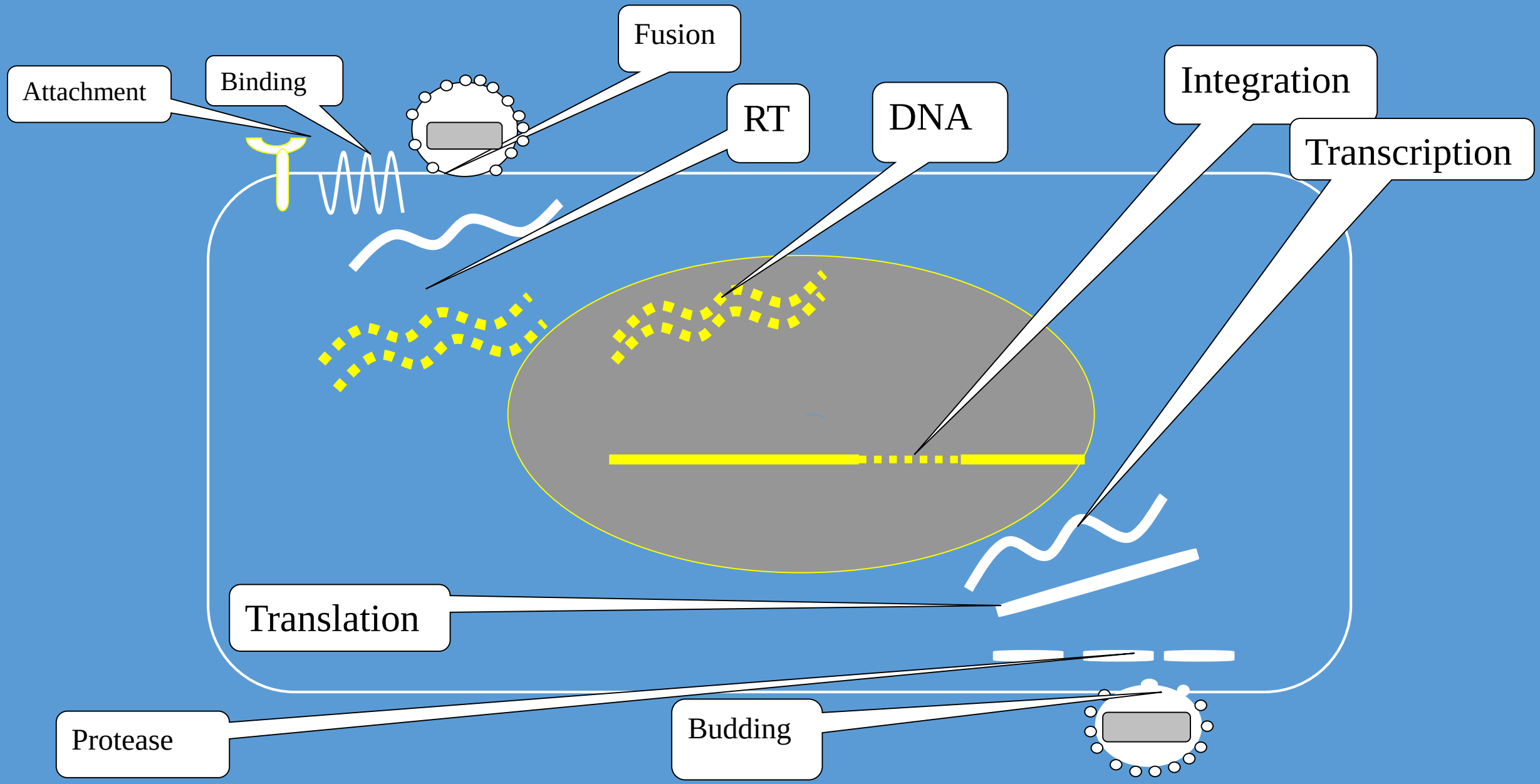
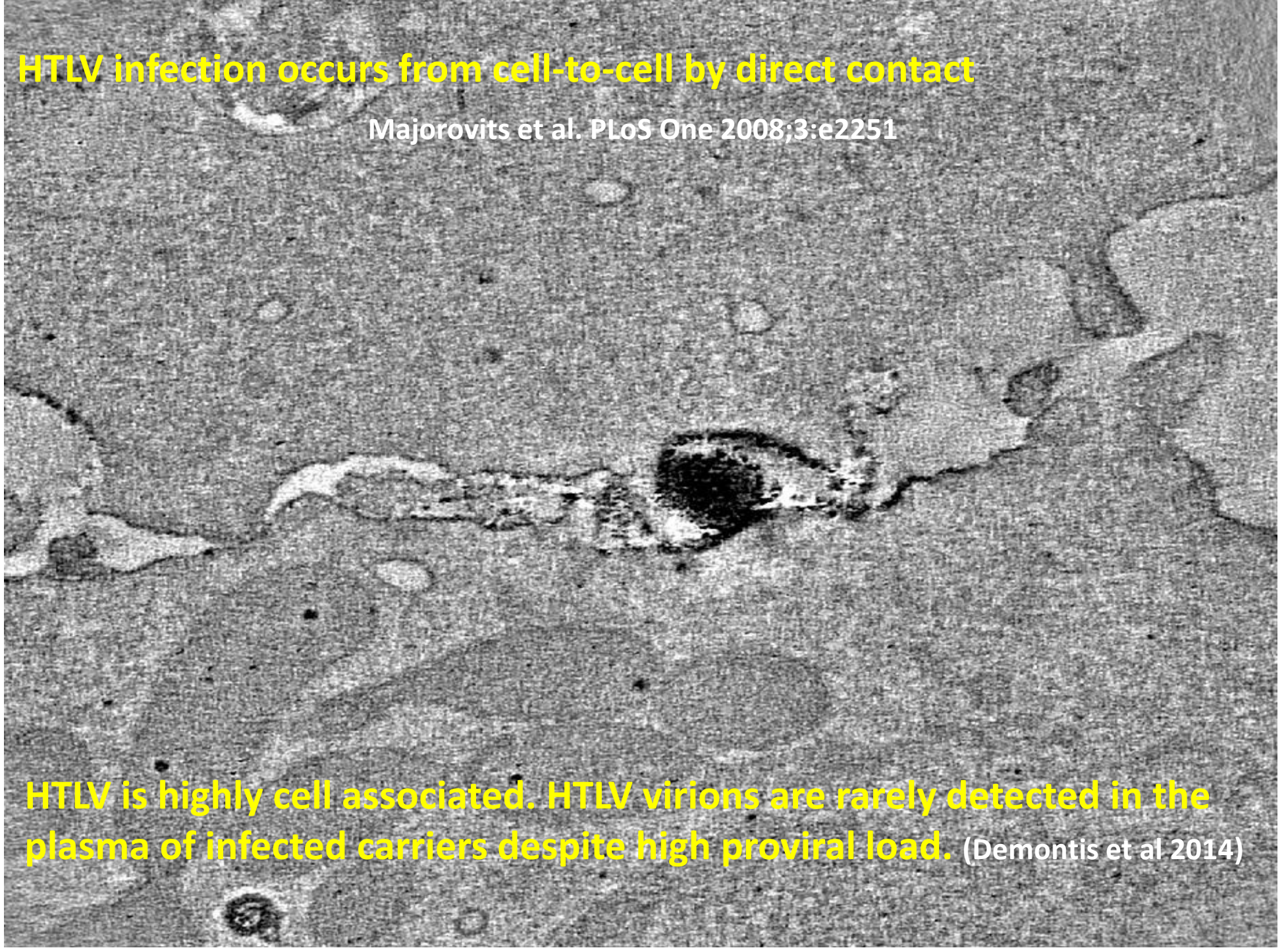
Human T-cell Lymphotropic Viruses

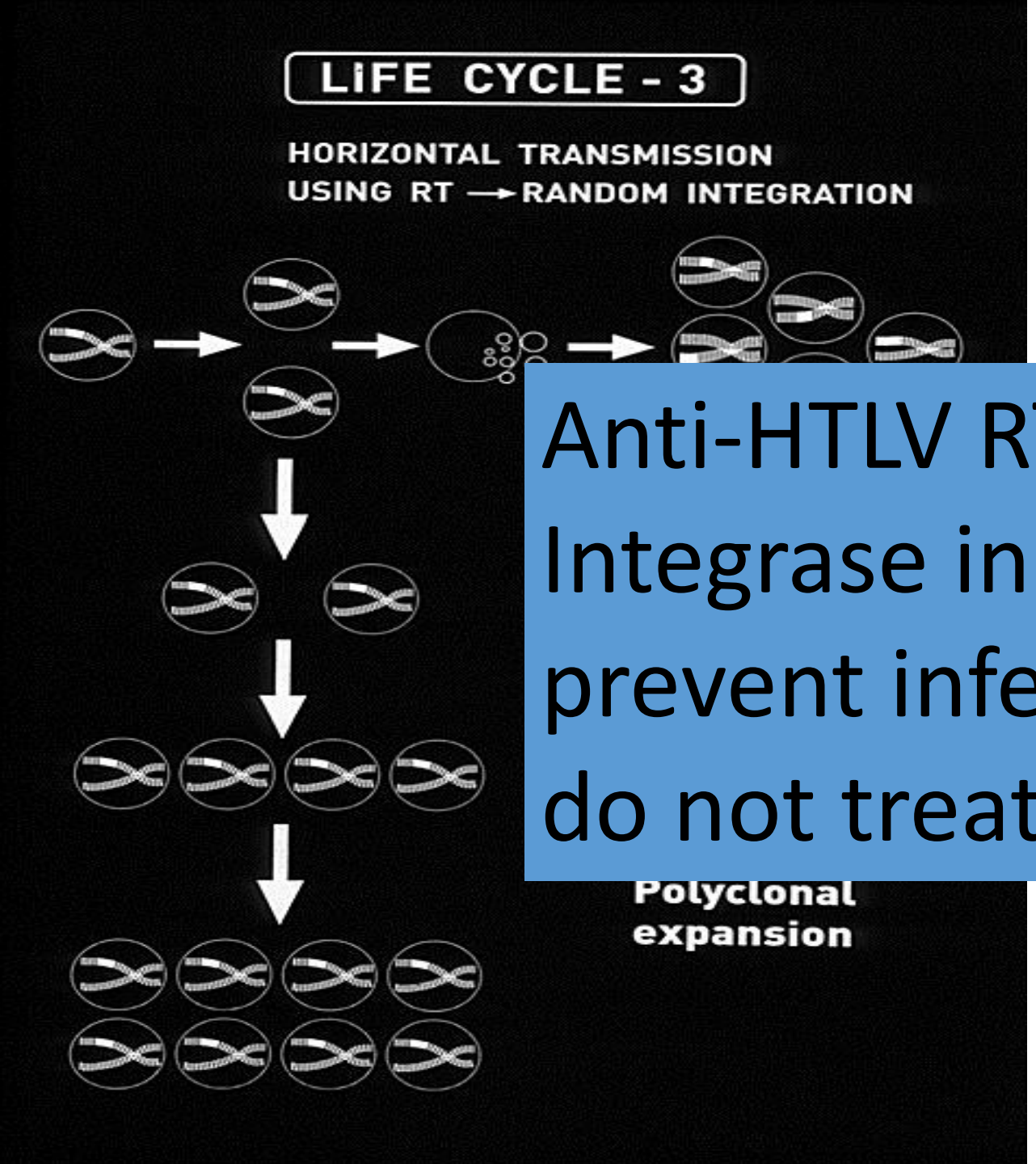
Graham P Taylor
Professor of Human Retrovirology
Imperial College London
g.p.taylor@imperial.ac.uk

- 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?



