



Figure 1 Scatter diagram and regression line (with 95% prediction interval) obtained from measurements of CD4 count and CD4% in 512 HIV-infected adults in Abidjan, Côte d'Ivoire, 1996–1997

Correlation coefficient between CD4 cell count and CD4% : $r = 0.88$
 Regression equation between CD4 cell count (dependent variable) and CD4% (independent variable):
 $(\text{CD4 count}) = -12.06 + 22.87 (\text{CD4}\%)$.
 Standard error of the slope : 0.56 $P < 0.0001$

(Coulter JT2, Coultronics, Paris, France). Our laboratory benefits from international programmes of haematology and flow cytometry quality control (College of American Pathologists, UKNEQAS and QASI programmes). As of December 1997, 512 patients were included in the cohort. Their mean age was 33 years, and the male:female ratio was 0.71:1. At inclusion, 182 (38%), 266 (56%) and 30 (6%) patients, respectively, were at stage 2, 3 and 4 of the WHO staging system for HIV infection.³

Parental age gap and child sex ratio—Fact or fiction?

From HELINÄ HAKKO, PIRKKO RÄSÄNEN, MARJO-RIITTA JÄRVELIN and JARI TIIHONEN

A recent report in *Nature* stated that the parental age gap predicted the sex of the first-born. An excess of sons was found in these couples where the husband was older than the wife.¹ However, this finding was not confirmed in three replications.²

We studied the finding by Manning *et al.*¹ using the Northern Finland Birth Cohort 1966 database, a genetically homogeneous population, in which information about the biological, socio-economic, environmental and health conditions have been collected from mid-pregnancy up to the age of 28 years.³ Only single births and infants of gestational age of 38–42 weeks were included in the present study ($n = 8712$). Logistic regression analysis was selected as the statistical method to assess the probability of having a male infant.

Figure 1 represents the scattergram and the regression line resulting from the analysis of the 512 CD4 measurements performed at inclusion. Based on the regression equation, 5%, 10%, 15%, 20% and 30% of CD4 cells correspond to an estimated CD4 absolute count of 102, 217, 331, 446 and 674 cells, respectively. These counts are about 50% higher than those resulting from the analysis of Yu.

In our previous study comparing CD4 measures in Africa and in Europe, the observed difference in CD4 count was related to a significantly higher total lymphocyte count in African subjects than in European ones. Although some African HIV-adults have long been known to present a relative hyperlymphocytosis due to absolute neutropenia, to our knowledge increased lymphocyte absolute count in African HIV+ patients have previously never been described. Further studies are needed in Africa to confirm this finding, and to understand better the underlying mechanisms. In between, our observations may help to adopt threshold values of CD4 cells when establishing clinical guidelines for prevention of opportunistic infections and antiretroviral treatments in African settings, as recently discussed at the 1997 African AIDS conference.⁴

References

- 1 Yu LM, Easterbrook P, Marshall T. Relationship between CD4 count and CD4% in HIV-infected people. *Int J Epidemiol* 1997;26:1367–72.
- 2 Anglaret X, Diagbouga S, Mortier E *et al.* CD4+ T-lymphocyte counts in HIV infection: Are European standards applicable to African patients? *J Acquir Immune Defic Syndr Hum Retrovirol* 1997;14:361–67.
- 3 The WHO International Collaborating Group for the Study of the WHO staging system. Proposed 'World Health Organization staging system for HIV infection and disease': preliminary testing by an international collaborative cross-sectional study. *AIDS* 1993;7:1711–18.
- 4 Agence Nationale de Recherches sur le SIDA (ANRS). *International Initiative: Place of antiretroviral drugs in the management of HIV infection in sub-Saharan Africa*. Paris: ANRS, 1997, pp.65.

The independent variables used were the parental age gap (exact age of wife subtracted from the exact age of husband) and the age of the mother at the infant's birth. The age gap was categorized as follows; D_0 = parental age gap between -1 and 1 year = no parental age gap, D_1 = husband 1–3 years older, D_2 = husband 3–6 years older, D_3 = husband ≥ 6 years and D_4 = wife > 1 year older than husband. As possible confounders, the following psychosocial variables were included in the statistical analysis: family's socioeconomic status (low/high/farmer), family type (two parent/single parent family), dwelling place (urban/rural), season of birth (spring = March–May/summer = June–August/autumn = September–November/winter = December–February). A more detailed description of the material and variables has been reported in earlier studies.^{4,5} Three logistic regression analyses were performed separately concerning first-borns only, 2nd and 3rd-borns together, and 4th- and later-borns together.

