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Serum LP(a) Levels in African Aboriginal Pygmies and Bantus, Compared with Caucasian and Asian Population Samples

C. Cobbaert,[1,*] *P. Mulder,*[2] *J. Lindemans,*[1] *and H. Kesteloot*[3]

[1]Central Clinical Chemical Laboratory, Dijkzigt Hospital, 3015 GD Rotterdam, The Netherlands,
[2]Department of Epidemiology and Biostatistics, Erasmus University, 3015 GD Rotterdam, The Netherlands,
and [3]Department of Epidemiology and Biostatistics, University Hospital Leuven, 3000 Leuven, Belgium

ABSTRACT. Serum lipoprotein(a) (Lp(a)) and its correlates were studied in African Aboriginal Pygmies (n = 146) and Bantus (n = 208) from Cameroon. Geometric mean Lp(a) levels were 274 and 289 mg/l in Bantu males and females, respectively, and 220 and 299 mg/l in Pygmy males and females, the gender difference being significant in Pygmies (p = 0.024). In Pygmies 41% and 52% of the males and females, respectively, had Lp(a) levels above 300 mg/l, compared with 47% and 55% in Bantus. Overall, Lp(a) levels did not significantly differ between Pygmies and Bantus, and did not correlate with age, body mass index (BMI), systolic and diastolic blood pressure. Compared with healthy Asian and Caucasian population samples, age- and BMI-adjusted geometric Lp(a) means were 2.3- to 5.0-fold higher in Pygmy and Bantu males, and 2.9- to 3.6-fold higher in Pygmy and Bantu females ($p \leq 0.05$). Across the population samples studied ethnicity predicted 12% and 17% of serum Lp(a) variance in males and females, respectively. J CLIN EPIDEMIOL 50;9:1045–1053, 1997. © 1997 Elsevier Science Inc.

KEY WORDS. Lipoprotein(a), cholesterol, Pygmy, Bantu, Caucasian, Asian

INTRODUCTION

Lipoprotein(a) (Lp(a)) is a cholesterol-rich complex lipoprotein macromolecule, consisting of a low density lipoprotein (LDL)-like particle attached by a disulfide bond to a unique glycoprotein, i.e., apolipoprotein(a) (apo(a)) [1]. Apo(a) is unique because of its structural analogy with plasminogen [2], and its size and functional polymorphism [3,4]. Most studies reported that serum Lp(a) levels are mainly genetically determined—variation at the apo(a) locus contributing to this heritability—and are hardly influenced by lifestyle, diet, or drugs [1,5–9]. On the other hand, a few studies have shown that the serum Lp(a) level is correlated with other variables, such as age [10–12], sex [11], smoking [10], blood pressure [13], waist-to-hip ratio [10], impaired glucose tolerance [14–16], proteinuria [17], fibrinogen levels [13,18,19], and use of medication [20,21].

So far, and despite the fact that Lp(a) had an attraction upon researchers like a "femme fatale," its physiological function is, 34 years after its discovery, still not unraveled. From experimental observations it is hypothesized that the cholesterol-rich Lp(a) lipoprotein particle probably exports cholesterol out of the liver providing a continuous peripheral supply of such Lp(a)-cholesterol, which is independent from diet and other factors and which is reflected by the highly stable Lp(a) concentration over long-time periods [22]. The most likely targets of Lp(a)-cholesterol are endocrine organs with high steroid hormone production. More is known about its pathophysiogical role. First, numerous epidemiological and clinical studies, mainly in Caucasians, demonstrated that Lp(a) was an independent risk factor for coronary heart disease (CHD) [6,23], stroke [24], and preclinical atherosclerosis [25]. Second, Rath *et al.* [26] demonstrated Lp(a) depositions in the vessel wall of grafted arteries of coronary bypass patients, and found an association with serum Lp(a) levels. Third, it is postulated that elevated Lp(a) levels might interfere with fibrinolysis, due to its structural analogy with plasminogen [27,28]. Therefore, an elevated Lp(a) level is considered to be a risk factor for both atherogenesis and thrombogenesis, at least in Caucasians [1,6,23].

