British HIV Association
BHIVA

marking World AIDS Day

FHIVA
federation of hiv associations

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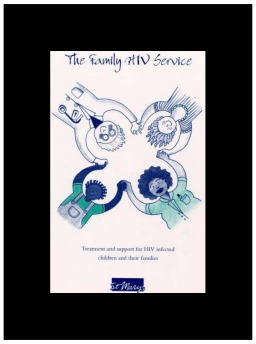
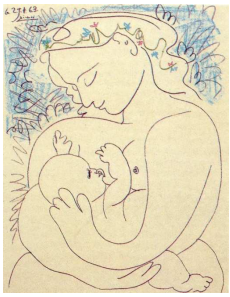
RCOG, London

2015 - Aiming for Zero Transmission HIV Exposed Uninfected Infants - HEUs are there any problems?



Hermione Lyall
Imperial Healthcare
NHS Trust
27.11.15

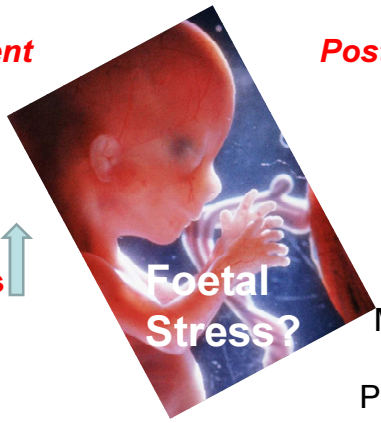


Acknowledgements:
Chrissie Jones, Andrew Prendergast, Pat Tookey, Claire Townsend, Claire Thorne, Graham Taylor, Gareth Tudor-Williams Marc Lallement, Catherine Peckham

The "foetal-infant" environment & HIV

Resource Rich ***Resource Poor***

Foetal environment
Genetics
Nutrition
Immune function
Immune activation
HIV Viral Load ↓
ART drugs ↑
Other drugs
Other infections
Prematurity
Smoking
etc



Post natal environment
Genetics
Environment
Nutrition
Breast / formula
Immune function
Immune activation
Maternal microbiome
Maternal well being
Poverty / Orphanhood
etc

HIV un-exposed un-infected	HUU
HIV exposed un-infected	HEU
HIV exposed infected	HEI

Effects of HIV / Drug exposure?

Resource Rich ***Resource Poor***

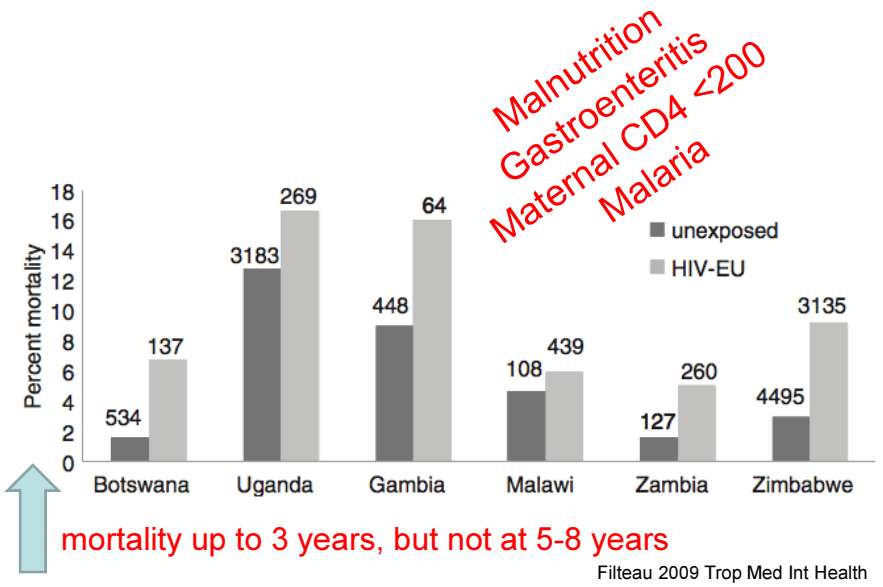
Mortality / Survival

Brain
Skin
Gut
Growth
Bones
Endocrine

Haematology
Cardiovascular
Infections
Immunology
Carcinogenesis
Mitochondria

OTHERS??

Mortality among HEU African infants



mortality up to 3 years, but not at 5-8 years

Filteau 2009 Trop Med Int Health

Infectious morbidity in HEU infants – in Africa

Low birth weight & low birth Neutrophils → ↑ morbidity & mortality

Hospitalisation for infection ↑↑ 20% in HEUs

↑↑ severe infections, more complications

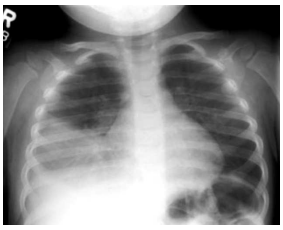
↑↑ LRTI (> in mothers with advanced HIV)

↑↑ Pneumococcal infections

↑↑ oral thrush

↑↑ TB (inc congenital TB)

OIs – PJP, CMV



↑↑ Post-operative infections & mortality (SA)

↑↑ diarrhoea, is probably related more to mode of feeding than HIV exposure.

