Biological and genetic determinants of serum apoC-III concentration: reference limits from the Stanislas Cohort

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Abstract **Apolipoprotein C-III (apoC-III) is involved in triglycerides metabolism, and is therefore important for the pathogenesis of coronary heart diseases. However, to our knowledge serum apoC-III variation factors and reference limits have never been determined, so the aim of this study was to establish them and facilitate clinical usefulness. We measured serum apoC-III concentration of apparently healthy subjects of the Stanislas Cohort by an immunoturbidimetric method. Genetic polymorphisms within the *APOC3*, *APOE*, *APOAIV*, and *LPL* genes were determined by a multiplex PCR. Serum apoC-III concentration varied from 28.2 mg/l to 225.8 mg/l in the overall sample and between subjects variability was about 30%. Factors influencing apoC-III concentration were age, BMI in adult men, alcohol consumption in adults, oral contraceptive intake in women, the post-pubescent status in boys. The *APOC3* 1100T allele in adult men and the *APOC3* −455C allele in boys were associated with increased apoC-III concentration. The *APOA4* 360His allele was associated with decreased apoC-III concentration in women. We also established reference limits of serum apoC-III concentration according to age and gender.**—Tilly, P., C. Sass, M. Vincent-Viry, D. Aguillon, G. Siest, and S. Visvikis. **Biological and genetic determinants of serum apoC-III concentration: reference limits from the Stanislas Cohort. *J. Lipid Res.* 2003.** 44: **430–436.**

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Apolipoprotein C-III (apoC-III), a major component of HDL, triglyceride-rich lipoproteins (TRL) (i.e., VLDL and chylomicrons), and, to a lesser extent LDL, plays an important role in the metabolism of these TRLs (1). Therefore, apoC-III concentration is highly and positively correlated to triglyceride concentrations (1). Over-expression of human apoC-III in the plasma of transgenic mice results in hypertriglyceridemia (2, 3) and an increase of atherosclerosis (3). In contrast, apoC-III-deficient mice are protected from postprandial hypertriglyceridemia and show reduced triglyceride concentrations (3). Serum concentration of apoC-III, especially non-HDL apoC-III present on TRL, has been found to be associated with coronary heart disease (CHD) (4, 5). It has been proposed that apolipoprotein composition of lipoproteins is more closely linked to CHD than the conventional measurement of lipid content (6).

Serum apoC-III concentration has been found at higher level in several pathological situations such as type 2 diabetes (7), hyperbilirubinemia (8), kidney deficiency (9), and decreased in thyroid dysfunction (10). Factors reported to influence apoC-III levels in healthy individuals are gender (11), age, menopause status (12), and genetic polymorphisms in the APOC3 gene (13–16). Genetic variants in the *APOE*, *APOA4*, and *LPL* genes are also potential determinants of apoC-III concentration. LPL and apoE are both involved in TRL metabolism (17, 18) and common *APOE* polymorphisms, and several polymorphisms in the *LPL* gene have been related to triglyceride concentration (19, 20). The *APOA4* gene is located in the 15 kb *APOA4-C3-A1* gene cluster (21) and is involved in triglyceride metabolism. Polymorphisms in the *APOA4* gene have been related to triglyceride concentrations (22).

ApoC-III is not frequently measured in clinical investigations, whereas apoA-I and apoB are well tested. Due to the important role of apoC-III in TRL metabolism and the increasing evidence of the implication of these particles in the pathogenesis of cardiovascular diseases, we judged it useful to determine both biological and genetic factors influencing serum apoC-III concentration and establish its reference limits for a Caucasian population coming from the Eastern part of France. Indeed, current values of apoC-III concentration have been evaluated through an immuno-

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turbidimetric method on only a small sample of 100 individuals (11) or on a larger population composed of non-Caucasian people (12). To our knowledge, serum apoC-III concentration reference limits had never been established in Caucasian populations.

MATERIALS AND METHODS

Sample population

The studied population has been taken from the Stanislas cohort, a longitudinal familial study that has been previously described (23). The sample population is composed of volunteers for a free 5-year periodic health examination. Subjects were Caucasian and came from the Vosges and the South of Meurthe et Moselle (Eastern part of France). All the individuals were apparently healthy: they were free from serious and/or chronic illnesses known and declared by them, none demonstrated clinical, biochemical or haematological evidence of cardiovascular, hepatic, or renal failures. Each subject gave written informed consent for participating in this study, which was approved by the Local Ethics Committee of Nancy.

