Epidemiological and molecular characteristics of HIV infection in Gabon, 1986–1994

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Objective: To describe trends in the prevalence of HIV-1 infection in different populations in Gabon, and the molecular characteristics of circulating HIV strains.

Methods: Data were collected on HIV prevalence through sentinel surveillance surveys in different populations in Libreville (the capital) and in Franceville. In Libreville, a total of 7082 individuals (hospitalized patients, tuberculosis patients, pregnant women, asymptomatic adults, prisoners) were recruited between 1986 and 1994. In Franceville, we tested 771 pregnant women and 886 healthy asymptomatic adults (1986–1988). Sera were screened for HIV antibodies by enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blot or line immunoassay (LIA). Reactive samples in ELISA were tested for the presence of antibodies to HIV-1 group O viruses by ELISA using V3 peptides from $HIV-1_{ANT-70}$ and $HIV-1_{MVP-5180}$ followed by confirmation by LIA and a specific Western blot. Seventeen HIV-1 strains were isolated (1988–1993) and a 900 base-pair fragment encoding the *env* region containing V3, V4, V5 and beginning of gp41 was sequenced and a phylogenetic tree was constructed.

Results: HIV prevalence was relatively low and remained stable (0.7–1.6% in pregnant women, 2.1–2.2% in the general population). The prevalence was also stable among prisoners (2.1–2.6%). Among hospitalized and tuberculosis patients prevalence was higher and increased (1.8–12.7% and 1.5–16.2%, respectively). Only three sera had antibodies to HIV-1 group O. The 17 HIV-1 strains represent six different genetic subtypes including type O.

Conclusion: Our data from 1986 to 1994 show a stable and low HIV prevalence in Gabon, and a high genetic diversity of HIV-1 strains. This, also observed in Cameroon, is in contrast to that found elsewhere in Africa. Differences in rate of spread of HIV infection are probably explained by interplay between numerous factors. The role of different HIV subtypes in the dynamics of the HIV epidemic should be examined further.

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Introduction

The course of the HIV/AIDS epidemic has shown wide variations between different regions in sub-Saharan Africa. In some Central African towns, such as Kinshasa (Zaïre), HIV prevalence among pregnant women has remained relatively low and stable since the mid-1980s, but in other large towns, such as Kampala (Uganda), Lusaka (Zambia) and Blantyre (Malawi), the epidemic has been explosive with HIV prevalence levels in pregnant women now well above 20% [1,2]. In all regions of sub-Saharan Africa the predominant mode of HIV transmission is through sexual intercourse between men and women. The reasons for the heterogeneity in the spread of HIV infection are poorly understood. Various factors can influence the efficiency of sexual transmission and can therefore play a role in the dynamics of HIV infection: patterns of risk behaviour, the incidence of other sexually transmitted diseases (STD), several demographic variables, and circumcision, which is considered a major factor [1–5]. The efficiency of HIV transmission can depend on biological factors: viral load, during early and large stages of the infection, may be raised severalfold [6].

The role of different HIV strains in the dynamics of the HIV epidemic remains the subject of controversy. There are strong suggestions that HIV-1 is more transmissible than HIV-2, which would explain why HIV-2 remains less prevalent than HIV-1 [7]. In terms of HIV-1 subtypes, recent data from Thailand suggest that HIV-1 subtype E may be more easily transmitted through heterosexual contact than HIV-1 subtype B [8].

There are two main groups of HIV-1, as determined by phylogenetic analysis of geographically divergent isolates: group M and group O. Group M, the major group, comprises at least nine different genetic subtypes (A to I) [9], all of which have been described in African patients. HIV-1 group O viruses are highly divergent HIV-1 viruses and have so far been found mainly in Cameroon or people from Cameroon living in France [10,11].