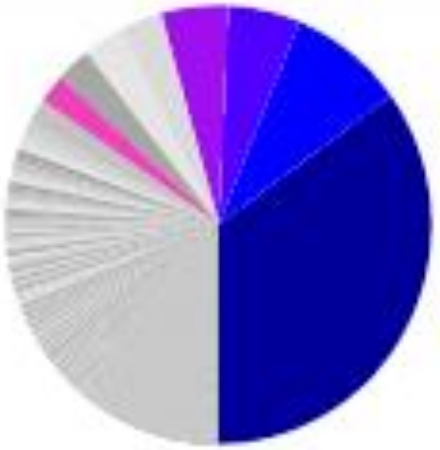
Looks like HIV but there are big differences

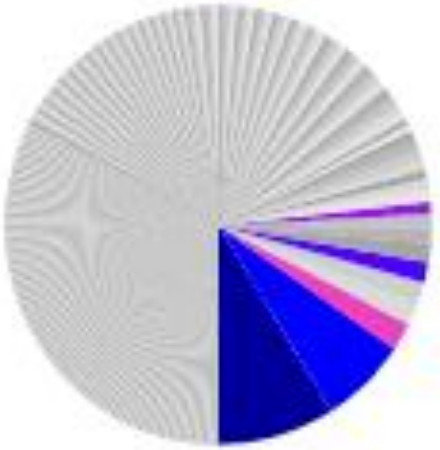

HTLV infection occurs from cell-to-cell by direct contact
Majorovits et al. PLoS One 2008;3:e2251
HTLV is highly cell associated. HTLV virions are rarely detected in the plasma of infected carriers despite high proviral load. (Demontis et al 2014)



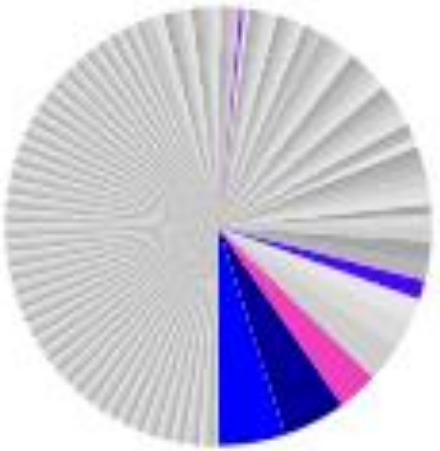
Anti-HTLV RT and Integrase inhibitors may prevent infection but do not treat infection

39 days after infection

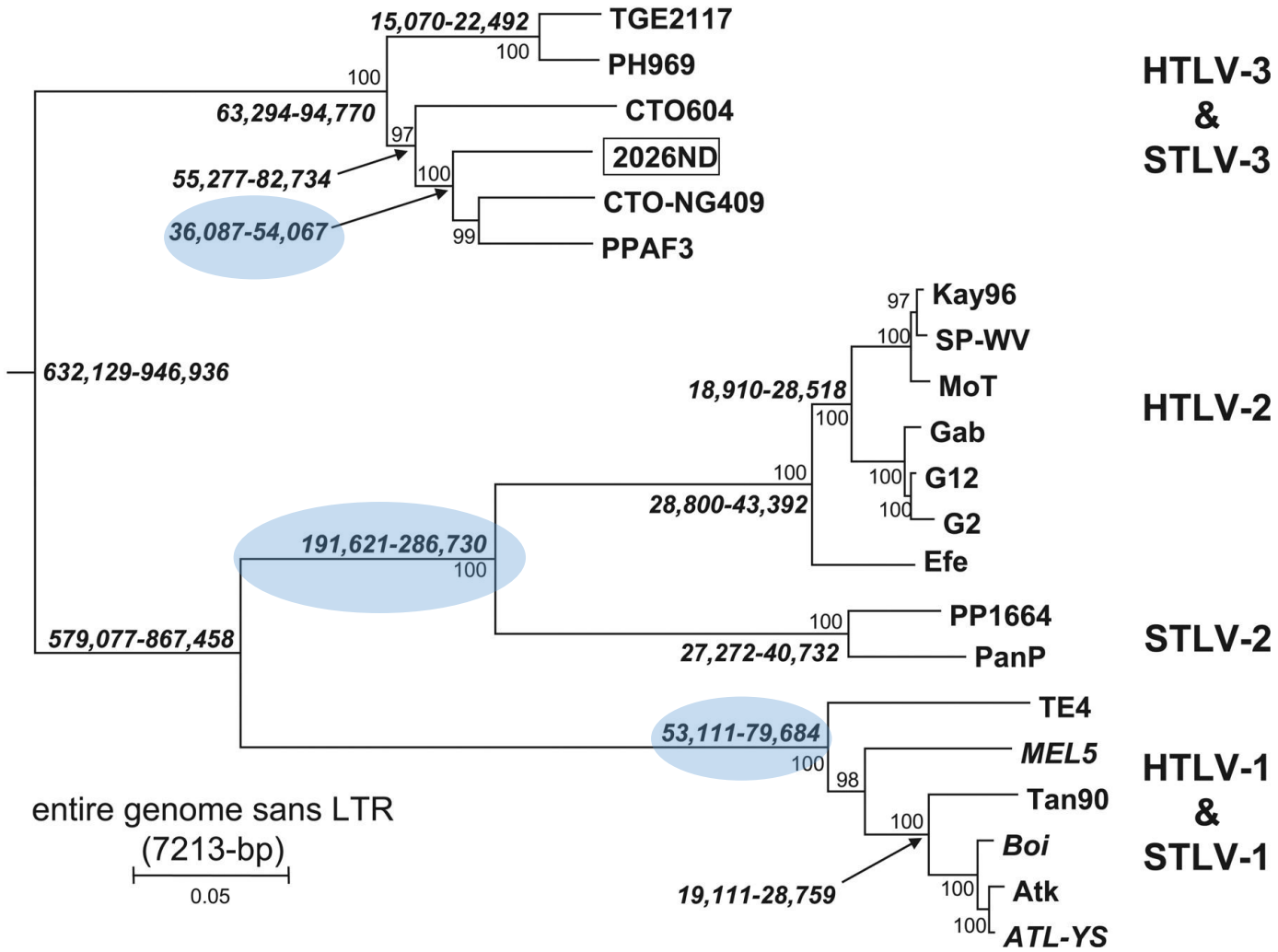




136 days after infection



HTLV's diverged from PTLVs ~40,000 (HTLV-3) ~60,000 (HTLV-1), ~200,000 (HTLV-2) years ago