For this study, the sample population included 865 individuals coming for the second health examination. These subjects did not take any cardiovascular medication. We excluded four subjects for abnormal liver metabolism with γ-glutamyltransferase (GGT) values higher than 300 U/l, alanine aminotransferase values greater than 200 U/l, aspartate aminotransferase greater than 200 U/l, and triglycerides and cholesterol concentrations higher than 10 mmol/l, and a pregnant woman. We also excluded two women with outliers values for apoC-III concentration (lower than 22 mg/l and greater than 240 mg/l) as these values are clearly outliers that do not belong to the reference distribution. The resulting sample contained 858 individuals aged 4 to 58 years old with complete biochemical and physical parameters. For genetic parameters, only 839 individuals among the 858 had complete data.

Blood samples and data collection

After an overnight fast, venous blood was collected in Vacutainer tubes containing either EDTA for DNA preparation or a gel for serum separation (Becton Dickinson). Puberty was determined using Tanner stages (24, 25): pubic hair and sexual maturation were scored by visual assessment (stage 1 represents pre-puberty, stage 2 represents early-puberty, stages 3 and 4 represent mid-puberty, and stage 5 represents late-puberty). Score used in this study is the addition of both sexual and pubic hair maturation scores.

Alcohol, tobacco, and drug consumption were collected during the blood sampling by a self-administered questionnaire. Current number of cigarettes, cigars, and pipes smoked daily were recorded. Cigars and pipes tobacco consumption was converted into equivalent cigarette tobacco consumption. Daily wine and beer consumption and weekly spirit consumption have been recorded. Beverages consumption has been convert in grams of alcohol daily consumed. BMI was calculated according to the Quetelet's formula: weight /height^2 (kg/m^2).

Analytical methods

DNA extraction was performed according to the salting out method described by Miller et al. (26). *APOC3* (−641T/C, −482C/T, −455T/C, 1100C/T, 3175C/G, and 3206T/G), *APOE* (Arg 112Cys and Arg158Cys), *APOA4* (Thr347Ser and Glu360His), and *LPL* Ser447Ter were determined by a PCR multilocus genotyping assay, essentially as previously described (27).

Biological measurements were determined by classical routine methods

Concentrations of serum apoC-III were determined by immunoturbidimetry, without any pre-treatment, using COBAS-Mira analyser (Roche Diagnostics) and Daiichi's kits (apoC-III AutoN "Daiichi", reference 241871) and calibrator (Apoauto N "Daiichi" High Calibrator). Antihuman apoC-III polyclonal antibodies from goat were used according to the manufacturer's recommendations. The performance of these assays was examined in control serum samples provided by the manufacturer with assigned values. Data from our assays were included when the values of the control serum samples were within the control ranges established for the control samples. The detection limits for the method used to test apoC-III were 4.38 mg/l for the smallest and 270 mg/l for the largest. The within-series imprecision of apoC-III measurements was estimated to be 2.5% on a serum pool made at the Centre for Preventive Medicine (mean apoC-III concentration of 77.6 mg/l). The day-to-day reproducibility was tested with the same serum pool and was 2.3%.

Statistical analysis

Statistical analyses were performed using BMDP® statistical software (University of California, Los Angeles, CA). Log-transformed values of apoC-III were used as the distribution was skewed. Data were stratified by gender and age with a cut-off value of 20 years for age in order to established reference limits according to age and gender as biological and genetic factors of variation can be different according to gender and age. Analyses were performed separately for four groups: adult men (called men group), adult women (called women group), boys, and girls. Twenty-two sons (21 to 30 years) and 20 daughters (21 to 28 years) were pooled together with fathers and mothers, respectively. Performing analysis without including the oldest children in these groups did not change the results, especially the genetic data. Pearson correlation coefficients between apoC-III concentrations and biological, clinical, and lifestyle variables were calculated. Factors significantly correlated to apoC-III concentration were next introduced in a stepwise multiple regression analysis that was used to determine the most important parameters of apoC-III variability and to quantify the relationships between the apoC-III concentration and these variables. These factors were also used for apoC-III adjustment before the estimation of apoC-III reference limits. We estimated the 2.5th, 5th, 50th, 95th, and 97.5th percentiles in men and women separately. Associations between genetic polymorphisms were investigated by analysis of variance after adjustment for the significant biological covariates. Multiple pairwise comparisons were also performed using a Student's *t*-test with Bonferroni corrections for multiple comparisons to determine difference between genotypic means. Polymorphisms showing significant relationship with apoC-III concentration were entered in a stepwise multiple regression analysis together with covariates to determine the most important genetic factors of apoC-III variation. Interactions between genetic polymorphisms and environmental factors (gender, age, BMI, or alcohol consumption) were also assessed in multiple regression analysis or in two-way ANOVA after adjustment for covariates.