Cotrimoxazole → ↓morbidity & mortality in HEU infants

Shapiro, J Inf Dis 2007; Koyanagi, PIDJ, 2011; McNally Lancet 2007; Kourtis AIDS. 2013

USA - HEU - morbidity & mortality during the first 2 yrs of life Women & Infants Transmission Study (WITS).

1990-2001 evaluation at birth, 1, 2, 4, 6, 9, 12, 18, 24 months
Growth, hospitalization, clinical disease (HEU 955, HEI 163)

Over 11 yrs - morbidity & mortality during the first 24 months of life decreased substantially for HEU infants.

HEU: ↑ short stature, poor weight gain & wasting compared to the general population.

Two or more changes in caretaker → growth deficiency

Fetal exposure to tobacco → height abnormalities.

Anemia common → associated with ZDV prophylaxis.

Paul et al, Pediatr Infect Dis J. 2005

Infectious morbidity in HEU infants – Europe

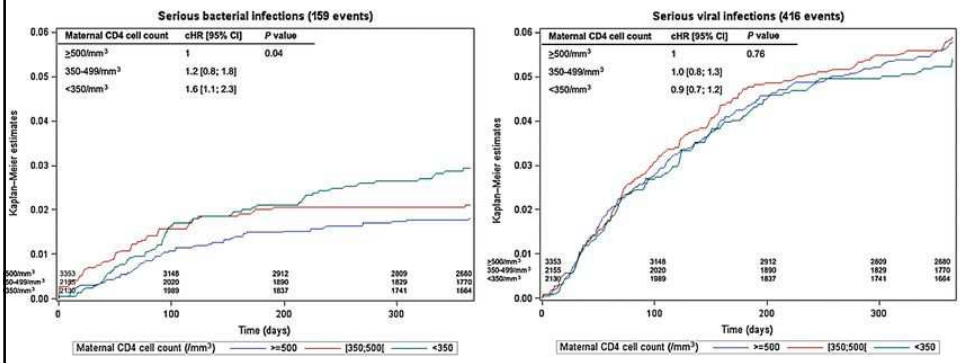
French Perinatal Cohort – n = 7638, 2002-10 (only HEU)

↑↑ hospitalisation for infection in first year of life (9.3%)

699 serious infections, 159 bacterial

Bacterial infection - ↑ with ↓ maternal CD4 (esp encapsulated)

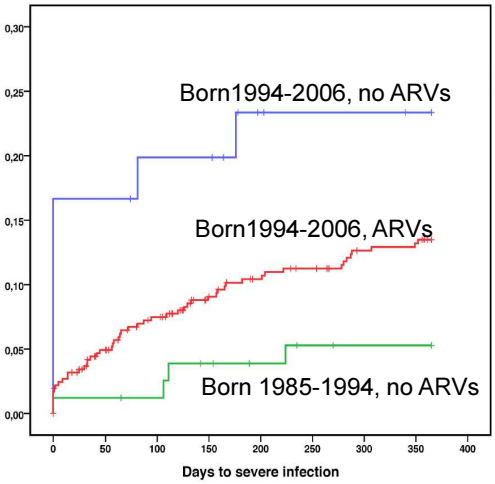
Viral infection – no effect of maternal CD4



Clement Taron-Brocard et al. Clin Infect Dis. 2014;59:1332-1345

Infectious morbidity in HEU infants – Belgium

Belgian single centre cohort, n= 537
Severe infections in 1st year of life – 16.8 /100 HUE years
Compared to general population: Strep pneumo ↑↑ 4x, Group B Strep ↑↑ 13x



Risk factors for severe infection in this cohort:

Prematurity →
↑↑ 21x neonatal period
↑↑ 3x post-neonatal

Born in post ARV era→
↑↑ with /without ART

Adler et al PLoS One 2015

Group B Strep infection ↑↑ in HEU

Africa – South Africa

antibodies to GBS:

↓ in pregnant women with HIV

↓ in new-born HEU infants (trans-placental)

↓ in HEU infants at 16 weeks of age

Increased risk of EOS and LOS disease

Europe – Belgium

HEU	HUU
1.55%	0.08%
6/322	16/20158

Late onset infection

5/6	2/16

HEU had more severe disease.

most were leukopaenic at presentation.

Le Doare K, Vaccine. 2015

Epalza C, Pediatrics. 2010

Increased risk of mortality from invasive pneumococcal disease in HEU infants aged <1 year in South Africa, 2009-2013.