Lipoprotein(a) is an inherited CHD risk factor which, to our knowledge, has not been investigated in Aboriginal African Pygmies yet [1,6]. Besides, knowledge of the genetic susceptibility of traditional populations may be valuable in order to anticipate *future* cardiovascular risks, especially if these populations would move from traditional lifestyles to more sedentary lifestyles [29–31]. After all, considerable ex-

*Address for correspondence: Dr. C. Cobbaert, Central Clinical Chemical Laboratory, Dijkzigt Hospital, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

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cess of coronary heart disease mortality and greatly increased prevalence of type 2 diabetes mellitus have been reported among expatriate "Westernized" Asian communities [29,30] as well as in Aborigines from Western Australian in transition to urbanization and Westernization [31]. As only a few hunter-gatherer populations remain throughout the World, African Pygmies being one of them [32–34], and as urbanization may occur in the future, it was decided to investigate the genetic susceptibility, i.e., serum Lp(a) levels, and lifestyle factors of traditional African Aboriginal Pygmy samples from South-West Cameroon, compared with Bantu samples from the same region. Because of the lack of international Lp(a) standardization [35], and to enable relative comparability across populations, serum Lp(a) levels in Pygmies and Bantus were compared with those of Caucasian and Asian population samples.

The objectives of this cross-sectional study were, first, to provide descriptive data upon serum Lp(a) levels in population-based samples of apparently healthy African Aboriginal Pygmies and neighboring Bantus, and to describe its relationships to other cardiovascular risk factors. Second, to compare serum Lp(a) concentrations in African Pygmies and Bantus to those in randomized Belgian, Hungarian, and Philippine population samples, displaying varying serum cholesterol levels and prevalences of CHD. Finally, to compare serum Lp(a) and serum cholesterol levels in Pygmies and Bantus with those in healthy and diseased Caucasians with overt CHD, respectively.

MATERIALS AND METHODS

Study Populations

This study was part of a wider survey of health in Pygmy and Bantu populations in Cameroon, and was carried out in January through February 1994, and in May through June 1994 [33,34]. Non-fasting sera from Bantus and aboriginal Pygmies living in South-West Cameroon were obtained as described by Kesteloot *et al.* [33,34]. Pygmies examined live in the tropical forests 3° to 4° north of the Equator in small communities of 60 to 100 individuals, including children. Two distinct Pygmy populations were investigated: One in the Mecasse region in the Dja reservation, consisting of three distinct communities spreaded out over a 30-km distance. The second Pygmy population was living in the region of Lolodorf, at a distance of about 80 km. The participation rate was estimated to be about 100% in three of the four Pygmy communities, whereas it was only 50% in the fourth Pygmy community due to a conflict of authority of part of the community to the tribal chief. Besides, three communities of neighboring Bantus were examined: one living in close contact with the Pygmies in the Mecasse region, one living in the Lolodorf region, and a separate community living in the village of Bengbis. In the Bantu population participation was essentially on a first-come, first-served basis due to time and blood sample collecting material restraints. Many more Bantus volunteered to participate but could not be accommodated. Consequently, it was impossible to examine a random sample of the population.

The Pygmies studied are pure hunter-gatherers, whereas the Bantus are agriculturers cultivating corn, manioc, and plantain. Since Pygmies do not know their age, the latter was estimated with the help of a Bantu teacher, by referral to important past events. After specimen collection and clot separation with a hand centrifuge, sera were frozen within eight hours and stored for maximum one month at −20°C, i.e., during the expedition period in Cameroon. Thereafter sera were shipped to Belgium and the Netherlands, stored at −70°C, and analyzed for serum Lp(a) within 8 months after sample collection.

Serum Lp(a) levels in Pygmies and Bantus were compared with fasting serum Lp(a) levels in Caucasian and Asian population samples (Belgians, $n = 905$; Hungarians, $n = 400$, and Philippines, $n = 195$). All Caucasian and Asian specimens investigated were from unrelated, apparently healthy, and randomly selected subjects. Firstly, Belgian sera were obtained from age- and sex-matched 20- to 39-year-old employees from each Belgian province. Recruitment was done in the context of a cross-sectional study investigating the contribution of environmental and genetically determined cardiovascular risk factors to regional serum cholesterol and cardiovascular mortality differences in Belgium (manuscript in preparation). Hitherto, employees of different socioeconomic status were invited to participate in this study, prior to a scheduled medical check-up. Previous randomization and subsequent invitation, and medical check-up were conducted by the Flemish IDEWE and the Wallonian CeSI, two "Centres de Services Interenterprises-Médecine du Travail". Informed consent was obtained from all participants. Individual questionnaires were distributed during the medical check-up; volunteers were invited to fill in their identity, home address, nationality, and to indicate their smoking, drinking, dietary and lifestyle habits, education and profession, use of hormonal contraception, consumption of lipid lowering or other medication, and so forth. The filled-in questionnaire was checked by the physician who did the medical check-up, and completed if necessary. In addition, height and weight, as well as blood pressure were measured by the physician. As the Belgian study group is well documented, it was used as a reference population sample in this comparative Lp(a) study. Randomized Hungarian samples were obtained via the National Institute of Food Hygiene and Nutrition, Budapest, Hungary [36], and were from adults living in Budapest, and in three different Hungarian regions, i.e., Fejér, Békés, Komárom-Esztergom. Philippine sera were from free-living individuals on Cebu Island and were randomized and obtained via the Philippine Heart Center in Quezon City.

