

## ISSUE SUMMARY: HTLV-1

### Overview

Recent media reports have highlighted the high prevalence of Human T-cell lymphotropic virus type 1 (HTLV-1) in some Aboriginal communities.<sup>1,2</sup> There is currently no vaccine for HTLV-1. With multiple strains of the virus in existence, HTLV-1c is the relevant sub-type in Australia,<sup>3</sup> targeting the CD4 positive T cells (similar to HIV-1 retrovirus). It is understood to be transmitted through sexual contact, blood-to-blood contact, prolonged breast feeding, and during pregnancy/labour.<sup>4,5</sup>

### Prevalence

HTLV-1 is not a notifiable infection in Western Australia. Between March 2006 and June 2014, the primary referral pathology laboratory for Western Australia, Pathwest, carried out 17,280 HTLV-1 tests. From this, 2.8%, or approximately 50 cases, returned positive results.<sup>4</sup> The data does not report Aboriginality. The PathWest data included public serology requests only, not those sent to private laboratories, or public laboratories in South Australia or the Northern Territory. Due to geographical proximity to test sites, laboratories in South Australia and the Northern Territory, conduct tests on samples from Western Australia.

Five, first-time, donors of blood in Western Australia tested positive for HTLV-1 according to Red Cross Blood Service (RCBS) data for the period 2007 to 2016.<sup>6</sup> Like PathWest, the RCBS data does not report Aboriginality.

In a study undertaken by the Northern Territory Government Pathology Service, which retrospectively applied the HTLV-1 serology test to blood received during 2008 and 2011, 368 positive tests were revealed. With the exception of one, all positive tests were on blood taken from Aboriginal patients, indicating that rates of HTLV-1 are higher in the Aboriginal population of Central Australia, than the non-Aboriginal population. The study involved only blood received at five Northern Territory hospitals, from the blood tests of patient's residing in the Ngaanyatjarra Shire of Western Australia. In comparison a 2014-15 study undertaken on blood HTLV-1 serology tests of patients of a single small remote Aboriginal community in the Northern Territory, 30 positive cases were revealed out of the 74 tests for HTLV-1.<sup>7</sup>

<sup>1</sup> Ancient virus lurking in remote Australia, affecting thousands of Aboriginal adults. *ABC News* [online]. 24 April 2018. Available: <http://www.abc.net.au/news/2018-04-24/ancient-virus-cousin-of-hiv-affecting-indigenous-australians/9688718>

<sup>2</sup> People are scared: the fight against a deadly virus no one has heard of. *Guardian Australia*. 24 April 2018. Available: <https://www.theguardian.com/australia-news/2018/apr/24/people-are-scared-the-fight-against-a-deadly-virus-no-one-has-heard-of>

<sup>3</sup> O Cassar. Human T-Cell Lymphotropic Virus Type 1 Subtype C molecular variants among Indigenous Australians: new insights into the molecular epidemiology of HTLV-1 in Australo-Melanesia. *PLoS: Neglected Tropical Diseases*. 2014. Available: <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0002418>

<sup>4</sup> C Bangham. HTLV-1 infections. *J Clin Path*. 2000; 53: 581-86. Available: <http://jcp.bmj.com/content/jclinpath/53/8/581.full.pdf>

<sup>5</sup> J Micallef et al. Public health aspects of HTLV-1: a literature review. Unpublished.

<sup>6</sup> C Seed et al (eds). *Transfusion-transmissible infections in Australia: 2017 surveillance report*. 2017. Sydney: UNSW and Australian Red Cross Blood Service. Available: <https://kirby.unsw.edu.au/report/transfusion-transmissible-infections-australia-surveillance-report-2017>

<sup>7</sup> L Einsiedel et al. The prevalence and clinical associations of HTLV-1 infection in a remote Indigenous community. *MJA*. 2015; 205(7): 305-309. <https://www.mja.com.au/journal/2016/205/7/prevalence-and-clinical-associations-htlv-1-infection-remote-indigenous?inline=true>

## Symptoms and associated diseases

There is strong evidence from cohort studies to suggest that HTLV-1 is a causal agent for adult T-cell leukaemia/lymphoma (ATL) and HTLV-1 associated myelopathy (HAM) which affects the central nervous system.<sup>3</sup> Research suggests that for people with HTLV-1 the lifetime risk of developing ATL is 3.0-5.0% and 0.25-3.0% for HAM.<sup>4</sup>

Studies suggest that HTLV-1 may also be associated with tuberculosis, uveitis (inflammatory eye disease), strongyloides stercoralis (roundworm) and bronchiectasis (lung disease).<sup>4</sup> A retrospective cohort study of bronchiectasis admissions to Alice Springs Hospital found that 55 out of 92 Aboriginal patients tested for HTLV-1 were seropositive.<sup>8</sup> A study of a remote Northern Territory community found that, of 30 HTLV-1 seropositive adults, nine had conditions possibly associated with HTLV-1- (namely, lung disease and strongyloides).<sup>8</sup> It has been posited that these comorbidities may be related to the role of HTLV-1 in the impairment/suppression of immunity.<sup>9</sup>

## Testing

To date, the Medicare Services Advisory Committee has not received an application for funding of the HTLV-1 blood test.<sup>10</sup> Two of the three private pathology laboratories in Western Australia refer HTLV-1 serology to PathWest. For Medicare-eligible patients, PathWest bill HTLV-1 serology to Medicare under item 69384 or similar (quantification of one antibody to microbial antigens not elsewhere described in the Schedule) at a cost of \$13.35. The vast majority of specimens do not require confirmatory testing and the turn-around time is 1-7 days; for specimens requiring confirmatory testing, turnaround time is 2-4 weeks.

