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The Circulatory Effects of Electrically Induced Changes in Ventricular Rate at Rest and during Exercise in Complete Heart Block *

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Measurements of the cardiac output in patients with congenital heart block were first made by indirect methods (1, 2), and later in a few patients by right heart catheterization at rest (3–5) and during exercise (6). These studies showed that the stroke volume was large and the cardiac output and pulmonary arterial and wedge pressures were normal at rest (3, 4) and during exercise (6). The rise in cardiac output during exercise was achieved mainly by the increase in ventricular rate which is characteristic of the congenital, but not the acquired, form of heart block (6, 7).

The acquired differs from the congenital form in that it occurs in an older age group, has a poorer prognosis, is often associated with underlying myocardial damage, and sometimes with congestive cardiac failure (7–9). The ventricular rate is lower at rest and generally remains unchanged or increases only slightly with exercise (7). In the first few patients studied in our laboratory (10, 11), the cardiac output at rest and during exercise was abnormally low and the pulmonary arterial and wedge pressures were high.

With the introduction of electrical pacemakers for use in heart block (12–15), it became important to determine the effects of the increase in heart rate and to define the optimal rates at which to stimulate the heart. Some observations concerning the latter have been reported in preliminary communications (16, 11) and in two patients with implanted myocardial electrodes (17). In the present investigation we have studied the influence of complete atrioventricular (A-V) block upon the systemic and pulmonary circulations at rest and during exercise and also the effects of changes in heart rate induced by an artificial pacemaker in the right ventricle.

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Methods

Patients. Fourteen patients with complete A-V block were studied, and details of their physical characteristics are given in Table I. The heart block was congenital in one patient (Patient 1) and was acquired in the rest. In four of these (Patients 4, 9, 11, and 12) there was a history of, or electrocardiographic changes to suggest, underlying ischemic heart disease. Patient 7 had had diphtheritic myocarditis 7 years before the onset of heart block, but in the remaining eight patients the etiology was obscure, there being no history of cardiac pain or rheumatic fever and no associated valve disease or hypertension. Patients 6 and 14 were in congestive heart failure at the time of study. The site of the idioventricular pacemaker as judged by the duration and form of the QRS complex was in the bundle of His in four patients (Patients 1, 6, 10, 12), in the right ventricle in three (Patients 8, 9, and 14), and in the left ventricle in the rest. One patient was in atrial fibrillation (Patient 12), and three patients (Patients 8, 12, and 14) were taking digoxin and chlorothiazide at the time of study. All the patients with acquired heart block were admitted to hospital because of uncontrolled Stokes-Adams attacks or heart failure.

Procedure. Arterial pressure was measured through an indwelling needle in the brachial artery. A double-lumen catheter was advanced into the lung so that its tip was wedged into a peripheral pulmonary artery while the proximal orifice lay in the pulmonary arterial trunk or one of its main branches.

The intravascular pressures were measured by capacitance manometers and recorded by a multichannel direct-writing instrument. The zero reference level for pressures was 10 cm above the plane of the catheterization table. Mean pressures were determined by planimetry, and all pressures were averaged over at least three respiratory cycles.

The cardiac output was measured by the direct Fick method. Expired gas was collected in a Tissot spirometer over a period of 3 minutes during which two samples each of arterial and mixed venous blood were taken

TABLE I

Individual values for heart rate, oxygen uptake, and cardiac output at rest, at idioventricular rhythm, and at various electrically induced heart rates in patients with complete heart block