Sera from diseased Caucasians were from unrelated Belgian male patients who underwent elective coronary artery

bypass grafting (CABG) (n = 100) as described previously [37], or presented with an acute myocardial infarction (n = 50) as diagnosed by WHO criteria. In the diseased group, serum Lp(a) was determined the day before bypass in the CABG patient group, and within 6 hours after onset of chest pain in the AMI patient group. All CABG and AMI patients included were free of insulin-dependent diabetes, renal insufficiency, cerebrovascular accidents, and liver disease. Notable is that in the CABG study group, only patients with preoperative serum cholesterol values between 4.66 and 7.24 mmol/l were included [37]. These highly selected, diseased Caucasian males were included to enable comparison of serum Lp(a) values in free-living Pygmies and Bantus and in healthy Caucasians to those in diseased Caucasians, using the same Lp(a) methodology.

Laboratory Methods

Serum Lp(a) was determined using an anti-apo(a) polyclonal capture ELISA from Biopool (TintElize lipoprotein(a), Cat. No. 610220; Biopool AB, Umea, Sweden). The capture polyclonal anti-apo(a) antibody does not cross-react with plasminogen up to 1000 mg/l. Lp(a) determinations in all population samples were performed using the TintElize Biopool kit, the assay being calibrated to total Lp(a) mass. Considering the lability of the Lp(a) lipoprotein particle [35], a maximum serum storage time of one year at −70°C was respected. At our experimental conditions, it was documented by means of frozen human serum pools that storage did not affect Lp(a) levels up to two years.

Cholesterol was determined enzymatically using CHOD-PAP reagents. Lipid analyses in the Belgian and Philippine population samples were performed at the University Hospital Leuven, Belgium, while all other determinations were performed at the Lipid Reference Laboratory of the University Hospital Rotterdam, The Netherlands. The Lipid Reference Laboratory (LRL) Rotterdam maintains total cholesterol standardization through the Lipid Standardization Panel of the Centers for Disease Control (CDC)-National Heart Lung and Blood Institute, Atlanta, Georgia. The LRL Rotterdam is also a permanent member of the Cholesterol Reference Method Laboratory Network (CRMLN) established and coordinated by CDC [38]. The cholesterol values determined in the Leuven University Hospital were also found to be traceable to the Abell-Kendall reference method: in subsets of the samples it was documented that the mean average cholesterol bias was in accordance with current NCEP performance guidelines (bias $\leq$ 3% versus the Abell-Kendall reference method) [39].

Statistical Methods

Basic statistical analysis, analysis of variance (ANOVA), and Pearson correlation analyses were performed using the SPSS/PC+ package (version 5.0.2). Lp(a) and cholesterol data were logarithmically (natural) transformed in all population samples, and geometric means were calculated. Gender differences within populations were evaluated using Student's t-test. Lp(a) differences among population samples were evaluated by one-way ANOVA in either gender. The multiple range test of Student-Newman-Keuls was used for multiple-comparison of sample means. Age and body mass index (BMI)-adjustments of geometric Lp(a) and cholesterol means were performed by means of multiple linear regression analysis (MLR). BMI was defined as weight (in kg)/height^2 (in m^2). On the aggregated population level a weighted least squares MLR analysis was performed to investigate whether mean BMI and mean age could predict male and female mean serum cholesterol and Lp(a) levels across populations, respectively. A statistical significance level of $\alpha = 0.05$ was adopted.

RESULTS

Table 1 displays mean (±SD) age, BMI, and cholesterol per gender for the population samples under study. Significant age, BMI and cholesterol differences existed among all five population samples (ANOVA, $p < 0.0001$).

