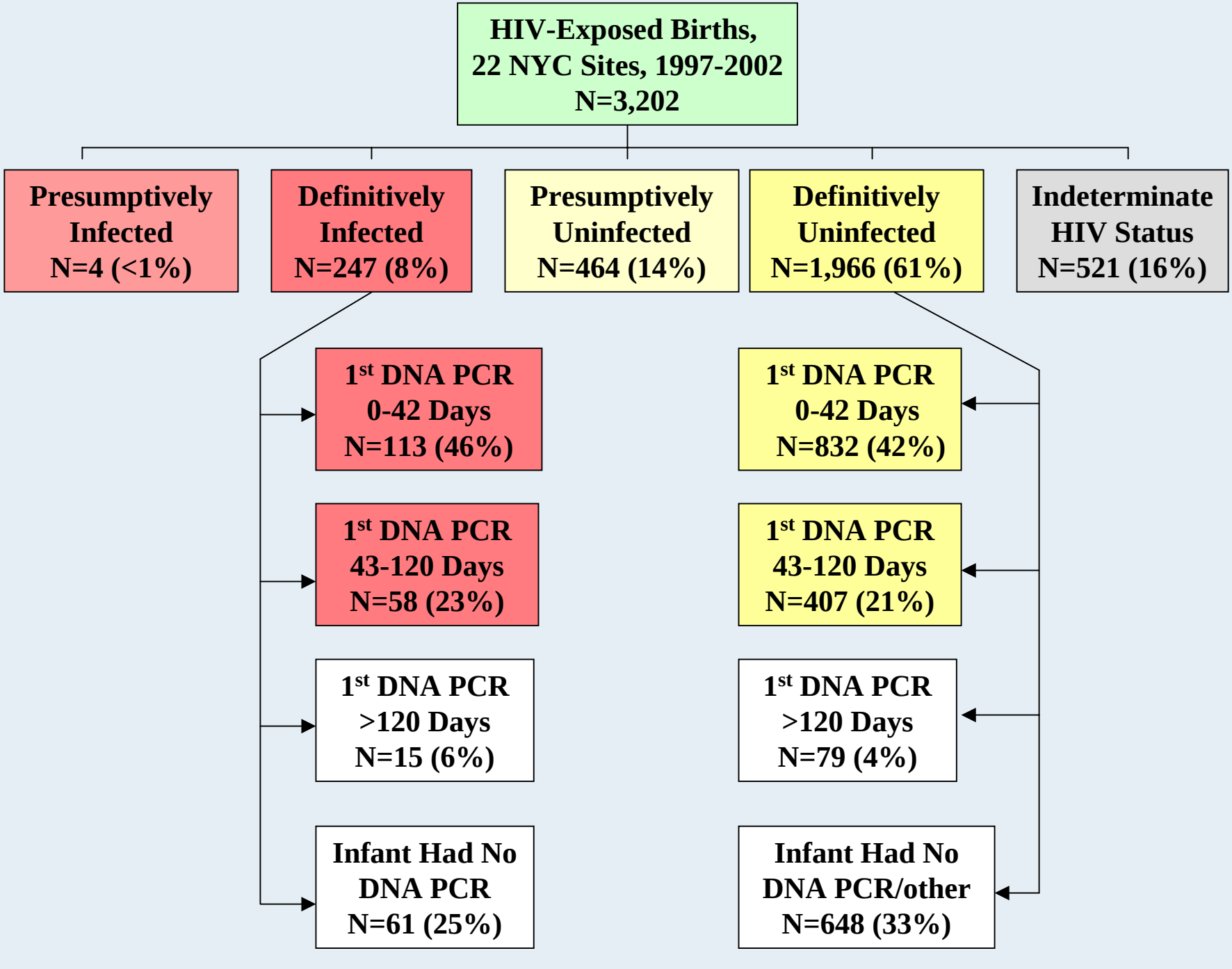
Methods-1

- 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-2

- 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%)
1st DNA PCR
43-120 Days
N=58 (23%)
1st DNA PCR
>120 Days
N=15 (6%)
Infant Had No DNA PCR
N=61 (25%)
1st DNA PCR
0-42 Days
N=832 (42%)
1st DNA PCR
43-120 Days
N=407 (21%)
1st DNA PCR
>120 Days
N=79 (4%)
Infant Had No DNA PCR/other
N=648 (33%)

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)

Age at DNA PCR	True Positive	False Positive	Positive Predictive Value	95% CI
0-42 days	92	0	100	95.4-97.6
43-120 days	21	0	100	96.9-99.2
>120 days	0	1	--	--

Results-2: Positive Predictive Value of 1st DNA PCR, HIV-Exposed Infants, 22 NYC sites, 1997-2002

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

Age at DNA PCR	True Positive	False Positive	Positive Predictive Value	95% CI
43-120 days	58	1	98.3	95.0-100
>120 days	--	0	--	--

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)

Age at DNA PCR	True Negative	False Negative	Negative Predictive Value	95% CI
0-42 days	832	45*	94.9	93.9-95.8
43-120 days	832	9	99.0	98.0-99.9
>120 days	832	0	100	99.0-100

* 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)

Age at DNA PCR	True Negative	False Negative	Negative Predictive Value	95% CI
43-120 days	407	2	99.5	99.0-100
>120 days	407	0	100	99.5-100

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.*

Conclusions-1

- 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.

Conclusions-2

- 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.

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- 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)
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