Patient	Sex	Age	Body surface area	Heart rate				Oxygen uptake				Cardiac output			
					E.S.R.†				E.S.R.				E.S.R.		
				I.V.R.*	50 to 65	70 to 83	85 to 100	I.V.R.	50 to 65	70 to 83	85 to 100	I.V.R.	50 to 65	70 to 83	85 to 100
		yrs	m^2	*beats/min*				*ml/min/m²*				*L/min/m²*			
1	M	21	1.66	39	64	78	91	180	191	195	191	3.7	4.4	4.4	4.2
2	M	52	1.52	30	60	73	92	140	151	161	141	3.4	3.3	3.9	3.6
3	F	68	1.51	38	50	79	90	126	161	164	169	2.0	2.8	3.0	3.2
4	M	77	1.59	27	50	83	97	135	128	148	138	2.4	2.2	2.5	2.4
5	M	63	1.55	32	57	73	95	142	155	164	161	1.7	2.6	2.9	2.5
6	M	65	1.71	35	56	78	90	137	147	153	154	2.0	2.4	2.8	2.9
7	M	42	1.98	32	54	79	87	134	140	157	169	2.5	3.3	3.9	4.0
8	M	62	1.91	44	65	83	100	114	121	123	129	1.6	2.2	2.3	2.5
9	F	50	1.55	42	53	75	97	123	130	133	130	2.4	2.5	2.9	2.9
10	F	70	1.56	38	53	74	93	129	141	137	128	2.4	3.0	3.0	3.1
11	M	71	1.88	29	51	77	92	113	122	133	137	1.4	1.4	1.8	1.7
12	M	67	1.86	32	52	73	85	160	188	153	152	2.1	2.4	2.4	2.4
13	M	64	1.74	37	60	73	88	94	115	126	122	1.5	1.8	2.1	2.1
14	M	66	2.14	30	51	72	95	141	134	164	129	2.1	2.1	3.1	2.2

* I.V.R. = idioventricular rate. † E.S.R. = electrically stimulated rate.

for the determination of the percentage of oxygen saturation (18). The blood oxygen capacity was determined photometrically, a sample being taken during each estimation of the cardiac output. Expired gas was analyzed in a Scholander apparatus. Pulmonary vascular resistance was calculated by the usual method (19).

Direct endocardial stimulation was carried out via a no. 6 catheter electrode inserted into the right ventricle. The external end of the catheter electrode was attached to a square wave generator that delivered a 5 millisecond pulse, dischargeable from 0 to 9 v at a rate that could be varied between 40 and 150 pulses per minute (10). The indifferent lead of the pacemaker was connected to a skin plate electrode of the type used for electrocardiograms, placed in the left pectoral region. The catheter electrode was inserted at the beginning of the procedure, the most sensitive site for achieving adequate myocardial response being the apical region of the right ventricle. The electrocardiogram was displayed on a cathode ray oscilloscope throughout the whole period of study.

Each patient was studied at rest in the supine position, without sedation, 6 hours after a light meal. Twelve patients were also studied during exercise. In each study the cardiac output and intravascular pressures were measured at the patient's idioventricular rate and during varying electrically stimulated heart rates ranging between 50 and 100 beats per minute. Cardiac output was measured once at idioventricular rate and then at the end of three separate 20-minute periods. In half of the patients the ventricular rate was artificially increased at the beginning of each period. In the other half the order of study was reversed so that the cardiac output was measured first during the highest ventricular rate and then at progressively decreasing rates until the pulse generator was switched off and a final measurement was made at idioventricular rate. Intravascular pressures were measured immediately before and after each estimate of cardiac output.

The patients then performed light exercise at a steady rate on a bicycle ergometer for 6 minutes. Cardiac output was measured during the fourth minute, and intravascular pressures were recorded during the third and fifth minutes of exercise. Each patient exercised twice with a 20-minute period of rest in between: once at their own idioventricular rate and once during an electrically stimulated ventricular rate ranging from 73 to 94 beats per minute. The order of study was also reversed in half of the group.

On completion of the study the catheter electrode was left in place in many patients for continued control of the heart rate until an inductive-coupled coil pacemaker was implanted (10).

Results

Tables I and II show the individual values at rest for cardiac output, oxygen uptake, and intravascular pressures at idioventricular and varying

artificially stimulated ventricular rates. The corresponding measurements during exercise are given in Tables V and VI. The mean values for these and other related measurements at rest and during exercise are given in Table III. The figures for heart rate and intravascular pressures represent the average of two measurements made immediately before and after each cardiac output.

Observations at rest at idioventricular rate (Tables I, II, and III)

The individual values for oxygen uptake, cardiac output, stroke volume, and pulmonary arterial mean and wedge pressures are illustrated in Figure 1, and the average values are given in Table III.

The average cardiac output was significantly lower ($t = 4.33$, $p < 0.001$) and the stroke volume significantly higher ($t = 4.06$, $p < 0.001$) than the average values obtained by a dye dilution method in ten normal elderly subjects (20). The oxygen uptake was not greatly different from the average values reported by Granath, Jonsson, and Strandell (21).

