Human T-cell Lymphotropic Viruses

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• What is HTLV?
• Where did it come from?
  • Where is it found?
  • What is its impact?
• How is it transmitted?
• What should we be doing?
Looks like HIV but there are big differences
HTLV infection occurs from cell-to-cell by direct contact


HTLV is highly cell associated. HTLV virions are rarely detected in the plasma of infected carriers despite high proviral load. (Demontis et al 2014)
Anti-HTLV RT and Integrase inhibitors may prevent infection but do not treat infection.
HTLV’s diverged from PTLVs ~40,000 (HTLV-3) ~60,000 (HTLV-1), ~200,000 (HTLV-2) years ago
FIGURE 2 | Geographical distribution of the main foci of HTLV-1 infection. Estimates of the number of HTLV-1 infected carriers, based on approximately 1.5 billion of individuals from known endemic areas and reliable epidemiological data obtained from studies among pregnant women and/or blood donors and/or different adult populations. In few countries, HTLV-1 endemic areas are limited to residents of certain regions such as Meshed in Iran, The Fujian Province in China, Turaco in Colombia and Central Australia.
High prevalence >1:10,000 first time blood donors

High prevalence >1:100 general population
HTLV-1 prevalence in Africa
HTLV-1 prevalence in Asia
HTLV-1 prevalence in North America

* The presence of HTLV-1 infection and cases of HTLV-1 associated diseases among indigenous inhabitants of Nunavut and British Columbia provinces of the Yukon and Northwest Territories have been reported (Annex I, Sibbald B et al., CMAJ, 2006).

** HTLV-1 seropositivity > 1: 10,000 among first time blood donors in some counties of states labelled with slanting stripes was associated with female sex, older age, non-white race/ethnicity, lower educational level, and residence in the western and south-western United States (Annex I, Chang et al., 2018).
HTLV-1 prevalence in South west Pacific

The highest reported prevalence of HTLV-1 is here 45%

5-10 million carriers worldwide is a conservative estimate
HTLV-1 Prevalence in Europe

High prevalence >1:10,000 first time blood donors
HTLV-I prevalence in the UK

- **1993 N London Blood Donors**  
  n = 96,000  
  – 1/20,000  
  Brennan et al BMJ 1993;307:1235-9

- **2000 N Thames Infant Heel Pricks**  
  n = 126,000  
  - 1/2,000  
  Ades et al BMJ 2000;320:1497-1501

- **Unpublished S London GU Clinic**  
  n = 2,553  
  - 1/330

- **2005 S London HIV+ patients**  
  n = 777  
  - 1/130  
HAM develops in 3% of cases.

- Spasticity/Weakness
- Hyperreflexia
- Bladder dysfunction
- Lumbar pain
- Constipation
- Impotence
Lymphocytic infiltration
Initially CD4 > CD8
Later CD8 predominate
Finally atrophy
The spinal cord become atrophied
There is evidence of widespread inflammation on PET scanning.

There is evidence of widespread inflammation on PET scanning.

Dimber et al J Nuc Med 2016 jnumed.116.1 75083
HTLV-associated inflammatory diseases

Life-time risk of HAM 3%

Uveitis ~1%

Life-time risk of other HTLV associated inflammation?
Adult T-cell Leukaemia/Lymphoma occurs in 5% of HTLV-1 carriers

- Median age of onset 51.5 years
- Generalised lymphadenopathy
- Hepatosplenomegaly
- Skin lesions
- Lytic bone lesions
- Hypercalcaemia
Adult T-cell Leukaemia/Lymphoma

Overall Survival ~8 months

Unchanged after 25 years

Overall Survival

<table>
<thead>
<tr>
<th>MST (months)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smouldering</td>
<td>55.0</td>
</tr>
<tr>
<td>Chronic</td>
<td>31.5</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>10.6</td>
</tr>
<tr>
<td>Acute</td>
<td>8.3</td>
</tr>
</tbody>
</table>

(P<.0001; \(\chi^2 = 207.8\); log-rank test)


ATLL is associated with infection in Infancy

ATLL can be prevented
Transmission of HTLV-1/2

- Mother-to-child
  - <33% with prolonged breastfeeding
- Sexual intercourse
- Blood transfusion
  - Cellular blood products ~ 30% transmission
  - Solid organ transplantation ~? 100%
- Sharing of injecting paraphernalia
- Self-flagellation

Emerging Infectious Diseases 2019
Tang et al
HTLV-1 infection is not transmitted within households

**Figure 1.** Number of children followed up and HTLV-I seropositive rates.

**Figure 2.** HTLV-I seropositive rates in children followed up long term.

Ando Y et al JID 2003 – Breast-fed children

Ando Y et al JID 2003 – Bottle fed children
Sexual Transmission

- Family studies indicate predominance of male-to-female transmission
- Miyazaki Cohort Study:
  - 1984-9: 534 Married couples
  - 342 HTLV- Concordant
  - 95 HTLV + Concordant
  - 33 M+F-: 5 seroconversions
  - 64 M-F+: 2 seroconversions
  - Relative Risk if -ve female 3.9

Heterosexual transmission of human T cell leukemia/lymphoma virus type I among married couples in southwestern Japan: an initial report from the Miyazaki Cohort Study.
J Infect Dis. 1993 Jan;167(1):57-65
Sero-prevalence data from Bahia, Salvador, Brazil

A blood donor’s story

HTLV-1 negative
UK Blood donation

5 months
New partner
Retiring to Spain
HTLV-1 positive

First symptoms

5 months
Wheelchair dependent

HTLV-1 seropositive

CASE REPORT
Rapid onset and progression of myelopathy following an STI: a case for screening?

Rachel J Caswell, Peter Nall, Meg Boothby, Graham P Taylor

STI 2019 June
What should we be doing?

Diagnose Carriers

Blood and Transplant

Sexual Health

Ante-natal Care

Prevention of transmission

Early detection/prevention of disease

30,000 HTLV carriers in UK (predominantly BME)

Indicator Diseases:

- Myelopathy
- Myositis
- Uveitis (especially recurrent)
- Keratitis
- Sjogren’s
- Thyroiditis
- Bronchiectasis
- Alveolitis
- Adult T-cell Leukaemia
- Persistent lymphocytosis
- Raised globulins
- Strongyloides stercoralis
- TB
- HIV
- Norwegian scabies
Making the diagnosis

Detects goat antibodies bound to human antibodies bound to HTLV-1/2 proteins

Detection of HTLV-1/2 infection
Sensitivity 100%
Specificity 99.7%

A sample with a signal equal to or greater than the assay cut-off is REACTIVE

Seroconversion window period of 6 – 8 weeks
Interpreting the initial serology
Confirming by Western Blot also distinguishes between HTLV-1 and HTLV-2.
Educating – patients

Health implications
Transmission risks,
Advocating safer sex
Contact Tracing

Referring

http://www.htlv.eu/

Colleagues

Indicator Diseases:
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In 2003 the Department of Health established a National HTLV Clinical Service

- Objectives
  1. To be the point of contact for HTLV infection
  2. To provide clinical expertise and health information for all patients with HTLV infections, their partners and relatives including blood donors
  3. To establish a critical mass of patients with these rare diseases to standardise and improve care
  4. To facilitate clinical and translational research
Development of a National HTLV Clinical Service

Access

Care

Diagnostics

Multidisciplinary

Public, patient participation

Research

Training

BASHH Guidelines on HTLVs – in preparation
THANK YOU