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Prevalence of Congenital Cardiovascular Malformations in Children of Human Immunodeficiency Virus-Infected Women: The Prospective P²C² HIV Multicenter Study

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Abstract

Objectives—The purpose of the study was to assess the effects of maternal HIV-1 (human immunodeficiency virus) infection and vertically transmitted HIV-1 infection on the prevalence of congenital cardiovascular malformations in children.

Background—In the United States, an estimated 7000 children are born to HIV-infected women annually. Previous limited reports have suggested an increase in the prevalence of congenital cardiovascular malformations in vertically transmitted HIV-infected children.

Methods—In a prospective longitudinal multicenter study, diagnostic echocardiograms were performed at 4–6-month intervals on two cohorts of children exposed to maternal HIV-1 infection: 1) a Neonatal Cohort of 90 HIV-infected, 449 HIV-uninfected and 19 HIV-indeterminate children; and 2) an Older HIV-Infected Cohort of 201 children with vertically transmitted HIV-1 infection recruited after 28 days of age.

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Results—In the Neonatal Cohort, 36 lesions were seen in 36 patients, yielding an overall congenital cardiovascular malformation prevalence of 6.5% (36/558), with a 8.9% (8/90) prevalence in HIV-infected children and a 5.6% (25/449) prevalence in HIV-uninfected children. Two children (2/558, 0.4%) had cyanotic lesions. In the Older HIV-Infected Cohort, there was a congenital cardiovascular malformation prevalence of 7.5% (15/201). The distribution of lesions did not differ significantly between the groups.

Conclusions—There was no statistically significant difference in congenital cardiovascular malformation prevalence in HIV-infected versus HIV-uninfected children born to HIV-infected women. With the use of early screening echocardiography, rates of congenital cardiovascular malformations in both the HIV-infected and HIV-uninfected children were five- to ten-fold higher than rates reported in population-based epidemiologic studies but not higher than in normal populations similarly screened. Potentially important subclinical congenital cardiovascular malformations were detected.

There has been a rapid rise in the number of women of child-bearing age infected with the human immunodeficiency virus type 1 (HIV-1) (1). In the United States, an estimated 7000 children are born to HIV-infected women annually, and mother-to-child transmission accounts for 95% of the reported AIDS cases in children under 4 years of age (2).

The association of vertically transmitted HIV-1 infection with left ventricular dysfunction and dilated cardiomyopathy has been well established in infants and children (3,4). However, the effect of maternal HIV-1 infection on the prevalence of congenital cardiovascular malformations is unknown. An abstract published in 1988 by Vogel and colleagues (5) reported a congenital cardiovascular malformation prevalence of 2.8% (5/175) in an uncontrolled study population of HIV-infected children. Three of the five patients required cardiac catheterization and surgery. That same year, the Italian Multicentre Study (6) reported a four-fold increase in the prevalence of congenital cardiovascular malformations in 165 HIV-infected children when compared to historical control data (2.4% vs. 0.6%).

The Prospective P²C² HIV Multicenter Study (P²C² HIV Study) was initiated to provide a systematic surveillance of *P*ediatric *P*ulmonary and *C*ardiovascular *C*omplications (P²C²) commonly seen in children exposed to maternal HIV-1 infection. The purpose of the present report was to examine the effects of maternal HIV-1 infection and vertically transmitted HIV-1 infection on the prevalence of congenital cardiovascular malformations in children born to HIV-infected women.

Methods

From May 1990 to January 1994, HIV-infected women and their children were recruited into the P²C² HIV Study at five clinical centers located in four major metropolitan areas. Studies evaluating the long-term effects of HIV-1 morbidity were performed in accordance with a protocol approved by the Institutional Review Board at each of the clinical centers. Informed consent to participate in the study was obtained from the appropriate family member of all patients. A detailed description of recruitment and retainment strategies for the P²C² HIV Study has been provided elsewhere (7).

