# Letters

## TOXOPLASMOSIS DIAGNOSIS IN PREGNANT WOMEN INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS I

To The Editors:

Because of the increase of human immunodeficiency virus 1 (HIV) infections in non-risk group-matching women, most of them of child-bearing age, congenital effects caused by this infection are an increasing problem in industrialized countries. Although only -20% of the newborn of HIV-positive mothers are congenitally infected with the virus (at least in Austria), some acquired immunodeficiency syndrome-associated pathogens are known to cause severe infections in the neonatal period and their importance may be underestimated during the surveillance of such high risk pregnancies. Congenital toxoplasmosis in unborn children of HIV-infected mothers can be a life-threatening cerebral, cardiac or hepatic infection. [1,2] Reactivation of latent *Toxoplasma* infection is a common event in acquired immunodeficiency syndrome patients whereas a primary *Toxoplasma* infection in HIV-positive patients seems to be rare. This observation may be attributed to the above average incidence of *Toxoplasma* seropositivity in HIV-infected individuals in Central Europe.[3] Thus congenital *Toxoplasma* infections in offspring of HIV-infected mothers is usually attributed to a reactivation in the mother, probably with a regular occurrence of chronic or intermittent parasitemia.[1,4,5] From unpublished data it is estimated that >50% of the pregnant women concurrently seropositive to HIV and *Toxoplasma gondii* congenitally infect their infants with the parasite. Thus in countries with a high incidence of latent *Toxoplasma* infections (e.g. 57% in the Austrian HIV-positive population[3] vs. 39% in pregnant women of the same age), the newborns of HW-infected mothers may bear a greater risk for acquiring a severe congenital toxoplasmosis than for acquiring a congenital HIV infection.

Because there is at least one report demonstrating the efficiency of therapy in time for a normal fetal outcome in a case of a maternal central nervous system toxoplasmosis,[6] a reliable diagnosis of the reactivation of the *Toxoplasma* infection in the pregnant women and/or of a congenital infection after the reactivation is of crucial importance. Diagnosis of toxoplasmosis in the newborn is insufficient in such cases, because there is an increased risk of severe damage already during the pregnancy. However, serodiagnosis of toxoplasmosis in HIV-positive persons is very difficult to carry out because of the subjects' reduced competence of a *de novo* synthesis of antibodies, and pregnancy may aggravate this problem. A chronic or intermittent maternal *Toxoplasma* parasitemia maybe life-threatening to the unborn but is often not to be suspected by the gynecologist because of clinical

silence. Moreover it cannot be detected by any imaging methods like computerized tomographic scanning or by conventional serodiagnosis inasmuch as antibody formation can be very exotic and inconclusive[7]; or by parasite DNA detection in amniotic fluid samples, because this technique is impracticable as a surveillance method.[8] In the European countries with public health systems that afford a regular toxoplasmosis screening of pregnant women such as in Austria (on an obligatory basis) or in Germany (voluntary), the situation is not better because physicians have ill conceived trust in standard laboratory findings, caused by a combination of a lack of information, ease and confidence in the traditional system.

Therefore a new intellectual approach is necessary for routine diagnosis of acute toxoplasmosis in HIV-infected pregnant women, applicable in cases of suspected acute infections as well as in cases of clinically silent reactivation and, especially for Europe, suitable as a screening technique. We propose that an attempt should be made to establish such a diagnosis on a regular basis, using a one step analysis of maternal blood combining an IgG antibody test with a parasite DNA detection by an amplification method (polymerase chain reaction). This procedure offers several undeniable advantages; (1) the test material is easily and cheaply obtained and the analyses may thus be repeated as often as necessary; (2) the detection of specific IgG antibodies practiced in almost any test system is an undisputed indicator of an infection even in immunosuppressed individuals[9]; and (3) *Toxoplasma* DNA detection in white blood cells seems to be a reliable marker of acute infections in humans.[10]

Having gained some experience in diagnosing acute toxoplasmosis by combining various serotests and an amplification method in immunocompetent pregnant women *(n* = 160)[11] and very limited experience with HIV-infected pregnant women *(n* = 3) we consider the above mentioned test combination as the most effective way for diagnosing a toxoplasmosis reactivation during pregnancy. Simultaneously the infection status of the pregnant woman is determined with the consequence of her education about avoiding a primary infection, and the existence of an acute toxoplasmosis is ascertained in cases under suspicion with the consequence of prompt induction of therapy. Moreover testing maternal blood requires only negligible changes in sample preparation and shipment for countries with an existing screening system.

