RNA would appear misplaced. In the landmark ACTG protocol 076 study, which demonstrated the efficacy of the only intervention proven to prevent maternal-fetal transmission [5], only a minor fraction of the treatment effect (9%–17%) could be explained by treatment-induced change in maternal RNA, suggesting that protective effect of zidovudine occurs mostly (though still in part) through mechanism(s) other than the reduction of maternal ''virus load'' [6].

Third, whether the observed reduction in maternal immune complex–dissociated (ICD) p24 antigen reflects removal of nonparticulate antigen by immune-complexing or by true clearance of particulate p24 cannot readily be determined. The ICD p24 antigen assay method could detect high baseline levels of p24 antigen (geometric mean, 219 pg/mL; range, 78–947) in 5 of our study patients who, prior to administration of HIVIG, had quantifiable levels of endogenous p24 antibody ranging to end point dilutions as high as 3794. This belies any suggestion that exogenously administered excess p24 antibody simply complexes antigen (implying at least some qualitative in addition to any quantitative factors at work in the observed suppression of detectable antigen). In any case, it would seem that reducing levels of antigen to which a fetus might be exposed in utero or intrapartum should be regarded as potentially beneficial in reducing transmission risk. Like RNA, antigen has been demonstrated on a population (though not an individual) basis to correlate positively with transmission risk [7, 8].

A definitive determination as to whether prophylactic passive immunization with specific hyperimmune globulin or other antibody products can or cannot prevent maternal-fetal HIV-1 transmission ultimately will require randomized, controlled trials. Regrettably, the parent study, ACTG protocol 185, will not provide an answer to the question of HIVIG efficacy for prophylactic immunization. At the first planned efficacy review of 379 evaluable patients in December 1996, there was a welcome but unexpectedly low overall transmission rate (4.8%). Therefore, it was determined that the study would possess insufficient statistical power with the existing 800 maternal-infant pair design to be able to detect an effect of HIVIG treatment if one was present, and further enrollment into the study was halted [9, 10]. However, other studies to evaluate this question are planned or ongoing, with some promising early results [11].

Finally, early postinoculation passive hyperimmune globulin therapy in the simian immunodeficiency virus/macaque model has shown that disease progression can be mitigated [12]. While information on disease progression in infected ACTG 185 infants awaits continued clinical follow-up, preliminary virologic data indicate that HIVIG treatment appears to be associated with a difference in age at first positive culture. Five of 8 infected intravenous immunoglobulin–treated infants exhibited positive cultures at birth, while 7 of 7 infected HIVIG-treated infants showed negative birth cultures ($P = .026$, Fisher's exact). This trend continues to be sustained as additional data are accumulated. Whether this will represent any modification in future disease development, time will tell.

J. S. Lambert, L. M. Mofenson, and J. Moye, Jr.

Institute of Human Virology, University of Maryland, Baltimore; Pediatric, Adolescent, and Maternal AIDS Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland

