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# IgE antibodies in toxoplasmosis

## Przeciwciała IgE w toksoplazmozie

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## Summary

Toxoplasmosis is a worldwide infection caused by the intracellular parasite *Toxoplasma gondii.* At least a third of the world human population is infected with the parasite, making it one of the most successful parasitic infections. Primary maternal infection may cause health-threatening sequelae for the fetus, or even cause death of the uterus. Reactivation of a latent infection in immune deficiency conditions such as AIDS and organ transplantation can cause fatal toxoplasmic encephalitis. Toxoplasmosis is a major cause of chorioretinitis, especially in individuals with impaired immune systems. In the acute phase, directly after invading the body, *T. gondii* begins to multiply rapidly. In the majority of cases acquired toxoplasmosis is asymptomatic. In the second week of infection, specific IgM antibodies are present in the blood. IgE antibodies appear at the same time, slightly preceding specific IgA antibodies. The concentration of IgE can be one of the parameters used for diagnosing an infection with *T. gondii*. Laboratory diagnosis, i.e. IgE and serologic assays, plays the main role in the diagnosis of congenital infection and assists in the confirmatory diagnosis of toxoplasmic encephalitis and ocular toxoplasmosis. This article is a review of IgE in toxoplasmosis.

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In parasitic invasions, especially in helminthic infections, there is observed an increase in the production of IgE antibodies. This defect results from disturbances in the regulation of antibody production by Th cells, which promotes a local inflammatory reaction. Through the release of mediators from mast cells IgE participates in the reaction of antibody-dependent cellular cytotoxicity (ADCC). There are two different cellular receptors which bind IgE. High-affinity IgE receptor FcεRII "classic"plays on the cells of the fattening indicate and basophils, and the low-affinity receptor for IgE (FcεRI) on granulocytes and lymphocytes. The FcεRII receptor participates in destruction of parasites by eosinophils (ADCC mechanism) and plays a role in the regulation of IgE synthesis [14].

Cytotoxic activity of the eosinophils is increased under the influence of cytokines (TNF-a and IL-5) released by mast cells, lymphocytes and macrophages. Th2 lympho-

cytes synthesize specific cytokines (IL-4, IL-5, IL-6, IL-10, IL-13 and IL-14) which play a major role in the pathogenesis of parasitic diseases. IL-5 is the major cytokine responsible for the increase in the eosinophil population in parasitoses, whereas IL-6 stimulates production of antibodies and exerts a pro-inflammatory effect by stimulating generation of acute phase proteins. IL-10 and IL-12 control the type of the immune response. The former inhibits cytokine synthesis and, by blocking the production of IL-6 and TNF-a, causes an advantage of the response occurring with Th2 involvement and B cell activation, while the latter, IL-12, facilitates the formation of a Th1 type response [3].

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## Specificity of IgE in maternal, fetal and congenital toxoplasmosis

Toxoplasmosis is an opportunistic invasion which usually progresses without any or with few symptoms. It can run a difficult clinical course when the functioning of the immune system is depressed. In the acquired form, infection with *T. gondii* shows a relation to the cells of the reticuloendothelial and muscular system. With a congenital invasion *T. gondii* localizes in the central nervous system and in the retina of the eye. In later stages of congenital toxoplasmosis we observe ophthalmic symptoms such as infections of the retina and the choroid. Congenital toxoplasmosis is dependent upon numerous factors such as gestational age, level of placental development, efficiency of the immune system of the mother and of the fetus, intensity of invasion and pathogenicity of *T. gondii.* Infection within the first trimester of pregnancy causes in utero death of the fetus, spontaneous abortion or birth of a neonate with symptoms of general occupation of the organs (hepatosplenomegaly, hepatitis, anemia, myocarditis, pneumonia, rash, renal failure, hemorrhagic condition) leading to death. Infection within the first trimester of pregnancy causes acute meningitis, hydrocephaly, nanocephaly, intracranial calcification, cerebral palsy, convulsions, muscle tone disorders, retinal-choroid infections, microphthalmia, and cataracts. Infection in the second trimester of pregnancy leads to formation of intracranial calcifications, hypoalbuminemia, and chorioretinitis [24].

