JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 1999, p. 3487–3490 Vol. 37, No. 11
0095-1137/99/$04.00+0

Detection of Specific Immunoglobulin E during Maternal, Fetal, and Congenital Toxoplasmosis

I. VILLENA,[1]†* D. AUBERT,[1]† V. BRODARD,[1]† C. QUEREUX,[2]† B. LEROUX,[3]† D. DUPOUY,[3]† G. REMY,[4]† F. FOUDRINIER,[1]† C. CHEMLA,[1]† J. E. GOMEZ-MARIN,[1,5]† AND J. M. PINON[1]†

Laboratory of Parasitology-Mycology, Team 4 (INSERM U.314), EA 2070, IFR 53,[1] Gynecology-Obstetrics Department, Centre Hospitalier Universitaire,[2] Pediatrics Department, Centre Hospitalier Universitaire,[3] and Infectious Diseases Department, Centre Hospitalier Universitaire,[4] Hôpital Maison Blanche, 51092 Reims, France, and Grupo de Patologia Infectiosa, Departamento de Medicina Interna, Hospital San Juan de Dios, Universidad Nacional de Colombia, Santafé de Bogota DC, Colombia[5]

Received 15 April 1999/Returned for modification 25 June 1999/Accepted 22 July 1999

Toxoplasma immunoglobulin E (IgE) antibodies in 664 serum samples were evaluated by using an immunocapture method with a suspension of tachyzoites prepared in the laboratory in order to evaluate its usefulness in the diagnosis of acute *Toxoplasma gondii* infection during pregnancy, congenital infection, and progressive toxoplasmosis. IgE antibodies were never detected in sera from seronegative women, from patients with chronic toxoplasma infection, or from infants without congenital toxoplasmosis. In contrast, they were detected in 86.6% of patients with toxoplasmic seroconversion, and compared with IgA and IgM, the short kinetics of IgE was useful to date the infection precisely. For the diagnosis of congenital toxoplasmosis, specific IgE detected was less frequently than IgM or IgA (25 versus 67.3%), but its detection during follow-up of children may be interesting, reflecting an immunological rebound. Finally, IgE was detected early and persisted longer in progressive toxoplasmosis with cervical adenopathies, so it was also a good marker of the evolution of toxoplasma infection.

Toxoplasma gondii infection is generally mild or subclinical in healthy adults, but it can have serious consequences when contracted during pregnancy, because of the risk of maternofetal transmission and congenital toxoplasmosis (CT).

The diagnosis of toxoplasmosis is usually based on immunological criteria. Most studies have focused on specific immunoglobulin G (IgG) and IgM (6, 18) and, more recently, specific IgA (2, 7, 16, 19). In acquired toxoplasmosis, the combined analysis of these three isotypes and their kinetics (20) can help to distinguish between an old infection (isolated IgG) and a recent infection (coexistence of IgG, IgM, and IgA, the latter validating the specificity of IgM by ruling out natural IgM). However, in addition to individual variations in the immune response, antitoxoplasmic IgM and IgA can persist for more than a year after infection (19, 20), hindering the precise dating of the infection. To improve the dating of *T. gondii* infection and to unmask longstanding progressive toxoplasmosis, we tried to identify an early, briefly appearing marker of recent infection. To this end, we developed an assay for antitoxoplasmic IgE (14, 25) and applied it to assessing the risk of toxoplasmosis in pregnant women and to the diagnosis of CT. We report our experience in these situations; reactivation in immunodeficient patients was the subject of a previous article (15).

MATERIALS AND METHODS

Immunological methods. IgG antibodies (Ab) were screened for by means of a previously described high-sensitivity direct agglutination (HSDA) method (13) with a positivity cutoff of 6 U/ml. Most adult sera in this study were also tested by enzyme-linked immunosorbent assay (ELISA) (Toxo G Ab EIA [Clonatec] or IMX Toxo IgG [Abbott]). Children's sera were also analyzed by using the comparative mother-child immunological profile method (CIP), which is based on enzyme-linked immunofiltration assay (ELIFA) (13).

