NRL
Science of Quality

HIV AIDS 2025 HTLV-1 SESSION

Update on Testing for HTLV-1

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Disclosure of Interests

- NRL conducts an Australian Scientific Conference on Infectious Diseases annually for which we seek and receive sponsorship from a range of IVD manufacturers selling into Australia (e.g. in 2023 - DiaSorin, Roche, Cepheid, Abbott, Integrated Sciences, AusDiagnostics, Qiagen, Grifols, Abacus, SpeeDx, Genetic Signatures, BD, Diagnostic Technology and Hologic.)

- NRL is designated as a WHO Collaborating Centre for Diagnostics and Laboratory support for HIV/AIDS and other blood borne infections and a WHO Prequalification Laboratory for the evaluation of test kits / assays for use in low- and middle-income countries on behalf of WHO.

- NRL also performs assessments of test kit performance on behalf of TGA and commercial IVD manufacturers under commercial arrangements and also provides scientific services to enable IVD Manufacturer's assays to achieve regulatory registration.

- NRL is the National Reference Laboratory for HTLV-1 in Australia and has supported the Longitudinal Study with HTLV-1 Confirmatory and PVL Testing services.

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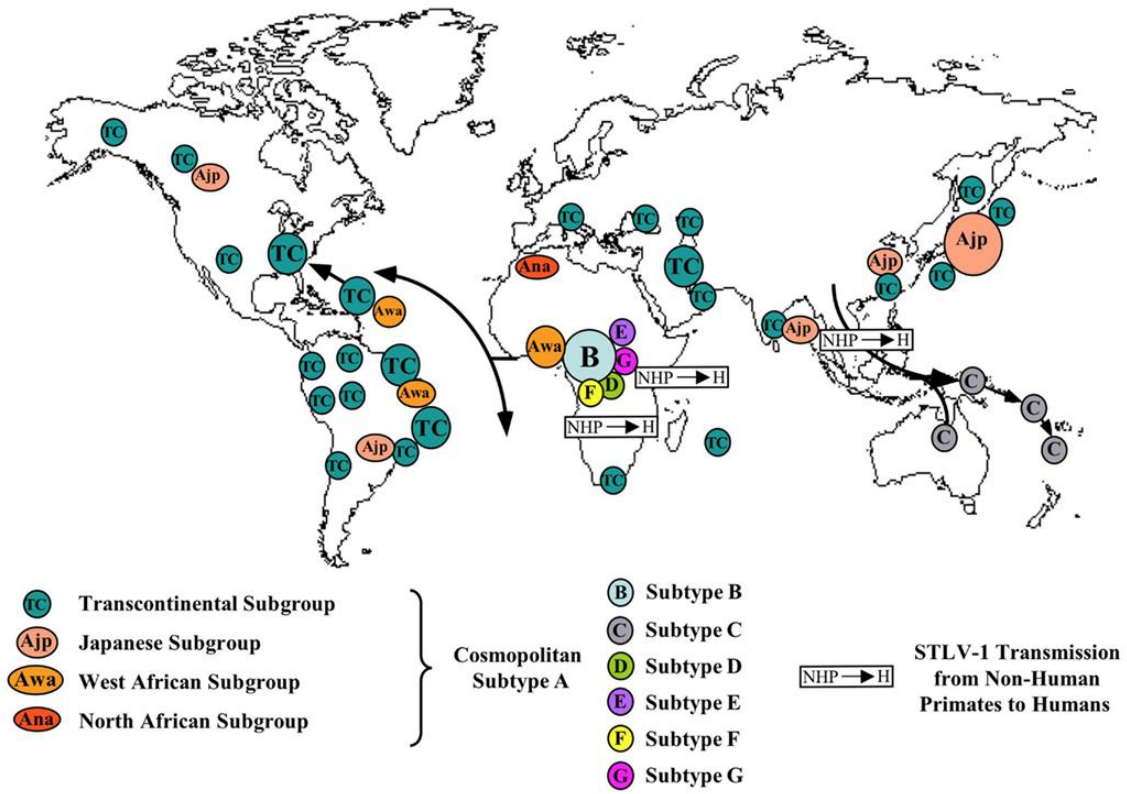
Overview

- Why do we test for HTLV?
- Elimination of Mother-to child transmission
- How do we diagnose for HTLV?
- What is happening in the context of testing services globally?
- Development of WHO HTLV-1 Clinical and Testing guidelines
- Summary
- Acknowledgments

