Immunological markers in HIV-infected pregnant women

The European Collaborative Study* and the Swiss HIV Pregnancy Cohort

Objective: To examine immunological markers in HIV-infected pregnant women.

Design: Women enrolled in the European Collaborative Study and the Swiss HIV Pregnancy Cohort were followed throughout pregnancy according to similar clinical and immunological protocols. Information was recorded at various times during pregnancy and, in some centres, also 6 weeks and 6 months post-partum.

Method: Locally-weighted linear regression analysis was used to investigate changes in markers of cellular and humoral immune function during pregnancy and immediately post-partum, taking into account the serial measurement data structure. Women who received zidovudine during pregnancy were excluded.

Results: Four hundred and thirty-eight women had two or more measurements during pregnancy or within 6 months of delivery. Twenty-four per cent (106) of the women reported injecting drugs during pregnancy. Mean CD4 and CD8 cell counts declined to a low level 6 months before delivery, increased gradually until delivery and rose sharply to a peak level 3 months post-partum. In contrast, CD4 and CD8 percentages were stable during pregnancy, and increased slightly thereafter. The same pattern was evident for transmitting women, those delivered by Cesarean section, and women who injected drugs during pregnancy, and there was no evidence for an association with immunosuppression. Total immunoglobulin (Ig) G levels declined gradually throughout pregnancy until delivery, and increased in the 6 month post-partum period. Total IgM and IgA levels remained stable throughout pregnancy.

Conclusions: These findings suggest that pregnancy does not accelerate HIV progression, but in view of the intrinsic variability in serial CD4 counts, caution should be exercised when assessing changes in immunological markers in individual pregnant women.

AIDS 1997, **11**:1859–1865

Keywords: HIV, pregnancy, immunological markers, Europe

Introduction

It has been speculated that pregnancy in an HIV-infected woman may accelerate the progression of immunosuppression. Pregnancy has been shown to be associated with altered immunity in both laboratory and clinical studies [1–3], which could enhance the immunosupression associated with HIV infection [1,4]. However, little information is available about the patterns of markers of immune function during pregnancy, and reported studies have been based on small numbers of women [5–7]. Observed changes during pregnancy

*Prepared by: M-L. Newell, C. Rudin†, D. Dunn and C. Peckham, from the European Collaborative Study Coordinating Centre, Department of Epidemiology and Biostatistics, Institute of Child Health, London, UK and the †University's Children's Hospital, Basel, Switzerland. See Appendix for list of collaborators.

Sponsorship: The Swiss HIV and Pregnancy study was supported by the Federal Office of Health (grant no. 90-7001 and 93-7131). European Collaborative Study Coordinating Centre support was from the UK Medical Research Council (MRC); collaborating centres received grants from the Ministero della Sanita/Instituto Superiore di Sanita, progretto AIDS 1995-96 (Padua, Genoa), the UK MRC, the AIDS Virus Education Research Trust, the Scottish Office Home and Health Department (Edinburgh), Praeventie-fonds no. 28-1704 (Amsterdam), Bundesminister für Gesundheit (Berlin), Fonds de la Recherche Scientifique Medicale (Brussels) and the Swedish MRC (Stockholm).

Note: The European Collaborative Study is a concerted action of the European Commission.

Requests for reprints to: Dr Marie-Louise Newell, Department of Epidemiology, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK.

Date of receipt: 13 May 1997; revised: 4 August 1997; accepted: 7 August 1997.

 ISSN 0269-9370

could also be associated with the effect of injecting drugs [8], and any analysis of trends of immune function markers over time needs to allow for maternal characteristics, such as clinical status and drug use.

In this paper, trends in lymphocyte subsets and immunoglobulins, as markers of immune function, are analysed over the course of the pregnancy and immediately post-partum, based on zidovudine-naive HIV-infected women enrolled in the European Collaborative Study (ECS) and the Swiss HIV Pregnancy Cohort (SHPC).

Methods

The ECS was set up in 1986 to estimate the risk of vertical transmission of HIV infection and the natural history of paediatric infection [9]. Currently the ECS includes 21 centres in seven European countries. The SHPC was established in 1990 [10,11], to complement the Swiss perinatal cohort [12] and the Swiss HIV Cohort Study [13]. In both studies similar protocols are used and clinical and immunological information is recorded at various times during pregnancy. In some centres information was also collected 6 weeks and 6 months post-partum.

