Effect of Posture on the Plasma Cholesterol Level

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Many studies of diet in relation to mortality from degenerative heart disease have shown that populations with high rates of coronary artery disease have high mean plasma cholesterol levels (Keys, 1957 ; Groen and Van der Heide, 1959). It is possible that the level of circulating cholesterol is causally related to the incidence and severity of coronary artery disease (Kannel *et al.*, 1964). Consequently there is considerable clinical interest in the plasma cholesterol level and in ways of lowering it.

It has long been known that changes in posture alter blood volume (Thompson *et al.*, 1928 ; Waterfield, 1931) and that there is a rise in concentration of plasma protein on changing from the lying to the standing position in man, due to a protein-poor fluid leaving the plasma under the influence of increased hydrostatic force (Fawcett and Wynn, 1960). As cholesterol in the plasma is non-filterable (Gerbrandy *et al.*, 1960), it seemed to us likely that its level in the plasma would vary with posture and that a failure to control this might mask the effect of treatment on the plasma cholesterol level. We therefore studied this together with estimations of plasma protein and haematocrit. In a few subjects the effect of posture on plasma calcium was also studied.

Subjects, Procedures, and Methods

Thirteen control subjects with normal levels of plasma protein and cholesterol and four patients with hypercholesterolaemia were studied. A plasma cholesterol level of 300 mg./100 ml. or more served to define the hypercholesterolaemic group. The tests were performed in the fasting state, blood samples being taken by means of an indwelling needle inserted into an antecubital vein at least 30 minutes before starting the test. This procedure avoided the need for venous compression. Most of the subjects had been recumbent since the previous evening ; in the remainder a minimum period of one hour in the horizontal position preceded the test.

The standard procedure (Fawcett and Wynn, 1960) was for the first two blood samples to be taken at a 15-minute interval with the subject lying down. The third sample was taken after a similar interval, during which the subject walked slowly about to ensure adequate circulation of blood in the lower extremities. The fourth sample was taken while the subject remained standing, after a sphygmomanometer cuff had been applied to the upper arm and inflated to 100 mg. Hg for two minutes with the hand kept clenched. Five postural studies were carried out in the reverse order—namely, the subjects, all of whom had been ambulant for at least one hour, had blood samples taken, and then resumed the horizontal position, blood being taken at five-minute intervals for 25 minutes.

Blood samples were collected into tubes containing lithium heparin, centrifuged, and the plasma separated. Plasma protein was determined by a semi-microKjeldahl method (Fawcett, 1954). Plasma cholesterol was estimated by Henly's (1957) modification of the method of Zlatkis *et al.* (1953) and plasma calcium by an ethylenediaminetetra-acetate titration method modified from the method of Wilkinson (1957). Estimations of cholesterol, plasma protein, and calcium were carried out at least in duplicate. For cholesterol the coefficient of variation (due to analytical error) was 1.4% for single determinations and 1% for means of duplicate determinations. The precision of the plasma protein and calcium estimations was also of this order. Haematocrit measurements were carried out in triplicate in Wintrobe tubes centrifuged at 3,000 r.p.m. for 30 minutes in a centrifuge of 14 cm. radius.

Effect of Changing from the Horizontal to the Vertical Position

The results are detailed in Tables I, II, and III. It can be seen (Table I) that there was no significant difference in plasma

TABLE I.—*Effect of Posture and Venous Compression on Plasma Cholesterol Level (mg./100 ml.)*

Subject	Lying			Standing		Standing with Venous Compression	
	A	B	Difference B–A	C	Difference C–B	D	Difference D–C
				Control Subjects			
1	168	163	−5	180	+17	191	+11
2	205	208	+3	233	+25	239	+6
3	124	—	—	131	—	131	0
4	176	178	+2	201	+23	211	+10
5	208	202	−6	237	+35	244	+7
6	100	99	−1	—	—	111	—
7	212	209	−3	225	+16	224	−1
9	156	157	+1	183	+26	168	−15
10	201	200	−1	229	+29	233	+4
11	158	155	−3	171	+16	176	+5
12	—	154	—	176	+22	195	+19
13	173	—	—	193	—	201	+8
Mean difference			−1·44		+23·2		+4·9
Standard deviation			3·09		6·41		8·56
t			1·4		10·9		1·9
			0·2 > P > 0·1		P < 0·001		0·1 > P > 0·05
				Hypercholesterolaemic Subjects			
15	471	448	−23	507	+59	523	+16
16	337	320	−17	370	+50	407	+37
17	300	294	−6	322	+28	340	+18
18	681	671	−10	720	+49	802	+82