For *APOE* common polymorphism, three variables, APOE4, APOE3, and APOE2 were generated. The APOE4 group was composed of subjects carrying the ε3/ε4 and ε4/ε4 genotypes; the APOE2 group included ε2/ε2, ε2/ε3 and ε2/ε4 genotypes. We decided to include subjects carrying the ε2/ε4 genotype in the APOE2 group because of the previously observed dominant effect of the ε2 allele on apoB and apoE in this genotype (28); the results were similar with or without the ε2/ε4 subjects in the APOE2 group. The APOE3 group included only subjects carrying the ε3/ε3 genotype.

TABLE 1. Characteristics of the sample population[a]

	Men (n = 219)	Women (n = 214)	Boys (n = 218)	Girls (n = 207)
Age (years)	42.4 (8.0)	40.8 (7.3)	15.2 (3.3)	15.2 (3.2)
BMI (kg/m^2)	25.2 (3.3)	23.8 (4.0)	20.1 (2.9)	20.3 (3.1)
Post puberty stage (%)	—	—	38.5	34.3
Menopause status (%)	—	5.1	—	—
Season of recruitment				
Winter (%)	26.0	26.2	28.0	23.7
Spring (%)	27.4	29.9	28.4	27.0
Summer (%)	24.7	24.3	22.0	26.6
Autumn (%)	21.9	19.6	21.6	22.7
Alcohol consumption (g/day)	24.4 (27.0)	7.1 (13.1)	1.7 (5.3)	0.7 (2.8)
Tobacco consumption (cig/day)	5.2 (10.2)	2.4 (6.5)	1.7 (4.5)	1.3 (3.8)
Oral contraceptive use (%)	—	26.6	—	18.4
Anti-inflammatory drug use (%)	6.8	5.1	0.5	4.3
Bilirubin (μmol/l)	13.6 (6.8)	10.6 (5.2)	13.5 (8.1)	10.7 (5.9)
Triglyceride (mmol/l)	1.37 (0.76)	1.02 (0.45)	0.87 (0.40)	0.92 (0.49)
Total Cholesterol (mmol/l)	5.71 (1.06)	5.58 (0.86)	4.27 (0.71)	4.63 (0.83)
HDL-Cholesterol (mmol/l)	1.44 (0.42)	1.80 (0.45)	1.44 (0.34)	1.58 (0.38)
ApoC-III (mg/l)	100.7 (35.6)	88.8 (26.4)	70.1 (18.4)	76.2 (24.8)
Median of ApoCIII (mg/l)	93.3	83.9	67.8	72.1

[a] Mean (SD) or percent.

For studying *APOC3* 3175 C/G, *APOA4* Thr347Ser and Glu360His, and *LPL* Ser447Ter polymorphisms, individuals homozygous and heterozygous for the less frequent allele were pooled together due to the small number of homozygous subjects. Statistical significance was set at $P < 0.05$.

RESULTS

Characteristics of the studied population

Characteristics of the sample population are presented in **Table 1**. They were in agreement with the recruitment of apparently healthy subjects (29). Most of the adults were middle-aged. Alcohol and tobacco consumption, as well as drug intake were moderate. All biological parameters had values within reference ranges and BMI values were almost within the reference ranges. **Table 2** indicates the allelic frequencies for all the studied polymorphisms, the genotype distribution for each polymorphism being in Hardy-Weinberg equilibrium.

Distribution of apoC-III concentration

Figure 1 showed apoC-III distribution among men, women, boys, and girls. Mean values and medians of serum apoC-III concentration are shown in Table 1. In the total sample, serum apoC-III concentration varied between 28.1 mg/l and 225.8 mg/l. Serum apoC-III concentration was significantly higher in men than in women ($P < 0.01$), and adults had higher serum apoC-III concentration than children ($P < 0.01$). There was no difference among children according to gender. The between-subjects variabilities were 35% for men, 30% for women, 26% in boys, and 32% for girls.