When a mother acquires a primary *T. gondii* infection during pregnancy, congenital infection may result, with severe consequences for the fetus. However, as the risk of fetal infection is very small when maternal infection occurs before conception, it is important to make a precise estimation of the timing of maternal infection. In the Ashburn et al. study [2], *Toxoplasma* specific IgE was detected in five out of six patients from group I (with definite or probable infection during pregnancy), but not in a patient who seroconverted, confirming the results of the IgM ELISA. Specific IgE was not detected in 8 of 11 pregnancies from 5 of 7 patients from group 2 (women with past or possible acute infection during 11 pregnancies). It has been suggested that specific IgE remains detectable for less than 4 months after infection. Positive IgE immunosorbent agglutination assay (ISAGA) results and low avidity antibodies were both able to confirm acute infection. The absence of specific IgE in patients from group 2 (women with past or possible acute infection during 11 pregnancies) may have been useful to exclude acute infection [2].

The aim of the study by Villena et al. [26] was to evaluate IgE antibodies as a specific marker of recent or progressive *T. gondii* infection. The method which was used to detect specific IgE was based on immunocapture with revelation through the use of a suspension of tachyzoites. The sensitivity of specific IgE detection by immunocapture was 86.6% in the study of Villena et al. [25], compared to 82.7% in the study of Gross et al. [12] and 63% in the study of Wong et al. [26] using the same technique. Villena et al. [25] found high titers of specific IgE in the first 2 months following seroconversion. Relative to the kinetics of IgE, the kinetics of specific IgA observed in this study are in keeping with those previously described [9]; 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.

Among women who seroconverted during pregnancy and whose children had congenital toxoplasmosis, the detection of IgE during pregnancy was not a predictive marker for congenital infection, as the kinetics and titers of these antibodies were similar to those observed in all seroconversions. In patients with progressive toxoplasmosis, IgE antibodies were detected very early and persisted for more than 6 months. For the diagnosis of congenital toxoplasmosis, specific IgE was detected less frequently than IgM or IgA (25% versus 67.3%). Isolation is never found, since its detection simply confirms diagnoses already based on other criteria. Performance poorer than that reported by Wong et al. [26] may be explained by at least two factors: Villena et al. [25] used only immunocapture, whereas Wong et al. [26] reported that ELISA was more sensitive for IgE in children, and in addition, all 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 for IgA detection at birth, as reported by Decoster et al. [5]. As the kinetics of IgE are shorter than those of other isotypes, it would appear that the IgE response was no longer detectable at birth in other infected children. Wong et al. [26] 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 the pregnancy.

Villena et al. [25] have previously reported that 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). Specific IgE was rarely found in children with congenital toxoplasmosis who developed chorioretinitis during the first year of life. These results conflict with previous reports [18] and data from Wong et al. [26] based on ELISA for IgE. The latter authors reported that ELISA was more sensitive than immunocapture in this setting. Screening for specific IgE antibodies is not useful as a first-line method when monitoring pregnancies at risk for *T. gondii* infection. However, when a *T. gondii* infection is demonstrated, IgE antibodies, 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 a progressive infection.

Foudrinier et al. [10] in their research describe marking specific IgE antibodies. The clinical value of immunoenzymatic detection of anti-*Toxoplasma* IgE was assessed by studying 2036 sera from 792 subjects, comprising seronegative controls and subjects with acute, active, reactivated, or congenital toxoplasmosis. Nonimmunized adults, pregnant women with recently acquired infection (acute toxoplasmosis), immunocompetent subjects with a recently acquired severe infection (active toxoplasmosis) expressed with fever, adenopathies, splenomegaly, pneumonia, meningitis, or disseminated infection were included; specific IgE antibodies were never detected in seronegative subjects. They were present, however, in 85.7% of asymptomatic seroconverters and in 100% of seroconverters with overt toxoplasmosis, following two different kinetics: in the former, the specific IgE titer generally presented a brief peak 2 to 3 months after infection and then fell rapidly, whereas specific IgE persisted at a very high titer for several months in the latter. IgE emerged concomitantly with an increase in IgG during *Toxoplasma* reactivation. For neonatal diagnosis of congenital toxoplasmosis IgE was less informative than IgM and IgA (sensitivities – 59.5%, 64.3% and 76.2%, respectively) and had a specificity of 91.9%. The diagnostic value of IgE detection at birth is slightly better than that of IgA but lower than that of IgM (respective specificities – 91.9%, 88% and 96.8%). In the neonatal period the IgE index was positive in 30 infants who were free of congenital toxoplasmosis. The index fell below the positivity cutoff by day 10 in all infants except one, in whom it remained positive until 2 months of age; it is noteworthy that this child's mother had a particularly high IgE index (>4). The presence of anti-*Toxoplasma* IgE in these uninfected infants may correspond to maternal antibodies which, as documented for IgA and IgM, may cross the damaged placental barrier. These specific maternal IgE antibodies are readily detectable when the relative nonspecific IgE concentration is very low in newborns. IgE assay can also contribute to neonatal diagnosis of congenital toxoplasmosis although the possibility of sample contamination by maternal antibodies means that a positive result must be confirmed on day 10 of life, as recommended for IgM and IgA.

