Lipoprotein[a] in the chimpanzee: relationship of apo[a] phenotype to elevated plasma Lp[a] levels

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Abstract Several studies have documented the presence of Lp[a] in nonhuman primates. However, data are lacking in great apes such as the chimpanzee. We have studied the quantitative distribution of Lp[a], as well as the frequency of apo[a] phenotypes, in a population of chimpanzees living in Gabon. Monoclonal antibody 14A12, directed against human apo[a], failed to recognize chimpanzee Lp[a]. Therefore, Lp[a] was assayed using an ELISA involving two polyclonal antibodies, an anti-human apo[a] and an anti-human apoB-100. Under these conditions, Lp[a] was detected in each of 28 animals. The plasma level of Lp[a] was found to be highly skewed toward elevated values: the mean Lp[a] level was 0.61 mg/ml (SD 0.45) as compared to 0.18 mg/ml (SD 0.16) in a normal Caucasian population ($P < 0.0001$). Phenotypes for apo[a] were identified by SDS-agarose-gel electrophoresis, followed by immunoblotting and detection by chemiluminescence. Seventeen different isoforms (ranging from 440 to 920 kDa) were found among all the animals as compared to 19 (540 to 960 kDa) in a human population of equivalent number. However, the distribution of apo[a] phenotypes was distinct between these populations. Thus isoforms of low molecular mass occurred with greater frequency in chimpanzee as compared to humans. In both populations, a strong inverse correlation between Lp[a] levels and apo[a] isoform sizes was found in chimpanzees ($r = -0.48$; $P < 0.01$) and in man ($r = -0.68$; $P < 0.0002$). Clearly then, chimpanzees differ not only from humans, but also from other nonhuman primates, such as the cynomolgus monkey and baboon, in both the distribution of their Lp[a] levels and the frequency of apo[a] isoforms.—**Doucet, C., T. Huby, J. Chapman, and J. Thillet.** Lipoprotein[a] in the chimpanzee: relationship of apo[a] phenotype to elevated plasma Lp[a] levels. *J. Lipid Res.* 1994. **35:** 263–270.

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Lipoprotein[a] (Lp[a]) is a serum lipoprotein particle, which was first described by Berg in 1963 (1). In human populations, high levels of Lp[a] represent a significant risk factor for the development of atherosclerotic disease (2). Lp[a] closely resembles low density lipoprotein (LDL) in its size and lipid composition, yet contains an additional glycoprotein called apo[a], which is attached to apoB-100 via a disulfide bridge. On the basis of the apo[a] cDNA sequence, the predicted protein structure is remarkably similar to that of plasminogen (3). Such a high degree of sequence homology implies that apo[a] may be involved in fibrinolytic mechanisms and suggests that apo[a] may constitute a link between atherosclerosis and thrombosis. In humans, apo[a] contains an inactive plasminogen-like protease domain, and two plasminogen-like kringle domains, kringles IV and V. The kringle IV domain is present in multiple tandem copies in the apo[a] sequence of both humans and rhesus monkey (3, 4). The kringle V domain, present in one copy in human apo[a], is however absent from the apo[a] cDNA sequence in the rhesus monkey (4). In humans, plasma Lp[a] levels vary considerably among individuals, and equally, the mean levels show marked variation among different ethnic groups (5, 6). These levels are highly heritable and inversely correlated with both apo[a] size and the number of kringle IV encoding domains present in the apo[a] gene (7).

Lp[a] levels are of great interest with respect to their role in the development of atherosclerotic disease. Equally, Lp[a] appears to be restricted to Old World primates and humans, with the exception of the hedgehog (8). Guo et al. (9) previously reported the presence of Lp[a] in the common marmoset, a New World monkey; in subsequent studies, we have not been able to reproduce these data. Hence, Old World monkeys are well suited as animal models for studies of Lp[a] and apo[a] phenotypes as risk factors in cardiovascular disease. Among the Old World monkey species, little attention has been focused on Lp[a] levels in populations, and data are limited to cynomolgus monkey and baboons, in which the distribution of Lp[a] levels and isoform sizes are similar to those in man (10, 11).

