

# Vertically acquired HIV diagnosed in adolescence and early adulthood in the United Kingdom and Ireland: findings from national surveillance

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## Objective

The aim of the study was to describe the characteristics of young people with vertically acquired HIV diagnosed aged  $\geq 13$  years.

## Methods

A retrospective review of HIV diagnoses reported to well-established national paediatric and adult HIV surveillance systems in the United Kingdom/Ireland was conducted.

## Results

Forty-two young people with vertically acquired HIV diagnosed aged  $\geq 13$  years were identified; 23 (55%) were female, 40 (95%) were black African and 36 (86%) were born in sub-Saharan Africa. The median age at HIV diagnosis was 14 years (range, 13–20 years). Half of the patients presented with symptoms; the remainder were screened for HIV following diagnosis of a relative. The median CD4 count at diagnosis was 210 cells/ $\mu$ L (range, 0–689 cells/ $\mu$ L), 12 patients (29%) were diagnosed with AIDS at HIV diagnosis or subsequently, and 34 (81%) started combination antiretroviral therapy (ART), most (31 of 34) within a year of diagnosis.

## Conclusion

A small number of young people with vertically acquired HIV survive childhood without ART and are diagnosed at age  $\geq 13$  years in the United Kingdom/Ireland. Half of the patients were asymptomatic, highlighting the importance of considering HIV testing for all offspring of HIV-infected women, regardless of age or symptoms. Increased awareness among clinicians and parents is required to reduce delayed presentation with advanced disease and to avoid onward transmission as these young people become sexually active.

**Keywords:** adolescence, late diagnosis, surveillance, UK & Ireland, vertical infection, young people

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## Introduction

Vertically acquired HIV diagnosed in adolescence or early adulthood has rarely been reported in the literature [1–3] and was previously assumed to be exceptional. However, although there are few good estimates of survival probabilities beyond 5 years, cohort data and modelling studies have suggested that at least 10% of untreated HIV-

infected infants, and possibly more, will reach adolescence [4,5].

Parents with HIV infection may be reluctant to test older, asymptomatic children as this would entail explanation of their own diagnosis [1,6]. Subsequent delay in diagnosis increases the likelihood of clinical complications, mortality (comparable to late presentation in horizontally infected adults) and risk of onward transmission of HIV [7–10].

In this report we describe the circumstances surrounding presentation to medical services and the clinical features of vertically infected young people diagnosed with HIV at 13 years of age or older in the United Kingdom or Ireland.

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## Methods

Young people with vertically acquired HIV diagnosed aged  $\geq 13$  years in the United Kingdom or Ireland were identified through routine paediatric and/or adult surveillance systems, and cases were cross-checked to remove duplicates. Individuals diagnosed in paediatric centres were identified through the National Study of HIV in Pregnancy and Childhood (NSHPC) and followed up in the Collaborative HIV Paediatric Study (CHIPS), which routinely collect mode of presentation and longitudinal data on infants born to HIV-infected women, and children presenting with HIV infection, in the United Kingdom or Ireland [11,12]; both studies have Multicentre Research Ethics Committee (MREC) approval. Data received by 1 October 2007 were used in this analysis. Additionally, young people were identified through the Health Protection Agency's (HPA) surveillance of new HIV diagnoses in the United Kingdom (diagnoses to end 2005, as reported to end 2006) and the 2005 annual Survey of Prevalent HIV Infections Diagnosed (England, Wales and Northern Ireland) [13]. The HPA is registered under Section 60 of the Health and Social Care Act 2001 and has approval from the Patient Information Advisory Group to handle data for purposes that include surveillance and the control of disease, even where specific patient consent has not been given. The HPA collects a more limited data set so supplementary data were collected for these individuals through case note review, with written agreement from reporting clinicians.

Route of transmission was determined by the reporting clinician, usually on the basis of history of maternal infection. In situations where the mother's status was unobtainable, and in the absence of identifiable risk factors for alternative routes of transmission, supportive data from family history (e.g. HIV-related deaths of family members) and medical history in early childhood (e.g. chronic lung disease with or without evidence of lymphocytic interstitial pneumonitis, herpes zoster, chronic parotitis, growth failure and delayed puberty) were regarded as highly suggestive of vertical infection in a young person. Reports received by the HPA where there was a questionable transmission category were further followed up with the reporting site as an additional check. Reports where the transmission route remained unclear were excluded from the analysis.

A common data set included demographic characteristics, date of arrival and of HIV diagnosis in the United Kingdom or Ireland, clinical status and CD4 cell count at diagnosis, and timing of combination antiretroviral therapy (ART). In addition, data on reason for HIV testing and clinical status were available for young people in paediatric centres. Descriptive statistics were generated using STATA 10 (StataCorp LP, College Station, TX, USA).