Specific IgA and IgM were detected by an immunocapture method using a suspension of tachyzoites prepared in the laboratory (ICT-A and -M, respectively) (16, 17). Briefly, tachyzoites of the RH strain of *T. gondii* from the peritoneal exudates of Swiss female mice infected 4 days earlier are collected in normal saline. After centrifugation, tachyzoites are treated with trypsin. The pellets are washed three times in phosphate-buffered saline (PBS) (75511; BioMérieux, Marcy l'Etoile, France) and incubated in Formol solution for 30 days at 4°C. After three washes in PBS, the concentration is adjusted to 2×10^8/ml, and the tachyzoites are stored in BABS buffer (73331; BioMérieux) with sodium azide (27967150; Prolabo, Fontenay-sous-Bois, France) at 4°C (8, 14). An IgA value of at least 2 was considered positive in adults, while the IgM cutoff was 9, because of possible interference by natural IgM (8, 17). For newborns and children, the positivity cutoff was 1 for both isotypes. IgM was also detected, in adults, by ELISA (Toxo M Ab EIA [Clonatec] or IMX Toxo IgM [Abbott]).

Antitoxoplasmic IgE was detected by using an ICT method (14) comparable to that used for specific IgA and IgM. Briefly, microtiter plates (96 wells; Nunc Microwell Polysorp 262 162) were sensitized with 100 μl of anti-human high-chain ε monoclonal antibodies (ANA B16; Argène Biosoft, Varilhes, France) diluted to 3 μg/ml. After 18 h of incubation at 4°C, the microtiter plates were washed and saturated in a storage solution containing PBS, sodium azide, and 1% bovine albumin fraction V (81003 TM; Miles). The microtiter plates can be stored at 4°C for up to 6 months and are washed in PBS (pH 7.2) just before use. The test sera were diluted 1/25 in PBS (1/5 for infants under 3 months) and distributed (100 μl) in three consecutive wells. After incubation for 3 h at 37°C, the plates were washed in PBS-Tween. A suspension of tachyzoites diluted in BABS buffer to a density of 1.5×10^7/ml was added in volumes of 100, 150, and 200 μl to the three wells of each serum sample. After incubation for 18 h at room temperature, the microtiter plates were read automatically with a spectrophotometer (Dynatech MR 5000 or 7000) coupled to software developed by our laboratory (Institute Jacques Boy, Reims, France). Scores were attributed to each well as follows: 0 for total tachyzoite sedimentation, 4 for complete agglutination, and 1, 2, or 3 for intermediate agglutination. The cumulative score for the three wells corresponding to a given serum sample could thus range from 0 to 12. A score of at least 2 (for adults) or 1 (for newborns) was considered positive.

The presence of specific IgM, IgA, or IgE at birth must be validated with a second sample obtained between days 5 and 10 of life if the mother also has these isotypes at delivery, to rule out transmission of maternal antibodies (13).

Samples. We tested 664 sera from 318 patients divided into 10 groups.

Group A (control group, 100 sera) was composed of 100 seronegative women whose sera were negative for IgG (HSDA titer of <6 U/ml) and IgM (by ELISA). Twelve of these women had natural IgM, with a titer of between 6/12

* Corresponding author. Mailing address: Laboratoire de Parasitologie-Mycologie, Hôpital Maison Blanche, 51092 Reims, France. Phone: 03-26-78-42-22. Fax: 03-26-78-73-28. E-mail: ivillena@chu-reims.fr.

† Member of the Reims Toxoplasmosis Group.

and 9/12 in ICT-M (11, 12). None of the 100 sera were positive for IgA (ICT-A titer of <2/12).

Group B (toxoplasmic seroconversion, 170 sera) was composed of 59 women (pregnant or not pregnant) who contracted toxoplasmosis (i.e., seroconverted) at a date known to within 1 month and who had a maximum follow-up of 274 days after seroconversion. Two of these women had cervical adenopathies during the seroconversion phase. Group C (toxoplasmic seroconversion, 87 sera) was composed of 38 women who seroconverted during pregnancy; 20 of the infants developed CT, and 18 were uninfected. For groups B and C, the criterion for seroconversion was a change of serology (negative to positive).