Table 2 presents the unadjusted serum Lp(a) levels in African Pygmies and Bantus, compared with Caucasian and Asian population samples. Geometric mean Lp(a) levels were 274 and 289 mg/l, respectively, in Bantu males (n = 93) and females (n = 115), and 220 and 299 mg/l in Pygmy males (n = 63) and females (n = 83). The gender difference was significant in Pygmies (p = 0.024) and not in Bantus. Likewise, Philippine females had higher Lp(a) values than males (p = 0.001). Lp(a) frequency distributions in Pygmy and Bantu were less skewed to the low concentration end, compared to Caucasian and Asian distributions (data not shown). In Pygmy males and females, respectively, 41% and 52% of the participants had Lp(a) levels above 300 mg/l, compared with 47% and 55% of the Bantus. Serum Lp(a) levels did not significantly differ between Pygmies and Bantus. Multiple-comparison of LnLp(a) means demonstrated that Lp(a) levels in Pygmies and Bantus were in either gender significantly higher compared with those measured in any other population sample (SNK-test; $p \leq 0.05$).

Overall upper reference ranges for men and women combined, defined as 75th percentiles, were lowest in Asians (162 mg/l), intermediate in Caucasians (204 mg/l), and highest in African Pygmies and Bantus (479 mg/l). The 75th percentile in the diseased Caucasian group was 349 mg/L (data not shown).

Lp(a) levels in Bantu males and females, and in Pygmy females were found to correlate with total cholesterol, LDL-cholesterol (LDL-c), and apolipoprotein B (apo B) but not with age, BMI, systolic and diastolic blood pressure, HDL-cholesterol, and apolipoprotein A-I (Table 3). Serum cholesterol was associated with age in Bantu males (r = 0.25; p = 0.02), while borderline significant in Pygmy males

TABLE 1. Age, body mass index, and serum cholesterol levels in African Pygmies and Bantus, stratified by sex, compared with Asian and Caucasian population samples

Population	*n*	Age (years) Mean	Age (years) SD	BMI (kg/m²) Mean	BMI (kg/m²) SD	Cholesterol (mmol/l) Mean	Cholesterol (mmol/l) SD
Men							
Apparently healthy population samples							
Africans							
Pygmies	63	33.8	16.6	20.0	2.4	2.885	0.693
Bantus	93	41.2	20.0	20.6	2.6	3.119	0.725
Caucasians							
Belgians	413	31.4	5.2	24.1	3.3	5.279	1.073
Hungarians	200	42.2	12.3	26.8	3.9	6.017	1.223
Asians							
Philippines	96	43.7	10.7	23.8	3.4	5.301	0.981
Diseased Caucasians (Belgians)							
CABG patients	100	53.8	4.8	25.8	2.6	5.589	0.891
AMI patients	50	59.5	11.6	25.5	3.1	5.551	1.025
Women							
Apparently healthy population samples							
Africans							
Pygmies	83	29.4	15.3	19.9	3.0	3.174	0.673
Bantus	115	44.8	17.4	20.9	2.9	3.559	0.714
Caucasians							
Belgians	492	30.2	5.3	22.2	3.1	5.117	0.971
Hungarians	200	40.3	10.5	26.0	5.6	5.702	1.162
Asians							
Philippines	99	46.9	10.4	23.1	3.9	5.433	1.155

TABLE 2. Serum lipoprotein(a) levels in African Pygmies and Bantus, stratified by sex, compared with randomly selected Caucasian and Asian population samples

Population	*n*	Lipoprotein(a) mass (mg/l) Geometric mean	Percentile 5	10	25	50	75	90	95	>300 mg/L (%)
Men										
Apparently healthy population samples										
Africans										
Pygmies	63	220[a]	37	62	141	234	424	530	758	41
Bantus	93	274	50	78	180	259	525	826	972	47
Caucasians										
Belgians	413	70	6	10	30	71	216	455	566	20
Hungarians	200	85	11	17	39	73	249	464	645	21
Asians										
Philippines	96	52[a]	9	12	24	52	127	269	323	7
Diseased Caucasians (Belgians)										
CABG patients	100	130	10	17	61	135	409	576	824	34
AMI patients	50	113	14	35	58	97	249	599	651	19
Women										
Apparently healthy population samples										
Africans										
Pygmies	83	299	86	125	192	331	557	669	928	52
Bantus	115	289	58	74	179	317	538	888	1111	55
Caucasians										
Belgians	492	67	7	11	27	67	186	411	553	16
Hungarians	200	86	12	19	34	74	237	566	776	22
Asians										
Philippines	99	86	18	21	44	88	176	294	399	9

[a] $p \leq 0.05$ for gender differences within population samples (Student's *t*-test).

