

## Screening transplant donors for HTLV-1 and -2

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### Introduction

Human T-cell leukemia virus-1 (HTLV-1) is the first pathogenic human retrovirus discovered in 1980.<sup>1</sup> HTLV-1 causes 2 devastating diseases: adult T-cell leukemia/lymphoma (ATL) and a neurological disorder, HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP or, more briefly, HAM). ATL becomes apparent in 2% to 5% of those infected with HTLV-1; another 1% to 2% will develop HAM.<sup>2</sup> There are usually 2 to 3 decades of latency after the infection before the onset of symptoms. A second HTLV (HTLV-2) isolated in 1982 has been causally linked to HAM, but not ATL.<sup>3</sup>

In other cases, HTLV-1 and HTLV-2 infection may remain asymptomatic for years while being transmitted from person-to-person through host cells in body fluids and breast milk, blood cell transfusions, and solid organ transplantation. There are no licensed vaccines to prevent HTLV-1 or HTLV-2 infections.

### Worldwide HTLV-1 distribution

Based on published data, at least 5 to 10 million people globally are infected with HTLV-1; this is certainly an underestimate because many highly populated regions such as China, India, and much of Africa and the Middle East have not been adequately assessed.<sup>4,5</sup> Known regions of high HTLV-1 endemicity include southern Japan, the Caribbean, South America, tropical and South Africa, Iran, Romania, and Melanesia.<sup>4,5</sup> Prevalence rates in the United States and Europe are relatively low and mainly because of immigrants from endemic areas.

Despite the apparent low prevalence, several cases of transplant-associated HTLV-1 myelopathy have been reported in recent years (Table 1). In the United States, these include 2 kidney transplant cases resulting in HAM.<sup>6,7</sup> HAM also was reported in a heart transplant case in France, and in 2 kidney and liver transplant cases in Spain.<sup>6</sup> In Germany, transplanted kidneys and a liver resulted in primary T-cell lymphoma in 3 patients.<sup>8</sup> In Japan, where significant clusters of HTLV-1 are present, 3 cases of HAM were reported following kidney transplants, along with 8 cases of ATL following kidney transplants, although donor status was not reported.<sup>2</sup> These posttransplant HAM cases occurred with rapid onset and rapid progression.<sup>9-11</sup> These findings call into question the current widespread view that systemic HTLV screening of donated organs is unnecessary: this view is based on the assumption that HTLV-1-associated diseases

will develop only in a small proportion of infected individuals and that progression to disease is slow compared with the average lifespan of humans and therefore poses no major threats to public health.

### Screening and transplantation

Thirty-five years after the discovery of HTLV-1, donor/recipient screening for the virus remains sporadic or nonexistent in most countries.<sup>12</sup> In 1993, a Centers for Disease Control and Prevention and a US Public Health Service Working Group recommended that those infected with HTLV-1 or HTLV-2 be counseled “not to donate blood, semen, body organs or other tissues.”<sup>13</sup> Nevertheless, on October 23, 2009, the US Organ Procurement and Transplant Network dropped its recommendation for universal HTLV-1/HTLV-2 screening in deceased organ donors because of the perception of low HTLV-1 prevalence in the United States, low positive predictive value of serologic screening tests, and a lack of serologic tests appropriate for use by organ procurement agencies.<sup>14</sup> Moreover, international transplant society guidelines provide no recommendations on HTLV-1 screening and use of donated organs.<sup>2</sup>

Yet the notion of safety in “low prevalence” regions may be questionable.<sup>15,16</sup> Pockets of high HTLV-1 prevalence have been found in some countries, including the United States and the European Union, and decades of refugee migration and immigration have altered the makeup of many urban and regional populations.<sup>4</sup> In particular, the ongoing migration from the Middle East and Africa is likely to significantly alter the prevalence of HTLV-1/HTLV-2 in many European Union countries.<sup>4</sup> Given these evolving foci of HTLV-1/HTLV-2 infections and the very poor prognosis of posttransplant HAM and ATL, there are calls for more widespread screening of live and deceased organ donors.