Table 1 Results of three logistic regression analysis for predicting the probability of male birth by mother's age and parental age gap after adjusting for socio-demographic characteristics of the family and season of birth in the Northern Finland 1966 Birth Cohort^a

Variable	First-borns (n = 2677) OR (95% CI)	2nd-3rd borns (n = 3624) OR (95% CI)	4th or later borns (n = 2411) OR (95% CI)
Age variables for parents			
<i>Age of mother (years)</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
<i>Parental age gap^b</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
No age gap (reference group)	1.00	1.00	1.00
1-3 years	1.00 (0.80-1.26)	1.12 (0.92-1.38)	1.04 (0.83-1.30)
3-6 years	0.91 (0.75-1.14)	1.06 (0.87-1.30)	1.08 (0.85-1.39)
>6 years	0.86 (0.67-1.11)	0.91 (0.73-1.14)	0.95 (0.73-1.23)
-1 year	0.97 (0.73-1.29)	0.96 (0.76-1.22)	1.19 (0.89-1.60)
Socio-demographic characteristics of family at child's birth			
<i>Social class</i>	<i>ns</i>	<i>ns</i>	<i>ns</i>
Low (reference group)	1.00	1.00	1.00
High	0.96 (0.80-1.15)	0.97 (0.83-1.12)	1.08 (0.86-1.34)
Farmer	0.98 (0.75-1.27)	0.85 (0.69-1.04)	1.00 (0.82-1.21)
<i>Family structure</i>	<i>ns</i>	<i>ns</i>	<i>0.05</i>
Two-parent family (reference group)	1.00	1.00	1.00
Single-parent family	1.01 (0.82-1.25)	1.05 (0.87-1.27)	0.81 (0.65-1.00)
<i>Dwelling place</i>	<i>ns</i>	<i>0.05</i>	<i>ns</i>
Rural (reference group)	1.00	1.00	0.01
Urban	0.97 (0.82-1.14)	0.87 (0.75-1.00)	1.24 (0.99-1.54)
Timing of birth			
<i>Season/quarter year</i>	<i>0.05</i>	<i>ns</i>	<i>ns</i>
Winter (reference group)	1.00	1.00	1.00
Spring	1.16 (0.93-1.43)	0.96 (0.80-1.15)	0.90 (0.72-1.12)
Summer	0.85 (0.69-1.07)	1.02 (0.85-1.24)	0.92 (0.74-1.16)
Autumn	1.01 (0.81-1.26)	1.07 (0.89-1.30)	0.92 (0.73-1.16)

^a The *P*-value of difference of deviations test to confirm the variable as a contributing factor of a male birth is shown in bold italics.

^b The exact age of wife subtracted from the exact age of husband.

The results (Table 1) showed that the probability of having a male first-born baby was not significantly related to the parental age gap. In fact, we observed a slight decrease in male first-borns as the parental age gap increased. Psychosocial factors were not related to the sex of the first-borns. Interestingly, there was a significant seasonal effect, showing a spring excess and a summer trough in births of male first-borns.

For the 2nd and 3rd-borns, we found a significant trough of male births, if the mother's dwelling place was in an urban area. For the 4th and later-borns, the probability of having a male infant decreased significantly, if the mother was the only parent in the family. Parental age gap, mother's age and season of birth had no influence on sex ratio in any of the later-borns. The logistic regression analyses were also repeated with the same categorization of parental age gap as used by Manning *et al.*¹ The results, however, remained unaltered.

Neither our study or previous replications² of the study by Manning *et al.* showed an excess of male first-borns among young women and older men. Compared with other replications, our study was performed in a large-scale, prospective and genetically homogeneous study sample and also included a more adequate categorization of parental age gap and adjustment for

confounders in a sophisticated statistical method. In particular it is essential to include confounding factors in the statistical analysis before one can obtain any evidence for a direct association between parental age gap and the sex of the child. However, further studies are needed in other populations and also with different combinations of socio-cultural, biological and climatic factors in order to estimate the scientific value of this phenomenon.

References

- Manning JT, Anderton RH, Shutt M. Parental age gap skews child sex ratio. *Nature* 1997;389:344.
- Arnold F, Rutstein S, James Wh, Boklage CE. Sex ratio unaffected by parental age gap. *Nature* 1997;390:242-43.
- Rantakallio P. The longitudinal study of the Northern Finland birth cohort of 1966. *Pediatr Perinat Epidemiol* 1988;2:59-88.
- Mäkikyrö T, Isohanni M, Moring J *et al.* Is a child's risk of early onset schizophrenia increased in the highest social class? *Schizophr Res* 1997; 23:245-52.
- Moiilanen I, Rantakallio P. The single parent family and the child's mental health. *Soc Sci Med* 1988;27:181-86.