Billing is complicated, but I can give you the basics:

- For Medicare-eligible community/GP patients, we bill HTLV serology to Medicare under item 69384 or similar (\$13.35 for 'Quantitation of 1 antibody to microbial antigens not elsewhere described in the Schedule');
- 2 of the 3 large private labs in WA refer HTLV serology to PathWest; the other refers interstate
- For specimens requiring confirmatory testing, turnaround time is 2-4 weeks
- For specimens not requiring confirmatory testing (the vast majority), turnaround time is 1-7 days, depending on where the specimen is received (e.g. metro vs regional); once the specimen gets to the testing lab (PathWest QE2), we have a result that day or the next working day

Since 1993, all donations of whole-blood and blood components in Australia are screened for HTLV-1. It has been proposed that only new donors will be tested in the future.<sup>11</sup>

<sup>8</sup> L Einsiedel et al. Bronchiectasis is associated with human T-lymphotropic virus 1 infection in an Indigenous Australian population. *Clinical Infectious Diseases*. 2012; 54: 43-50. Available: <https://academic.oup.com/cid/article/54/1/43/368532>

<sup>9</sup> S Honarbakhsh and G Taylor. High prevalence of bronchiectasis is linked to HTLV-1-associated inflammatory disease. *BMC Infectious Diseases*. 2015; 15: 258. Available: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4491414/pdf/12879\\_2015\\_Article\\_1002.pdf](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4491414/pdf/12879_2015_Article_1002.pdf)

<sup>10</sup> L Allam and J McCurry. World experts call for Australia to act on devastating HTLV-1 virus. *Guardian*. 28 April 2018. Available: <https://www.theguardian.com/australia-news/2018/apr/28/world-experts-call-for-australia-to-act-on-devastating-htlv-1-virus>

<sup>11</sup> C Styles et al. Reconsideration of blood donation testing strategy for human T-cell lymphotropic virus in Australia. *Vox Sanguinis*. 2017; 112(8): 723-732.



HTLV-1 testing is not included in Australian routine antenatal screening guidelines.<sup>12</sup> Grivas and colleagues' retrospective study of HTLV-1 serology requests made to the Northern Territory Government Pathology Service found 284 requests relating to Aboriginal women aged 15 to 35 years between 2008 and 2011.<sup>6</sup> No published Western Australian data about HTLV-1 antenatal testing rates are currently available.

In 2017, the United Kingdom National Screening Committee recommended against systematic population screening for HTLV in pregnancy.<sup>13</sup> The rationale for the decision included the fact that HTLV is not common in the UK, the low risk of vertical transmission, and potential harms associated with receiving a positive diagnosis, including anxiety and stigma.

However, antenatal screening is conducted in high prevalence settings including Japan, Martinique and Brazil.<sup>14</sup> At a HTLV-1 Round Table discussion hosted by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine it was suggested that "antenatal testing should/could be a regional guideline".<sup>15</sup>

The 2006 National HIV Testing Policy noted that that HTLV testing is "carried out as clinically indicated in people who have blood diacrasias, neurological signs, severe scabies or Strongyloides infection."<sup>16</sup> The Central Australian Rural Practitioners' Association *Standard Treatment Manual* recommends that HTLV-1 testing should form part of investigations for dementia and crusted scabies.<sup>17</sup>

Additionally, the Thoracic Society of Australia and New Zealand recommends that, when undertaking baseline investigations for chronic suppurative lung disease and bronchiectasis, HTLV-1 testing should be considered after discussion with a specialist.<sup>18</sup> However, an audit of adult bronchiectasis admissions in six Kimberley hospitals between 2011 and 2016 found that none of the patients in the sample were tested for HTLV-1.<sup>19</sup>

## Counselling

Guidelines developed by the United States Centres for Disease Control and Prevention recommend that patients who test positive for HTLV-1 should be advised to:

<sup>12</sup> Royal College of Pathologists of Australasia. *Antenatal screening*. 4 February 2015. Available: <https://www.rcpa.edu.au/Library/Practising-Pathology/RCPA-Manual/Items/Clinical-Problems/A/Antenatal-screening>

<sup>13</sup> UK National Screening Committee. *UK NSC recommendation on screening for Human T-cell lymphotropic virus (HTLV) in pregnancy*. December 2017. Available: [https://legacyscreening.phe.org.uk/policydb\\_download.php?doc=781](https://legacyscreening.phe.org.uk/policydb_download.php?doc=781)

<sup>14</sup> A. Carneiro-Proietti et al. Mother-to-child transmission of human T-cell lymphotropic viruses-1/2: what we know, and what are the gaps in understanding and preventing this route of infection. *Journal of Pediatric Infectious Diseases*. 2014; 3(1): SS24-29. Available:

[https://academic.oup.com/jpids/article/3/suppl\\_1/S24/905784#supplementary-data](https://academic.oup.com/jpids/article/3/suppl_1/S24/905784#supplementary-data)

<sup>15</sup> ASHM. HTLV-1 Round Table- Summary. 15 November 2016. Unpublished.