Sensini [22] in his research describes infection with *T. gondii* during pregnancy. IgE antibody detection has been proposed as a way of defining the stage of the infection, because IgE is found only in serum samples from patients with acute infection, and the duration of IgE seropositivity is shorter than that of IgM and IgA. Enzyme immunoassays (EIAs) and ISAGA tests have been used for IgE determination, but these assays are home-made and have been applied in only a few reference centers. However, Foudrinier et al. [10] reported limited (a few months) IgE seropositivity in 85.7% of asymptomatic seroconverters, and long persistence at a very high titer in 100% of seroconverters with overt toxoplasmosis. Furthermore, IgE emerged concomitantly with the increase of IgG during reactivation. Addressing congenital toxoplasmosis in neonates, Sensini writes [22]: „IgE has been found in serum samples from congenitally infected neonates, but the sensitivity of IgE detection is lower than that of IgM and IgA. Emergence of specific IgE during post-natal treatment is considered to be a sign of poor adherence or inadequate dosing. Nevertheless, simultaneous measurement of IgM, IgA and IgE improves the diagnostic yield."

Ege et al. [8] in their study present infection with *T. gondii* in pregnant women who are at risk of coming into contact with the parasite. Pregnant women in the third trimester of pregnancy were recruited. Women who lived on farms where any kind of livestock was kept were assigned to the farm group. Specific IgM and IgG antibodies were determined. Additionally, specific IgE antibodies in the mother and 2-month-old children were determined. In this study previous infection with *T. gondii* exerted its effect only in the stratum of mothers who had exposure to cats during their first year of life, but not in mothers only recently exposed. The association of the maternal *T. gondii* infection in infancy with reduced IgE production against seasonal allergens in the offspring might reflect an epigenetic effect.

Olariu et al. [17] describe congenital toxoplasmosis in the USA. One or more severe clinical manifestations of congenital toxoplasmosis were reported in 84% of the infants and included eye diseases (92.2%), brain calcifications (79.6%), and hydrocephalus (67.7%). *T. gondii*-specific IgM, IgG and IgE antibodies were demonstrable in 86.6%, 77.4% and 40.2% of the infants, respectively.

Abdul-Gani [1] attempted to assess the diagnosis of congenital toxoplasmosis. Primary maternal infection with *T. gondii* acquired during pregnancy may result in congenital infection with serious sequelae in the neonatal period or years after birth [20]. Prenatal diagnosis of congenital toxoplasmosis (CT) is based on ultrasonography, amniocentesis, and fetal-blood sampling [4,7]. Infection of the fetus early in the pregnancy leads to death in utero or severe neurological damage [20]. Definitive diagnosis of congenital infection later requires cultures of amniotic fluid (AF) and fetal

blood, in both mice and fibroblast cell culture [6,7]. Since amniocentesis can be easily performed as early as week 15 of gestation, polymerase chain reaction (PCR) diagnosis of congenital infection from AF between weeks 15 and 19 of gestation was reported to be possible [13]. It was found that the detection of the *T. gondii* SAG1 gene by PCR had a higher sensitivity than conventional serologic testing because even the most sensitive method of measuring IgM detects the infection in only 75% of infants [25]. The *Toxoplasma* SAG1 gene was detected within 24 h of obtaining the cells from cerebrospinal fluid (CSF) at 37 days of life while serum IgM antibody was negative on the same day [27].

PCR represents a revolution in the diagnosis of congenital *T. gondii* infection in that it facilitates the process with respect to time, sampling ease and reliability [21].