The analysis excluded 109 women who had received zidovudine treatment during pregnancy. Most of these women were enrolled between early 1989 and late 1994, before the introduction of zidovudine treatment to reduce vertical transmission [14], and had more advanced HIV disease, as evidenced by their lower CD4 count.

Although in the ECS CD4 and CD8 counts were determined locally [15], and in the SHPC in three reference centres [10], centre differences were minimal when the methods were compared in healthy antibody-negative children [15]. Immunoglobulins were determined locally using an immunoturbidometric method, according to the manufacturer's instructions.

Statistical methods

Immunological measurements were analysed relative to the date of delivery, because women with low CD4 cell counts tend to deliver earlier than those with CD4 counts above 200 cells $\times 10^6$/l [9]. Locally-weighted linear regression analysis [16] was used to investigate changes in the mean value of each immunological parameter during pregnancy and in the post-partum period. The smallest band width that did not give rise to an excessive number of turning points (30 days) was selected. The analysis took into account the serial measurement data structure, but this model makes no assumption about how parameters change over pregnancy. This model only includes women with two or more measurements at any point during or after pregnancy, as women with a single measurement provide no information on immunological changes.

Results

The analysis is based on a total of 438 women with two or more immunological measurements during pregnancy or within 6 months of delivery. Three hundred and forty-two (342, 78%) women were white and of European origin, and 106 (24%) reported injecting drugs during pregnancy.

Cellular immunity

A total of 1115 measurements of CD4 lymphocyte counts were available for 414 women (Fig. 1). Fewer measurements were taken in the first trimester of pregnancy than in the second and third trimester, and many were concentrated near the time of delivery. The post-partum measurements reflected the timing of the scheduled visits: about 6 weeks, 3 and 6 months after delivery.

Figure 2 shows mean CD4 cell counts relative to the date of delivery. The mean CD4 cell count declined during the first trimester of pregnancy to its lowest level 6 months before delivery. Subsequently it increased gradually until delivery, and then rose sharply to a peak level at around 3 months post-partum. Thereafter the CD4 counts declined gradually to reach baseline levels by 6 months post-partum. The pattern of CD8 counts over time was similar to that of the CD4 counts (Fig. 3).

In contrast to the CD4 cell count, the CD4 percentage was stable during pregnancy, at about 28%, and there

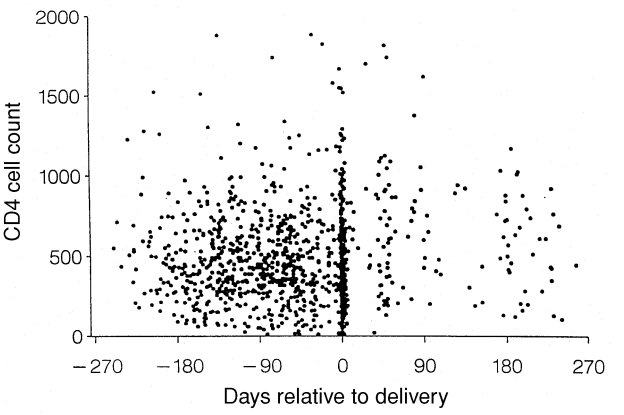

Fig. 1. Timing of CD4 cell count measurements.