Our knowledge on the geographical distribution of the different HIV-1 genotypes in Africa is incomplete, but the few data that are available suggest that the relative prevalence of each genotype differs from region to region [12]. It has been suggested that these differences in the distribution of HIV-1 subtypes could explain, at least in part, the wide variations in the course of the HIV epidemic in sub-Saharan Africa.

Surveillance of HIV infection in different population groups was started in Gabon, Western Equatorial Africa, in 1986. It soon became clear that there is a large variety of HIV strains, including HIV-2 and group O strains, circulating in the population of Gabon [13–15]. Furthermore chimpanzees naturally infected by an HIV-1-like virus [16,17] were originally found in Gabon. These observations have led to speculation on the origins and evolution of HIV viruses in this part of the world.

In this study we describe trends in the prevalence of HIV-1 infection in different populations in Gabon since the start of sentinel surveillance in 1986, as well as the molecular characteristics of circulating HIV strains.

Materials and methods

Study population

Gabon is situated in Western Equatorial Africa and has a population of about 1.2 million inhabitants. During the last decade, the population of Gabon became mainly urban. In Libreville, the capital city, the population ranged from 200 000 inhabitants in 1980 to 450 000 inhabitants in 1994; 75% of the population lives in urban areas. A high number of immigrants (about 200 000) are living in the main towns of Gabon, mostly from neighbouring countries and West Africa.

Data were collected on HIV prevalence through planned random surveys in different populations in Libreville and Franceville, which is situated in a semi-rural area in the south-eastern part of the country. In Libreville, a random selection of patients admitted to the Infectious Diseases Department of the General Hospital was tested each year from 1988 to 1994 (n = 864); random samples of tuberculosis patients were screened between 1990 and 1994 (n = 477). Sentinel surveillance among pregnant women attending antenatal clinics around Libreville provided prevalence data for 1988, 1993 and 1994 (n = 2753). In addition, in each of the years 1986, 1988 and 1989 a population-based survey was carried out on HIV prevalence among adults (n = 1180).

The methods of these surveys are described in more detail elsewhere [13,18]. In each of these surveys between 350 and 400 adults in the age group 15–49 years were randomly selected from the general population by two-stage cluster sampling [13,18]. In 1986 and 1994 a survey among prisoners (n = 1808) was also carried out. In Franceville, data were collected on pregnant women in 1986 and 1987 (n = 771), and general population surveys were carried out in 1986 and 1988 (n = 886).

HIV serology

Sera were screened for the presence of HIV antibodies by either one of the following enzyme-linked immunosorbent assays (ELISA): Elavia mixt or Genelavia mixt (Diagnostics Pasteur, Marnes-La-Coquette, France); HIV ELISA (Dupont-de-Nemours, Wellington, Delaware, USA); Vironostica (Organon Teknika, Oss, The Netherlands); or Innotest HIV-1/HIV-2 (Innogenetics, Ghent, Belgium). Reactive samples were confirmed either by a commercial HIV Western blot (Dupont-de-Nemours or Diagnostics Pasteur) or by a line immunoassay (LIA) based on recombinant proteins and synthetic peptides of HIV-1 and HIV-2 (INNOLIA HIV-1+2, Innogenetics) [19].