Factors of biological variation and reference limits of serum apoC-III concentration

No influence of tobacco consumption, bilirubin concentration, anti-inflammatory treatment, or the season during which the blood collection had been done was found ($P > 0.10$) (data not shown). In contrast, both men and boys serum apoC-III concentration was significantly correlated with age and BMI (**Table 3**). Serum apoC-III concentration was significantly linked to alcohol consumption in adults. The post-pubescent status was related to serum apoC-III concentration in boys and oral contraceptive intake was significantly related to increased serum apoC-III concentration in females. Menopausal status seemed to have no significant influence on serum apoC-III concentration ($P = 0.082$).

The main biological factors of serum apoC-III concentration, determined by stepwise multiple regression analysis, were age ($\beta = 0.0028$, $P = 0.022$), BMI ($\beta = 0.0086$, $P = 0.004$), and alcohol consumption ($\beta = 0.77\ 10^{-3}$, $P = 0.035$) in men. In women, they were alcohol consumption, oral contraceptive intake, and age ($\beta = 0.0025$, $P < 0.001$; $\beta = 0.092$, $P < 0.001$ and $\beta = 0.0029$, $P = 0.030$ respectively). The main factor of serum apoC-III variation in boys was the post-pubescent status ($\beta = 0.046$, $P = 0.003$) and in girls it was the oral contraceptive intake ($\beta = 0.083$, $P = 0.001$).

Reference limits for serum apoC-III concentration were obtained after adjustment for significant biological covariates in

TABLE 2. Allelic frequencies in the population of the studied polymorphisms

Allele	Allelic Frequency
APOC3 −641 C	0.414
APOC3 −482 T	0.297
APOC3 −455 C	0.399
APOC3 1100 T	0.277
APOC3 3206 G	0.354
APOC3 3175 G	0.101
APOA4 347Ser	0.213
APOA4 360His	0.100
APOE 2	0.106
APOE 3	0.769
APOE 4	0.125
LPL 447Ter	0.125

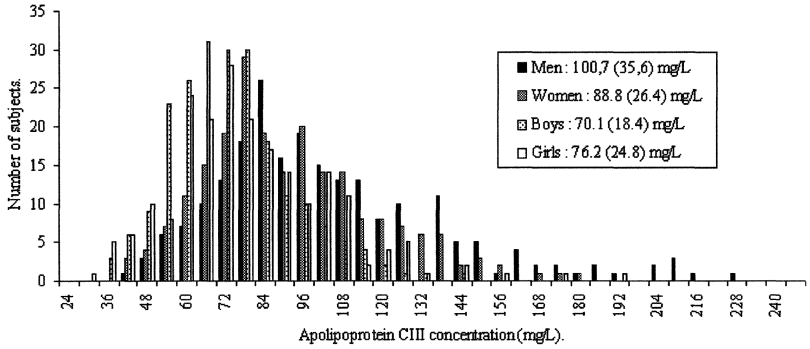

Fig. 1. Distribution of serum apoC-III concentration among men, women, boys, and girls.

each group. **Table 4** presents percentiles of serum apoC-III concentration according to age and gender used as partition criteria. Subjects aged 4 to 20 years were pooled together as apoC-III medians were not found significantly different in (4–13), (14–17), and (18–20) age groups. Concerning the 50th percentile, values of serum apoC-III concentration increased regularly with age in both males and females.

Genetic factors of apoC-III concentration variation

LPL Ser447Ter polymorphism had no significant influence on serum apoC-III levels. In contrast, in males, serum apoC-III concentration was significantly associated with *APOC3* polymorphisms at different loci: −641T/C ($P = 0.02$ in boys), −482C/T ($P = 0.05$ in men and $P = 0.02$ in boys), −455T/C ($P = 0.007$ in boys), 1100C/T ($P < 0.001$ in men), 3175C/G ($P = 0.05$ in men), and 3206T/G ($P = 0.01$ in men), with the rare allele or the homozygous for the rare allele related to an increase in serum apoC-III concentration. The −455T/C and 1100C/T polymorphisms are the more important apoC-III genetic variation contributing to apoC-III concentration in boys and men, respectively (**Table 5**). In females, carriers of the *APOA4* 360His allele presented significant lower serum apoC-III concentration compared to the *APOA4* 360 Glu/Glu carriers ($P = 0.037$ in women and $P = 0.003$ in girls) (Table 5). In women also, apoC-III concentration decreased significantly in subjects carrying the *APOE* ε3/ε4 or ε4/ε4 genotypes compared to the carriers of the *APOE* ε2/ε2 or ε2/ε4 genotypes ($P = 0.023$) (Table 5).