TABLE 3. Pearson correlations of LnLp(a) with anthropometric data and serum lipids in African Pygmies and Bantus, with respect to gender

	Bantu		Pygmy	
Variable	Males $n = 92$	Females $n = 113$	Males $n = 63$	Females $n = 83$
Age	−0.06	0.06	−0.10	0.16
BMI	0.12	−0.15	0.06	0.10
SBP	−0.07	−0.09	−0.01	0.09
DBP	−0.06	0.15	−0.04	0.02
Heart rate	−0.03	−0.04	0.13	0.08
Apo A-I	0.11	−0.00	−0.00	−0.05
HDL-cholesterol	0.06	−0.02	−0.04	0.12
Apo B	0.38[c]	0.31[b]	0.19	0.31[b]
LDL-cholesterol	0.50[c]	0.39[c]	0.03	0.35[b]
Cholesterol	0.35[c]	0.28[b]	0.06	0.28[a]
Netto triglycerides	−0.26[a]	−0.02	0.13	−0.13

[a] $p < 0.05$.
[b] $p < 0.01$.
[c] $p < 0.001$.

($r = 0.22$; $p = 0.08$). In contrast, serum cholesterol was not significantly associated with age in Pygmy respectively Bantu females (data not shown).

Table 4 depicts age- and BMI-adjusted geometric Lp(a) and cholesterol means per gender for the population samples studied. *P*-values are given, versus the Belgian population sample, the latter being the reference population sample in the MLR analysis. Pygmy and Bantu concentrations differed significantly from Belgian levels ($p < 0.0001$), Pygmies and Bantus having the lowest serum cholesterol, and the highest serum Lp(a) levels among the population samples studied. Philippine males had Lp(a) levels that were significantly lower compared with those in Belgian males, while Hungarian females displayed significantly higher Lp(a) levels compared to Belgian females. Both Hungarian males and females had significantly higher cholesterol values compared to Belgians. Age- and BMI-adjusted geometric Lp(a) means were 2.8-and 4.3-fold higher in male respectively female Pygmies compared to Belgian males and females, and 3.5- and 3.9-fold higher in male and female Bantus ($p < 0.0001$). Finally, age- and BMI-adjusted serum Lp(a) levels in diseased Belgian males were significantly higher than in apparently healthy Belgian males: 131 mg/l in CABG patients and 114 mg/l in AMI patients, compared with 72 mg/l in healthy male participants.

MLR analysis pointed out that BMI, age, and ethnicity explained 12% and 17% of serum Lp(a) variance in males and females, respectively, compared with 60% and 51% of serum cholesterol variance. BMI and age alone explained maximum 3% of Lp(a) variance. After adjusting for ethnicity BMI remained a borderline significant predictor in either gender (BMI in males: $p = 0.08$; BMI in females: $p = 0.09$), in contrast with age. Moreover, Table 5 demon-

TABLE 4. Age- and BMI-adjusted geometric mean values of serum lipoprotein(a) and serum cholesterol in African Pygmies and Bantus, stratified by sex, compared with randomly selected Caucasian and Asian population samples

Population	*n*	Cholesterol (mmol/l)	*p*-Value vs. Belgians of the same gender	Lipoprotein(a) (mg/l)	*p*-Value vs. Belgians of the same gender
Men					
Apparently healthy population samples					
Africans					
Pygmies	63	3.017	<0.0001	204	<0.0001
Bantus	93	3.159	<0.0001	253	<0.0001
Caucasians					
Belgians	413	5.336	—	72	—
Hungarians	200	5.659	0.0012	88	NS
Asians					
Philippines	96	5.159	NS	51	0.0243
Diseased Caucasians (Belgians)					
CABG patients	100	5.159	NS	131	0.0003
AMI patients	50	4.895	0.0164	114	0.0545
Women					
Apparently healthy population samples					
Africans					
Pygmies	83	3.241	<0.0001	289	<0.0001
Bantus	115	3.445	<0.0001	264	<0.0001
Caucasians					
Belgians	492	5.104	—	67	—
Hungarians	200	5.296	0.036	90	0.0129
Asians					
Philippines	99	5.111	NS	81	NS

Abbreviation: NS = not significant.

