Since the beginning of HIV pandemic 25 years ago, Kaposi’s sarcoma (KS) has been detected in AIDS patients, and it is considered an AIDS-defining illness. The first report on disseminated KS in younger homosexual men from the USA contrasted with the three forms of KS previously described in elderly persons from Mediterranean countries, in children and adults from the sub-Saharan countries, and in post-transplant patients receiving corticosteroid and immunossuppressive therapies. KS in AIDS patients assumed a more aggressive pattern, disseminating into the viscera and being associated with a greater likelihood of death.

KS in AIDS or ‘epidemic’ KS has been detected worldwide and is related to mode of HIV transmission: high frequencies of KS have been observed among homosexual men and low frequencies among haemophiliacs, suggesting that a sexually transmitted agent could account for the tumour. In 1994 a novel human herpesvirus provisionally called Kaposi’s sarcoma-associated herpesvirus (KSHV) and more recently named human herpesvirus 8 (HHV-8) was detected in KS lesions from AIDS patients. The same herpesvirus was subsequently detected in all forms of KS, classic, endemic, and iatrogenic.

Interestingly, after the introduction of HAART, a reduction in the number of KS/AIDS cases was observed in the Western world. In vitro and in vivo studies supported the benefit of antiretroviral therapy in controlling HHV-8 growth and disease development and progression. The tat protein of HIV was implicated in enhancing the entry of HHV-8 into endothelial cells, and in increasing HHV-8 viral load by reactivation of HHV-8 from a latent state. Antiretroviral therapy could therefore have a synergistic effect on KS/AIDS, allowing immune reconstitution and the clearance of HIV and consequently of HHV-8.

In 1994, antiretroviral treatment in AIDS patients was started in Brazil, first with transcriptase inhibitors, and from 1996 also with protease inhibitors. Since then, a decrease in the number of KS/AIDS cases has been detected by the Brazilian Ministry of Health. In São Paulo, Brazil, a seroepidemiological study conducted by our group in HIV/AIDS patients receiving antiretroviral therapy revealed 17% HHV-8-seropositive cases, and a 5-year follow-up showed that only 2% of these patients developed KS. This result contrasts with the 20% prevalence of KS in AIDS patients detected in the same region before the HAART era. Taking these data into account, we advocated the use of antiretroviral therapy in developing countries where KS is endemic, such as in sub-Saharan Africa, in order to fight both HIV and HHV-8 infections and diseases.

Using DNA sequencing of HHV-8 ORF K1 we were able to detect the three most common HHV-8 subtypes described around the world (A, B and C) in HIV/AIDS patients from São Paulo, south-east Brazil, and subtype B in a similar population from Salvador (north-east Brazil). These data may reflect the ethnic background of the individuals who live in these regions; São Paulo received European and Asiatic immigrants during its colonisation and has a mixed race/colour population, while Salvador was colonised by black individuals from Africa during the African slave trade, so black/mullatto is the predominant population.

Furthermore, among Indians from the Amazon region (northern Brazil) we detected HHV-8 subtype E, which is phylogenetically related to subtype D (Australasia) and subtype Hok (North of Japan), along with HHV-8 subtype A. We
suggested virus transmission in populations living in poor
HIV/AIDS, especially in Africa where KS is endemic.
therefore help developing countries to fight and control
from endemic areas.3
horizontal transmission for infection in children and infants
regions; sexual virus transmission could account for KS
transmission differ between endemic and epidemic HHV-8
On the other hand, it seems evident that the routes of virus
cost.
it could be used in developing countries because of its low
We still do not know whether there is a correlation between
HHV-8 subtype and virus pathogenicity, but we are attempting
to correlate HHV-8 subtype and tumour aggressiveness.

On the other hand, it seems evident that the routes of virus
transmission differ between endemic and epidemic HHV-8
regions; sexual virus transmission could account for KS
infection in adults from endemic and epidemic areas, and
horizontal transmission for infection in children and infants
from endemic areas.3

Using nested PCR for detecting several DNA segments of HHV-
8, we confirmed HHV-8 shedding in blood, saliva, and urine
from HIV/AIDS patients with and without KS, and suggested
virus transmission/acquisition by these body fluids.24 In
addition, we recently found HHV-8 shedding in urine and
suggested virus transmission in populations living in poor
socioeconomic and sanitary conditions,25 as previously
demonstrated in a study conducted among Ugandan families
with limited access to water and consequently poor hygiene.26
Several sanitary practices that prevent contact with saliva and
urine could therefore be employed in developing countries to
avoid virus transmission/acquisition.

