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Brasília Letter: Proposal for Toxoplasmosis Control in Brazil with a Multidisciplinary Approach and a Pan-American Cooperation Perspective

Carta de Brasília: Proposta para o Controle da Toxoplasmose no Brasil com Abordagem Multidisciplinar e Perspectiva de Cooperação Pan-Americana

Brazilian Toxoplasmosis Research Network/Coordinating Committee of the VI Brazilian Symposium on Toxoplasmosis and III International Symposium on Toxoplasmosis, members of the roundtable "Pan-American Cooperation: Strategic Partnerships in Addressing Toxoplasmosis," and all participants of the plenary session.*

ABSTRACT

A diverse group of professionals gathered in Brasília for the VI Brazilian Symposium on Toxoplasmosis and III International Symposium on Toxoplasmosis from October 17 to 19, 2023. Guided by the 'One Health' concept, the event addressed toxoplasmosis in its human, animal, and environmental dimensions. Participants discussed strategies to improve the prevention, diagnosis, and treatment of the disease in Brazil, also emphasizing a Pan-American cooperation. The resulting document, the *Brasília Letter: Proposal for Toxoplasmosis Control in Brazil with a Multidisciplinary Approach and a Pan-American Cooperation Perspective*, synthesizes the specialists' concerns and proposes actions for the development of public health policies in Brazil and other countries in the Americas. This initiative aims to promote significant advances in toxoplasmosis control, benefiting society's health on a continental and global scale.

Key words: *Toxoplasma gondii*; Toxoplasmosis prevention; control; Public health; One Health; Preventive medicine; Research; Education; Environmental epidemiology; Molecular epidemiology.

RESUMO

Reuniu-se em Brasília para o VI Simpósio Brasileiro sobre Toxoplasmose e o III Simpósio Internacional sobre Toxoplasmose, um grupo diversificado de profissionais, no período de 17 a 19 de outubro de 2023. Guiado pelo conceito de 'Saúde Única', o evento abordou a toxoplasmose em suas dimensões humana, animal e ambiental. Os participantes discutiram estratégias para melhorar prevenção, diagnóstico e tratamento da doença no Brasil, enfatizando também uma cooperação panamericana. O documento resultante, *Carta de Brasília: Proposta para o Controle da Toxoplasmose no Brasil com Abordagem Multidisciplinar e Perspectiva de Cooperação Panamericana*, sintetiza as preocupações dos especialistas e propõe ações para o desenvolvimento de políticas de saúde pública no Brasil e em outros países das Américas. Esta iniciativa visa promover avanços significativos no controle da toxoplasmose, beneficiando a saúde da sociedade em escala continental e global.

Palavras-chave: *Toxoplasma gondii*; Prevenção; Controle; Saúde pública; Saúde Única; Medicina preventiva; Pesquisa; Educação; Epidemiologia ambiental; Epidemiologia molecular.

HISTORICAL CONTEXT AND DOCUMENT PURPOSE

In an important milestone in our journey, we recall the days of September 20 and 21, 2008, during the Toxoplasmosis Centennial Congress, in the activities of the First National Symposium on Toxoplasmosis, held in Armação dos Búzios, Rio de Janeiro, Brazil. In this pioneering event, we gathered a diverse group of professionals, including researchers, healthcare professionals, epidemiologists, and public health specialists, with the central objective of discussing the control of congenital toxoplasmosis in Brazil. It was in

that context that the idea of forming the Brazilian Toxoplasmosis Research Network - Brazilian Toxo Net - emerged. Its purpose was to foster research collaboration and share experiences in clinical care, with the aim of finding comprehensive solutions for toxoplasmosis, benefiting a broad group of the Brazilian population.

The Brazilian Toxo Net, an active and operational non-governmental organization, operates as a non-profit private law association established for an indefinite period with scientific, social, and educational objectives. It has had legal personality since 2016 and is governed by its own

bylaws and relevant legal provisions. It functions as a continuous dialogue space among national researchers, international partners, and professionals in human, animal, and environmental health, also serving as advocates urging authorities to implement public policies for the control of toxoplasmosis. One of the outcomes of the First National Symposium on Toxoplasmosis was the *Búzios Letter*¹, a document that outlined fundamental concerns and proposals for cooperation between researchers and health managers. This letter became an important milestone in the approach to toxoplasmosis in Brazil, proposing guidelines and concrete actions to improve the understanding and control of this disease. The proposed measures aimed to protect the health of the population against the risks associated with toxoplasmosis, with a special focus on pregnant women and children.