Group D (fetal blood, 13 samples) was composed of 13 fetuses whose mothers underwent antenatal diagnosis (amniocentesis and fetal blood sampling) and who were found to be positive (IgM and/or IgA in fetal blood). Detection of toxoplasmic DNA by PCR-based methods with amniotic fluid was not done for all of the diagnoses.

Group E (progressive toxoplasmosis, 40 sera) was composed of 10 patients (12 to 51 years of age) monitored for toxoplasmosis who had a high titer of IgG and the presence of IgM and IgA for at least 6 months after seroconversion (three cases of cervical adenopathies).

Group F (control group, 27 sera) was composed of 27 asymptomatic women who were pregnant or attempting to become pregnant and whose sera were submitted to the laboratory to determine their toxoplasmic immunological status. All of these sera were positive for IgG (HSDA titer of between 12 and 400 U/ml); the ICT-M titer was below 9, and the IgM ELISA and ICT-A were negative. These women thus had a pattern corresponding to longstanding immunity.

Group G (CT, 82 sera) was composed of 52 children with clinical manifestations (i.e., chorioretinitis and intracranial calcifications) or purely biological CT. The diagnoses were confirmed by parasite isolation (from amniotic fluid, fetal blood, or placenta) and/or by specific immunological tests (IgM and/or IgA Ab and/or neo-Ab in the children's blood detected by CIP-ELIFA [11]) and the persistence of specific IgG at 12 months. The sera tested were obtained during the first month of life.

Group H (CT, 61 sera) was composed of 30 children with CT who, between 5 and 33 months after birth, had a clear immunological rebound as shown by (i) a rise in IgG levels (>2 titers in HSDA), (ii) the emergence of specific IgM and/or IgA, and/or (iii) the emergence or increase of precipitating Ab (by ELIFA). Immunological rebounds are frequent on treatment cessation and when treatment is inadequate (because of insufficient doses or poor compliance); they can also occur during correctly prescribed and administered treatment (23), although this is rare. Overall, we identified 37 immunological rebounds in these 30 children (five children had two rebounds and one child had three).

Group I (chorioretinitis in children with CT, 23 sera) was composed of nine children with CT who developed chorioretinitis during their first year of life, with regular immunological monitoring from birth to the onset of the lesion (23).

Group J (Control group, 61 sera) was composed of 10 children who were free of CT and whose mothers had progressive toxoplasmosis during the pregnancy. These children were monitored clinically and serologically from birth up to the age of at least 12 months, at which time their specific IgG had totally disappeared (HSDA titer of 0 U/ml between 9 and 12 months). None of these children had clinical manifestations of CT.

RESULTS

Control groups (groups A, F, and J). IgE Ab were never detected in samples from groups A, F, and J.

Toxoplasmic seroconversion (groups B and C). Seven of the 59 women in group B consistently tested negative for specific IgE. In the remaining 52 patients, IgE Ab appeared within days of the infection, at the same time as IgM but before IgA and well before IgG. The IgE titer increased rapidly to reach a maximum within 2 to 3 weeks, with marked individual differences. IgE Ab persisted at a plateau for 1 month and then tailed off rapidly, reaching mean values of 2/12 at 3 months and 1/12 at 6 months (Table 1) and being undetectable thereafter. In some subjects IgE Ab were highly transient, while in others they persisted beyond month 4 (four sera from two seroconverters with cervical adenopathies).

Among the 38 women in group C, 17 whose children had CT and 15 whose children were free of infection had IgE Ab during the seroconversion phase. The kinetics of maternal IgE Ab was not influenced by whether or not their children had CT (data not shown). The remaining six women had no IgE Ab.

Fetal blood (group D). Among the 13 fetal blood samples positive for IgM and/or IgA, only 3 contained specific IgE (titers of 2/12 in one sample and 12/12 in two samples).

