Brighton and Sussex University Hospitals NHS Trust

CHIPS Collaborative HIV Paediatric Study

brighton and sussex medical school

To Determine the Prevalence of HIV Seroreversion in 5 Collaborating Paediatric HIV Centres in the UK

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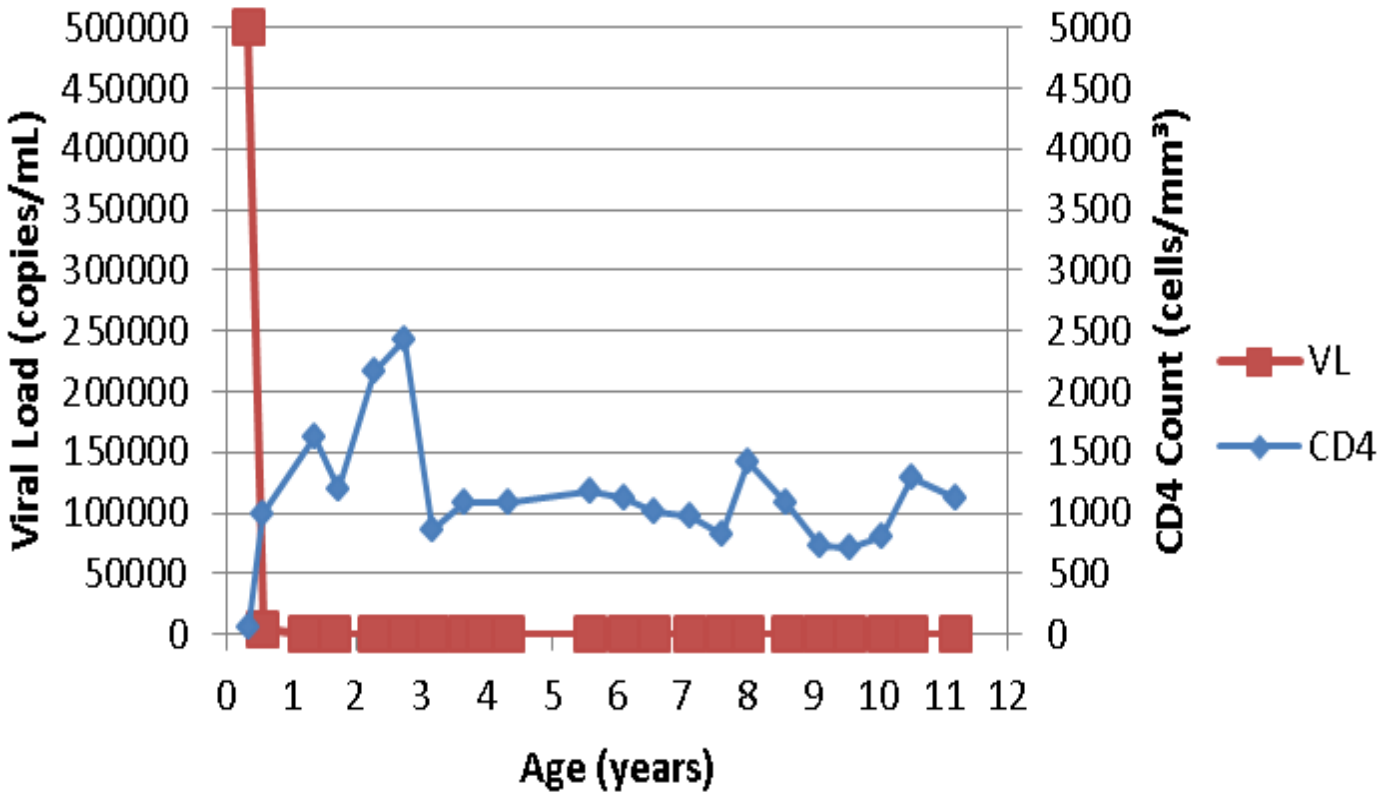
Case

- 12 year old girl
- Diagnosed with HIV @ 3/12 old
- ART since 3/12
- FU
  - very well,
  - excellent CD4,
  - VL<40,
  - Side effect of Rx-lipoatrophy/high cholesterol
  - Darunavir monotherapy

Routine appt: negative HIV Antibody test…

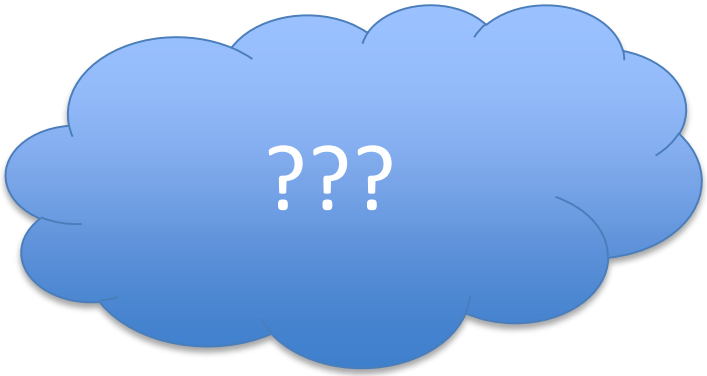
? Diagnosis correct



How common is seroreversion in children?

