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HÆMODYNAMIC EFFECTS OF NITROGLYCERIN IN PATIENTS WITH CORONARY HEART DISEASE

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The usefulness of nitroglycerin (glyceryl trinitrate) in relieving angina pectoris is undisputed: it has one of the clearest pharmacological effects in man. However, the mechanism of its action is not well understood (Gorlin, 1962; Case and Roven, 1963). In animal experiments the nitrites cause relaxation of smooth muscle, notably in the vessels, and an increased coronary flow can easily be demonstrated (Charlier, 1961). However, it is doubtful whether nitroglycerin relieves angina pectoris by dilatation of the coronary arteries. In the first place, ischæmia by itself provides a very powerful vasodilator stimulus due to the accumulation of vasodilating substances in the anoxic tissue, so that it is unlikely that artificial vasodilator agents can act upon vessels already under a maximal influence of endogenous metabolites. An action of nitroglycerin on the larger arteriosclerotic coronary arteries also seems unlikely. Another mechanism of action of nitrites may be through reduction of the work of the heart. Brunton (1867) pointed out that amyl nitrite diminished the tension of the pulse, and it has also been found that the cardiac output at rest is decreased after nitroglycerin (Gorlin, 1962).

Other mechanisms of action have also been proposed but so far none has been found acceptable, and the general opinion appears to favour a direct dilatation of coronary vessels (or collaterals) in combination with a reduction of cardiac work as the most likely mode of action of nitrites.

In the course of a study of the hæmodynamic pattern during exercise in patients with coronary heart disease it was sometimes necessary to give nitroglycerin. Observations could, therefore, be made of the action of the drug on cardiac output and arterial blood pressure during exercise in such patients. Similar observations have apparently not been made hitherto. A short account of the main findings has been given (Christensson, Karlefors, and Westling, 1964).

Subjects and Methods

The subjects were examined 2 to 3 hours after a light morning meal. Polythene tubes were inserted in one or both brachial arteries (Bernéus *et al.*, 1954) under local anæsthesia. Another tube was put into a cubital vein and advanced to the subclavian vein or the right atrium. Expired air was collected in Douglas bags and analysed for O_2 and CO_2 content according to Scholander. Cardiac output was measured with the indicator dilution technique. Bromsulphalein was injected into the venous tube and arterial blood samples were taken every second by free flow into small test-tubes in a rotating disk (Wassén, 1956). Arterial pressures were registered by inductance manometers and recorded, with the electrocardiogram, on an ink-writing electrocardiograph (equipment: AB Elema, Stockholm, Sweden). The experimental procedure will be described in the results. Exercise tests in the recumbent position were carried out on the examination table. The patient was pedalling an electrically-braked bicycle ergometer (AB Elema) with the centre of

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rotation approximately at heart level. Exercise tests in the sitting position were carried out in the "natural position" for bicycling.

The subjects comprised 32 patients with angina pectoris of varying degree. The mean age was 52, range 41–67 years. Most of them were incapacitated and admitted to the Cardiology Department for consideration of surgical therapy. All patients were used to the action of glyceryl trinitrate and took it to relieve anginal pain. A clinical diagnosis of previous infarction had been made in slightly more than half of them. The resting arterial blood pressure was normal in all; cardiac enlargement was seen on chest radiograph in 6. Coronary arteriography was performed and pathological changes were present in all patients. Occlusion of a main coronary branch was observed in two-thirds.

The effect of nitroglycerin at rest was studied in 19 patients. Of these, 7 were also studied during recumbent exercise and 4 during sitting exercise (at a later examination). Observations on the effect of nitroglycerin during recumbent exercise were also made in 7 patients not studied at rest. In addition to the 4 also studied at rest, observations during sitting exercise were made on 6 not studied previously and in 2 studied during recumbent exercise at a previous examination. Six patients had been operated on for cardiopericardiopexy (Beck-I procedure, as described by Hallén, 1964) between the first and second examination, as indicated in the Tables.

The hæmodynamic effects of nitroglycerin at rest were also examined in 5 healthy volunteers.

