

MEETING REPORT

**PUBLIC HEALTH
IMPACT AND IMPLICATIONS
FOR FUTURE ACTIONS:
WHO GLOBAL CONSULTATION
ON THE HUMAN
T-LYMPHOTROPIC
VIRUS TYPE 1**

TOKYO, JAPAN, 13-15 NOVEMBER 2019



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ABBREVIATIONS AND ACRONYMS

ATL	adult T-cell leukaemia/lymphoma
HAM/TSP	HTLV-1-associated myelopathy or tropical spastic paraparesis
HTLV-1	human T-lymphotropic virus type 1
IARC	International Agency for Research on Cancer
IRVA	International Retrovirology Association
MSM	men who have sex with men
NAT	nucleic acid testing
PWID	people who inject drugs
STI	sexually transmitted infection
WHO	World Health Organization

INTRODUCTION

Background

The human T-lymphotropic virus type 1 (HTLV-1, also known as the human T-cell leukaemia virus type 1), was the first oncogenic human retrovirus discovered 40 years ago. It was shown to be the cause of an aggressive haematological malignancy known as adult T-cell leukaemia/lymphoma (ATL). Transmission of HTLV-1 occurs when the viral RNA genome from infected donor cells transfers and permanently integrates a copy of proviral DNA into the cells of a recipient host. This results in lifelong infection of the new host. Surveys of HTLV-1 prevalence found that the infection was concentrated geographically, with high levels of prevalence in particular regions and populations. HTLV-1 infection was subsequently identified in the mid-1980s as the cause of a progressive neurological condition that became known as HTLV-1-associated myelopathy or tropical spastic paraparesis (HAM/TSP). Case investigations and epidemiological studies identified the main routes of transmission of HTLV-1 infection as sexual, parenteral (primarily through transfusion of cellular blood components) and vertical from mother to child (primarily through breastfeeding). Most high-income countries have introduced HTLV-1 screening of blood donations, but few other public health measures have been implemented to prevent infection or its consequences, or to manage ATL and HAM/TSP. Furthermore, there are major gaps in the epidemiology of HTLV-1 infection, which makes it difficult to assess its public health burden and trends.

WHO global consultation

Rationale

The World Health Organization (WHO) has published a number of technical reports on HTLV-1, including: reports from the 1988 and 1992 meetings of the WHO Western Pacific Regional Office Scientific Group on HTLV-1 Infections and Associated Diseases; an evaluation of commercial HTLV-1 test kits in 1995; and monographs of the International Agency for Research on Cancer (IARC) on HTLV-1 in 1996 and 2012. In 2018, a group of HTLV-1 experts and other stakeholders called upon WHO to take up HTLV-1. Given the increasing public awareness of HTLV-1 infection in some populations and interest expressed by a number of Member States, an expert consultation was planned to assess the current global situation from a public health perspective. The consultation aimed to review existing global epidemiology, clinical and public health evidence so as to better understand the public health implications of HTLV-1 infection and disease, identify major gaps in knowledge requiring further research and identify possible public health measures to be undertaken.

Objectives

The consultation had the following objectives:

- review evidence on the global and regional epidemiology and transmission routes of HTLV-1 infection;
- review evidence on the diseases associated with HTLV-1 infection and broader health consequences;
- review evidence on the effectiveness of HTLV-1 interventions, including prevention, testing, treatment and care interventions;
- review the scope of country and community responses to HTLV-1;
- identify priorities for research, public health action and community engagement; and
- agree on a process to produce a series of WHO technical reports covering the areas of HTLV-1 epidemiology, health consequences, and clinical and public health interventions.