Invasive pneumococcal disease, n = 2099 cases, 2009 / 2013
92% known HIV exposure status, 86% known outcomes

Exposure	IPD rate / 100,000		Case Fatality	
	2009	2013	overall	< 6mths of age
HEI	654	272	34%	
HEU	88	33	29%	37%*
HUU	28	18	25%	32%

*rel risk 1.76x

Need to prioritise HEU for pneumococcal immunisation

von Mollendorf, Clin Infect Dis. 2015

Congenital CMV and HEU infants

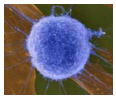
Canadian study n = 1255 – 2.2% cCMV
↑↑ in mothers with ↓↓ CD4 counts, born earlier, lower birth weight
Gantt S, J Med Virol. 2015

South African study n = 748 – 2.9% cCMV (96% of women on ART)
↑↑ 2.9x in mothers ↓↓ CD4 <200
No significant effect of: maternal age, type of ART, length of ART, gest age / birth weight.
Manicklal S, Clin Infect Dis. 2014

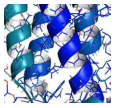
French Perinatal Cohort n = 4797 – overall 2.3% cCMV
HEI 10.3% HEU 2.2%
HEU 1997- 1998 3.5% 2003 - 2004 1.2%
Logistical regression analysis – significant factors:
Delivery period, maternal age, maternal CD4 < 200, time of starting ART.
Guibert G, Clin Infect Dis. 2009

Postnatal CMV infection in HEU ↑ if mother not on ART, or CD4<200
Frederick et al Clin Infect Dis. 2012

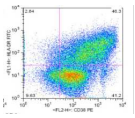
Immune abnormalities in HIV-exposed, uninfected infants



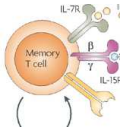
CD4 ↓ CD8↑



Cytokines ↓↑



Immune activation ↑



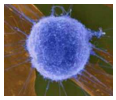
Naïve T cell ↓ Memory T cell ↑

Reviewed in Afran 2013, Clin Exp Imm

Immune abnormalities in HIV-exposed, uninfected infants

Feature	Reference
Reduced transfer of maternal antibody including IgG	de Moraes-Pinto *et al.* [40]; Farquhar *et al.* [46]; Cumberland *et al.* [42]; Scott *et al.* [45]; Bunders *et al.* [44]; Jones *et al.* [93]
Altered CD4⁺ and CD8⁺ T cell counts	Clerici *et al.* [33]; Miles *et al.* [98]; Slogrove *et al.* [11]; Borges-Almeida, *et al.* [126]
Increased proinflammatory responses in cord blood to polyclonal stimulation	Hygino *et al.* [47]; Hygino *et al.* [48]
Increased T cell immune activation	Rich *et al.* [36]; Clerici *et al.* [33]; Romano *et al.* [59]; Vigano *et al.* [54]
Skewed T cell memory and differentiation subset distributions	Rich *et al.* [36]; Clerici *et al.* [33]; Nielson *et al.* [128]; Vigano *et al.* [54]; Miles *et al.* [98]
Increased susceptibility to T cell apoptosis	Economides *et al.* [49]
Increased plasma IL-7 levels	Clerici *et al.* [33]
Altered DC phenotype and *in-vitro* IL-12 production	Chougnet *et al.* [51]; Velilla *et al.* [53]
Reduced thymic size	Kolte *et al.* [56]
Reduced TREC levels in periphery	Nielson *et al.* [128]
Skewed maturation of B cell subsets and susceptibility to apoptosis	Bunders *et al.* [44]; Miyamoto *et al.* [129]; Borges-Almeida *et al.* [126]

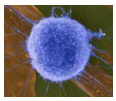
IgG = immunoglobulin G; IL = interleukin; TREC = T cell receptor excision circles.



Clinical & Experimental Immunology

Afran 2013

Immunology in HEU



European Collaborative Study n= 1663 HEU,
followed from birth – for at least 8 yrs
Standard protocol to measure TLC, CD4 & CD8 cell counts.

Ethnicity

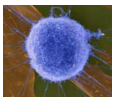
black children - ↓TLC, CD4, CD8 cell counts than white
black children - ↑ TLC, CD4 & CD8 lymphopaenic counts

ART exposure

ART - ↓ TLC & CD4 cell counts in 1st year of life
ART - ↓ CD8 cell counts until at least 8 years of age
ART duration & intensity - associated with TLC levels

Bunders et al, AIDS. 2005

Placental transfer of maternal antibody – reduced in HEU



HEU infants are more vulnerable to infections

- Timely infant vaccination
- Consider immunisation in pregnancy to protect in early life

Table 2. Influence of Maternal HIV Infection on Placental Antibody Transfer

Specific Antibody	Placental Transfer, Median (IQR)[a]: HIV-Infected Mother–Exposed Uninfected Infant Pairs	Placental Transfer, Median (IQR)[a]: HIV-Uninfected Mother–Unexposed Infant Pairs	Reduction, %[b]	*P* Value[c]
Haemophilus influenzae type b	0.57 (0.45-0.79)	0.74 (0.61-1.00)	23	.002
Bordetella pertussis	0.91 (0.61-1.20)	1.51 (1.15-2.06)	40	<.001
Pneumococcus	0.62 (0.41-0.77)	0.73 (0.53-0.94)	15	.05
Tetanus toxoid	0.95 (0.60-1.12)	1.30 (1.03-1.86)	27	<.001