Results

1. *Effects of Nitroglycerin at Rest* (*Tables I and II**). In 19 patients the hæmodynamic effects were studied at rest in the horizontal position. In all 19 nitroglycerin (0·5 mg. sublingually) caused a fall in arterial blood pressure with a diminished pulse amplitude and a slight increase in pulse rate. The cardiac output was measured after 4 to 6 minutes and was decreased in 14 patients; the stroke volume decreased in all 19. It was found that the patients with more severe coronary insufficiency tended to have a relatively bigger fall in cardiac output and stroke volume, especially in comparison with the group of normal subjects (Table III) in which hardly any change occurred in these parameters.

The blood pressure decreased largely in parallel with the cardiac output; thus major changes in total systemic vascular resistance should not have occurred.

2. *Effects of Nitroglycerin During Exercise. Supine position* (*Tables IV–VI*). Most of the patients were subjected to an exercise test in the supine position. Circulatory measurements were made at the 4th to 8th minute of exercise. Two tests were carried out with an interval of about 45 minutes, one of them being preceded by giving the patient 0·5 mg. nitroglycerin sublingually. Half the patients were given nitroglycerin before the first exercise and the other half before the second test. This was done to eliminate the influence of a systematic difference between the two exercise tests. Table IV shows that there was in fact a tendency towards a lower cardiac output and arterial pressure during the second exercise. However, differences were not significant.

Exercise under the influence of nitroglycerin differed significantly from the control test in the following respects: lower cardiac output and stroke volume and a higher calculated arteriovenous difference in oxygen content. After excluding 2 patients, because the time between nitroglycerin administration and circulatory measurements was more than 10 minutes and 2 others because the work intensity was 150 kilopond-metres/min. (kpm), the average changes become larger (Table VI).

The incidence of anginal pain is shown in Table VII. Pain occurred only in exercise tests that were not preceded by nitroglycerin. Eight instances of anginal pain occurred in 14 tests without nitroglycerin, 5 in the first and 3 in the second test.

Sitting position (*Tables VIII and IX*). In view of the probable mode of action of nitroglycerin, it was felt that an examination of the effects of the drug during exercise in the sitting position might be worth while. Twelve patients were subjected to exercise for 8 to 10 minutes in the sitting position. After a steady pulse rate had been reached, the first determination of cardiac output was made after about 4 minutes of exercise. Without interrupting exercise, nitroglycerin was given to 6 patients (the remaining 6 had an inert pill) and a new determination of cardiac output was made 4 to

* All 9 Tables are set out at the end of the paper in an Appendix.

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5 minutes later. It will be seen (Table IX) that nitroglycerin caused an increase in pulse rate, a fall in cardiac output, and thus a big reduction in the stroke volume (Fig. 1). In fact, nitroglycerin decreased the cardiac output during sitting exercise to values that were often similar to those at rest in the supine position. Arterial mean pressure was slightly decreased. Oxygen consumption was measured during sitting exercise in 3 patients only, 2 of whom had been given nitroglycerin. The oxygen uptake was unchanged after nitroglycerin in these 2; as was the case in the patients studied in the supine position. Since the cardiac output decreased considerably during sitting exercise, it is likely that the arteriovenous difference in oxygen content reached quite high values.

In 3 of the 6 patients given nitroglycerin moderate anginal pain had developed during the 3rd to 4th minute of exercise. The administration of nitroglycerin led to a disappearance of

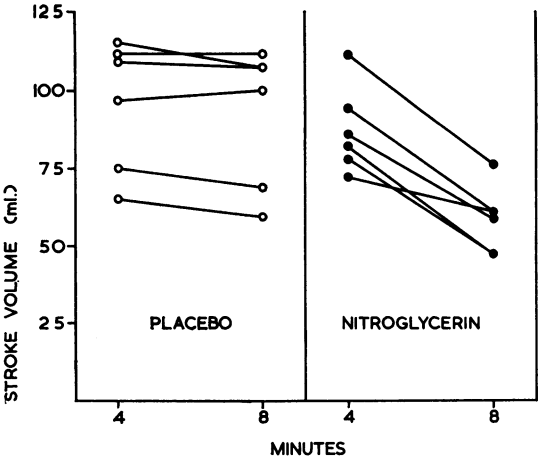

FIG. 1.—Changes in stroke volume after nitroglycerin during sitting exercise. Measurements were made at 4 and about 8 minutes of continuous exercise. Note that the administration of an inert pill between the measurements had hardly any effect on stroke volume, whereas there was a considerable fall after nitroglycerin.