Global application of HTLV Testing



Gessain A & Cassar O *Frontiers Microbiol* 2012 3:388

Diagnose and manage patients

- Unprotected sexual intercourse
- Exposure to blood
- IV drug use – shared needles
- High endemic area screening
- Clinical symptoms of HTLV-I

Prevent transmission:

- Blood donor screening
- Solid organ and Tissue donor screening
- Antenatal screening
- Mandatory notification of cases and contact tracing

Elimination - transmission from mother to child

Japan

- Achieved maternal to child elimination (targeted late1980s; universal antenatal screen 2010)[1]
- Continuing prevalence from sexually transmitted HTLV-1 infection

Brazil

- 14 – 20% MTCT transmission in urban areas (16.5k - 23.5k new cases annually)[2]
- Universal antenatal screening from September 2025
- Target elimination of Maternal to Child transmission by 2030
- Expansion of clinical and testing services

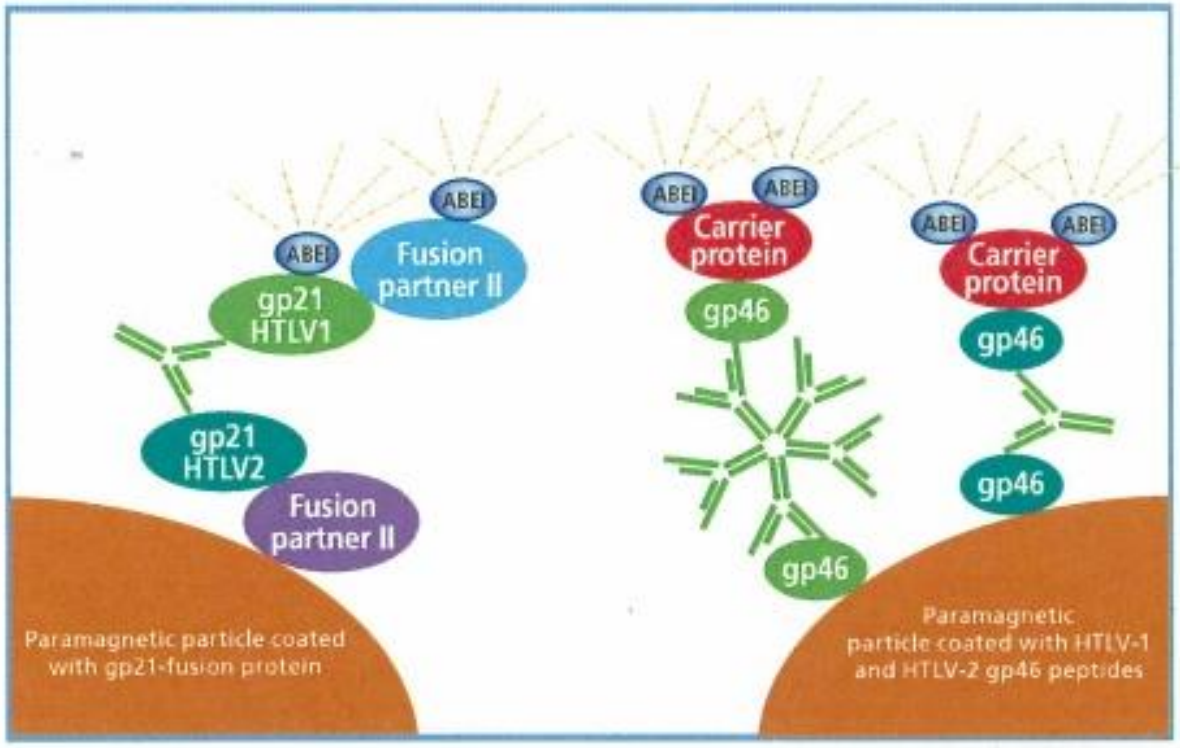
Australia

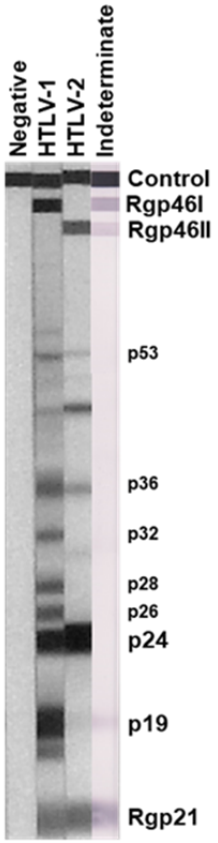
- Clinical Guidelines on HTLV-1 for Aboriginal Primary Health Care settings launched May 2025
- Offering antenatal screening to pregnant aboriginal people

