International health policy forum for the elimination of HTLV
Advancing HTLV Health Policies around the World

10 November 2021
Meeting Report
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# ACRONYMS AND ABBREVIATIONS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>ATLL</td>
<td>Adult T cell leukemia/lymphoma</td>
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<td>HAM</td>
<td>HTLV-1 associated myelopathy</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HTLV</td>
<td>Human T cell lymphotropic virus</td>
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<tr>
<td>MTCT</td>
<td>Mother-to-child transmission</td>
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<td>NCHR</td>
<td>National Centre for Human Retrovirology</td>
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<td>PAHO</td>
<td>Pan American Health Organization</td>
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<td>PLHTLV</td>
<td>People living with HTLV</td>
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<td>STIs</td>
<td>Sexually transmitted infections</td>
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<td>UK</td>
<td>United Kingdom</td>
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<td>WHO</td>
<td>World Health Organization</td>
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**SUMMARY**

This report highlights some of the main interventions available for the prevention and control of human T cell lymphotropic virus (HTLV) infection and its consequences and summarizes national and institutional experiences, discussions, successes, and challenges associated with the implementation of public health policies toward the elimination of HTLV infection. These topics were presented at the webinar “HTLV World Day 2021: International health policy forum for the elimination of HTLV – Advancing HTLV health policies around the world.”

It is evident that HTLV-1 is the etiologic agent of severe diseases, and its socioeconomic impact should not be underestimated. Adequate care for people living with HTLV (PLHTLV) is complex, and a multidisciplinary team is needed. The United Kingdom (UK) has implemented a successful model to provide care for PLHTLV, the National Centre for Human Retrovirology (NCHR). NCHR is centered on patients, but its role extends beyond patient care. Brazil has been one of the leading protagonists on the implementation of HTLV-related public health policies. Recent advances observed in this country followed the integration of HTLV into the program of sexually transmitted infections (STIs) of the Brazilian Ministry of Health and were linked to strong collaborations among the government, HTLV scientists, and patients. In Australia, the implementation of policies to prevent new infections has been limited despite the high prevalence of HTLV-1 infection in Aboriginal communities. A challenge in this setting is the dichotomy between health care workers and the affected communities with respect to understanding HTLV-1 infection and its impact. Patients’ representatives shared their experiences and identified their priorities: (1) increase HTLV awareness, including among health care workers; (2) promote antenatal screening and access to milk substitutes; (3) include HTLV in other health care programs such as STI programs; (4) develop a point of care test to allow early diagnosis and surveillance; (5) improve access to specialized care, including mental health support; and (6) invest in research.

Public health policies for HTLV-1/2 are considered scarce in the Region of the Americas and are usually limited to screening of blood donors. Scaling up HTLV-1/2 testing should be prioritized, and counseling of those living with HTLV-1 is an opportunity to prevent transmission. Testing pregnant women, followed by avoidance of or limited breastfeeding, should be a priority, and targeted testing for those at high risk of infection should be considered. Lack of awareness about HTLV is a major challenge, and PAHO/WHO engagement is crucial to surpass this obstacle. Inclusion of HTLV in existing programs, such as STI and maternal health, and programs focused on elimination of infectious diseases and neglected infections, was identified as an opportunity to facilitate implementation of health policies relating to HTLV-1/2 in the Region. Investment in research is needed to close gaps in knowledge and to develop cost-effective policies and tools supporting the advancement of successful public health responses such as low-cost point of care tests for HTLV-1/2 diagnosis.

Finally, specifics of HTLV infection in the Americas were discussed, including the negative impact of HTLV-1 on the outcomes of co-infections that are common in the Region, including tuberculosis, strongyloidiasis, STIs, and mycosis. Genetic, environmental, and sociocultural aspects may influence HTLV-1 clustering or disease outcomes in the Region. Familial aggregation is also important and should be considered when evaluating the impact of HTLV-1 infections and designing policies to combat this virus. HTLV-2 is the predominant
virus type among Amerindians. Successful policies to control this infection should rely on a combined approach to overcoming linguistic, cultural, and geographic barriers. The partnership between HTLV researchers and the Brazilian Ministry of Health’s Special Secretary of Indigenous Health (DSEI/SESAI) has been successful in the Region.

RATIONALE

Human T cell lymphotropic virus (HTLV) infection affects mainly vulnerable population groups: people living in poverty in areas with very low human development indexes, sex workers, men who have sex with men, people who inject drugs, and epidemiologically closed and semi-closed population groups including traditional populations and indigenous people. This virus and its consequences have been neglected for decades, despite the high morbidity and mortality attributable to HTLV infection.

In this context, in 2018 an open letter to the World Health Organization (WHO) from HTLV researchers was published in the Lancet (1) emphasizing that the time had come to eliminate this infection. In response to this request, the initial step is to shine light on HTLV and support an international effort toward the elimination of HTLV-1/2. Following the publication of a technical report on HTLV 1 by WHO (2), the Pan American Health Organization, in partnership with the HTLV Channel, a platform designed to increase awareness of HTLV, organized a webinar on November 10, 2021. This date was established in 2018 as HTLV World Day by the International Retrovirology Association (IRVA) and has been celebrated by the HTLV community since 2019. The webinar “HTLV World Day 2021: International health policy forum for the elimination of HTLV” aimed to discuss the health policies already implemented in several countries, which may contribute to achieving the goal of HTLV elimination. Taken together, these actions can be an inspiration for those countries that are still in early stages of establishing national strategies for the prevention and control of HTLV-1/2 and can propel proposals for the elimination of these viruses.

OBJECTIVES

The main objectives of this meeting included:

- Promoting discussions regarding health policies related to the prevention and control of HTLV-1/2
- Identifying priorities, potential barriers, and opportunities to advance toward HTLV-1/2 elimination
SECTIONS

The webinar was divided into three sessions. During the first session, experiences in providing services and establishing public health policies in three countries were presented, and the perspectives of people living with HTLV in Brazil, the United Kingdom, and Argentina were shared. A discussion about public policies on HTLV in the Americas was conducted during session 2, and, finally, some particularities of this infection in the Region were addressed in session 3. The program is available as Appendix 1. A total of 20 speakers from eight countries (Argentina, Australia, Belize, Brazil, Jamaica, Peru, the United Kingdom, and the United States of America) participated in the meeting. The audience comprised nearly 360 attendees from 43 countries. Live interaction was possible via chat.