Switzer W M et al. J. Virol. 2006;80:7427-7438

Journal of Virology

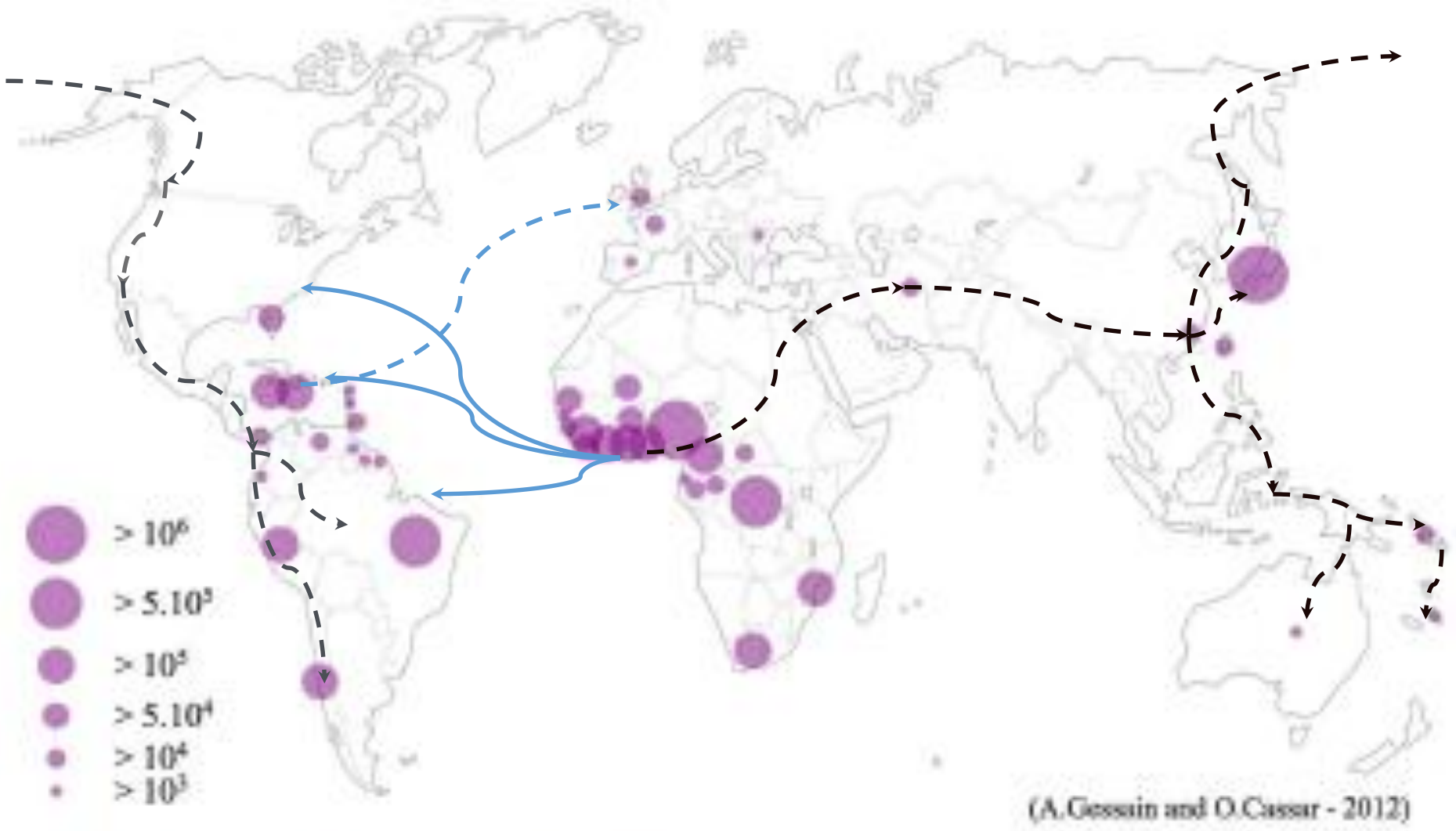


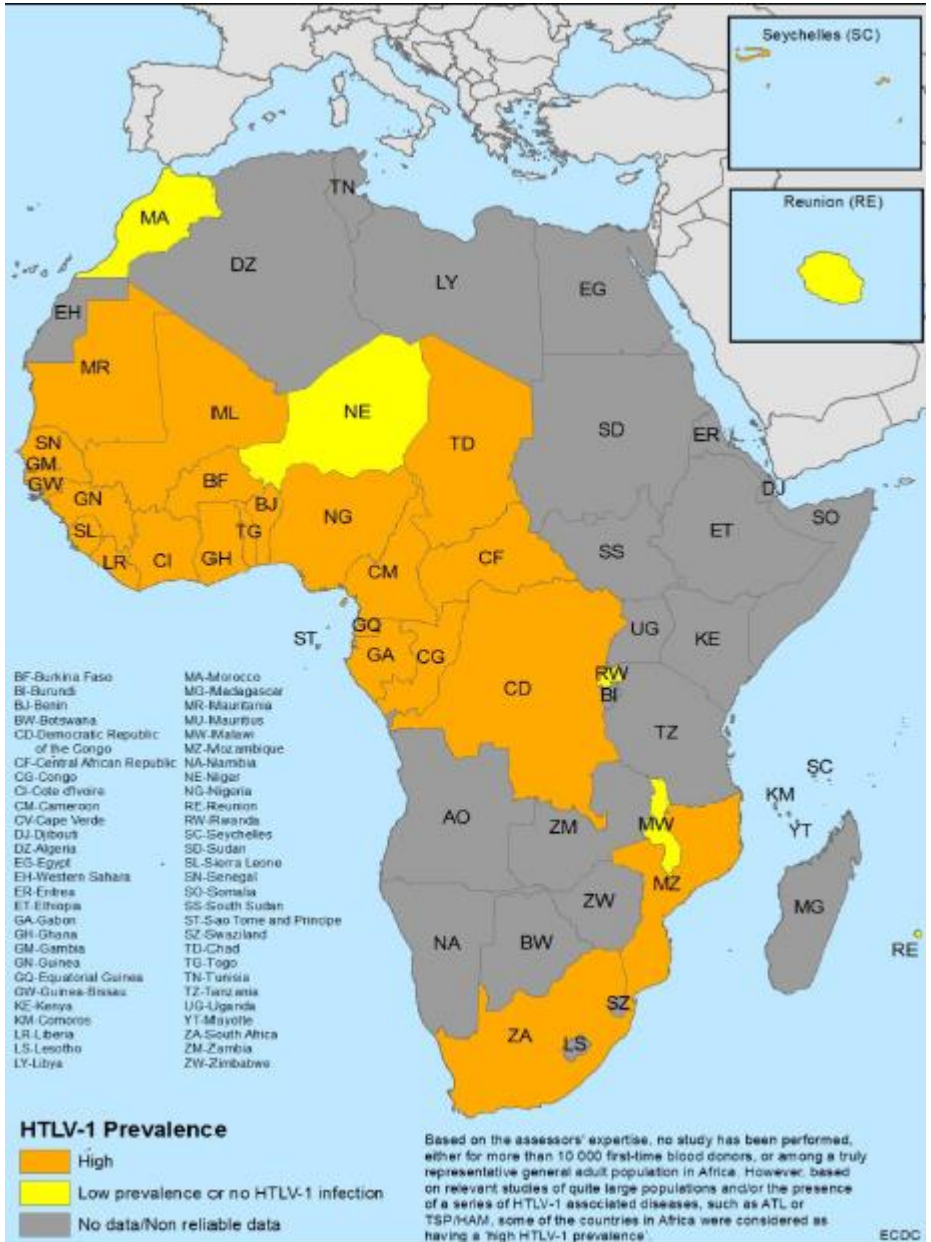
FIGURE 2 | Geographical distribution of the main foci of HTLV-1 infection. Estimates of the number of HTLV-1 infected carriers, based on approximately 1.5 billion of individuals from known endemic areas and reliable epidemiological data obtained from studies among pregnant women and/or blood donors and/or different adult populations. In few countries, HTLV-1 endemic areas are limited to residents of certain regions such as Mashad in Iran, The Fujian Province in China, Tumaco in Colombia and Central Australia.

S America & The Caribbean

High prevalence >1:10,000 first time blood donors

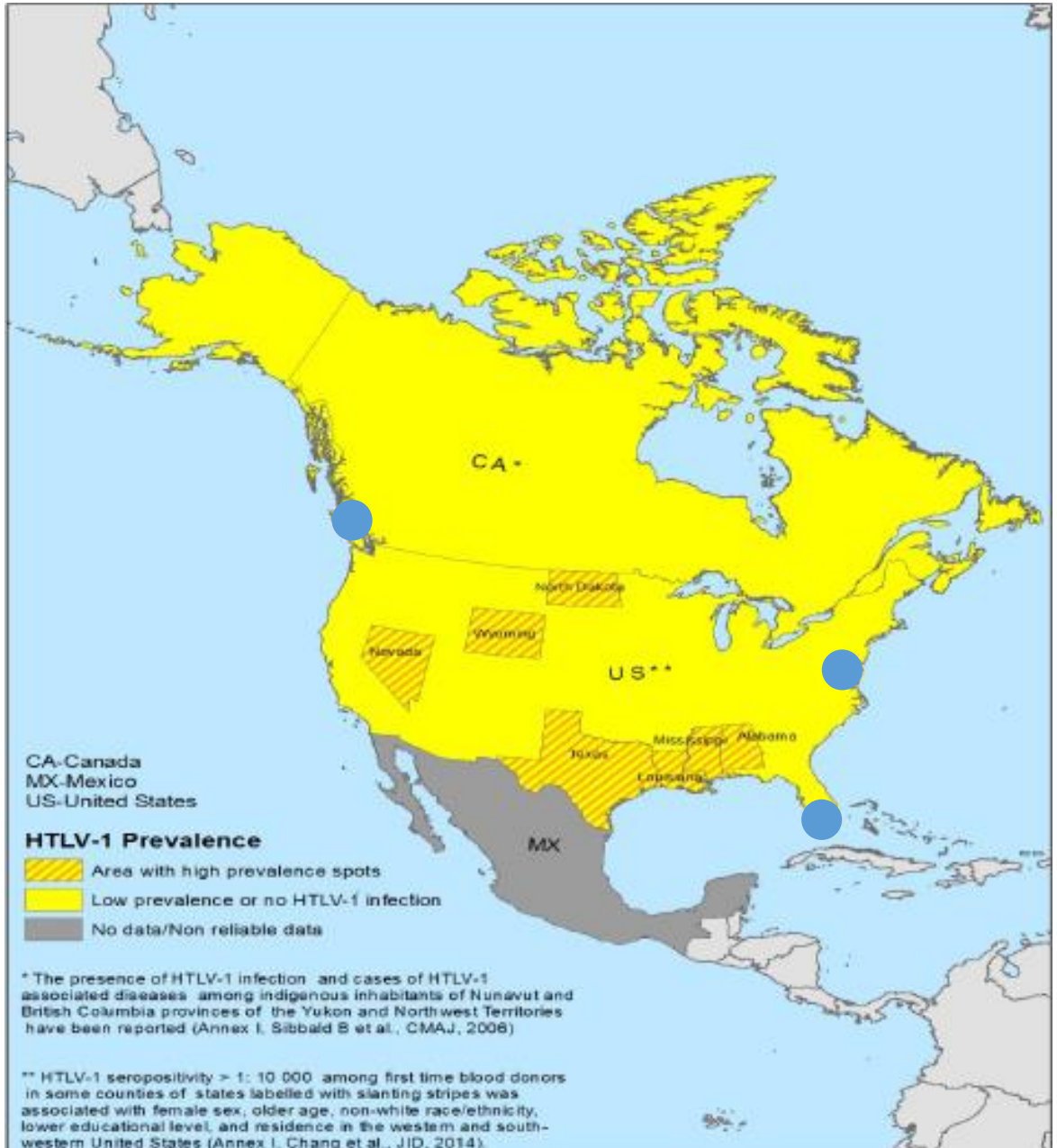
High prevalence >1:100 general population