1. Nishijima T, Shimada S, Noda H, Miyake K. Towards the elimination of HTLV-1 infection in Japan. Lancet Infect Dis Elsevier. 2019;19:15–6.
2. Rosadas C, Malik B, Taylor GP, Puccioni-Sohler M. Estimation of HTLV-1 vertical transmission cases in Brazil per annum. Althouse B, editor. PLoS Negl Trop Dis. Public Library of Science; 2018;12: e0006913. doi: 10.1371/journal.pntd.0006913 [DOI

How do we diagnose HTLV?

Screen blood to **detect HTLV antibody**





Confirm antibody presence by repeat screening and a confirmatory test – **Western Blot**

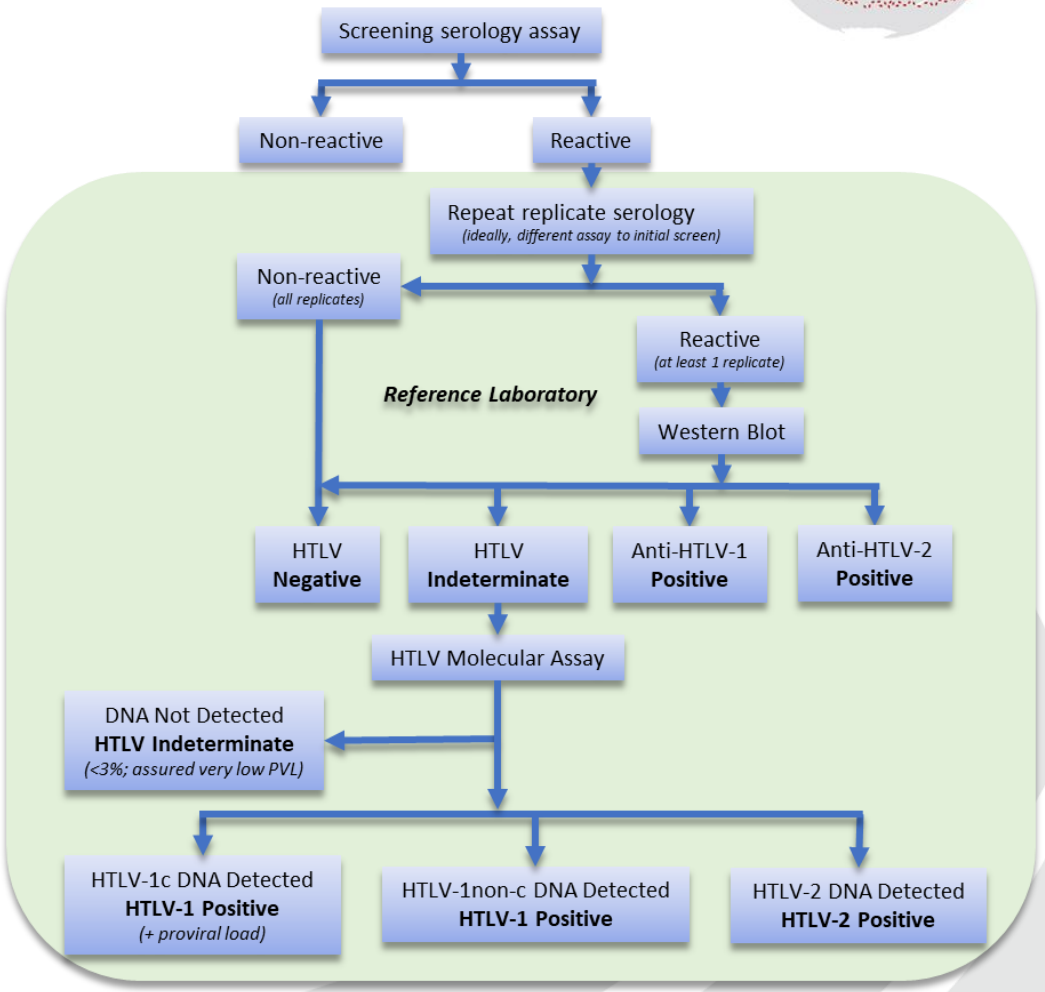
Seronegative for HTLV:	No bands
Seropositive for HTLV-1:	Rgp21 and Rgp46I and p19 ***or*** p19 and p24 (p19 ≥ p24) and Rgp21
Seropositive for HTLV-2:	Rgp21 and Rgp46II and p24 ***or*** p19 and p24 (p19 < p24) and Rgp21
Indeterminate for HTLV:	All other banding patterns