The P²C² HIV Study recruited two study cohorts. The *Neonatal Cohort* (also referred to as group II in other P²C² publications) was composed of infants born to HIV-infected women enrolled during gestation or by 28 days after birth. A randomly selected group of HIV-uninfected children from this cohort was followed throughout the study as a comparison group (Neonatal Cohort/Comparison Group) for the HIV-infected children (Neonatal Cohort/HIV-Infected Group). The *Older HIV-Infected Cohort* (also referred to as group I in other P²C² publications) was composed of children enrolled at more than 28 days of age with documented vertically transmitted HIV-1 infection. This group was selected to provide information on the later stages of HIV-1 infection in childhood. Children who were classified as P-2, subclass E (cancer), at enrollment according to the 1987 Revised Centers for Disease Control Classification System were excluded from the study (8).

Maternal HIV-1 status was determined by antibody testing with an enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blot. The HIV-1 status of the infant was determined by viral culture upon recruitment, at 3 months, and at 6 months of age. An HIV-negative status was confirmed by antibody testing at a minimum of 15 months of age. Children who were lost to follow-up or died prior to confirmation of HIV-1 status were classified as HIV-indeterminate. Measurements of maternal CD4 lymphocyte number and percent were obtained at delivery in laboratories that used AIDS Clinical Trials Group quality assurance protocols.

Throughout the study, a screening physical examination was routinely performed by a P²C² nurse prior to each echocardiogram. The presence or absence of a murmur was recorded. From March 1994 to January 1997, the P²C² HIV Study protocol included physical examination findings of a pediatric cardiologist on all patients suspected of having a congenital cardiovascular malformation or congestive heart failure.

Diagnostic anatomical echocardiograms and left ventricular function and contractility analyses were performed according to the P²C² protocol at 10 designated noninvasive laboratories affiliated with the five participating clinical centers. Echocardiograms were performed upon enrollment into the study and at 4-month intervals prior to determination of HIV-infection status. Echocardiograms continued at 4-month intervals throughout the study for the HIV-infected children. Chloral hydrate was used for sedation in children under 3 years of age when necessary. Children who were determined to be HIV-negative subsequently obtained echocardiograms at 6-month intervals without sedation.

Echocardiograms were recorded on VHS or SVHS videotapes for subsequent review. The studies were supervised and reviewed by staff pediatric cardiologists at the clinical centers. The finding of a congenital cardiovascular malformation and its status on later studies were reported to a central data coordinating center. The persistence of a congenital cardiovascular malformation at 1 year of age was established by notation of the malformation on an echocardiogram at or beyond 1 year of age.

Several quality assessments were performed to ensure uniformity of quality and diagnostic capability of the echocardiograms. During the initial stages of the study, a random sample of 44 echocardiograms with normal and abnormal findings was collected for a blind review by

a P²C² cardiologist at another clinical center. Thereafter, only studies positive for a congenital cardiovascular malformation were routinely reviewed by a second P²C² cardiologist. After completion of the data collection phase, a subsequent blind review of 25 Neonatal Cohort studies with abnormal findings was performed by a single P²C² cardiologist (S.E.D.) to further refine the study diagnostic criteria for congenital cardiovascular malformations. There was agreement on the primary diagnosis in 21 of the 25 cases reviewed (84%). Based on this blind review and other quality assurance measures, the diagnostic criteria for congenital cardiovascular malformations were then modified to exclude transient right-sided flow lesions. There was agreement between the initial reading and blind review in all of the cases ultimately included in the primary rate calculations, excluding the diagnosis of patent foramen ovale.