Since age does not affect the pulmonary arterial and wedge pressures (21), the results for these measurements have been compared to the observations made in our own series of normal subjects studied under similar conditions, the mean values for which are shown in Table IV. Both the pulmonary arterial and wedge pressures were significantly higher ($t = 10.30$, 10.12, $p < 0.001$) as was the pulmonary vascular resistance ($t = 3.39$, $p < 0.01$).

Effects of increasing ventricular rate at rest (Tables I, II, and III)

The average values for the systemic and pulmonary intravascular pressures and cardiac output at varying heart rates from idioventricular rate to 100 beats per minute are shown in Figure 2.

Although there was some individual variation, on the average the cardiac output increased with the heart rate and reached its highest level between 70 and 83 beats per minute when it was restored to normal (20, 21). Further increments in heart rate produced no substantial rise in cardiac output, and in six patients there was a fall. In five patients the cardiac output increased by 0.1 to 0.2 L

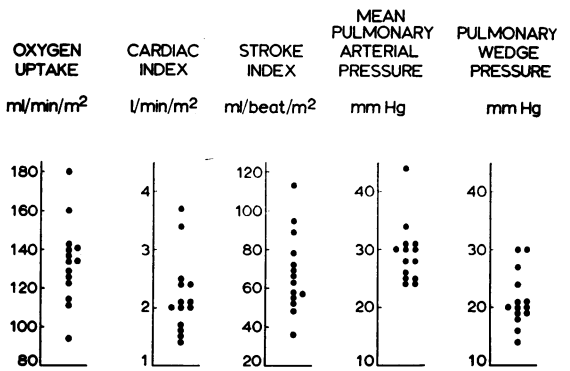

FIG. 1. INDIVIDUAL VALUES FOR OXYGEN UPTAKE, CARDIAC OUTPUT, AND PULMONARY ARTERIAL MEAN AND WEDGE PRESSURES IN PATIENTS WITH COMPLETE HEART BLOCK AT REST AT IDIOVENTRICULAR RATE.

per minute per m², and in three there was no change. The cardiac output at rates of 70 to 83 beats per minute was significantly greater than that at idioventricular rhythm ($t = 5.52$, $p < 0.001$) and at 50 to 65 beats per minute ($t = 2.86$, $p < 0.02$) but was not essentially different from that at 85 to 100 beats per minute ($t = 0.79$, $p < 0.10$). The stroke volume fell with each increment in heart rate from a mean of 65 ml per m² at idioventricular rate to 31 ml per m²

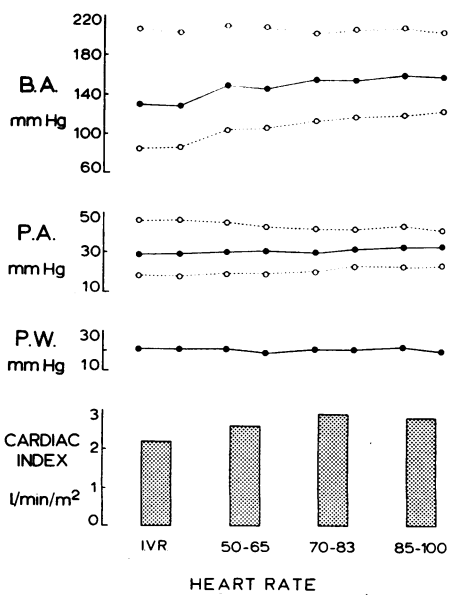

FIG. 2. MEAN VALUES AT REST FOR BRACHIAL ARTERIAL (B.A.), PULMONARY ARTERIAL (P.A.), AND WEDGE PRESSURES (P.W.) AND CARDIAC OUTPUT AT IDIOVENTRICULAR RATE (I.V.R.) AND ELECTRICALLY STIMULATED HEART RATES IN 14 PATIENTS WITH COMPLETE HEART BLOCK.