## Acute, subacute and chronic toxoplasmosis; symptomatic and asymptomatic (latent) toxoplasmosis

In patients with a correctly functioning immune system the infection progresses asymptomatically or limits itself to local changes in the lymph nodes. The period of an asymptomatic parasitemia is 1-3 weeks long. Specific antibodies IgM, IgA, IgE and IgG (seroconversion) are created, which causes inhibition of propagation of the parasite and leads to the development of cysts in the tissue. Acquired toxoplasmosis in 85%-90% of cases is asymptomatic. It can be expressed as lymphadenopathy mainly of the throat, neck and head. Lymphadenopathy persists and returns for a period of time ranging from a few to several months. The enlargement of the lymph nodes is an immunologic reaction of the host to the presence of the *T. gondii* parasite or its metabolic products. The IgG antibodies are evidence of having come into contact with the parasite. In the general form of toxoplasmosis the symptoms involving internal organs are pneumonia, myocarditis, pleuritis, hemorrhagic condition, hepatosplenomegaly, anemia and less frequently encephalitis and myositis.

In research described by Kodym et al. [15] 106 people with acute form of toxoplasmosis (primarily with lymphadenopathy) were studied, as well as 368 patients with asymptomatic toxoplasmosis, using 5 different serological tests utilized to detect the presence of IgA, IgE, IgM and IgG antibodies. It has been demonstrated that the IgG avidity and assayed IgE demonstrated the highest specificity (97.7% and 91.7% respectively) and the highest positive predictive value (respectively 89.4% and 75.6%). The best correlation between serological results and clinical symptoms was observed in assaying IgE antibodies. The only drawback was that the presence of these antibodies in blood circulation was too brief, since IgM test positive for a period of 12-18 months, IgA for 6-9 months and IgE for 4-6 months. Avidity of IgG remains at a low level for 4 months at most and later shows a rising tendency, which correlates with enlargement of lymph nodes and increased production of IgE. Hence, measuring IgE is a highly specific test which can be used to diagnose acute forms of toxoplasmosis provided that detection is achieved using very sensitive tests. According to Gross et al. [12] IgE antibodies can be an indicator of the disease becoming active.

Wong et al. [25] cite the research of Pinon et al. [18] and Poirriez et al. [19] describing the presence of specific IgE antibodies which have been assayed using the ISAGA method in patients with an acute *Toxoplasma* infection, congenital toxoplasmosis, or toxoplasmic chorioretinitis. Congenital toxoplasmosis was diagnosed through the presence of neurologic disease including hydrocephalus, chorioretinitis, and/or the presence of cerebral calcifications. IgE antibodies were detected (by ELISA or ISAGA) in 100% of women who seroconverted during pregnancy. In their study Wong et al. were able to detect a greater percentage of women who seroconverted during pregnancy (100%) in both of IgE assays, but the decline of IgE antibodies (detected by ELISA and ISAGA) in individual patients varied considerably, and serum from one patient which remained positive for IgE by both ELISA and ISAGA for 37 weeks after seroconversion was documented [26].

In their work Suzuki et al. [23] illustrate the presence of IgE antibodies in acute acquired toxoplasmosis. Specific IgE antibodies appear early in a *T. gondii* infection, almost simultaneously with IgM and IgA antibodies. Significant levels of specific IgE antibodies have been demonstrated in 63-100% of patients with toxoplasmosis. Pinon et al. [18] reported that the IgE ISAGA was positive in sera from 25 (86%) of 29 women who seroconverted during gestation or had specific IgA and IgM antibodies. Specific IgE was present early in the infection, simultaneously with IgM antibodies, but slightly preceding the presence of IgA antibodies. In sequential sera from 23 patients with toxoplasmosis, IgE antibodies never persisted for longer than 4 months after the beginning of the infection.

*T. gondii* is a parasite which enters the body of individuals who have a depressed immune system endogenously. Toxoplasmosis accompanies organ transplantation (the heart, lungs, bone marrow), neoplasms (Hodgkin's disease, lymphomas, leukemia) and AIDS. During the course of AIDS chorioretinitis, pneumonia, the general form of toxoplasmosis, myocarditis, and pericarditis appear. According to Kodym et al. [15] if lymphadenopathy and acute toxoplasmosis persist longer than one year it may be related to the impaired immunological response. In patients with toxoplasmic lymphadenopathy, high IgE antibody titers were detected by ELISA and ISAGA in virtually all patients within 12 weeks of the onset of clinical illness. These data confirm the results of previous reports on the usefulness of serologic tests in the diagnosis of toxoplasmic lymphadenopathy. In patients with congenital toxoplasmosis, toxoplasmic lymphadenopathy, and toxoplasmic chorioretinitis, the IgE ELISA appears to be more sensitive and may be the more appropriate test [26].