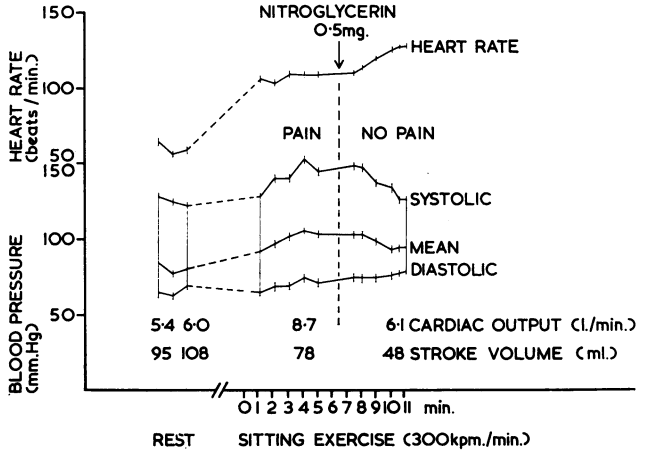

FIG. 2.—Hæmodynamic response to 0·5 mg. nitroglycerin sublingually during sitting exercise.

pain, in spite of continued exercise at the same intensity. Fig. 2 shows the development of the circulatory effects of nitroglycerin during exercise. The pulse rate increased and the pulse amplitude decreased, both at 1 to 2 minutes after giving nitroglycerin. At the same time the patient reported "easing" of chest pain. At the time when the maximal effect of nitroglycerin had developed pain was entirely absent.

The hæmodynamic changes seen after giving the inert pill were small (Table IX) and may be regarded as representative for the errors in the methods used.

DISCUSSION

It appears certain from the present observations on patients with ischæmic heart disease that the principal effect of nitroglycerin at rest and during exercise is on the stroke volume and the output

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of the heart. The reduction of the arterial blood pressure was relatively small and less pronounced than the fall in cardiac output. Thus the total vascular resistance in the systemic circulation is likely to have increased after nitroglycerin. This may be taken as evidence against arteriolar dilatation. On the contrary, available evidence indicates that the most important primary mechanism of action of nitroglycerin is to diminish venous tone. The action of nitrites on the venous system was described many years ago by Weiss, Wilkins, and Haynes (1937) and Wilkins, Haynes, and Weiss (1937) and has been studied further by Sharpey-Schafer and Ginsburg (1962), Åblad and Johnsson (1963), and Åblad, Henning, and Johnsson (unpublished observations, 1964).

A reduction of the venous tone should lead to a diminished cardiac filling. This effect should be more pronounced in the vertical position. The present experiments indicate that such an influence of posture can be demonstrated during exercise in subjects with coronary heart disease, since the actions of nitroglycerin were more pronounced in patients who bicycled in the "natural position" than in those who pedalled with the legs at heart level.

The difference in response to nitroglycerin at rest between normal subjects and patients with ischæmic heart disease is worthy of comment. Since the healthy subjects were younger than the patients, too much emphasis must not be laid upon this finding, but the possibility obviously exists that patients with coronary heart disease are more sensitive to the actions of nitroglycerin. This might depend upon an increased venous tone (c.f. Radó, Gonda, and Kovács, 1958). Further experiments, particularly on normal subjects during exercise, are required to solve this problem.

In our opinion, the results obtained give strong support for the view that nitroglycerin may relieve angina pectoris by reducing the work of the heart. Some subjects studied here were thus able to perform an exercise which normally caused severe anginal pain, with a cardiac output that was not much different from that at rest when they were free from pain. The reduction of cardiac output must mean that the exercise during nitroglycerin was performed with a high arteriovenous oxygen difference. Nitroglycerin might thus be regarded as a drug that makes the circulatory system more economical as regards flow and pressures.