Reactive samples from the epidemiological surveys were tested for the presence of antibodies to HIV-1 group O viruses, as well as indeterminate samples and samples that were positive on ELISA but negative on Western blot. In addition, the following samples were tested for antibodies to HIV-1 group O: 205 HIV-1 antibody-positive sera and 79 indeterminate sera (i.e. ELISA-positive but without antibodies to HIV envelope proteins by Western blot) collected between 1992 and 1994 at the bloodbank and the National Laboratory in Libreville; and 409 sera (272 HIV-1 confirmed, 226 HIV Western blot indeterminate and 62 HIV ELISA-positive and Western blot-negative) from the International Centre of Medical Research [Centre International de Recherches Médicales (CIRM)] in Franceville. A previous study has shown that in Africa, and more specifically in Central Africa, indeterminate HIV Western blots are relatively frequent. They were mainly a result of early ELISA tests and the low prevalence in the population studied. These are usually considered as non-specific reactions even if a seroconversion or a reaction with an HIV variant cannot be excluded [20]. Sera were screened by an improved ELISA using V3 peptides from HIV-1$_{ANT-70}$ and HIV-1$_{MVP-5180}$ followed by confirmation by LIA where different biotinylated V3 peptides from various HIV-1 strains (consensus peptide, Mn, Mal, Eli, ANT-70, MVP-5180 and SIVcpz-gab) were applied as a streptavidin complex in parallel lines on nylon strips. The V3 ELISA and LIA were research products kindly provided by Innogenetics. ELISA-reactive sera were also retested in the in-house HIV-1$_{ANT-70}$ Western blot. Western blot strips were prepared as previously described [21]. Sera were considered as having antibodies to HIV-1 group O if they showed a strong and specific reaction with the ANT-70 or MVP-5180 peptide on LIA, and if they have also antibodies to the gp120 of HIV-1$_{ANT-70}$ on Western blot.

Genetic analysis

A total of 17 virus strains were isolated between 1988 and 1993, as previously described [22]; 10 strains were from Libreville. Of these 10 strains, four were isolated from asymptomatic seropositive persons identified in the general population survey of 1988 (LBV2-3, LBV10-5, LBV21-7, LBV23-10); six were collected between 1989 and 1993 from AIDS patients admitted to the Infectious Diseases Department of the General Hospital (VI685 in 1992, VI1686 in 1992, VI1076 in 1993, VI525 in 1990, VI526 in 1990, VI354 in 1989). The seven remaining strains (G41, G98, G109, G134, G135, G139, G141) were isolated from AIDS patients living in Franceville and were collected between 1988 and 1989. All 17 persons were from Gabon, except for one man who was from Niger (strain G98). The results of the genotyping of strains LBV21-7 and VI525 have been previously published [14]. VI686 was previously classified in HIV-1 group O based on phylogenetic analysis of part of the *pol* gene [15].

Preparation of DNA template for polymerase chain reaction (PCR) was performed as described elsewhere [22]. A nested PCR was performed in 50 µl reaction mixture containing 50 mmol/l KCl; 10 mmol/l Tris-HCl (pH 8.3); 2.5 mmol/l MgCl$_2$; 0.01% gelatin; 0.2 mmol/l deoxyribonucleotides (dATP, dCTP, dGTP, dTTP); 0.4 µmol/l of each primer and 1.25 U *Taq* DNA polymerase (Perkin-Elmer Cetus, Zaventem, Belgium). Restriction sites were added to the 5′ end of the primers for cloning purposes. An aliquot corresponding to 1 µg DNA was subjected to a first PCR round of 35 cycles. Gabonese isolates were amplified as previously described [23] except for strains LBV10-5, G134, G139 and G141 which were amplified with the outer primers WOU26 and WOU29 (WOU26: 5′-GCATCTCCTATG GCAGGAAGAAG-3′; WOU29: 5′-TGTAAGTCATT GGTCTTAAAGGTACCTG-3′). Cycling conditions were 1 min at 94°C, 1 min at 50°C and 5 min at 72°C in a thermal DNA cycler (Perkin-Elmer Cetus). Two microlitres of the amplified DNA were subjected to a second round of 25 cycles using the inner primers JFES and WOU28 (JFES: 5′-cgctgaattcAGAGCAGAAGAC AGTGGCAATG-3′ WOU28: 5′-ccgtctagaTTTGAC CACCACTTGCCACCCAT-3′). Cycling conditions were 1 min at 94°C, 1 min at 55°C and 5 min at 72°C.