Pinon et al. [18] previously reported that *Toxoplasma* IgE antibodies were detected using the ISAGA technique in two of three patients with AIDS and toxoplasmic ence-

phalitis. In this study, when low-positive results were included, IgE antibodies were detected in 83% of the sera of 12 adult patients with AIDS and toxoplasmic encephalitis by ISAGA and in 50% by ELISA. These data are promising and warrant further study of the use of these methods for the diagnosis of toxoplasmic encephalitis in this type of patient population. In patients with AIDS and suspected toxoplasmic encephalitis a panel of serologic tests should provide a more accurate means of assessing whether the infection is presently active or quiescent.

In the majority of patients with toxoplasmic chorioretinitis, and those with toxoplasmic encephalitis, reactivation of a latent infection is a postulated pathogenetic mechanism of the disease. The Wong et al. data are consistent with their hypothesis that recrudescence of IgE antibodies in patients with disease caused by reactivation may be a marker for the study of immune regulation of immunoglobulin switching in patients with this infection [26].

In the study by Wong et al. [26], *Toxoplasma* IgE antibodies were detected in patients with toxoplasmic chorioretinitis which had resulted from a reactivation of a chronic (latent) infection. When low-positive results were included, more patients with toxoplasmic chorioretinitis had detectable IgE antibodies by ELISA (54%) than by ISAGA (36%). These results are similar to the 46% reported by Pinon et al. (18) in patients with congenital toxoplasmic chorioretinitis. In a separate study of sera from nine patients who had serologic evidence of an acute infection and ocular manifestations including uveitis and chorioretinitis, all had high IgE titers by ELISA.

Garweg et al. [11] reported immunoglobulin in human ocular toxoplasmosis. Using quantitative ELISA, specific antibodies of the IgA, IgM, and IgE types have been demonstrated to occur in ocular toxoplasmosis patients at the following frequencies: IgA, from 26% through 52% to 63% in the aqueous humor; IgM, from <1% to 11% in the aqueous humor and to 50% in the serum; IgE, from 0% to 14% in the vitreous fluid and to 66% in the serum. The levels of IgE within the aqueous humor have not been determined, which is surprising given the purported role of this class of immunoglobulin in ocular toxoplasmosis – related to hypersensitivity and autoimmunity. Immunoblotting for IgM and IgE failed to yield any useful information, which accords with previously published data relating to adult patients, although in young children those classes of immunoglobulin may be of greater importance. Hence, they do not recommend the evaluation of IgM and IgE on a routine basis. Indeed, local production of IgE would be expected to contribute to inflammatory eye diseases, including ocular toxoplasmosis.

London et al. [16] described patients with ocular toxoplasmosis. A number of atypical presentations of ocular toxoplasmosis have been reported, including neuroretinitis, retrobulbar optic neuritis, papillitis, scleritis, outer retinochoroiditis, anterior optic neuropathy, rhegmatogenous and serous retinal detachment, and retinal vascular occlusion. Ocular toxoplasmosis was a common cause of uveitis in patients in a clinic in northern California and patients with ocular toxoplasmosis were more likely than general uveitis patients to be young, male, and Latino, often having emigrated from Mexico to the USA.

Detection of *Toxoplasma* IgE antibodies for the diagnosis of acute *Toxoplasma* infection (seroconversion during pregnancy and toxoplasmic lymphadenopathy) and for congenital *Toxoplasma* infection serves as a useful adjunct to currently available tests. Detection of IgE *Toxoplasma* antibodies also appears to be associated with reactivated chronic (latent) infections and may be important for the diagnosis of these conditions.

## Conclusion

The absence of natural IgE, together with the early emergence of specific IgE during seroconversion, its brief peak between 2 and 3 months after infection, and its shorter kinetics relative to IgM and IgA make specific IgE antibodies a useful complementary tool for fine dating of seroconversion. The persistence of specific IgE several months after seroconversion is suggestive of active toxoplasmosis and should be taken into account in the risk assessment both during pregnancy and prior to conception. Specific IgE is almost always present in symptomatic acquired toxoplasmosis and can thus contribute to the etiologic diagnosis of lymphadenopathies.