HTLV-1 prevalence in Africa

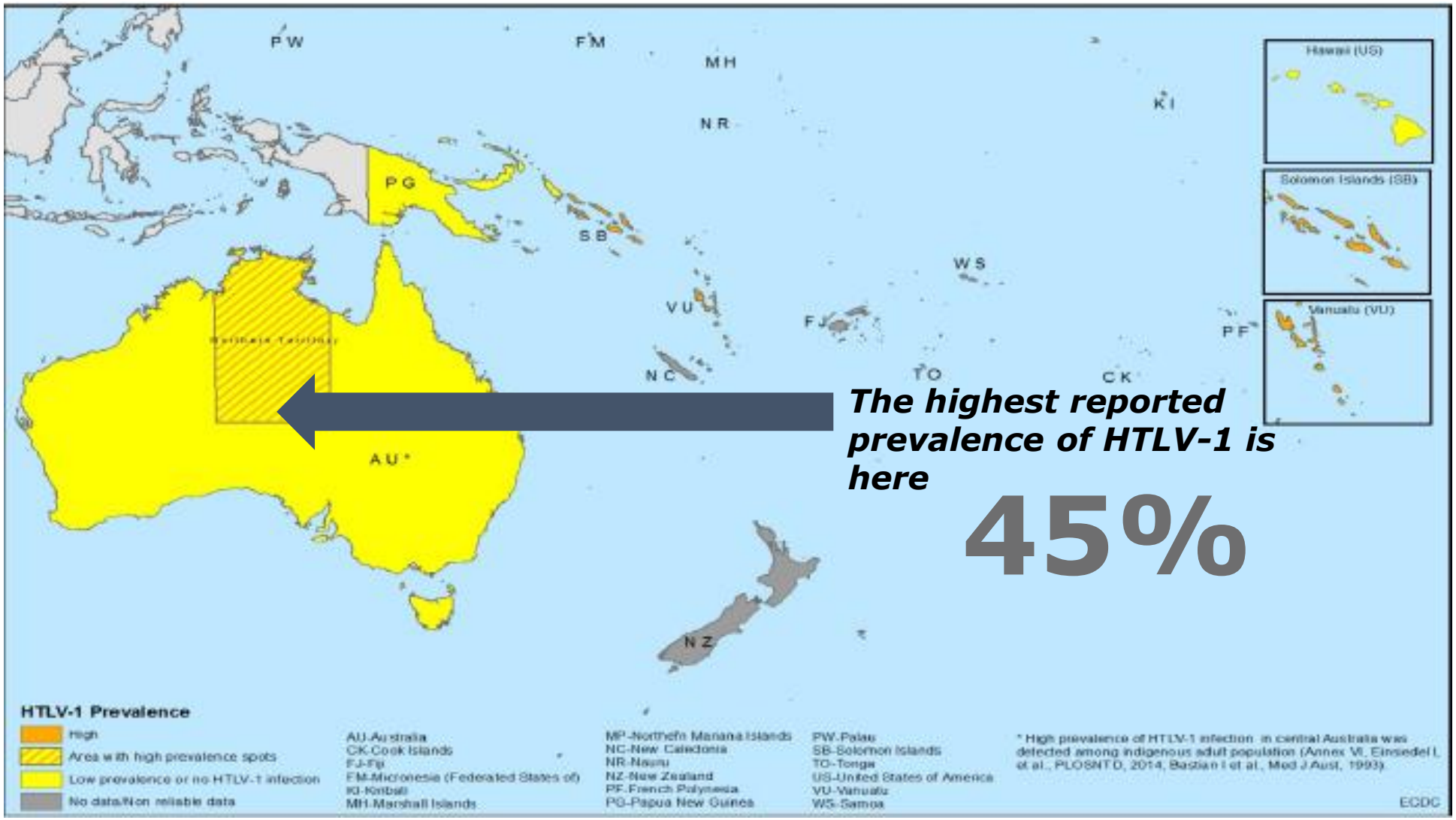


HTLV-1 prevalence in Asia

HTLV-1 prevalence in North America



HTLV-1 prevalence in South west Pacific



5-10 million carriers worldwide is a conservative estimate

HTLV-1 Prevalence in Europe

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 Cooke et al J Med Virol 2005;76:143 - 5