TABLE II

Individual values for brachial and pulmonary arterial and pulmonary wedge

Patient	Idioventricular rate Pressure							Heart rate, 50 to 65 beats/min Pressure						
	Brachial arterial			Pulmonary arterial			Pulmonary wedge	Brachial arterial			Pulmonary arterial			Pulmonary wedge
	S*	D	M	S	D	M	M	S	D	M	S	D	M	M
	mm Hg							*mm Hg*						
1	184	96	128	41	15	28	20	187	103	136	37	16	26	16
2	189	70	107	40	17	24	20	207	96	137	40	16	31	19
3	201	78	119	42	15	25	19	205	86	132	43	17	27	22
4	239	91	148	41	11	28	14	230	121	158	33	14	23	17
5	209	68	125	42	16	30	20	214	90	150	38	18	28	17
6	260	98	180	67	30	44	30	258	123	191	60	30	43	30
7	187	90	124	39	13	24	16	179	115	139	38	17	27	19
8	137	64	92	48	20	31	20	200	113	149	48	24	34	22
9	188	92	130	47	19	30	24	194	101	138	47	19	31	18
10	228	78	127	42	19	26	19	240	107	159	42	16	25	18
11	226	88	127	39	16	25	20	229	110	148	39	20	26	24
12	207	83	117	54	23	31	27	196	89	131	56	21	32	20
13	199	106	148	51	18	30	18	185	109	141	42	17	26	14
14	198	88	132	52	18	34	30	194	104	151	54	21	39	28

* S = systolic, D = diastolic, and M = mean.

at a rate between 85 and 100 beats per minute. The variation in stroke volume between the different rates was significant (analysis of variance, $p < 0.001$).

The oxygen uptake continued to rise as the heart rate increased, reaching a maximal value between 70 and 83 beats per minute. The variation in oxygen uptake between the different heart rates was significant (analysis of variance, $p < 0.001$). The expired volume and respiratory exchange ratio varied little during the changes in ventricular rate (Table III). The a-v oxygen difference fell with each increment in heart rate, reaching its lowest level between 70 and 83 beats per minute (Table III), when it was significantly different from the value at idioventricular rate ($t = 4.08$, $p < 0.001$) and at 50 to 65 beats per minute ($t = 2.99$, $p < 0.02$).

The brachial and pulmonary arterial mean and diastolic pressures rose with an increasing heart rate, but the average systolic pressure changed little. The pulmonary wedge pressure was essentially unaffected by the changes in heart rate, and the pulmonary vascular resistance remained unaltered.

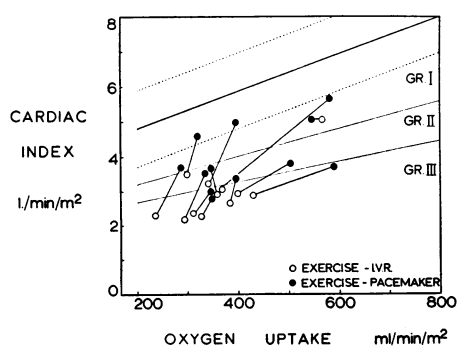

FIG. 3. INDIVIDUAL VALUES FOR CARDIAC OUTPUT PLOTTED AGAINST OXYGEN UPTAKE DURING EXERCISE AT IDIOVENTRICULAR (I.V.R.) AND ELECTRICALLY STIMULATED HEART RATES (PACEMAKER). The regression line and 95% confidence limits of cardiac output on oxygen uptake in normal subjects during exercise (24), and three arbitrary grades of impairment of the response of cardiac output to exercise (22), are shown.

Observations during exercise (Tables III, V, and VI)

The individual values for cardiac output and oxygen uptake during exercise at both idioventricular and electrically stimulated heart rates are shown in Figure 3.

Exercise at idioventricular rate. The exercise performed by this group was very light, since most were unable to do more, and the mean oxygen uptake during the fourth minute of exercise was only 354 ml per minute per m^2. The average cardiac output increased significantly from the average resting value of 2.2 L per minute per m^2 to 3.0 L per minute per m^2 ($t = 5.50$, $p < 0.001$). The mean a-v oxygen difference rose from the

TABLE II

pressures at rest and at various heart rates in patients with complete heart block