**Table 1.** The diagnostic algorithm to differentiate congenital and acquired toxoplasmosis

| Patients infected with *Toxoplasma gondii* | | | |
|---|---|---|---|
| **congenital toxoplasmosis** | | **acquired toxoplasmosis** | |
| acute toxoplasmosis | chronic toxoplasmosis | acute toxoplasmosis | chronic toxoplasmosis |
| IgM+ (12-18 months) | IgM- | IgM+ (12-18 months) | IgM- |
| IgG+ avidity (max. of 4 months, after which avidity increased) | IgG avidity + | IgG+ (max. of 4 months, after which avidity increased) | IgG avidity + |
| IgA+ (6-9 months) | IgA+/- | IgA+ (6-9 months) | IgA+/- |
| IgE+ (4-6 months) | IgE- | IgE+ (4-6 months) | IgE- |

## References

[1] Abdul-Ghani R.: Polymerase chain reaction in the diagnosis of congenital toxoplasmosis: more than two decades of development and evaluation. Parasitol. Res., 2011; 108: 505-512

[2] Ashburn D., Joss A.W., Pennington T.H., Ho-Yen D.O.: Do IgA, IgE, and IgG avidity tests have any value in the diagnosis of toxoplasma infection in pregnancy? J. Clin. Pathol., 1998; 51: 312-315

[3] Bliss S.K., Marshall A.J., Zhang Y., Denkers E.Y.: Human polymorphonuclear leukocytes produce IL-12, TNF-α and the chemokines macrophage-inflammatory protein-1α and -1β in response to *Toxoplasma gondii* antigens. J. Immunol., 1999; 162: 7369-7375

[4] Daffos F., Capella-Pavlovsky M., Forestier F.: Fetal blood sampling during pregnancy with use of a needle guided by ultrasound: a study of 606 consecutive cases. Am. J. Obstet. Gynecol., 1985; 153: 655-660

[5] Decoster A., Slizewics B., Simon J., Bazin C., Darcy F., Vittu G., Boulanger C., Champeau Y., Demory J.L., Duhamel M.: Platelia-Toxo IgA, a new kit for early diagnosis of congenital toxoplasmosis by detection of anti-P30 immunoglobulin A antibodies. J. Clin. Microbiol., 1991; 29: 2291-2295

[6] Desmonts G., Couvreur J., Thulliez P.: Congenital toxoplasmosis. 5 cases of mother-to-child transmission of pre-pregnancy infection. Presse Med., 1990; 19: 1445-1449

[7] Desmonts G., Daffos F., Forestier F., Capella-Pavlovsky M., Thulliez P., Chartier M.: Prenatal diagnosis of congenital toxoplasmosis. Lancet, 1985; 1: 500-504

[8] Ege M.J., Herzum I., Büchele G., Krauss-Etschmann S., Lauener R.P., Bitter S., Roponen M., Remes S., Vuitton D.A., Riedler J., Brunekreef B., Dalphin J.C., Braun-Fahrländer C., Pekkanen J., Renz H., von Mutius E., PASTURE Study Group: Specific IgE to allergens in cord blood is associated with maternal immunity to *Toxoplasma gondii* and rubella virus. Allergy, 2008; 63: 1505-1511

[9] Foudrinier F., Marx-Chemla C., Aubert D., Bonhomme A., Pinon J.M.: Value of specific immunoglobulin A detection by two immunocapture assays in the diagnosis of toxoplasmosis. Eur. J. Clin. Microbiol. Infect. Dis., 1995; 14: 585-590

[10] Foudrinier F., Villena I., Jaussaud R., Aubert D., Chemla C., Martinot F., Pinon J.M.: Clinical value of specific immunoglobulin E detection by enzyme-linked immunosorbent assay in cases of acquired and congenital toxoplasmosis. J. Clin. Microbiol., 2003; 41: 1681-1686

[11] Garweg J.G., Garweg S.D., Flueckiger F., Jacquier P., Boehnke M.: Aqueous humor and serum immunoblotting for immunoglobulin types G, A, M, and E in cases of human ocular toxoplasmosis. J. Clin. Microbiol., 2004; 42: 4593-4598