PCR fragments were digested with their respective restriction enzymes, electrophoresed on a 1% agarose gel, purified, ligated into a pUC18 or pBR322 cloning vector and introduced in *Escherichia coli*. One clone was sequenced for each isolate. Purified plasmid DNA (Qiagen plasmid kit; Westburg, Leiden, The Netherlands) was used as template and sequencing reactions were performed. Electrophoresis and data collection were done on a Pharmacia automated laser fluorescence sequencer. Sequences were always obtained for both DNA strands and additional sequencing was performed in case of unsolved ambiguities.

The 17 Gabonese HIV *env* sequences were aligned with 29 previously known sequences of HIV-1 isolates of diverse geographical origin and the SIVcpz-gab sequence on the basis of primary structure. The previously reported HIV-1 sequences are of the strains, LAI, MN, SF2, D687, U455, OYI, Z321, NDK, Z2Z6, ELI, D747, NOF, CA13, VI557, BZ126, BZ163, LBV21-7, V1525, C113, C122, CA4, CA5, CA10, CA16, CA20, CM239, CM235, MVP5180, VAU and ANT-70.

The nucleotide sequence data were deposited in the European Molecular Biology Laboratory, GenBank and DNA Data Bank of Japan Nucleotide Sequence Databases under the following accession numbers. (X90912 to X90924 and X96526).

Statistical analysis

Statistical comparison of the groups was done by χ^2 analysis with or without Yates' correction and by χ^2 test for linear trend. The calculations were performed using

Table 1. HIV seroprevalence rates by years in different population groups

Years	No. tested	No. HIV+ (no. HIV-2)	HIV+ (%)	χ^2	P
Libreville					
Infectious Diseases patients					
1988	125	2	1.6	19.05	0.00001
1990	99	3	3.0		
1991	74	4	5.4		
1992	190	8	4.7		
1993 .	156	13(1)	8.3		
1994 .	220	2(1)	12.7		
Tuberculosis patients					
1990	199	3	1.5	25.47	0.00001
1992	120	11	9.2		
1993	35	9(1)	25.7		
1994	123	20(1)	16.2		
Pregnant women					
1988	539	4	0.7	1.182	0.28 (NS)
1993	530	12	2.2		
1994	1684	28	1.7		
General population					
1986	383	8	2.1	0.23	0.88 (NS)
1988	397	9(1)	2.2		
1989	400	9(1)	1.7		
Prisoners					
1986	650	14	2.1	0.48 (NS)	
1994	1158	31(2)	2.7		
Franceville					
Pregnant women					
1986	473	4	0.8	0.08 (NS)*	
1987	298	4	1.3		
General population					
1986	384	1	0.3	1.35 (NS)*	
1988	502	4	0.8		

* With Yate's correction. NS, Not significant.

EpiInfo Programme (5.01 a; Centers for Disease Control Epidemiology Program Office, Atlanta, Georgia, USA).

Results

HIV prevalence in the different population groups
Table 1 shows the prevalence data for the groups in different years. In Libreville, the HIV prevalence among pregnant women ranged between 0.7 and 2.2% from 1988 to 1994, without evidence of a significant increase over this 6-year time period. Similarly, the HIV prevalence in the general population remained relatively low and stable between 1986 and 1989, ranging between 1.7 and 2.2%. The prevalence among 1158 prisoners tested in 1994 was nearly the same as the prevalence among 650 prisoners tested in 1986 (2.1 versus 2.7%). The prevalence data from Franceville also show low levels of infection in the general population. In 1986 and 1987 the HIV infection rates among pregnant women were 0.8 and 1.3%, respectively. The general population surveys gave levels of 0.3 and 0.8% in 1986 and 1988, respectively.

Among patients admitted to the Infectious Diseases Department and among tuberculosis patients higher HIV prevalences were found than in the general population, as expected. There was also a marked increase of the prevalence in these groups of patients between 1988 and 1994. Among the patients admitted to the Infectious Diseases Department the percentage of HIV-infected patients increased from 1.6% in 1988 to 12.7% in 1994 (χ^2 for trend, 19.05; $P = 10^{-5}$). Among the tuberculosis patients, the HIV seroprevalence increased from 1.5% in 1990 to 16.2% in 1994 (χ^2 for trend, 25.47; $P = 10^{-5}$).

