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Central Haemodynamics at Rest and during Exercise in Severe Chronic Obstructive Lung Disease

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ABSTRACT

Twenty-five patients of ages 39–72 years, with a maximum ventilatory capacity (MVV_F) of $\leqslant 35\%$ of the predicted values, were classified into a respiratory insufficiency (R) and a comparison (C) group according to the clinical progress of the disease. With the patients in their habitual state, the total haemoglobin (THb, g), the pulmonary and systemic pressures, cardiac output ($\dot{Q}$, l/min) and pulmonary (PVR) and systemic (SVR) vascular resistance in (mmHg/l) · min were measured at rest and during work.

The mean values and S.E.M. in groups R and C were as follows: for THb 7.4 ± 0.3 and 8.6 ± 0.5 g/kg, blood volume 59.1 ± 2.0 and 64.9 ± 2.8 ml/kg, $S_{a\bar{O}_2}$ 86.2 ± 2.2 and 90.4 ± 1.4 %, $a\bar{v}_{O_2}$ 48.5 ± 2.5 and 53.2 ± 2.6 ml/l, pulmonary arterial mean pressure 31 ± 2 and 26 ± 2 mmHg, PVR 4.7 ± 0.5 and 3.2 ± 0.3 (mmHg/l) · min, arterial mean pressure 105 ± 4 and 102 ± 4 mmHg, SVR 23.1 ± 1.2 and 23.9 ± 1.8 (mmHg/l) · min. $\dot{Q}$ was 4.5 ± 0.2 in the R-group male patients and 4.7 ± 0.3 l/min in the females, and 4.5 ± 0.3 in the C-group male patients and 3.5 l/min in the one female patient.

During work (not performed in all patients of group R) at mean work loads of 160 kpm/min in 4 male patients of group R, $\dot{Q}$ was 6.5 ± 0.5 l/min, at 90 kpm/min in 3 female patients of group R 6.4 ± 0.2 l/min, at 150 kpm/min in 10 male patients of group C 6.7 ± 0.4 l/min and at 150 kpm/min in the female patient of group C 5.2 l/min. It is emphasized that both the right and left ventricular function may be impaired in these patients.

INTRODUCTION

The aim of this investigation was to study central haemodynamic conditions in patients with severe chronic obstructive pulmonary disease, in their habitual state, in an attempt to find out whether periods of manifest respiratory insufficiency could be due to the pulmonary disease alone or partly to other factors. Such possible factors are the degree of circulatory and cardiac adjustment to the disease, myocardial disease, coronary arterial sclerosis or the mode of response to hypoxia, hyperoxia, hypercapnoea and physical work. The patients, who had a maximum ventilatory capacity (MVV_F) of $\leqslant 35\%$ of predicted normal values, were classified as follows: (1) a respiratory insufficiency (R) group, if they had had one or several periods of respiratory insufficiency demanding breathing assistance (either intensive physiotherapy combined with medicinal and oxygen treatment, or the use of a respirator) and (2) a comparison (C) group, if they had never needed breathing assistance. In this paper the haemodynamic studies performed at rest and during work are reported and the R and C groups are compared.

MATERIAL

The material consisted of 25 persons, selected among patients treated in 1968–70 at the Department of Pulmonary Diseases, University Hospital, Uppsala, for chronic obstructive pulmonary disease (COLD), diagnosed according to the ATS criteria (3) and as described by Brundin & Tammivaara-Hilty (8), and having a ventilatory capacity (MVV_F) of $\leqslant 35\%$ of predicted normal values on investigation under ordinary daily medication. Details of the clinical history of the disease, changes in the ventilatory capacity and lung volumes, ECG and physical working capacity are given elsewhere (8, 42). The patients were classified into two groups: (1) a respiratory insufficiency (R) group, consisting of 14 patients (8 male, 6 female) and (2) a comparison (C) group, consisting of 11 patients (10 male, one female), according to whether or not they had had periods of absolute insufficiency demanding breathing assistance. The age, weight, body surface area (11), resting metabolic rate (RMR), total haemoglobin (THb, g/Kg), and blood volume (BV, ml/kg), ventilatory capacity (MVV_F, l/min), and maximal physical working capacity (W_{max}, kpm/min) in the sitting posture on the day before catheterization are presented in Table I for each of the R- and C-group patients and as mean values $\pm$S.E.M. for the different groups.

