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Blood Lipids as Related to Cardiovascular and Neuroendocrine Functions Under Different Conditions in Healthy Males and Females

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LUNDBERG, U., M. FREDRIKSON, L. WALLIN, B. MELIN AND M. FRANKENHAEUSER. *Blood lipids as related to cardiovascular and neuroendocrine functions under different conditions in healthy males and females.* PHARMACOL BIOCHEM BEHAV **33**(2) 381–386, 1989.—Correlations were calculated between, on the one hand, total serum cholesterol, low-density (LDL) and high-density (HDL) lipoprotein cholesterol, and triglycerides, and, on the other hand, systolic (SBP) and diastolic blood pressure (DBP), heart rate (HR), urinary epinephrine, norepinephrine, and cortisol in 30 healthy males and 30 healthy females, aged 30–50. The cardiovascular and neuroendocrine measurements were obtained under different real-life and laboratory conditions. The most striking finding was that, in men, but not in women, total serum cholesterol was significantly positively correlated with SBP in all conditions (LDL and HDL cholesterol followed the same pattern). In women, but not in men, epinephrine and norepinephrine during laboratory-induced mental stress were significantly positively correlated with total cholesterol, LDL and triglycerides.

Serum cholesterol Triglycerides Blood pressure Catecholamines Sex differences

DATA concerning relationships between blood lipids and cardiovascular functions are scarce. Epidemiological investigations, however, indicate positive correlations between different risk factors for coronary heart disease including lipids (8, 15, 16). Recent experimental studies have shown an association between serum lipids (cholesterol, triglycerides) and heart rate acceleration (7) and stress responses in blood pressure (10), respectively.

Serum cholesterol is regarded as a primary risk factor for coronary heart disease (CHD) (11, 12, 18). Leren *et al.* (8) found low but significant positive correlations between cholesterol and blood pressure in a sample of 14000 men. Stamler *et al.* (16) examined a population of 13000 white and black men and women and found a significant relation between serum cholesterol and blood pressure for white males aged 30–44. Salonen and Puska (15) found a positive association between changes in blood pressure and changes in serum cholesterol over a five year period in a sample of 600 men and women. Variations in life-style, particularly diet, suggested that changes in fat consumption were related to changes in serum cholesterol as well as in blood pressure. Studies on relaxation and biofeedback training (13) have also supported a relationship between life-style changes and reduced blood pressure and cholesterol levels.

Findings of a weak positive association between serum cholesterol and blood pressure in normal healthy subjects are generally based on single measurements of blood pressure, usually taken at rest. Little is known about the relationship between blood lipids and cardiovascular functions under active conditions, particularly in naturalistic settings.

In the present study, which forms part of a larger project (4) concerned with environmental stress in healthy male and female white collar workers, fasting blood lipids (total serum cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglycerides) in healthy males and females were related to repeated measurements of systolic and diastolic blood pressures, and heart rate obtained under the following conditions: 1) a day at work, 2) a day at home, 3) laboratory-induced stress, and 4) laboratory rest. In addition, lipids were related to urinary catecholamines and cortisol measured under the same conditions.

METHOD

Subjects

Thirty male and 30 female nonsmoking white collar workers

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TABLE 1

MEANS AND STANDARD DEVIATIONS (SD) OF AGE, HEIGHT (m), WEIGHT (kg), AND BODY MASS INDEX (BMI) IN HEALTHY MALES AND FEMALES

	Men		Women	
	Mean	SD	Mean	SD
Age	41.20	6.19	41.10	5.75
Height	1.77	0.055	1.66	0.066
Weight	79.30	7.44	59.9	6.56
BMI*	25.14	2.03	21.78	2.04

*Body mass index = weight (kg)/height (m)^2.

TABLE 2

MEANS AND STANDARD DEVIATIONS (SD) FOR CARDIOVASCULAR AND NEUROENDOCRINE MEASUREMENTS IN HEALTHY MALES AND FEMALES [BASED ON FRANKENHAEUSER *ET AL.* (4)]