Diagnostic criteria and excluded diagnoses

Standard diagnostic definitions were utilized for congenital cardiovascular malformations. In all cases, the diagnosis of a congenital cardiovascular malformation required verification of the lesion upon subsequent review by a P²C² cardiologist at the clinical center in which the study was performed. Structural lesions believed to be possibly normal stages of cardiovascular development were excluded from the primary calculations of congenital cardiovascular malformation prevalence: an atrial septal defect at less than 2 months of age, a patent ductus arteriosus at less than 2 months of age, and a patent foramen ovale at any age. After quality assurance review, transient right-sided flow abnormalities without a hemodynamically significant gradient (defined as a gradient of 10 mm Hg or greater) were also excluded. Only right-sided flow lesions that were identified on two or more echocardiograms, with at least one notation beyond 1 year of life, were included in the analyses.

Statistical analysis

The prevalence of congenital cardiovascular malformations was estimated as a proportion. Confidence intervals (CI 95%) were calculated for prevalence rates within each study cohort and by HIV-1 status within the Neonatal Cohort. The prevalence rates were compared between groups using a chi-square test or a Fisher exact test. Maternal CD4 lymphocyte count and percent were compared by the HIV-1 status of the child and separately by the congenital cardiovascular malformation status of the child using the Wilcoxon rank-sum test. Logistic regression was used to examine the joint association of HIV-1 status and congenital cardiovascular malformation status on the detection of a cardiac murmur.

Results

Patients

A total of 611 fetuses or live-born infants were enrolled in the Neonatal Cohort including 11 fetuses and 600 live births. Of the 600 live-born children, 558 had one or more echocardiograms (n = 90 HIV-positive, n = 449 HIV-negative, and n = 19 HIV-indeterminate) and formed the study population. Forty-two children had no echocardiograms, including 8 children who died (n = 2 HIV-positive and n = 6 HIV-indeterminate), 28 lost to follow-up (n = 1 HIV-positive, n = 8 HIV-negative, and n = 19

HIV-indeterminate), and 6 children randomized off study without having an echocardiogram (all HIV-negative). Two hundred sixteen HIV-uninfected children from 204 mothers were randomly selected to be followed as a comparison group (Neonatal Cohort/Comparison Group) from the HIV-negative infants.

Among the 558 infants from the Neonatal Cohort with one or more echocardiograms, 291 (52.2%) were male. Most of the infants were either black ($n = 282$, 50.5%) or Hispanic ($n = 175$, 31.4%). The demographic profiles of the HIV-infected and HIV-uninfected groups were similar. Among the 85 HIV-infected and 412 HIV-uninfected children who had two or more echocardiograms, the median number of echocardiograms completed in the first year of life was four and three, respectively.

There were a total of 205 children enrolled in the Older HIV-Infected Cohort. Among the 201 children with one or more echocardiograms, the median age at the time of enrollment was 23.0 months, with a range of 1.7 to 166.0 months. A majority of the 201 children were female ($n = 109$, 54.2%), and most were either black ($n = 88$, 43.8%) or Hispanic ($n = 79$, 39.3%). The gender and race characteristics of the Older HIV-Infected Cohort were not significantly different from the Neonatal Cohort.

Neonatal cohort/HIV-infected and comparison groups

The overall prevalence of congenital cardiovascular malformations was 6.5% (36/558) among children in the Neonatal Cohort with a median age at cardiovascular diagnosis of 102 days (Table 1). There was no statistically significant difference in the rates of congenital cardiovascular malformation prevalence obtained at the five clinical centers: Baylor (5.1%), Boston (9.6%), Mt. Sinai (8.3%), Presbyterian (3.7%), and UCLA (8.0%). There was no statistically significant difference detected in the congenital cardiovascular malformation prevalence among HIV-infected (8.9%) and HIV-uninfected (5.6%) children. The observed difference in congenital cardiovascular malformation prevalence rates between HIV-infected and HIV-uninfected children was 3.3% with a 95% CI of -3.0% to 9.5% . There was no statistically significant difference in the median age at first detection between the HIV-infected group and the HIV-uninfected group (29 vs. 107 days, $p = 0.42$).