The organizers also invited researchers, health care workers, civil society representatives, and other stakeholders to send abstracts to be presented during the webinar. Seventeen manuscripts were received and presented in the format of video posters, which are fully available at the HTLV Channel (https://youtube.com/c/HTLVChannel). All abstracts have been made available in a Web annex to this report that is available at https://www.paho.org/en/international-health-policy-forum-elimination-htlv.

OVERVIEW OF HTLV PUBLIC POLICIES IN THE AMERICAS

Dr. Rubén Mayorga-Sagastume

PAHO/WHO, USA

Dr. Rubén Mayorga-Sagastume started his presentation with an overview about HTLV-1 infection, focusing on the Region of the Americas. There are an estimated 5-10 million people living with HTLV-1 (PLHTLV) in the world. However, this might be an underestimate due to the lack of robust data from many highly populated countries. The Region of the Americas is one of the WHO regions with the most available data regarding HTLV prevalence, with 66 published studies (21 among blood donors, 22 among pregnant women, 17 in the general population, and 6 in diverse populations); however, these studies are not enough to unveil the complete burden and impact of HTLV infection. Table 1 shows the range of HTLV-1 prevalence in the PAHO region according to selected population groups. In addition, higher HTLV-1 prevalence is observed among populations at high risk of sexually transmitted infections (STIs), including sex workers (ranging from 2.8% to 21.8%) and men who have sex with men (6.2%).

Table 1. HTLV-1 prevalence in the PAHO region according to population group

<table>
<thead>
<tr>
<th>Population Group</th>
<th>HTLV-1 prevalence: PAHO region (minimum-maximum %)</th>
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<tbody>
<tr>
<td>Blood donors</td>
<td>0.001–2.4</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>0.1–5.7</td>
</tr>
<tr>
<td>General population</td>
<td>0.26–6.7</td>
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HTLV-1 transmission rates vary according to transmission route. Mother-to-child transmission (MTCT), in the absence of intervention, is around 20%; the rate for blood products with cellular components ranges from 28% to 63%; and transmission following infected organ transplantation is as high as 87%. Infection rates among sexual partners of PLHTLV range between 20.2% and 65.2%.

Dr. Mayorga-Sagastume also highlighted that although HTLV-1 is traditionally associated with adult T cell leukemia/lymphoma (ATLL), HTLV-1 associated myelopathy (HAM), HTLV-1 associated uveitis, and infective dermatitis, the consequences of HTLV-1 in those affected are probably much broader, but evidence is not as strong yet.

HTLV-1 has been included in global and regional public health agendas since 1988 (Figure 1). Actions have focused on screening blood donors and recognizing HTLV-1 as a human carcinogen. More recently, WHO held a consultation on HTLV-1, followed by the publication of a meeting report in 2019 and a technical report in 2021 (2). In 2020, PAHO’s Strategic and Technical Advisory Group on Disease Elimination recommended that PAHO should consider HTLV-1 as a candidate for elimination (3).

**Figure 1.** Timeline of the global and regional public health agenda on HTLV
Similarly, PAHO has encouraged blood services to screen for HTLV-1 since 1998 (Figure 1). According to information reported by 36 countries, regional coverage of HTLV-1/2 screening of blood units collected in Latin America and the Caribbean was 90% in 2016 and 2017. Most countries and territories (27) reported screening of all blood units (Argentina, Aruba, Bahamas, Barbados, Bermuda, Brazil, Cayman Islands, Chile, Colombia, Costa Rica, Curacao, Dominica, Dominican Republic, Guyana, Haiti, Honduras, Jamaica, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Turks and Caicos Islands, Uruguay). Seven countries did not screen blood products for HTLV-1 or did not report this information to PAHO (Anguilla, Belize, Bolivia, Cuba, El Salvador, Mexico, Nicaragua). Guatemala tested 94% of blood products in 2016 but reported 0% screening coverage in 2017. Ecuador reported low coverage, with approximately 10% of blood units tested each year (4).

Regarding interventions to prevent MTCT of HTLV-1, antenatal screening, followed by avoidance or shortening the duration of breastfeeding, is associated with a reduced risk of MTCT. Japan is the only country with universal antenatal screening. France, Brazil, and Chile have reported screening of pregnant women in some regions or according to identification of risk factors. In addition, Brazil, Chile, and Japan recommend testing infants whose mothers are seropositive, but no standard algorithm has been defined. Breast milk donors are tested in France and the UK only, and testing is limited to those considered as having a high risk of infection.

With respect to HTLV diagnosis, some limitations have been identified: (1) there is no international standard; (2) multiple assays are required; (3) local prevalence may affect decisions on the best algorithm (and epidemiological data are lacking in some areas); (4) there are limited numbers of tests approved by the United States Food and Drug Administration (FDA) and other stringent regulatory authorities, and there are no tests with WHO prequalification; (5) cross-reactivity has been reported (including with Plasmodium falciparum); and (6) cost should be considered, particularly in low prevalence settings. Regarding HTLV care, the evidence obtained on best management from clinical trials is limited and mainly focused on ATLL and HAM.

Finally, Dr. Mayorga-Sagastume acknowledged that HTLV-1 causes a range of severe diseases with high burdens in some communities and geographic locations. He recognized that there are still major gaps in knowledge and data, which in turn make it difficult to assess the real public health impact of HTLV-1 infection. Interventions are available to prevent mother-to-child, sexual, and blood transmission, but there is a lack of international public health policy guidance to prevent and manage HTLV-1 infection and disease. He urged the community to take advantage of the renewed interest in HTLV and recommended increasing public awareness (civil society activism and media reports) and improving dissemination of emerging scientific findings by scientific and professional networks such as the International Retrovirology Association and the Global Virus Network. He also stressed that WHO Member States, scientists, and communities should continue engaging with WHO and calling for action. He pointed out that WHO is expected to (1) provide guidance on surveillance and prevention of, as well as screening and care for, HTLV-1 infection and associated conditions; (2) promote a comprehensive public health response to HTLV-1 infection, helping with integration; and (3) support research to close knowledge gaps.
SESSION 1.
HEALTH POLICIES AROUND THE WORLD

Chair: Professor Graham Taylor
Imperial College London, UK

It is time to eliminate HTLV: Why?