Jones, 2011,
Le Doare, Vaccine, 2014
De Moraes-Pinto, 1996 & 1998
Cumberland, 2007
Scott, 2007

JAMA The Journal of the American Medical Association

Responses to Vaccination in HEU and HUU

Higher in exposed

Similar in exposed & unexposed

Lower in exposed

	HEU	HUU	Ref
Diphtheria	Similar	Similar	Simani, AIDS, 2014
Tetanus	Similar	Similar	Jones, JAMA, 2011
	Similar	Similar	Reikie, CVI, 2013
	Similar	Similar	Simani, AIDS, 2014
Pertussis (PT & FHA)	Higher	Lower	Jones, JAMA, 2011
	Higher	Lower	Reikie, CVI, 2013
PT	Higher	lower	Simani, AIDS, 2014
FHA	Similar	Similar	Simani, AIDS, 2014
Hib (PRP)	Similar	Similar	Jones, JAMA, 2011
	Similar	Similar	Reikie, CVI, 2013
	Similar	Similar	Simani, AIDS, 2014
PRP SBA	Similar	Similar	Simani, AIDS, 2014

Higher in exposed

Similar in exposed & unexposed

Lower in exposed

	HEU	HUU	Ref
HBsAg	Lower	Higher	Simani, AIDS, 2014
	Higher proportion of non-responders and good responders	Lower proportion of no-responders or good responders	Abramczuk, CVI, 2011
	Similar	Similar	Reikie, CVI, 2013
Pneumococcus	Higher	Lower	Jones, JAMA, 2011
Serotype-specific	Similar	Similar	Madhi, JID, 2010
OPA	Similar (except serotype 19F)	Similar	Madhi, JID, 2010
Measles 1st dose	Higher	Lower	Simani, AIDS, 2013
	Similar	Similar	Reikie, CVI, 2013
Measles 2nd dose	Lower	Higher	Simani, AIDS, 2013

Responses to Vaccination in HEU and HUU

Higher in exposed

Similar in exposed & unexposed

Lower in exposed

	HEU	HUU	Ref
BCG at birth	Altered patterns		Van Rie, 2008, CVI
BCG at 6 weeks	Similar	Similar	Jones, AIDS, 2014
BCG at birth	Similar	Similar	Mansoor, JID, 2009
BCG at birth	Similar	Similar	Elliott, 2010, Vaccine
BCG	Similar @ 6/52	Similar @ 6/52	Kidzeru, 2014, AIDS
	Higher @ 14/52	Lower @ 14/52	
	Lower polyfunc	Higher polyfunc	
BCG	Higher CD4	Lower CD4	Mazzola, 2011, AIDS
	Lower GD	Higher GD	

In general, HEU infants mount a robust antibody responses to vaccines and are likely to be equally protected as HUU

Intra-uterine Growth in European HUE

European Collaborative Study - weight, height, & OFC, n=1912

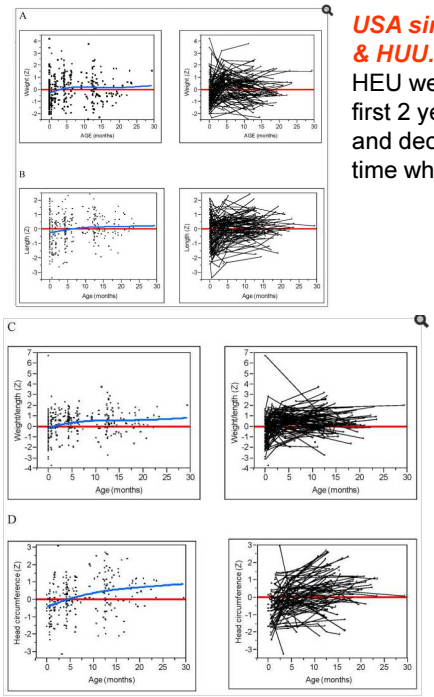
Birth weight / OFC

Born at term or before 34 weeks no difference if exposed to mono/ no ART or cART

Born at 34 -36 weeks, increased weight if on cART

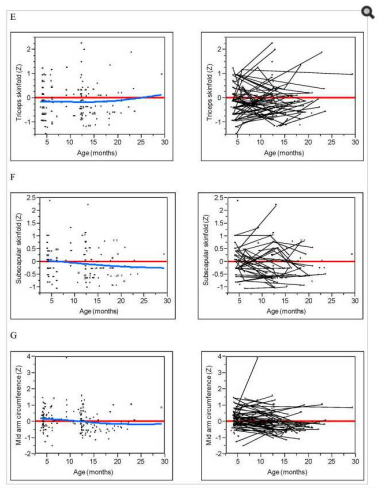
Gestational age and maternal illicit drug use were strongly associated with growth, effect of cART was marginal.

Hankin et al, J Acquir Immune Defic Syndr. 2005



USA similar growth & body composition - HEU & HUU.