Thirty-six congenital cardiovascular malformations were diagnosed in 36 children within the Neonatal Cohort (Table 2). The distribution of congenital cardiovascular malformations in HIV-infected versus HIV-uninfected children was similar, and rare or uncommon malformations were not identified at unexpectedly high rates (Tables 2 and 3). Only one case of patent ductus arteriosus was associated with prematurity. A number of normally subclinical congenital cardiovascular malformations, such as a bicuspid aortic valve without stenosis or regurgitation, a persistent left superior vena cava, and a small coronary arteriovenous fistula, were identified on the screening echocardiograms. These lesions comprised 6 out of the 36 congenital cardiovascular malformations detected (16.7%) in the Neonatal Cohort.

A heart murmur was noted on 24.2% (129/534) of children with a known HIV-1 status within the Neonatal Cohort. A murmur was more common among HIV-infected infants (35.6% vs. 21.9%, $p = 0.008$) and tended to be more frequent among infants with a

congenital cardiovascular malformation (39.4% vs. 23.2%, $p = 0.05$). Among the group of 36 Neonatal Cohort children with a congenital cardiovascular malformation, 14 (38.9%) had a murmur detected.

The two children with a cyanotic congenital cardiovascular malformation (2/558, 0.4%) underwent successful surgical repair. A patient with obstructed total anomalous pulmonary venous return was repaired at 2 days of age, and a patient with a ventricular septal defect and pulmonary stenosis was corrected at 3 years of age. No other child studied required cardiac catheterization or surgical intervention for a congenital cardiovascular malformation. Two children with a secundum atrial septal defect had evidence of right ventricular hypertrophy on electrocardiogram. Neither had evidence of persistent right ventricular volume overload on echocardiogram (as defined by diastolic septal flattening). In addition, no child with an isolated ventricular septal defect or patent ductus arteriosus had evidence of a hemodynamically significant left to right shunt on echocardiogram (as defined by left ventricular dilatation).

Persistence of a congenital cardiovascular malformation was documented on a follow-up echocardiogram in 56% (19/34) of children with a known HIV-1 status at 1 year of age (Table 3). There was a trend toward congenital cardiovascular malformation persistence in HIV-infected (6/85, 7.1%) versus HIV-uninfected children (13/412, 3.2%; $p = 0.11$).

Congenital cardiovascular malformation status of the child did not correlate with severity of maternal HIV-1 infection as measured by CD4 cell count. There was no significant difference in median values of maternal CD4 number and percent between the children with a congenital cardiovascular malformation ($n = 29$, 484 cells/mm³ and 29%) versus the control group children ($n = 454$, 423 cells/mm³ and 27%).

Older HIV-infected cohort

The prevalence of congenital cardiovascular malformations in the Older HIV-Infected Cohort was 7.5% (95% CI 4.2%, 12.0%). Sixteen lesions were diagnosed in 15 children (Table 4). Median age at the time of diagnosis was 16.8 months. The congenital cardiovascular malformation prevalence was similar in the Older HIV-Infected Cohort and the Neonatal Cohort/HIV-Infected Group (7.5% and 8.9%, respectively). There was also no statistically significant difference in the prevalence of congenital cardiovascular malformations between children in the Older HIV-Infected Cohort and the Neonatal Cohort as a whole.

Patent foramen ovale

A patent foramen ovale was seen after 1 year of age in 13 children within the Neonatal Cohort (13/534, 2.4%). Two of the 13 children were HIV-infected, and 11 were HIV-uninfected. A patent foramen ovale was seen after 1 year of age in 10 children within the Older HIV-Infected Cohort (10/201, 5.0%). The inclusion of patent foramen ovale in the calculations of congenital cardiovascular malformation prevalence did not result in any statistically significant increases (Table 5). Three infants in the Neonatal Cohort had a patent foramen ovale in addition to another congenital cardiovascular malformation, resulting in 49 lesions among 46 infants.