TABLE 1. Mean titers of IgG (HSDA) and IgM, IgA, and IgE (ICT) Ab in group B (toxoplasmic seroconversion, 59 women, 170 sera) in the 9 months following infection

Mo	Titer (mean ± SD)			
	HSDA (U/ml)	ICT (/12)[a]		
		IgM	IgA	IgE
0–1	65 ± 153	11.04 ± 1.43	7.28 ± 4.37	8.35 ± 3.68
1–2	619 ± 730	10.93 ± 1.53	7.97 ± 3.44	7.92 ± 4.64
2–3	690 ± 690	10.14 ± 20	6.88 ± 3.84	2.27 ± 3.39
3–4	1,014 ± 1006	9.57 ± 1.54	5.50 ± 3.48	1.42 ± 2.20
4–5	1,089 ± 928	9.25 ± 2.18	5.06 ± 3.79	1.38 ± 1.51
5–6	575 ± 601	7.87 ± 2.83	4.83 ± 2.00	1.35 ± 1.63
6–7	90 ± 71	7.50 ± 3.30	3.40 ± 2.41	0.87 ± 1.24
7–8	91 ± 77	6.70 ± 3.68	1.83 ± 1.65	0.50 ± 0.50
8–9	91 ± 77	6.66 ± 3.32	1.66 ± 1.90	0.37 ± 0.65

[a] Agglutination score. For adults, an IgM score of ≥9 is positive and an IgA or IgE score of ≥2 is positive.

Progressive toxoplasmosis (group E). The 10 patients with suspected progressive toxoplasmosis (persistently high IgG, IgM, and IgA levels at 6 months after infection) had high levels of IgE Ab (scores of 6/12 to 12/12) during the first month after infection. In eight cases the IgE Ab persisted 6 months after infection (as did IgM and IgA), with a wide range of values (3.5/12 to 12/12). Five patients had a high level of IgE Ab (8/12 to 12/12) 4 months after the beginning of seroconversion (Table 2). Three patients had cervical adenopathies during the seroconversion phase, and all had persistent IgE Ab 6 months later.

CT (groups G and H). In the month following birth, 41 of the 52 children with CT tested positive for IgM and/or IgA (Table 3). Twenty-nine children (46 sera) were simultaneously positive for IgM and IgA, and 12 (20 sera) were separately positive for IgM (6 cases) or IgA (6 cases). IgE was found together with IgM and IgA in 13 children (20 sera); all 13 children were born to mothers who seroconverted during the last trimester.

Thirty of the 52 children with CT had 37 immunological rebounds. IgM and/or IgA was positive in 17 patients, of whom 12 also had IgE Ab (Table 4); in the latter cases the three isotypes appeared concomitantly. In five rebounds only IgM and/or IgA was detected, while in another seven rebounds only

TABLE 2. Changes in specific IgE Ab titers (ICT) in group E (progressive toxoplasmosis; 10 patients, 40 sera)

Patient	ICT-E titer (/12)[a] at mo:					
	1	2	3	4	6	>6
1	12	12	ND[b]	12	12	12
2	12	ND	12	ND	ND	12
3	6	ND	ND	4	ND	ND
4	12	8.5	ND	8	ND	0
5[c]	10	12	ND	ND	4	ND
6[c]	12	12	ND	ND	5	3
7	12	9	9.5	12	12	ND
8	12	ND	ND	ND	5	ND
9[c]	12	ND	ND	11	6	ND
10	12	ND	2	ND	3.5	ND

[a] Agglutination score. For adults, an IgM score of ≥9 is positive and an IgA or IgE score of ≥2 is positive.
[b] ND, not done.
[c] Patient with cervical adenopathy at the time of seroconversion.

TABLE 3. Detection of specific antitoxoplasmic IgM, IgA, and IgE Ab in the first month of life in group G (CT; 52 children, 82 sera)

No. of patients (no. of sera)	Ab[a]		
	IgM	IgA	IgE
13 (20)	+	+	+
16 (26)	+	+	−
6 (10)	+	−	−
6 (10)	−	+	−
11 (16)	−	−	−

[a] +, presence of Ab; −, absence of Ab.