Brazil and Africa share several sociodemographic
characteristics and sanitary conditions: South America and
Africa are both large continents, their populations are
educationally and socioeconomically diverse, rural and urban
areas in both have very different populations and sanitary
differences, and both experience a large number of tropical
and infectious diseases. In spite of this, Brazil has earned
international acclaim in the fight against AIDS by a series of
programmes including prevention and free access to
antiretroviral treatment for all patients.22,23 The lessons learned
in Brazil, our experiences and the data we have gathered could
therefore help developing countries to fight and control
HIV/AIDS, especially in Africa where KS is endemic.

REFERENCES
1. Friedman-Klein AE. Disseminated Kaposi’s sarcoma syndrome in young
2. Goedert JJ. The epidemiology of acquired immune deficiency syndrome
3. Hengen LR, Ruzicka T, Tyring SK, et al. Update on Kaposi’s sarcoma and other
HHV-8 associated diseases Part 1: epidemiology, environmental predisposition,
4. Haverkos HW, Dritman DP. Prevalence of Kaposi’s sarcoma among patients with
5. Brail V, Peterman TA, Berkelman RL, Jaffe HW. Kaposi’s sarcoma among persons
6. Tappero JW, Cori A, Wolfe SE, Benjamin TG. Kaposi’s sarcoma. Epidemiology,
pathogenesis, histology, clinical spectrum, staging criteria and therapy. J Am
8. Jones AL, Hanson DL, Dworkin MS, Jaffe HW. Incidence and trends in Kaposi’s
sarcoma in the era of effective antiretroviral therapy. J Acquir Immune Defic
Syndr 2003; 24(4): 270-274.
therapy with protease inhibitors on HIV-related Kaposi’s sarcoma. AIDS 1998;
12: 145-149.
syndrome-related Kaposi’s sarcoma regression after highly active antiviral
11. Rezza G, Donorso M, Rainero D, et al. Incidence of Kaposi’s sarcoma and HHV-
8 seroprevalence among homosexual men with known dates of HIV
12. Aoki Y, Totsu G. HIV-1 Tat enhances Kaposi’s sarcoma-associated herpesvirus
Lancet 1997; 349: 774-775.
association between the presence of HHV-8 antibodies and the development of
Kaposi’s sarcoma in HIV-1-infected patients receiving antiretroviral therapy.
15. Caterino-de-Araujo A, Carbone PHL, Martinez FLB, et al. Lack in detecting an
association between the presence of human herpesvirus 8 antibodies and the
development of Kaposi’s sarcoma in HIV-1-infected patients receiving anti-
retroviral therapy. Paper presented at the XIII International AIDS Conference,
of human herpesvirus 8 (HHV-8) with age confirms HHV-8 endemicity in
17. Caterino-de-Araujo A, Calabrò ML, Santos-Fortuna E, Sultman J, Chiesa-
Bianchi L. Searching for human herpesvirus 8 antibodies in serum samples from
patients infected with human immunodeficiency virus type 1 and blood donors
18. Caterino-de-Araujo A, Deltolla SEL. Searching for antibodies to HHV-8 in
children born to HIV-1 infected mothers from São Paulo, Brazil. Relationship to
19. Caterino-de-Araujo A, Santos-Fortuna E, Carbone PHL, Calabrò SE, Moreira AA.
Human herpesvirus 8 (HHV-8) antibodies among women from São Paulo, Brazil.
Association with behavioral factors and Kaposi’s sarcoma. Braz J Infect Dis
of HHV-8 infection in the pediatric population of two university hospitals in Rio
patients from São Paulo, Brazil. Presentation of a new HHV-8 subtyping
method. Paper presented at the XV International Conference on AIDS, Barcelona,
22. Moreira AA. Pesquisa de sítios de restrição enzimática em segmento da ORF K1
do genoma de herpesvírus humano tipo 8 (HHV-8) em isolados cênicos de São
Paulo: relação com subtipos virais e implantação da técnica de RFLP (Restriction
Fragment Length Polymorphism Analysis) para determinar subtipos virais. São
Paulo, 2003. [Dissertação de Mestrado. Faculdade de Ciências Farmacêuticas da
23. Cunha AMG, Costa SCB, Costa FE, Caterino-de-Araujo A, Galvão Castro B.
Serological and molecular detection of HHV-8 in Brazilian populations. 2
24. Santos-Fortuna E. Herpesvirus humano tipo 8 (HHV-8): Estudo de segmentos
alvo do genoma viral em amostras de sangue, saliva e urina de pacientes
infectados pelo HIV/Aids, com e sem sarcoma de Kaposi. Doctoral Thesis,
25. Santos-Fortuna E, Caterino-de-Araujo A. Confirming shedding of human
herpesvirus 8 in urine from Brazilian infected patients. J Clin Microbiol 2003;
41(2): 1008.
26. Miltukayte SM, Biggar RJ, Pfeiffer RM, et al. Water, socioeconomic factors, and
human herpesvirus 8 infection in Ugandan children and their mothers. J
(suppl 4): S1-53.