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HIV and antiretroviral treatment exposure in fetal and early life

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HIV in children

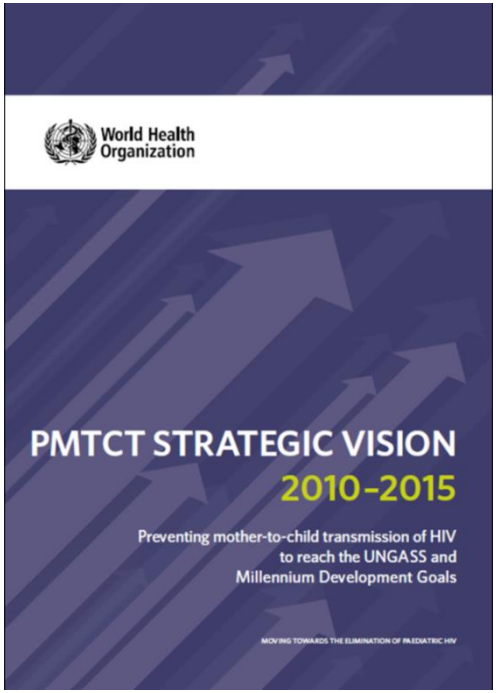
- Globally, in 2014, an estimated 220,000 children were newly infected with HIV
- The overwhelming majority of children born to HIV-infected women are in sub-Saharan Africa
- Of the estimated 600 new paediatric infections each day in children < 15 years of age, nearly all are attributable to mother-to-child transmission (MTCT) and mostly in sub-Saharan Africa
- The prevalence of HIV among pregnant women varies from less than 1% in the UK and Europe to over 40% in some areas of southern Africa

UNAIDS 2015

Mother-to-child transmission

- Mother-to-child transmission of HIV can occur before, during or after delivery
- Without interventions, the rates at 18 months postpartum in a breastfed population can be over 30%, and even without breastfeeding, peripartum transmission rates can be as high as 15%
- Risk factors associated with MTCT include maternal HIV disease progression (CD4 and RNA levels), vaginal delivery, prematurity and breastfeeding
- Postnatal transmission risk through breastfeeding is substantial and continues as long as breastfeeding continues

Towards Elimination of Mother-to-Child Transmission



With plasma HIV load being the dominant risk factor for transmission, ART has become the main approach in the prevention of mother-to-child transmission

ART and preterm delivery

- In pooled analysis of European and USA data, ART was associated with a seven-fold reduction in MTCT compared to monotherapy, but a 1.4-fold increase in premature and a 2-fold increase in severely premature deliveries

  Townsend et al, BJOG 2010 and Antiviral Therapy 2010

- Studies in Botswana showed women on either ART or short-course PMTCT ART were at increased risk of adverse pregnancy outcomes, including stillbirths, preterm delivery, SGA and early neonatal deaths.
  - ART was associated with a 1.8-fold increased risk of adverse pregnancy outcomes

  Powis et al JID 2011;204:5-6-514

- Unlikely this ART effect is associated with a particular drug, but more likely an indication of effective HIV treatment in combination regimen

  Fiore et al J Reprod Immunol 2006; 70: 143-150

ART exposure in fetal and early life: impact on developing immune system?

- Infant mortality is increased for SGA infants, and there may be long-term developmental consequences
- Clinical implications of possibly altered immune system development are likely to be limited in at least the short term
- Effects may be subtle and only manifest in adulthood - risk of not reaching optimal potential may have society impact

Bunders et al, AIDS 2004
Bunders et al, AIDS Res Hum Retroviruses 2010

PIMS in Cape Town

- NIH-funded cohort of pregnant women and their children
  - pregnancy dating by ultrasound before 21 weeks
  - Assessment of placental implementation and maintenance
  - Metabolomics in pregnancy and the neonate
  - Innate immunity during pregnancy and in the placenta in cases (preterm or SGA) and controls (matched for duration of ART exposure and maternal age)

  to inform understanding of mechanisms underlying the increased rate of preterm and SGA deliveries in women who are on ART from before or early pregnancy

- Further research is planned on infant outcomes during the first year of life and developmental assessment at age 4-5 years or later