HAM develops in 3%

Spasticity/Weakness

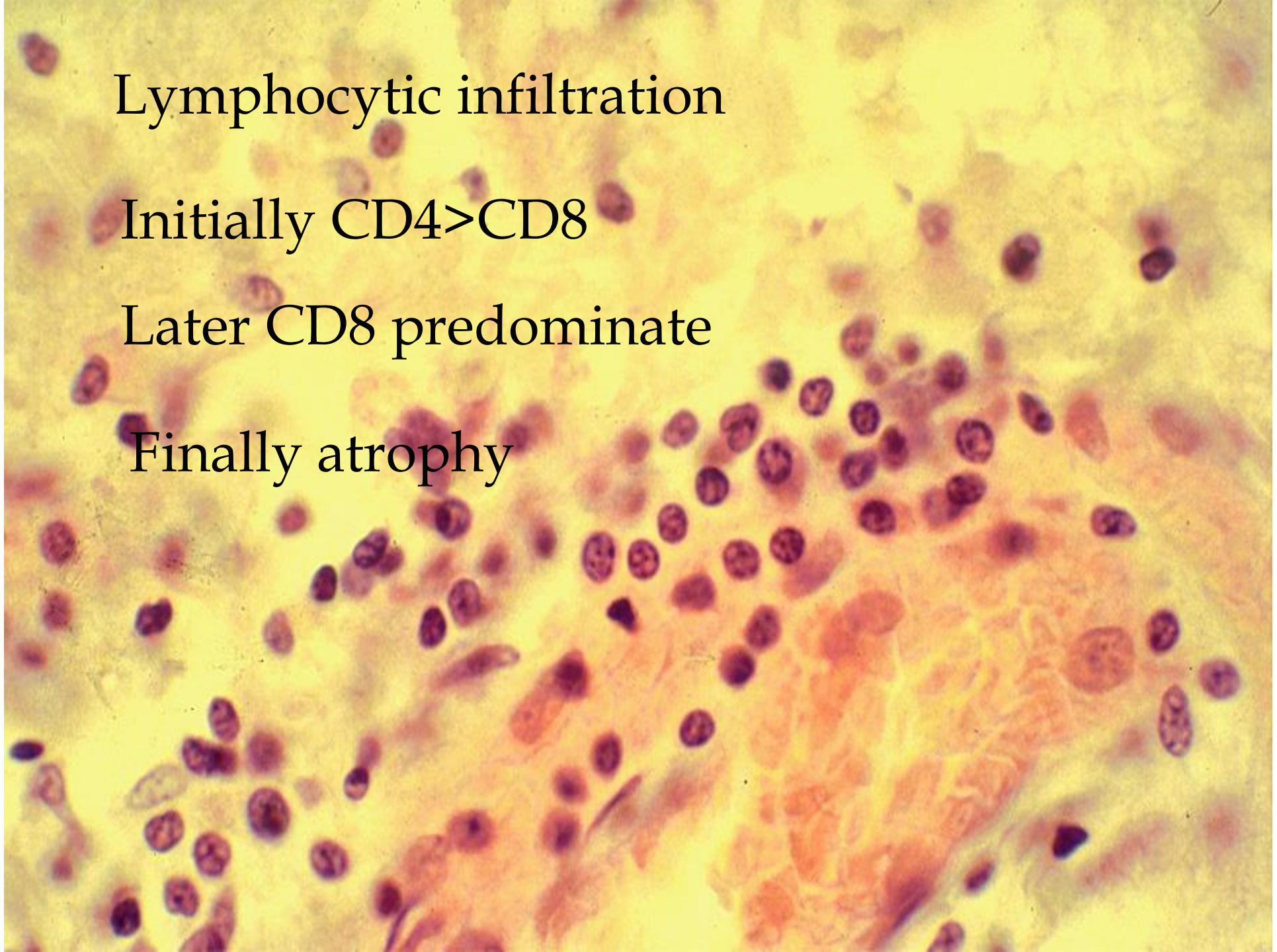
Hyperreflexia

Bladder dysfunction

Lumbar pain

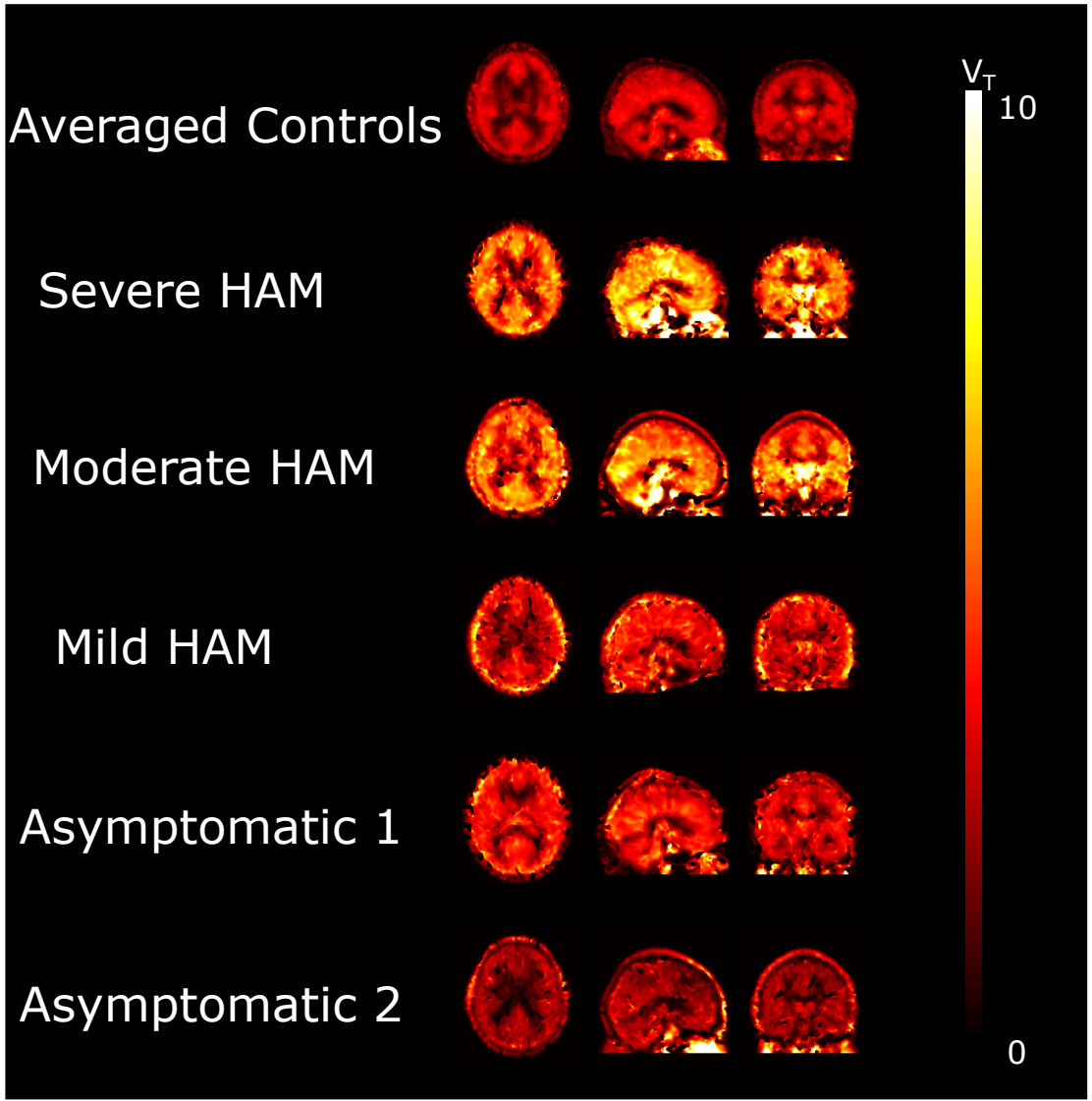
Constipation

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



Dimber et al J Nuc Med 2016 jnumed.116.175083

HTLV-associated inflammatory diseases

Life-time risk of HAM 3%

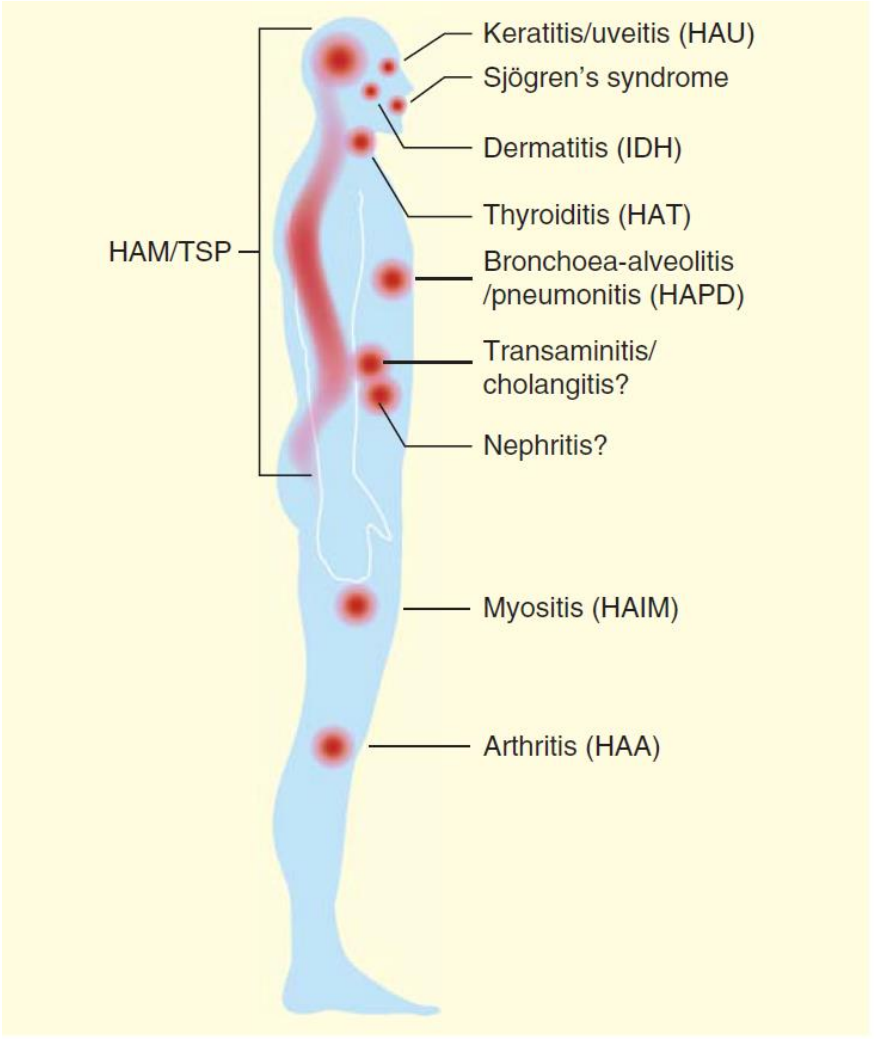


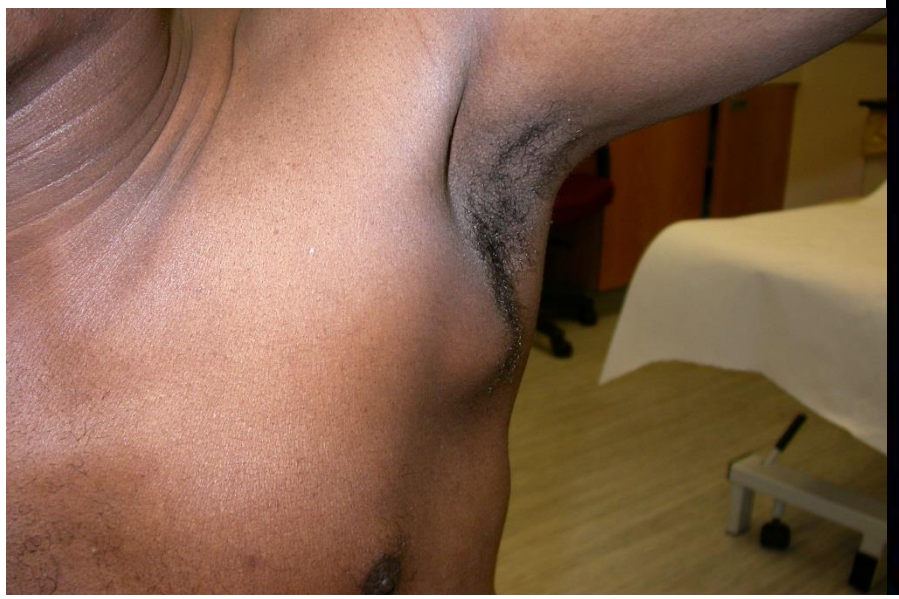
Figure 2. Distribution of human T lymphotropic virus type 1-associated inflammatory diseases by body sites.

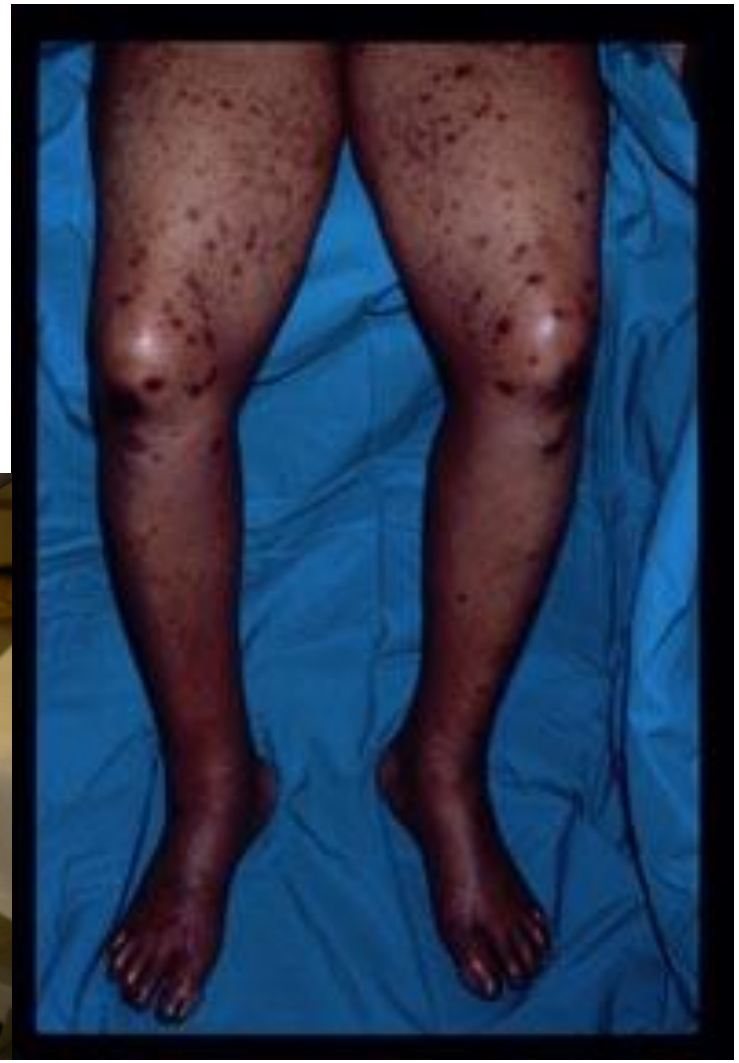
Uveitis ~1%

Life-time risk of other HTLV associated inflammation ?

Adult T-cell Leukaemia/Lymphoma occurs in 5% of HTLV-1 carriers

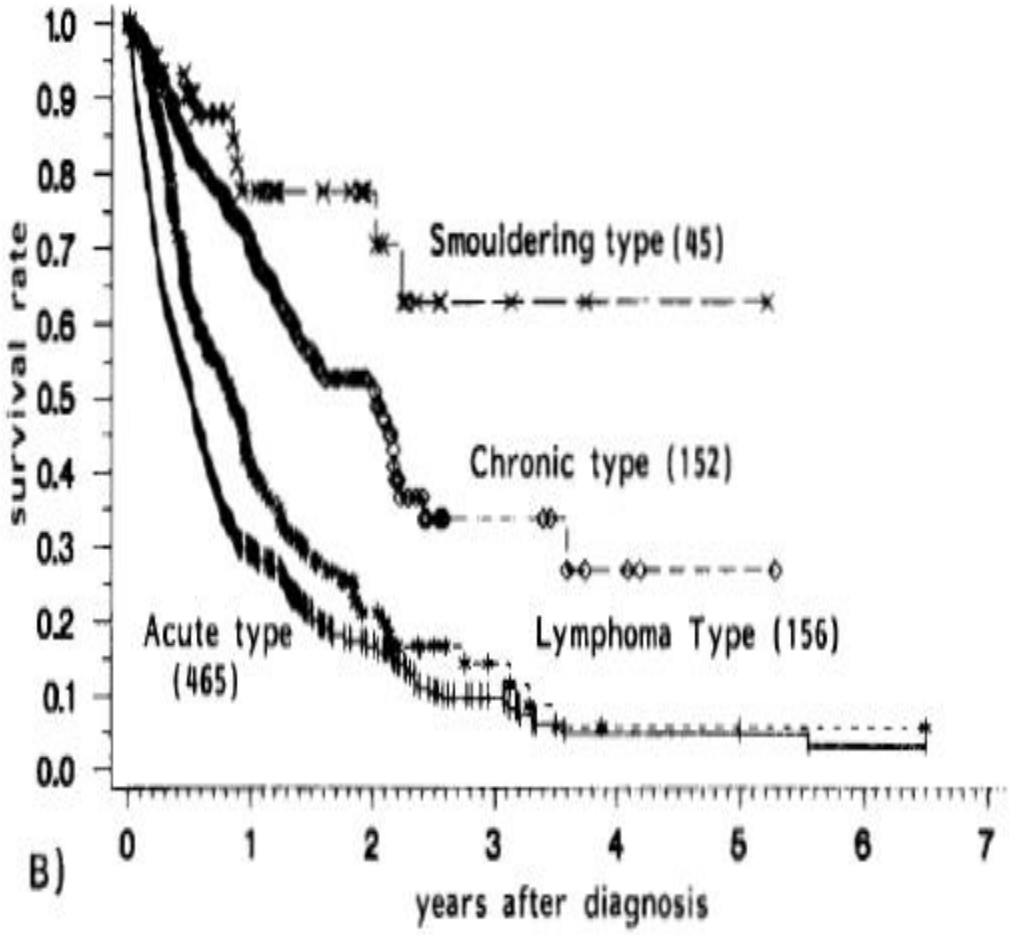
- Median age of onset 51.5 years
- Generalised lymphadenopathy
- Hepatosplenomegaly
- Skin lesions
- Lytic bone lesions
- Hypercalcaemia