Discussion

Effect of maternal HIV-1 infection

Development within the uterine environment of an HIV-infected woman may have untoward effects on fetal cardiac development regardless of the status of HIV-1 transmission to the fetus. As previously published, self-reported rates of maternal illicit drug use, smoking and alcohol consumption were high in our study population, but the rates were similar in mothers of HIV-infected and mothers of HIV-uninfected children (9).

The congenital cardiovascular malformation prevalence in both the Neonatal Cohort and the Older HIV-Infected Cohort was five- to ten-fold higher than the 0.4% to 1.4% prevalence reported in population-based epidemiologic studies (10–14). The children in either P²C² study cohort underwent multiple echocardiographic examinations that yielded a high rate of structural lesions. Of the patients with a congenital cardiovascular malformation, <40% had a murmur detected. Many of these lesions would not have been reported in population-based studies in which cases were primarily identified after referral for evaluation of a murmur or for clinical evidence of congestive heart failure.

Several reports describe the prevalence of congenital cardiovascular malformations based on screening echocardiography at an early age. Ooshima and colleagues (15) examined 502 consecutive neonates and discovered 19 cases (3.8%) of congenital cardiovascular malformations: 10 ventricular septal defect (2.0%), 4 atrial septal defect (0.8%), 2 pulmonary stenosis (0.4%), and 1 each of aortic stenosis, endocardial cushion defect and tricuspid regurgitation (0.2%). During the first 12 months, 8 of 10 ventricular septal defects and all 4 atrial septal defects closed spontaneously, giving a 1.0% prevalence of congenital cardiovascular malformations at 1 year. Hirashi and colleagues (16) reported a 2.0% prevalence of muscular ventricular septal defect in a cohort of 1028 newborns with a 76% spontaneous closure rate by 1 year of age. A murmur was present in 42% of the patients at the time of initial echocardiographic examination. Roguin and colleagues (17) reported a 5.3% prevalence of muscular ventricular septal defect in 1053 newborns with an 89% spontaneous closure rate by 10 months of age. Only 11% of the patients had clinical evidence of a ventricular septal defect at the time of echocardiographic diagnosis.

In our Neonatal Cohort, children of HIV-infected women, 9 of the 12 ventricular septal defects were muscular in location (including a patient with a ventricular septal defect and pulmonary stenosis), yielding a 1.6% prevalence of muscular ventricular septal defect. There was a 1.3% prevalence of secundum atrial septal defect. Both of these rates are comparable to the available normal population data as determined by early screening echocardiography.

Because of the high rate of early spontaneous resolution of certain lesions, the timing of echocardiographic screening may affect the number of congenital cardiovascular malformations detected. Spontaneous closure of an atrial septal defect (18,19) or a ventricular septal defect (15–17) within the first several years of life has been well documented in a large percentage of patients. In contrast, spontaneous closure of a patent ductus arteriosus after 3 months of age is rare (20,21). To date, there are no studies describing the course of a trivial patent ductus arteriosus using serial echocardiography.

Effect of vertically transmitted HIV-infection

In contrast to earlier limited reports (5,6), the prevalence of congenital cardiovascular malformations was not significantly different between HIV-infected (8.9%) and HIV-uninfected (5.6%) children. With sample sizes available, this study had over 80% statistical power to detect differences in the prevalence of congenital cardiovascular malformations of 6% in HIV-uninfected children versus 16% in HIV-infected children (significance level = 0.05, one-sided). The power of the study to detect statistically significant differences was somewhat diminished because of a lower than originally anticipated vertical transmission rate of 16.7% for the Neonatal Cohort.

It is likely that HIV-1 infection in a substantial percentage of vertically transmitted cases occurs after the completion of cardiac development at 6 to 8 weeks of fetal age (8 to 10 weeks' gestational age). Studies on children indicate that a majority of vertically transmitted cases occurs either late in pregnancy or during the perinatal period (22,23).

