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Perspective

Screening for HTLV-1 infection should be expanded in Europe[☆]Vicente Soriano^{1,*}, Carmen de Mendoza², on behalf of the Spanish HTLV Network¹ Helath Sciences School & Medical Center, International University of La Rioja (UNIR), Madrid, Spain² Department of Internal Medicine, Puerta de Hierro University Hospital, Madrid, Spain

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ABSTRACT

Human T-cell lymphotropic virus type 1 (HTLV-1) infection is spreading globally at an uncertain speed. Sexual, mother-to-child, and parenteral exposure are the major transmission routes. Neither vaccines nor antivirals have been developed to confront HTLV-1, despite infecting over 10 million people globally and causing life-threatening illnesses in 10% of carriers. It is time to place this long-neglected disease firmly into the 2030 elimination agenda. Current evidence supports once-in-life testing for HTLV-1, as recommended for HIV, hepatitis B and C, along with targeted screening of pregnant women, blood donors, and people who attended clinics for sexually transmitted infections (STIs). Similar targeted screening strategies are already being performed for Chagas disease in some Western countries in persons from Latin America. Given the high risk of rapid-onset HTLV-1-associated myelopathy, universal screening of solid organ donors is warranted. To minimize organ wastage, however, the specificity of HTLV screening tests must be improved. HTLV screening of organ donors in Europe has become mandatory in Spain and the United Kingdom. The advent of HTLV point-of-care kits would facilitate testing. Finally, increasing awareness of HTLV-1 will help those living with HTLV-1 to be tested, clinically monitored, and informed about transmission-preventive measures.

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Introduction

Human T-cell lymphotropic virus type 1 (HTLV-1) infection is spreading globally at an uncertain speed [1,2]. This is not surprising because viral transmission occurs following sexual, parenteral, and vertical exposure, and HTLV testing is rare in most regions. Moreover, as only 10% of carriers develop serious clinical manifestations lifelong, the HTLV-1 pandemic largely runs silently involving people unaware of their infection [3]. Finally, to date, there is no protective vaccine or antiviral therapy.

The World Health Organization (WHO) has recently recognized HTLV-1 as a neglected infection of global concern [4]. It has been included in the WHO's strategic planning for STI control for 2030 [5]. To achieve this target, timely HTLV testing is crucial, as most asymptomatic individuals are unaware of their HTLV status, allowing ongoing viral transmission. In this regard, the good experience from Japan is very illustrative [6]. There, universal HTLV screening was introduced years ago in pregnant women, blood donors, organ donors and recipients, and certain high-risk populations such as injection drug users, sex workers, individuals with STIs, and health care workers with a high risk of blood exposure (surgeons, etc.).

The lack of awareness about HTLV-1 infection by the general population and specifically about self-carrier status are major challenges. These two facts preclude taking any preventive actions. For instance, HTLV-1 pregnant women who know their status and avoid breastfeeding reduce the chances of infecting their newborns from 15–20% to less than 1–2% [7,8]. Hence, HTLV-1 antenatal testing in endemic regions should be considered a priority. Regarding Japan, the implementation of antenatal HTLV screening has annulled vertical transmission in that country [6].

In non-endemic countries, emerging data increasingly favors HTLV-1 screening of pregnant women. Taking Spain as an example, of 9813 consecutive pregnant women who attended 11 sites across the country since 2021, five (0.05%) were HTLV-1 positive. All were Latin American migrants. Indeed, HTLV-1 seroprevalence in this group increased to 0.6% [9]. These figures are much higher than rates for other well-accepted screening tests performed on all pregnant women, such as HIV, hepatitis B surface antigen, or syphilis. Accordingly, HTLV testing should be part of antenatal screening, at least in pregnant women from Latin America. Of note, a targeted screening like the one proposed is not something new, because it is already being performed for Chagas disease [10].

Because HTLV-1 transmission globally mostly occurs following sexual exposure [11], HTLV testing of people with multiple sex partners or attending STI clinics should be effective for unveiling asymptomatic carriers. In Spain, a recent survey tested 2524 individuals who attended six STI clinics during the last year. Five individuals were HTLV-1 positive. All but one were from Latin America, increasing the HTLV-1 seroprevalence in this group to 0.67%. Three were men who had sex with men, of whom two were HIV-1 positive and another was under pre-exposure prophylaxis [12].

The transplantation setting merits special consideration. Transmission of viral infection to recipients of HTLV-1-contaminated organs is the rule. Moreover, unusual rapid progressive myelopathy has been reported among transplant recipients of solid organs from HTLV-1+ donors [13]. Hence, HTLV-1 screening should be considered universal in the transplantation setting [14]. However, HTLV screening of organ donations in the United States is largely suboptimal, with only deceased individuals from endemic regions being recommended for testing. In contrast, HTLV screening of all organ donors in Europe has become mandatory in Spain and in the United Kingdom.