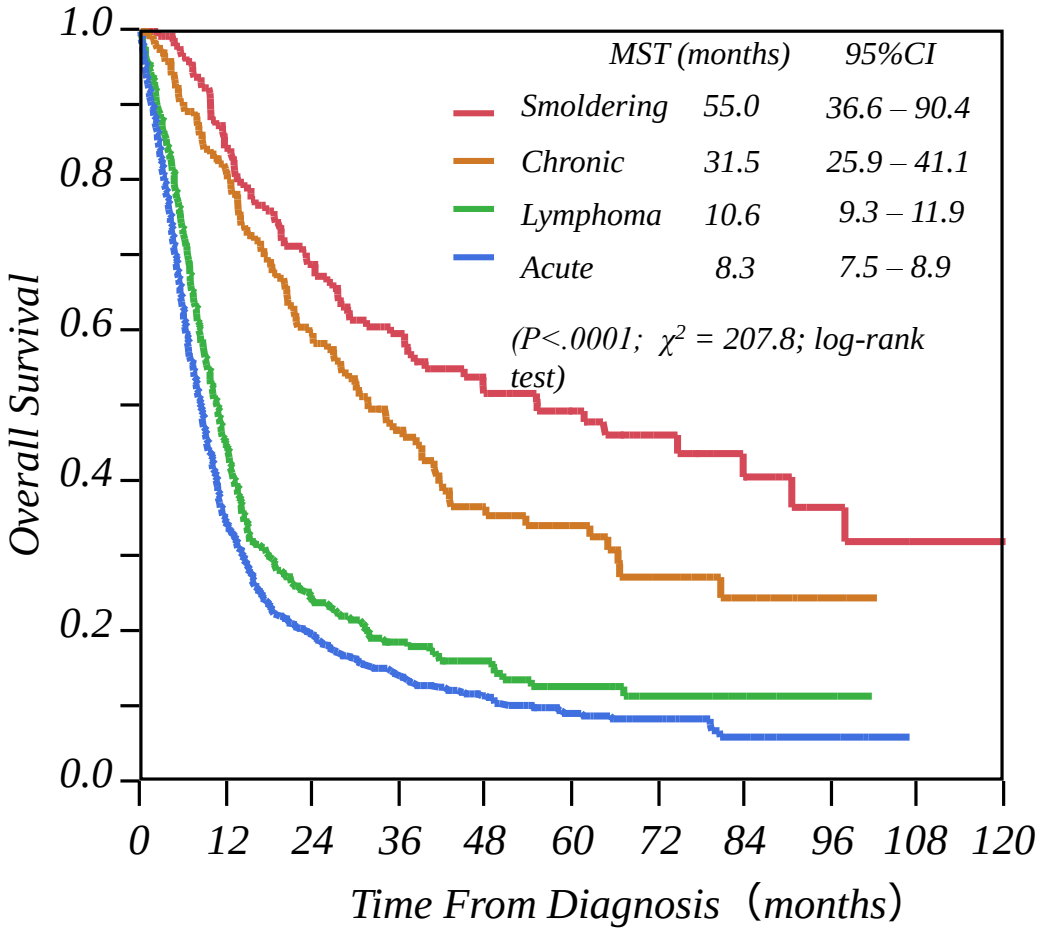
Adult T-cell Leukaemia/Lymphoma

Overall Survival ~8 months



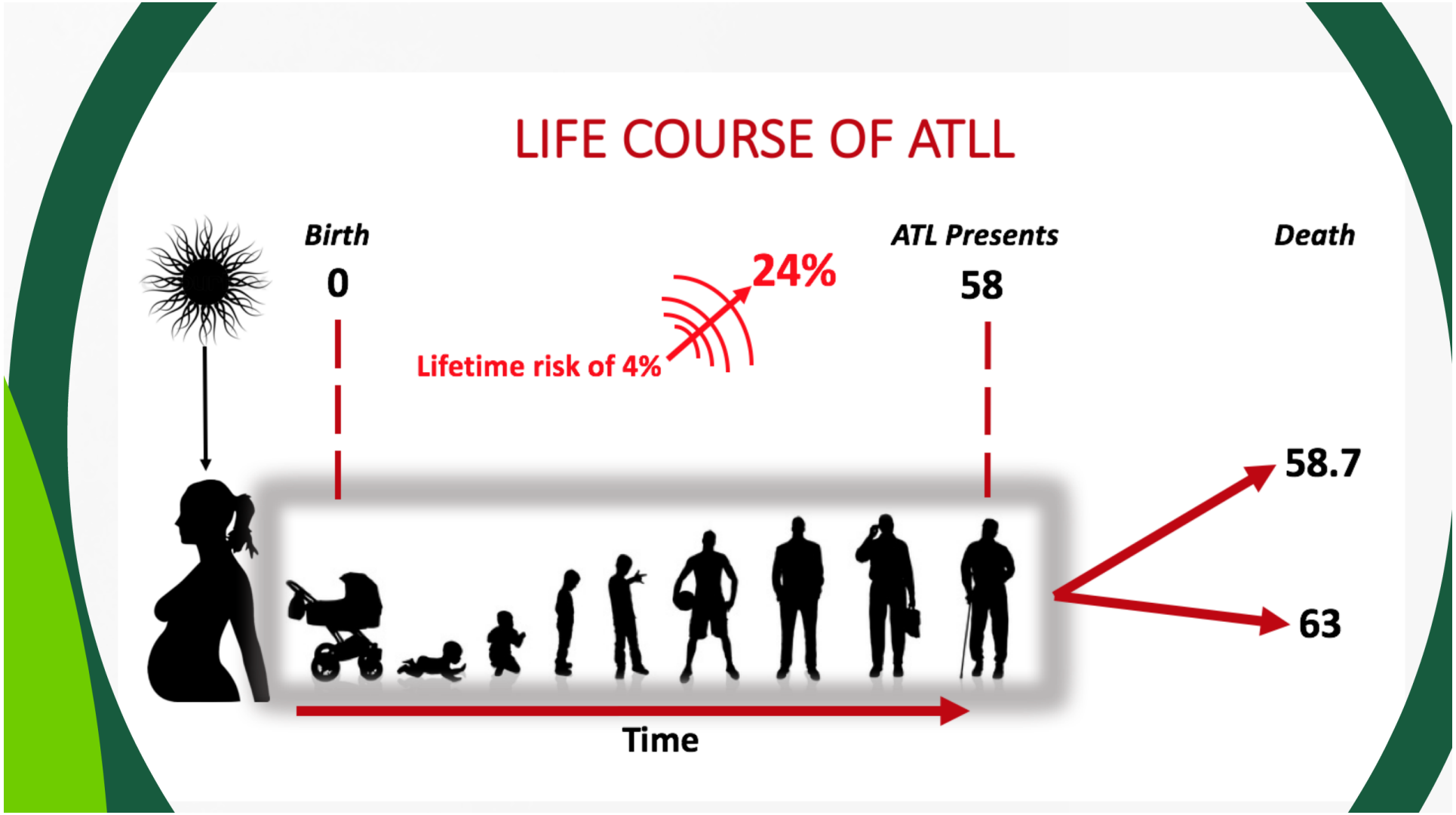
Shimoyama M, Br J Haematol 1991;79:428-437

Unchanged after 25 years



Katsuya H, et al, Blood 2015;126:2570-7

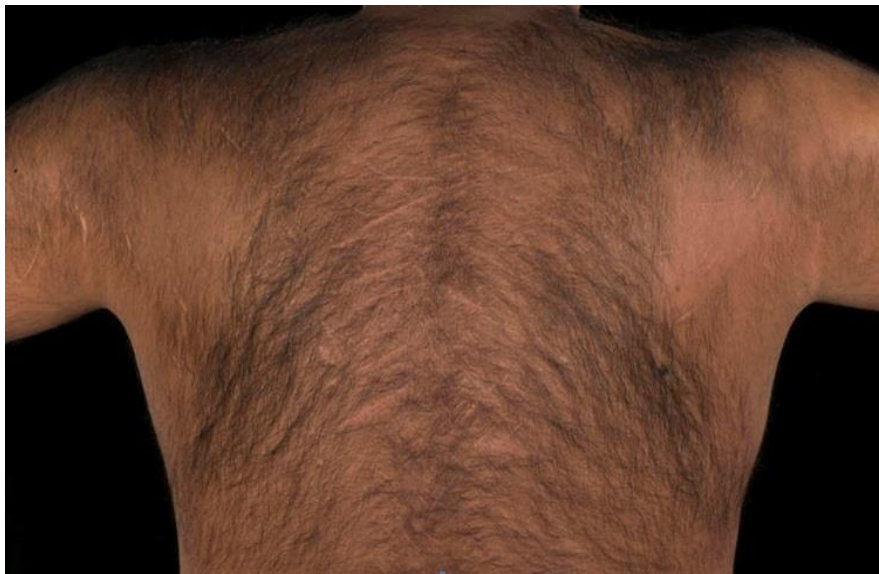
ATLL is associated with infection in Infancy



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

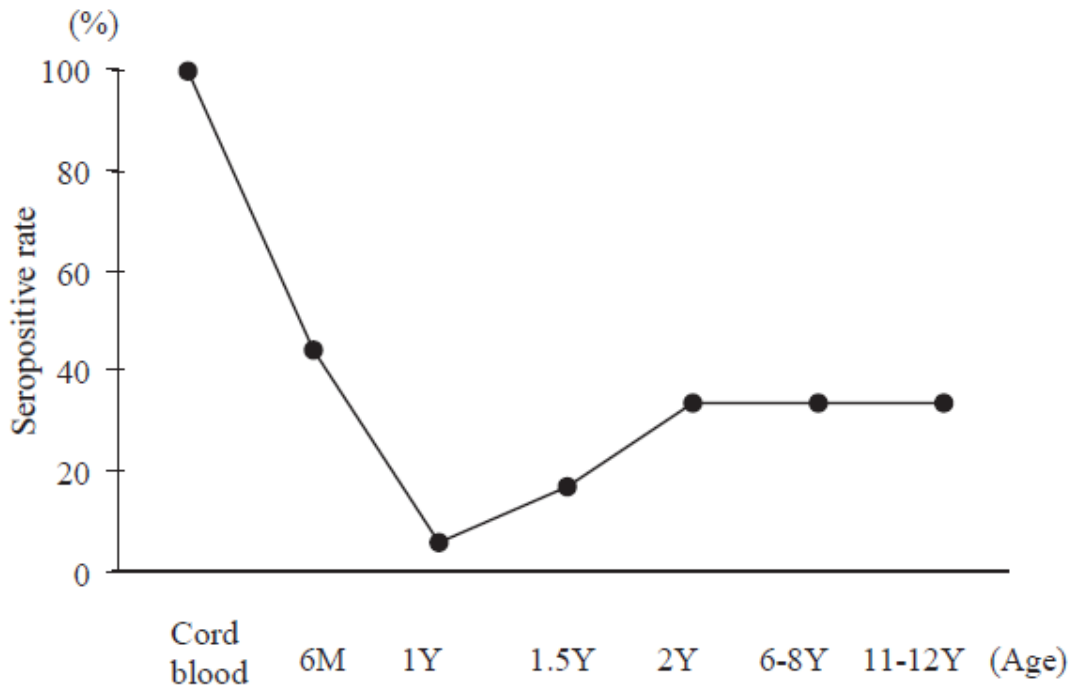


Figure 2. HTLV-I seropositive rates in children followed up long term.