IgE was detected. Finally, no specific IgM, IgA, or IgE was detected in 13 cases.

Chorioretinitis in children with CT (group I). Only one of the nine children with CT who developed chorioretinitis during the first year of life had IgE and IgA at birth. An immunological rebound with IgE was found in two children at the time chorioretinitis was diagnosed. Thus, IgE was positive in only three of the nine CT patients with chorioretinitis.

DISCUSSION

The aim of this study was to evaluate IgE Ab as a specific marker of recent or progressive *T. gondii* infection. Few studies on this isotype have been published (1, 10, 14, 15, 25). The method that we used to detect specific IgE was based on immunocapture with revelation by use of a suspension of tachyzoites. In contrast to Wong et al. (25), we will not discuss the ELISA method; the conflicts between our results and those of Wong et al. may be due, at least in part, to kinetic variations observed with different techniques, as reported for other isotypes (20). Seronegative women and children free of CT never tested positive for specific IgE, confirming the high specificity of this marker for *T. gondii* infection (20, 25). The detection of specific IgE thus points to recent or progressive infection (in the absence of natural IgE), as specific IgE is never found in subjects with old infection.

During seroconversion, IgE was detected in the diagnostic serum sample, together with IgM. In a previous study (14) we observed a case in which IgE was the first isotype to emerge, and Wong et al. have described a similar case (25). The sensitivity of specific IgE detection by immunocapture was 86.6% in our study (groups B and C), compared to 82.7% in the study of Gross et al. (10) and 63% in the study of Wong et al. (25) using the same technique. However, Wong et al. obtained 100% sensitivity in ELISA for IgE, with a kinetic pattern shifted to the right, but in a smaller number of patients (8 patients, versus 52 in our study). These authors nonetheless recommended the ISAGA-IgE method (equivalent to our ICT-E assay) for immunological monitoring of seronegative pregnant women, because of the early emergence of this marker. In addition, ELISA for IgE remains positive for a longer period, which would hinder fine dating of an infection acquired during pregnancy. We found high titers of specific IgE in the first 2 months following seroconversion, albeit with marked individual differences (8/12 to 12/12); this isotype tailed off very rapidly during the third and fourth months, being undetectable beyond 4 months after seroconversion, as previously reported by us (14) and by others (1, 10).

TABLE 4. Detection of specific antitoxoplasmic IgM, IgA, and IgE Ab during immunological rebounds in group H (CT; 30 children, 61 sera)

No. of immunological rebounds (no. of sera)	Ab[a]	
	IgM and/or IgA	IgE
12 (23)	+	+
5 (8)	+	−
7 (10)	−	+
13 (20)	−	−

[a] +, presence of Ab; −, absence of Ab.

Relative to the kinetics of IgE, the kinetics of specific IgA observed here is in keeping with that previously described (2, 7, 9, 19); this isotype emerged during the first month after infection, remained at a plateau for 2 months, and then fell gradually to become undetectable 6 to 8 months after infection. Large individual differences were observed, and 5 to 10% of women seroconverted without detectable IgA (2, 7). Finally, while the absence of specific IgM rules out recent infection, its persistence beyond 12 months in immunocapture assays hinders dating of the infection (8, 20). Compared with IgA and IgM, the short kinetics of IgE offers a clear advantage in this respect.

Among the women who seroconverted during pregnancy and whose children had CT (20 cases), the detection of IgE during the pregnancy was not a predictive marker of congenital infection, as the kinetics and titers of these antibodies were similar to those observed in all seroconversions.

In the group of patients considered to have progressive toxoplasmosis (group E, persistent IgM and IgA), IgE Ab were detected very early, and they persisted for more than 6 months in three patients with cervical adenopathies (no precise clinical information was available in the other cases). The presence of IgE Ab in progressive or disseminated infection has been reported by other authors (1, 3, 4, 25) and confirms the value of serologic investigations for the diagnosis of toxoplasmic lymphadenitis. Indeed, the diagnosis of progressive *T. gondii* infection can be made by direct detection of the parasite in pathological specimens and by mouse inoculation, cell culture, or, more recently, detection of toxoplasmic DNA by PCR-based methods; however, these techniques are reserved for a limited number of situations and specialized laboratories.