While people at high risk may go for HTLV testing after perceived risk exposure, persons at low risk are rarely diagnosed early. Then it is generally too late to prevent transmission to sex partners

or newborns. As shown in Table 1, the benefits of expanded testing for other viruses are more evident and compelling. For instance, hepatitis B vaccination can be offered to people with markers of susceptibility. Knowledge of HIV and hepatitis C infection status is helpful because earlier prescriptions of specific antivirals may suppress viral replication and lead to immune restoration (for HIV) or complete cure (for hepatitis C). In contrast, being HIV-negative for persons with high-risk behaviors provides a chance to protect themselves using pre-exposure prophylaxis.

Given that there is no vaccine or antivirals to confront HTLV-1 infection, the reasons for pushing testing would be limited to halting further transmission. However, besides stopping further transmissions, screening of family relatives and sex partners of HTLV-1+ persons may unveil asymptomatic carriers that would benefit from adequate clinical monitoring. People living with HTLV-1 have a 57% increase in the risk of premature death compared to uninfected individuals [15] because persistent immune inflammatory phenomena due to chronic viral infection might lead to accelerated aging.

Some low-income countries where HTLV-1 is endemic do not screen blood donations. Risk assessments in European countries and North America have supported the discontinuation of HTLV-1 screening of blood donations after performing universal testing for a while. The HTLV prevalence was too low. Nowadays, only targeted or selective screening on first-time blood donors is advised or when blood products have not been leukoreduced [16].

HTLV-1 testing has shifted from scenarios where only clinical suspicion of sick people was considered for universal screening. In between, there are two strategic screening alternatives that could be more cost-effective. The first is once-in-life testing and the second is targeted screening of special groups.

For the general population between the ages of 13 and 64 years, the Centers for Disease Control and Prevention (CDC) recommends testing for HIV at least once in life [17]. For people with certain ongoing risk factors, testing should be made at least once a year if previously negative. For other viral infections that are similarly transmitted, parenterally or following sexual contact, SUCH as hepatitis B or C, the CDC recommends screening all adults aged 18 years and older at least once in their lifetime [18,19]. For hepatitis B, testing may unveil susceptible persons that could benefit from hepatitis B vaccination. For hepatitis C, screening must be repeated periodically for people who test negative, while risky behaviors persist. Testing should be carried out regardless of risk disclosures, as many people might be reluctant to disclose stigmatizing behaviors.

There is no doubt that a rapid and cheap HTLV point-of-care test will be crucial to reach clinically vulnerable and underserved populations or in places with limited access to health care services [20]. The development of HTLV rapid tests and/or self-testing tools would largely contribute to unveiling asymptomatic carriers. A point-of-care test is a powerful tool for the easy and rapid detection of infections without the requirement for expensive instruments and laboratory equipment; however, serological point-of-care test kits for HTLV-1 are not widely available worldwide. In Japan, a lateral flow assay has recently been marketed as a point-of-care test kit for HTLV-1 immunoglobulin G detection. It exhibits relatively good sensitivity and specificity.

It is time to place this long-neglected disease firmly into the 2030 elimination agenda. Despite the scarcity of large and updated HTLV surveys in many regions, current evidence supports HTLV-1 testing once in life, as recommended for HIV, and hepatitis B and C [21]; and targeted screening of pregnant women, people who attended STI clinics, and blood donors. Given the high risk of rapid-onset myelopathy, HTLV-1 screening of solid organ donors should be mandatory. To minimize organ wastage, the specificity of HTLV screening tests must be improved. Re-assessing and increasing the thresholds for seroreactivity in screening assays would reduce the

Table 1
Benefits of early viral testing

	Estimated infected population (millions)	Antiviral therapy	Vaccine	Halt transmission	Clinical monitoring
Hepatitis B	316	yes	yes	yes	yes
Hepatitis C	57	yes	no	yes	yes
HIV	38	yes	no	yes	yes
HTLV-1	10	no	no	Yes*	yes

*Breastfeeding, sexual and transfusions/transplants
In bold the greater benefits

rate of false positives, at least by testing low-risk populations such as blood donors in non-endemic regions [10]. The advent of point-of-care kits will facilitate HTLV testing in most sites. Finally, further efforts must be made to raise awareness of HTLV-1 to ensure that those living with the virus are tested, clinically monitored, and informed about transmission mechanisms to others.

Declaration of competing interest

None.

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Author contributions

VS wrote the first draft. CdM reviewed the text and added comments. All authors of the Spanish HTLV Network read the final draft and provided comments.

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