	Men		Women	
	Mean	SD	Mean	SD
SBP (mmHg)				
Work	130.5	13.9	120.6	10.2
Home	124.5	10.0	116.7	11.8
Stress	139.4	15.3	128.5	11.2
Rest	125.6	13.8	115.4	11.7
DBP (mmHg)				
Work	87.4	9.9	85.6	8.7
Home	83.2	9.2	82.0	8.5
Stress	88.1	10.1	79.3	9.7
Rest	81.7	7.3	78.5	9.7
HR (beats/min)				
Work	67.5	10.6	73.2	9.8
Home	66.1	10.4	71.8	9.5
Stress	70.5	10.6	78.3	12.1
Rest	57.8	7.6	64.2	7.6
Epinephrine (pmol/min/kg)				
Work	0.42	0.15	0.44	0.21
Home	0.29	0.11	0.33	0.23
Stress	0.50	0.26	0.53	0.35
Rest	0.39	0.17	0.39	0.17
Norepinephrine (pmol/min/kg)				
Work	1.91	0.54	2.22	0.78
Home	1.76	0.48	2.25	0.77
Stress	1.61	0.53	2.45	1.30
Rest	2.06	0.61	2.34	0.70
Cortisol (pmol/min/kg)				
Work	1.57	1.02	1.20	0.69
Home	1.57	0.99	1.45	0.67
Stress	3.59	3.42	3.60	3.17
Rest	2.15	3.31	2.08	2.03

participated in the study. A medical check-up confirmed that they were in good health. The male and female groups were matched for age (range 30–50). Mean age, body weight, height, and body mass index are shown in Table 1.

Blood Lipids

At 8 a.m. after 12–14 hr fasting, a venous blood sample was drawn from each subject and analysed for serum cholesterol, triglycerides (Technicon, SMACK 2) and high density lipoprotein (HDL) cholesterol (Boehringer). In menstruating women, blood samples were obtained between day 10 and 14 of the menstrual cycle. Low density lipoprotein (LDL) cholesterol was calculated according to the following formula: LDL = total cholesterol-HDL-triglycerides·0.453. (Highest triglyceride value = 2.6 mmol/l). A blood sample from one women was lost due to a technical mishap.

Cardiovascular and Neuroendocrine Measurements

Cardiovascular and neuroendocrine measurements were available from the main study (4), which comprised four different conditions: 1) a normal day at work (9 a.m.–5 p.m.), 2) a work-free day at home (9 a.m.–5 p.m.), 3) experimental stress (60 min) and 4) laboratory rest (50 min). Measurements at home were obtained one week after the day at work, the laboratory experiment was performed four months later (one week after blood sampling). For the measurements at work and at home, the day of the cycle was recorded for menstruating women (but not kept constant). For a summary of the data, see Table 2.

Systolic (SBP) and diastolic blood pressure (DBP) and heart rate (HR) were recorded every hour (fixed interval), using a semiautomated blood pressure device (digital sphygmomanometer UD-510), from 9 a.m. to 5 p.m. during the day at work and the day at home. Each recording was the median of three measurements and mean values were calculated from the nine recordings each day. In the laboratory [for details see (6)], SBP, DBP and HR were recorded successively by an automatic device (Dinamap 846, Mingocard 6) during a 60 min stress period (about 9–10 a.m.) comprising six different tests (star-tracing, mental arithmetic, color-word conflict, cold pressor, hand-grip and a Type A interview) and by a manual sphygmomanometer during a subsequent 50 min period of rest (about 11 a.m.–12 noon). Automatic and manual measurements were calibrated in the morning for each subject. Parallel measurements were found highly correlated and in no case did the two sets of measurements differ significantly (4). Minor differences in mean values (Table 2) due to the different measurement techniques would not influence the correlational analyses below. Thus, mean values based on 19 measurements during stress and 6 measurements during rest were available.

Two-hour measurements of catecholamine and cortisol excretion were obtained at 11 a.m., and at 1, 3, and 5 p.m. during the day at work and the day at home, respectively. Mean values for catecholamines (fluorophotometric assay) and cortisol excretion (radioimmunoassay) were calculated from the four measurements the day on the job and the day at home, respectively. In the laboratory, one urine sample (about 60 min) was obtained after the mental stress tests and one after (50 min) rest. According to the normal circadian variation during morning hours (catecholamine levels increasing, cortisol decreasing), stress levels (9–10 a.m.) of catecholamines were underestimated and cortisol overestimated as compared to rest (about 11 a.m.–12 noon).

Statistical Analyses

Product-moment correlations were calculated for total cholesterol, HDL, LDL, and triglycerides and for SBP, DBP, HR, catecholamine, and cortisol measurements in the four different conditions for males and females, respectively. Partial correlations were calculated after removing the (linear) effects of age.

