THE HISTORICAL QUESTION OF ACQUIRED IMMUNODEFICIENCY SYNDROME IN THE 1960s IN THE CONGO RIVER BASIN AREA IN RELATION TO CRYPTOCOCCAL MENINGITIS

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Abstract. In Europe before the advent of the acquired immunodeficiency syndrome (AIDS), fatal cases of infection with Cryptococcus neoformans resembling acute meningitis were rarely described and never in young adults. However, rapidly fatal cryptococcal meningitis in young Africans has been known to exist in central Africa for at least 30 years, mainly in the lower area of the Congo River basin. Cases have been reported in this area since 1953, particularly in young patients during the 1950s. It is also known that central African AIDS patients frequently suffer from cryptococcosis, and there is a possibility that earlier clinical reports of encephalitis were actually fatal cases of AIDS in young Africans. It appears possible that the central part of the African continent is the area where human immunodeficiency virus originated.

Rapidly fatal acute cryptococcal meningitis of the young African has been known to exist in the Congo River basin area for more than 30 years. Molez and others reported in 1982 a lethal form of acute cryptococcosis in a young Congolese adult who died in the Military Hospital of Brazzaville in 1981. This infection, then considered to be extremely rare in young subjects, caught our attention. We discovered that there existed a well-documented bibliography on this pathology in the young adults of central Africa, 

CRYPTOCOCCOSIS INFECTION

Pathology and neurotropism. Cryptococcus neoformans is a ubiquitous yeast with a cosmopolitan distribution; independent of its classic associations (lymphoreticular disorder, neoplasm, and immunodeficiency in older subjects), it sometimes presents as an attack on the central nervous system that is sometimes rapidly fatal. Cases of cryptococcosis (systemic mycoccocosis) seen before the 1950s were rare in both Europe and in Africa, and only 11 cases of cryptococcosis were reported in sub-Saharan Africa between 1940 and 1950. Since 1953, infection with Cryptococcus has been detected in most central African The accumulation of 20 years (1947–1968) of histopathologic data in Francophone central Africa (Chad to the Congo) showed that 65 cases of cryptococcosis (always associated with encephalitis) were reported in these countries.

Cryptococcosis is associated with a disorder of the lymphoreticuloendothelial system in 30% of the cases, 

Increased cryptococcosis and acquired immunodeficiency syndrome (AIDS). An initial analysis of C. neoformans infections was done in 1956 with the report of 350 cases worldwide published between 1894 and 1955. The frequency of cryptococcosis showed a marked increase primarily after the development of immunosuppressive therapy in developed countries at the beginning of the 1960s. Hay and others reported 1.4 cases per year in the literature between 1963 and 1968, and 7.4 cases per year between 1973 and 1978. However, the frequency of cases of cryptococcosis worldwide is still low. In sub-Saharan Africa the use of these therapies is less widespread, and when one considers the life expectancy and the pyramid of ages (completely reversed in comparison with those in developed countries), cancers and immunosuppressive pathologies, etc. of older subjects are not a factor related to the increase in the number of cases of cryptococcosis infection.

Information on the pathology due to Cryptococcus (frequency and characteristics) was not accurately known until the number of cases due to infection with human immunodeficiency virus (HIV) resulted in increased monitoring of this infection. Cryptococcosis has now acquired importance and is now the second most common opportunistic infection of the central nervous system observed in the evolution of AIDS since the latter appeared in human viroepidemiology. The study of the first 1,000 cases of AIDS recorded in the United States showed that two-thirds of the cases of Cryptococcus infection appeared as the only clinical manifestation in HIV infection. Cryptococcosis meningitis has been observed in one-fourth of the cases of AIDS as the initial manifestation; in three cases, the meningeval syndrome was the principal clinical risk in two of them.
Central African specificities and AIDS. In Europe, the frequency of cases of cryptococcosis associated with AIDS is 3–8%, 17, 23, 25, 26 In Africa, the prevalence of cryptococcosis with HIV ranges from 8% to 36% in central Africa25, 26, 27 and from 4% to 6% in west Africa.28, 29 However, the technical means (culture and serology) used by laboratories to obtain these data must be taken into account: thus, for subjects examined in Africa, the prevalence is 8–13%.20–23 while it is 33–36% for central African subjects studied in Europe.34–36 We found that the prevalence of cryptococcal meningitis, particularly in Central Africa, increases as ones gets closer to the Congo River basin area.31–33, 37, 38

In addition, the isolation of *C. neoformans* in hut wood and in the digestive contents of cockroaches (mainly from houses of patients who died of AIDS associated with cryptocciosis) allowed Swinne and others to demonstrate that the humid tropical environment in Kinshasa, Zaire39 or in Bujumbura, Burundi40 is rich in this pathogenic agent.

CRYPTOCOCCOSIS IN THE CONGO RIVER BASIN AREA

1950–1960. Cryptococcus pathogen has been found in young subjects in the Congo River basin area for more than 30 years. Cases of cryptococcal meningitis were reported in 1953, 40 and in 1954 in a nine-year-old boy.41 In 1959, two fatal cases (with acute meningitis) were reported in an 18-year-old woman in Brazzaville42 and in an 11-year-old girl in Kinshasa.43 At the same time, two other clinical observations were reported at the other end of the Congo River basin area.41, 42

1960–1980. During the 1960s in Kinshasa, approximately one patient per year was found to have cryptococcal meningitis.3, 14 With the beginning of the expansion of AIDS, cryptococcal meningitis began to be investigated in Central Africa more often,43, 44 and the neurotropism associated with *Cryptococcus* was observed in this region.45–48

In Zaire, the recorded cases of cryptococcal meningitis were found in particularly young patients; from 1960 to 1978 (21 cases) the average age of the subjects was 17 years, and from 1978 to 1984 (44 cases), the average age was 33 years.45, 49 In another study of 15 fatal cases in Kinshasa (from 1980 to 1981),50 the average age was 33.7 years, with the youngest being a 10-year-old boy.

