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Editorial

Epidemiological and clinical aspects of human T-cell leukemia virus infection types 1 and 2: an introduction

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Human T-cell leukemia virus (HTLV) is a retrovirus that only infects humans. It causes a lifelong infection. HTLV is an ancient retrovirus that has been present in human populations since tens of thousands of years.[1,2] There are several different types and subtypes of the virus, most of which originated separately from different simian T-cell leukemia virus (STLV) strains. These viral (sub)types entered the human population in distinct simian-to-human transmission events, mainly in Africa. HTLV spread from Africa to the rest of the world accompanying different migration waves in human history.[1–3] The most important types are HTLV-1 and HTLV-2.[1–4]

Nowadays, HTLV-1 infection is present on all continents, but its distribution is heterogeneous.[5] Countries that have reported a high prevalence of HTLV-1 in the general population (more than 1%) include Peru, Jamaica, Martinique, Guinea-Bissau, Togo, Gabon, Cameroon, Papua New Guinea, the Solomon Islands, Vanuatu, and Japan.[3,5,6] The HTLV-1 prevalence is very low (<0.1%) in the general population in Europe and in the United States.[3,5,6] Regardless of the country, the prevalence of HTLV-1 can reach high levels in certain population groups, such as people with specific ethnic backgrounds (e.g. Aboriginal Australians and Amerindians in the Andes region), immigrants from HTLV-1-endemic regions, and injection drug users and their contacts.[3,5–8] HTLV-1 seroprevalence appears to increase with age, especially in women.[3,5,8]

HTLV-2 is concentrated in isolated populations in central Africa and in the Amazon region in South America, and among injection drug users in Europe and the USA.[4] It has been estimated that word-wide, there are at least 5–10 million people living with HTLV-1.[5] The number of people living with HTLV-2 is not well known.

HTLV-1 is a virus that is very closely linked to its human host cells (predominantly CD4 lymphocytes). When a CD4 lymphocyte is infected, the HTLV-1 provirus is integrated in the host cell genome. The HTLV-1 provirus stimulates mitosis and the number of proviral copies increases through clonal expansion of CD4 lymphocytes rather than through viral replication.[3,9] Hence, the replication system of HTLV-1 is very different than that of HIV.[9]

One consequence of this special mechanism of viral persistence of HTLV-1 is that the mutation rate is exceptionally low.[2] Another consequence is that HTLV-1-infected people have normal or increased CD4 lymphocyte counts. A third consequence is that the amount of free HTLV-1 in human plasma (HTLV-1 viral load) is so low that it cannot be detected in normal, ex-vivo conditions. What can be measured is the HTLV-1 proviral load, i.e. the proportion of peripheral blood mononuclear cells that contain HTLV-1 provirus.[10] The HTLV-1 provirus load varies a lot between HTLV-1-infected people and tends to remain relatively constant over time in an infected individual. Subgroups of people with clinical complications of HTLV-1 have, on average, a higher proviral load than subgroups without such complications, but the clinical significance of the proviral load for monitoring the prognosis at the individual level remains unclear.[10]

A fourth consequence of the special HTLV-1 persistence strategy (more mitosis stimulation than viral replication) is that virus transmission from one person to another requires the transfer of infected cells. The main routes of HTLV-1 transmission are through breastfeeding, sexual intercourse, contaminated blood products containing cells, and organ transplantation.[3, 6] In HTLV-1-endemic regions, the proportion of children of infected mothers that acquire HTLV-1 ranges between 15% and 25%. With a shorter duration of breastfeeding, the proportion of transmission drops.[3, 6] The incidence of sexual transmission has been estimated in about 1 per 100 person years in HTLV-1-discordant couples.[11] The risk of infection after transfusion of contaminated blood has been estimated in 10%–45%, depending on storage time and type of transfusion.[12]

Both HTLV-1 and HTLV-2 infections can be diagnosed with serological and molecular techniques. The serological techniques used for screening are commercial enzyme immunoassays (most frequently used), particle agglutination tests, and chemiluminescence assays. Serological confirmation is based on line immunoassay or western blot. Molecular techniques (mostly in-house methods) are usually reserved for cases with inconclusive serological results or research settings.[13] In several countries, candidate blood donors are systematically screened for HTLV infection in order to prevent HTLV transmission via blood transfusion (Brazil, Colombia, Peru, Uruguay, USA, Canada, France,

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United Kingdom, Iran, Japan, and Australia among others) .[12] In Japan, HTLV screening is also offered to pregnant women so that HTLV transmission via breastfeeding can be avoided.[14]

HTLV-1 was first described in 1980, and various clinical complications of HTLV-1 infection have been described over the years and are still being reported nowadays. We have classified these HTLV-1-associated diseases into three groups: neoplastic, inflammatory, and infectious diseases.[3] The most important neoplastic complication is ATLL, a malignancy of CD4 cells with a bad prognosis.[15] The most important inflammatory complication is HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). People with HAM/TSP have a spastic gait and may lose the ability to walk.[16] Many HAM/TSP patients also have urinary problems, constipation, back pain, and other inflammatory manifestations such as uveitis, dry eye syndrome, or thyroiditis.[16, 17] Infections that tend to be more frequent in HTLV-1-infected compared to HTLV-1-negative subjects include strongyloidiasis, scabies, tuberculosis, mycoses of skin and nail, among others.[3, 18, 19]

We have estimated that over a lifetime, up to 10% of the HTLV-1-infected people develop one or another complication. It is unknown why the majority of the HTLV-1-infected people remain asymptomatic while others develop associated diseases.[3] There are no vaccines to prevent or drugs to cure HTLV-1 infection, but it is important to treat HTLV-1-associated diseases to prevent further complications and to improve the quality of life of people living with HTLV-1.

The clinical consequences of HTLV-2 infection are less well known. The literature on HTLV-2 is limited, but some studies have shown associations with spastic paraparesis and other neurological syndromes, pneumonia and bronchitis, inflammatory conditions such as arthritis, and perhaps with increased mortality.[4]

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