In the present study, we have examined variation in Lp[a] levels and apo[a] isoforms in a chimpanzee population. The chimpanzee was selected as the qualitative and quantitative aspects of the other major lipoproteins and

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apolipoproteins in this primate closely resemble those typical of normolipidemic human subjects (12, 13).

MATERIAL AND METHODS

Subjects and samples

All animals are housed at the Regional Centre for Training and Research in Human Reproduction in Gabon. The colony was maintained on a classic vegetarian diet with fruits and vegetables supplemented with 750 ml/day of Cerelac (Nestlé).

Sixteen female and 13 male chimpanzees ranging in age from 6 to 19 years (mean 13 yr ± 3) were investigated. Little information was available on the pedigree of these animals. Blood samples were taken on EDTA from fasted animals and plasmas were transported frozen by air to Paris. Previous examination of human plasmas demonstrated the absence of any effect of freezing the samples on Lp[a] assays over a three-month period (personal observation, C. Doucet and J. Thillet).

Controls were 27 healthy normolipidemic human subjects. In this case, after overnight fasting, blood samples were taken on EDTA and frozen before use.

Lipid and apolipoprotein analyses

Plasma total cholesterol and triglyceride concentrations were determined enzymatically with BioMerieux kits.

Plasma HDL cholesterol was estimated enzymatically by the same method as total cholesterol; apoB-100-containing lipoproteins were initially precipitated with phosphotungstate/$MgCl_2$. LDL cholesterol was calculated according to the formula of Friedewald [LDL cholesterol = total cholesterol − (HDL cholesterol + triglycerides/5)] (14).

The quantification of apolipoproteins A-I and B-100 in whole plasma was performed by electroimmunodiffusion using commercially available plates (Sebia, Issy les Moulineaux).

Purification of Lp[a]

Chimpanzee plasma pooled from all animals was used for the purification of Lp[a]. To prevent degradation of lipoproteins, PMSF (1 mM), BHT (4.4 μg/ml), gentamycin (0.005%), NaN_3 (0.01%), and EDTA (0.01%) were added to the plasmas. The solvent density of the plasma was adjusted with solid KBr to 1.050 g/ml and centrifuged at 100,000 *g* and 10°C for 24 h in a Ti70 rotor (Beckman). The floating lipoproteins were removed and the infranatant was adjusted with KBr to 1.100 g/ml and recentrifuged under the same conditions for 48 h. The 1.050–1.100 g/ml Lp[a]-enriched fraction was subjected to gel filtration chromatography on a Bio-Gel A-15m column (Bio-Rad) equilibrated with PBS at 4°C. The fractions from the first UV-absorbing peak, containing pure Lp[a], were pooled, concentrated against Aquacid II (Calbiochem), and dialyzed overnight against PBS (pH 7). The purity of the preparation was assessed by SDS-PAGE followed by Western blotting and by double rocket electroimmunodiffusion (15). These experiments showed that the Lp[a] preparation was less than 5% contaminated by LDL. The weight % chemical composition of chimpanzee Lp[a] (25.5% protein, 33.1% cholesteryl ester, 7.3% free cholesterol, 14.6% triglycerides, and 19.5% phospholipids) was similar to that previously described for human Lp[a] (16).

Quantitation of lipoprotein[a]

Lp[a] was quantified using two different ELISA assays; the first method involved use of two monoclonal antibodies developed in the laboratory (17). An anti-human apo[a] monoclonal antibody (MAB 14A12) was used as the "capture" antibody and a peroxidase-conjugated anti-human Lp[a] monoclonal antibody (MAB 3A3) as the detecting antibody.