Ando Y et al JID 2003 – Breast-fed children

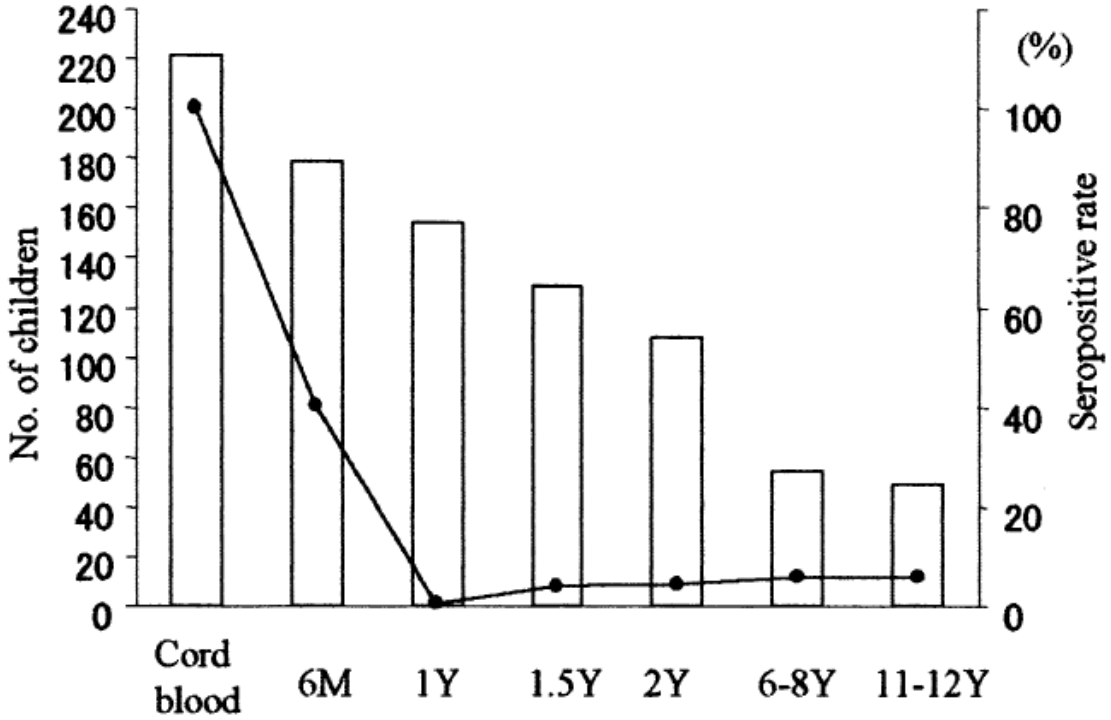


Figure 1. Number of children followed up and HTLV-I seropositive rates.

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

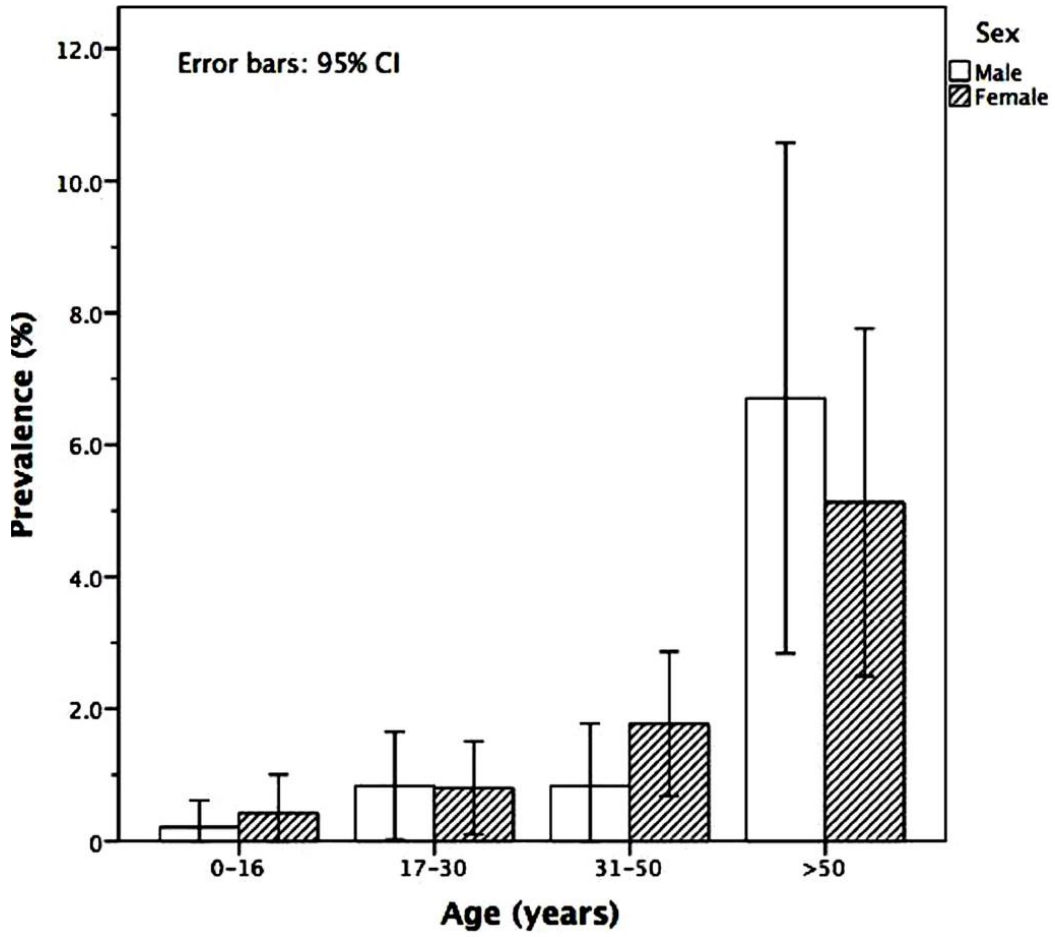
  64 M-F+ 2 seroconversions

  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.

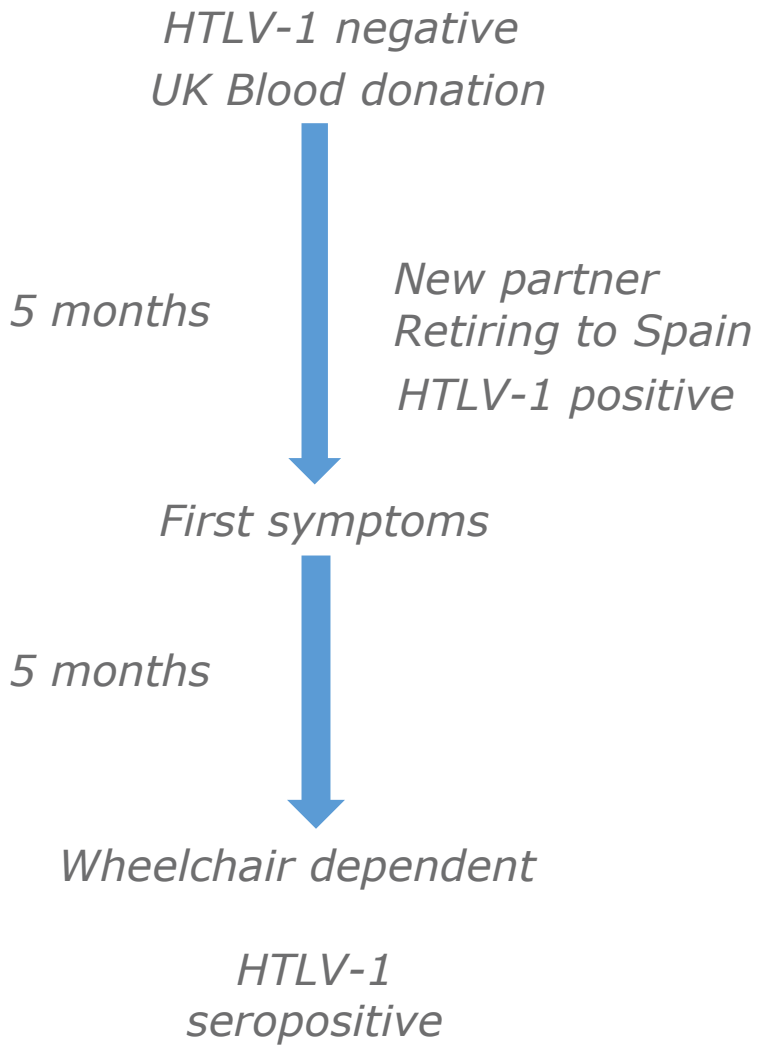
J Infect Dis. 1993 Jan;167(1):57-65

Sero-prevalence data from Bahia, Salvador, Brazil



Nunes et al PLoS ONE 12(2): e0171303.

A blood donor's story



CASE REPORT

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

Rachel J Caswell,[1] Peter Nall,[2] Meg Boothby,[1] Graham P Taylor[2]

STI 2019 June

What should we be doing?