Improved Diagnostic Testing Algorithm

mission
TO PROMOTE THE QUALITY OF TESTS AND TESTING FOR INFECTIOUS DISEASES GLOBALLY

NRLs next generation HTLV molecular assay (ACH4 funding)

- **Distinguishes between HTLV-1 and HTLV-2**
- **Distinguishes between endemic (HTLV-1_c) and non-endemic (HTLV-$1_{non\text{-}c}$)**
- **Provides a proviral load for HTLV-1_c (endemic to CA)**
- Excellent analytical performance, requires clinical validation
  - HTLV-$1_{non\text{-}c}$ and HTLV-2 validation panel has been sourced
  - HTLV-1_c panel: Longitudinal Study samples ***provided ethical use of residual extracts for this purpose can be obtained***



✓ **Reduce IND rates from 10% to <3%**
✓ **Provides PVL for HTLV-1c POS**

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What is a HTLV-1 Proviral Load (PVL)?

- Quantifies the amount of virus circulating by counting the number of HTLV infected lymphocytes in the blood stream
- Can be designed to distinguish HTLV-1 from HTLV-2
- **Can be used as a Confirmatory assay (with Western Blot)**

- Can be used to predict likely risk of transmissi… those at risk of developing associated dise…
  - High PVL pre-dates and is associ… both inflammatory and proliferativ… s.
  - Low PVL predicts asymp… infection and less risk of these diseas…

No commercial test for virus available globally

…veitis
Myopathy
Thyroiditis
Pulmonary disease
ATLL (clonal expansion)
HAM / TSP (activated T cells)

Citation: Taylor, G.P.; Evans,W.; Rosadas, C. High HTLV-1 Proviral Load Predates and Predicts HTLV-1-Associated Disease: Literature Review and the London Experience. Pathogens **2024**, 13, 553. https://doi.org/10.3390/pathogens13070553

Testing consensus

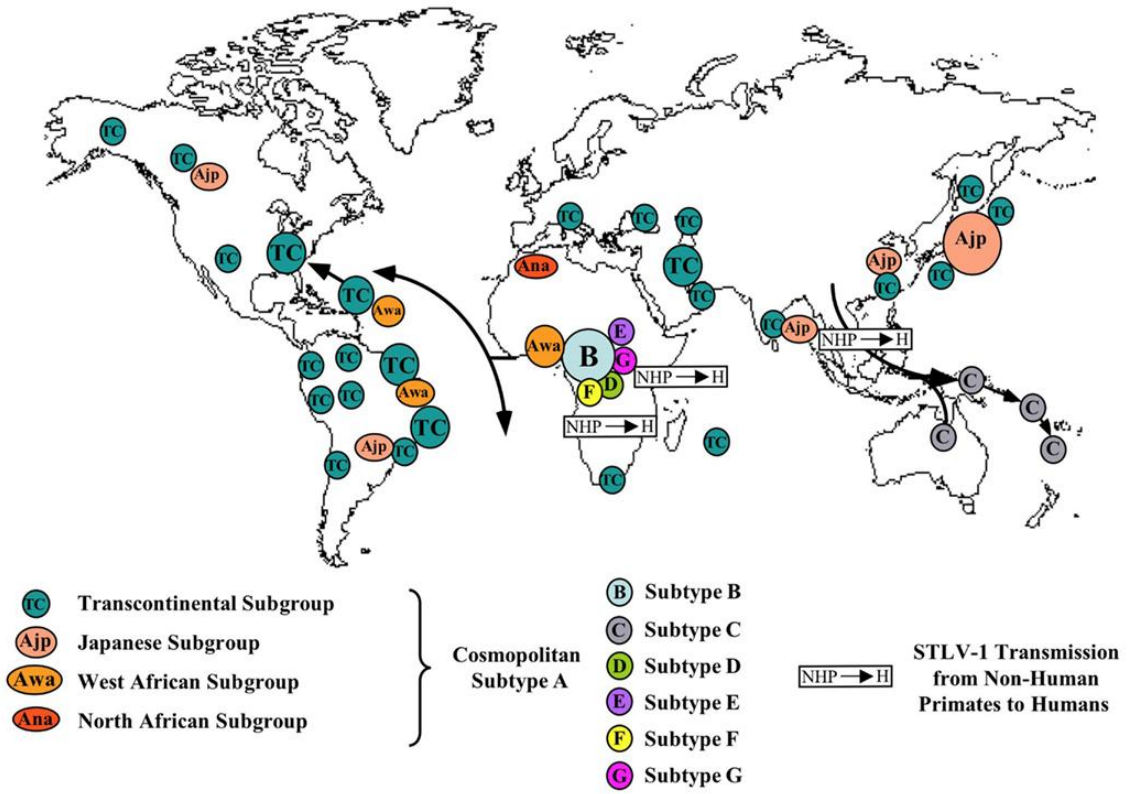
- PVL helpful to identify who is at risk but lacks specificity
- Strong evidence of effective control of the virus in some individuals
- Gaps in understanding of timing of disease onset & who will remain healthy