The second assay was developed with two polyclonal antibodies, both prepared in sheep. An anti-human apo[a] antibody (17) was used as the "capture" antibody and a peroxidase-conjugated anti-human apoB-100 antibody as the detecting antibody. Both antibodies were purified by caprylic acid precipitation (18) and then concentrated by ammonium sulfate precipitation (40%). Polystyrene microtiter plates (96-well immunoplates, Costar, Cambridge, U.K.) were coated overnight at 4°C with 100 μl of a 10 μg/ml dilution of anti-apo[a] antibody in a phosphate-buffered saline, pH 7.4 (PBS). After washing to remove unbound antibodies (washing buffer: PBS containing 0.05% Tween), the wells were blocked by incubation with 3% BSA in PBS at room temperature for 1 h. After a further wash, 100 μl of appropriately diluted Lp[a] samples, in PBS containing 0.05% Tween and 1% BSA at pH 7.4, was added to the wells. The plates were incubated for 2 h at 37°C; they were then washed and a peroxidase-labeled anti-apoB-100 antibody (1:800 in PBS/Tween/BSA) was added. After an additional incubation for 90 min at 37°C, the plates were washed and the substrate, (1 mg/ml O-phenylenediamine dihydrochloride (OPD, Sigma) in 0.05 M citrate buffer at pH 5.5 containing 0.01% H_2O_2), was added. The reaction was allowed to proceed in the dark for 20 min and stopped with 3 N HCl. Absorbance was then read at 492 nm using a Titertek multiscan microplate reader. Each plate contained eight dilutions (0.4–40 ng total Lp[a]/well) of a reference standard (Immuno-France). Periodically, purified Lp[a] was compared to the reference standard for calibration purposes. For the present ELISA, the working concentration range was 4 ng–0.4 μg/ml Lp[a] lipoprotein mass. Intra- and inter-coefficients of variation for this ELISA assay were 1% and 2.6%, respectively.

Determination of apo[a] phenotype

Apo[a] isoform size was determined by agarose gel electrophoresis as described by Kamboh, Ferrell, and Kottke (19) with slight modifications.

Plasma samples were diluted (vol/vol) with reducing buffer (20 mM Tris-HCl, 1% SDS and 40 mM dithiothreitol at pH 8.8, containing 0.25% bromophenol blue). Fifty–300 ng Lp[a] mass, based on the ELISA measurements, was applied in order to visualize all apo[a] isoforms. The mixture was heated at 100°C for 3 min. Electrophoresis was performed on a 1.5% agarose submarine gel by using a USB submarine-gel unit. Agarose gels (12 × 14 cm) were cast using a solution of 75 ml of 1.5% agarose (Bio-Rad low M_r) dissolved in 100 mM Tris, 100 mM boric acid, 0.002 M EDTA, and 0.1% SDS. Electrophoresis was carried out in tank buffer (50 mM Tris, 50 mM boric acid, 0.001 M EDTA, 0.1% SDS) for 4 h at constant 50 mA at room temperature. A standard (Immuno-France) was run on each gel, containing four different isoforms corresponding to the F, S1, S2, and S3 isoforms in the nomenclature of Utermann et al. (20). As this electrophoretic system is able to detect at least 25 different isoforms instead of 6 as in Utermann's system (19), we decided to attribute an arbitrary molecular mass to the isoforms of the standard, which facilitated the identification of an unknown isoform (see Results).

After electrophoresis, proteins were transferred to a PVDF membrane (Millipore) by simple diffusion. After protein transfer, the membrane was incubated overnight in a solution of 5% powered skim milk dissolved in PBS to block the remaining protein-binding sites. The filter was then immersed for 1 h in a sheep polyclonal anti-apo[a] antibody. After extensive washing, the filter was incubated for 15 min with a second antibody, rabbit anti-sheep IgG, conjugated with alkaline phosphatase enzyme (Bio-Rad). AMPPD (Tropix), a chemiluminescent substrate of this enzyme, was used for revelation (21).

Statistical analyses

Results are expressed as mean ± SD. Statistical analyses were performed with the Statview TM II computer program (Abacus Inc.). Pairwise comparisons were performed by the Mann-Whitney test. Correlations were obtained by the Spierman test. The statistical level of significance was set at 5%.