Heart rate, 70 to 83 beats/min Pressure							Heart rate, 85 to 100 beats/min Pressure						
Brachial arterial			Pulmonary arterial			Pulmonary wedge	Brachial arterial			Pulmonary arterial			Pulmonary wedge
S	D	M	S	D	M	M	S	D	M	S	D	M	M
mm Hg							*mm Hg*						
188	116	139	35	18	26	13	204	130	155	42	25	33	16
200	100	139	39	16	27	23	203	106	149	43	14	31	21
212	114	159	54	23	40	33	215	114	161	48	28	38	26
220	129	181	40	24	31	20	242	152	193	46	29	36	26
197	94	143	35	17	25	16	200	105	150	38	19	28	16
249	138	194	52	31	41	31	248	150	206	49	29	39	29
172	110	139	40	20	31	19	176	112	140	42	24	34	23
194	117	145	47	24	34	20	198	117	151	47	27	35	21
196	116	150	46	25	35	20	190	118	150	44	27	34	20
230	122	168	39	19	27	19	230	129	171	36	19	25	14
235	135	169	39	21	29	22	241	145	181	44	24	34	27
198	112	145	43	19	28	17	189	117	140	47	22	28	16
176	108	139	38	17	27	14	167	105	134	34	18	26	13
190	106	156	42	16	30	20	186	108	148	55	22	40	31

resting value of 6.3 vol per 100 ml to 12.2 vol per 100 ml. The response to exercise, however, was less than normal (23) in all and severely impaired in nine patients.

During exercise the heart rate of the patient with congenital heart block increased from 39 to 53. In this patient the increase in the cardiac output was proportional to the change in rate, and the stroke volume remained the same. Only two patients (Patients 2 and 4) with acquired heart block showed an increase in heart rate of a similar magnitude, and in these, the cardiac output increased despite a decrease in stroke volume. Among the remaining patients, the greatest increase in heart rate during exercise was 5 beats per minute. Despite the relative constancy of the heart rate all except one (Patient 8) of these patients developed some increase in the cardiac output during exercise, and this was achieved by an increase in stroke volume. The average stroke volume rose from 65 ml per m^2 to 78 ml per m^2 ($t = 3.36$, $p < 0.01$).

There was a slight increase in the average brachial arterial mean and systolic pressures, no change in the diastolic pressure, and a slight widening of the pulse pressure. The average pulmonary arterial mean pressure increased by 12 mm Hg, and the pulmonary wedge pressure by 8 mm Hg. The pulmonary vascular resistance did not change significantly. The pulmonary arterial and wedge pressures were both significantly greater ($t = 5.23, 5.01$, $p < 0.001$) than the values observed in normal subjects studied in this laboratory and higher than the average values recorded in normal old men (21). Pulmonary ventilation during exercise was normal with respect to oxygen uptake (24) except for Patient 6, who was in heart failure.

The patient with congenital heart block had a normal cardiac output at rest and was able to perform more strenuous work than the others. He had the greatest increase in cardiac output and heart rate during exercise although the response was still less than normal. The pulmonary arterial and wedge pressures were abnormally high, both at rest and during exercise.

Exercise at electrically stimulated rates. The patients were able to perform more work, as judged by the oxygen uptake, during exercise at an average electrically stimulated rate of 79 beats per minute than at the idioventricular rate. In each patient there was a significant rise in cardiac output from rest to exercise at a heart rate in the range of 73 to 94 beats per minute. The average cardiac output increased from the resting value of 2.9 L per minute per m^2 to 4.0 L per minute per m^2 ($t = 6.46$, $p < 0.001$). The response of the cardiac output was still abnormal (Figure 3), but had improved in every patient except the one with congenital heart block, in whom it remained un-

TABLE III

Mean values for cardiac output, intravascular pressures, and related measures at rest and during exercise at various heart rates in patients with complete heart block