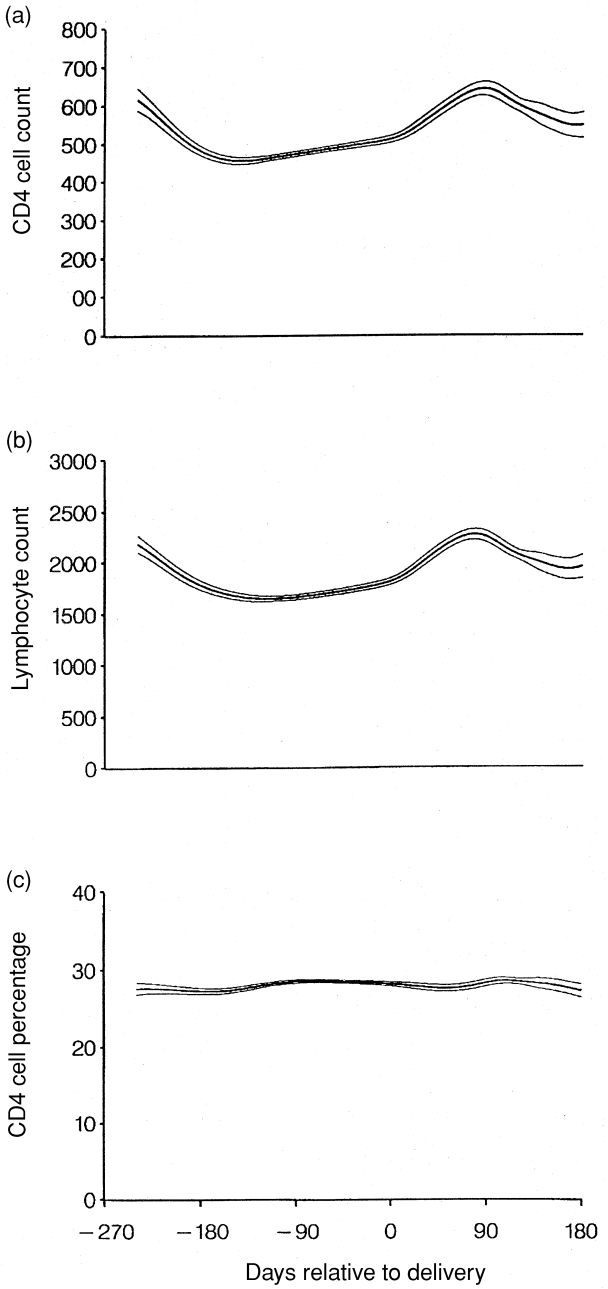

Fig. 2. Pattern of CD4 cell count (top panel), absolute lymphocyte count (middle panel) and CD4 cell percentage during pregnancy and up to 6 months post-partum. Mean with 95% confidence interval.

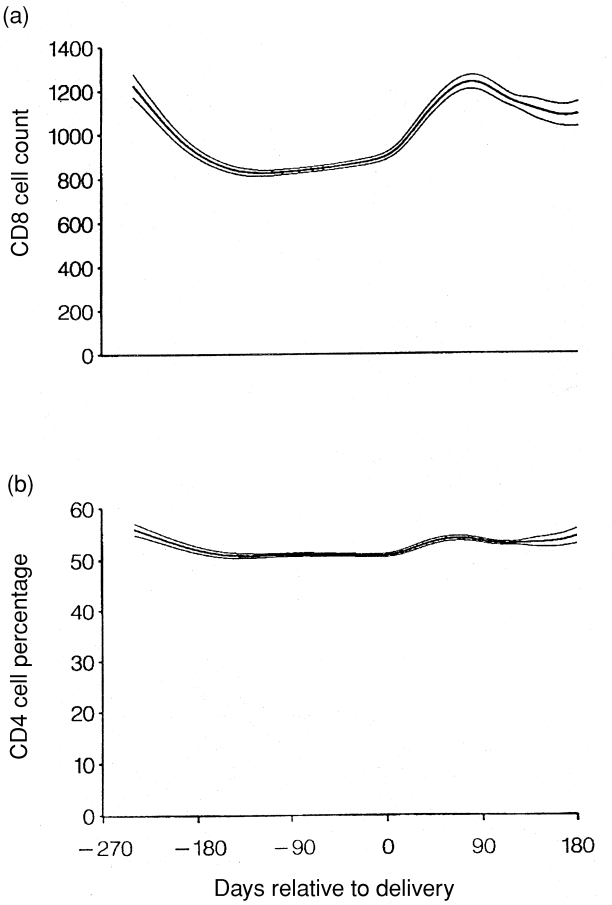

Fig. 3. Pattern of CD8 cell count (top) and CD8 cell percentage (bottom) during pregnancy and up to 6 months post-partum. Mean with 95% confidence interval.

was a slight increase of approximately 2%, 3 months after the delivery (Fig. 2). Similarly, the CD8 percentage was stable throughout pregnancy, with a small increase in the first 3 months post-partum (Fig. 3). This stability in the percentages, as opposed to the absolute count, would suggest that some of the increase in CD4 cell count during and after pregnancy was due to an increase in absolute lymphocyte count (Fig. 2). Indeed, the changes in lymphocyte counts over and after pregnancy were similar to the changes of CD4 and CD8 counts described above.

These analyses were repeated for the following subgroups: women whose infants were infected, those delivered by Cesarean section, and women who were injecting drug users during their pregnancy. The same pattern was evident in all subgroups, and there was no evidence that the pattern was associated with levels of immunosuppression as measured by CD4 percentage.