Blood pressure levels in menstruating women were correlated

TABLE 3

MEANS, STANDARD DEVIATIONS AND RANGES FOR SERUM LIPID LEVELS (mmol/l)

	Men			Women		
	Mean	SD	Range	Mean	SD	Range
Cholesterol	6.45	1.04	4.1–9.5	6.12	1.08	4.2–9.2
HDL	1.20	0.25	0.9–1.9	1.63	0.35	0.9–2.7
LDL	4.67	0.94	2.5–7.2	4.04	1.04	2.1–6.6
Triglycerides	1.31	0.49	0.8–2.6	0.96	0.37	0.5–2.4

with day of the cycle, but no significant association was found at work (SBP: r = .00, DBP: r = .01) or at home (SBP: r = .04, DBP: r = −.23), which is consistent with data from Collins *et al.* (3). (In the laboratory experiment, phase of the menstrual cycle was controlled.) Four menopausal women (no menstruation for the last 6 months) and three women taking oral contraceptives were examined separately, but since their data did not change the results in any noticeable way, all 29 women were included in the final analyses.

RESULTS

Blood Lipid Levels

Means, standard deviations and the range of blood lipids in males and females, respectively, are presented in Table 3. The majority of values were within or close to normal Swedish reference levels (17) for males and females, respectively. Men had higher LDL ($t=2.41$, $p<0.05$) and triglyceride levels ($t=3.10$, $p<0.01$) and lower HDL levels ($t=5.37$, $p<0.001$) than women. The sex difference in total cholesterol did not reach significance ($p>0.20$).

Correlations between the four lipid values are shown in Table 4. As expected, total cholesterol and LDL cholesterol were highly correlated in both sexes. However, in males but not in females, total cholesterol was significantly correlated with HDL cholesterol and, in females but not in males, triglycerides were significantly correlated with total cholesterol and LDL cholesterol.

Correlations Between Blood Lipids and Cardiovascular Measurements

Product moment correlations between blood lipids and cardiovascular measurements in the four different conditions are shown in Fig. 1 for males and females, respectively. In men, there was a consistent pattern showing that total cholesterol, as well as LDL and HDL cholesterol, were significantly positively correlated with SBP. Corresponding correlations for women were close to zero. Moreover, in men but not in women total cholesterol and triglycerides were positively correlated with DBP. HR was not significantly correlated with lipids in any case.

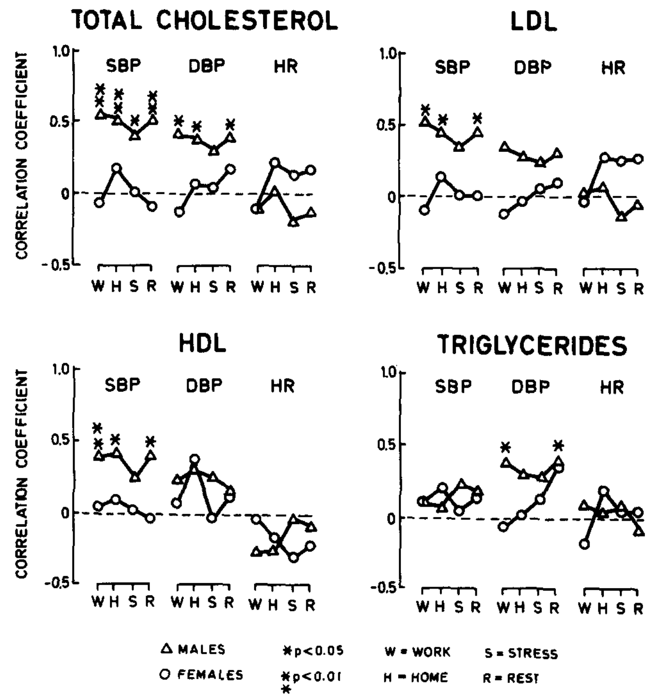

FIG. 1. Product moment correlations between serum lipids and cardiovascular measurements in different conditions for healthy males and females. W = Work: day at work (9 a.m.– 5 p.m.); H = Home: workfree day at home (9 a.m.–5 p.m.); S = Stress: experimental stress in the laboratory (60 min); R = Rest: resting in the laboratory (50 min).