Of the 226 sera which were HIV-positive, 218 (96.5%) were with HIV-1-positive and only eight (3.5%) were HIV-2-positive.

HIV-1 group O antibodies
A total of 1089 sera were tested for the presence of antibodies to group O viruses (Table 2). Of these, 185 HIV-positive sera were collected in epidemiological surveys. Only two of these sera were found to be positive for HIV-1 group O, one was from a patient admitted to the Infectious Disease Department in Libreville, in 1992, the other was from a pregnant woman attending an antenatal clinic in 1993. Both women were Gabonese. In Libreville, 205 HIV-1-positive and 79 indeterminate sera, collected between 1992 and 1994 from the blood bank and the national laboratory, were negative for group O antibodies. In Franceville, one out of the 272 HIV-1-positive sera from CIRM was positive for antibodies to group O, but none of the 226 indeterminate and 62 ELISA-positive but Western blot-negative sera had group O antibodies. The relative frequency of HIV-1 group O

Table 2. Number of sera with antibodies to HIV-1 group O among HIV-1-positive, HIV-indeterminant and HIV-negative sera in different population groups from Libreville and Franceville.

Population group	City	Years	No. tested	No. with antibody to HIV group O
HIV-1				
Infectious Diseases patients	L	1990–1994	55	1
Tuberculosis patients	L	1992–1994	36	–
Pregnant women	L	1988–1994	39	1
General population	L	1986–1989	9	–
Prisoners	L	1994	28	–
Blood donors from the Screening National Laboratory	L	1992–1994	201	–
Pregnant women/general population	F	1980–1988	8	–
CIRM Screening Clinical Laboratory	F	1988–1994	272	1
Total			648	3
Indeterminate				
Infectious Disease patients	L	1990–1994	1	–
Pregnant women	L	1988–1994	8	–
Prisoners	L	1994		–
Blood donors from the Screening National Laboratory	L	1992–1994	79	–
CIRM Screening Clinical Laboratory	F	1988–1994	226	–
Total			320	
ELISA-positive, WB/LIA-negative				
Infectious Disease patients	L	1990–1994	13	–
Pregnant women	L	1988–1994	30	–
Prisoners	L	1994	16	–
CIRM Screening Clinical Laboratory	F	1988–1994	62	–
Total			121	

CIRM, Centre International de Recherches Médicales; WB/LIA, Western blot/line immunoassay; L, Libreville; F, Franceville.

infection in HIV-1-positive sera was therefore 0.5% (two out of 390) in Libreville and 0.4% (one out of 272) in Franceville.

Genetic analysis

The sequence diversity of a 900 base-pair fragment encoding part of the *env* region containing V3, V4 and V5 and the beginning of gp41 was studied, and a phylogenetic tree was constructed based on 872 unambiguously aligned positions. The 17 Gabonese HIV-1 strains represent six different genetic subtypes. In the tree (Fig. 1) eight group M subtypes can be distinguished, containing sequences representative for subtypes A to H. Seven (VI685, G41, G135, LBV2-3, G139, VI1076, LBV23-10) of the 17 isolates belong to subtype A, supported by 100% of the bootstrap trees. Four Gabonese isolates (LBV21-7, G98, VI525, VI526) are from subtype G, supported by 999 out of 1000 bootstrap trees. One isolate (VI354) clustered with subtype F strains from Brazil and Cameroon in 772 out of 1000 bootstrap trees. Subtype C, supported by all bootstrap trees, consists of two statistically highly supported clusters; one cluster harbours two Gabonese isolates (LBV10-5, G134) and other cluster contains the South-African strain NOF and the strain D747. Subtype D, supported by all bootstraps contains two Gabonese isolates (G109, G141). Finally, one isolate VI686 belonged to group O.