[12] Gross U., Keksel O., Dardé M.L.: Value of detecting immunoglobulin E antibodies for the serological diagnosis of *Toxoplasma gondii* infection. Clin. Diagn. Lab. Immunol., 1997; 4: 247-251

[13] Grover C.M., Thulliez P., Remington J.S., Boothroyd J.C.: Rapid prenatal diagnosis of congenital *Toxoplasma* infection by using polymerase chain reaction and amniotic fluid. J. Clin. Microbiol., 1990; 28: 2297-2301

[14] Joseph M., Gounni A.S., Kusnierz J.P., Vorng H., Sarfati M., Kinet J.P., Tonnel A.B., Capron A., Capron M.: Expression and functions of the high-affinity IgE receptor on human platelets and megakaryocyte precursors. Eur. J. Immunol., 1997; 27: 2212-2218

[15] Kodym P., Machala L., Rohácová H., Sirocká B., Maly M.: Evaluation of a commercial IgE ELISA in comparison with IgA and IgM ELISAs, IgG avidity assay and complement fixation for the diagnosis of acute toxoplasmosis. Clin. Microbiol. Infect., 2007; 13: 40-47

[16] London N.J., Hovakimyan A., Cubillan L.D., Siverio C.D.Jr., Cunningham E.T.Jr.: Prevalence, clinical characteristics, and causes of vision loss in patients with ocular toxoplasmosis. Eur. J. Ophthalmol., 2011; 21: 811-819

[17] Olariu T.R., Remington J.S., McLeod R., Alam A., Montoya J.G.: Severe congenital toxoplasmosis in the United States: clinical and serologic findings in untreated infants. Pediatr. Infect. Dis. J., 2011; 30: 1056-1061

[18] Pinon J.M., Toubas D., Marx C., Mougeot G., Bonnin A., Bonhomme A., Villaume M., Foudrinier F., Lepan H.: Detection of specific immunoglobulin E in patients with toxoplasmosis. J. Clin. Microbiol., 1990; 28: 1739-1743

[19] Porriez J., Puygauthier-Toubas D., Marx-Chemla D., Pouletty P., Bonhomme A., Pluot M., Pinon J.M.: Comparison of ELIFA and IGM-immunocapture technics in the diagnosis of 50 cases of congenital toxoplasmosis. Ann. Biol. Clin., 1988; 46: 811-814

[20] Remington J.S., Desmonts G.: Toxoplasmosis. In: Remington J.S., Klein J.O. (eds) Infection diseases of the fetus and newborn infant. W.B. Saunders, Philadelphia, 1990; 89-195

[21] Saadatnia G., Golkar M.: A review on human toxoplasmosis. Scand. J. Infect. Dis., 2012; 44: 805-814

[22] Sensini A.: *Toxoplasma gondii* infections in pregnancy: opportunities and pitfalls of serological diagnosis. Clin. Microbiol. Infect., 2006; 12: 504-512

[23] Suzuki L.A., Rocha R.J., Rossi C.L.: Evaluation of serological markers for the immunodiagnosis of acute acquired toxoplasmosis. J. Med. Microbiol., 2001; 50: 62-70

[24] Swisher C.N., Boyer K., McLeod R.: Congenital toxoplasmosis. The Toxoplasmosis Study Group. Semin. Pediatr. Neurol., 1994; 1: 4-25

[25] Villena I., Aubert D., Brodard V., Quereux C., Leroux B., Dupouy D., Remy G., Foudrinier F., Chemla C., Gomez-Marin J.E., Pinon J.M.: Detection of specific immunoglobulin E during maternal, fetal, and congenital toxoplasmosis. J. Clin. Microbiol., 1999; 37: 3487-3490

[26] Wong S.Y., Hajdu M.P., Ramirez R., Thulliez P., McLeod R., Remington J.S.: Role of specific immunoglobulin E in diagnosis of acute toxoplasma infection and toxoplasmosis. J. Clin. Microbiol., 1993; 31: 2952-2959

[27] Yamakawa R., Yamashita Y., Yano A., Morita J., Kato H.: Congenital toxoplasmosis complicated by central diabetes insipidus in an infant with Down syndrome. Brain Dev., 1996; 18: 75-77

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The authors have no potential conflicts of interest to declare.