PRIMEVIEW

HAM/TSP

nature REVIEWS DISEASE PRIMERS

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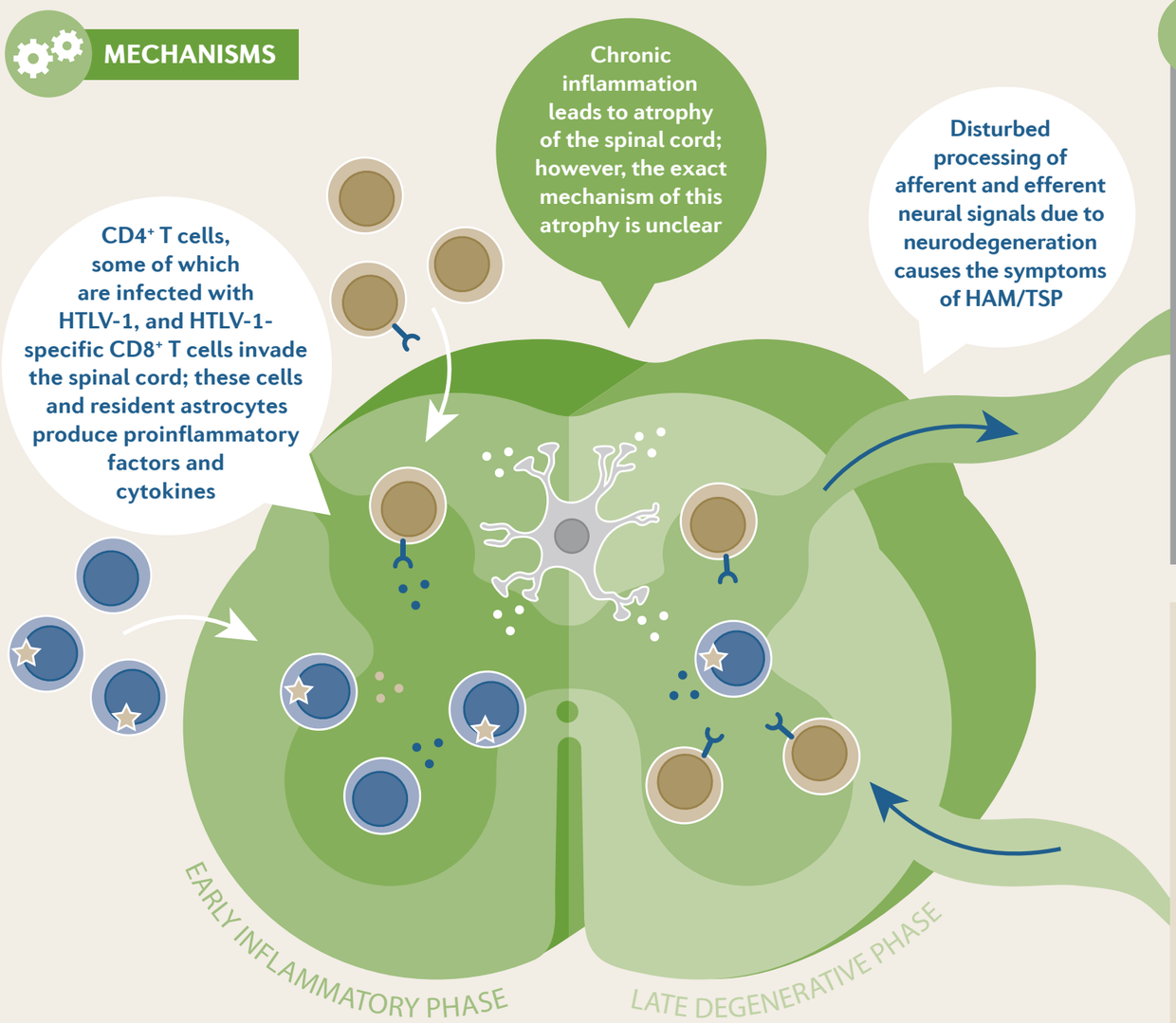
Tropical spastic paraparesis (TSP) was first described in the nineteenth century in the Caribbean. Its aetiology remained unclear until the 1980s, when infection with human T-lymphotropic virus 1 (HTLV-1) was identified as the cause. Since then, TSP is also known as HTLV-1-associated myelopathy (HAM). HAM/TSP affects the spinal cord and leads to paralysis of the legs, back pain and urinary symptoms.