HEU weigh less at birth → slightly ↑ growth in the first 2 years of life. HEU had less subcutaneous fat and decreasing mid-upper arm circumference over time when compared with US standards.



Neri et al, J Pediatr. 2013

Growth & Development in Zambian HEU / HUU

111 HEU, 279 HUU, aged 6-12 years, assessed →

Anthropometry

Health questionnaire & clinical exam

BP, Hb, HbA1c, glucose, cholest, CRP

Most recent school report

- HEU smaller and less fat than HUU
  - difference became non-significant when adjusted for socio-demographic variables
- HEU ↑ minor illness and ↑ meds prescribed
- No difference between HEU and HUU in biochemical markers
- HEU lower maths grades
  - difference maintained when adjusted for socio-demographic variables

Nicholson et al, BMC Pediatr. 2015

Growth, Bones & Tenofovir

Infant growth outcomes after maternal tenofovir use during pregnancy.

IMPAACT P1025 (infants born 2002-2011)

n=2025 at birth (31% TDF exposed); n=1496 at 6 mths (31% TDF exposed)

By most measures, in utero exposure to tenofovir did not significantly predict infant birth weight or growth through 6 months of age.

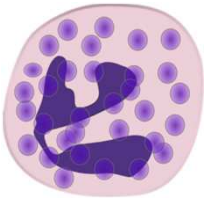
Ransom et al, J Acquir Immune Defic Syndr. 2013

New born meconium TDF concentrations

↑ meconium TFV concentrations → greater gestational ages ($\rho = 0.29$, $P = 0.03$) and lower maternal HIV RNA before delivery ($\rho = -0.29$, $P = 0.04$). Meconium TFV concentrations were not associated with infant weight, length ($n = 58$) or bone mineral content ($n = 49$).

Pediatric HIVAIDS Cohort Study (PHACS), PIDJ 2015

Haematology - Neutrophils



ECS - Levels and patterns of neutrophil counts for first 8 years of life. HEI n=156 HEU n=1533

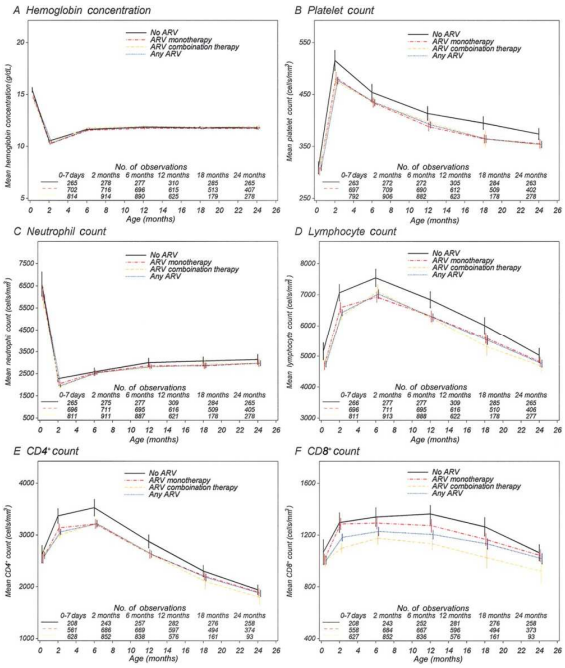
HIV-infection: after 4 months of age, neutrophil counts were consistently and substantially lower. Advanced HIV disease & ARV ↓↓ neutrophil count.

Ethnicity: black children ↓ lower counts than white across the age range

HEU: male gender, & ARV exposure were associated with reduced neutrophil count until at least 8 years of age.

clinical relevance of reduced levels of neutrophils?

European Collaborative Study.AIDS. 2004



USA Women & Infants Transmission Study (WITS)

HEU n=1820 ARV-exposed
HEU n= 351 ARV-unexposed
0 – 24 months of age

0-2 mths ART-exposed:
↓ Hb, Neut, TLC, CD4+

6-24 mths ART-exposed:
↓ platelet, TLC, CD4+
↓ CD8+

cART compared to mono-ART:
↓ Neut, TLC, CD8+ at 0-2 mths
↓ CD8+ at 6-24 mths

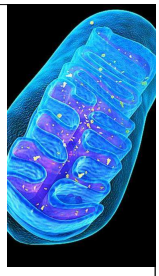
Small differences – is there a clinical significance?

Susan E. Pacheco et al. J Infect Dis. 2006;194:1089-1097

HEU Mitochondrial Morbidity & Exposure to Nucleoside Analogues?