## Results

Forty-two vertically infected young people were identified as having been diagnosed with HIV infection aged  $\geq 13$  years, 36 (86%) in paediatric centres and six (14%) in adult

**Table 1** Characteristics of vertically HIV-infected young people diagnosed in the United Kingdom or Ireland aged  $\geq 13$  years ( $n = 42$ )\*

Characteristic	<i>n</i> (%) unless otherwise stated
Reported to	
Paediatric surveillance system	36 (86%)
Adult surveillance system (after removing duplicates; see Methods)	6 (14%)
Sex	
Female	23 (55%)
Male	19 (45%)
Ethnicity	
Black African	40 (95%)
Mixed	2 (5%)
Country of birth	
United Kingdom/Ireland	6 (14%)
Sub-Saharan Africa	36 (86%)
Age at arrival in the United Kingdom or Ireland for those born abroad (years)	
Median (range)	12 (1–16)
Interval between arrival and diagnosis (years)	
Median (range)	2 (0–13)
$\geq 5$ years	8 (32%) <sup>†</sup>
Age at HIV diagnosis (years)	
Median (range)	14 (13–20)
Reason for HIV test <sup>‡</sup>	
Symptomatic	
Non-class B/C	9 (25%)
Class B	5 (14%)
AIDS	4 (11%)
Diagnosis of relative	17 (47%)
Not known	1 (3%)
Mode of presentation (CDC classification)**	
Non-AIDS	33 (80%)
AIDS	8 (20%)
CD4 count at diagnosis (cells/ $\mu$ L)	
Median (range)	210 (0–689)
$< 200$ cells/ $\mu$ L	17 (47%)
ART status ever	
Naïve	8 (19%)
Initiated ART	34 (81%)
Interval between HIV diagnosis and starting ART (years)	
Median (range)	0.1 (0–3)
Clinical status ever <sup>‡</sup>	
Not or mildly symptomatic (CDC stage A)	19 (53%)
CDC stage B	9 (25%)
CDC stage C	8 (22%)
Died	0
Status at last follow-up	
Receiving care from paediatric or adult services	27 (64%)
Transferred from paediatric to adult services	12 (29%)
Left country/lost to follow-up	2 (5%)
Died	1 (2%)

\*Data are for young people attending paediatric services to the end of September 2007 and adult services to the end of 2005.

<sup>†</sup>Data missing for 11 participants.

<sup>‡</sup>Paediatric services only.

\*\*Mode of presentation missing for one young person.

ART, antiretroviral therapy; CDC, Centers for Disease Control and Prevention.

centres (see Table 1). The earliest year of diagnosis was 1998. Most (95%) were of black African ethnicity and just over half (55%) were female. The majority (86%) were born in sub-Saharan Africa, with a median age at arrival in the United Kingdom or Ireland of 12 years (range, 1–16 years); the median interval between arrival and diagnosis was 2 years (range, 0–13 years), and eight children were diagnosed  $\geq 5$  years after arrival.

Overall the median age at HIV diagnosis was 14 years (range, 13–20 years). Reasons for HIV testing were mainly HIV-related symptoms (50%) and diagnosis of a relative (47%). At diagnosis 17% had one or more AIDS-defining illness; these included cytomegalovirus (two patients), oesophageal candidiasis (three), tuberculosis (three), cryptosporidiosis (one) and *Pneumocystis carinii* pneumonia (one). The median CD4 count at diagnosis was 210 cells/ $\mu$ L (range, 0–689 cells/ $\mu$ L) and 47% had a CD4 count of  $< 200$  cells/ $\mu$ L. Four-fifths (81%) started combination ART within 3 years of HIV diagnosis. Of those not starting ART, one young person died of pulmonary tuberculosis shortly after diagnosis and the remainder all had CD4 counts of  $> 250$  cells/ $\mu$ L at diagnosis. At last follow-up, 93% were still receiving care in the United Kingdom or Ireland.

## Discussion

This report is the first to describe the clinical features and circumstances of new HIV diagnoses in vertically infected young people aged  $\geq 13$  years in the United Kingdom and Ireland. It combines data from both paediatric-specific and population-wide surveillance systems, giving as complete case ascertainment as possible. However, it is possible that we have slightly underestimated the number of vertically infected HIV-positive young people identified in adult services; teenagers diagnosed in adult centres may be incorrectly recorded as horizontally infected if it is assumed that they are too old to have survived perinatal infection. Furthermore, for this analysis surveillance data for adult services were only available for diagnoses made by the end of 2005 as reported to the end of 2006. Subsequent scrutiny of diagnoses made in adult services in 2006 and 2007, and comparison with cases reported to the paediatric system, suggest that up to 13 additional young people with vertically acquired infection were diagnosed in the United Kingdom between the ages of 16 and 20 years (B. Rice, personal communication, Health Protection Agency Centre for Infections, London; P. Tookey, personal communication, UCL Institute of Child Health, London). However, most of these young people were born abroad, and it is likely that some would have been diagnosed before arrival in the United Kingdom and thus excluded from our analysis.