Attempts at calculation of left ventricular work were not made, since the present observations were not detailed enough; in particular the left ventricular filling pressure was not known. However, the reduction in stroke volume and ejection pressure in combination with the probable reduction in ventricular volume should have caused a considerable decrease of the energy demands of the left ventricle (Levine and Wagman, 1962), especially in the sitting position.

Summary

The hæmodynamic effects of 0·5 mg. nitroglycerin (glyceryl trinitrate) sublingually have been examined at rest (19 patients) and during exercise on a bicycle ergometer with the patient supine (14 patients) or sitting (6 patients) on the bicycle. Arterial blood pressure, cardiac output (indicator dilution technique), and oxygen consumption were measured.

At rest the cardiac output and stroke volume decreased after nitroglycerin. A moderate tachycardia and a slight decrease in mean arterial pressure occurred. After nitroglycerin, exercise in the supine position was performed with a lowered cardiac output and stroke volume and a higher calculated arteriovenous O_2-difference. These effects were more pronounced in the sitting position.

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APPENDIX

TABLE I

PHYSIOLOGICAL CHARACTERISTICS AND HÆMODYNAMIC OBSERVATIONS IN 19 PATIENTS WITH CORONARY HEART DISEASE AT REST IN SUPINE POSITION BEFORE AND AFTER ADMINISTRATION OF 0·5 MG. NITROGLYCERIN SUBLINGUALLY

Case No.	Age (yr.)	B.S.A. ($m.^2$)	Min. after nitroglycerin	Heart rate (beats/min.)	Cardiac output (l./min.)	Stroke volume (ml./min.)	Pressure in brachial artery (mm. Hg)			Oxygen uptake (ml./min.)
							S	D	Mean	
1	63	1·80	—	78	6·6	85	157	70	107	—
			4·0	83	4·6	55	143	74	83	—
2	53	1·85	—	70	4·3	61	147	68	95	—
			4·0	97	3·6	37	81	52	70	—
3	53	1·96	—	72	7·4	103	128	62	85	—
			4·0	80	6·5	81	126	73	92	—
4	56	1·96	—	57	6·5	114	150	65	101	—
			4·5	78	5·5	71	114	67	78	—
6	55	2·01	—	72	7·8	108	142	76	109	—
			4·0	103	6·3	61	124	84	100	—
8	57	1·70	—	77	5·3	69	127	69	91	—
			4·5	85	4·2	49	114	70	88	—
9	48	1·80	—	69	4·0	58	115	60	84	—
			4·0	73	4·0	55	119	64	82	—
10	53	2·28	—	58	6·4	110	138	69	90	—
			3·5	69	6·7	97	116	63	84	—
11	65	2·10	—	64	6·7	105	140	65	101	—
			4·5	80	6·7	84	128	75	96	—
12	59	1·85	—	64	4·4	69	133	73	98	—
			4·0	75	4·1	55	116	70	93	—
13	51	1·61	—	82	4·0	49	141	85	107	—
			4·0	106	3·0	28	119	81	94	—
14	45	2·00	—	80	5·8	73	—	—	90	—
			5·0	102	5·1	50	109	74	83	—
15	55	1·77	—	60	5·1	85	129	67	94	
			4·0	70	4·8	69	110	64	82	—
17	52	1·95	—	50	5·8	116	99	57	74	—
			7·0	63	4·9	78	90	58	70	—
20	55	1·92	—	74	5·4	73	123	76	95	287
			4·0	82	5·7	70	118	74	88	290
22	50	2·05	—	52	5·2	100	—	—	80	—
			3·5	78	3·6	46	97	60	70	—
23	55	1·94	—	91	5·4	59	140	93	113	—
			4·5	115	3·9	34	—	—	106	—
24	54	1·82	—	74	5·3	72	100	66	78	296
			5·0	83	5·4	65	95	64	73	295
25	61	1·89	—	93	5·3	57	93	59	74	300
			4·5	104	4·8	46	76	50	64	234

B.S.A. is body surface area.