Recognizing the magnitude of the impact of toxoplasmosis on the Brazilian population and the need for effective coordination, we, a diverse group of researchers and healthcare professionals, dedicated to the study of the parasite *Toxoplasma gondii* and its repercussions on the environment and living beings, gathered again in Brasília, during the VI Brazilian Symposium on Toxoplasmosis and the III International Symposium on Toxoplasmosis, from October 17 to 19, 2023, united by the concept of 'One Health'. This meeting reinforced our mission to address the various aspects of toxoplasmosis, encompassing human, animal, and environmental health through cooperation among multiple sectors, disciplines, and communities at various levels of society.

At this internationally scoped meeting, we also had the opportunity to discuss the relevance and feasibility of collaborations in research and health actions focused on toxoplasmosis, encompassing the three Americas (South, Center and North). Considering the impact of the recommendations of the *Búzios Letter* on the construction, management, and execution of health actions and policies, we now renew and expand our commitment to improving public health in Brazil through the proposition of new guidelines gathered in this document.

This document was prepared by the Board of Directors of Brazilian Toxo Net, the event organizing committee, members of the roundtable "Pan-American Cooperation: Strategic Partnerships in Addressing Toxoplasmosis," with the contribution and approval of the plenary at the scientific meeting, which consisted of academics, researchers and active professionals in health management and care. The focus was on providing propositions that support the mission of Brazilian Toxo Net, as expressed at the scientific meeting held in October 2023 in Brasília.

ACTION PROPOSALS

The following proposals are the result of extensive discussions and collaborations among experts in the field of toxoplasmosis. They are designed to be implemented as public health policies in Brazil, addressing the multifaceted challenges posed by toxoplasmosis through a One Health approach. We urge health authorities to consider these recommendations for improving toxoplasmosis control and prevention across the country.

Interdisciplinary integration

The importance of interdisciplinary collaboration involving professionals working at the human-animal-environment interface and dedicated to the study and actions related to toxoplasmosis is reaffirmed. This synergy is essential to effectively combat toxoplasmosis. It is necessary to expand and diversify the channels for disseminating knowledge about the parasite and the disease symptoms it causes in the context of government healthcare management (in the Sistema Único de Saúde – SUS, private, and complementary services – health plans and philanthropic) at the municipal, state, and federal levels.

Support should be provided for the implementation and expansion of policies that address the needs of groups most vulnerable to infection, such as pregnant women and newborns, people living with Human Immunodeficiency Virus (HIV) and other conditions of permanent or transitory immunological vulnerability². Additionally, it is necessary to seek support for the implementation and expansion of these policies among specific population groups, such as indigenous peoples³, riverside communities, and quilombola communities (descendants of Afro-Brazilian slaves who formed autonomous settlements)⁴. Consideration should also be given to support for the implementation and expansion of policies that address groups of animals with greater susceptibility to clinical manifestations of toxoplasmosis.

In this context, the critical role of organized civil society in all the actions proposed in this letter is recognized and encouraged, from those aimed at increasing the visibility of preventive measures to those fostering knowledge and control of toxoplasmosis at the national level.

One Health: Integrating Human, Animal, and Environmental Approaches to Toxoplasmosis Control

It is proposed to invest in the control of toxoplasmosis within the One Health approach, recognizing that human, animal, and environmental health are intrinsically interconnected. This holistic approach is fundamental for understanding and mitigating this health threat. In this context, the importance of primary health care is highlighted as the population's primary point of contact with the health system.

The team of professionals working at this level of care should be encouraged to:

- Share knowledge about toxoplasmosis in its various aspects.
- Identify risks.
- Assess needs.
- Address the health demands of the community members under their care.
- Monitor the flow of patients among the various points of the health care system, whose characteristic is the hierarchical flow based on the complexity of the cases.

Another strategy to control toxoplasmosis should include reducing the population of stray cats, incorporating sterilization programs for both domestic and feral cats.

Therefore, it is important to reinforce the participation of representatives from official government agencies (Ministry of Health, Ministry of Agriculture, Livestock and Supply, and Ministry of the Environment), along with members of the Brazilian Toxo Net, in exchanging information regarding the monitoring of human, animal, and environmental health. This collaboration aims to plan effective control measures to limit the spread of *T. gondii*.

In this scenario, it is essential to involve not only human health professionals but also those dedicated to animal health and welfare, as well as specialists in environmental conservation, protection, and recovery, along with their respective organizations across Brazil.

Universal Prenatal and Neonatal Screening

The importance of actions aimed at preventing and minimizing the damage caused by congenital toxoplasmosis is reiterated. Among these actions, it is essential to conduct early and effective prenatal screening, ideally with monthly serological monitoring during pregnancy for seronegative pregnant women, preferably using

point-of-care tests during prenatal care. This approach makes early detection of seroconversion feasible at a low cost.