In our study most of the young people were born abroad; the median interval between arrival in the United Kingdom or Ireland and diagnosis was 2 years, and eight children had arrived over 5 years previously. There may therefore have been missed opportunities for earlier diagnosis in some cases. As the databases used for analysis do not collect data on past medical history we were unable to ascertain whether this group of young people had previously been diagnosed with HIV-related or AIDS-defining illnesses before their HIV diagnosis in adolescence. Had this been the case there may have been further opportunities for earlier diagnosis. By the time they were diagnosed, the majority had advanced HIV disease: a fifth had already developed AIDS, nearly half were severely immune suppressed with CD4 counts of  $< 200$  cells/ $\mu$ L and most started ART shortly after diagnosis.

Our findings highlight the importance of considering HIV testing for all offspring of HIV-infected women, regardless of age or symptoms. Increased awareness among both healthcare professionals and HIV-positive parents is urgently required to reduce delay in HIV diagnosis, prevent presentation with advanced disease and reduce ongoing transmission as this population becomes sexually active [14].

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contributions from AJ and PAT. All authors contributed to the interpretation of the data, commented on the draft and approved the final version.

## References

- 1 Hay P, Majewska W, Railton J, Sharland M, Scullard G, Pakianathan M. Vertically transmitted HIV presenting in adulthood. Poster 14.1/1, *European AIDS Clinical Society Conference*, Warsaw, October 2003.
- 2 Español T, Figueras MC, Soriano V, Caragol I, Hernandez M, Bertran JM. Very late presentation of vertically transmitted HIV-1 infection. *Acta Paediatr* 1996; **85**: 755–757.
- 3 Richardson MP, Sharland M. Late diagnosis of paediatric HIV infection in south west London. *BMJ* 1998; **316**: 271–272.
- 4 The European Collaborative Study. Fluctuations in symptoms in human immunodeficiency virus-infected children: the first 10 years of life. *Pediatrics* 2001; **108**: 116–122.
- 5 Marston M, Zaba B, Salomon JA, Brahmbhatt H, Bagenda D. Estimating the net effect of HIV on child mortality in African populations affected by generalized HIV epidemics. *J AIDS* 2005; **38**: 219–227.
- 6 Eisenhut M, Sharma V, Kawsar M, Balachandran T. Knowledge of their children's HIV status in HIV-positive mothers attending a genitourinary medicine clinic in the UK. *HIV Med* 2008; **9**: 257–259.
- 7 Jerene D, Endale A, Hailu Y, Lindtjorn B. Predictors of early death in a cohort of Ethiopian patients treated with HAART. *BMC Infect Dis* 2006; **6**: 136.
- 8 Hogg RS, Yip B, Chan KJ *et al.* Rates of disease progression by baseline CD4 cell count and viral load after initiating triple-drug therapy. *JAMA* 2001; **286**: 2597–2599.
- 9 Bolton-Moore C, Mubiana-Mbewe M, Cantrell RA *et al.* Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia. *JAMA* 2007; **298**: 1888–1899.
- 10 Burns FM, Johnson AM, Nazroo J *et al.* Missed opportunities for earlier HIV diagnosis within primary and secondary healthcare settings in the UK. *AIDS* 2008; **22**: 115–122.
- 11 Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Trends in management and outcome of pregnancies in HIV-infected women in the UK and Ireland, 1990–2006. *Br J Obstet Gynaecol* 2008; **115**: 1078–1086.
- 12 Judd A, Doerholt K, Tookey PA *et al.* Morbidity, mortality, and response to treatment by children in the UK and Ireland with perinatally acquired HIV infection during 1996–2006: planning for teenage and adult care. *Clin Infect Dis* 2007; **45**: 918–924.
- 13 The UK Collaborative Group for HIV and STI Surveillance. *Testing Times – HIV and Other Sexually Transmitted Infections in the UK: 2007*. London: Health Protection Agency, Centre for Infections, 2007.
- 14 Chadborn TR, Delpech VC, Sabin CA, Sinka K, Evans BG. The late diagnosis and consequent short-term mortality of HIV-infected heterosexuals (England and Wales, 2000–2004). *AIDS* 2006; **20**: 2371–2379.