Dr. Fabiola Martin
Queensland University, Australia
President of the International Retrovirology Association

To argue why it is important to eliminate HTLV-1, Dr. Fabiola Martin started her lecture pointing out the consequences of this infection. HTLV-1 causes a multitude of high-mortality and high-morbidity diseases. Some patients will have ATLL, which has a median survival of 8-10 months with low quality of life, despite adequate care. This has not improved over time; for example, the number of deaths caused by ATLL in Japan has not significantly declined over the past 18 years (5). HAM is another condition caused by HTLV-1, and its consequences include pain, leg stiffness, urinary incontinence, sexual dysfunction, and difficulty walking, with many patients becoming wheelchair bound. This disease has a huge social impact as it impairs patients’ mobility, autonomy, ability to work, and social relations. In addition, HTLV-1 may cause uveitis, impairing patients’ sight; dermatitis, resulting in disfiguring skin lesions; pulmonary lesions; chronic pain due to inflammation; and increased severity of co-infections. It is also associated with increased mortality and premature death.

A relevant point that is usually underappreciated is the socioeconomic impact of HTLV-1 infection. This virus has negative effects with respect to education, job opportunities, poverty, and mental health, and it is associated with stigma and ostracism. HTLV-1 is an incurable STI, and those living with HTLV-1 carry the burden of the risk of transmitting the virus to their loved ones, including their babies.

Dr. Martin also discussed some possible reasons contributing to the limited advances in HTLV health policies worldwide: (1) a lack of investment in research and restricted numbers of researchers in the field; (2) health inequities (as HTLV affects mainly vulnerable populations); and (3) a lack of awareness. Those mostly affected (low-income groups, women, indigenous communities) are those usually discriminated against, with insufficient or no health and sexual education; such factors contribute to maintaining the virus within this population. Thus, it is important to empower these individuals. Finally, Dr. Martin highlighted the importance of engaging with PLHTLV in research design, service development, and scientific meetings so that their voices are heard and their experiences and perspectives are considered in the planning of HTLV-1 policies.
Public policies for HTLV in England and the London experience

Dr. Divya Dhasmana
National Centre for Human Retrovirology, UK

Dr. Divya Dhasmana focused her presentation on the organization of the national center for HTLV care (National Centre for Human Retrovirology, NCHR) in England and its role beyond patient care. It is estimated that there are 20,000 PLHTLV in the UK, but only around 900 are aware of their infection. The majority are female (65%) and Afro-Caribbean (60%) (6). Despite the relatively low prevalence of HTLV-1/2 infection in the country, England has implemented screening of blood donors (in 2003), transplant donors (in 2017), those undergoing fertility treatment (in 2014; limited to people with a high risk of infection), and breast milk donors (at risk only). The NCHR is linked to the Department of Sexual Health and HIV at St. Mary’s Hospital, which in turn is linked to Imperial College London; spoke clinics are located in Birmingham, Manchester, and York. The hub-and-spoke organization model adopted by the NCHR facilitates access to medical care. The anchor establishment (hub), located in London, offers a complete array of services and is complemented by secondary establishments (spokes) that offer more limited service, routing patients with more specific needs to the hub (7).

PLHTLV are at the core of the NCHR. The center needs to be accessible, so those who must travel outside their local area have their costs refunded. The facility is also adapted to secure accessibility for those with limited mobility. Patient and public involvement ensure that patients’ perspectives are considered. Specific diagnostic laboratory and research facilities support the center. This fosters research and facilitates translating results into patient benefit. External activities include providing information to health care professionals and the public and engaging with government bodies and medical education professionals (Figure 2). HTLV care is complex, so a multidisciplinary team is needed. The clinical team at the NCHR includes doctors, a specialist HTLV neurologist and hematologist, a specialist nurse, and a neurophysiotherapist. Referrals to other specialists may be necessary, as well as access to specialized tests.

Figure 2. Graphic representation of the basis of NCHR model
An important observation was that NCHR activities are not limited to patient care but also comprise awareness campaigns, engagement with policymakers, and medical education. Some examples were highlighted during the talk: (1) development of a clinical guideline for sexual health practitioners to encourage HTLV testing in this target population; (2) publication of a guideline for needle exposure and collaboration with UK advisory bodies to understand risks among health care workers; (3) advocacy with policymakers to ensure evidence-based decisions on universal antenatal screening; (4) engagement with patients so that they can advocate on their own behalf for the implementation of effective health policies; (5) collaboration with the UK Health and Security Agency, which gathers epidemiological data on HTLV and manages the national voluntary register system; and (6) provision of information about HTLV infection (e.g., via the website www.htlv.eu).

**HTLV-1 in Australia: Characteristics, public health response, and barriers to preventing HTLV**

Dr. Lloyd Einsiedel  
*Baker Heart and Diabetes Institute, Australia*

Dr. Lloyd Einsiedel began his presentation by noting that HTLV-1 subtype c is the circulating strain in Australia. Community- and hospital-based studies have shown that around 10% of PLHTLV have HTLV-1 associated diseases (bronchiectasis/bronchiolitis, HAM, uveitis, infective dermatitis, myositis) and that HTLV-1 is associated with increased mortality. In Central Australia, HTLV-1 prevalence reaches 39% in the adult population in remote Aboriginal communities (8), with likely predominant sexual transmission. Despite this high prevalence, public health policies are limited to screening of blood donors and screening of health care workers with occupational exposures, followed by administration of antiretroviral prophylaxis (even though the evidence to support this policy is limited). Surveillance is restricted to HTLV-1 seropositive and ATLL patients in the Northern Territory. The Department of Health funded a long-term study to identify the impact of HTLV-1 infection on people in Central Australia after having considered, in 2018, that only a small proportion of those affected by the virus will develop disease (HAM and ATLL) and that there is not enough evidence of a broader impact of the virus on patients’ health. The lack of policies to prevent transmission in communities with a high prevalence of infection was identified as a major drawback in Australia's response to HTLV-1 infection.