Humoral immunity

The concentration of circulating total immunoglobulin (Ig) G declined gradually throughout pregnancy until delivery, before increasing in the 6 months post-partum period (Fig. 4). Total IgM and IgA levels remained stable throughout pregnancy, increasing slightly in the 3 months following delivery, and dipping thereafter (Fig. 4).

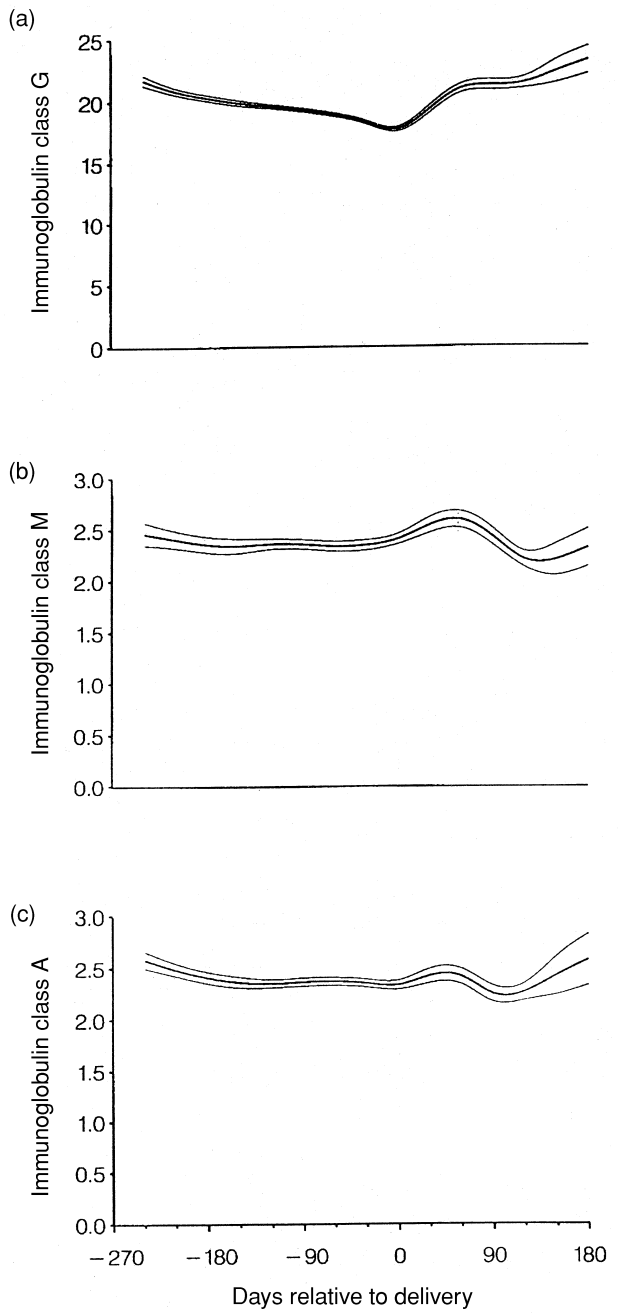

Fig. 4. Immunoglobulin (Ig) G (top), IgM (middle) and IgA (bottom) patterns during pregnancy and in the 6 month period after delivery. Mean with 95% confidence interval.

Discussion

The findings from the ECS and the SHPC support the view that pregnancy does not accelerate the course of HIV disease in a population of HIV-infected women, who did not receive zidovudine therapy during pregnancy and most of whom were asymptomatic. Concern about a possible interaction between pregnancy and HIV infection was triggered by early case reports of HIV-infected women with opportunistic infections during pregnancy [17,18]. However, these reports suffered from selection bias towards women with severe immune depression and subsequent studies based on cohorts in New York and Edinburgh demonstrated no acceleration of disease associated with pregnancy, in women without advanced HIV disease [8,19,20].

There is some evidence to suggest that, in HIV-uninfected women, pregnancy *per se* is associated with the suppression of humoral and cellular immunity [1,3,7], but it is unclear whether this is exaggerated in HIV-infected women. Wide variations in markers of immune function in HIV-infected women have been reported [5,6,8,21], but these studies included only small numbers of women, and analyses were largely cross-sectional, which makes it difficult to describe the patterns over a period of time. In the ECS and the SHPC, multiple measurements were available for 438 women and it was possible to analyse trends over and after pregnancy, thus providing more definitive results than those reported previously.