TABLE II.—*Effect of Posture and Venous Compression on Plasma Protein Level (g./100 ml.)*

Subject	Lying			Standing		Standing with Venous Compression	
	A	B	Difference B–A	C	Difference C–D	D	Difference D–C
1	6·55	6·63	+0·08	7·0	+0·37	7·3	+0·3
2	6·9	6·9	0	7·8	+0·9	7·9	+0·1
6	7·5	7·5	0	8·6	+1·1	8·4	−0·2
7	8·3	8·3	0	8·1	−0·2	8·0	−0·1
8	7·58	7·61	+0·03	7·92	+0·31	—	—
9	7·58	7·50	−0·08	8·08	+0·58	8·32	+0·24
10	6·5	6·3	−0·2	7·3	+1·0	7·3	0
11	6·7	6·5	−0·2	7·1	+0·6	7·7	+0·6
12	—	5·94	—	7·4	+1·46	7·1	−0·3
15	7·4	7·4	0	8·7	+1·30	8·9	+0·2
17	6·53	6·90	+0·37	7·35	+0·45	7·5	+0·15
18	6·8	6·84	+0·04	7·2	+0·36	8·2	+1·0
Mean difference			+0·0036		+0·686		+0·18
Standard deviation			0·188		0·477		0·369
t			0·71		4·98		1·62
			0·5 > P > 0·2		P < 0·01		0·2 > P > 0·1

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cholesterol level between the two samples, A and B, taken before there was a change of posture (0.2>P>0.1). Subsequent differences were therefore attributed to change in posture or to venous compression. In the control subjects the mean rise of plasma cholesterol after 15 minutes in the vertical position was 12.9%, and the range 7.7–17.3%. The mean rise of plasma protein level (Table II) was 8.5% (range 2.4–17.6%) and of haematocrit (Table III) 8.6% (range 4.9–14.7%). These changes are all statistically significant. In the hypercholesterolaemic group (Table I) the mean percentage rise of cholesterol was also 12.9%, with a range of 7.3–21.9%.

Venous occlusion applied in the vertical position caused a further rise of plasma cholesterol in 8 out of the 11 control subjects tested, but the rise was not statistically significant. Venous compression produced a further substantial rise in plasma cholesterol in all four hypercholesterolaemic subjects.

TABLE III.—*Effect of Posture and Venous Compression on Haematocrit* (%)

Subject	Lying			Standing		Standing with Venous Compression	
	A	B	Difference B–A	C	Difference C–B	D	Difference D–C
1	40·9	40·7	−0·2	43·7	+3·0	45·9	+2·2
2	42·5	42·5	0	45·7	+3·2	46·7	+1·0
6	39·2	38·2	−1·0	43·2	+5·0	43·0	−0·2
7	40·0	39·0	−1·0	41·5	+2·5	41·7	+0·2
8	39·3	40·0	+0·7	42·0	+2·0	—	—
9	36·0	36·5	+0·5	38·3	+1·8	39·2	+0·9
10	34·0	34·0	0	37·0	+3·0	37·4	+0·4
11	45·9	44·7	−1·2	48·6	+3·9	50·4	+1·8
12	—	38·7	—	44·4	+5·7	45·2	+0·8
13	29·5	29·4	−0·1	33·4	+4·0	32·7	−0·7
15	41·7	41·3	−0·4	44·7	+3·4	—	—
17	33·9	34·6	+0·7	36·9	+2·3	40·6	+3·7
18	42·5	42·0	−0·5	45·7	+3·7	46·5	+0·8
Mean difference			−0·208		+3·34		+1·12
Standard deviation			0·647		1·17		1·09
.. .. ..			1·11		10·03		3·41
			0·5 > P > 0·2		P < 0·001		P < 0·01

TABLE IV.—*Effect of Posture and Venous Compression on Plasma Calcium Level (mg./100 ml.)*

Subject	Lying	Standing		Standing with Venous Compression	
	B	C	Difference C–B	D	Difference D–C
1	9·3	9·9	+0·6	9·8	−0·1
2	9·3	9·7	+0·4	9·8	+0·1
13	8·7	9·3	+0·6	9·2	−0·1
14	9·4	10·7	+1·3	10·3	−0·4
15	9·3	9·7	+0·4	10·0	+0·3
17	11·8	12·0	+0·2	—	—

The effect of assuming the vertical position on the plasma calcium level is shown by the results in six subjects in Table IV. A mean rise of 0.50 mg./100 ml. (6.7%, range 3.4–13.8%) occurred without further effect from additional venous compression.