A highlight of the talk was the discussion about barriers to preventing HTLV-1 transmission in Australia. The assumptions of local medical elites and the concerns of the Aboriginal community were assessed. Although there are some particularities, the results can be easily extrapolated to other scenarios. Medical elites consider that HTLV-1 is not clinically significant. Mortality is used as a measure of impact and is considered rare and restricted to ATLL. It is claimed that perfect epidemiology is needed to prove disease association. These clinical assumptions differ among hospital specialists and primary care physicians. Medical elites also share some ethical concerns such as testing and increasing awareness without target therapies available, disregard for available evidence/clinical guidelines, and competition with high burden noncommunicable diseases. Finally, medical elites assume that Aboriginal people are unable to understand HTLV-1, and HTLV-1 knowledge will harm them. They consider that this virus is not a priority for Aboriginal people and that other treatable diseases are more important. The Aboriginal community has identified some concerns regarding health policies related to HTLV, including (1) potential stigmatization from contact tracing, (2) gender issues and sexual health, (3) limited access to safe breast milk alternatives, (4) cultural sensitivities regarding modes of transmission, and (5) the effects of colonization. An understanding of
these barriers is critical for the development of effective HTLV-1 policies in this setting. Lack of information is at the heart of this issue, so it is important to reiterate a statement from an Aboriginal individual as captured in the presentation “Education is power.” (9).

**Brazil’s response to HTLV**

*Professor Angelica Miranda*

*Ministry of Health, Brazil*

Brazil is an endemic country for HTLV-1/2 and has been implementing public policies related to this virus since 1993. Professor Angelica Miranda opened her talk by describing some of these policies (Figure 3). Universal screening of blood, organ, and tissue donors and publication of clinical guidelines, including guidelines on the clinical management of PLHTLV and infants whose mothers are seropositive, are examples of policies that have been implemented nationally. There is a national recommendation that women who are seropositive for HTLV-1 avoid breastfeeding and provide formula milk; however, HTLV-1 antenatal screening is limited to some states.

An important step that contributed to the recent advances observed in the government’s response to HTLV-1/2 was the inclusion of HTLV-1/2 in the coordination of STIs (Brazilian Ministry of Health) in 2019. This centralized the response to HTLV-1/2 and facilitated the progress of health policies in the country. The strategies used to stimulate the inclusion of HTLV in the agenda were to increase awareness about HTLV-1/2 infection and establish a close collaboration among policymakers, specialist researchers, and patients’ representatives. Brazil used the network of the STI program to increase awareness about HTLV-1/2 among community and health care workers. Thus, a chapter about HTLV-1/2 was included in the clinical protocol and therapeutic guidelines for STIs (10). This was also expanded and published as a manuscript in peer-reviewed scientific journals and is available in Portuguese, Spanish, and English (11, 12). In addition, HTLV-1 is part of an online training program for health care workers about STIs, and two dedicated webinars were organized: one discussing the HTLV chapter in the STI protocol and the other focusing on the recently published guidelines for the management of PLHTLV (13). A calendar with diagnostic flowcharts of STIs, including HTLV-1/2, was distributed to primary health care units in the country. A media campaign focused on HTLV-1/2 was also advertised via the Brazilian Ministry of Health’s social media platforms and website.

There are still some barriers to preventing HTLV-1/2 infection in the country, and Professor Miranda pointed to the lack of epidemiological data for some regions, the lack of consensus and guidelines (e.g., a protocol for testing infants whose mothers are seropositive), and the costs of health technologies and supplies. In Brazil, all health technologies that are approved for incorporation in the public health system should have integral costs covered by the government. Moving forward, the next steps should be (1) implementation of universal HTLV-1/2 antenatal screening, (2) compulsory notification of pregnant women who are seropositive for HTLV-1/2, (3) inclusion of confirmatory tests for all seropositive patients, (4) inclusion of HTLV-1/2 testing for patients with STIs, (5) stimulation of prevalence studies, and (6) continuance of efforts to increase awareness about HTLV-1/2 infection.
Figure 3. Timeline of public health policies implemented for HTLV infection in Brazil

<table>
<thead>
<tr>
<th>Year</th>
<th>Policy Description</th>
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<tbody>
<tr>
<td>1993</td>
<td>Ministerial decree (#1376/93) establishing HTLV screening for blood product donors</td>
</tr>
<tr>
<td>1998</td>
<td>Publication of the HTLV Technical Report for hemotherapy services and Public Health laboratories</td>
</tr>
<tr>
<td>2009</td>
<td>Ministerial decree (#2600/09) establishing HTLV screening in tissues and cell product donors</td>
</tr>
<tr>
<td>2014</td>
<td>Ministerial decree establishing confirmatory test for people with ATLL and the regulation of AZT use</td>
</tr>
<tr>
<td>2016</td>
<td>Ministerial decree establishing guidance for newborns care</td>
</tr>
<tr>
<td>2019</td>
<td>Ministry of Health - Coordination for STI - and inclusion of HTLV in this coordination</td>
</tr>
<tr>
<td>2021</td>
<td>Publication by the Ministry of Health of the Clinical Management Guidelines for patients with HTLV - 3rd edition</td>
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Capturing patients’ voices on the current HTLV context

Ms. Adjeane Oliveira, HTLV Vida, Brazil
Ms. Ema Moyano, Grupo HTLV Argentina, Argentina
Ms. Kristy Blakeborough, UK

Experiences and perspectives of people living with HTLV-1/2 were heard during the webinar. Patients’ representatives from Brazil, Argentina, and the UK expressed the main challenges that they face and highlighted their priorities. The lack of knowledge about HTLV-1/2 among health care professionals was unanimously stressed as a major challenge faced by patients. This not only delays the diagnosis and prevention of new infections but also contributes to feelings of abandonment. The socioeconomic impact of HTLV-1 infection was also addressed, as exemplified by the need for early retirement faced by many patients. Stigma, fear of disclosing their diagnosis, and what they called “social death” is a reality and a concern among them. Familial aggregation of HTLV-1/2 infection also poses obstacles to patients; it is not uncommon to have more than one family member infected by this virus, which may cause diseases with severe outcomes, including death, as experienced by Ema Moyano and Adjeane Oliveira.