30,000 HTLV carriers in UK (predominantly BME)

Diagnose Carriers

Blood and Transplant

Sexual Health

Ante-natal Care

Prevention of transmission

Early detection/prevention of disease

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

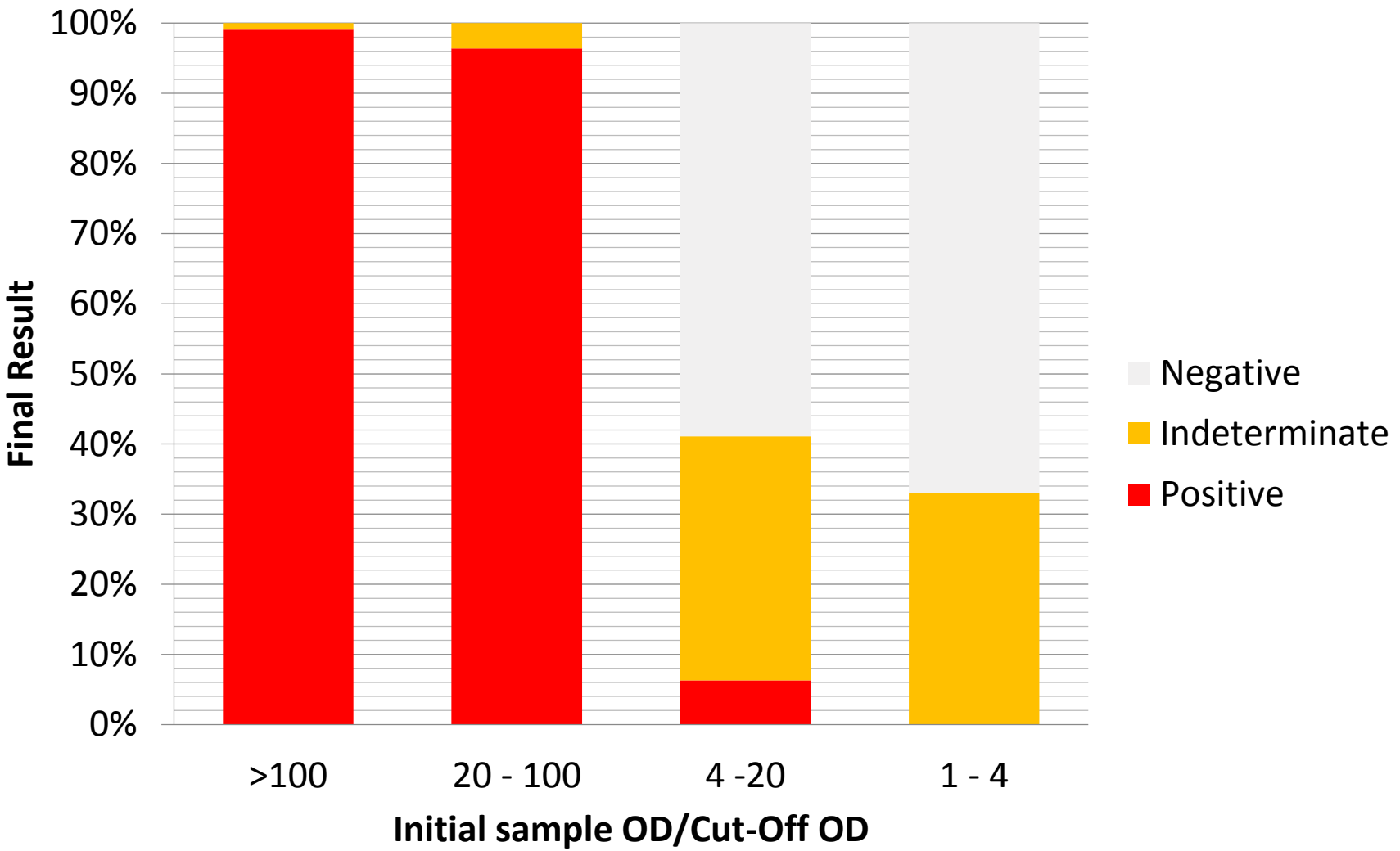
Detection of HTLV-1/2 infection
Sensitivity 100%

Specificity 99.7%

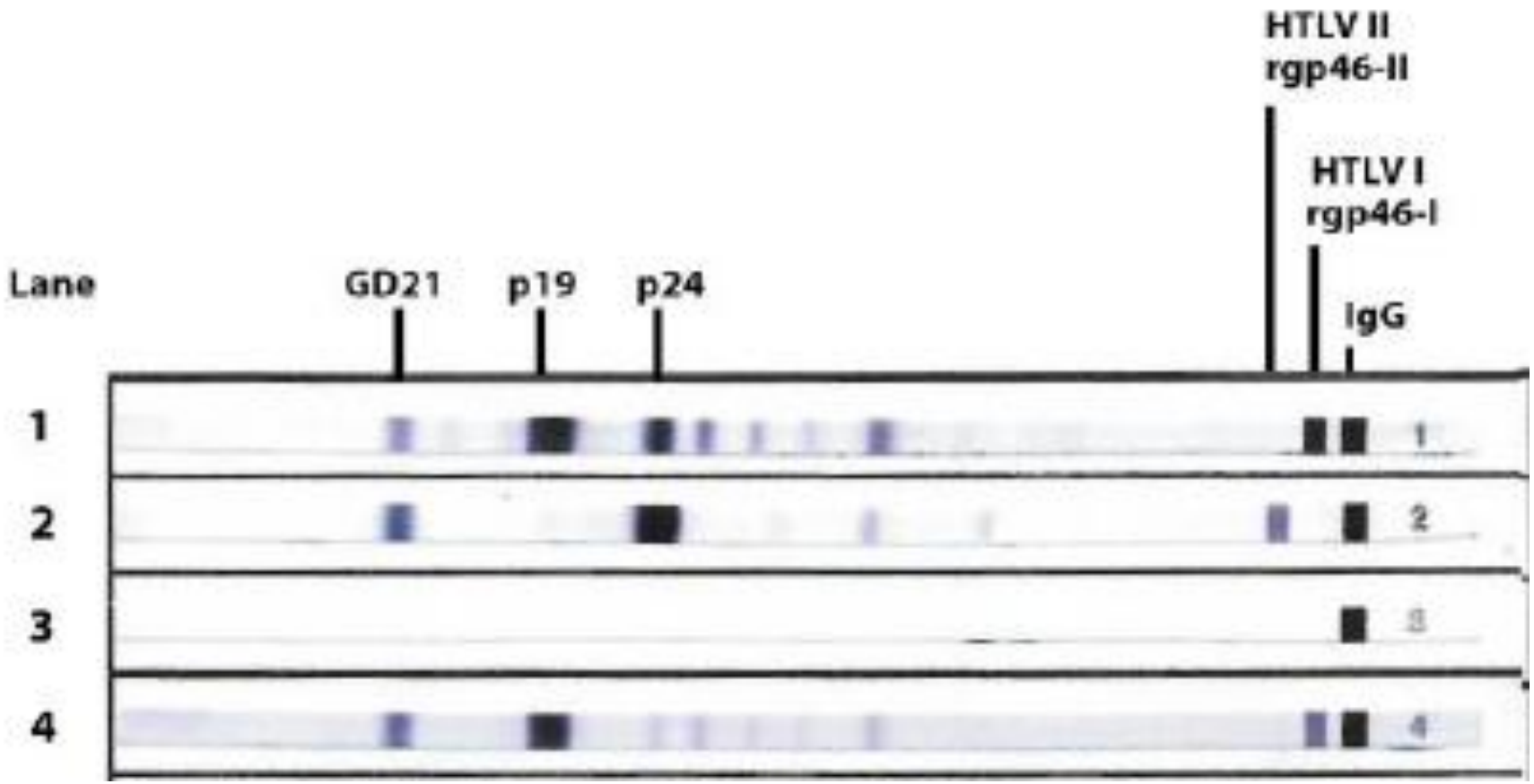
A sample with a signal equal to or greater than the assay cut-off is REACTIVE

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:

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

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

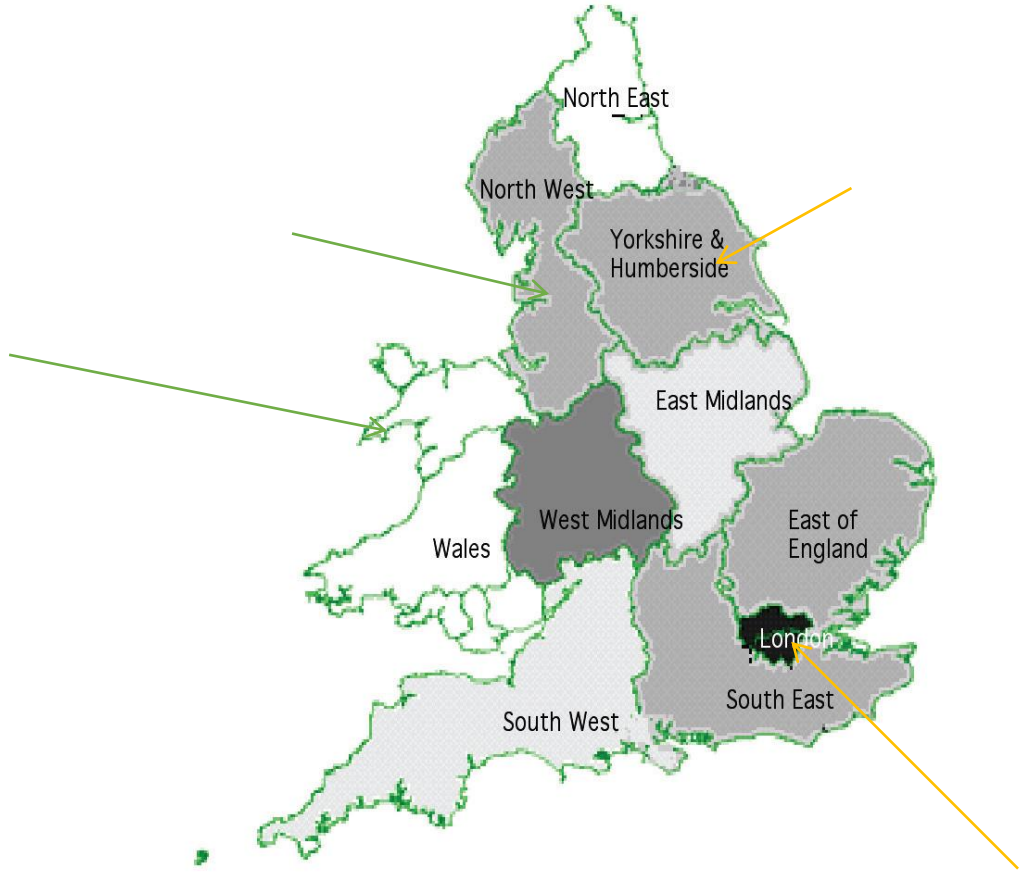
Diagnostics

Multidisciplinary

Public, patient participation

Research

Training



BASHH Guidelines on HTLVs – in preparation

THANK YOU