TABLE 5. Weighted least squares multiple linear regression analysis in aggregated Caucasian, Asian, and African population samples (n = 5), stratified by sex, with mean serum lipoprotein(a) and mean serum cholesterol as dependent variables, and with mean age and mean BMI as independent variables

Dependent variable	Predictors	Coefficient	S.E.	p Value
Men				
Mean Ln Lp(a)	Mean BMI (kg/m^2)	−0.1873	0.1174	NS
(Ln mg/l)	Mean age (year)	0.0316	0.0447	NS
	Constant	7.8378	2.9511	NS
Mean Ln cholesterol	Mean BMI (kg/m^2)	0.1148	0.0250	0.04
(Ln mmol/l)	Mean age (year)	−0.0085	0.0095	NS
	Constant	−0.8720	0.6284	NS
Women				
Mean Ln Lp(a)	Mean BMI (kg/m^2)	−0.2071	0.1610	NS
(Ln mg/l)	Mean age (year)	0.0510	0.0445	NS
	Constant	7.4687	3.4060	NS
Mean Ln cholesterol	Mean BMI (kg/m^2)	0.0885	0.0445	NS
(Ln mmol/l)	Mean age (year)	−0.0087	0.0123	NS
	Constant	−0.1421	0.9421	NS
Men and women				
Mean Ln Lp(a)	Sex (female)	−0.1272	0.3170	NS
(Ln mg/l)	Mean BMI (kg/m^2)	−0.1954	0.0812	0.05
	Mean age (year)	0.0435	0.0258	NS
	Constant	7.5961	1.9049	0.007

Abbreviation: NS = not significant.

strates that at the aggregated level, i.e., across the population samples studied, overall mean BMI was negatively correlated with overall mean Lp(a) levels (p = 0.05) if men and women were grouped.

DISCUSSION

The Pygmies studied are pure hunter-gatherers and are the Aborigines in Africa south of the Sahara. They were overrun by the Bantu who, from 1200–1400 A.D. gradually spread from the upper Nile Valley and the region of Lake Chad southward and westward over the continent [32]. Up to now, Pygmies live in isolated groups among the Bantu and along the Equator. As described by Kesteloot *et al.* [33,40], the characteristic diminutive Pygmy stature together with the consistent Pygmy body measurements, lifestyle factors and serum lipid levels compared to previous reports [32], are a reflection of the homogeneity of the Pygmy race and of the fact that a representative sample was taken. The Pygmy sample investigated, though partly consisting of related individuals as children were included, was derived from four different communities living in and nearby the Dja reservation in South-West Cameroon. Due to the high participation rate the Pygmy sample is a good representation of the current Pygmy cohabitation in those specific regions. However, the representativeness for the total African Pygmy population is unknown. The same holds for the Bantu sample investigated: volunteers from three neighboring communities, mainly entered on a first-come, first-served basis and partly containing relatives, were studied. Notwithstanding the fact that the Bantu population sample was not randomly gathered, it reflects the Bantu cultures from the Mecasse and the Lolodorf region, and the city of Bengbis.

In this study, we focused upon the genetically determined Lp(a) lipoprotein risk factor, in relation to the modifiable serum cholesterol risk factor and to ethnicity. Notable features of our study are the exceptionally low mean serum cholesterol levels in Pygmies, the absent or minor cholesterol increase with estimated age, as well as the two- to fivefold higher mean Lp(a) levels (Tables 2 and 4) compared with Asians and Caucasians. Bantus had the same mean Lp(a) level as Pygmies, while age- and BMI-adjusted serum cholesterol levels were approximately 5% higher both in males and females, and increased significantly with age in Bantu males. From Table 2 it can be seen that 41–55% of Pygmies and Bantus had serum Lp(a) levels above 300 mg/l, the universally accepted upper reference limit in Caucasians. As presence of CHD is very unlikely in African Pygmies [32] and Bantus, the high serum Lp(a) concentrations samples must either be counteracted by other factors, or be in itself an insufficient cause for developing atherosclerosis. Consequently, we agree with others [41,42] that for identifying subjects at increased risk of coronary heart disease, ethnicity-related cutoff values, based on 75th percentiles, should be used for Lp(a).