The patients’ representatives underscored the importance of PAHO/WHO in pushing for discussions about public policies on HTLV-1/2 worldwide and specifically in their own countries. They also voiced their priorities, as follows:

- Increase HTLV awareness, including among health care workers
- Promote antenatal screening and access to milk substitutes
- Include HTLV in other health care programs, such as STI programs
- Develop a point of care test to allow early diagnosis and surveillance
• Improve access to specialized care, including mental health support
• Invest in research

The patient representatives also discussed the role of civil society in the development of public policies. In this regard, it is worth noting the experience from HTLVida. This patients’ association in Bahia, Brazil, has been playing a central role in the development of public health policies in the State of Bahia that recently culminated in the approval of an integral care program for those living with HTLV-1. Oliveira stressed the importance of a strong collaboration among civil society, researchers, and policymakers to achieve such a positive outcome. Patient forums and patient and public involvement workshops are important UK initiatives that were mentioned by Kristy Blakeborough. These are good opportunities for patients to share their concerns, experiences, and perspectives with other patients and with health care professionals. Patients understand that work as a group is important, but the reduced mobility caused by HTLV-1 and the psychological burden of this infection may hamper group activities. The patient representatives also identified that patients may encourage general practitioners to engage with HTLV-1 specialists so that health care workers can feel empowered to include HTLV-1/2 in their local public health programs and clinical routines. Finally, the participants stressed that patients should collaborate by volunteering in research projects to help advance knowledge about this infection.

It is time to eliminate HTLV: How?
Professor Graham Taylor
Imperial College London, UK

Professor Graham Taylor addressed some common myths about HTLV-1/2 that need to be tackled to facilitate the advance of HTLV policies. He focused on arguments raised by the UK National Antenatal Screening Committee, which decided not to implement universal antenatal screening in the country in 2017. There is enough evidence to argue against the myth that “HTLV rarely causes disease.” Although we may not fully understand how and the degree to which HTLV-1 affects patients’ lives, this should not be underrecognized. Professor Taylor urged scientists and medical writers to avoid perpetuating this misleading statement. Another statement that needs to be revised is “Not many people are infected.” People should reflect on whether there is a number that should be considered sufficient to justify implementation of policies, and another important discussion is whether implementation will depend on the population that is affected. Other common statements and questions include “Since there is no treatment for mothers, we should not test for HTLV-1” and “What is the impact of testing during pregnancy on the mental health of pregnant mothers?” However, there is also a need to think about how seropositive mothers feel about not knowing that they are infected and transmitting the infection to their babies. Still another argument that has been used is “Babies don’t get sick,” but antenatal screening should not be limited to diseases that affect only infants.

Finally, Professor Taylor commented that there are still many geographic areas where the prevalence of infection is unknown. Evidence from London, where the population has a diverse background and origins, indicates that HTLV-1/2 is prevalent in many of those areas. The community should be able to better define HTLV-1/2 distribution. Sexual transmission is one of the major transmission routes, and although we are testing for many sexually transmitted diseases, HTLV-1/2 tests are not offered. He concluded that there is a need to increase testing for HTLV-1/2.
Dr. Noreen Jack  
PAHO/WHO, Belize

Dr. Noreen Jack described how we can achieve meaningful progress on HTLV-1/2 public health responses. Her statement “If we do not look, we will not find” summarizes the need to improve HTLV-1/2 surveillance and conduct epidemiological and pathogenesis studies to better understand the burden and spread of HTLV-1/2. In regard to HTLV-1/2 testing, she emphasized that several serological assays with high sensitivity and specificity are commercially available and can be combined to allow accurate diagnosis. There are also several qualitative and quantitative nucleic acid tests, but none are commercially available. There is a need to develop low-cost rapid tests that can be easily scaled up to quickly identify those infected so that they can be referred to appropriate care and transmission can be prevented.

She acknowledged that many strategies related to HTLV-1 prevention are currently implemented in different settings. Thus, there is a need to develop guidance on testing strategies and cost-effectiveness policies to prevent HTLV-1/2 transmission that are feasible in low-resource settings. Integrating HTLV-1 into existing platforms such as the PAHO/WHO Integrated Sustainable Framework for the Elimination of Communicable Diseases in the Americas is also a good strategy. There is a clear need to invest in research for the development of effective treatments, vaccines, and point of care tests. Finally, Dr. Jack stressed that there is a need for greater patient advocacy and removal of stigma and discrimination and that elimination plans must be made collectively as a global community.
SESSION 2.
PUBLIC HEALTH POLICIES FOR HTLV IN THE AMERICAS

Chair: Professor Ricardo Ishak
Universidade Federal do Pará, Brazil

Panelists:
Professor Edward Murphy, University of California, San Francisco, USA
Professor Peter Figueroa, The University of the West Indies, Mona, Jamaica
Professor Patricia Garcia, School of Public Health at Cayetano Heredia University; former member of the Ministry of Health, Peru
Dr. Mirna Biglione, CONICET, University of Buenos Aires, Institute for Biomedical Research in Retroviruses and AIDS, Argentina

Opening remarks

Session 2 of the webinar took the format of a panel discussion focused on the public health response to HTLV-1/2 in selected countries in the Region of the Americas. The panelists started the session with brief opening remarks. It was clear from these remarks that HTLV-1/2 public health policies are considered scarce in the represented settings (USA, Jamaica, Peru, and Argentina). Policies are limited to the screening of blood units in all of these countries and are considered incomplete, as confirmatory testing for seroreactive donors is not available in the public health care system, nor is counseling of seropositive individuals. In Argentina, confirmation of infection and counseling are conducted by HTLV-INBIRS (UBA-CONICET) without governmental support. An interesting platform presented by Dr. Mirna Biglione involved the webpage https://www.htlvconsciente.com, where information about HTLV is shared in Spanish. In the USA, screening of organ donors was reversed recently due to concerns about the number of false-positive results and the consequent discard of organs. In the same country, recommendations regarding health policies related to HTLV were published in 1993, but there has been no subsequent update. In Peru, although a taskforce developed recommendations regarding HTLV-1/2 policies, the document has not been approved as of yet.