The pattern in CD4 cell percentage described here using data from the ECS and the SHPC was similar to that reported recently from a New York study [22], in which measurements on 148 HIV-negative and 192 HIV-infected women during and for up to 2 years after pregnancy were compared. In this latter study a decline in mean CD4 percentage in HIV-infected women was reported throughout the period of observation, especially during the 2 years after delivery, whereas HIV-uninfected women showed a gradual increase in CD4 percentage in the third trimester of pregnancy followed by stable levels post-partum. In contrast, the HIV-infected women in the ECS and the SHPC showed stable levels of CD4 percentages throughout pregnancy and up to 6 months post-partum. A larger proportion of the HIV-infected women in the New York study were severely immunosuppressed compared with the women enrolled in the ECS and SHPC [23], and the decline of CD4 percentage in the 2 years post-partum is likely to reflect the natural history of HIV infection rather than pregnancy-related immunosuppression. In a recent study from Sweden, which included African women, CD4 cell counts were highest around the time of delivery and declined during the 6 month period thereafter to values close to those of early pregnancy [24].

Temmerman *et al.* [25] reported no association between duration of pregnancy and immune status, and the patterns of immunological markers described for HIV-infected women were similar to those of uninfected controls. CD4 cell percentage was lower post-partum than antenatally, in both infected and uninfected women, but this was not the case for absolute CD4 cell counts. CD8 cell percentage and counts were significantly higher post-partum than ante-

natally. In 89 pregnant Malawian women (54 HIV-infected and 35 uninfected) there was an increase in absolute CD4 and CD8 cell counts in both infected and uninfected women, but no parallel increase in CD4 or CD8 percentage [21]. Both the Nairobi and the Malawi study suggest that HIV-infected women are no more immunosuppressed during pregnancy than uninfected controls. Although the analysis in these studies was cross-sectional and it is difficult therefore to comment on the patterns in immunological markers before and after pregnancy, the findings from the ECS and SHPC on HIV-infected women were similar to those from these African studies. The stability of levels of total IgM and IgA and the relatively minor changes in total IgG are likely to reflect the asymptomatic nature of the disease, and provides further evidence for a lack of immune deterioration in pregnancy.

It has been suggested that the effect of injecting drug use on immune markers is greater than the effect of HIV [8,26], but in our study the pattern in immunological markers over pregnancy was similar for HIV-infected women who continued to inject illicit drugs during pregnancy and for those who did not.

The lack of data relating to the first trimester of pregnancy in our cohorts did not allow us to describe the pattern in CD4 counts during that time. However, the graph presented in Fig. 2a suggested a decline in CD4 count from early in pregnancy to a nadir a little after 3 months. This would confirm previous reports in HIV-uninfected women [27] of a significant decline in CD4 count as early as 4 weeks after conception, concomitant with the human chorionic gonadotropin peak and compatible with immune changes and fetal graft tolerance [28]. It has been suggested that the changes observed could be due to recompartmentalization, rather than an increase in susceptibility [28].

Similar to the finding of the ECS and SHPC that changes in immunological markers show no short-term detrimental effects of pregnancy on HIV infection, there was no evidence of increased virological activity during pregnancy in a Swedish study [24], although there was some suggestion of resumed virological activity in the 6 months after delivery. Weiser *et al.* [29] investigated 19 mother–child pairs and showed that although HIV viral load varied between women, it remained stable over time (18–65 weeks post-partum) within women.

The trend in CD4 percentage during and after pregnancy observed in the ECS and SHPC was not associated with the level of the percentage. This would suggest that even for women with more advanced HIV disease there is likely to be little or no pregnancy-related adverse effect on the progression of HIV disease. Although the lack of an HIV-uninfected control group hinders a definitive conclusion, it is likely that the sharp reductions in CD4 counts in the first trimester of pregnancy are pregnancy-related rather than evidence of progression of HIV. Similarly the increases in CD4 counts in the later stages of pregnancy are likely to be pregnancy-related and this would need to be taken into account when assessing response to antiretroviral treatment. However, in view of the large individual variability in patterns of immunological markers over time between women, which are also present in non-HIV infected pregnant controls (data not shown), caution should be exercised when assessing changes in immunological markers in individual pregnant women.