Prognostic Biomarkers can change clinical care:

- Support how to discuss transmission and disease risk with patients
- Provide choice to patients about the next steps
- To treat or not treat healthy people at risk of disease
- Decide what treatment & when

Citation: Taylor, G.P.; Evans,W.; Rosadas, C. High HTLV-1 Proviral Load Predates and Predicts HTLV-1-Associated Disease: Literature Review and the London Experience. Pathogens **2024**, 13, 553. https://doi.org/10.3390/pathogens13070553

IRVA International Testing Group



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Representation of Clinical and Laboratory experts from:

- **Argentina**
- **Australia**
- **Brazil (2 labs)**
- **Japan (3 labs)**
- **Peru**
- **United Kingdom (2 labs)**
- **Iran &**
- **USA**

Issues:

- *Poor equity in access to testing services – many at risk populations are untested*
- *High cost of testing services*
- *Variable capability of Testing services*
- *Variable quality and accuracy of testing*
- *Emerging availability of Point-of-Care Tests*
- *No molecular commercial test available*

IRVA International Testing Group

AIMS:

- Publish guidance regarding test methods, protocols and testing guidelines.
- Develop recommended testing guidelines and advice
- Support laboratories with cost effective solutions
- Standardise assays – source and develop an international standard and QA programs
- Publish test methods
- Establish a Prognostics Biomarker Subgroup

- Strengthened capacity and capability in Brazil and Argentina
- Broaden access to HTLV PVL - focus on sharing knowledge and protocols
- Improving consistency of testing across labs in-country
- Provide support to improve accuracy and also reduce cost

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HTLV-I Prognostic Biomarker Working Group

AIMS:

- Provide advice and support for design, development and implementation of prognostic tests to predict the development of HTLV-1-related diseases, including to:
  - Understand the predictive ability of tests.
  - Publish methods for prognostic testing.
- Work towards the standardisation of assays and development of recommended testing guidelines

OUTCOMES:

1. **Guidance and leadership regarding types of tests - guidelines, protocols and methods**
2. **Disseminated prognostic testing algorithms and guidelines along with protocols and methods**
3. **Survey of access to testing services including prognostic biomarkers**
4. **Planning to conduct comparative blind testing of a sample set across laboratories**

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WHO HTLV-1 Clinical and testing guidelines

- Appointed a consultant to lead the development
  - Collected existing country clinical guidelines
  - Systematic review of clinical guidelines conducted

<Interruption to US funding of WHO>

- Development of Diagnostics Landscape Overview and registration of all tests available globally including Point-of-care tests
- Systematic review to support testing guidelines underway
- Consideration of Pre-qual Evaluation of test kits for HTLV-1

Summary

- Progress in being made to improve diagnostic accuracy in Australia
- Progress being made to improve access to HTLV-1 PVL testing globally
- Progress underway to improve the quality of testing
- Progress being made towards being able to identify asymptomatic individuals at risk of developing of disease
- WHO committed to developing HTLV-1 Clinical and Testing Guidelines
- Point-of-care Test options becoming available and are under evaluation

Acknowledgements & Thanks

IRVA Testing Working Group Members

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