Blood pressure as well as total cholesterol and LDL have been shown to increase with age (2). In our subjects there was a positive but nonsignificant ($p<0.10$) correlation between age and total cholesterol (and LDL) in both men and women (Table 5). In order to remove the (linear) effects of age on the relationship between lipid values and cardiovascular measurements, partial correlations were calculated. Table 6 shows that the partial correlations were slightly lower (cf. Fig. 1), but the pattern remained the same. Significant partial correlations were obtained between SBP and total cholesterol/LDL/HDL (and between total cholesterol and DBP at work) in men. The positive correlations between triglycerides and DBP in men increased slightly after removing the effect of age, and reached significance ($p<0.05$) in three out of the four conditions (Table 6).

TABLE 4

PRODUCT MOMENT CORRELATIONS BETWEEN SERUM LIPID MEASUREMENTS

	Men			Women		
	Total Choles-terol	HDL	LDL	Total Choles-terol	HDL	LDL
HDL	0.40*			−0.06		
LDL	0.96†	0.28		0.95†	−0.35	
Trigl	0.10	−0.40*	−0.01	0.66†	−0.28	0.62†

*$p<0.05$; †$p<0.01$.

Correlations Between Blood Lipid Levels and Neuroendocrine Measurements

Partial correlations between blood lipids and neuroendocrine measurements were calculated (after removing the linear effects of age) as shown in Table 7. As data from one "extreme" woman, who had both the highest catecholamine and the highest blood lipid values, markedly affected the magnitude of the correlations, her data were excluded from Table 7.

During experimental stress, norepinephrine was significantly

TABLE 5

PRODUCT MOMENT CORRELATIONS BETWEEN SERUM LIPIDS AND AGE, HEIGHT, WEIGHT AND BODY MASS INDEX (BMI) IN HEALTHY MALES AND FEMALES

	Total Cholesterol		HDL		LDL		Triglycerides	
	Men	Women	Men	Women	Men	Women	Men	Women
Age	0.35*	0.35*	0.21	−0.03	0.33	0.32	0.07	0.29
Height	−0.01	0.06	0.21	0.02	−0.04	0.03	−0.23	0.15
Weight	0.01	0.13	−0.13	0.16	0.18	0.07	0.08	0.11
BMI	0.02	0.10	−0.29	0.16	0.03	0.05	0.26	0.01

*$p<0.10$.

TABLE 6

PARTIAL CORRELATIONS BETWEEN SERUM LIPIDS AND CARDIOVASCULAR MEASUREMENTS IN DIFFERENT CONDITIONS FOR HEALTHY MALES AND FEMALES AFTER REMOVING THE LINEAR EFFECTS OF AGE

	Total Cholesterol		HDL		LDL		Triglycerides	
	Men	Women	Men	Women	Men	Women	Men	Women
SBP								
Work	0.50†	−0.27	0.33	0.08	0.45*	−0.28	0.08	−0.08
Home	0.44*	0.06	0.38*	0.13	0.37*	−0.01	0.07	0.16
Stress	0.37*	−0.08	0.23	0.03	0.30	−0.09	0.19	0.08
Rest	0.50†	−0.17	0.49†	−0.01	0.40*	−0.16	0.11	0.01
DBP								
Work	0.40*	−0.17	0.11	0.06	0.31	−0.18	0.41*	−0.09
Home	0.27	0.09	0.09	0.36*	0.16	−0.06	0.44*	0.06
Stress	0.32	−0.14	0.19	−0.01	0.23	−0.14	0.32	−0.02
Rest	0.32	−0.18	0.16	0.12	0.22	−0.22	0.42*	−0.02
HR								
Work	−0.08	−0.14	−0.39*	−0.05	0.01	0.08	0.01	−0.28
Home	−0.05	0.06	−0.29	−0.20	0.03	0.14	−0.02	0.04
Stress	−0.09	0.08	−0.05	−0.30	−0.09	0.21	0.04	−0.04
Rest	−0.17	0.10	−0.11	−0.24	−0.10	0.20	−0.04	−0.01

*$p<0.05$; †$p<0.01$.
Work: Day at work (9 a.m.–5 p.m.).
Home: Workfree day at home (9 a.m.–5 p.m.).
Stress: Experimental stress in the laboratory (60 min).
Rest: Resting in the laboratory (50 min).

positively correlated with total cholesterol ($p<0.01$), LDL cholesterol ($p<0.01$) and triglycerides ($p<0.05$) in women. Before excluding the "extreme" woman, corresponding correlations reached significance ($p<0.01$) for epinephrine, too. There was no other consistent pattern of correlations.