Discussion

The prevalence data of the pregnant women and the results of the repeated population surveys indicate that between 1986 and 1994 the prevalence of HIV infection in the general population of Libreville remained relatively low and stable. However the time span for which data are available is too short to allow us to draw any firm conclusions as to the future course of the HIV epidemic in Gabon. At this stage it is impossible to say whether prevalence levels will remain low or whether the epidemic in Gabon is still in its earlier stages and the prevalence data represent datapoints on the low end of an exponential curve which will rise sharply in the next few years. However, the increase in HIV prevalence among patients admitted to the Infectious Diseases Department and among tuberculosis patients suggests that the HIV epidemic in Gabon is still in its early stages and may not yet have reached a plateau.

Although the results from the epidemiological studies suggest a relatively recent start of the epidemic in Libreville, the genetic characteristics of the circulating virus strains suggest that HIV viruses have been circulating in Gabon for a very long time. Our sample size of 17 HIV-positive isolates is rather small, yet we were able to document the presence of at least five different group M sub-
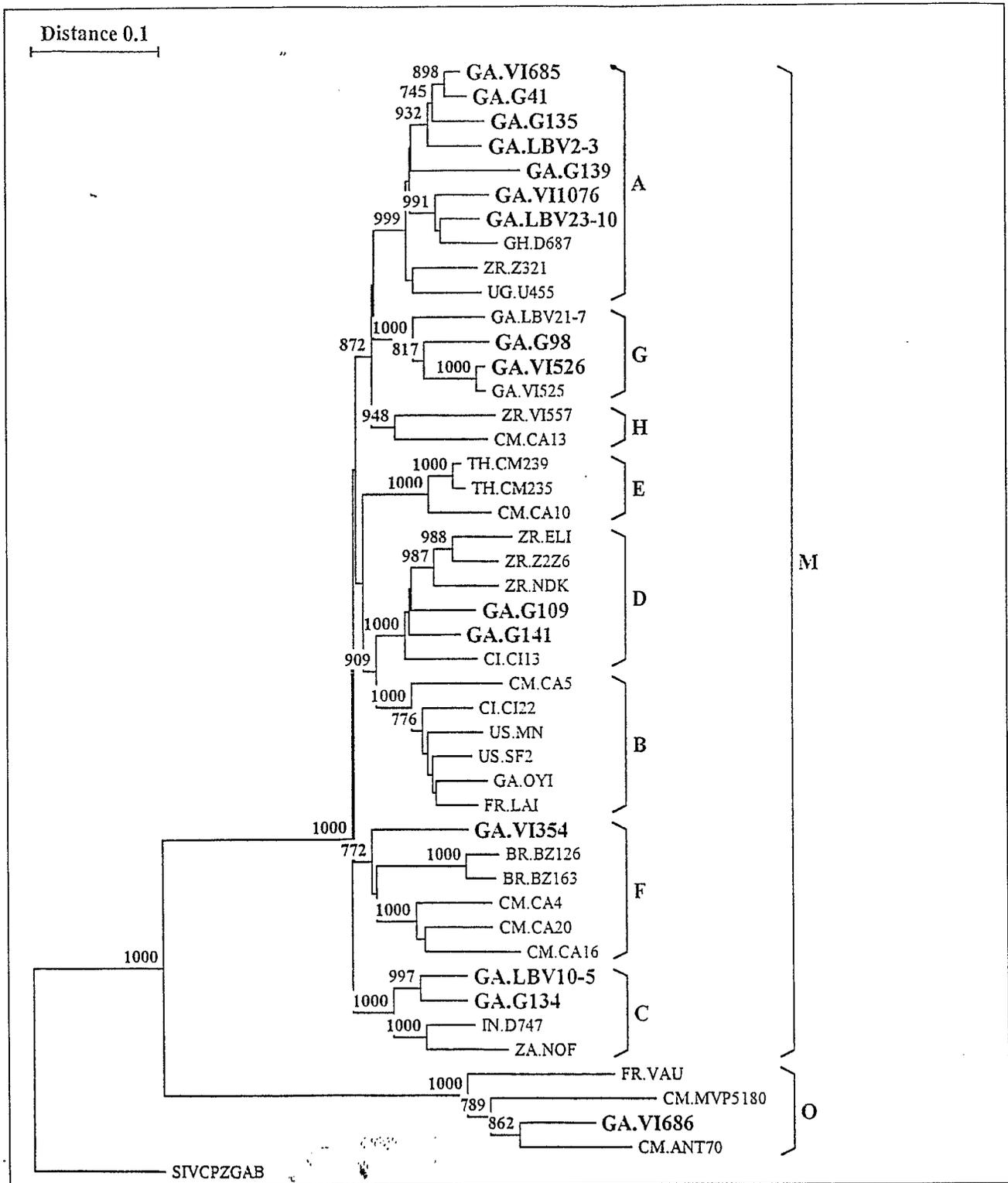
Distance 0.1