We tested potential interactions between *APOC3* −455C, 1100T, *APOA4* 360 His, *APOE* ε4 alleles, and environmental factors (gender, age, BMI, alcohol, or contraceptive pill). Significant interactions were found in adults between *APOC3* 1100C/T polymorphism and gender (from two-way ANOVA $P = 0.0035$ for *APOC3* 1100T × gender) and in males between *APOC3* 1100C/T polymorphism and age ($P = 0.0010$ for *APOC3* 1100T × age over 20 years old). No other significant interactions between apoC-III covariates and genetic polymorphisms was observed.

DISCUSSION

Herein, we reported factors of apoC-III biological variation and provide reference limits for apoC-III, measured by immunoturbidimetry assay.

We found that the between individual variability of serum apoC-III concentration was important (from 26% to 35%) and similar to those already reported for other apolipoproteins such as apoB (30), apoAI (31), and apoE (32).

Bilirubin did not affect serum apoC-III concentration as reported by Rifai et al. (11), who used the same immunoturbidimetric method. In the study of Davit-Spraul et al. (8), a hyperbilirubinemia higher than 100 μmol/l was associated with elevated concentrations of apoC-III. However, in the present study, bilirubinemia was less than 100 μmol/l (less than 61 μmol/l) as expected for healthy subjects. therefore, the lack of association observed between serum apoC-III concentration and bilirubin was not surprising. A borderline significant relationship was observed between serum apoC-III concentration and menopausal status in the present study. This is probably due to the small number of menopaused women in our study (only 11 women representing 5% of the women). The absence of significant effect of tobacco consumption on serum apoC-III concentration was already reported by Peacock et al. (14).

In both men and women, we found that age was related to increase of apoC-III. Noma et al. (12) reported a decrease of serum apoC-III concentration after 60 years that cannot be evidenced in the present study because of the younger age of our sample population (<56 years for men and <54 years for women). ApoC-III concentration increased with postpubescent status in boys as observed for triglyceride (33) and

TABLE 3. Correlations between biological variables and apoCIII concentration[a]

	Correlation Coefficient			
	Men (n = 219)	Women (n = 214)	Boys (n = 218)	Girls (n = 207)
Age	0.237[b]	0.045	0.134[d]	0.133[e]
BMI	0.270[b]	0.047	0.173[d]	0.085
Post puberty	—	—	0.200[c]	−0.008
Menopause	—	0.119[e]	—	—
Alcohol consumption	0.227[b]	0.225[b]	0.085	0.100
Oral contraceptive intake	—	0.188[c]	—	0.232[b]

[a] Only variables presenting correlation with P value <0.10 in at least one group are presented.
[b] $P < 0.001$.
[c] $P < 0.01$.
[d] $P < 0.05$.
[e] $P < 0.10$.

TABLE 4. Reference limits of apoC-III concentration

			Percentiles									
	Number		2.5		5		50		95		97.5	
Age	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
4–20	218	207	41.0	39.4	44.5	43.5	68.5	72.4	103.3	120.8	111.9	133.4
21–45	138	168	50.0	48.0	55.3	52.5	88.1	82.8	157.4	133.0	173.8	145.5
46–55[a]	79	46	52.7	54.5	58.2	59.0	100.0	91.4	161.8	134.6	178.6	145.9

Apolipoprotein C-III values were adjusted on all biological covariables affecting apoC-III concentration (alcohol consumption and BMI for men and puberty for boys, alcohol consumption for women and oral contraceptive intake for females) as followed: in boys (4–20) y = Log apoC-III − 0.046 × (puberty status −0.385) with puberty status = 1 if after puberty, else puberty status = 0; in men (21–55) y = Log apoC-III − 0.0099 × (BMI −25.2) − 0.923 10^{-3} × (alcohol −24.4); in girls (4–20) y = Log apoC-III – 0.083 × (oral contraceptive intake −0.184) with oral contraceptive intake = 1 if use, else = 0; in women (21−53) y = Log apoC-III – 0.068 × (oral contraceptive intake −0.266) − 0.0026 × (alcohol −7.11).

[a] For women 46–53.

apoE concentrations (32). Indeed, as reported in the literature, apoC-III concentration was highly correlated to triglycerides in our population ($P < 0.0001$).

ApoC-III concentration was affected by alcohol consumption in adults, in the same way that triglyceride concentration increases with alcohol consumption. This agrees with Lecomte et al. (34), who showed that apoC-III and lipoproteins containing apoC-III concentration were related to ethanol consumption and that they decreased after alcohol withdrawal treatment.

Oral contraceptive intake was found associated with an elevation in serum apoC-III concentration with a similar impact to that reported for triglycerides (29).