How long can it last?

What factors are associated with seroreversion?
Why only seen in some patients?
- Genetic ?
- Timing of Rx?
- Maternal factors?



What are the implications of seroreversion?
- Prognostic implications?
- Immunological?

Background: Seroreversion

Negative HIV antibody test despite confirmed HIV infection

- 1997: Luzuriaga *et al* – first reported in 2 infants
- 2005: Hainaut *et al*, Belgium
  - 14 babies ART <2/12, 5 FU to 18/12 with full viral suppression, 4/5 (80%) neg Ab, no long term FU
- 2013: Asang *et al*, Germany
  - 37 children ART<5/12, full viral suppression, 11/37(30%) Ab neg,
  - mean age FU 6.6 7/8 HLA DQB1*03
- 2014: Ejeliogu *et al*, Nigeria
  - 19/66 (29%) babies Ab neg at 21/12. All 19 ART< 6/12 and had full viral suppression

UK prevalence unknown

Luzuriago K et al; NEJM 1997, 336:1343-9
Hainaut M et al; letter CID 2005(41)
Asang C et al; AIDS. 2013(27)
Eleliogu et al; BJMMR 2014, 10, 4/30, 4892-4900

Aims

1. To determine the prevalence of seroreversion, in children with HIV, in 6 paediatric HIV centres in the UK.

2. To determine factors associated with seroreversion

3. To determine if seroreversion has any affect on long term outcome
    1. Clinically
    2. Immunologically

    } Work in progress

Methods

- Approval obtained from the steering committee of the Collaborative HIV in Paediatrics Study (CHIPS) in 2013
- Survey requesting anonymous data sent to 6 Collaborating Paediatric HIV centres early 2014

Initial Survey	
How many paediatric patients with HIV do you look after in your hospital?	
How many have started Antiretroviral therapy (ARVs) under 1 year of age?	
Of these, how many have had a HIV antibody test after the age of 2 years?	
Of these, How many patients have a negative antibody test?	
Of these, how many had an initially positive Antibody test < 1 year of age?	

- Royal Alexandra Children's Hospital, Brighton
- Great Ormond Street Hospital, London
- Heartlands Hospital, Birmingham
- Evelina Children's Hospital, London
- St George's Hospital, London
- St Mary's Hospital, London

Methods

- Anonymous data on patients with a negative HIV antibody test from the CHIPS database- April 2014
    - Basic demographics
    - Age at HIV diagnosis
    - Age of ART initiation
    - ART Regimen
    - Initial /Most recent VL
    - Initial/Most recent CD4 count
    - Opportunistic infections

- 2015: work in progress
    - Comparison of pts with negative and positive AB test

Results 1: Prevalence

Centre	No of patients	No pts tested	No negative Ab
1	9	9	1
2	115	105	4
3	103	103	3
4	56	56	2
5	115	15	1
Total	398	288	11

- 288 actually tested
    - all those who commenced ART < 2 years of age tested
- Prevalence=11/288= 3.8 % of tested
- Probable *total* prevalence= 11/398= 2.8%

Results 2: median age at diagnosis

Patient	Gender	Age at Diagnosis (years)	Initial VL (copies/mL)	Initial CD4 Count (cells/mm³)	Age at ARV initiation (years)	Number of ARVs Initiated	Time to Undetectable VL (years)	Current Age (years)	Current CD4 Count (cells/mm³)	Current VL (copies/mL)	Presentation at Diagnosis
1	M	0.25	148,302	280	0.32	4	0.84	8.87	780	<20	PCP
2	F	0.0	220	3129	0.0	3	0.27	2.00	2013	<20	NA
3	M	0.24	75,000	953	0.27	3	1.09	10.98	596	<40	CMV,FTT,PCP
4	M	0.0	27,000	550	0.38	3	1.37	13.58	958	<20	CMV,PCP
5	M	0.31	>500,000	60	0.37	4	1.30	12.14	1117	<40	CMV,PCP
6	F	0.25	>500,000	280	0.30	4	0.66	9.91	1106	<20	PCP
7	F	0.18	246	4900	0.23	4	0.85	14.25	1341	<50	CMV,PCP
8	M	0.19	>500,000	205	0.24	3	2.38	8.46	429	230	Pancytopenia, seizure,
9	F	0.00	2732	1532	0.0	3	0.50	8.05	1233	<20	NA
10	M	0.00	58	2421	0.0	3	0.84	2.64	1501	<40	NA
11	F	0.11	>500,000	1645	0.26	U	0.50	4.73	2240	<40	Ringworm