The HIV-infection status of the child did not correlate with maternal lymphocyte subsets (CD4 cell count and percent). More detailed analyses of immunologic characteristics associated with mother–infant HIV-1 transmission are provided elsewhere (24). Recent advances in the understanding of vertical HIV-1 infection have yielded additional tools for the study of the mother, fetus and infant exposed to HIV-1 that were not available at the onset of the P²C² HIV Study.

Subclinical cardiovascular malformations and patent foramen ovale

Because of their potential long-term clinical impact, subclinical lesions, defined as uniformly silent lesions, were included in the P²C² analyses of congenital cardiovascular malformation prevalence. The subclinical lesions seen in the Neonatal Cohort were bicuspid aortic valve without stenosis or regurgitation, persistent left superior vena cava and coronary arteriovenous fistula. These subclinical lesions accounted for 6 of the 36 lesions diagnosed (16.7%) and 5 of the 18 lesions that persisted at 1 year of age (27.8%) in the Neonatal Cohort.

The fate of a small coronary arteriovenous fistula diagnosed in childhood is not established. The incidence of small coronary arteriovenous fistulae is not insignificant in adult populations (0.02% to 2.1%) (25–27), with an incidence of 0.18% reported in the largest series (25). Small coronary arteriovenous fistulae, such as the three identified in our Neonatal Cohort, are usually clinically silent with no accompanying murmurs or symptoms (28,29).

Diagnosis of a patent foramen ovale on a screening echocardiogram is of potential clinical importance because of its possible association with cerebral and peripheral embolic events (30). Because of its high prevalence in normal patients, however, the diagnosis of a patent foramen ovale was not included in the primary analyses of congenital cardiovascular malformation prevalence in the P²C² study.

Study limitations

The study examined only the rates of congenital cardiovascular malformations in live-born children and did not address the rate and potential causes of fetal loss secondary to HIV-1 infection. Potentially, there may have been additional cases of congenital cardiovascular malformations that were not included in the study due to fetal demise.

Conventional clinical diagnostic criteria were utilized for the diagnosis of structural lesions. By several quality control measures, there was good agreement on the diagnosis of major and minor congenital cardiovascular malformations. The lack of uniform criteria for the diagnosis of congenital cardiovascular malformations could not be corrected retrospectively because imaging studies were not directed at the identification or exclusion of all minor structural lesions. Based on the quality control assessment, it is reasonably anticipated that any bias inherent in the study owing to diagnostic criteria would have been evenly divided between HIV-infected and HIV-uninfected children. The unique feature of this report relates to the comprehensive echocardiographic evaluation and follow-up of large cohorts of HIV-infected and HIV-uninfected children of HIV-infected women.

Conclusions

In a prospective study of children born to HIV-infected women, there was no statistically significant difference in the prevalence of congenital cardiovascular malformations in HIV-infected versus HIV-uninfected children. Rates of congenital cardiovascular malformations in both the HIV-infected and HIV-uninfected children, as determined by early screening echocardiography, were five- to ten-fold higher than rates reported in population-based epidemiologic studies but not higher than in normal populations similarly screened. The use of echocardiography as the method of case detection and the timing of screening were important in comparisons of congenital cardiovascular malformation prevalence. Potentially important subclinical congenital cardiovascular malformations were detected by screening echocardiography, but both their natural history and impact on the clinical course of children exposed to maternal HIV-1 infection are unknown.

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Appendix

A partial listing of participants in the P²C² HIV Study is listed below. For a full list, see ref. 7.