The French Perinatal Cohort **Stephane Blanche et al 2002**

* Crude rate in French cohort		3 / 1000
Observed back ground rate		1 / 10 000
	ART exposed	Un-exposed
French Cohort	2644	1748
MITOCHONDROPATHY		
Significant evidence for:	28	1
"Possible"	14	0
"Established"*	7	0



USA retrospective review of perinatal exposure to ART in PACTS Study.
No NRTI exposed HEU died of mitochondrial disorders (n=118 deaths < 5 years)
No living HUEs had symptoms of mitochondrial dysfunction (n=1951).
Bulterys et al, Ann N Y Acad Sci. 2000

"MITOC" study commissioned by EMA → results still awaited……

Transient lactic acidemia in HEU infants exposed to perinatal ART

Plasma lactate > normal,at least once in 35 / 38 (92%) infants

Reached levels > 5 mmol/l in 10 (26%) infants

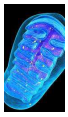
78 /117 (68%) lactates were elevated (11 > 5 mmol/l)

No infants received ART beyond 6 weeks

Elevated lactates persisted up to age 6 months

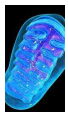
2 infants had symptoms consistent with lactic academia

No association between the infant peak lactate and the type or duration of ART during pregnancy



Alimenti et al, Pediatr Infect Dis J. 2003

In utero NRTI exposure & possible mitochondrial dysfunction in HEU.



PACTG 219/219C n=1037 HEU born 1991-2002

Possible cases with signs of MD according to "Enquête Périnatale Française" criteria were identified retrospectively

Cases (n = 20) significantly more likely to be male and born in earlier years than non-cases (n = 1017)

Overall no association between in NRTI exposure & MD

When adjusted for year of birth the odds of first exposure in the third trimester to 3TC (OR, 10.57; 95% CI, 1.93-75.61) and ZDV/3TC (OR, 9.84; 95% CI, 1.77-71.68) higher among cases than non-cases.

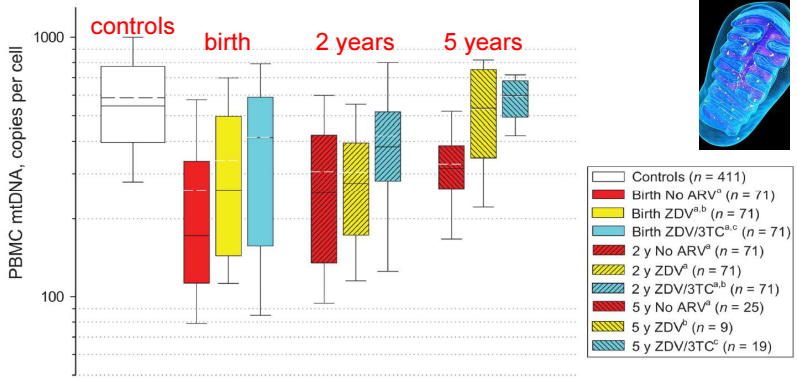
Unable to control for confounding by maternal viral load or psychoactive drug use.

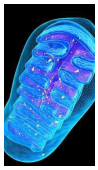
Brogly et al, AIDS. 2007

Some evidence of small changes in mDNA in cases.

Brogly et al, AIDS Res Hum Retroviruses. 2011

Antiretroviral exposure and lymphocyte mtDNA content among HEU





Is it HIV or ART?

mtDNA - stored PBMCs (Primagen Retina Mitox assay)
411 HUU and 213 HEU (+/- in-utero and neonatal ARV)
mtDNA ↓ in HEU compared to HUU
mtDNA ↑ in HEU+ART compared to HEU-ART
By 5 years of age:
mtDNA ↑ to normal levels in HEU+ART, but remain lower in HEU-ART

Aldrovandi et al, Pediatrics. 2009

Cardiac effects of in-utero exposure to antiretroviral therapy in HEU children.

Pediatric HIV/AIDS Cohort Study's Surveillance Monitoring for ART Toxicities study.

No significant differences in echocardiographic Z-scores between 417 HEU and 98 HUU, aged 2-7 years.

Subclinical differences in left ventricular structure and function with 1st trimester exposure to cART.

lower stress-velocity Z-scores
lower LV dimension Z-scores
higher mean LV posterior wall thickness
lower mean LV wall stress Z-scores

Lipshultz et al, AIDS. 2015

Brain - cognitive & academic outcomes

USA Pediatric HIVAIDS Cohort Study HEU 5-13 yrs.

Test	number	% ART exposure
WPPSI-IIIs	350	84%
WASI	337	64%
WIAT-II-A	415	67%

Cognitive Performance: No association with ART regime or class

Same factors as associated with lower performance in general pop applied in this cohort: prematurity; SGA; maternal alcohol; lower maternal IQ etc.

Nozyce, Pediatr Infect Dis J. 2014

USA PACT 219/219C n = 1840, born 1993-2006, 92% ART exposed

Bayley Scales of Infant Development (BSID) at 2yrs of age

No effect of ART exposure on BSID scores

LBW infants had higher scores if ART exposed

17% of mothers used illicit drugs, no effect on BSID scores

Williams et al, Pediatrics. 2010

Cognitive & Academic outcomes in HEU compared to HUU

Zambia – B+ era, ART exposure (inutero & BF)

Capute Full-Scale Develop quotient HEU n=97 HUU n=103

No significant difference in performance Ngoma et al, AIDS. 2014

Thailand & Cambodia – HEU n = 160, HUU n = 167

Beery Visual Motor Integration (VMI) test, Color Trails, Perdue Pegboard, and Child Behavior Checklist (CBCL), Thai children (n = 202) also completed the Wechsler Intelligence Scale (IQ) and Stanford-Binet II memory tests.