0.18

Results 2: median age at ART initiation

Patient	Gender	Age at Diagnosis (years)	Initial VL (copies/mL)	Initial CD4 Count (cells/mm³)	Age at ART initiation (years)	Number of ARVs Initiated	Time to Undetectable VL (years)	Current Age (years)	Current CD4 Count (cells/mm³)	Current VL (copies/mL)	Presentation at Diagnosis
1	M	0.25	148,302	280	0.32	4	0.84	8.87	780	<20	PCP
2	F	0.0	220	3129	0.0	3	0.27	2.00	2013	<20	NA
3	M	0.24	75,000	953	0.27	3	1.09	10.98	596	<40	CMV,FTT,PCP
4	M	0.0	27,000	550	0.38	3	1.37	13.58	958	<20	CMV,PCP
5	M	0.31	>500,000	60	0.37	4	1.30	12.14	1117	<40	CMV,PCP
6	F	0.25	>500,000	280	0.30	4	0.66	9.91	1106	<20	PCP
7	F	0.18	246	4900	0.23	4	0.85	14.25	1341	<50	CMV,PCP
8	M	0.19	>500,000	205	0.24	3	2.38	8.46	429	230	Pancytopenia, seizure,
9	F	0.00	2732	1532	0.0	3	0.50	8.05	1233	<20	NA
10	M	0.00	58	2421	0.0	3	0.84	2.64	1501	<40	NA
11	F	0.11	1,526,940	1645	0.26	U	0.50	4.73	2240	<40	Ringworm

0.26

Results 2: time to undetectable VL

Patient	Gender	Age at Diagnosis (years)	Initial VL (copies/mL)	Initial CD4 Count (cells/mm³)	Age at ARV initiation (years)	Number of ARVs Initiated	Time to Undetectable VL (years)	Current Age (years)	Current CD4 Count (cells/mm³)	Current VL (copies/mL)	Presentation at Diagnosis
1	M	0.25	148,302	280	0.32	4	0.84	8.87	780	<20	PCP
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3	M	0.24	75,000	953	0.27	3	1.09	10.98	596	<40	CMV,FTT,PCP
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5	M	0.31	>500,000	60	0.37	4	1.30	12.14	1117	<40	CMV,PCP
6	F	0.25	>500,000	280	0.30	4	0.66	9.91	1106	<20	PCP
7	F	0.18	246	4900	0.23	4	0.85	14.25	1341	<50	CMV,PCP
8	M	0.19	>500,000	205	0.24	3	2.38	8.46	429	230	Pancytopenia, seizure,
9	F	0.00	2732	1532	0.0	3	0.50	8.05	1233	<20	NA
10	M	0.00	58	2421	0.0	3	0.84	2.64	1501	<40	NA
11	F	0.11	1,526,940	1645	0.26	U	0.50	4.73	2240	<40	Ringworm

0.84

Results 2: current age and CD4 count

Patient	Gender	Age at Diagnosis (years)	Initial VL (copies/mL)	Initial CD4 Count (cells/mm³)	Age at ARV initiation (years)	Number of ARVs Initiated	Time to Undetectable VL (years)	Current Age (years)	Current CD4 Count (cells/mm³)	Current VL (copies/mL)	Presentation at Diagnosis
1	M	0.25	148,302	280	0.32	4	0.84	8.87	780	<20	PCP
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5	M	0.31	>500,000	60	0.37	4	1.30	12.14	1117	<40	CMV,PCP
6	F	0.25	>500,000	280	0.30	4	0.66	9.91	1106	<20	PCP
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9	F	0.00	2732	1532	0.0	3	0.50	8.05	1233	<20	NA
10	M	0.00	58	2421	0.0	3	0.84	2.64	1501	<40	NA
11	F	0.11	1,526,940	1645	0.26	U	0.50	4.73	2240	<40	Ringworm

8.87 1117

Results 2: prevalence in children starting ART < 6 months of age

- 11 seroreverted and 47 seropositive children who started ART < 6 months of age in the 5 centres
- Prevalence 11/58=19%

Centre	Ab neg	Ab pos	total
1	1	2	3
2	4	22	26
3	3	6	9
4	2	10	12
5	1	7	8
Total	11	47	58

Results 3: Impact on outcome?

Work in progress

Comparison of seroreverted vs seropositive children who started ART < 6 months of age in the 5 centres

- 9 antibody negative *vs.* 44 antibody positive
- NO difference in
  - Age/sex
  - most recent CD4
  - Viral suppression (all suppressed)

Discussion

- Seroreversion
  - Treatment factors
  - Host factors
  - Other

- Long term implications as children still young?

- Immunologically different?
  - ? HIV resevoirs
  - T cell function

- Counselling these children who will have a negative HIV test?

Conclusions

- Pilot study in 5 UK centres:
- Prevalence of seroreversion in children on ART< 6/12 is 19% (CI 10-31%)
- Seroreversion is associated with early initiation of ARVs

Brighton and Sussex University Hospitals NHS Trust

brighton and sussex medical school

Great Ormond Street Hospital

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CHIPS Collaborative HIV Paediatric Study

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the alex Children's Hospital

Birmingham Children's Hospital