Significant association between apoC-III concentration and *APOC3* polymorphisms was observed in males only. This finding is consistent with our previous observation of the lack of association between the *APOC3* 1100C/T polymorphism and triglycerides in women (35). This agrees also with Groenendijk et al. (16), who found no association between the *APOC3* promoter polymorphisms and APOC-III concentration in spouses of familial combined hyperlipidemia probands. In contrast to this study, Peacock et al. (20) reported that the relation between APOC3 1100C/T polymorphism and apoC-III occurs in both sexes, but the study was done in Icelander sample population, a specific population. Dallongeville et al. (13) found an association between the *APOC3* −482 C/T in women only, but most of the effect was observed in the postmenopausal group and in our study, postmenopausal women were very few. Our results together with other reports reinforced the idea that the relation between *APOC3* polymorphisms and apoC-III and other lipids traits may vary according to gender (13, 14, 35).

Polymorphisms in the 3′ region of the *APOC3* gene were more particularly associated with apoC-III in adult men whereas polymorphisms in the promoter region were in boys. This may indicate age-dependent relationship. Very few data exist in children. In contrast to this study, Shoulders et al. (36) showed in a community-based sample of Italian school children that the polymorphisms in the *APOC3* promoter were not related to apoC-III concentration whereas the *APOC3* 3175C/G was.

Adult men bearing the less frequent allele of the *APOC3* 1100, 3175, and 3206 polymorphisms had higher APOC-III concentration. These results are consistent with previous association studies that have shown significant

TABLE 5. ApoC-III concentration according to significant studied polymorphisms

APOC3 1100C/T	CC	CT	TT	
Men	n = 122	n = 82	n = 15	
	89.1 (1.37)	100.0 (1.31)	122.2 (1.44)	$P = 0.0002$[a]
APOC3 –455T/C	TT	TC	CC	
Boys	n = 80	n = 94	n = 44	
	64.6 (1.31)	66.1 (1.26)	75.9 (1.28)	$P = 0.007$[b]
APOA4 Glu360His	Glu/Glu	Glu/His + His/His		
Women	n = 180	n = 35		
	86.9 (1.32)	78.5 (1.30)		$P = 0.037$
Girls	n = 165	n = 39		
	74.5 (1.35)	63.4 (1.38)		$P = 0.003$
APOE	ε2	ε3/ε3	ε4	
Women	n = 44	n = 123	n = 39	
	91.0 (1.26)	85.5 (1.32)	77.8 (1.33)	$P = 0.023$

Means (SD) adjusted for age, BMI, alcohol consumption in men; age, alcohol consumption, and oral contraception in women; puberty status in boys; and oral contraception in girls. Tests are performed on Log-transformed values but untransformed values are shown. Student's *t*-test pairwise comparison with Bonferroni correction for multiple comparison:

[a] $P < 0.05$ C/C versus C/T , $P < 0.01$ C/C versus T/T, and $P < 0.10$ C/T versus T/T.

[b] $P < 0.01$ C/C versus T/T and $P < 0.05$ C/C versus C/T.

effects of these polymorphisms on apoC-III (37) and triglyceride (38) concentrations even if these results were not observed in all studies (13, 39).

To our knowledge, this is the first study showing association between *APOA4* polymorphism and apoC-III concentration. The *APOA4* 360His allele was associated with decreased of serum apoC-III concentration in females with a more important impact in girls. In accordance with our results, some studies have previously found that this allele was related to reduced fasting triglyceride and increase HDL concentrations (22), even if some studies failed to show these effects. ApoA-IV is involved in transport, use, and storage of triglycerides and variation in its gene could lead to a modification in the metabolism of triglycerides and thus to variation of apoC-III concentration. Furthermore, the *APOA4* gene is located next the *APOC3* gene in the same gene cluster. Therefore, variation in the *APOA4* gene or in linkage disequilibrium with variation in the intergenic region of the cluster could play a role in the regulation of *APOC3* transcription, which could explain the decrease in serum apoC-III concentration observed in women. Indeed, common enhancers for the expression of apoC-III and apoA-IV have been described (40). The association was evidenced in females only, indicating possible hormonal regulation.

In conclusion, we have determined biological and genetic factors of variation of the serum apoC-III concentration in a healthy middle-aged Caucasian population. For the first time, we established reference limits for serum apoC-III concentration, measured by immunoturbidimetric method, in a Caucasian population sample issued from the Eastern part of France. This work provided information to take into account for the interpretation of serum apoC-III measurements in clinical laboratories.

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