Rev. Inst. Med. trop. S. Paulo
44 (3):119-120, May-June, 2002.

EDITORIAL

TOXOPLASMOSIS AND THE LABORATORY: DIAGNOSIS AND A CONSTANT STRIVING FOR IMPROVEMENT

Antonio Walter FERREIRA & Mário E. CAMARGO

Almost half a century has elapsed since the early studies of Sabin and Feldman about the diagnosis of Toxoplasmosis. Traditional manual laboratory methods adequate for small routines have been replaced with automated or semi-automated procedures involving little manipulation and risk of human error, which can be used for large routines at reasonable prices.

Indeed, continuous scientific and technical evolution has led to a decisive progress in diagnosis through the search of "gold standard" tests that will provide safe information about the real health status of the patient. However, in our opinion, faults are often observed in the training of clinicians or laboratory technicians concerning the selection of tests and mainly their use at an opportune time and the correct interpretation of their results with respect to the clinical signs and symptoms presented by the patients. Fortunately, great efforts are being made in this respect both by Health Offices and by medical societies and entities in various States in Brazil. The serological profiles observed during the course of Toxoplasmosis are classical, respectively representing recent infection, previous infection or a transition phase, and have been defined by experienced investigators such as G. DESMONT in France, J.S. REMINGTON in the United States, and others, including Brazilian researchers, such as M.E. CAMARGO from this Tropical Medicine Institute. Successively available immunological resources, such as the Complement Fixation test, Indirect Hemagglutination and detection of anti-*Toxoplasma gondii* IgG and IgM antibodies especially by ELISA and Immunofluorescence, have been thoroughly investigated. For years these serological profiles of toxoplasmosis have been exhaustively taught at medical and paramedical schools and discussed at Congresses and Scientific Meetings, being unanimously accepted in laboratory diagnostic routine. However, technology has evolved, especially with the development of more sensitive automated equipment. The Universities, historical seats of research, have been rapidly superseded by large industries which have heavily invested in the development of new products and in equipment of high sensitivity. However, some errors have started to arise especially in the search for IgM antibodies by attributing excessive value to their residual levels, which are nonsignificant and erroneously interpreted as positive results indicating current infection, with serious consequences especially for women in the early phase of pregnancy, who are submitted to unnecessary treatment or even to interruption of pregnancy. Fortunately, research and development have continued to advance and new parameters have been developed for the diagnosis of toxoplasmosis in its different phases, such as the avidity test of IgG antibodies and detection of the parasite by a molecular method such as the polymerase chain reaction (PCR). IgG antibodies of low avidity characterize the beginning of infection, being present up to the third or fourth month, whereas the PCR method permits to confirm fetal infection by detection of the parasite DNA in amniotic fluid.

Thus, the following algorithm could be suggested for the diagnosis of toxoplasmosis:

Search for IgG antibodies using a sensitive and specific automatic method;

Search for IgM antibodies by immunocapture and, in the case of their presence at levels exceeding those established by the manufacturer, i.e., above the reactivity threshold of the test, use of the avidity test of IgG antibodies.

When combined and properly interpreted, these tests help define the disease, permitting the identification of important information that will guide the conduct of the clinician in the "recent acute", or "non-acute" phase. Only the presence of IgG antibodies indicates immunity when they are detected at satisfactory levels using highly specific reagents, whereas IgM antibodies characterize current infection. The Indirect Immunofluorescence test could be used in small routines, with care taken to avoid false-positive IgM antibodies. All sera should be routinely absorbed with RF absorbent before processing, a fact that makes the test more onerous for the laboratories.

A serious mistake, unfortunately quite frequent and with often serious consequences, is to consider pregnant women who are seronegative for anti-toxoplasma antibodies to be at no risk to transmit toxoplasmosis to the fetus. This is due to the fact that the professionals believe that this serological negativity excludes maternal infection by toxoplasma, as would be the case for negative tests for other conditions such as Chagas disease, syphilis etc. In contrast, a negative serological test for

Instituto de Medicina Tropical de São Paulo - Universidade de São Paulo, SP, Brasil, Av. Dr. Enéas de Carvalho Aguiar 470, 05403-000 São Paulo, SP, Brasil

toxoplasmosis requires frequent repetition in pregnant women throughout gestation due to the risk of the mother to become infected since she has no defense antibodies and therefore could transmit the parasite to the fetus, who is highly vulnerable to severe mortal infection or serious irreversible lesions, mainly of the brain. The tests should be repeated monthly or at two month intervals while they remain negative, and if positivity should occur it will be imperative to treat immediately both the pregnant woman and the newborn.

REFERENCES

1. ASHBURN, D.; JOSS, A.W.L.; 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. Path., 51**: 312-315, 1998.

2. CAMARGO, M.E. - Toxoplasmose. In: FERREIRA, A.W. & ÁVILA, S.L.M., ed. **Diagnóstico laboratorial das principais doenças infecciosas e auto-imunes.** Rio de Janeiro, Guanabara Koogan, 2001. p. 278-288.

3. CAMARGO, M.E.; LESER, P.G. & LESER, W.S.P. – Definição de perfis sorológicos na toxoplasmose. Importância diagnóstica e epidemiológica. **Rev. bras. Pat. clin**. **13:** 113-127, 1977.

4. CAMARGO, M.E.; LESER, P.G. & ROCCA, A. – Rheumatoid factor as cause for false positive IgM anti-toxoplasma fluorescent tests. A technique for specific results. **Rev. Inst. Med. trop. S. Paulo, 14:** 310-313, 1972.

5. COZON, G.J.N.; FERRANDIZ, J.; NEBHI, H.; WALLON, M. & PEYRON, F. – Estimation of the avidity of immunoglobulin G for routine diagnosis of chronic *Toxoplasma gondii* infection in pregnant women. **Europ. J. clin. Microbiol. infect. Dis., 17:** 32-36, 1998.

6. REMINGTON, J.S.; McLEOD, R. & DESMONTS, G. – Toxoplasmosis. In: REMINGTON, J.S. & KLEIN, J.O., ed. **Infectious diseases of the fetus and newborn infant.** 4. ed. Philadelphia, W.B. Saunders, 1995. p. 140-267.

7. SUZUKI, L.A.; ROCHA, R.J. & ROSSI, C.L. – Evaluation of serological markers for the immuno diagnosis of acute acquired toxoplasmosis. **J. med. Microbiol., 50**: 62-70, 2001.

8. WILSON, M.; REMINGTON, J.S.; CLAVET, C. *et al.* – Evaluation of six commercial kits for detection of human immunoglobulin M antibodies to *Toxoplasma gondii*. The FDA Toxoplasmosis Ad Hoc Working Group. **J. clin. Microbiol., 35**: 3112-3115, 1997.

Received: 29 April 2002