The question is unanswered whether the detection of *Toxoplasma* DNA in the blood of a pregnant woman is a proof of parasitemia (living, infectious parasites floating in the bloodstream) with its potential for damaging the unborn child. Because any controlled studies in this field would be ethically problematic and presumably technically impracticable, this decision will remain a question of personal estimation for a long time. We believe that until the contrary has been proved, parasite DNA detection in white blood cells is the most reliable and practicable technique for detection of acute toxoplasmosis in HIV-infected pregnant women. We hope that our suggestion may contribute to prevention of congenital infections in children of mothers with acquired immunodeficiency syndrome.

**Acknowledgment.** Financial support was provided by EU Concerted Action BMH1-CT92-1535.

Andreas Hassl, Ph.D., D.Sc.
Wolfgang Tuma, Ph.D.

Clinical Institute of Hygiene
University of Vienna
Vienna, Austria (AH)

GeneLab
Institute of Molecular Diagnostics
Gelsenkirchen, Germany (WT)

Accepted for publication July 31, 1995.

Address for reprints: Dr. Andreas Hassl, Clinical Institute of Hygiene, University of Vienna, Kinderspitalgasse 15, Vienna A-1095, Austria.

Key words: Concurrent congenital infection, human immunodeficiency virus, toxoplasmosis, diagnosis, amplification method.

1. Marty P, Bongain A, Rahal A, et al. Prenatal diagnosis of severe fetal toxoplasmosis as a result of toxoplasmic reactivation in an HIV-1 seropositive woman. Prenat Diagn 1994; 14:414-5.
2. Medlock MD, Tilleli JT, Pearl GS. Congenital cardiac toxoplasmosis in a newborn with acquired immunodeficiency syndrome. Pediatr Infect Dis J 1990;9:129-32.
3. Aspöck H, Hassl A. Parasitic infections in HIV patients in Austria: first results of a long-term study. Int J Med Microbiol 1990;272:540-6.
4. Mitchell CD, Erlich SS, Mastrucci MT, Hutto SC, Parks WP, Scott GB. Congenital toxoplasmosis occurring in infants perinatally infected with human immunodeficiency virus 1. Pediatr Infect Dis J 1990;9:512-8.
5. Remington J, Desmonts G. Toxoplasmosis. In: Reminton J, Klein J, eds. Infectious diseases of the fetus and newborn infant. Philadelphia: Saunders, 1990:89-195.
6. Hedriana HL, Mitchell JL, Brown GM, Williams SB. Normal fetal outcome in a pregnancy with central nervous system toxoplasmosis and human immunodeficiency virus infection: a case report. J Reprod Med 1993;38:747-50.
7. Jaqueti J, Martinez Hernandez D, Navarro Gallar F, Garcia Esteban RJ. Lack of development of *anti-Toxoplasma gondii* IgG antibodies in an HIV-positive pregnant woman with positive *anti-Toxoplasma* IgM. Med Clin Barc 1990;94:358.
8. Hohlfeld P, Daffos F, Costa JM, Thulliez P, Forestier F, Vidaud M. Prenatal diagnosis of congenital toxoplasmosis with a polymerase-chain-reaction test on amniotic fluid. N Engl J Med 1994;331:695-9.
9. Zangerle R, Allerberger F. High risk of developing toxoplasmic encephalitis in AIDS patients seropositive to *Toxoplasma gondii.* J Acquir Immune Defic Syndr 1994;7:207-8.
10. Ho Yen DO, Joss AW, Balfour AH, Smyth ET, Baird D, Chatterton JM. Use of the polymerase chain reaction to detect *Toxoplasma gondii* in human blood samples. J Clin Pathol 1992;45:910-3.
11. Tuma W, Weber E, Hassl A, et al. Detection of *Toxoplasma gondii* nucleic acid in pregnancy. Lab Med 1994;18:512-6.