EPIDEMIOLOGY

As HAM/TSP only occurs in HTLV-1-infected individuals, its prevalence is highest in areas where the virus is endemic. HTLV-1 infection is most common in Japan, South America, the Caribbean, parts of Africa and central Australia. In these countries, prevalence can exceed 50% in certain ethnic groups. For example, more than 1 million people are infected in Japan and a similar number in Brazil. HTLV-1 can be transmitted through sexual contact, breastfeeding, blood transfusions and organ transplantations. This requirement for close contact explains the regional differences in prevalence. However, data on HTLV-1 prevalence are limited for large parts of the world. Only 0.25–3.7% of infected individuals will develop HAM/TSP depending on ethnicity and the duration of infection.

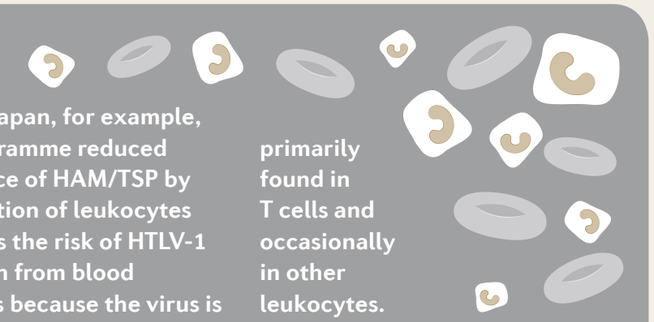
Risk factors for the development of HAM/TSP are genetic background, age, female sex, duration of infection and high HTLV-1 proviral loads in peripheral blood mononuclear cells

MECHANISMS



SCREENING & PREVENTION

Currently, there are no prophylactic measures that reduce the risk of developing HAM/TSP except avoiding infection with HTLV-1. Some countries have blood and tissue screening programmes for HTLV-1. In Japan, for example, such a programme reduced the incidence of HAM/TSP by 16%. Depletion of leukocytes also reduces the risk of HTLV-1 transmission from blood transfusions because the virus is primarily found in T cells and occasionally in other leukocytes.



MANAGEMENT

No curative treatment is available for HAM/TSP and, therefore, clinical care focuses on reduction of symptoms and on counselling. Several drugs, including corticosteroids, interferon and antiretrovirals, have been tried in relatively small, mostly open-label trials and some have shown benefits such as reduced symptoms and lower viral loads. Immunomodulatory drugs seem to be particularly useful in the initial, inflammatory phase of the disease; later, when neurodegeneration predominates, these drugs are less effective. In addition, symptomatic treatments are used to manage spasticity, motor dysfunction, pain, constipation and urinary complications.

OUTLOOK

HAM/TSP is a chronic, progressive disease with major consequences for the affected patients, including growing disability, shortened life expectancy and very limited therapeutic options. Improved biomarkers and neuroimaging are needed to facilitate better monitoring and diagnosis. Also, new drugs raise hope for more effective treatment of HAM/TSP. Currently, CCR4-specific monoclonal antibodies are in clinical trials; the chemokine receptor CCR4 is expressed on most HTLV-1-infected T cells. This treatment is an example of how a better understanding of the basic biology underlying HAM/TSP can advance the clinical management of the disease.

Currently, no treatment is available for the neurodegeneration that is characteristic of HAM/TSP; preclinical advances in 'neuroregenerative' approaches offer an exciting prospect

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