Professor Peter Figueroa summarized his top five recommendations: (1) screen blood donors in countries where HTLV is prevalent; (2) prioritize screening of pregnant women, with counseling to limit the duration of breastfeeding or use milk substitutes; (3) integrate HTLV-1/2 more explicitly with STI and HIV control programs; (4) test people at high risk of STIs; and (5) notify and counsel sexual partners of PLHTLV. Resources are limited, so it is important to perform cost-effectiveness studies. There is a need for seed funding for countries in the Region so that they can start working on HTLV control. Finally, it was noted that the absence of or limited HTLV-1 health policies supports inequities, and there needs to be a global response to this neglected infection.

Is it feasible to eliminate HTLV-1/2?

Professor Patricia Garcia stressed that the recommendation to include HTLV-1 as a potential pathogen to be eliminated during the meeting of the PAHO Strategic and Technical Advisory Group on Disease Elimination in 2020 was strategic and intended to increase awareness
about this virus. The Region has achieved successful results toward the elimination of HIV and congenital syphilis, demonstrating that elimination of HTLV-1 is possible. Professor Figueroa pointed out that instead of focusing on establishing targets for assessing elimination, scaling up HTLV-1 testing should be prioritized. Identification of those living with HTLV-1 is an opportunity to prevent transmission. Testing pregnant women allows counseling and reducing new infections and their associated diseases. Targeted testing for those at high risk of infection should be considered. Counseling of those diagnosed with HTLV-1 is key, and countries are missing opportunities to prevent new infections.

The panelists also mentioned that it is important to understand how the steady increase in STIs and the expansion of STI and HIV prevention interventions, such as pre-exposure prophylaxis (PrEP), would relate to the HTLV-1/2 epidemic. Development of rapid tests for HTLV-1 is critical to progress in policies targeting this virus. The importance of PAHO and the webinar as a catalyst in increasing awareness and promoting discussion about HTLV among policymakers was stressed.

How can sufficient and adequate epidemiological information be obtained?

Surveillance of blood donors, although not ideal, was identified as a potential opportunity to gather epidemiological data. Professor Edward Murphy pointed out that testing first-time blood donors with confirmatory testing, at least for a certain proportion of donors, would allow accurate measurement of prevalence. Testing repeat blood donors allows determining HTLV-1 incidence. It should be considered that this population has a low risk of infection, and the real burden of these viruses may be underestimated. This approach has allowed the identification of some interesting data; for example, the HTLV-1 prevalence among blood donors has been declining in the USA but increasing among urban youth from Japan and Brazil.

Dr. Biglione reported that prevalence data from Argentina are obtained by researchers, but no epidemiological data are produced by government authorities. She noted that an important aspect is the need to strengthen the link between specialized researchers and local policymakers and that PAHO can assist in this regard.

Is it possible to work on prevention and control without having accurate epidemiological data?

Professor Garcia stressed that there are many areas with sufficient studies showing a significant prevalence of HTLV-1/2, but this information is not shared with policymakers, which is critical to transforming research into meaningful programs and policies related to HTLV-1/2. Working without data is difficult, and thus it is important to have register systems and compulsory notification of seropositive patients. This provides epidemiological information, facilitating advocacy for funding, and will help to evaluate the impact of policies. Professor Figueroa exemplified the feasibility of this strategy, explaining that implementation of antenatal screening would concomitantly provide epidemiological data and allow scale up of interventions and evaluation of the efficacy of policies. He identified as a major drawback that countries are testing blood donors but are not gathering epidemiological data. In addition, counseling of those who test positive to avoid transmission is not adequate, and screening their sexual partners is not offered. Dr. Biglione noted that some measures such as surveillance of blood donors and training health care workers involve low costs but would be highly beneficial.

What are the main obstacles to the implementation of effective HTLV-1/2 health policies, and what can we learn from the experiences of other programs?

The panelists agreed that lack of awareness about HTLV-1 is a major obstacle and that PAHO/WHO engagement is pivotal to change this scenario. In Professor Figueroa’s view, there are
many demands in public health but limited resources, and thus PAHO should take the first step to support local voices in promoting HTLV-1/2 on the agenda and should include HTLV in a meeting of the Directing Council, recognize it as a problem, and recommend policies to Member States. In his opinion, once countries have an initial program in place, it can be easily expanded to other high-risk groups (e.g., sexual partners, STI patients, sex workers). Professor Garcia highlighted that raising patients’ voice is also crucial and, starting with antenatal screening programs, may help to decrease stigma. The development of affordable point of care tests for HTLV would also facilitate testing uptake.

**What barriers to accessing adequate health care are faced by PLHTLV in your setting?**

Professor Murphy explained that the health care system organization in the USA may present challenges to health care service delivery and access. Despite the progress observed in recent years, lack of access to the national health insurance system still affects different groups and populations, especially low-income and Afro-descendent communities, which are usually the most affected by HTLV-1 in the USA.

Dr. Biglione highlighted that lack of knowledge on HTLV among health care workers also impairs access to adequate care. This results in a lack of counseling and linkage to care among blood donors reactive to HTLV screening and in inaccurate information provided to PLHTLV, delaying access to interventions that will impact their lives.

**What are the next steps to include HTLV-1 in a positive agenda?**

Professor Garcia recommended that WHO should include HTLV-1/2 more explicitly in its guidelines and directives. She identified five priorities to be tackled: lack of awareness, lack of diagnosis capacities, training of professionals for counseling, establishment of services for adequate follow-up of patients, and development of guidance on health policies. Funding for research is also essential.

In Professor Figueroa’s view, there is a need to prioritize elimination of HTLV-1 MTCT. Countries are working on elimination of HIV and congenital syphilis MTCT and should add HTLV-1 to that list. He also highlighted the responsibility of health care professionals to inform the mother, explain risks and benefits of avoidance and/or shortening of breastfeeding, and together, help her to make an informed decision that best suits her.

The panelists concluded that researchers and policymakers should advocate with international and national research funding agencies for funding for HTLV-1. Civil society organizations may also take part in these advocacy efforts to increase allocation of resources to research on and the public health response to HTLV.