References

1. Moore JP. Clinical trials of IVIG [letter]. J Infect Dis **1998**;178:597–8.
2. Lambert JS, Mofenson LM, Fletcher CV, et al. Safety and pharmacokinetics of hyperimmune anti–human immunodeficiency virus (HIV) immunoglobulin administered to HIV-infected pregnant women and their newborns. J Infect Dis **1997**;175:283–91.
3. Cao Y, Krogstad P, Korber BT, Koup RA, et al. Maternal HIV-1 viral load and vertical transmission of infection: the Ariel Project for the prevention of HIV transmission from mother to infant. Nat Med **1997**;3:549–52.
4. Melvin AJ, Burchett SK, Watts DH, et al. Effect of pregnancy and zidovudine therapy on viral load in HIV-1 infection women. J Acquir Immune Defic Syndr Hum Retrovirol **1997**;14:232–6.
5. Connor E, Sperling R, Gelber R, et al. Decreased maternal-infant transmission of human immunodeficiency virus 1 associated with zidovudine treatment. N Engl J Med **1994**;331:1173–80.
6. Sperling RS, Shapiro DE, Coombs RW, et al. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. N Engl J Med **1996**;335:1621–9.
7. Boyer PJ, Dillon M, Navaie M, et al. Factors predictive of maternal-fetal transmission of HIV-1. Preliminary analysis of zidovudine given during pregnancy and/or delivery. JAMA **1994**;271:1925–30.
8. Rich KC, Janda W, Kalish LA, et al. Immune complex–dissociated p24 antigen in congenital or perinatal HIV infection: role in the diagnosis and assessment of risk of infection in infants. J Acquir Immune Defic Syndr Hum Retrovirol **1997**;15:198–203.
9. National Institutes of Health, National Institute of Child Health and Human Development. NIH News Advisory: ACTG Protocol 185. Bethesda, MD: NIH, 26 March **1997**.
10. Mofenson LM, Stiehm ER, Lambert J, et al. Efficacy of zidovudine in reducing perinatal HIV-1 transmission in HIV-1–infected women with advanced disease [abstract I-117]. In: Program and abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy (Toronto). Washington, DC: American Society for Microbiology, **1997**.
11. Guay L, Musoke P, Mmiro F, et al. Phase I/II trial of HIVIG for the prevention of HIV-1 vertical transmission in Uganda [abstract 071]. In: A Conference on Global Strategies for the Prevention of HIV Transmission from Mothers to Infants (Washington, DC). Washington, DC: American Society for Microbiology, **1997**.
12. Haigwood NL, Watson A, Sutton WF, et al. Passive immune globulin therapy in the SIV/macaque model: early intervention can alter disease profile. Immunol Lett **1996**;51:107–14.

Reprints or correspondence: Dr. John S. Lambert, Institute of Human Virology, University of Maryland at Baltimore, 725 W. Lombard St., N548, Baltimore, MD 21201 (lambert@umib.umd.edu).

The Journal of Infectious Diseases 1998;178:598–9

0022–1899/98/7802–0050$02.00

Value of Cytomegalovirus (CMV) IgG Avidity Index for the Diagnosis of Primary CMV Infection

To the Editor—There are several methods used to detect antibodies to cytomegalovirus (CMV), including a commercial Western blot test. However, the reliability of these tests for the diagnosis of primary CMV infection, reactivation, or reinfection has not been evaluated for clinical laboratory use. In an interesting paper, Grangeot-Keros et al. [1] reported on the reliability of low-avidity IgG in the diagnosis of recent primary CMV infection. My colleagues and I have done similar research and wish to add our results to the discussion [2–5].

We studied the value the Enzygnost CMV-IgG test (Behringwerke, Marburg, Germany), an ELISA that interprets the absorbance obtained in each sample through an α-method [6]. This automated method calculates the titer of IgG, using one dilution of sample and 2 positive controls. The value obtained for the positive controls in each assay depends on the nominal value, limit values, and characteristics of the reagents used (antigen and anti-IgG), allowing extrapolation of a curve for each assay and establishing a relation between the absorbance and titer of antibodies. An important concern in antibody detection is the variability in control values and reagents; however, use of the α-method eliminates day-to-day variations in laboratory conditions and variations between laboratories.

The α-method is useful for detecting specific IgG [7]. Grangeot-Keros et al. [1] studied the levels of low-avidity IgG in recent acute CMV infection, using modifications in time and in the value for clinical diagnosis. On the basis of the findings in [7], we think the avidity index as calculated by Grangeot-Keros et al. was not correct for the following reasons: It is not possible to directly compare the absorbance values obtained in wells with urea with those obtained in wells without urea; it is necessary to consider the absorbance obtained in the positive control in each assay; it is necessary to know the level of low-avidity IgG present in the positive control; and it is necessary that sera from the same patients be studied simultaneously to demonstrate the change of low-avidity IgG over a long period of time.

We feel it is necessary for Grangeot-Keros et al. to recalculate their results. This clarification would allow others to use this test in clinical laboratories on a regular basis. Also, it is possible that the rate of low-avidity IgG designed by Grangeot-Keros et al. [1] better approximates the results obtained by our group using the Enzygnost test.