RESULTS

Plasma levels of lipids and apolipoproteins

In order to determine whether our animals were normolipidemic, we examined lipid, lipoprotein-lipid, and apolipoprotein levels in our chimpanzee population, although such data have been previously published (12, 13). **Table 1** compares lipid and apolipoprotein levels in chimpanzee and human populations of equivalent number. The concentrations of total and LDL cholesterol were slightly but significantly lower in chimpanzees than in humans ($P < 0.05$ and $P < 0.01$, respectively), whereas previous studies have documented comparable levels in chimpanzee and humans. Such a discrepancy could have several explanations. In one study, the animals were non-fasted, which might have had an effect on their cholesterol levels (12); in another, the number of animals was small and could not be compared statistically (13).

On the other hand, triglyceride levels were slightly elevated in chimpanzees as compared to humans ($P < 0.05$). This observation could be related to the uncertainty with respect to the fasting state of the animals, as they were maintained in semi-freedom. Among the chimpanzee population, no significant difference was observed between males and females.

With the exception of the above differences in lipid levels, other parameters were normal and we considered the animals as normolipidemic, with the exception of two.

TABLE 1. Comparison of plasma concentrations of lipids and apolipoproteins in chimpanzee and human populations

	Human			Chimpanzee		
	Total[a] n = 27	Male n = 17	Female n = 10	Total n = 28	Male n = 13	Female n = 15
CT	1.84 ± 0.35	1.83 ± 0.36	1.86 ± 0.34	1.63 ± 0.28[b]	1.57 ± 0.25	1.68 ± 0.30
TG	0.72 ± 0.39	0.80 ± 0.41	0.58 ± 0.33	1.00 ± 0.57[b]	1.11 ± 0.74	0.91 ± 0.38
C-HDL	0.48 ± 0.11	0.44 ± 0.11	0.54 ± 0.08	0.50 ± 0.15	0.48 ± 0.13	0.52 ± 0.16
C-LDL	1.22 ± 0.30	1.23 ± 0.32	1.20 ± 0.28	0.93 ± 0.21[c]	0.90 ± 0.14	0.98 ± 0.22
apoA-I	1.43 ± 0.31	1.32 ± 0.28	1.60 ± 0.28	1.53 ± 0.26	1.42 ± 0.17	1.62 ± 0.29
apoB	0.83 ± 0.21	0.81 ± 0.22	0.88 ± 0.21	0.78 ± 0.18	0.77 ± 0.16	0.79 ± 0.20

CT, total cholesterol; C-HDL, HDL cholesterol; C-LDL, LDL cholesterol; TG, triglycerides; apoA-I and B, apolipoproteins A-I and B-100.
[a]All concentrations were expressed in mg/ml and are mean ± SD.
[b]Significantly different between human and chimpanzee populations ($P < 0.05$).
[c]Significantly different between human and chimpanzee populations ($P < 0.001$).

One animal displayed a very high triglyceride level (>10 mg/ml) and was consequently discarded from both statistical analyses and from the rest of the study. Another animal exhibited a low apoB-100 level (0.37 mg/ml); however, since other lipid parameters were normal, this animal was included in the study.

Lp[a] quantification

A quantitative sandwich ELISA built with two monoclonal antibodies had been previously set up in the laboratory to assay Lp[a] in human plasma samples (17). However, it has not been possible to assay chimpanzee plasmas with this ELISA. Further experiments by Western blot analysis revealed that one of the two monoclonal antibodies (14A12) failed to recognize apo[a] from chimpanzee. However, the immunological cross-reactivity between chimpanzee and human Lp[a] had been previously described (22). We have confirmed this result by Ouchterlony immunodiffusion (data not shown). Together, these data attest to the common presence of major antigenic determinants in human and chimpanzee Lp[a].