Adjusted for caregiver education, parent as caregiver, income, age, ethnicity.

Slightly lower scores on verbal IQ, full-scale IQ, & Binet Bead Memory in HEU, uncertain significance.

No differences in performance IQ, other Binet memory domains, Color Trail, Perdue Pegboard, Beery VMI, or CBCL test scores.

Kerr et al, AIDS Care. 2014

ART & Language Outcomes in HEU Infants.

Risk for late language emergence after in utero ART exposure in HEU infants.

1129 language assessments were conducted among 792 1- and 2-year-old children. In utero cARV exposure showed little association with LLE, except for higher risk of language delay observed in 1-year-old infants with atazanavir exposure.

Pediatric HIVAIDS Cohort Study (PHACS), Pediatr Infect Dis J. 2013

Meconium ART concentrations

↑ meconium atazanavir concentrations were protective against developmental language delays at 1 year, suggesting the importance of fetal ATV detoxification into meconium. This supports ATV exposure safety for infant language development.

Pediatric HIVAIDS Cohort Study (PHACS), Pediatr Infect Dis J. 2015

Malignancy? – no data yet
NSHPC Data linkage - flagging

- Office for National Statistics
- Births, deaths, cancer registration, emigration
- Flagging studies provide event notification
- UK born infants born to infected women being flagged (no names – complex procedure)

- Numbers for babies
- Other data linkage possibilities
- Ethics and consent issues – public health considerations

Specific drug effects - Kaletra newborn toxicity

Kaletra liquid - 42% ethanol, & 15% propylene glycol
Neonatal ⇓ liver metabolism – CP3A / alcohol dehydrogenase

FDA adverse events reporting system (AERS) <2yrs
10 cases of severe toxicity, 8 prems (28-35 wks)
7 Cardiac toxicity (cardiac failure, AV block, bradycardia)
5 acute renal failure (⇑ K common); 3 CNS effects
1 death (assoc with an over dose), rest improved on d/c Kal
Rx started on day 1 of life in 7/10
NB – no denominator data;

FDA safety alert 8.3.11 – avoid Kaletra in <14 day old infants unless no alternatives – monitor organ function closely

Association of prenatal & postnatal exposure to lopinavir-ritonavir & adrenal dysfunction among uninfected infants of HIV-infected mothers

JAMA. 2011 Jul 6;306(1):70-8. ANRS French Perinatal Cohort Study Group

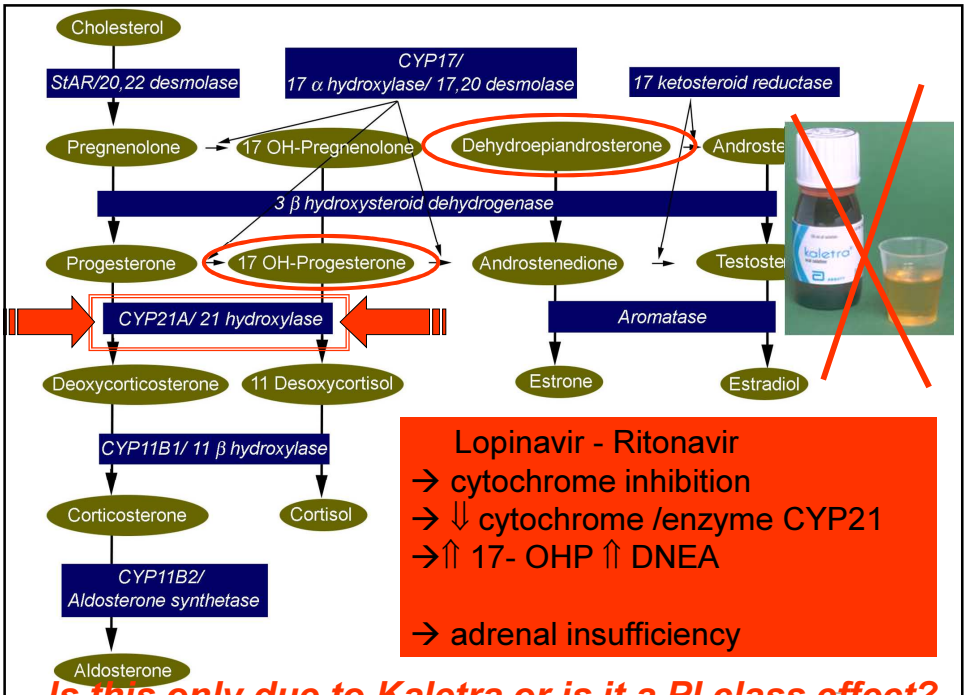
French cohort
All term newborns on lopinavir-ritonavir were asymptomatic