Another relevant and necessary action, complementary to prenatal screening, is neonatal screening for toxoplasmosis. This is particularly important in Brazil considering: (a) the territorial extent of Brazil, (b) the social and economic diversity of its population, (c) the heterogeneity of access to diagnosis during pregnancy, (d) the risk of infection/reinfection of pregnant women due to the considerable genetic diversity of the parasite and its ubiquitous presence in the environment, (e) the higher probability of transplacental transmission in the third trimester of pregnancy, and (f) the severity of ocular disease, which also presents impairments in neurological, auditory, motor, and cognitive functions

In accordance with Law 14,154, dated May 26, 2021⁵, which included toxoplasmosis in the Universal Neonatal Screening Program of Brazil, the group discussed the importance of supporting the process of its implementation in partnership with the Ministry of Health, state and municipal health departments, philanthropic institutions, and educational institutions, respecting their particularities.

Within this perspective, the following needs are highlighted:

- Ensure the availability of specific medications for the treatment of pregnant women with toxoplasmosis, avoiding any interruptions in the supply of these medications.
- Provide the necessary resources for early confirmation of infection in cases identified by screening, including serological tests, neuroimaging exams, and ophthalmological evaluations.
- Make efforts to develop pediatric formulations of the medications used in congenital toxoplasmosis, simplifying their management, reconstitution, and storage, a necessary condition to ensure drug stability and thus provide adequate treatment for children with congenital toxoplasmosis.
- Promote rehabilitation strategies, including early stimulation of children at risk of neuropsychomotor developmental delays due to congenital toxoplasmosis.
- Ensure facilitated and timely access to the Health Care Network for People with Disabilities, providing the necessary interventions for the appropriate development of these children.
- Expand the Low Vision care network with the objective of making access easy and timely for the prevention of visual impairment and visual rehabilitation in individuals with greater impairment, seeking to enable children and adults to perform daily life activities with a better quality of life.

Advancing Toxoplasmosis R&D: Strategic Priorities and Collaborative Initiatives

The importance of encouraging research on toxoplasmosis in its various aspects, including environmental, human, and animal health impacts, is reaffirmed. In this context, it is essential to launch public calls for proposals to promote studies in this area. The Ministry of Health can play a fundamental role in fostering this initiative. According to its competencies established by legislation, the Ministry is responsible for promoting the exchange of knowledge and experiences with different entities, whether they are public or private institutions, as well as the technical-scientific community and international organizations, in addition to initiatives in the field of digital health⁶. This role is essential to stimulate and support innovative and collaborative research on toxoplasmosis, addressing its various facets and impacts.

There are several important themes to be considered:

- Assess the applicability and cost-benefit of:
 - Neonatal screening for toxoplasmosis currently underway in Brazil.
 - Monthly serological monitoring during pregnancy with tests for the rapid recognition of seroconversion.
 - Instituting early treatment at the point of care for acutely infected pregnant women with available and effective medications.
- Promote studies that support earlier fetal treatment, as infections in the early stages of pregnancy result in more serious fetal impairments.
- Conduct local or national cohort studies of children identified with toxoplasmosis through neonatal screening as well as prenatal screening.
- Develop pediatric formulations for the treatment of congenital toxoplasmosis.
- Evaluate the magnitude and impact of toxoplasmosis in people living with HIV.
- Evaluate the magnitude and impact of toxoplasmosis in companion, livestock, and wild animals at the national level.
- Collaborate with the National Council for the Control of Animal Experimentation (CONCEA) of the Ministry of Science, Technology, and Innovation in Public Health Event (PHE) situations. These are situations that demand the urgent implementation of measures for the prevention, control, and containment of risks, damages, and harm to public health.
- Disseminate scientific events on toxoplasmosis on the Brazilian Toxo Net's website.
- Conduct studies on the relationship between prenatal databases and notification data of pregnant women with acute toxoplasmosis.
- Perform studies on host-parasite interactions and the discovery of new and repurposed compounds for the treatment of toxoplasmosis.
- Seek technical and political support from civil society for the inclusion of toxoplasmosis as a topic in the research lines of funding agencies.

Enhancing Toxoplasmosis Surveillance and Control: Integrating Data-Driven Strategies for Comprehensive Public Health Management

The importance of actions aimed at the surveillance of toxoplasmosis in pregnancy and congenital toxoplasmosis, cerebral toxoplasmosis, and ocular toxoplasmosis for the development and evaluation of public health policies is reiterated. To achieve this goal, we propose to:

1. Foster Data Collection and Analysis:

- Promote routine analyses and discussions of toxoplasmosis data collected in service, in conjunction with other diseases, conditions, and health determinants, to support local actions.
- Provide information regarding the prevalence, incidence, mortality, and morbidity of the different forms of toxoplasmosis.
- Develop specific notification forms for the different clinical presentations of the disease to qualify epidemiological information in public databases.
- Adapt health information systems to receive data on the characteristics of the various clinical presentations of toxoplasmosis.