Thus, we constructed a quantitative sandwich ELISA by using two polyclonal antibodies (see Material and Methods). Under these conditions, standard human plasma and purified chimpanzee Lp[a] gave strictly superimposable standard curves (**Fig. 1**). A comparison had been previously established between a human serum standard and purified human Lp[a] that had given the same results (23). This ELISA was used to determine Lp[a] levels in plasma from the 28 available chimpanzees. As shown in **Fig. 2,** the distribution of monkey plasma Lp[a] levels (Fig. 2A) was completely different from that obtained in plasmas from an equivalent number of human

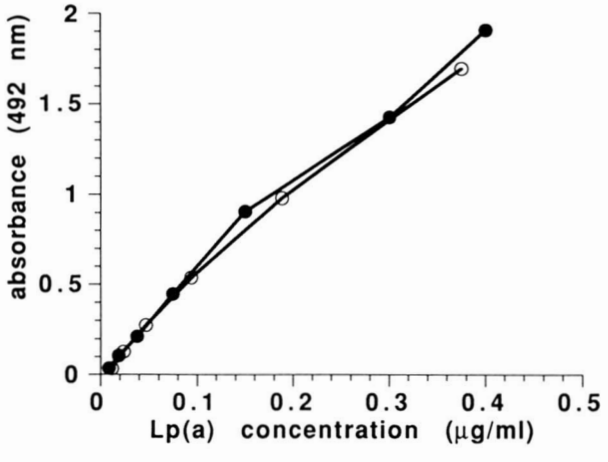

Fig. 1. Standardization of the Lp[a] assay. A sandwich ELISA using an anti-human apo[a] polyclonal antibody for coating and an anti-human apoB-100 polyclonal antibody (conjugated to horseradish peroxidase) for detection was used to compare the quantification of a human serum standard containing known amounts of Lp[a] (●) and known amounts of purified Lp[a] from chimpanzee (○). Lp[a] concentrations are given as Lp[a] lipoprotein mass.

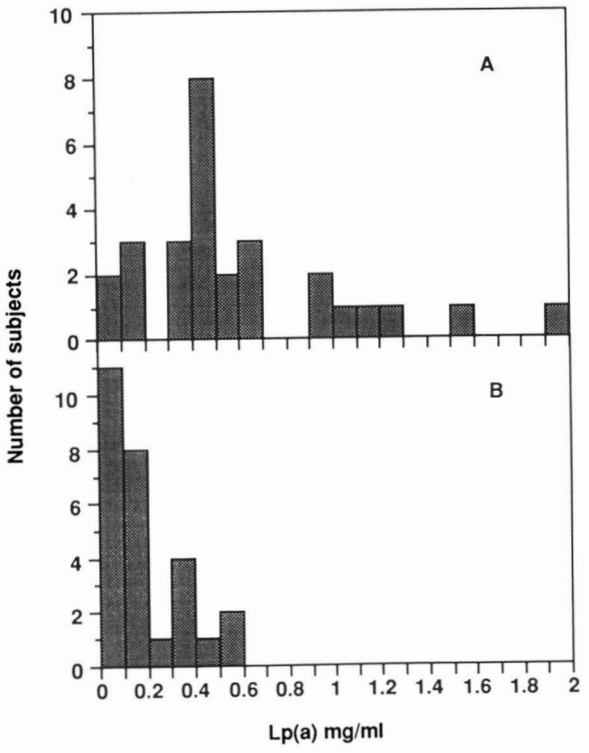

Fig. 2. Comparison of the distribution of Lp[a] levels in (A) the chimpanzee population and (B) a healthy, normal human control population. Lp[a] was quantified by our ELISA procedure (see Methods).

subjects (Fig. 2B). The range of monkey plasma Lp[a] levels was from 0.03 to 1.96 mg/ml as compared to the human range of 0.01–0.53 mg/ml. The mean level was 0.61 ± 0.45 mg/ml (median 0.47 mg/ml) for chimpanzee and 0.18 ± 0.16 mg/ml (median 0.13 mg/ml) for human. The difference was highly significant ($P \leq 0.0001$). The chimpanzee distribution was skewed towards high Lp[a] values in contrast to the human distribution which, as usual, was highly skewed towards the low values.