	Rest				Exercise	
	I.V.R.*	50 to 65	70 to 83	85 to 100	I.V.R.	E.S.R.†
Rate, *beats/min*	35	55	77	92	39	79
Oxygen uptake, *ml/min/m²*	133 (20.8)‡	145 (23.3)	151 (19.3)	147 (20.2)	354 (82.5)	415 (112.2)
Pulmonary ventilation, *L/min/m²*	4.6 (1.3)	4.6 (1.2)	4.5 (1.0)	4.4 (1.0)	11.3 (3.2)	11.9 (4.9)
Respiratory exchange ratio	0.79 (0.06)	0.79 (0.08)	0.79 (0.06)	0.78 (0.04)	0.84 (0.06)	0.85 (0.06)
A-v oxygen difference, *vol/100 ml*	6.3 (1.6)	5.9 (1.6)	5.4 (1.2)	5.4 (1.3)	12.2 (2.0)	10.8 (2.9)
Cardiac output, *L/min/m²*	2.2 (0.66)	2.6 (0.74)	2.9 (0.73)	2.8 (0.73)	3.0 (0.79)	4.0 (0.87)
Stroke volume, *ml/m²*	65 (20.4)	47 (11.9)	39 (9.9)	31 (8.3)	78 (14.5)	51 (12.4)
Brachial arterial pressure, *mm Hg* S§	204 (29.3)	209 (23.0)	204 (22.4)	206 (25.5)	232 (30.7)	226 (27.6)
D	85 (12.1)	105 (10.8)	116 (12.4)	122 (16.6)	84 (10.4)	109 (18.3)
M	129 (20.5)	147 (15.6)	155 (17.5)	159 (21.1)	140 (23.6)	158 (25.0)
Pulmonary arterial pressure, S	48 (7.9)	44 (7.4)	42 (5.8)	43 (5.7)	67 (9.8)	61 (15.4)
mm Hg D	18 (4.6)	19 (4.1)	21 (4.3)	23 (4.6)	25 (5.7)	28 (10.1)
M	29 (5.2)	30 (5.7)	31 (5.0)	33 (3.8)	41 (7.0)	42 (11.7)
Pulmonary wedge pressure, *mm Hg*	21 (4.8)	20 (4.5)	21 (5.6)	21 (5.8)	29 (4.8)	28 (10.7)
Pulmonary vascular resistance, *dyne-sec-cm⁻⁵*	180 (106)	176 (77)	181 (63.5)	198 (46.5)	202 (91.8)	183 (89.3)

* I.V.R. = idioventricular rhythm.
† E.S.R. = electrically stimulated rate.
‡ The figures in parentheses are standard deviations.
§ S = systolic; D = diastolic; M = mean.

changed. In Patients 3 and 7 the response to exercise was restored to normal. Since the average oxygen uptake during exercise was greater under electrical stimulation than at idioventricular rate, the levels of cardiac output achieved under these two circumstances cannot be directly compared. This subject has been considered in detail elsewhere (23). We prefer to present the data as shown in Figure 3, where it is apparent that the effect of electrical stimulation is to bring the relationship between cardiac output and oxygen uptake during exercise closer to the normal expectation. An alternative way of analyzing these results is to calculate the increase in cardiac output per 100 ml increase in oxygen uptake during exercise. For the patients with acquired heart block this figure averaged 0.29 L per minute per m² at idioventricular rate and 0.43 L per minute per m²

TABLE IV

Physical characteristics, cardiac output, intravascular pressures, and related measurements in 77 normal subjects (45 men, 32 women), at rest in supine position

	Mean	SD	Range
Age, *yrs*	33.5	14.4	14–60
Body surface area, *m²*	1.74	0.19	1.38–2.23
Oxygen uptake, *ml/min/m²*, STPD*	143.0	16.7	110–192
Pulmonary ventilation, *L/min/m²*, BTPS†	4.94	1.84	2.5–8.3
A-v oxygen difference, *vol/100 ml*	3.60	0.62	2.4–5.7
Cardiac output, *L/min/m²*	4.04	0.64	2.6–5.8
Heart rate, *beats/min*	89.9	12.2	62–118
Stroke volume, *ml/m²*	45.8	9.1	32–70
Brachial arterial pressure,‡ *mm Hg* S§	136.0	17.7	98–165
D	79.8	10.1	60–95
M	102.9	13.5	73–134
Pulmonary arterial pressure,‡ *mm Hg* S	24.9	4.9	12–35
D	11.4	3.1	5–19
M	17.9	3.2	12–26
Pulmonary wedge pressure,‖ *mm Hg*	10.5	2.7	4–16
Systemic vascular resistance,‡ *dyne-sec-cm⁻⁵*	1,187.4	294.5	593–2100
Pulmonary vascular resistance,‖ *dyne-sec-cm⁻⁵*	88.4	39.2	11–172

* STPD = Standard temperature, pressure, dry.
† BTPS = Body temperature, pressure, saturated with water.
‡ 67 subjects.
§ S = systolic; D = diastolic; M = mean.
‖ 51 subjects.