RETROSPECTIVE ANALYSIS OF HIV IN THE CONGO RIVER BASIN AREA

Historical presence of the virus. It would seem that the central equatorial region of Africa is perhaps where HIV originated,51–53 and what remains to be determined is the time at which HIV began to circulate. Two cases of AIDS were confirmed in two sailors having frequented harbors located on African coasts between 1955 and 1957; one was an English sailor who died in 1959,54, 55 and the other was a Norwegian sailor who died in 1975.56

In analyzing 818 plasma samples obtained since 1959 from central Africa (Zaire, Rwanda, Burundi, and southern Sudan), American epidemiologists57 reported that an African subject originating from central Africa had been in contact with the HIV-1 (or a related virus) 25 years earlier. After testing by Western blotting and indirect immunofluorescence, 21 of 672 sera were positive for HIV. One of these 21 sera, selected for its high positivity, reacted with the main proteins of the HIV-1 coded by the *ga* and *env* genes, as well as with the proteins coded by the *cabc* gene of the simian virus. This serum was also highly positive in an ELISA.

In addition, in a Zairian village located in the Congo rain forest, which has been the object of a serologic investigation of Lassa fever over a 10-year period (1976–1986),58 no increase in HIV seroprevalence was found (its rate remained stable at 0.8%). Thus, in rural rain forest areas, where the inhabitants are scattered, HIV can be circumscribed.

The Congolese hypothesis. The presence of cryptococcal meningitis is sufficient to be diagnostic for AIDS,23, 34, 32 and this idea has been advanced since 1985 by the World Health Organization.59 It is possible that acute encephalitic infections due to *C. neoformans* that were reported in the scientific literature from 1950 to 1960 concerning the Congo River basin area were linked to the appearance of the AIDS virus in humans. With regard to the period 1970–1980, investigators66, 67 have reported some highly suspected clinical cases of AIDS with no link to a cryptococcal infection. The cases detected in Zairian children in 197768 were probably cases of AIDS.

Only a few investigators in the former Belgian Congo and the former French Congo had insisted on the specificity of those cases of acute cryptococcosis with lethal meningitis in young Congolese individuals without any other associated pathology. Thus, there is an accumulation of facts that makes one believe that cases of AIDS might have existed in the Congo River basin area since the 1950s.

It is likely that the virus was present in this area in the past because it appeared in such an explosive way, given that the virus remained latent during the previous decades. This allows one to consider a certain continuity of all cases of cryptococcosis linked to the Congo River basin area and corresponds to a possible AIDS dynamic in this area. In view of the hypothesis on the historic origin of the HIV, one can speculate about the means of propagation of this pathogenic agent out of the forest of the Congo River basin area.

THE HAITIAN INCIDENCE

The Haitian question. One of the more historic and geographic repercussions of HIV concerns Haiti because the Dominican Republic, which borders Haiti and is located on the same island (Hispaniola), does not have the same prevalence of HIV.65 For a long time, the Haitian people were accused of having introduced HIV infection into the United States while Haiti was a place of sexual tourism until 1985.64, 66 However, given the history of Haiti during the last 20 years, one cannot help but notice the links between this Caribbean island and the African continent (Congo River basin area). There was a migration of a large number of people that took place between Haiti and central Africa between 1960 and 1965 and between 1970 and 1975. However, it is very difficult to evaluate this migratory pattern and the causes of death of the subjects because there are no available published data.

The Haitian exile. After Francois Duvalier (Papa Doc) took political power in 1957, there was an emigration of certain social classes of the Haitian population due to polit-
The viral diseases that exist in the great rain forest region of equatorial Africa are very numerous. Viruses (mainly the arboviruses) linked with a vector ensures their transmission only in tropical areas, but in the past 10 years a series of unknown virus (Marburg, Lassa, Ebola, etc.) have emerged from this area where they were previously undetected. It is probable that for the HIV to appear in such an explosive a manner, it must have been present in some specific but unknown and ignored habitat.

In Cryptococcus infections with encephalitis, some consciousness problems have been be noted such as drowsiness, disorientation, and equilibrium problems. In Brazzaville in a subject who died of cryptococcal meningitis, we observed acute pallico-chin reflexes that would evoke sleeping sickness. In the Congo River basin area, these encephalitic signs, which are associated with slimming, could have led to a confusion between AIDS pathology and the African trypanosomiasis, which has been present in central Africa for many decades.

Knowing well that it is very difficult to determine from all of our observations the real geographic origin of HIV, it appears that the lethal pathology caused by C. neoformans has been present in the Congo River basin area since the 1950s, especially if one reviews the published reports concerning this pathogenic agent during this period. There are few historical epidemiologic reports concerning the dynamics of the emergence of HIV;54,55,56 thus, any new explanation has a certain epidemiologic interest.

Concerning the implication of the Haitian migration in the emergence of the HIV from the Congo River basin area, complementary research would be necessary to confirm or deny the hypothesis given in this report. This historical research belongs to the demographers and anthropologists; they would have the means to have access and exploit the migratory data in the various countries concerned (if these data exist).

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