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TABLE II

SUMMARY OF HÆMODYNAMIC EFFECTS OF NITROGLYCERIN AT REST IN 19 PATIENTS WITH CORONARY HEART DISEASE

	Mean value before nitroglycerin	S.E.M.*	No of observations	Mean change caused by nitroglycerin	S.E.M. of difference	No. of observations	p value
Pulse rate (beats/min.)	70	2·7	19	+15	1·9	19	<0·001
Cardiac output (l./min.)	5·6	0·25	19	−0·7	0·15	19	<0·001
Cardiac index (l./min./m.²)	2·9	0·11	19	−0·4	0·08	19	<0·001
Stroke volume (ml.)	82	5·1	19	−23	3·3	19	<0·001
Stroke index (ml./m.²)	43	2·2	19	−12	1·6	19	<0·001
Arterial blood pressure (mm. Hg)							
systolic	130	4·5	17	−17	4·0	16	<0·001
diastolic	69	2·2	17	±0	1·8	16	—
mean	93	2·7	19	−9	1·8	19	<0·001

* Standard error of the mean.

TABLE III

SUMMARY OF HÆMODYNAMIC EFFECTS OF NITROGLYCERIN IN 5 HEALTHY MALE VOLUNTEERS (AGED 22, 22, 27, 47, AND 51) AT REST IN SUPINE POSITION

	Mean value before nitroglycerin	S.E.M.	Mean change caused by nitroglycerin	S.E.M. of difference	p value
Pulse rate (beats/min.)	61	3·2	+7·6	2·0	<0·05
Cardiac output (l./min.)	5·4	0·42	+0·4	0·30	—
Cardiac index (l./min./m.²)	2·9	0·22	+0·2	0·18	—
Stroke volume (ml.)	89	3·4	−3	6·2	—
Stroke index (ml./m.²)	48	1·7	−1·4	3·2	—
Arterial blood pressure (mm. Hg)					
systolic	120	3·1	−7	4·6	—
diastolic	72	2·9	±0	4·7	—
mean	90	3·0	−2	3·7	—

TABLE IV

SUMMARY OF HÆMODYNAMIC CHANGES IN TWO EXERCISE TESTS

	Mean value for first exercise*	S.E.M.	No. of observations	Mean difference between 1st and 2nd exercise	S.E.M. of difference	No. of observations	p value
Pulse rate (beats/min.)	102	4·30	14	2·6	2·8	14	—
Cardiac output (l./min.)	9·1	0·4	14	0·65	0·5	14	—
Stroke volume (ml.)	92	6·2	14	6·6	5·5	14	—
Arterial blood pressure (mm. Hg)							
systolic	152	5·2	14	4·6	4·0	14	—
diastolic	81	2·3	14	1·0	3·0	14	—
mean	110	3·8	14	3·6	2·4	14	—
Oxygen consumption (ml./min.)	944	21·5	11	32	42	11	—
Arteriovenous oxygen difference; calculated (ml./l.)	103	5·4	11	−6·4	6·1	11	—

* 7 patients with and 7 without nitroglycerin.
14 patients: 7 performed first exercise without and second preceded by 0·5 mg. nitroglycerin; and in 7 others the procedure was reversed. Recumbent exercise, 300 kpm/min. in 12, 150 kpm/min. in 2 patients.

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TABLE V: PHYSIOLOGICAL CHARACTERISTICS AND HÆMODYNAMIC OBSERVATIONS IN 14 PATIENTS WITH CORONARY HEART DISEASE DURING EXERCISE IN SUPINE POSITION BEFORE AND AFTER ADMINISTRATION OF 0·5 MG. NITROGLYCERIN (Ni) SUBLINGUALLY

