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A technique for dating toxoplasmosis in pregnancy and comparison with the Vidas anti-toxoplasma IgG avidity test

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ABSTRACT

A comparative evaluation of 384 selected sera was performed using the Beckman Coulter Access and Abbott Axsym Toxo-IgG assays. The Axsym assay yields positive early results following infection, while the Access assay gives higher titres during chronic infection. The ratio between the two complementary tests, Axsym Toxo-IgG/Access Toxo-IgG (Ax/Ac), was compared with the Vidas anti-*Toxoplasma* IgG avidity index (AI). The Ax/Ac ratio decreased progressively as the time between infection and sampling increased. The mean Ax/Ac values (±SE) were 2.50 (±0.26), 2.14 (±0.13), 2.33 (±0.22), 1.34 (±0.09), 1.32 (±0.10), 0.92 (±0.08) and 0.74 (±0.07) for groups of sera sampled at 1, 2, 3, 4–5, 6–8, 9–12 and 13–24 months, respectively, after infection in pregnant women. These values were much smaller for cases with chronic infection (>24 months), i.e., 0.56 (±0.03), 0.44 (±0.04) and 0.53 (±0.04), respectively, for pregnant women and immunodepressed patients with and without reactivation. Taking a ratio of 1 as a threshold for recent infection, the patients in the groups sampled at 1, 2 and 3 months had Ax/Ac ratios >1 in 49/50 (98%), 53/55 (96.4%) and 36/36 (100%) cases, respectively. Thus, an Ax/Ac ratio of <1 in serum from a pregnant woman allows a recent infection (<3 months) to be excluded. This technique has the advantage of yielding positive results that develop much more rapidly than the AI, thereby helping to reassure large numbers of pregnant women and avoiding costly and unnecessary prophylactic treatment and follow-up.

Keywords Avidity index, congenital toxoplasmosis, diagnosis, IgG kinetics, pregnancy, *Toxoplasma gondii*

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INTRODUCTION

The follow-up of obstetrical toxoplasmosis depends mainly on the detection of anti-*Toxoplasma*-specific IgM and IgG [1–3]. When an individual is positive for both IgM and IgG in the absence of a previously diagnosed infection, complementary tests are required to differentiate between a recently acquired infection (<3 months) and a more chronic infection. Such tests include the detection of specific IgA and IgE antibodies [4,5], but the avidity index (AI), a technique developed about 15 years ago [6], is the test used most widely [1–3]. An elevated AI in the first trimester of pregnancy excludes a recent infection and helps to prevent unnecessary follow-up and treatment. Different techniques to measure the AI in pregnancy have been developed, evaluated and compared in a number of studies [5,7–16]. Although the AI has been universally accepted as a reliable test, recent studies [10,11,16] have shown that the evolution of a positive reaction is slow, so that its use for excluding infections that have occurred only a few months before pregnancy is limited. Using 271 sera, it was recently demonstrated that an avidity threshold of 0.2 was reached 6–24 months after infection (mean 11.49 ± 3.9 months), and that the avidity threshold of 0.3 was reached 7 - >24 months after infection (mean 14.20 ± 4.8 months) [10]. This slow evolution of positive results, which varies

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according to the technique used for detection, is the principal limitation of this test and justifies the use of complementary assays [16].

Another dating technique that compares the results of two serological tests with different antigenic targets (i.e., predominantly membranous antigen and predominantly cytoplasmic antigen) has also been studied with a view to differentiating recent and chronic infection [17,18]. One approach involves comparing the kinetics of two commercially available assays in parallel, e.g., the Axsym Toxo-IgG assay (Abbot Diagnostic, Rungis, France) and the Assess Toxo-IgG assay (Beckman Coulter, Roissy, France). The principles and the techniques of these two automated tests are very similar. Axsym Toxo-IgG uses a microparticle enzyme immunoassay, while Access Toxo-IgG uses a chemiluminescence immunoassay with microparticles, and both use a two-step indirect antibody test. Axsym Toxo-IgG seems to become IgG-positive earlier, and gives significantly elevated IgG titres, compared with Access Toxo-IgG, with sera taken in the first 3 months after infection. The present study used 384 selected sera to compare these two commercial immunoassays in terms of their sensitivity and speed in detecting acute and chronic infection, and also investigated the use of the Axsym Toxo-IgG/Access Toxo-IgG (Ax/Ac) ratio as a new technique for dating toxoplasmosis infection. The kinetics of this ratio and its correlation with the time after infection were evaluated and compared with the kinetics of the AI.

MATERIALS AND METHODS

Follow-up of pregnant women and immunodepressed patients

The majority of sera (304/384) were from pregnant women with known dates of infection (part 1), and the remainder (80/384) were from cases of chronic toxoplasmosis with known seroconversions >24 months previously (part 2), during the period July 1998 to July 2005. All samples were stored at −20°C before investigation.

Part 1 of the study included 79 pregnant women with seroconversion. The mean age at the time of seroconversion was 28.8 ± 4.9 years (range 16–39 years). Clinical follow-up of the pregnant women and their neonates was continued for up to 1 year for 65 of these women. This group included 23 infants who were born with congenital toxoplasmosis, and 43 infants (including one pair of twins) who did not acquire the disease (Table 1). The 304 sera were obtained from the 79 pregnant women at 1–24 months after infection, and were divided into seven equal sample groups on the basis of the interval between sampling and infection (1, 2, 3, 4–5, 6–8, 9–12 and 13–24 months (±15 days).

It was possible to date infections because of the obligatory monthly serological screening policy in France. Dating was based on the following serological kinetic criteria. The first IgM-positive (or doubtful) serum according to the ISAgA assay (bioMérieux, Durham, NC, USA) or the Toxo-IgM Access assay (Beckman Coulter), with or without IgG, was dated as 1 month (±15 days) after infection. If IgG was absent from the first serum (IgM-positive, IgG-negative), its presence (according to the Access and Axsym Toxo-IgG) during the follow-up period was obligatory for confirming infection. It was necessary for the interval between the first positive serum (IgM with or without IgG) and the preceding negative serum to be >2 months for inclusion in the study. Using these dating criteria, the decision to start treatment was made as follows: (i) no treatment was given when diagnosis was made at delivery or following spontaneous abortion (13/79 cases); or (ii) treatment with spiramycin (9 MIU/mL) was continued for a minimum of 15 days (66/79 cases), with changes made as necessary (pyrimethamine + sulfadiazine for 9/66 cases), as described previously by Flori *et al.* [6].

Table 1. Characteristics of 79 pregnant women with seroconversion and their infants

Time of maternal infection (WG)	Mothers		Infants		
	No. of seroconversions	No. treated during pregnancy	No. lost to follow-up before 1 year of age	No. with proven maternofetal transmission	Fetal and paediatric disease
−6–4	10	10 (100%)	2/10 (20%)	0/8 (0%)	No cases
5–14	24	23 (96%)	6/25 (24%) (one pair of twins)	2/19 (11%)	1 spontaneous abortion 1 clinical infection
15–27	24	24 (100%)	4/24 (17%)	11/20 (55%)	3 terminations of pregnancy 2 clinical infections[a] 6 subclinical infections
28–40	21	9 (45%)	2/21 (10%)	10/19 (53%)	10 subclinical infections
Total	79	66 (84%)	14/80 (17.5%)	23/66 (35%)	1 spontaneous abortion 3 terminations of pregnancy 3 clinical infections[a] 16 subclinical infections

WG, week of gestation.
[a]Cerebral calcifications and/or chorioretinal scar without severe visual impairment at an age of 1 year.