Using MLR serum Lp(a) variances could be explained up to 12% and 17% in males and females, respectively, across the healthy population samples studied, and were predicted exclusively by ethnicity and barely by age or BMI. However,

at the aggregated level, mean BMI was negatively correlated with mean Lp(a) if men and women were combined, while no significant correlation was observed with mean age (Table 5). Finally, the tight univariate correlations demonstrated with total cholesterol, apo B and LDL-c in Pygmies and Bantus could be explained by the high relative percentage of Lp(a)-cholesterol and Lp(a)-apo B compared with Asians and Caucasians (Table 3).

The large differences in serum Lp(a) between African Pygmies and Bantus compared with Asians [43,44] and Caucasians [10 13,41,43,45,46], and the absence of association with many other variables except serum lipids, are consistent with previous reports that state that Lp(a) levels are largely genetically determined [1,5,6]. Also, the height and distribution of the serum Lp(a) levels in Pygmies and Bantus seem to be comparable or even higher than those described in Nigerians [43], Congolese [47], Sudanese [48] and American blacks [19,25,49–53]. The high Lp(a) levels in blacks, without corresponding high prevalence of CHD, suggest that race and gender differences in apo(a) phenotypes, hemostatic activity, or other unrelated factors may contribute to this paradox. However, from twin studies it became clear that neither behavioral or environmental correlates, nor variation in the apo(a) size phenotype appeared to explain the higher mean Lp(a) levels among blacks compared to whites [7]. Rather these findings corroborate the hypothesis that Lp(a) is a continuous supplier of liver cholesterol to peripheral endocrine organs independent of triglycerides or dietary cholesterol intake, being preferentially preserved during human evolution in black African populations of which the food supply was not as regulated as that of Caucasian and Asian populations. In contrast, in civilized human populations, Lp(a) may have lost its phylogenetical importance since other cholesterol-rich lipoproteins, notably LDL, are highly abundant. Moreover, potential adverse effects of high Lp(a) levels should become overt especially in these civilized populations. This may be in line with the significant shift-to-the-right of the Lp(a) distributions (Table 2) and of the geometric means (Table 4) in Caucasian CABG and AMI patients, respectively, compared with healthy Caucasians, notwithstanding similar (CABG group) or even lower (AMI group) mean cholesterol levels in the diseased Caucasian groups (Table 4). The shift-to-the right is also in accordance with the findings of numerous other authors [6,22]. Although CHD is a multifactorial disease, the 1.6- and 1.8-fold higher, respectively, adjusted Lp(a) means in diseased compared with healthy Caucasians may be elements aggravating the atherosclerosis risk of these subjects and contributing to their disease. In contrast, the high Lp(a) levels in Pygmies and Bantus without concomitant high prevalence of CHD are difficult to understand. Yet, according to Maher *et al.* [54] Lp(a) is especially atherogenic in combination with high (LDL-) cholesterol levels or other acquired risk factors, e.g., due to Westernization [29–31], that can nurture Lp(a) into a more potent risk factor. To draw firm conclusions regarding the Lp(a) pathogenicity in Pygmies, Bantus, and other population samples prospective studies are warranted that document Lp(a) atherogenicity and its determinants in different populations.

Major strengths of this study are the fact that serum Lp(a) levels were obtained using one and the same method in all population samples, and were determined in frozen sera that were adequately stored for less than one year. Therefore, storage time and temperature did not confound the measured Lp(a) results [35]. Limitations of this study are related to the cross-sectional study design and the relatively small sample sizes. Moreover, Pygmy and Bantu samples were not completely randomized, in contrast with the Asian and Caucasian samples. Consequently, extrapolation of these data to whole populations should be done with caution. Also, the diseased Caucasians represent two strongly selected groups that were, with the exception of BMI and age, not matched or adjusted for other cardiovascular risk factors.

We conclude that African Aboriginal Pygmies and Bantus have serum Lp(a) levels that are comparable, with adjusted Lp(a) means being up to fivefold higher compared with Asian and Caucasian means. In contrast, adjusted serum cholesterol means were 0.57- to 0.67-fold the Caucasian and Asian means. In the light of the virtual absence of CHD in Aboriginal African Pygmies and Bantus, high serum Lp(a) levels do not *seem* to be very deleterious in these population samples. Consequently, ethnicity-related upper reference values should be used for Lp(a). Also, longitudinal studies are warranted to determine the pathogenicity of Lp(a) in different populations with variable interrelationships between *nature* and *nurture*.

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