For the diagnosis of CT, specific IgE was detected less frequently than IgM or IgA (25 versus 67.3%). Never found in isolation, its detection simply confirms a diagnosis already based on other criteria. The poorer performance than that reported by Wong et al. (25) may be explained by at least two factors: we used only immunocapture, whereas Wong et al. reported that ELISA was more sensitive for IgE in children, and in addition, all 13 children in whom IgE was detected at birth were born to mothers who seroconverted during the last trimester. This suggests that the children's IgE response was very recent, as reported by Decoster et al. (7) for IgA detection at birth. As the kinetics of IgE is shorter than that of other isotypes, it would appear that the IgE response was no longer detectable at birth in the other infected children. Wong et al. (25) gave no information on the date of maternal infection, raising the possibility that the children in whom they detected specific IgE were also infected late in pregnancy.

Among the 11 children with CT in whom we did not detect specific IgM, IgA, or IgE at birth, the positive antenatal diagnosis had led to maternofetal treatment. As we (22) and others (5, 12) have previously reported, such treatment can eradicate markers of congenital infection usually found at birth (absence of IgM, IgA and/or IgE; low or nonspecific titers of IgG; and/or negative placental inoculation).

For the antenatal diagnosis of CT, screening for specific IgE in fetal blood seems to be less effective than testing for IgM

and/or IgA (11). However, with recent progress in molecular biology, testing of fetal blood samples is being abandoned in favor of amniocentesis alone, and therefore a full assessment of this isotype under these conditions will probably never be done.

IgE Ab do not appear to have much value for the diagnosis of CT, as the combination of CIP-ELIFA and ICT-M and -A performs far better (13). In contrast, detection of specific IgE during laboratory monitoring of children at risk may be useful, as IgE (like IgM and IgA) can emerge or reemerge during follow-up, reflecting an immunological rebound. These isotypes are not always found simultaneously, meaning that all three must be screened for at the same time as IgG, another marker of immunological rebound; the qualitative information provided by CIP-ELIFA is also essential, because of its precocity (13). Immunological rebound can occur on treatment cessation and even during treatment, in which case it may reflect poor compliance; it may also be the forerunner of a clinical relapse, meaning that it should be tested for routinely in children at risk (23).

Specific IgE was rarely found in children with CT who developed chorioretinitis during the first year of life. These results conflict with previous reports (14) and data from Wong et al. based on ELISA for IgE (25). The latter authors reported that ELISA was more sensitive than immunocapture in this setting.

Screening for specific IgE Ab is not useful as a first-line method when monitoring pregnancies at risk for *T. gondii* infection. However, when *T. gondii* infection is demonstrated, IgE Ab, which emerge rapidly and disappear after a short time, can help to date the infection precisely, a key factor in determining whether antenatal diagnosis is warranted. Moreover, the persistence of specific IgE beyond 6 months after seroconversion points to progressive infection. If biological markers of progression are detected, we (21), like Vogel et al. (24), recommend close monitoring of the pregnancy, even if the seroconversion occurred before conception. In regard to CT, tests for specific IgE appear to be more useful in the course of biological monitoring (detection of immunological rebound) than for diagnostic purposes, even though ELISA detection may be more frequent in this case. Finally, screening for specific IgE can also be useful for the etiological diagnosis of toxoplasmic lymphadenitis.

ACKNOWLEDGMENTS

This work was supported by the Programme Hospitalier de Recherche Clinique, Ministère de la Santé et de la Ville, Paris, France.

We thank D. Young for checking the English.