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Abbreviations and Acronyms

HIV	human immunodeficiency virus
P²C²	pediatric pulmonary and cardiac complications

Table 1
Prevalence of Congenital Cardiovascular Malformations (CCM) in Infants (Neonatal Cohort) of HIV-Infected Mothers

Group	No. Infants	No. CCM	%	95% CI	Median Age CCM Identified (days)
HIV-infected	90	8	8.9	3.9%, 16.8%	29
HIV-uninfected	449	25	5.6	3.6%, 8.1%	107
HIV-indeterminate	19	3	15.8	3.4%, 39.6%	64
HIV-infected and HIV-uninfected	539	33	6.1	4.3%, 8.5%	105
All infants	558	36	6.5	4.6%, 8.8%	102

Patent ductus arteriosus (PDA) and atrial septal defect (ASD) in infants <2 months of age, right-sided lesions that did not persist, and all patent foramen ovale (PFOs) were excluded.

Table 2
Summary of All Congenital Cardiovascular Malformations (CCM) Among 558 Infants
From the Neonatal Cohort

CCM	Frequency	%
Cyanotic Lesions		
Total anomalous pulmonary venous return	1	0.2
Ventricular septal defect and valvar pulmonary stenosis	1	0.2
Shunt Lesions		
Secundum atrial septal defect	7	1.3
Ventricular septal defect	11	2.0
Patent ductus arteriosus	9	1.6
Right-sided Lesions		
Supravalvar pulmonary stenosis	1	0.2
Left-sided Lesions		
Bicuspid aortic valve	2	0.4
Miscellaneous Lesions		
Persistent left superior vena cava	1	0.2
Coronary arteriovenous fistula	3	0.5
Total	36	6.5

Table 3
Prevalence of Congenital Cardiovascular Malformations (CCM) and Lesion Status at One Year of Age Among the Neonatal Cohort

CCM	HIV-Infected (n = 90)			Follow-up HIV-Infected (n = 85)			HIV-Uninfected (n = 449)			Follow-up HIV-Uninfected (n = 412)		
	No. Infants	%		Persisted	Resolved	Unknown	No. Infants	%		Persisted	Resolved	Unknown
Cyanotic lesion	1	1.1		1			1	0.2		1		
Secundum atrial septal defect	2	2.2		1	1		5	1.1		3	2	
Ventricular septal defect	3	3.3		2	1		8	1.8		1	6	1
Patent ductus arteriosus*	1	1.1		1			5	1.1		3	1	1
Supravalvar pulmonary stenosis	1	1.1		1			0					
Bicuspid aortic valve	0						2	0.5		2		
Persistent left superior vena cava	0						1	0.2		1		
Coronary arteriovenous fistula	0						3	0.7		2	1	
No. infants and percent	8	8.9		6/85	2/85	0/85	25	5.6		13/412	10/412	2/412
				7.1%	2.4%	0.0%				3.2%	2.4%	0.5%

* Each of the three HIV indeterminate infants with a CCM had a patent ductus arteriosus.

Table 4
Summary of All Congenital Cardiovascular Malformations (CCM) Among 201 Infants
From the Older HIV-Infected Cohort

Abnormality	Frequency	%
Shunt Lesions		
Secundum atrial septal defect	4	2.0
Ventricular septal defect	1	0.5
Patent ductus arteriosus	2	1.0
Right-sided Lesions		
Tricuspid valve prolapse	1	0.5
Valvar pulmonary stenosis	1	0.5
Left-sided Lesions		
Mitral valve prolapse	5	2.5
Subaortic stenosis	1	0.5
Miscellaneous Lesions		
Single coronary artery system	1	0.5
Total	15*	7.5%*

* Sixteen lesions in 15 infants and children.

Table 5
Prevalence of Congenital Cardiovascular Malformations (CCM) Among the Neonatal Cohort Including Patent Foramen Ovale in Children Over One Year of Age

Group	No. Infants	No. CCM	%
HIV-infected	90	9	10.0
HIV-uninfected	449	34	7.6
HIV-indeterminate	19	3	15.8
All infants	558	46*	8.2

PDA and ASD in infants <2 months of age, right-sided lesions that did not persist, and PFOs in children less than 1 year were excluded.

* Three infants had a PFO plus an additional lesion resulting in 49 lesions among 46 infants.