Comparison of apo[a] phenotypes in chimpanzee and man

To determine whether chimpanzee displayed an apo[a] size heterogeneity similar to humans, plasma samples of each individual chimpanzee were subjected to immunoblot analysis. In comparison with acrylamide gels, the agarose-gel system detects a larger number of apo[a] isoforms (19). Therefore, it was necessary to develop a nomenclature different from that of Utermann (20), which discriminates between only six different isoforms. We attributed an arbitrary molecular mass to the four isoforms present in our standard. As apoB-100 (550 kDa) migrated to a position exactly intermediate between that of the F and S1 isoforms, we used values of 500, 600, 700, and 800 kDa for F, S1, S2, and S3, respectively. The apparent molecular mass of the different isoforms was then

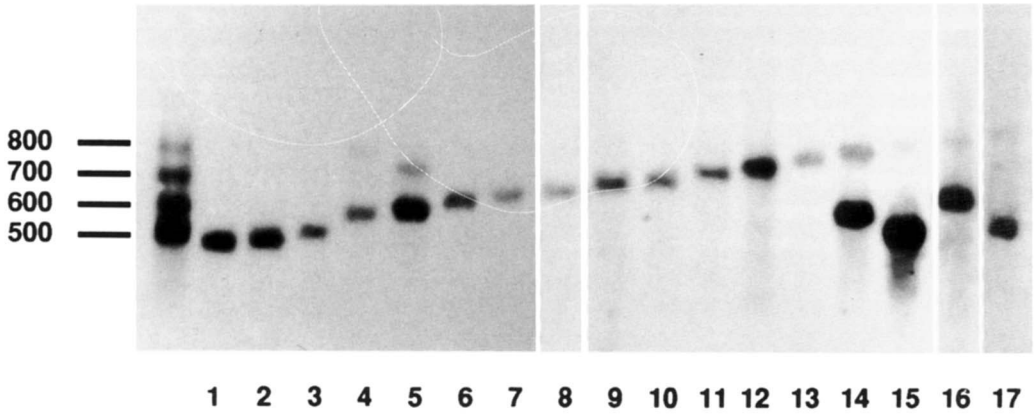

Fig. 3. Demonstration of different apo[a] phenotypes in individual chimpanzee plasma samples. Apo[a] phenotypes were resolved by electrophoresis in 1.5% SDS-agarose-gel followed by immunoblotting and revealed by chemiluminescence. An isoform standard was applied at left, containing the F, S1, S2, and S3 isoforms; their apparent molecular mass (in kDa) is indicated.

calculated according to their migration with respect to the standard.

Fig. 3 illustrates the different apo[a] isoforms detected in chimpanzees using SDS-agarose-gel electrophoresis and immunoblotting. Individual monkeys had apo[a] isoforms of apparent molecular mass varying between 440 and 920 kDa, and which presented as either single- or double-band phenotypes. Of the 28 monkey plasmas used for this analysis, 43% had two apo[a] isoforms. A total of 17 different isoforms was detected in the chimpanzee plasmas based on molecular mass differences. Under the same experimental conditions, 19 different isoforms were detected among a normal human population. These isoforms ranged from 540 to 960 kDa and the number of heterozygotes was equivalent to that found in the chimpanzee population (41%). The apparent molecular mass distribution of the apo[a] isoforms was different between both populations as illustrated in **Fig. 4.** The mean value of apo[a] isoform size was 665 ± 121 kDa (median 640) for chimpanzee as compared to 789 ± 114 (median 810) for human. This difference was also evident when the correlations between apo[a] isoforms and Lp[a] levels were compared (**Fig. 5**). For individuals displaying