Effect of Changing from the Vertical to the Horizontal Position

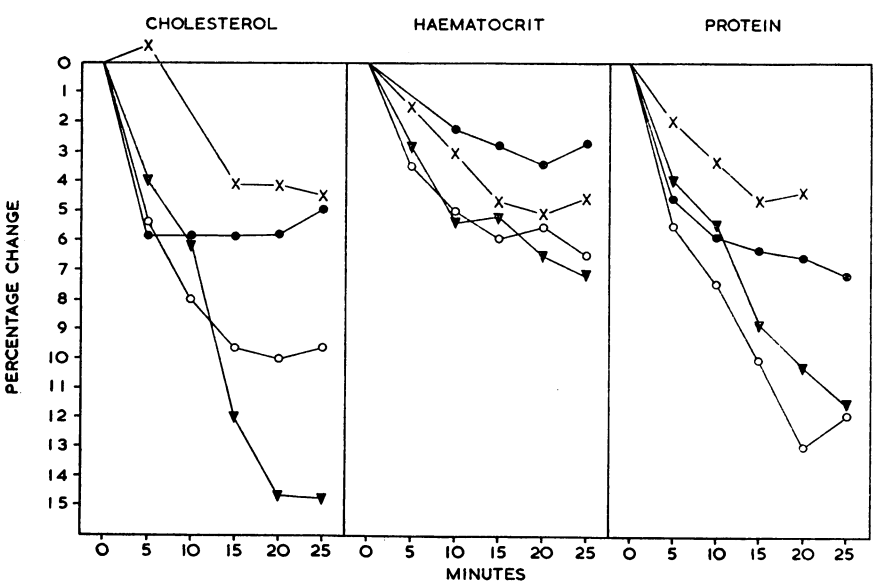
Four control subjects were studied by observing the plasma levels of cholesterol and protein and the haematocrit when the posture was changed from vertical to horizontal. The results, shown in the Chart, suggest that though certain of the falls in concentration were completed earlier most of the subjects required 20 minutes in the lying position for the achievements of basal levels.

Discussion

These data show that standing for a quarter of an hour results in a mean increase of 12.9% in the circulating cholesterol level, which is statistically highly significant, and that this is accompanied by similar rises in protein level and haematocrit, and to a lesser degree (6.7%) in calcium level, which are consistent with the finding that less than half of the plasma calcium is not filterable (Gerbrandy *et al.*, 1960). The reverse effect occurs when the subject lies down. Our subjects did not remain completely still when they were vertical, as in stationary subjects haemoconcentration is greater in the leg than in the arm (Youmans *et al.*, 1934).

Over the years various workers have reported " spontaneous " fluctuations in blood lipid levels and especially cholesterol values (McEachern and Gilmour, 1932 ; Peterson *et al.*, 1960). These changes have occurred without regard to treatment, dietary change, unusual stress, or intercurrent illness, and seem to be particularly marked in patients with hypercholesterolaemia. Changes over a few hours have been attributed to normal diurnal variation (Shapiro *et al.*, 1959) and stress (Peterson *et al.*, 1962). Segall and Neufeld (1960) reported falls in cholesterol levels in two patients observed over several years during periods in hospital, and thought this observation was not in favour of a rise in plasma cholesterol with stress. In contradistinction to the above reports, Turner and Steiner (1939) found remarkable constancy of serum cholesterol levels over 24-hour periods. In these reports of serial blood cholesterol estimations we have found no reference to the position of the patient when blood was withdrawn. It seems probable that in some groups—for example, patients in hospital and blood donors—blood is more likely to be withdrawn with the patient in the horizontal position. The findings of Segall and Neufeld (1960) of a fall in serum cholesterol of 15.7%, 31.4%, and 22.5% respectively in three patients admitted to hospital for treatment of chest pains, and that of Nicolaysen and Westland (1963) that the level of cholesterol in blood donors was between 10% and 20% below that of other groups studied, suggest that part, at least, of the difference could have been due to postural cause.