Acknowledgements

We acknowledge the help we have received from C. Kully, J. Callis and C. Thorne. We also thank L. Chieco-Bianchi, F. Zacchello, R. D'Elia, A.M. Laverda, S. Cozzani, C. Cattelan, A. Mazza, B. Grella, A.R. Del Mistro, V. Jiacomet, O. Rambon, S. Oletto (Padua); M. Langhof, R. Schulz, A. Steinmüller (Berlin); S. Burns, R. Hague, P.L. Yap, J. Peutherer, G. Bird, F. Mitchell, C. Lockhart (Edinburgh); B. Sancho, G. Fontan-Casanego, M.L. Gonzalez, M.L. Prieto (Madrid); Dr M.C. Otero, Dr A. Perez Tamarit, Dr M. Gobernado, Dr J.L. Lopez, Dr M. Sanchez (Valencia); G. Mulder, M. Kreyenbroek, T. Kosten, M.C.A. van Leeuwen, the participants of the Dutch Collaborative Study of HIV-infected Women and Their Children (Amsterdam); C. Ottenblad, K. Elfgren, B. Christensson, G. Lidin-Jansson, R. Ljung (Sweden); C. Gotta, F. Melica, C. Cirillo, M. Bellomo, G. Di Siena, P. Rocca (Genoa); B. Martinez de Tejada, L. Zamora (Hospital Clinic, Barcelona); J. Llorens, M. Vinolas, M.A. López-Vílchez (Hospital del Mar, Barcelona); G. Zucotti (Ospedale San Paolo, Milan); M. Carla Re (Bologna); C. Christini, F. Castelli, A. Rodella (Brescia); I. Quinti, A. Pachí (Rome); G. Noia (Rome); A. Maccabruni, A. Spinillo (Pavia); G. Ferraris (Clinica Mangiagalli, Milan).

References

1. Weinberg ED: **Pregnancy-associated depression of cell-mediated immunity.** *Rev Infect Dis* 1984, **6**:814–831.
2. Sridama V, Pacini F, Yang S, Moawad A, Reilly M, DeGroot LJ: **Decreased levels of helper T cells: a possible cause of immunodeficiency in pregnancy.** *N Engl J Med* 1982, **307**:352–356.
3. Biedermann K, Flepp M, Fierz W, Joller-Jemelka H, Kleihues P: **Pregnancy, immunosuppression and reactivation of latent toxoplasmosis.** *J Perinat Med* 1995, **23**:191–203.
4. Hocke C, Morlat P, Chene G, Dequae L, Dabis F, Group d'Epidémiologie Clinique du Sida en Aquitaine: **Prospective cohort study of the effect of pregnancy on the progression of**