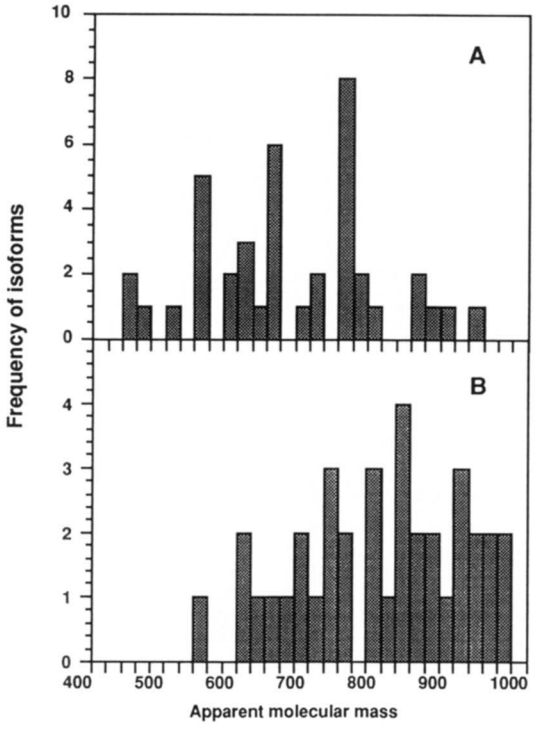

Fig. 4. Comparison of the distribution of apo[a] isoform size in (A) the chimpanzee population and (B) a normal human population. Apparent molecular mass was determined as described in the Results section. Both bands were included in the case of double-band phenotypes.

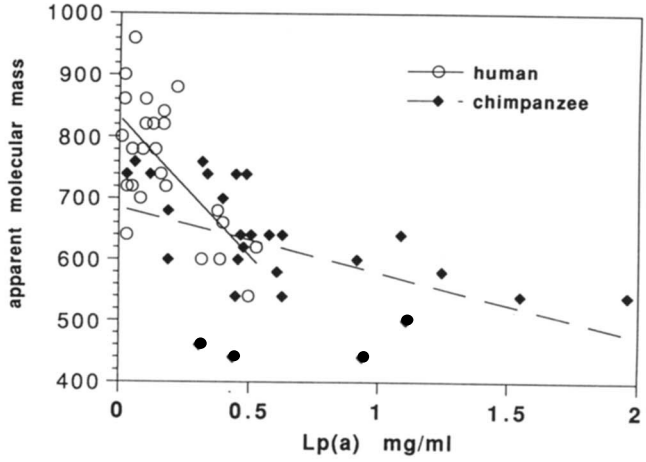

Fig. 5. Correlation between Lp[a] levels and apo[a] isoform size in both chimpanzee (—◆—) and human populations (—○—) ($r = -0.48$ for chimpanzees and $r = -0.68$ for humans). Only the smallest isoform was included in the case of double-band phenotypes (see Results).

double-band phenotypes, we have considered only the smallest band, because, in most cases, this isoform was present in greatest amount. In both populations, there was a negative correlation between Lp[a] levels and apo[a] phenotypes ($r = -0.68$; $P < 0.0002$, and $r = -0.48$; $P < 0.01$, for human and chimpanzee, respectively). Clearly, the overall distribution of Lp[a] levels and of apo[a] phenotypes was quite distinct between chimpanzees and humans.

DISCUSSION

In this study, we have demonstrated that the distribution of Lp[a] levels and apo[a] phenotypes in a chimpanzee population is distinct from that found in cynomolgus monkey (10) and baboon (11, 24) populations. In contrast to these monkey populations, we have shown that the distribution of plasma Lp[a] concentrations in normolipidemic chimpanzees is completely different from that of a human population (Fig. 2). The mean and median values are highly skewed towards high values. In the monkey population, 82% of individuals had levels greater than or equal to 0.3 mg/ml, which is the level estimated as the threshold for elevated cardiovascular risk in humans. Twenty-five percent of human subjects had levels above this concentration. If the large number of different isoforms found in this population is considered (Fig. 4), then our population of chimpanzees would thus appear to be representative, consisting mainly of unrelated individuals. Recently, the finding that Lp[a] levels are skewed towards low values in a Caucasian population could not be confirmed among other ethnic groups (5, 6). Clearly, in a similar manner, the chimpanzee distribution was distinct from that of other monkey populations (10, 11).