Case No.	Age (yr.)	B.S.A. (m^2)	Order of exercise	Treatment	Time interval† (min.)	Heart rate (beats/min.)	Cardiac output (l./min.)	Stroke volume (ml.)	Pressures brachial artery (mm. Hg) S	D	Mean	Oxygen uptake (ml./min.)	Art.-ven. oxygen diff. (calculated) (ml./l.)
1*	65	1·75	I	Ni	5·5	112	7·5	67	140	80	107	999	133
			II	—	—	106	6·2	59	150	79	107	649	105
6*	56	2·01	I	—	—	104	11·0	106	166	81	116	980	89
			II	Ni	12·0	94	8·3	88	141	74	102	832	100
15	55	1·77	I	Ni	14·0	89	8·9	100	146	73	104	—	—
			II	—	—	85	8·0	94	148	77	109	—	—
16	44	2·32	I	—	—	79	9·1	115	142	82	113	—	—
			II	Ni	14·0	86	7·2	84	144	85	114	—	—
20	55	1·92	I	—	—	89	11·5	129	160	80	108	938	82
			II	Ni	6·5	85	8·7	102	142	68	94	901	104
22	50	2·05	I	—	—	87	11·0	126	149	75	106	884	80
			II	Ni	6·0	90	8·4	93	142	85	104	882	105
24	54	1·82	I	—	—	91	10·0	110	142	72	103	1060	106
			II	Ni	6·0	97	7·2	74	123	68	87	1090	151
25	61	1·89	I	—	—	121	8·3	69	110	50	78	817	98
			II	Ni	6·5	116	9·1	78	121	68	82	936	103
26	56	1·96	I	Ni	5·0	135	9·9	73	193	108	142	894	90
			II	—	—	102	10·0	98	183	88	131	900	90
27	46	1·87	I	Ni	6·5	90	8·9	99	136	75	106	937	105
			II	—	—	92	9·6	104	165	92	119	1100	114
28	62	1·94	I	Ni	5·5	94	6·3	67	145	91	104	—	—
			II	—	—	92	9·9	108	133	79	103	—	—
31	46	1·84	I	Ni	7·0	116	9·2	79	155	91	112	937	102
			II	—	—	112	9·9	88	159	87	115	820	83
32	53	1·87	I	Ni	6·0	116	7·4	64	167	99	128	898	121
			II	—	—	118	7·7	65	153	90	116	909	118
39	49	1·98	I	—	—	104	8·1	78	172	78	115	1030	127
			II	Ni	5·5	116	7·8	67	156	81	108	1020	130

Work intensity 300 kpm/min.; in Case 1 and 6, 150 kpm/min.

The statistical values in Table VI are based upon the data from the last 10 patients above, because of the difference in work intensity (Case 1 and 6) and the longer duration between administration of nitroglycerin and the estimation of cardiac output (Case 15 and 16). The statistical values in Table IV are based on all 14 patients.

* Patients operated *ad modum* Beck (cardio-pericardiopexy).

† The time between the administration of nitroglycerin (Ni) and the determination of cardiac output.

TABLE VI: SUMMARY OF HÆMODYNAMIC EFFECTS OF NITROGLYCERIN DURING RECUMBENT EXERCISE*

	Mean value during control exercise	No. of observations	Mean change caused by nitroglycerin	S.E.M. of difference	No. of observations	p value
Pulse rate (beats/min.)	101	10	+4·7	3·5	10	—
Cardiac output (l.min.)	9·6	10	−1·3	0·47	10	<0·05
Cardiac index (l./min./m^2)	5·0	10	−0·7	0·25	10	<0·05
Stroke volume (ml.)	98	10	−18	5·2	10	<0·01
Stroke index (ml./m^2)	50	10	−9	2·7	10	<0·01
Arterial blood pressure (mm. Hg)						
systolic	153	10	−5	5·0	10	—
diastolic	79	10	+4	3·9	10	—
mean	109	10	−3	3·1	10	—
Oxygen uptake (ml./min.)	940	9	+3	28·0	9	—
Arteriovenous oxygen difference; calculated (ml./l.)	100	9	+12	5·4	9	—

* Same observations as in Table IV (see text).

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TABLE VII

INCIDENCE OF ANGINAL PAIN DURING RECUMBENT EXERCISE

	Exercise Tests			Nitroglycerin		
	First	Second	Total	Without	With	Total
Anginal pain	5	3	8	8	0	8
No pain	9	11	20	6	14	20
Total	14	14		14	14	

Two exercise tests in 14 patients. Experimental procedure is described in Table IV. Hæmodynamic observations are given in Tables IV and VI.