human immunodeficiency virus infection. *Obstet Gynecol* 1995, **86**:886–891.
5. Biggar RJ, Pahwa S, Minkoff H, *et al.*: **Immunosuppression in pregnant women infected with human immunodeficiency virus.** *Am J Obstet Gynecol* 1989, **161**:1239–1244.
6. Rich KC, Siegel JN, Jennings C, Rydman RJ, Landay AL: **CD4+ lymphocytes in perinatal human immunodeficiency virus (HIV) infection: evidence for pregnancy-induced immune depression in uninfected and HIV-infected women.** *J Infect Dis* 1995, **172**:1221–1227.
7. Kumar A, Madden DL, Nankervis GA: **Humoral and cell-mediated immune responses to herpesvirus antigens during pregnancy — a longitudinal study.** *J Clin Immunol* 1984, **4**:12–17.
8. Brettle RP, Raab GM, Ross A, Fielding KL, Gore SM, Bird AG: **HIV infection in women: immunological markers and the influence of pregnancy.** *AIDS* 1995, **9**:1177–1184.
9. European Collaborative Study: **Vertical transmission of HIV-1: maternal immune status and obstetric factors.** *AIDS* 1996, **10**:1675–1681.
10. Rudin C, Camli C, Schnriger H, *et al.*: **HIV und Schwangerschaft.** *Schweiz Med Wochenschr* 1995, **125**: 2322–2329.
11. Erb P, Kuchi S, Burgin D, *et al.*: **Quantitative anti-p24 determinations can predict the risk of vertical transmission.** *J Acquir Immun Defic Syndr* 1994, **7**:261–264.
12. Kind C, Brandle B, Wyler C, *et al.*: **Epidemiology of vertically transmitted HIV-1 infection in Switzerland: results of a nationwide prospective study.** *Eur J Pediatr* 1992, **151**:442–448.
13. Ledergerber B, von Overbeck J, Egger M, Luethy R: **The Swiss HIV Cohort Study: rationale, organization and selected baseline characteristics.** *Soz Praeventivmed* 1994, **39**:387–394.
14. Connor EM, Sperling RS, Gelber R, *et al.*: **Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment.** *N Engl J Med* 1994, **331**:1173–1180.
15. European Collaborative Study: **Age-related standards for T lymphocyte subsets based on uninfected children born to human immunodeficiency virus 1-infected women.** *Pediatr Infect Dis J* 1992, **11**:1018–1026.
16. Hastie TJ, Tibshirani RJ: *Generalized Additive Models*. New York: Chapman and Hall; 1990.
17. Scott GB, Fischl MA, Klimas N, *et al.*: **Mothers of infants with the acquired immunodeficiency syndrome evidence for both symptomatic and asymptomatic carriers.** *JAMA* 1985, **253**:363–366.
18. Minkoff H, Nanda D, Meneg R, Fikrig S: **Pregnancies resulting in infants with acquired immunodeficiency syndrome or AIDS-related complex: follow-up of mothers, children and subsequent born siblings.** *Obstet Gynecol* 1987, **69**:288–291.
19. Minkoff HL, Henderson C, Mendez H, *et al.*: **Pregnancy outcomes among mothers infected with human immunodeficiency virus and uninfected control subjects.** *Am J Obstet Gynecol* 1990, **163**:1598–1604.
20. Alger LS, Farley JJ, Robinson BA, Hines SE, Berchin JM, Johnson JP: **Interactions of human immunodeficiency virus infection and pregnancy.** *Obstet Gynecol* 1993, **82**:787–796.
21. Miotti PG, Liomba G, Dallabetta GA, Hoover DR, Chiphangwi JD, Saah AJ: **T lymphocyte subsets during and after pregnancy: analysis in human immunodeficiency type 1-infected and -uninfected Malawian mothers.** *J Infect Dis* 1992, **165**:1116–1119.
22. Burns DN, Nourjah P, Minkoff H, *et al.*: **Changes in CD4+ and CD8+ cell levels during pregnancy and post partum in women seropositive and seronegative for human immunodeficiency virus-1.** *Am J Obstet Gynecol* 1996, **174**:1461–1468.
23. European Collaborative Study: **Characteristics of pregnant HIV-1 infected women in Europe.** *AIDS Care* 1996, **8**:33–42.
24. Lindgren S, Martin C, Anzen B, Strand H, Bredberg-Raden U, Ehrnst A: **Pattern of HIV viraemia and CD4 levels in relation to pregnancy in HIV-1 infected women.** *Scand J Infect Dis* 1996, **28**:425–433.
25. Temmerman M, Nagelkerke N, Bwayo J, Chomba EN, Ndinya-Achola J, Piot P: **HIV-1 and immunological changes during pregnancy: a comparison between HIV-1-seropositive and HIV-1-seronegative women in Nairobi, Kenya.** *AIDS* 1995, **9**:1057–1060.
26. Mauri A, Piccione E, Deiana P, Volpe A: **Obstetric and perinatal outcome in human immunodeficiency virus-infected pregnant women with and without opiate addiction.** *Eur J Obstet Gynecol Reprod Biol* 1995, **58**:135–140.
27. Degenne D, Canepa S, Lecomte C, Renoux M, Bardos P: **Serial study of T-lymphocyte subsets in women during very early pregnancy.** *Clin Immunol Immunopath* 1988, **48**:187–191.
28. Johnstone FD, Thong KJ, Bird G, Whitelaw J: **Lymphocyte subpopulations in early human pregnancy.** *Obstet Gynecol* 1994, **83**:941–946.
29. Weiser B, Nachman S, Tropper P, *et al.*: **Quantification of human immunodeficiency virus type 1 during pregnancy: relationship of viral titer to mother-to-chid transmission and stability of viral load.** *Proc Natl Acad Sci USA* 1994, **91**:8037–8041.