REFERENCES

1. **Ashburn, D., A. W. Joss, T. H. Pennington, and D. O. Ho-Yen.** 1995. Specificity and usefulness of an IgE immunosorbent agglutination assay for toxoplasmosis. J. Clin. Pathol. **48:**64–69.
2. **Bessieres, M. H., C. Roques, A. Berrebi, V. Barre, M. Cazaux, and J. P. Seguela.** 1992. IgA antibody response during acquired and congenital toxoplasmosis. J. Clin. Pathol. **45:**605–608.
3. **Bossi, P., E. Caumes, L. Paris, M. L. Dardé, and F. Bricaire.** 1998. *Toxoplasma gondii*-associated Guillain-Barré syndrome in an immunocompetent patient. J. Clin. Microbiol. **36:**3724–3725.
4. **Brooks, R. G., R. E. McCabe, and J. S. Remington.** 1987. Role of serology in the diagnosis of toxoplasmic lymophadenopathy. Rev. Infect. Dis. **9:**1055–1062.
5. **Couvreur, J., P. Thulliez, F. Daffos, C. Auffrant, Y. Bompard, A. Gesquiere, and G. Desmonts.** 1993. In utero treatment of toxoplasmosis foetopathy with the combination pyrimethamine-sulfadiazine. Fetal Diagn. Ther. **8:**45–50.
6. **Dannemann, B. R., W. C. Vaughan, P. Thulliez, and J. S. Remington.** 1990. Differential agglutination test for diagnosis of recently acquired infection with *Toxoplasma gondii*. J. Clin. Microbiol. **28:**1928–1933.
7. **Decoster, A., B. Slizewics, J. Simon, C. Bazin, F. Darcy, G. Vittu, C. Boulanger, Y. Champeau, J. L. Demory, M. Duhamel, and A. Capron.** 1991. Platelia Toxo IgA, a new kit for early diagnosis of congenital toxoplasmosis by detection of anti-P30 immunoglobulin A antibodies. J. Clin. Microbiol. **29:**2291–2295.
8. **Desmonts, G., Y. Naot, and J. S. Remington.** 1981. Immunoglobulin M immunosorbent agglutination assay for diagnosis of infectious diseases: diagnosis of acute congenital and acquired *Toxoplasma* infections. J. Clin. Microbiol. **14:**486–491.
9. **Foudrinier, F., C. Chemla, D. Aubert, A. Bonhomme, and J. M. Pinon.** 1995. Value of specific immunoglobulin A detection by two immunocapture assays in the diagnosis of toxoplasmosis. Eur. J. Clin. Microbiol. Infect. Dis. **14:**585–590.
10. **Gross, U., O. Keksel, and M. L. Dardé.** 1997. Value of detecting immunoglobulin E antibodies for the serological diagnosis of *Toxoplasma gondii* infection. Clin. Diagn. Lab. Immunol. **4:**247–251.
11. **Hezard, N., C. Chemla, F. Foudrinier, I. Villena, C. Quereux, B. Leroux, D. Dupouy, M. Talmud, and J. M. Pinon.** 1997. Antenatal diagnosis of congenital toxoplasmosis in 261 pregnancies. Prenat. Diagn. **17:**1047–54.
12. **Hohlfeld, P., F. Daffos, P. Thulliez, C. Aufrant, J. Couvreur, J. McAleese, D. Descombey, and F. Forestier.** 1989. Fetal toxoplasmosis: outcome of pregnancy and infant follow-up after in utero treatment. J. Pediatr. **115:**765–769.
13. **Pinon, J. M., C. Chemla, I. Villena, F. Foudrinier, D. Aubert, D. Toubas, B. Leroux, D. Dupouy, C. Quereux, M. Talmud, T. Trenque, G. Potron, M. Pluot, G. Remy, and A. Bonhomme.** 1996. Early neonatal diagnosis of congenital toxoplasmosis: value of comparative enzyme-linked immunofiltration assay immunological profiles and anti-*Toxoplasma gondii* immunoglobulin M (IgM) or IgA immunocapture and implications for postnatal therapeutic strategies. J. Clin. Microbiol. **34:**579–583.