Final remarks were presented by Professor Ricardo Ishak. He addressed the similarities of the different scenarios discussed, despite the distinct stages of health access within the countries. According to Professor Ishak, it is necessary to (1) increase screening for HTLV-1/2; (2) more clearly outline the role of HTLV-1/2 as an STI; (3) include compulsory notification of infection and disease; (4) continue to push for increases in the availability of funds to produce new knowledge on the different aspects of disease epidemiology (particularly the emphasis on transmission, which can have a rapid impact on prevention), infection outcomes, and mechanisms of pathogenesis; (5) prepare trained personnel to recognize infection and disease; (6) set appropriate diagnosis standards; and (7) provide reliable information on the existence of the virus and its extensive life toll to change its status as a neglected condition.
SESSION 3.
SPECIFICS OF HTLV INFECTION IN THE AMERICAS

Chair: Dr. Carolina Rosadas
Imperial College London, UK
HTLV Channel, Brazil

**HTLV and co-infections**

*Professor Eduardo Gotuzzo*
Universidad Caetano Heredia, Peru

Professor Eduardo Gotuzzo opened his talk by stressing that HTLV-1 is a neglected disease that affects people with low incomes and contributes to increasing poverty. He highlighted that the impact of HTLV on mortality, morbidity, disability, and immunosuppression is underrecognized. HTLV-1 may cause proliferative and inflammatory disease, but it can also cause selective immune dysfunction. This immune dysfunction may impact co-infection outcomes, and this was the focus of Professor Gotuzzo`s presentation.

Several examples of neglected tropical infections that are negatively affected by HTLV-1 and have a high prevalence in America were described during the talk, including infective dermatitis, strongyloidiasis, tuberculosis, fungal co-infections, and other STIs. Infective dermatitis, a chronic skin disorder associated with HTLV-1 infection, is common in Latin America and the Caribbean. Its onset is usually in early childhood, and this disease is now considered a sentinel event of HAM and ATLL.

HTLV sexual transmission results in a high prevalence of infection among sex workers as well as high rates of co-infection with other STIs. This highlights the importance of testing patients with STIs for HTLV-1. In addition, HTLV-1/HIV co-infection is associated with higher mortality and lower survival time than HIV mono-infection. The negative effect of HTLV-1 in co-infections with pathogens commonly seen in the Americas is also evidenced by the higher risk of developing tuberculosis, severe strongyloidiasis, and crusted scabies among individuals living with HTLV-1.

In conclusion, recognizing the broader impact of HTLV-1 infection on patients’ health is important. This strengthens the need for public health policies to tackle this virus.

**Risk factors for HAM**

*Dr. Tatiane Assone*
Universidade de São Paulo, Brazil
HTLV Channel, Brazil

Dr. Tatiane Assone highlighted some of the risk factors for developing HAM. From a public health perspective, one important observation is that HTLV-1 is not only more prevalent in women than men, but HAM is also more frequently observed in women. This is important to consider when designing policies to prevent transmission and to provide adequate care. A high proviral load is known to be associated with a higher risk of disease onset; however,
it is not sufficient to cause disease. Some genes and genetic polymorphisms have been identified as associated with an increased risk of or protection from the development of HTLV-1 associated diseases. Dr. Assone also touched on familial aggregation of HTLV-1 infection and associated diseases. This increases the burden on those affected. In addition to limited research funding, the admixture population observed in the Americas is considered a challenge to identifying genetic markers associated with susceptibility to or protection from HTLV-1 infection or progression to disease.

There is also a need to understand how environmental and sociocultural aspects may influence HTLV-1 clustering or disease outcomes in different areas of the world. There is a need to determine the extent to which underdiagnosis of HTLV-1 associated diseases may contribute to the differences observed in infection outcomes (e.g., ATLL diagnosis is considered rare in the Americas relative to Japan).

**HTLV in indigenous people**

Professor Antonio Vallinoto  
*Universidade Federal do Pará, Brazil*

Professor Antonio Vallinoto began his talk by describing the heterogeneous geographic distribution of HTLV-1/2 in the world and how HTLV-1/2 was introduced in the Americas after emerging in Africa (through human migration via the Bering Strait and/or the slave trade during the colonial period). HTLV-1 is endemic in many Amerindian communities, with the prevalence varying from 0.4% to 9.8%. However, HTLV-1 infection is considered rare among indigenous people from the Brazilian Amazon region. In contrast, there is known to be a high prevalence of HTLV-2 infection in this group.

An interesting study showed that more than 30% of the members of the Kayapo community are infected with HTLV-2, with a high prevalence among children and increasing prevalence with age; this confirms that both mother-to-child and sexual transmission are ongoing in that community. Familial aggregation is also observed among indigenous people and should be addressed when implementing policies to prevent infection. In addition, HTLV-2 distribution is heterogeneous between different communities. The Arawete and Asurini communities, for example, have remained free from HTLV-1/2 despite being related geographically to other communities with a high prevalence of infection. Cultural and social isolation may explain this finding.

Researchers have been consistently urging for policies to tackle HTLV-1/2 among Amerindians for decades. The complexity of HTLV-1/2 infection in this population makes a combined approach, focused on sociocultural aspects, essential. Professor Vallinoto pointed out that linguistic and cultural barriers hinder the implementation of effective policies in this setting. Barrier methods to prevent STIs, for example, have poor acceptance among male indigenous individuals, and cross breastfeeding is a common practice among Amerindians that may facilitate HTLV-1 spread via vertical transmission.

Positive initiatives were also shared during the lecture. The research group has been engaging with the Brazilian Ministry of Health, more specifically the Special Secretary of Indigenous Health (DSEI/SESAI), to increase awareness of and advance health polices for HTLV-1/2 in this particular population. Specifically, a technical report about the epidemiology of HTLV-1/2 among Brazilian Amerindians and prevention strategies was shared with policymakers. Recommendations included the following: (1) serological screening in indigenous communities and confirmation of infection for seroreactive individuals, (2) clinical follow-
up of positive cases, (3) provision of information and technical training for health care staff members working with indigenous communities, (4) design of information booklets in indigenous languages, (5) provision of milk substitutes, and (6) continuance of condom provision. Positive outcomes of this collaboration between academia and policymakers also included the organization of two webinars focused on increasing health care workers’ awareness about HTLV-1/2 among indigenous people and distribution of the guidelines for HTLV-1/2 published by the Brazilian Ministry of Health in 2021 (13) for all 34 DSEI/SESAI units in the country. Professor Vallinoto concluded by highlighting the necessity to consider difficulties in accessing these geographically isolated communities when designing health policies aimed at them.