898	GA.VI685
745	GA.G41
932	GA.G135
	GA.LBV2-3
	GA.G139
991	GA.VI1076
999	GA.LBV23-10
	GH.D687
	ZR.Z321
	UG.U455

A

1000	GA.LBV21-7
872	GA.G98
817	1000 GA.VI526
	GA.VI525

G

948	ZR.VI557
	CM.CA13

H

1000	TH.CM239
1000	TH.CM235
	CM.CA10

E

988	ZR.ELI
987	ZR.Z2Z6
	ZR.NDK
1000	GA.G109
	GA.G141
	CI.CI13

D

1000	CM.CA5
776	CI.CI22
	US.MN
	US.SF2
	GA.OYI
	FR.LAI

B

1000	GA.VI354
772	1000 BR.BZ126
	BR.BZ163
1000	CM.CA4
	CM.CA20
	CM.CA16

F

909

997	GA.LBV10-5
1000	GA.G134
1000	IN.D747
	ZA.NOF

C

1000

1000	FR.VAU
789	CM.MVP5180
862	GA.VI686
	CM.ANT70

O

M

SIVCPZGAB

Fig. 1 Phylogenetic tree based on 872 unambiguously aligned positions of HIV-1 *env* gene sequences from 44 different subjects, for which the country code is indicated, and the simian immunodeficiency virus (SIV)cpz-gab. The sequences determined in this study are indicated in bold type. The distance between two sequences is obtained by summing the lengths of the connecting branches using the scale at the top. The number of bootstrap trees out of 1000 replications supporting a particular phylogenetic group in more than 75% is placed alongside the node considered.

types as well as one group O subtype. A similar large variety of HIV-1 subtypes has been found in Cameroon and the Central African Republic [24]. In Cameroon, subtypes A, B, E, F and H are circulating, as well as group O viruses [25]. In the Central African Republic, subtypes A, C, D, E, G and H have been found. The large variety

of circulating subtypes in Central Africa seems to be quite different from what has been found so far in other parts of the world, including other regions of Africa [23,26] where, on a similar number of samples, circulating strains belong only to a few different HIV-1 subtypes. This co-circulation of all known HIV-1 subtypes in Central Africa would be an argument in favour of the hypothesis that the HIV viruses somehow originate from this part of Africa.

An additional argument in favour of his hypothesis is the isolation of two different HIV-1-like viruses (SIVcpz-gab, SIVcpz-gab2) from naturally infected chimpanzees in Gabon. However, the prevalence of SIVcpz infection among chimpanzees is probably low, which argues against the chimpanzee being the natural host of HIV-1 viruses [27]. On the other hand, the close phylogenetic relationship between HIV-1 and SIVcpz would suggest that both humans and chimpanzees are infected by viruses from a third, as yet unidentified, primate species. There are two possible explanations for the large variety of subtypes found in humans. The first is that the different subtypes are the result of different, independent cross-species transmission events. However this presupposes a high prevalence of the different subtypes in the natural host and a high frequency of cross-species transmissions. Alternatively, the different subtypes are the result of differentiation within the human host. This in turn presupposes that the virus has been circulating for a very long time in the human population in Central Africa. In this report, retrospective serologic studies have shown that HIV existed in humans as early as the late 1950s [28]. It is also interesting to note that the first three patients with AIDS, described in France in 1978, (i.e. before the AIDS epidemic) came from Gabon and Congo [29].