Fawcett and Wynn (1960) showed that variations in protein and haematocrit due to changes in posture are complete in 15 minutes in the normal subject, and we assume that the same is true for cholesterol. These workers also showed that variations in plasma volume due to changes in posture were greater when there was hypoalbuminaemia, and that the full change takes as long as an hour to develop. Eisenberg (1963) confirmed the



Percentage changes in haematocrit and in plasma cholesterol and protein levels in four normal subjects on changing from the vertical to the horizontal posture.

importance of hypoalbuminaemia in these postural shifts. While we have not studied this point in the present work, it is likely that variations in cholesterol level due to postural changes will be greater in patients with reduced plasma albumin levels than in healthy people. In view of the relationship of plasma cholesterol concentration to plasma volume change, the recent work of Eisenberg and Wolf (1965) is of interest. These authors showed that in quiet standing the decrease in plasma volume in a hypertensive group of subjects (13.2%) significantly exceeded that in their normal group (7.3%). Though cholesterol levels were not estimated, one would expect rises commensurate with those they observed in serum protein and haematocrit. The significance of these findings lies in the fact that hypertensive patients are likely to be assessed for evidence of coronary artery disease and raised plasma cholesterol levels, and changes in these levels due to the influence of posture are likely to be greater in them than in normal subjects.

The effect of local venous hydrostatic changes on withdrawing blood from a dependent limb has been studied by Eisenberg (1963) by estimation of haematocrit and serum protein levels. The rise in concentration of these values is in accord with the rise we found over the levels in the vertical subject after increasing venous pressure. Venous compression, without reference to postural alterations, has been shown to cause significant increases in plasma protein, cholesterol, and calcium (Gerbrandy, 1960) and in plasma protein and cholesterol (Koerselman *et al.*, 1961 ; Page and Moinuddin, 1962). For example, Page and Moinuddin (1962) applied sphygmomanometer-cuff pressure of 100 mm. Hg and after five minutes found a rise in concentration of cholesterol of 5.4–19.8% and a 6–20% rise of plasma protein concentration.

The demand for serial estimations of blood cholesterol will not diminish in the foreseeable future. The Framingham study (Kannel *et al.*, 1964) has shown that neither the various lipid indices nor independent lipid levels surpassed the serum cholesterol level as the most important contributor to risk of coronary artery disease. If for this reason added significance is to be placed on the circulating cholesterol level, it is important to exclude the uncontrolled effect of posture. As one would expect the findings to apply equally to all protein and protein-bound constituents of the blood, ideally one should advise a period of some 20 minutes' lying down for the patient before a blood sample is withdrawn, with a minimum of venous compression.

Summary

When the posture is changed from lying to standing for a quarter of an hour a mean increase of 12.9% in the level of plasma cholesterol results in normal subjects. A similar change occurs in the haematocrit and plasma protein levels, and, by inference, in all non-filterable elements of the blood. The reverse process occurs on lying down, though it takes rather longer. The significance of these findings is discussed, especially with regard to serial readings during attempts to reduce the blood cholesterol level.

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Medical Memoranda

Hypotension after Exercise

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Ever since Bradbury and Eggleston (1925) described the syndrome of orthostatic hypotension the mechanism of functional derangement has been the subject of numerous physiological studies. In the case presented here the clinical picture was dominated by neurological symptoms due to a profound fall in blood-pressure after exercise. With variations in posture, changes in the filling pressure of the right atrium preceded alterations in arterial pressure, an order of events suggesting a disturbance of venous tone.

Case Report

A 55-year-old police inspector complained of transient visual disturbances for two years. Sometimes he saw coloured lights, and on other occasions there was blurring, lack of colour, and constriction of the visual fields. These episodes were bilateral, lasted one to five minutes, and usually occurred when he rested after exertion. They were often accompanied by a sensation of unsteadiness, though he never fell or lost consciousness. Occasionally they were associated with dysarthria, and once with dysphagia. He had noticed poor sweating for 10 years, and he had been impotent for three years.

Examination revealed a dry skin, with a Parkinsonian facies. The only other abnormalities were mild rigidity of the right arm and lack of facility with repetitive movements in the right hand and foot. There was no tremor.

Routine blood and urine studies were normal, including glucose-tolerance test and W.R. There was no significant abnormality in radiographs of the skull, cervical spine, or chest. Sweating could be provoked all over the body, though the response was poor in the face, hands, and feet.

The following vascular reflexes were observed.

Posture.—When the patient got himself up from lying to standing there was a fall of 12 mm. Hg in right atrial pressure, recorded from a cardiac catheter. This was accompanied by a rather slower