TABLE V

Individual values for cardiac output, oxygen uptake, heart rate, and intravascular pressures during exercise at idioventricular rate in patients with complete heart block

Patient	Heart rate	Oxygen uptake	Cardiac output	Pressure						
				Brachial arterial			Pulmonary arterial			Pulmonary wedge
				S*	D	M	S	D	M	M
	beats/min	*ml/min/m²*	*L/min/m²*	*mm Hg*						
1	53	557	5.1	200	83	122	52	15	32	24
2	43	297	3.6	225	78	122	56	20	34	26
3	43	375	3.2	214	72	133	74	27	43	33
4	38	428	2.9	265	97	181	74	24	46	32
5	31	290	2.2	221	66	139	66	24	43	31
6	38	390	2.9	270	99	188	88	39	49	40
7	31	331	3.1	214	79	117	55	22	35	31
8	44	323	2.3	218	92	135	65	28	40	27
9	41	233	2.3	207	80	125	64	23	39	29
10	39	344	3.0	251	92	149	69	24	37	17
11	26	306	2.4	295	95	150	66	27	40	26
12	35	379	2.8	203	81	118	70	27	40	31

* S = systolic; D = diastolic; M = mean.

at electrically stimulated rate. The difference between these two figures was significant ($t = 2.58$, $p < 0.02$).

Since the heart rate under artificial stimulation remained unchanged during exercise, the rise in cardiac output was achieved by an increase in stroke volume. The mean stroke volume increased from 39 to 51 ml per m², which was significant ($t = 4.98$, $p < 0.001$).

Pulmonary ventilation during exercise remained normal with respect to oxygen uptake (24).

The changes in systemic arterial, pulmonary arterial, and wedge pressures were similar to those observed when the patients exercised at idioventricular rhythm (Table III).

Discussion

The cardiac output in the patients with acquired complete heart block was less than normal, even allowing for their advanced age. The stroke volume was larger than normal, but this increase was insufficient to maintain a normal cardiac output in the face of the extreme bradycardia. The low cardiac output appears to have been due to a combination of the simple effects of bradycardia

TABLE VI

Individual values for cardiac output, oxygen uptake, heart rate, and intravascular pressures during exercise at electrically stimulated heart rates in patients with complete heart block

Patient	Heart rate	Oxygen uptake	Cardiac ouptut	Pressure						
				Brachial arterial			Pulmonary arterial			Pulmonary wedge
				S*	D	M	S	D	M	M
	beats/min	*ml/min/m²*	*L/min/m²*	*mm Hg*						
1	79	555	5.1	203	104	136	38	18	28	18
2	75	318	4.6	215	96	142	49	17	31	27
3	73	598	5.7	223	90	144	77	38	57	46
4	77	580	3.7	257	123	187	61	26	42	26
5	74	336	3.6	215	86	140	48	16	30	12
6	78	505	3.8	268	132	202	86	46	62	46
7	76	383	5.0	191	88	128	37	15	26	15
8	80	341	2.9	219	111	152	64	34	47	31
9	94	286	3.7	210	116	160	70	37	52	27
10	77	337	3.7	238	114	176	65	24	39	21
11	78	346	3.0	276	146	193	61	29	43	31
12	82	394	3.5	200	107	139	75	33	48	32

* S = systolic; D = diastolic; M = mean.

and a degree of impaired contractility of the myocardium. Impaired contractility might be expected to be associated with ischemic lesions in the myocardium, but to some extent it may also be a physiological function of bradycardia itself (25–27). The influence of bradycardia alone, or of bradycardia plus the physiological "staircase effect," may be deduced from the fact that the cardiac output could be restored to normal by increasing the rate. Yet, even under these circumstances, the wedge pressure remained abnormally high, which would suggest that the normal cardiac output was only achieved in the presence of an increased left ventricular filling pressure.

The high wedge pressure may itself have been due to a specific impairment of the contractility of the left ventricle. However, the fact that the highest wedge pressure was observed in the two patients with overt congestive cardiac failure suggests that hypervolemia may also have been an important factor. The elevation of the wedge pressure was not due to the bradycardia alone, since the pressure remained unchanged while the heart rate increased. This constancy of the wedge pressure contrasts with observations made in patients with mitral stenosis (28). The relationship between heart rate and mean wedge pressure would, in any case, be expected to be a complex one because of the presumably nonlinear distensibility of the cardiac chambers, the inconstancy of the resistance of the mitral valve, and the variable rate of the flow of blood into the ventricle.