Previous studies have shown that a polyclonal anti-human apo[a] antibody was able to recognize Lp[a] in every Old World primate tested (25). We confirmed this finding with our ELISA assay involving use of such an antibody (Fig. 1). However, one monoclonal antibody raised against human apo[a] (14A12) failed to recognize chimpanzee apo[a] or Lp[a]. This antibody had been previously characterized and found to react with every human apo[a] isoform (17). These data strongly suggest that certain antigenic determinants of chimpanzee apo[a] are distinct from those of human apo[a]. Moreover, a second monoclonal antibody (73A7) to human apo[a], which is known to compete with MAB 14A12 (17), did not react with apo[a] from chimpanzee. However, the mapping of these antibodies to specific epitopes remains to be established. Consequently, the possibility that 14A12 antibody may represent an anti-kringle V antibody cannot be excluded. In this case, it would appear that the kringle V sequence may be absent from chimpanzee apo[a], as it is from rhesus apo[a] (4). It may be also noted that MAB 14A12 failed to recognize apo[a] from rhesus monkey (C. Doucet and J. Thillet, unpublished results). Further work is currently in progress to analyze this finding.

Using SDS-PAGE and immunoblotting, Utermann et al. (20) resolved 6 apo[a] isoforms, which they designated F, B, S1, S2, S3, and S4 on the basis of their electrophoretic mobility. By application of the same technique, Gaubatz et al. (26) detected 11 different apo[a] isoforms. However, using genomic blotting after pulse gel electrophoresis, Boerwinckle et al. (7) were able to distinguish 19 different genotypes. From the size difference between the smallest and the largest apo[a] isoforms and the size of one kringle IV repeat, one may calculate a total number of 20–30 possible isoforms. Such a number is beyond the resolution of the SDS-PAGE system, but corresponds to the resolution of an agarose-gel system (19). Consequently, we used this latter system (Fig. 3). Taken together, we detected a total number of 24 distinct isoforms in humans and chimpanzees, which was in the range of the theoretical calculation. Due to the large number of possible isoforms as compared to the number of individuals tested, it was difficult to statistically analyze the results. However, the distribution of apo[a] isoforms was clearly distinct between chimpanzee and human populations (Fig. 4). To our knowledge, this is a unique feature. Thus, when different human ethnic groups were compared, then the phenotype distribution did not differ, although Lp[a] levels varied considerably (5, 6).

Despite the increased sensitivity of our immunoblot procedure, the number of double-band phenotypes (43% and 41% for chimpanzees and humans, respectively) was still considerably less than would be expected from the observation of Lackner et al. (27), who found that 94% of individuals had two different alleles as analyzed by pulsed field gel electrophoresis of DNA fragments. Our finding was not unique and was similar to those reported in most immunoblotting studies (5, 6, 7, 20, 26). One possible explanation for this discrepancy could be that in double-band genotypes, one of the genes was either expressed in small amounts or, alternatively, was not expressed at the protein level in some individuals. Such a suggestion is in good agreement with the finding that in most subjects, the smallest isoform was expressed in greater amounts than that of largest size in humans (28). The same result was found in our chimpanzee population.

Our results also revealed a negative correlation between Lp[a] levels and apo[a] isoform size in the chimpanzee population (Fig. 5) and confirmed this correlation in the control human population. For this purpose, we put together homozygotes and heterozygotes, considering the smallest isoform in the latter case. This was done according to Sandholzer et al. (29) who analyzed the phenotypes of different human populations in the same manner. A strong correlation was found between Lp[a] levels and apo[a] phenotypes in both populations ($r = -0.68$ and

−0.48 for human and chimpanzee, respectively). Again, the chimpanzee population was displaced both towards high concentrations and small isoforms as compared to the human one, but followed the rule concerning the inverse relationship between apo[a] size and Lp[a] level previously described in human populations (28). However, it is notable that the slopes of the regression curves are different. This finding could indicate that Lp[a] levels in chimpanzee are less dependent on apo[a] isoform size than those of human. The fact that the distribution of apo[a] isoforms was shifted to lower sizes in the case of chimpanzee as compared to human, could however partly account for the higher Lp[a] levels in chimpanzee.

In summary, although the plasma lipid and apolipoprotein levels in chimpanzee closely resemble those in humans, this nonhuman primate presents quantitative and qualitative aspects of Lp[a] and apo[a] that are exceptional. This finding raises the question of the evolution of Lp[a] in various species, as the chimpanzee is the nonhuman primate most closely related to humans.

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