TABLE VIII

PHYSIOLOGICAL CHARACTERISTICS AND HÆMODYNAMIC OBSERVATIONS IN 12 PATIENTS WITH CORONARY HEART DISEASE DURING EXERCISE IN THE SITTING POSITION (WORK INTENSITY 300 KPM/MIN.)

Case No.	Age (yr.)	B.S.A. ($m.^2$)	Time of exercise† (min.)	Treatment	Time interval‡ (min.)	Heart rate (beats/min.)	Cardiac output (l./min.)	Stroke volume (ml.)	Pressures brachial artery (mm. Hg)			Oxygen uptake (ml./min.)
									S	D	Mean	
3*	55	2·01	3·0	—	—	108	9·3	86	150	83	105	—
			7·0	Ni	3·5	130	7·7	59	122	78	95	—
7*	58	1·98	5·0	—	—	112	8·7	78	149	76	108	—
			10·5	Ni	4·0	128	6·1	48	128	78	96	—
33	41	1·89	4·5	—	—	98	8·1	83	145	75	109	—
			10·0	Ni	3·5	135	6·5	48	122	83	99	—
35	50	1·97	5·5	—	—	75	8·4	112	129	76	101	—
			12·0	Ni	5·5	86	6·5	76	124	80	95	—
43	65	1·76	6·0	—	—	82	7·9	96	183	89	118	1140
			12·0	Ni	5·0	108	6·5	60	135	85	107	1090
44	40	1·76	5·0	—	—	120	8·7	73	176	88	111	987
			12·0	Ni	5·0	155	9·2	59	144	81	105	968
11	67	2·08	4·0	—		95	9·3	98	145	70	95	—
			10·0	Placebo		102	10·1	99	145	70	97	—
12*	60	1·82	4·5	—		104	7·8	75	181	90	121	—
			9·5	Placebo		110	7·7	70	163	72	104	—
14*	46	1·96	5·0	—		126	8·2	65	133	75	101	—
			9·0	Placebo		123	7·2	59	136	78	99	—
16	45	2·35	4·5	—		92	10·2	111	163	100	123	1150
			12·0	Placebo		97	10·5	108	159	96	123	1160
20	56	1·96	4·0	—		82	9·4	115	149	65	95	—
			8·5	Placebo		83	8·9	107	141	65	98	—
40	50	1·86	5·0	—		90	10·1	112	168	78	100	—
			10·0	Placebo		95	10·5	111	162	79	101	—

* Patients operated *ad modum* Bech (cardio-pericardiopexy).
† Indicates the time point during exercise, when the hæmodynamic observations were made.
‡ The time between administration of nitroglycerin and the determination of cardiac output.

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TABLE IX

SUMMARY OF HÆMODYNAMIC EFFECTS OF NITROGLYCERIN DURING SITTING EXERCISE

	Mean value during exercise before nitroglycerin	Change after nitroglycerin mean±S.E.M.	p value	Mean value during exercise before placebo	Change after placebo: mean±S.E.M.	p value
Pulse rate (beats/min.)	99	+25·0±4·2	<0·01	98	+4·0±1·5	—
Cardiac output (l./min.)	8·5	− 1·4±0·42	<0·05	9·2	±0·0±0·27	—
Cardiac index (l./min./m.^{2})	4·5	− 0·7±0·22	<0·05	4·6	±0·0±0·14	—
Stroke volume (ml.)	88	−30·0±3·5	<0·001	96	−4·0±1·4	—
Stroke index (ml./m.^{2})	47	−16·0±2·1	<0·001	48	−2·0±0·8	—
Arterial blood pressure (mm. Hg)						
systolic	155	−26·0±5·8	<0·01	157	−6·0±3·0	—
diastolic	81	− 0·3±2·4	—	80	−3·0±3·1	—
mean	109	− 9·0±1·1	<0·001	106	−2·0±3·1	—

Work intensity 300 kpm/min. 6 patients were given nitroglycerin and 6 placebo. 6 observations in all groups.

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