Tedla et al suggested that organ procurement organizations and transplant programs should determine local prevalence to guide screening efforts.<sup>17</sup> Ramanan et al recommended targeted screening of potential high-risk living (and deceased) donors for HTLV-1/HTLV-2 seropositivity to inform transplant candidates of the potential risk of infection and disease and to reduce or prevent the occurrence of HAM in solid organ transplant recipients.<sup>18</sup> Suggestions also have been put

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**Table 1. Recently reported transplant cases resulting in HAM or ATL from HTLV-1–infected organs**

Country	Transplanted organ	Disease	Cases	Reference
France	Heart	HAM	1	6
Germany	Kidney	ATL	2	8
Germany	Liver	ATL	1	8
Jamaica	Kidney	ATL	1	2
Japan	Kidney	ATL	8	2
Japan	Kidney	HAM	3	9-11
Spain	Kidney	HAM	2	6
Spain	Liver	HAM	1	6
United Kingdom	Kidney	ATL	1	2
United States	Kidney	HAM	2	6,7

forward for national or international registries of all HTLV-1–affected transplants.<sup>19</sup> Alerted to the dangers of rapid-onset HAM following HTLV-1–infected organ transplants in late 2014, the Japanese Ministry of Health, Labor and Welfare started working with the Japan Society for Transplantation and the Japanese Society for Clinical Renal Transplantation to begin HTLV-1 screening of all kidney donations (Y. Yamano, St. Marianna University, written communication, 12 December 2014). Similarly, the United Kingdom issued new transplantation guidance on HTLV-1/HTLV-2 screening of cadaveric solid organs in 2011.<sup>20</sup>

The Global Virus Network (GVN; [gvn.org](http://gvn.org)) joins with these investigators and others in calling for more systematic HTLV-1/HTLV-2 screening before solid organ transplantation.

## GVN

The GVN is an international coalition of leading medical virologists collaborating and cooperating on research into human viral diseases. Established in 2011, the GVN currently consists of 34 affiliated laboratories in 24 countries. It supports research; promotes training in medical virology for young scientists; serves as a technical resource for governments, businesses, and international organizations; facilitates international scientific cooperation; and advocates for funds for the field and evidence-based public policies.

In 2014, the GVN formed a task force of international experts on HTLV-1 and the diseases this virus causes. The mission of the HTLV-1 Task Force is to help speed the discovery of therapies to prevent virus transmission and progression from infection to disease and to educate the public about this virus, the serious diseases it causes, and how to prevent its spread. One critical recommendation emerging from recent expert discussions is to improve local and regional screening efforts to prevent virus transmission and to better understand the prevalence of HTLV-1 infection and the burden of HTLV-1–associated diseases in countries with potentially vulnerable populations.

In an editorial, Taylor noted that, “Whereas not screening donors...for human immunodeficiency virus infection would be considered unethical, the same is not the case of HTLV-1, another human retrovirus, where risk assessments are made based on the predicted prevalence of cases among donors, the probable risk of transmission, and the subsequent likelihood of disease.”<sup>19</sup> Yet, those risk assessments are based on inadequate national epidemiology, ignoring changing demographics in many countries, and a poor understanding of the natural history of transplant-acquired HTLV-1 and posttransplant disease progression. The screening costs for HTLV-1 are small in comparison with the cost of

posttransplant illness and death, lost productivity, and treatment expenditures associated with HAM and ATL following HTLV-1 infection.

## Conclusion

For these reasons, the GVN Task Force on HTLV-1 recommends and urges transplant societies to make wider use of available screening assays and to educate donors and recipients about HTLV-1/HTLV-2 infection, transmission, and disease prevention. Improved assays and institutional screening practices will help to reduce virus transmission and may provide better information about the incidence of and prognosis of HTLV-1–associated diseases after organ transplants. In addition, the US Centers for Disease Control and Prevention and other health prevention agencies should consider updating their policy recommendations on organ transplant screening.<sup>13</sup>

## Authorship

Contribution: E.M. drafted the article; R.C.G., L.W., and H.H. undertook critical revision of the article for important intellectual content and the final approval of the article.

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A complete list of the members of the Global Virus Network’s Task Force on HTLV-1 appears in “Appendix.”

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## Appendix

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