

HIV TESTING IN THE NEONATAL PERIOD

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CONTENT

- **Evolving PMTCT interventions & 6-week HIV PCR testing**
- **The diagnostic performance of HIV PCR at birth**
- **When should neonates have an HIV PCR test?**
- **Optimal response to a neonatal HIV PCR result that is:**
 - **positive**
 - **negative**
 - **indeterminate**

Evolving PMTCT interventions and 6-week HIV PCR testing

2000

Serial HIV ELISA tests to 18 months of age in HIV-exposed infants

2004

Single HIV DNA PCR test at 6 weeks of age to detect virtually all **perinatal** (in utero & intrapartum) infections (Sherman et al. PIDJ 2005)

sd NVP at birth

① High HIV-related mortality that occurs prior to testing at 6 weeks of age

CHER study – initiate cART at ± 7 weeks of age to reduce morbidity and mortality (Violari, NEJM, 2008)

$\pm 20\%$ mortality in perinatal HIV-infected infants by 13 weeks of age (Marston, Int J Epidemiol, 2011)

$\pm 20\%$ of IU-infected infants LTFU or die by 6 weeks

② Effect of maternal and infant PMTCT prophylaxis on sensitivity of HIV PCR test

2010 SA PMTCT guidelines

Simultaneous introduction of

- daily dose NVP for 6 weeks to infant
- HIV TNA PCR test replaced HIV DNA PCR

HIV TNA PCR on same day as final dose of NVP,
a potent viral load lowering drug

ARV & HIV PCR (In)Sensitivity

- In in utero infected infants, **sdNVP** reduced infant VL to below the limit of detection in 38% at 5 days of age and 17% at 2 weeks of age (Mphatswe AIDS 2007, Lilian JCM 2012)
- the probability of a positive HIV PCR at age 6 weeks in perinatally HIV-infected infants is decreased with **multi-drug maternal and/or infant PMTCT** prophylaxis (Shapiro IAS, 2011)
- in formula fed infants who received 6 weeks of postpartum **AZT**, with or without other antiretrovirals, 32% of IP-infected infants tested HIV DNA PCR negative at 6-weeks of age but positive at 3 months of age (Nielsen-Saines NEJM 2012)
- **Case studies** (Haeri Mazenderani SAMJ 2014, Connolly PIDJ 2013)

6 week PCR is too

- **LATE** to reduce early morbidity & mortality
- **EARLY** to identify all perinatal HIV infections