14. **Pinon, J. M., D. Toubas, C. Marx, G. Mougeot, A. Bonnin, A. Bonhomme, M. Villaume, F. Foudrinier, and H. Lepan.** 1990. Detection of specific immunoglobulin E in patients with toxoplasmosis. J. Clin. Microbiol. **28:**1739–1743.
15. **Pinon, J. M., F. Foudrinier, G. Mougeot, C. Marx, D. Aubert, O. Toupance, G. Niel, M. Danis, P. Camerlynck, G. Remy, J. Frottier, D. Jolly, M. H. Bessieres, D. Richard-Lenoble, and A. Bonhomme.** 1995. Evaluation of risk and diagnostic value of quantitative assays for anti-*Toxoplasma gondii* immunoglobulin A (IgA), IgE, and IgM and analytical study of specific IgG in immunodeficient patients. J. Clin. Microbiol. **33:**878–884.
16. **Pinon, J. M., H. Thoannes, P. Pouletty, J. Poirriez, J. Damiens, and P. Pelletier.** 1986. Detection of IgA specific for toxoplasmosis in serum and cerebrospinal fluid using a nonenzymatic IgA capture assay. Diagn. Immunol. **4:**223–227.
17. **Pouletty, P., J. Kadouche, M. Garcia-Gonzalez, E. Mihaesco, G. Desmonts, P. Thulliez, H. Thoannes, and J. M. Pinon.** 1985. An anti-human μ chain monoclonal antibody: use for detection of IgM antibodies to *Toxoplasma gondii* by reverse immunosorbent assay. J. Immunol. Methods **76:**289–298.
18. **Remington, J. S., and G. Desmonts.** 1990. Toxoplasmosis, p. 89–195. *In* J. S. Remington and J. O. Klein (ed.), Infectious diseases of the fetus and newborn infant, 3rd ed. The W. B. Saunders Co., Philadelphia, Pa.
19. **Stepick-Biek, P., P. Thulliez, F. G. Araujo, and J. S. Remington.** 1990. IGA antibodies for diagnosis of acute congenital and acquired toxoplasmosis. J. Infect. Dis. **162:**270–273.
20. **Turunen, H., K. A. Vuorio, and P. O. Leinikki.** 1983. Determination of IgG, IgM and IgA antibody responses in human toxoplasmosis by enzyme-linked immunosorbent assay (ELISA). Scand. J. Infect. Dis. **15:**307–311.
21. **Villena, I., C. Chemla, C. Quereux, D. Dupouy, B. Leroux, F. Foudrinier, and J. M. Pinon.** 1998. Prenatal diagnosis of congenital toxoplasmosis transmitted by an immunocompetent woman infected before conception. Prenat. Diagn. **18:**1079–1081.
22. **Villena, I., C. Quereux, and J. M. Pinon.** 1998. Congenital toxoplasmosis: value of prenatal treatment with pyrimethamine-sulfadoxine combination. Prenat. Diagn. **18:**754–756.
23. **Villena, I., D. Aubert, B. Leroux, D. Dupouy, M. Talmud, C. Chemla, T. Trenque, G. Schmit, C. Quereux, M. Guenounou, M. Pluot, A. Bonhomme, and J. M. Pinon.** 1998. Pyrimethamine-sulfadoxine treatment of congenital toxoplasmosis: follow-up of 78 cases between 1980 and 1997. Scand. J. Infect. Dis. **30:**295–300.
24. **Vogel, N., M. Kirisits, E. Michael, H. Bach, M. Hostetter, K. Boyer, R. Simpson, E. Holfels, J. Hopkins, D. Mack, M. B. Mets, C. N. Swisher, D. Patel, N. Roizen, L. Stein, M. Stein, S. Withers, E. Mui, C. Egwuagu, J. Remington, R. Dorfman, and R. McLeod.** 1996. Congenital toxoplasmosis transmitted from an immunologically competent mother infected before conception. Clin. Infect. Dis. **23:**1055–1060.
25. **Wong, S. Y., M. P. Hadju, R. Ramirez, P. Thulliez, R. McLeod, and J. S. Remington.** 1993. Role of specific immunoglobulin E in diagnosis of acute *Toxoplasma* infection and toxoplasmosis. J. Clin. Microbiol. **31:**2952–2959.