So, if we can assume that the populations of Gabon have been exposed to HIV viruses for a very long time or that these viruses have been circulating among humans for a number of decades already, or both, how can it then be explained that the prevalence levels of HIV infection are still so low, compared to other regions in Africa where prevalence levels of well over 20% were reached in less than 10 years? Several researchers have reflected on the paradox that there is molecular evidence that HIV has been prevalent in human populations for a very long time — over one century according to some estimates — yet that it only became apparent over the last 15 years. May and Anderson [30] offer a possible explanation based on work with mathematical models: initial chains of infection in relatively isolated populations, such as rural villages, stutter to extinction, but throw off sparks that start another chain of infections in another village [30]. The number of sparks will increase steadily until a large-scale epidemic starts off with an exponential increase in prevalence levels. It seems, at least for the time being, that the HIV epidemic in Libreville consists of multiple 'sparks' or smaller epidemics that are the result

of outside contact. The reasons why these sparks have not yet resulted in a large-scale epidemic such as the ones in Abidjan and Kampala [31] are not clear. A survey among pregnant women in Libreville carried out in 1994 found high prevalence rates of other STD: 9% of the women had a chlamydial infection, 2% gonococcal infection, 18% were found with trichomoniasis and 3% were positive for syphilis [32]. These data indicate high levels of high-risk sexual behaviour. However, we do not have any data on sexual behaviour patterns, more specifically sexual mixing patterns and concurrent partnerships, which have been suggested as critical determinants of the rate of spread of HIV infection in populations [33]. These sexual patterns and concurrent partnerships, as well as circumcision status of the male partner, might be an important determinant in explaining the differences in the course of the HIV epidemic between different parts of Africa. In Gabon, circumcision is commonly practised on men, and this factor is believed to be a protective factor against the spread of HIV infection. Other factors related to the efficiency of virus transmission include sexual practises such as intercourse during menses or anal intercourse; the presence of another STD; condom use; and disease stage of the infected partner.

Other potential factors involved in the spread of the HIV infection could be related to demographic variables and genetic characteristics of the virus or the population, or both. In countries where the epidemic is spreading dramatically, a massive migration of rural inhabitants to urban centres has been frequently observed [34], but in Gabon, at least at present, rapid urbanization is not associated with rapid spread of HIV infection.

The genetic subtype of the virus can also be a factor in the difference of the HIV spread [10,11]. The extent to which different subtypes of HIV-1 would play a role in the dynamics of HIV-1 in Africa remains unknown, but it cannot be excluded that a different genetic HIV-1 subtype could have a different biological behaviour. In East Africa [29] and in Côte d'Ivoire [23], where the epidemic has been increasing rapidly, HIV-1 subtype A is highly predominant in contrast with Gabon or Cameroon where the HIV seroprevalence remains stable and low and where numerous genetic subtypes of HIV-1 are circulating. Is this indicating that subtype A strain is more virulent than the other strains and becomes dominant in the same way that HIV-1 dominates HIV-2 in some West African countries? Or is this indicating that the first infection occurred by subtype A and then in these countries social and behavioural factors made the epidemic explosive?

Finally, human leukocyte antigen characteristics and natural resistance to HIV of some populations is a potential factor which has to be considered but for which no data are currently available.

A better understanding of the reasons for the differences in spread of HIV infection is urgently needed for the design of more cost-effective interventions to control the spread of HIV infection, and would thus enable more accurate predictions of the future spread of HIV infection.

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