2. Strengthen Prevention and Control Measures:

- Enhance disease prevention and control actions based on scientific evidence and patient care service data.
- Reinforce disease prevention and control actions based on scientific evidence and mandatory reporting data from the federal health registration system in Brazil.

3. Promote Service Integration:

- Encourage integration between services that attend to patients with toxoplasmosis, both adults and children, especially patients co-infected with HIV, to ensure rational planning and broad availability of specific medications for the treatment of toxoplasmosis for all individuals.

4. Develop Environmental Surveillance:

- Establish an interministerial environmental surveillance program to:
 - Identify water sources and food groups with the highest likelihood of *T. gondii* contamination.
 - Create effective mitigation strategies to reduce oocyst contamination in the environment.

5. Standardize Laboratory Methods:

- Encourage the standardization and interlaboratory validation of procedures for the isolation, recovery, and efficacy testing in the detection of oocysts in environmental samples, including water and food.

Enhancing Outbreak Investigation Capabilities: A Multi-Agency Collaborative Approach

Brazil has recorded the most frequent occurrences of toxoplasmosis outbreaks and the largest (in terms of the number of affected individuals) outbreaks documented in the medical-scientific literature to date. This unique position underscores the critical importance of robust outbreak investigation capabilities in the country. Strengthening these capabilities is essential for early detection, rapid response, and effective management of toxoplasmosis outbreaks, ultimately contributing to better public health outcomes and providing valuable insights for global toxoplasmosis control efforts. This objective involves coordinated action among various essential agencies and actors, including:

- National Health Surveillance Agency (ANVISA)
- Ministry of Agriculture and Livestock (MAPA)
- Ministry of Fisheries and Aquaculture (MPA)
- Ministry of Education (MEC)
- Ministry of Environment and Climate Change (MMA)
- National Health Foundation (FUNASA)
- Secretariat for Indigenous Health (SESAI)
- As well as the sectors of Primary and Specialized Care and Health Surveillance in healthcare.

To strengthen toxoplasmosis outbreak investigation, the following recommendations are proposed:

1. Professional Development:

- Invest in specialized training and courses to enhance the technical skills of professionals involved in toxoplasmosis outbreak investigation.

2. Technical and Scientific Capacity Building:

- Strengthen the capabilities of various governmental spheres, Central Laboratories (LACENS), and educational and research institutions.
- Ensure the use of state-of-the-art tools and knowledge available in research centers and universities to support outbreak investigations.

3. Collaborative Funding:

- Guarantee funding for partnerships between different levels of government and educational and research institutions.
- Establish strategic collaborations to support the investigation and resolution of outbreaks.

Investing in Primary Prevention Educational Programs

Recognizing the crucial role of education in preventing toxoplasmosis, the following recommendations were proposed:

1. Educational Measures for Teachers and Students:

- Support and encourage educational initiatives about toxoplasmosis for teachers and students across all levels of education.
- Extend these educational efforts to populations at highest risk for the disease.

2. Continuing Education for Health Professionals:

- Strengthen ongoing educational programs for health professionals who provide care to individuals with toxoplasmosis.

3. Integration with Existing School Health Programs:

- Disseminate educational prevention actions within the framework of the School Health Program⁷.

4. Engagement with Education Professionals:

- Promote meetings and workshops with basic and secondary education professionals to discuss toxoplasmosis and its prevention.

PAN-AMERICAN RESEARCH AND COOPERATION NETWORK

The proposal for a Pan-American Toxoplasmosis Network emerged from a collaborative initiative aimed at enhancing research on *T. gondii* and toxoplasmosis across the Americas. This endeavor was inspired by the successful trajectory of the Brazilian Toxo Net and was conceptualized during a debate organized at the symposium. The event convened researchers from Argentina, Brazil, Colombia, the Dominican Republic, Mexico, and the United States of America, fostering a truly pan-American perspective. The collective consensus reached by the participants underscores the urgent need to consolidate efforts across the Americas. Whether through the establishment of a network, consortium, or any other collaborative structure, the primary objective is to strengthen collective capacities and experiences in *T. gondii* and toxoplasmosis research. These multidisciplinary collaborations between diverse regions, involving both seasoned professionals and early-career researchers, aim to surmount existing limitations and pave the way for significant advancements in various domains, including:

- Health education.
- Epidemiology.