Jose Gutiérrez, Gonzalo Piédrola, and Maria del Carmen Maroto

Microbiology Department, University Hospital San Cecilio, Granada University, Granada, Spain

References

1. Grangeot-Keros L, Mayaux MF, Lebon P, et al. Value of cytomegalovirus (CMV) IgG avidity index for the diagnosis of primary CMV infection in pregnant women. J Infect Dis **1997**;175:944–6.
2. Gutiérrez J, Rodríguez M, Maroto MC, Piédrola G. Reliability of four methods for the diagnosis of acute infection by Epstein-Barr virus. J Clin Lab Anal **1997**;11:78–81.
3. Gutiérrez J, Maroto MC. Are IgG antibody avidity assays useful in the diagnosis of infectious diseases? A review. Microbios **1996**;87:113–21.
4. Gutiérrez J, Rodríquez M, Piédrola G, Maroto MC, Peiron J. Behavior of IgG antibody avidity for the antigen and of IgA in active cytomegalovirus, Epstein-Barr virus, herpes simplex virus and human herpes virus 6 infections. Adaptation of a commercial test. J Infect **1997**;35:25–30.
5. Gutiérrez J, Rodríquez M, Piédrola G, Maroto MC. Detection of IgA and low avidity IgG antibodies for the diagnosis of recent active toxoplasmosis. Clin Microbiol Infect **1997**;3:658–62.
6. Gutiérrez J, Maroto MC, Piédrola G. Evaluation of a new reagent for anti-cytomegalovirus and anti–Epstein-Barr virus IgG. J Clin Microbiol **1994**; 32:2603–5.
7. Dopatka HD, Giesendorf B. Single point quantification of antibody by ELISA without need of a reference curve. J Clin Lab Anal **1992**;6: 417–22.

Reprints or correspondence: Dr. Jose Gutiérrez, C/Camino Bajo de Huetor, nº 84, 1ºA, E-18008 Granada, Spain (josegf@goliat.ugr.es).

The Journal of Infectious Diseases 1998;178:599–600

0022–1899/98/7802–0051$02.00

Reply

To the Editor—We appreciate the interest of Gutiérrez et al. in our paper. As they say, the α-method recommended by the manufacturer of the indirect EIA (Enzygnost CMV-IgG; Behringwerke, Marburg, Germany) that we used does improve the reproducibility of the results; thus, if we wanted to compare concentrations obtained in different experiments, we would use this method. However, when we calculate an avidity index, we compare (in the same test) absorbance values that are obtained in wells with and in wells without urea. The optical densities are slightly different from one test to another, but we do not think that the ratios differ enough to change the clinical significance of the results. In each experiment, we always include a low-avidity and a high-avidity index control. Furthermore, as suggested by us [1] and others [2], all serum samples from individual patients are always simultaneously included in order to study the change in the avidity index over time.

Liliane Grangeot-Keros, Marie Jeanne Mayaux, Pierre Lebon, François Freymuth, Geneviève Eugene, René Stricker, and Elisabeth Dussaix

Hôpital Antoine Béclère, Clamart; Unité 292 INSERM, Hôpital de Bicêtre, Le Kremlin-Bicêtre; Hôpital Saint-Vincent de Paul, Paris; Centre Hospitalier Universitaire, Caen, France; Dianalab, Geneva, Switzerland

References

1. Grangeot-Keros L, Mayaux MJ, Lebon P, et al. Value of cytomegalovirus (CMV) IgG avidity index for the diagnosis of primary CMV infection in pregnant women. J Infect Dis **1997**;175:944–6.
2. Dussaix E, Chantot S, Harzic M, Grangeot-Keros L. CMV-IgG avidity and CMV IgM concentration in both immunocompromised and immunocompetent patients. Pathol Biol **1996**;44:405–10.

Reprints or correspondence: Dr. Liliane Grangeot-Keros, Laboratoire de Bactériologie-Virologie, Hôpital Antoine Béclère, 157 rue de la Porte-de-Trivaux, BP 405, 92141 Clamart, France.

The Journal of Infectious Diseases 1998;178:600

0022–1899/98/7802–0052$02.00