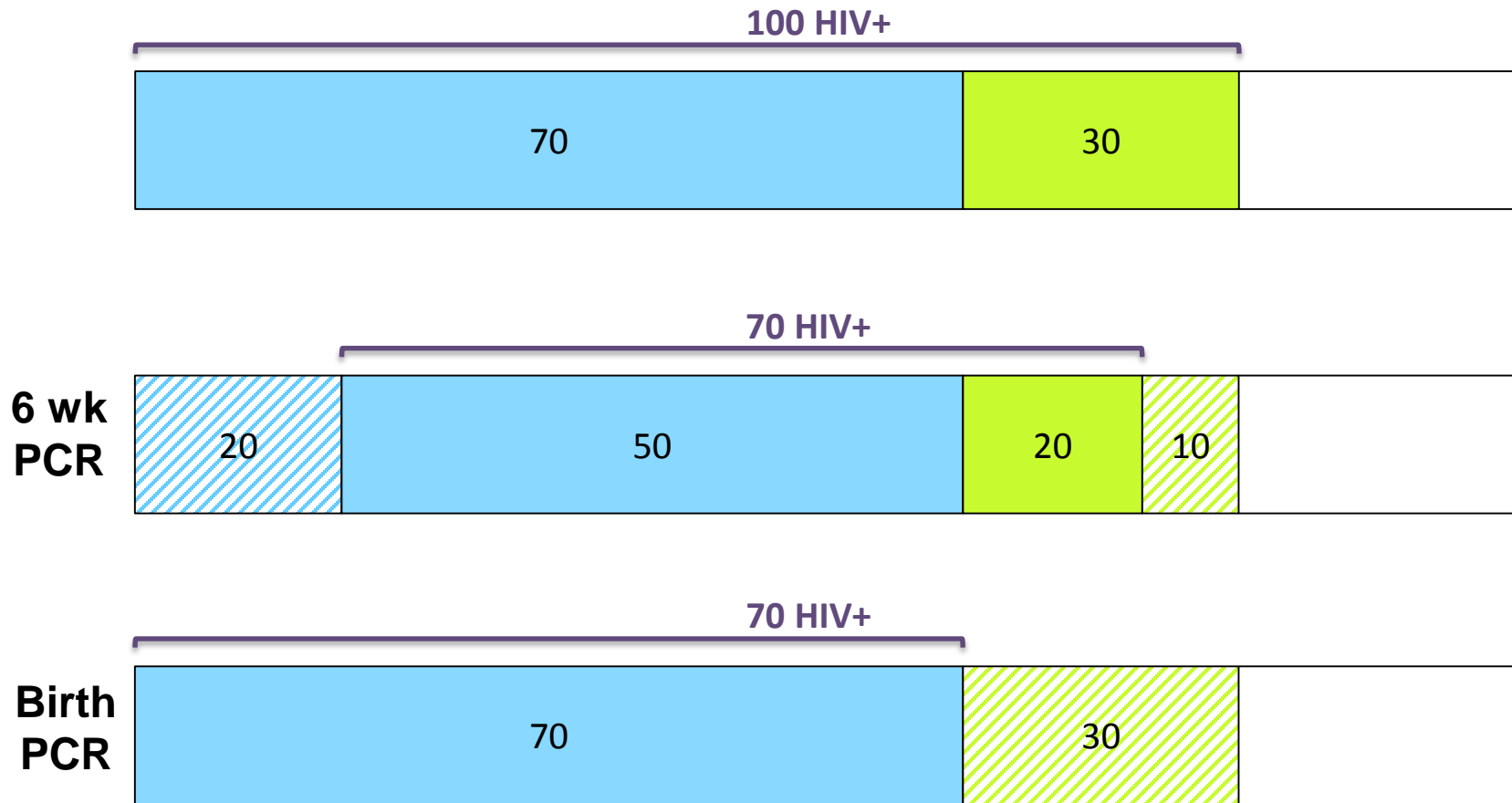
HIV PCR at birth

- Birth HIV PCR sensitivity for perinatal HIV infection <100%
- Prior to PMTCT or standardized HIV PCR tests - **38%** of all perinatal HIV infections detectable at birth (Dunn 1995)
- WHO Option A & sdNVP to infant – **76%** of all perinatal infections detectable at birth (Lilian PIDJ 2012)
- Birth testing:
 - majority women in SA deliver in facilities in SA therefore $\pm \frac{3}{4}$ of all perinatal infections detectable with $\pm 100\%$ coverage
 - no routine neonatal visits at delivery facility for HIV PCR result to be returned to neonate
 - intrapartum infections undetected unless additional HIV PCR test performed

In utero

Intrapartum

Postnatal



When should neonates have an HIV PCR test?

- In SA, no diagnosis of neonatal HIV infection because no HIV PCR test recommended (unless symptomatic)
- No accurate national data for HIV-related neonatal mortality
- Modeling the optimal timing of HIV PCR testing in South Africa considering birth, 6-, 10- & 14-week EPI visits
 - 1 HIV PCR test – identifies the same number of HIV+ infants at birth as at 6-weeks
 - 2 HIV PCR tests – most HIV+ infants identified at birth and 10-weeks of age (Lilian JAIDS in press)

When should neonates have an HIV PCR test?

Targeted birth testing for neonates at high risk of infection
e.g.

- Neonate premature or LBW
- Mother diagnosed at delivery or detectable VL

Universal birth testing – test all HIV-exposed neonates

Evaluate:

- Evidence for ‘high risk factors’
- Cost of universal birth PCR test vs ease of implementation
- Implications for public health system of changing guidelines

Optimal response: **POSITIVE birth HIV PCR result**

- urgent call back – communication with labs & follow up to link all HIV PCR+ to care,
- confirmation of diagnosis with 2nd virological assay
- initiate cART

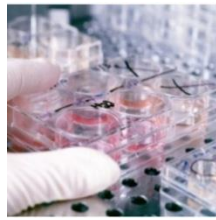
Don't delay cART for confirmatory assay but obtain confirmatory results ASAP because progressively more difficult on ARVs to detect HIV either on VL or HIV PCR

Optimal response: **NEGATIVE birth HIV PCR result**

- Birth test negative, ideally repeat test at 10 weeks
- SA National guidelines recommend 6 weeks
- US guidelines recommend virological assay 2-4 weeks after combination ARV infant prophylaxis has discontinued if HIV PCR negative during prophylaxis
- As for all HIV-exposed and –uninfected infants, HIV PCR is recommended
 - Clinical features suggestive of HIV infection
 - 6 weeks post weaning of breastmilk (unless >18months of age at test – HRT/ELISA)

Optimal response: **INDETERMINATE birth HIV PCR result**

- Increase in indeterminate HIV PCR test results – creates confusion and reduced efficiency in field
- Occur at 6 weeks and birth
- ???????????



ACKNOWLEDGEMENTS

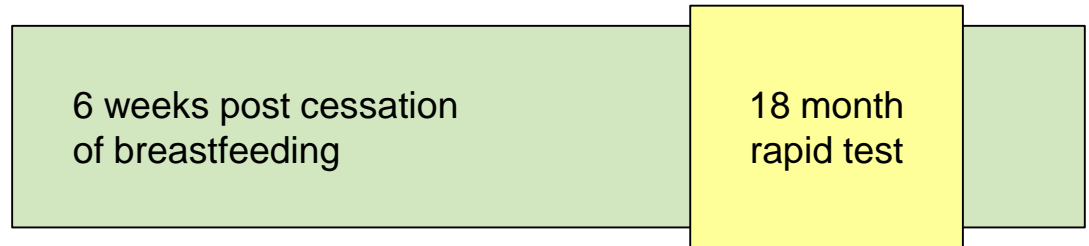
- Mother and infant study participants
 - Rivka Lilian, Kapila Bhowan
Paediatric HIV Diagnostics, Wits Health Consortium
 - Ashraf Coovadia, Karl Technau et al
Rahima Moosa Mother & Child Hospital
 - Sergio Carmona, Lucia Hans, Perry Hlalele & Sue Candy
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Ideal Algorithm ?

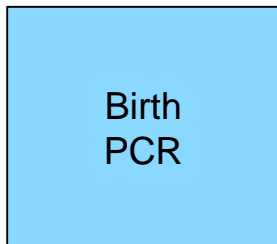
PCR



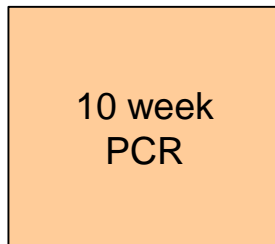
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PCR



PCR



PCR (20%)