Meeting participation and agenda

With the support of the governments of Australia and Japan, two countries with high HTLV-1 prevalence in limited and specific geographical areas and populations, WHO organized a global consultation on 13–15 November 2019, hosted by the National Center for Global Health and Medicine, Tokyo, Japan. Over 50 participants were invited from 20 countries, representing all WHO regions. Participants included experts in the areas of basic sciences epidemiology, infectious diseases and public health, and affected communities. Experts were invited from national public health/communicable disease programmes of high-burden countries, and from existing research, technical and policy networks at national and international levels (Annex 2 – list of participants). The meeting was chaired by Professor Brendan Murphy, Chief Medical Officer, Australian Government Department of Health, and Professor Toshiki Watanabe, from the University of Tokyo and President of the International Retrovirology Association (IRVA). The meeting was opened by Dr Yasuhiro Suzuki, Chief Medical and Global Health Officer and Vice Minister of Health, Ministry of Health, Labour and Welfare of Japan, and Professor Norihiro Kokudo, President of the National Center for Global Health and Medicine, Tokyo.

The participants reviewed background papers that had been commissioned by WHO to inform the meeting deliberations. These were on: (i) HTLV-1 epidemiology, transmission and diagnosis; (ii) health consequences of HTLV-1 infection; and (iii) HTLV-1 prevention, testing, treatment and care interventions, and national policies and guidelines (Annex 1 – agenda). Meeting participants reached consensus on the following set of findings and recommendations.

MEETING PROCEEDINGS AND RECOMMENDATIONS

Geographical distribution and surveillance

Based on the available prevalence data, the geographical distribution of HTLV-1 infection continues to be highly focal, with known areas of high prevalence in Japan, and a number of countries in central and west Africa, the Caribbean, Europe, Latin America, Oceania and the Middle East. Whereas migration has contributed to increased detection of HTLV-1 cases in some low-prevalence countries, there is little evidence of ongoing expansion beyond known endemic areas. There remain large populations for which the prevalence of HTLV-1 is unknown, e.g. countries in south and south-east Asia, and north and east Africa. Additionally, reports of ATL and HAM/TSP in populous countries (e.g. India) with little HTLV-1 prevalence data currently available reflects the need for larger-scale studies. There are also gaps in information concerning the variation in prevalence within endemic countries, and about prevalence in subpopulations that might be at higher risk, e.g. people who inject drugs (PWID) and men who have sex with men (MSM). No country has yet adopted systematic approaches to the surveillance of HTLV-1.

Recommendation 1: Guidance should be developed on HTLV-1 surveillance methods to cover infection, its complications and public health responses.

Recommendation 2: Guidance should be developed on rapid assessment methods to determine HTLV-1 prevalence and country/endemic context, to generate key data to inform national policies, priorities and investments.

Recommendation 3: Guidance should be developed for low-resource settings on testing approaches and strategies for detection of HTLV-1 that are appropriate to the setting and the purpose.

Recommendation 4: Guidance should be developed on HTLV-1 testing approaches, including on who should be offered testing for HTLV-1, accompanied by strategies for communicating test outcomes to individuals and to communities.

HTLV-1 transmission and prevention

The major modes of HTLV-1 transmission are well established by research. Mother-to-infant transmission occurs primarily through breastfeeding at an average rate of around 20%, with shorter durations of breastfeeding associated with lower rates of transmission. Male-to-female sexual transmission is more frequent than female to male. There are limited data on transmission between same-sex couples. Transfusion of cellular blood products from a person with HTLV-1 infection carries a high risk of transmission (up to 60%), as does solid organ transplantation. However, transfusion of cell-free plasma carries a low or no risk of transmission. The risk of nosocomial transmission or transmission associated with injecting drug use is unknown. It is well established that higher levels of HTLV-1 proviral load is a risk factor for transmission, but the transmission risk associated with very low or undetectable levels remains unknown. Prevention strategies explicitly directed at HTLV-1 transmission remain limited to screening of blood donations and, in a limited number of settings (Japan and some Latin American countries), the screening of pregnant women and support to limit breastfeeding for those found to have infection. It is likely that existing strategies for

Testing strategies for HTLV-1 infection

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