Appendix

European Collaborative Study: collaborators

C. Giaquinto, E. Ruga, A. De Rossi, D. Truscia (Universita degli Studi di Padova, Padova, Italy); I. Grosch-Wörner, A. Schäfer (Universitätsklinikum Rudolf Virchow, Berlin, Germany); J. Mok, F. Johnstone (City Hospital, Edinburgh, UK); J. Jiminez, C. de Alba, F. Omenaca-Teres (Hospital 12 De Octubre, Madrid, Spain), M.C. Garcia-Rodriguez, I. Bates, I. de José, F. Hawkins, R. Martinez Zapico (Hospital Infantil La Paz, Madrid, Spain); C.A. Canosa, A. Gonzalez-Molina, F. Asensi Bonet (Hospital La Fe, Valencia, Spain); H. Scherpbier, K. Boer (Academisch Medisch Centrum, Amsterdam, The Netherlands); A.B. Bohlin, S. Lindgren, A. Ehrnst, B. Anzén, E. Belfrage (Huddinge and Danderyd Hospitals, Stockholm, Sweden); J. Levy, A. Alimenti, P. Barlow (Hospital St Pierre, Brussels, Belgium); A. Ferrazin, A. De Maria, C. Gotta, Dr Maritati (Hospital San Martino, Genoa, Italy); A. Mûr, M.T. Rovira Puges (Hospital del Mar, Laboratorio Referencia de Cataluña, Barcelona, Spain); O. Coll, C. Fortuny (Hospital Clinic, Barcelona, Spain); J. Boguña (Hospital Sant Joan de Deu, Barcelona, Spain); M. Casellas Caro (Hospital Vall D'Hebron, Barcelona, Spain); Y. Canet (Hospital Parc Tauli de Sabadell, Barcelona, Spain); G. Pardi, M. Ravizza, E. Semprini, C. Castagna, S. Fiore (Ospedale San Paolo, Milan, Italy); B. Guerra, P. Dallacasa, S. Bianchi, L. Bovicelli (Policlinico S Orsola, Bologna, Italy); E. Prati, S. Zanelli, M. Duse, A. Soresina (Universita di Brescia, Brescia, Italy); G. Scaravelli, M. Stegagno (Universita La Sapienza, Rome, Italy); M. De Santis (Universita Cattolica, Rome, Italy); M.L. Muggiasca, P. Marchisio (Ospedale L. Sacco, Milan, Italy); A. Iasci, A. Spinillo (Policlinico S Matteo, Pavia, Italy); A. Bucceri, E. Grossi, L. Rancilio (Clinica Mangiagalli and Clinica De Marchi, Milan, Italy).

Swiss HIV Pregnancy Cohort: collaborators

C. Camli, H. Schnuriger, M. Weisser, C. Kully, R. Berger, U.B. Schaad (University Children's Hospital, Basel); N. Deslex, N. Pavic, J. Bizer, M. Schnegg, A. Schwendke (University Women's Hospital, Basel); P. Erb (Institute of Medical Microbiology, Basel), A. Tichelli (University Hospital, Basel); K. Biedermann,

U. Lauper, M. Zurrer, G. Khan (University Women's Hospital, Zurich); W. Fierz, H.I. Joller (Laboratory for Clinical Immunology, Zurich); O. Irion, A.P. Brunelli (Department of Gynaecology and Obstetrics, Geneva) L. Perrin, S. Yerli (Laboratory of Virology, Geneva); G. Spoletini, J.P. Chave, A. Schreyer (Department of Gynecology and Obstetrics, Lausanne); M. Isenschmid, F. Mathezioic, C. Ott (University Women's Hospital, Berne); G. Drack, K. Keller (Women's Hospital, St Gallen); M. Etienne-Turchi, E. Saurenmann, S. Heller (Canonal Hospital, Luzern); T. Paly, D. Passwer (Women's Hospital, Aarau); S. Heinzl, K. Knotek (Cantonal Hospital, Bruderholz); J.C. Spira (Cantonal Hospital, Liestal); B. Hollinger, W. Schneider (Cantonal Hospital, Baden); M. Spreng (Cantonal Hospital, Fribourg); R. Dahler (Cantonal Hospital, Glarus); H. Stamm (Regional Hospital, Montreux); M. Delaloye (Regional Hospital, Morges); A. Saurina (Cantonal Hospital, Solothurn); R. Fleischmann, J. Frohlicher, B. Grob (Cantonal Hospital, Winterthur); T. Paly, R. Leuppi, B. Wenk (Cantonal Hospital, Zug); F. Limmacher (Regional Hospital, Grabs); S. Huber (Cantonal Hospital, Otten); C. Braschler (Cantonal Hospital, Schaffhausen); P. Cornu (Cantonal Hospital, La Chaux-de-Fonds); G. Gerretsen (Ita Wegman Hospital, Basel); P. Affentranger, M. Poorbeik (Central Laboratory of the Swiss Red Cross) and C. Kind (Coordinator of the Swiss Neonatal HIV Study, St Gallen).