- Biology.
- Treatment.
- Food safety.
- Diagnostic.

Key recommendations:

1. Strengthen Collaborative Work:

- Focus on enhancing cooperation within the countries of North, Central, and South America.
- Aim to reduce costs and increase the feasibility of monthly point-of-care testing during prenatal care.
- Work towards making early detection of seroconversion a low-cost reality.

2. Address Existing Challenges:

- Recognize significant obstacles, such as training health personnel in the use and interpretation of laboratory tests.
- Acknowledge that access to medications after diagnosis constitutes a bottleneck in some services.

3. Prioritize Prevention and Treatment:

- Maintain the goal of implementing all available tools for education, diagnosis, and treatment during pregnancy.
- Emphasize that ideally, prevention of infection is paramount, followed by treatment during pregnancy when necessary.

4. Neonatal Screening:

- It is essential to maintain neonatal screening until universal coverage of diagnosis and treatment during pregnancy is achieved. Additionally, it must be sustained until the risk of environmental transmission is significantly reduced for the most vulnerable populations, especially those economically disadvantaged.
- Work towards significantly reducing the risk of environmental transmission.

5. Strategic Objectives:

- Reduce infection rates in the population by improving education and water treatment.
- Strive for universal coverage of diagnosis and treatment during pregnancy.

This collaborative approach aims to leverage the strengths of different regions and disciplines to address the complex challenges posed by toxoplasmosis across the Americas. By promoting cooperation and knowledge sharing, we can work towards more effective strategies for prevention, diagnosis, and treatment strategies for this disease, which poses a significant concern in the realm of public health.

CONCLUSIONS AND FINAL CONSIDERATIONS

As we conclude this document, it is crucial to synthesize the main points discussed and emphasize the importance of the proposed actions for advancing toxoplasmosis control and research in the Americas.

Summary of key points:

1. The formation of the Pan-American Toxoplasmosis Network represents a significant milestone in international collaboration for the study and control of this disease.

2. We have identified key areas for advancement, including health education, epidemiology, parasite biology, treatment, food safety, and diagnosis.
3. We recognize the need to strengthen cooperation among countries in the three Americas, focusing on improving early diagnosis and treatment during pregnancy.
4. We emphasize the importance of neonatal screening as a temporary measure until diagnosis and treatment during pregnancy achieve universal coverage and the risk of environmental contamination by the parasite significantly decreases from its current level.
5. We emphasize the One Health approach, recognizing the interconnection between human, animal, and environmental health in controlling toxoplasmosis.

Reiteration of the importance of proposed actions:

The actions proposed in this document are fundamental to addressing the challenges presented by toxoplasmosis in our region. Multidisciplinary and international collaboration is essential to:

- Develop more effective prevention and control strategies.
- Improve access to early diagnosis and treatment.
- Reduce infection rates in the population through education and improved water treatment.
- Advance understanding of the diversity of *T. gondii* strains and their impact on public health.
- Implement environmental and veterinary control measures to reduce parasite transmission.

Call to action for health authorities and professionals:

We call upon health authorities, researchers, and health professionals from all countries in the Americas to:

1. Support and actively participate in the Pan-American Toxoplasmosis Network.
2. Implement the recommendations proposed in this document in their respective countries and institutions.
3. Prioritize funding and support for collaborative research on toxoplasmosis.
4. Work towards implementing public policies aimed at prevention, early diagnosis, and adequate treatment of toxoplasmosis.
5. Adopt a One Health approach, integrating efforts across human, animal, and environmental health.

Through this document, we reaffirm our commitment to improving the health of the population in the Americas concerning the harms caused by toxoplasmosis. We open avenues for collaboration in basic and translational research, as well as health cooperation actions among the countries of the American continent.

We recognize significant similarities between the situations in Brazil and Latin America due to shared socioeconomic challenges, which differ from those found in North America, particularly in Canada and the United States. Furthermore, South America exhibits significantly greater genetic diversity of *T. gondii* strains compared to North America, which may have implications for reinfection episodes during pregnancy and a higher prevalence of severe clinical manifestations of the disease. We hope that the *Brasília Letter* will serve as an important indicator for the development of public health policies by authorities in this sector, both in Brazil and across other countries of the American continent, much

like the *Búzios Letter* did for Brazil in the recent past. By translating the proposed actions into concrete measures, we aim to benefit and continue to enhance the well-being and health of society. This initiative will promote significant advances in the prevention, diagnosis, and treatment of toxoplasmosis, thereby strengthening human, animal, and environmental public health on both a continental and global scale.

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