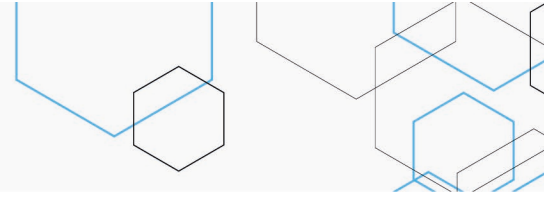


Newborn Screening for Congenital Toxoplasmosis



Technology: Expansion of newborn screening (heel prick test) for congenital toxoplasmosis

Indication: Congenital toxoplasmosis

Applicant: Health Surveillance Department of the Ministry of Health of Brazil

Background: Congenital toxoplasmosis (CT) is an infectious disease that results from the transplacental transmission of *Toxoplasma gondii* to the fetus, due to maternal primary infection during pregnancy. Newborns who have clinical manifestations may have signs in the neonatal period or in the first months of life. These cases tend to have, more frequently, severe sequelae, such as visual impairment in varying degrees, mental retardation, seizures, motor abnormalities and deafness. The prevalence of toxoplasmosis is high in Brazil, ranging from 64.9% to 91.6%, depending on the region. A high percentage (50-80%) of women of childbearing age are IgG positive, and 20-50% are susceptible (IgG and IgM negative) and at risk of acquiring the infection during pregnancy. Studies carried out in Brazil have shown that 5-23 children are born infected per 10,000 live births. The inclusion of toxoplasmosis in the Neonatal Screening Program, which complements the maternal screening in Brazil, has been suggested by several specialists. According to Neto and colleagues, although the long-term efficacy of treatment of CT has not been well documented, in view of the availability of reliable diagnostics, functional logistics, and networking for screening, the insidious nature of the sequelae and the very high prevalence of the disease, neonatal screening for CT should be considered an alternative to no screening at all.

Question: Is newborn screening test for congenital toxoplasmosis by analysis of anti-*Toxoplasma gondii* IgM antibodies in blood spots collected on filter paper, safe, effective and efficient enough to change immediate and long-term practices and outcomes in patients diagnosed?

Scientific evidence: According to data from a national study in Brazil, neonatal screening identified cases of infection not detected by obtaining only one or two serum samples from pregnant women for *T. gondii* serology, mainly when infection was acquired in late pregnancy. The immunosorbent agglutination assay (ISAGA) is the serological test for the diagnosis of CT that has shown the highest sensitivity (54-87%) and specificity (77.7-100%). There are no randomized trials evaluating antiparasitic therapy in infants, so the evidence comes from observational studies. Compared with historical controls (untreated or treated for one month), combination treatment for 12 months was associated with improved neurologic, cognitive, and auditory outcomes and prevention of new eye lesions.

Economic evaluation: With no screening of the population, the cost would be BRL 11.42 per birth, or about BRL 33,555,477.36 for all births in Brazil in 2018. The expansion of newborn screening for congenital toxoplasmosis, including costs of screening as well as treatment during the first year of life, was estimated to be BRL 8.19 per birth, and BRL 24,064,742.52 for all births. Among the strategies tested, prenatal screening had the highest cost, BRL 57.96 per birth, including screening in the three trimesters of pregnancy, and treatment of pregnant



women and children. In one year, the total cost of prenatal screening would be BRL 170,304,331.68. The costs saved by performing neonatal screening were estimated to be BRL 13,516,216.80, when compared with no screening. Considering avoided CT related adverse outcomes, although the total costs for the neonatal screening were estimated to be lower, it was less effective than prenatal screening. The 1-year incremental cost-effectiveness ratio showed that prenatal screening would require investing BRL 50.02 to avoid one adverse event compared with neonatal screening. No screening at all was found to be dominated by the screenings assessed.

Budget impact analysis: In the first scenario, considering the cost of BRL 8.19 per birth obtained in the economic evaluation, the budget impact would be around BRL 23.9 million. Considering a maternal-fetal transmission rate of 18.5% identified in a Brazilian epidemiological study, the budget impact was estimated to be approximately BRL 55 million, after five years, and considering a lower transmission rate of 3.5%, it would be approximately BRL 54 million. In the last scenario, considering the prevalence of congenital toxoplasmosis of 6/10,000 live births, the budget impact was estimated to range from BRL 55.44 to BRL 55.56 million.

International recommendations: Toxoplasmosis prevention strategies, adopted by the several public health systems, are not uniform across different countries. The neonatal screening has been adopted in Poland, Denmark and some cities in the United States – these three countries have low prevalence of congenital toxoplasmosis. Countries with high incidence of infection, such as France, Austria and Slovenia, implemented prenatal screening. The United Kingdom, where congenital toxoplasmosis is rare, has no universal serologic screening program.

Considerations: Congenital toxoplasmosis is an important health problem, prevalent in Brazil (5-23 infected children for every 10,000 live births), and often associated with severe sequelae. CT is diagnosed by detection of IgM in the neonatal period in more than 80% of cases. Early treatment may reduce the damage caused by the disease. The analysis of anti-*T. gondii* IgM for neonatal screening has already been applied in different regions in Brazil, and the cost-benefit ratio of early diagnosis is favorable in the absence of a well-implemented prenatal screening.

Initial Recommendation: Conitec, at its 84th Ordinary Meeting, on December 4th, 2019, decided that the subject matter should be made available in a public consultation with a favorable preliminary recommendation to the expansion of newborn screening (heel prick test) for congenital toxoplasmosis, in the scope of the Brazilian Public Health System (SUS). Congenital toxoplasmosis is a public health problem, and early diagnosis and treatment may reduce the sequelae of the disease in children.

Public consultation: The Conitec's Recommendation Report was made available through the Public Consultation No. 84/2019 between January 2nd and 21st, 2020. Two hundred forty-four contributions were received, 110 of which were technical-scientific contributions, and 134 were experience or opinion contributions. After analyzing the contributions received in the



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Public Consultation, Conitec's plenary session decided that there was not sufficient reason to change the preliminary recommendation.

Final Recommendation: The Conitec's members present at the 85th Ordinary Meeting, on February 5th, 2020, unanimously decided to recommend the expansion of newborn screening (heel prick test) for congenital toxoplasmosis. The Deliberation Record N^o 507/2020 was signed.

Decision: To expand newborn screening (heel prick test) for congenital toxoplasmosis, in the scope of SUS, according to Ordinance N^o 5, published in the Official Gazette of the Federal Executive N^o 44, Section 1, page 130, on March 5th, 2020.