The abnormally high pulmonary arterial pressure appears to be due to the raised wedge pressure. Although the pulmonary vascular resistance was higher than would be normal in younger people, this could be entirely due to age. There are no direct measurements of the pulmonary vascular resistance in normal elderly people, but the observations that the cardiac output is reduced (20, 21) while the pulmonary arterial and wedge pressures remain the same as in young people suggest that the resistance rises with age.

At idioventricular rate the response of the cardiac output to exercise was severely impaired. In the normal subject exercising in the supine position the increase in cardiac output is largely due to the increase in heart rate, stroke volume increasing but little (29). An impaired response was therefore to be expected in these patients, since the heart rate did not increase appreciably during exercise. A simliar but less severe impairment of response has been observed when the normal increase in heart rate during exercise is prevented by the administration of pronethalol to supine normal subjects (30). The small increase in cardiac output that did occur was due to a rise in stroke volume, the extent of the increase being similar to that seen in normal subjects.

When the heart rate during exercise was increased by electrical stimulation, the response of cardiac output was improved, and it became normal in some patients. Although this supports the view that bradycardia was an important reason for the impaired response at idioventricular rate, it is necessary to consider why the cardiac output response was usually still abnormal at faster electrically stimulated rates. One explanation is that the heart rate, although much faster than the idioventricular rate, was still less than would have occurred in normal subjects performing similar exercise. The heart rate of young subjects under these conditions ranged from 87 to 115 beats per minute (24), and that of normal older subjects would have been greater. The mean electrically stimulated rate of 79 beats per minute (range, 73 to 94) probably did not allow cardiac output to rise to levels it would have reached at more normal heart rates. Impaired myocardial contractility may have played some part in the inadequate response, especially in view of the high wedge pressure. Finally, since the heart was very large in some of the patients, functional tricuspid incompetence may have contributed to the impaired response of the cardiac output as suggested by McMichael and Shillingford (31).

The resting oxygen uptake, which was normal at idioventricular rates, increased significantly as the heart rate was increased. The pulmonary ventilation and respiratory exchange ratio remained unaltered, and the patients were in a steady respiratory and cardiac state. The heart was the only organ whose requirement seems certain to have increased, although the myocardial oxygen uptake has not been measured in such patients, nor its variation with heart rate at rest.

There is considerable evidence from experiments in animals that myocardial oxygen con-

sumption is a function of heart rate and systolic blood pressure (32, 33). In normal subjects the myocardial oxygen uptake is about 16 ml per minute per m^2, which is approximately equal to the increase of total oxygen uptake at electrically stimulated rate in the patients with heart block. The present findings are, therefore, consistent with the suggestion that a twofold increase in heart rate doubled the myocardial oxygen uptake.

There was a range of heart rates at which cardiac output reached a maximum, further increases in rate often being associated with a decrease in cardiac output. This optimal rate lay between 70 and 83 beats per minute, and at these rates the patients felt most comfortable. They were also able to exercise more readily, since they were not troubled by the symptoms of weakness and fatigue that were experienced at idioventricular rates. Possibly, however, they would have noted further improvement, and cardiac output during exercise would have been closer to normality at faster heart rates than were used in this study. Breathlessness was not a complaint in these patients, providing further evidence that this symptom is determined by factors other than the cardiac output.

The findings in patients with acquired heart block differ in some respects from those previously reported for patients with congenital heart block (3–6), in whom the heart rate tends to be faster and less fixed. Others have reported that in patients with congenital heart block the cardiac output is normal and responds normally to exercise, and that pressures in the pulmonary circulation are also normal (6). In the one patient with congenital heart block in the present study, however, the cardiac output although normal at rest did not respond normally to exercise, and the pulmonary wedge pressure was elevated.

Summary

Fourteen patients with complete heart block (13 acquired and 1 congenital) were studied at rest and during exercise in the supine position, both at idioventricular and various electrically stimulated heart rates.

Cardiac output at rest was abnormally low, despite an increased stroke volume, and the response of cardiac output to exercise was greatly impaired. Pulmonary arterial and wedge pressures were abnormally high at rest and during exercise.

At faster, electrically stimulated rates, the cardiac output at rest rose to normal levels, and there was an improvement in the response of cardiac output to exercise. The optimal rate at rest usually lay between 70 and 83 beats per minute.

The resting oxygen uptake was normal at idioventricular rates but increased significantly when the heart rate rose.

The hemodynamic abnormalities in these patients appear to be due to a combination of bradycardia and impaired myocardial contractility.

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