<sup>16</sup> National HIV Testing Policy 2006. Available: [http://www.ilo.org/wcmsp5/groups/public/---ed\\_protect/---protrav/--ilo\\_aids/documents/legaldocument/wcms\\_115835.pdf](http://www.ilo.org/wcmsp5/groups/public/---ed_protect/---protrav/--ilo_aids/documents/legaldocument/wcms_115835.pdf)

<sup>17</sup> Central Australian Aboriginal Congress et al. *Standard Treatment Manual*. 2017. Available:

<https://www.remotephcmanuals.com.au/home.html>

<sup>18</sup> Thoracic Society of Australia and New Zealand. *Clinical Guideline: Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand*. Available:

[https://www.thoracic.org.au/clinical-documents/command/download\\_file/id/17/filename/Clinical\\_guideline\\_-\\_CHRONIC\\_SUPPURATIVE\\_LUNG\\_DISEASE\\_AND\\_BRONCHIECTASIS\\_IN\\_CHILDREN\\_AND\\_ADULTS\\_IN\\_AUSTRALIA\\_AND\\_NEW\\_ZEALAND.pdf](https://www.thoracic.org.au/clinical-documents/command/download_file/id/17/filename/Clinical_guideline_-_CHRONIC_SUPPURATIVE_LUNG_DISEASE_AND_BRONCHIECTASIS_IN_CHILDREN_AND_ADULTS_IN_AUSTRALIA_AND_NEW_ZEALAND.pdf)

<sup>19</sup> J Barron et al. Bronchiectasis in the Kimberley region of Western Australia. *Australian Journal of Rural Health*. 2018. Available: <https://onlinelibrary.wiley.com/doi/abs/10.1111/ajr.12411>

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- Share the information with their physician
- Refrain from donating blood, semen and tissues
- Refrain from sharing needles or syringes with anyone
- Refrain from breast-feeding
- Consider the use of condoms during sex
- Arrange for their sexual partner to be tested
- Be aware of the risk of vertical transmission if attempting to conceive
- Be aware of the risk of acquiring other sexually transmissible infections.<sup>20</sup>

In Japan, where HTLV-1 prevalence has been high, obstetricians generally recommend that infants of HTLV-1 seropositive mothers are either formula-fed, given frozen-thawed breast milk (which is believed to destroy HTLV-1 infected cells) or breast-fed only for the first three-months of the life.<sup>21</sup>

The recommendation against breastfeeding is a source of contention in resource-poor regions, given the immuno-protective role of breastmilk and the potential difficulty of obtaining suitable alternatives.<sup>15</sup> It has been argued that HTLV-1 recommendations should be consistent with the 2010 UNAIDS guidelines which “advise at least 6 months of exclusive breastfeeding and advise to continue breastfeeding after this time if replacement feeding is not feasible, even when antiretroviral drugs are not available”.<sup>22</sup>

### Treatment

There is currently no cure for HTLV-1. Treatments are available for diseases which may be associated with HTLV-1, such as ATL and bronchiectasis. Currently, there is no established treatment for HAM, although some trials have produced promising results.<sup>23</sup>

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<sup>20</sup> Centres for Disease Control and Prevention. Recommendations for Counseling Persons Infected with Human T-Lymphotropic Virus, Types I and II. *MMWR*. 1993; 42(RR-9): 1-13. Available: <https://www.cdc.gov/mmwr/preview/mmwrhtml/00021234.htm>

<sup>21</sup> S Suzuki et al. Current status of the nutritional guidance of baby to human T-cell leukemia/lymphoma virus type 1 carriers by Japanese obstetricians. *International Journal of Clinical Pediatrics*. 2015; 4(1): 143-144. Available: [file:///C:/Users/dvujcich/Downloads/201-1028-1-PB%20\(1\).pdf](file:///C:/Users/dvujcich/Downloads/201-1028-1-PB%20(1).pdf)

<sup>22</sup> C van Tienen et al. Stopping breastfeeding to prevent vertical transmission of HTLV-1 in resource-poor settings: beneficial or harmful? *Arch Gynecol Obstet*, 2012; 286: 255-256. Available: [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3374111/pdf/404\\_2011\\_Article\\_2211.pdf](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3374111/pdf/404_2011_Article_2211.pdf)

<sup>23</sup> T Sato et al. Mogamulizumab (anti-CCR4) in HTLV-1-associated myelopathy. *New England Journal of Medicine*. 2018; 378: 529-38.