CLOSING REMARKS

Dr. Leandro Sereno
PAHO/WHO, USA

Dr. Leandro Sereno closed the meeting by highlighting that investment in research is needed to close gaps. As observed for other communicable diseases such as HIV, international funding of national programs and research has been decreasing in recent years. This is particularly the case in the Americas, as donors redirect their priorities to higher burden and lower income countries on other continents. Hence, allocation of national funding is crucial to allow sustainability of the response against HTLV-1/2. As economic resources are limited, it is important to develop strategies to integrate HTLV-1/2 into existing programs such as HIV, STI, maternal health, and communicable disease elimination programs.

In addition, there is a need to define effective interventions and develop cost-effectiveness studies, which will facilitate better programmatic planning and advocacy for inclusion of HTLV-1/2 in the global health agenda. Acknowledging the impact of HTLV-1 in health beyond ATLL and HAM was addressed, along with how it may influence cost-effectiveness analyses and decision making.

There are still gaps in key information and evidence, but the response can start immediately. WHO has expressed its intentions and commitment to promote a broader response to HTLV-1/2, and initial actions should include addressing these specific questions. Generating strategic information and evidence on prevention, diagnosis, care, and treatment interventions will allow the development of WHO recommendations and guidance regarding the public health response to HTLV-1/2. Likewise, with clear goals and targets it will be possible to measure the efficacy of public health policies toward the elimination of HTLV-1/2 infection and the related burden.
CONCLUSIONS

HTLV-1 is a neglected infection that causes severe disease mainly in vulnerable populations. Priority topics that have been identified and will certainly drive the HTLV agenda in the Region of the Americas, as well around the world include:

1. It is essential to increase awareness about HTLV-1/2 among health care workers with the inclusion of this topic in basic and continued education and capacity building activities.

2. Increasing awareness is also needed among the general population with communication campaigns, empowering individuals, and communities to identify risks and seek for care, as well as to reduce stigma and discrimination.

3. There is a need to include/expand HTLV-1/2 screening targeting priority and most affected population groups.

4. Elimination of mother-to-child transmission should be considered a priority, and adoption and scale up of prevention measures are needed.

5. Countries should design and implement national policies for HTLV prevention and control, including the priority topics above. PAHO/WHO support may be an important catalytic to promote HTLV-1/2 on the global and national public health agendas.

Additionally, the meeting has identified a number of opportunities that national programs can leverage to implement and expand HTLV 1/2 public health response, notably:

1. Integration of HTLV into HIV, STI and/or other relevant health programs.

2. Integration of HTLV-1 testing into antenatal care, together with additional care and prevention measures.

3. Integration of HTLV into elimination programs, such as EMTCT and other broader communicable diseases elimination initiatives.

4. Generation of date on HTLV-1/2 prevalence obtained by screening of target populations such as blood donors and seize this opportunity for counseling and prevention of new infections, as well as to strengthen linkage to care.

Finally, several activities and products are expected to impact and move forward the HTLV global agenda, paving the way for the implementation of comprehensive public health response to HTLV-1/2 in our Region. PAHO/WHO’s support and leadership may be important to:

1. develop technical guidelines on HTLV-1/2 testing and diagnosis and strategies to prevent transmission.

2. increase awareness about HTLV-1 infection among policy makers in the Region.

3. strengthen collaboration with experts across the different Regions.

4. promote the integration of HTLV-1 care and prevention into existing health programs

5. consolidate HTLV on the international public health agenda

6. promote and facilitate research on HTLV-1/2
REFERENCES


Appendix  - Program and Agenda

Webinar HTLV World Day 2021:
International health policy forum for the elimination of HTLV
Advancing HTLV health policies around the world

Program
November 10, 2021. 8:00 a.m. - Brasília (GMT-3)

8:00 - 8:10 Opening ceremony
PAHO/WHO, Brazilian Ministry of Health, Organizing Committee

8:10 - 8:30 Overview of the global public health agenda on HTLV-1/2
Dr. Rubén Mayorga-Sagastume (PAHO/WHO)

Session 1: Health Policies around the World
Chair: Professor Graham Taylor

8:30 - 8:45 It is time to eliminate HTLV: Why?
Dr. Fabiola Martin (Australia)

9:00 - 9:15 Public policies for HTLV in England and the London experience
Dr. Divya Dhasmana (UK)

9:15 - 9:30 HTLV-1 in Central Australia: The long road to public health
Dr. Lloyd Einsiedel (Australia)

9:30 - 9:45 Public Policies for HTLV-1/2 in Brazil
Professor Angelica E. Miranda (Brazil)

9:45 - 10:05 Capturing patients’ voices on the current HTLV context
Ms. Adjeane Oliveira (Brazil)  
Ms. Ema Moyano (Argentina)  
Ms. Kristy Blakeborough (UK)

10:05 - 10:30 Q&A

10:30 - 10:45 It is time to eliminate HTLV: How?
Professor Graham Taylor (UK)  
Dr. Noreen Jack (Belize)

Session 2: Public Health Policies for HTLV in the Americas
Chair: Professor Ricardo Ishak (Brazil)

11:00 - 12:00
Professor Edward Murphy - USA
Professor Peter Figueroa - Jamaica
Professor Patricia Garcia - Peru
Dr. Mirna Biglione - Argentina

12:00 - 12:20 Q&A

12:20 - 12:30 Closing remarks
Professor Ricardo Ishak (Brazil)

12:30 - 14:00 Interval

Session 3: Specifics of HTLV Infection in the Americas
Chair: Carolina Rosadas (UK / Brazil)

14:00 - 14:15 HTLV and co-infections
Professor Eduardo Gotuzzo (Peru)

14:15 - 14:30 Risk factors for HAM
Dr. Tatiane Assone (Brazil)

14:30 - 14:45 HTLV in indigenous people
Professor Antonio Vallinoto (Brazil)

14:45 - 15:00 Closing session
Dr. Leandro Sereno (PAHO/WHO)