DISCUSSION

In view of the large number of correlations calculated (almost 200), only consistent patterns in the data should be interpreted. The most striking finding was that serum cholesterol and blood pressure within the normal range were positively correlated in healthy males, also after removing the effects of age. The correlations were higher than those reported earlier (8). One reason for this could be that the present blood pressure measurements represent means of a great number of recordings, thus considerably reducing the influence of momentary fluctuations [cf. (9)]. Another possible reason is that our healthy subjects were more homogenous than earlier samples with regard to factors influencing blood lipids and/or blood pressure. They were all nonsmoking white collar workers aged 30–50, and they had been asked to refrain from the consumption of alcohol and all pharmacological agents before measurements (4).

No association was found between blood lipids and blood pressure in women (Fig. 1). Moreover, the correlations between the different blood lipids also differed between males and females (Table 4). It is known that cholesterol levels vary somewhat during the menstrual cycle and LDL cholesterol tends to decrease during the luteal phase (1). However, blood samples were taken in the follicular phase and, hence cyclic variations in lipid levels are not likely to have contributed to the sex differences in correlational pattern. As blood pressure was not associated with different phases

TABLE 7

PARTIAL CORRELATIONS BETWEEN SERUM LIPIDS AND NEUROENDOCRINE MEASUREMENTS IN DIFFERENT CONDITIONS FOR HEALTHY MALES AND FEMALES AFTER REMOVING THE LINEAR EFFECTS OF AGE AND DATA FROM ONE "EXTREME" WOMAN

	Total Cholesterol		HDL		LDL		Triglycerides	
	Men	Women	Men	Women	Men	Women	Men	Women
Epinephrine								
Work	0.36*	0.06	0.23	0.26	0.20	−0.02	0.13	−0.17
Home	0.19	0.34	0.28	0.10	0.20	0.27	−0.26	0.21
Stress	−0.01	0.35	0.31	0.04	0.02	0.05	−0.41*	0.32
Rest	0.21	0.08	0.05	0.12	0.27	0.04	−0.19	−0.04
Norepinephrine								
Work	0.29	0.28	0.04	0.12	0.28	0.04	0.10	−0.04
Home	−0.03	0.07	−0.11	−0.20	0.01	0.14†	−0.09	0.11
Stress	−0.25	0.52†	−0.01	−0.11	−0.18	0.50†	−0.38*	0.40*
Rest	−0.20	0.26	−0.01	−0.10	−0.12	0.29	−0.41*	0.04
Cortisol								
Work	−0.04	−0.19	0.05	0.11	−0.01	−0.20	−0.13	−0.22
Home	−0.04	0.22	0.14	−0.07	−0.02	0.24	−0.24	−0.06
Stress	0.31	−0.20	0.28	−0.29	0.35	−0.07	−0.31	−0.16
Rest	0.17	0.07	0.27	−0.23	0.17	0.18	−0.27	−0.17

*$p<0.05$; †$p<0.01$.
Work: Day at work (9 a.m.–5 p.m.).
Home: Workfree day at home (9 a.m.–5 p.m.).
Stress: Experimental stress in the laboratory (60 min).
Rest: Resting in the laboratory (50 min).

of the menstrual cycle, the interpretation of the sex differences in Table 6 remains open.

Single significant correlations should be interpreted with caution. However, it is interesting to note that, in agreement with our findings, McKinney *et al.* (10) found that triglyceride levels correlated with DBP in a group of 50 patients.

Data on cardiovascular reactivity of the present subjects (6), show that subjects with total cholesterol levels above the group median were more reactive in terms of SBP than those below. This was true of both men and women. Taken together, our results show that in men, serum cholesterol was associated with both absolute SBP level and stress-induced change in SBP (reactivity), whereas in women reactivity only was related to cholesterol.

One "extreme" woman contributed very much to the correlation between blood lipids and catecholamine excretion during stress in the female group. However, correlations remained significant for norepinephrine after excluding her values. The corresponding correlations for men tended to be negative. These findings seem at variance with those of Fredrikson and Blumenthal (5), who found that male postinfarction patients with high total cholesterol/HDL ratios had higher resting levels of plasma catecholamines and greater increase during mental arithmetic than men with lower levels. Thus, the association between cholesterol level and catecholamine responses to stress remains unclear.

Below the age of 50–55 women have lower serum cholesterol levels (2), lower blood pressure and are less likely to develop CHD than men. Above this age these sex differences tend to disappear. In view of these established facts and the present findings, it seems particularly important to examine the association between different CHD risk factors in older men and women.

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