

Is the HIV-2 pandemic vanishing?

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The first AIDS patients were diagnosed in 1981 in California. Most were white men having sex with men. The causative agent could not be isolated until 1983. It was a retrovirus, human immunodeficiency virus (HIV)-1. By then, AIDS had already spread to almost every continent, and the patients were of all ethnicities. AIDS was also present in women and children. In most cases, there was a history of drug addiction, transfusions, sexually transmitted infections, etc. In 1985, the first HIV diagnostic tests were marketed, which were blood antibody tests.

By the mid-80s, there were many HIV-positive people in sub-Saharan Africa, and heterosexual transmission was by far the main route of transmission (De Cock et al., *Lancet* 2002). In pregnant women, contagion of babies was frequent, especially if breastfeeding had been prolonged. HIV transmission also occurs through transfusions and intramuscular injections with unsterilized needles after exposure to contaminated blood.

In 1986, African AIDS patients who did not have antibodies to HIV were described (Clavel et al., *N Engl J Med* 1987). Most were from former Portuguese and French colonies in West Africa, such as Guinea-Bissau, Ivory Coast, Gabon, and Cameroon. A French group identified the second AIDS virus in these patients. It was called HIV-2 (Clavel et al., *Nature* 1986). In the laboratory, it was a less virulent retrovirus than HIV-1. In the clinic, patients developed AIDS more slowly. In addition, HIV-2 is transmitted less than HIV-1 by sexual and vertical routes, that is, from mothers to their babies (De Mendoza et al., *AIDS* 2017).

HIV-2 in Spain

In Spain, the first cases of HIV-2 infection were described in 1988 on the Catalan coast, North of Barcelona (Soriano et al., *Eur J Clin Microbiol Infect Dis* 1989). There was a group of migrants from West Africa who worked in the collection of fruits and flowers. They came mainly from Gambia, Senegal, Ivory Coast, Cameroon, Gabon, and Equatorial Guinea. Many were asymptomatic, but some had the first manifestations of AIDS.

In 1989, the Spanish HIV-2 group was formed, which maintains a national register of cases to date (De Mendoza et al., *AIDS* 2017). A total of 425 HIV-2 infections have been reported in Spain. The average age at diagnosis is 42 years. Overall, 64% are men. More than 75% are African migrants, but about 15% are native Spaniards who have lived in West Africa and/or have had sex with people from those regions.

In recent years, there has been a decrease in the number of HIV-2 cases diagnosed in Spain. Since the COVID-19 pandemic, fewer than 10 cases have been reported annually. The Canary Islands, Almeria, Madrid, Catalonia, and the Balearic Islands are the places with the highest number of diagnoses. These are the areas with the highest rates of migration of Africans from endemic areas (De Mendoza et al., *Int J Infect Dis*, 2024).

HIV-2 decline in West Africa

The World Health Organization estimates that the number of people infected with HIV-2 worldwide ranges between 1 and 2 million. By comparison, those infected with

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HIV-1, the classic AIDS virus, are 40 million. While new HIV-1 infections are stabilizing at around 1.3 million/year, diagnoses of HIV-2 infection are in decline and estimated to be below a thousand new cases per year.

After the recognition of the epicenter of HIV-2 cases in West Africa at the end of the twentieth century, HIV-2 has been declining for decades. A Spanish collaborative study in the Ivory Coast has highlighted that, at present, < 5% of patients treated with antiretrovirals are HIV-2 carriers (Konan *et al.*, *AIDS Rev* 2024). This fact is paradoxical since HIV-2 originated precisely in the Tai forest in Ivory Coast, from the jump to humans (zoonoses) of the retrovirus from infected monkeys, which are the animal reservoir (Peeters *et al.*, *AIDS Res Hum Retroviruses* 1994).

Multiple factors have been postulated as the cause of the apparent control of the HIV-2 pandemic, such as the lower virulence and transmissibility of the virus, frequent screening of the population at risk, the extensive use of antiretroviral medication (which inhibits both HIV-1 and HIV-2), etc. (Gottlieb *et al.*, *Lancet HIV* 2018). Other prevention measures, such as fewer sexual partners or the use of condoms, do not seem to contribute

since sexually transmitted infections are on the rise (Soriano *et al.*, *AIDS Rev* 2023).

Future of the HIV-2 epidemic

Some epidemiological models have suggested that the HIV-2 pandemic could be extinguished before 2050 (Fryer *et al.*, *AIDS* 2015). In reality, even if the incidence of new cases continues to fall, it is very unlikely to reach zero. The asymptomatic period in HIV-2 infection can be several decades, and a proportion of carriers do not know they are infected. In this way, these people could continue to infect others, especially through sexual relationships.

There is no doubt that the evolution of the HIV-2 pandemic has reached a turning point. However, so far, only one infectious disease, smallpox, has been eradicated from the planet. The vaccine was the key tool. We do not have a vaccine for HIV-2, although we have good diagnostic tests and effective, suppressive antiretroviral medication (De Mendoza *et al.*, *AIDS Rev* 2020). HIV-2 infection must not become a neglected disease. Maintaining a high index of suspicion of HIV-2 infection is the best strategy to achieve its eradication.