3 premature infants life-threatening symptoms compatible → adrenal in-sufficiency (hyponatremia, hyperkalemia with, in 1 case, cardiogenic shock)

All symptoms resolved off lopinavir-ritonavir treatment

- Kaletra 7 / 50 ⇑ 17OHP levels – 14%
- Controls (ZDV) 0 / 108 ⇑ 17OHP levels

- French Guthrie Card National rate ⇑ 17OHP levels – 0.03%

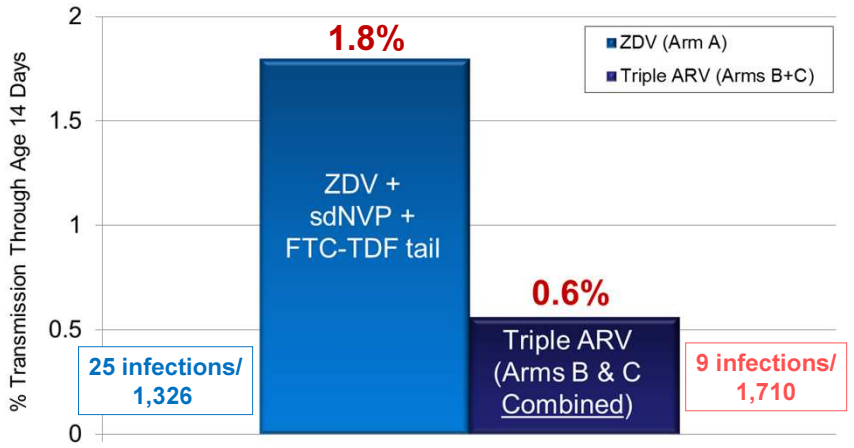


Lopinavir - Ritonavir
→ cytochrome inhibition
→ ⇓ cytochrome /enzyme CYP21
→⇑ 17- OHP ⇑ DNEA

→ adrenal insufficiency

Is this only due to Kaletra or is it a PI class effect?

PROMISE MTCT Through Age 14 Days Significantly Lower in Triple ARV Arms



Difference in MTCT Risk (Repeated Confidence Interval):
-1.28% (95% CI -2.11%, -0.44%)

PROMISE summary of 1077BF/FF Antepartum Component Infant Safety Results

- There were no significant differences in infant signs/symptoms and lab AEs by study arm.
- There were 60 early infant deaths by 14 days; including 28 deaths in version 3.0.
- In V 3.0, there was a significantly lower risk of infant death for **ZDV/3TC vs TDF/FTC**:
  - **0.6%(2/346) vs. 4.4% (15/341), p=0.001**

The difference was primarily seen in deaths among infants less than <34 weeks gestation –why?

Effects of HIV / ART exposure?

Resource Rich ***Resource Poor***

Mortality / Survival

With maternal ART

⇓ Infant HIV Tx
⇓ HEU infections
⇑ Prematurity
⇑ Drug toxicities

Without maternal ART

⇑ Infant HIV Tx
⇑ Immune dysfunction
⇑ HEU infections
⇑ Orphans / poverty

Well designed – large long term follow up studies in resource poor settings are essential to assess these effects

NSHPC

Children enrolled in CHART

n = 307 children enrolled (born 1996-2003)

No health or developmental problem	107 (35%)
At least one "usual" problem	179 (58%)
e.g. childhood infections, asthma, gastroenteritis	
Specific health / developmental problem	21 (7%)

Congenital abnormalities (7)

- Posterior urethral valves
- Cleft lip & palate
- Hydrocephalus (aqueduct stenosis)
- Spina bifida & hydrocephalus
- Ovarian cyst
- Pulmonary stenosis
- Talipes

Others (14)

- Febrile seizure (5)
- Sickle cell disease (4)
- Cerebral palsy 2° to prematurity
- Intraventricular haemorrhage (prem)
- Head injury & 2° developmental delay
- Atopy with seizure
- Autism

Follow up of uninfected children exposed to ART: UK CHART study 2002-05

Investigated logistics of long-term follow up of uninfected HIV-exposed children

Explored whether serious adverse outcomes associated with exposure to ART in fetal/early life were apparent in early childhood

Incorporated NSHPC data on ART exposure, delivery etc.

CHART data on health/development in early childhood

Prevalence of abnormal outcomes within UK norms, but numbers small and duration of follow up limited

Comprehensive long-term clinic-based follow up not feasible in UK

alternative approaches required, e.g. secure data linkage protocols

NSHPC

Hankin CD et al. AIDS Care 2009, 19(1):482-486

Elimination of infant HIV →

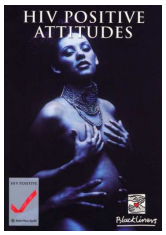
A dream in 1994 → Reality in 2015

access to HIV tests & effective ART

There are consequences for HIV & ART exposed uninfected infants –

its our job to minimise these effects and optimise outcomes –

How to do long term surveillance?



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