Table I. *Age, weight, body surface area, resting metabolic rate (RMR), total haemoglobin (THb) and blood volume (BV) in relation to kg body weight, maximum voluntary ventilation (MVV_F, l/min), and maximum physical working capacity (W_{max}, kpm/min), measured in the sitting posture, on the day before right heart catheterization as individual values and as mean and S.E.M. in the male and female patients of groups R and C*

Pat. ident. Sex	Age (y.)	Weight (kg)	Body surf. area (m^2)	RMR (%)	THb body weight (g/kg)	BV body weight (ml/kg)	MVV_F (l/min)	W_{max} (kpm/min)
R1 M	50	55	1.67	+36	6.9	52.7	21	150
R2 M	55	70	1.90	+9	5.6	57.1	18	235
R3 M	59	57	1.66	+43	10.1	75.4	34	450
R4 M	64	48	1.64	+24	6.9	58.3	13	0
R5 M	66	59	1.62	+27	7.1	54.2	25	300
R6 M	66	52	1.62	+20	7.4	63.5	16	80
R7 M	67	63	1.79	+7	7.9	63.5	18	50
R8 M	69	82	2.08	−9	7.4	62.2	22	250
R11 F	57	47	1.46	+14	7.2	55.3	14	25
R12 F	57	40	1.38	+35	8.1	70.0	19	50
R13 F	65	47	1.52	+45	7.7	59.6	21	200
R14 F	67	70	1.74	+15	6.6	52.9	34	200
R15 F	68	73	1.80	+3	7.2	46.6	20	200
R16 F	72	43	1.43	+31	7.0	55.8	34	30
RM	62±2	61±4	1.75±0.06	+25±8	7.4±0.45	60.9±2.5	21±2	189±52
RF	64±3	53±6	1.56±0.07	+24±6	7.3±0.28	56.7±3.2	24±3	118±37
R M+F	63±2			+24±5	7.4±0.27	59.1±2.0	22±2	
C1 M	39	54	1.57	+5	8.2	61.1	15	200
C2 M	39	56	1.76	+27	10.6	76.8	26	400
C3 M	55	54	1.68	+11	6.8	64.8	16	265
C4 M	57	64	1.75	+29	9.2	57.8	28	400
C5 M	62	70	1.90	+15	6.6	57.1	22	225
C6 M	66	83	1.95	+13	9.1	57.8	13	100
C7 M	68	61	1.74	+30	10.0	72.1	35	400
C8 M	68	64	1.80	+15	8.0	60.9	16	50
C9 M	70	53	1.60	+36	11.0	81.1	23	335
C10 M	70	65	1.75	+12	5.4	52.3	10	185
C11 F	56	46	1.43	+26	9.5	71.7	23	200
CM	59±4	62±3	1.75±0.04	+19±3	8.5±0.58	64.2±3.0	20±3	251±37
CF	56	46	1.43	+26	9.5	71.7	23	200
C M+F	59±3			+20±3	8.6±0.53	64.9±2.8	21±2	

METHODS

The total haemoglobin (THb, g) measurement by the alveolar CO method (22, 37) was modified by prolonging the lung N_2 wash-out period to 15 min. The coefficient of variation for 19 duplicate THb measurements was 4.5%. For different reasons (smoking and high initial alveolar CO-concentration, distress caused by the investigation or methodological errors) the given THb value is in 6 patients (R 12, 13, 16 and C 4, 8, 11) taken from a single determination. In our laboratory the coefficient of variation for duplicate THb measurements varied between 2.6–6.1% at the time of this investigation. The blood volume (BV, l) was calculated in the conventional manner by considering the body haematocrit to be 91% of the haematocrit measured in the arterial blood in the sitting posture. Both THb and BV are given in relation to body weight.

The principles for arterial catheter introduction, arterial pressure measurements, expiratory gas collection, and different analytical methods and calculations have been described by Bäcklund & Tammivaara-Hilty (10). The resting metabolic rate (RMR, %) was calculated from the obtained oxygen uptake ($\dot{V}_{O_2}$, ml STPD/min) at rest during the right heart catheterization with the aid of the current tables (18).

The patients were investigated in a state of fasting and abstinence from smoking, lasting from about 5 p.m. on the previous day. In the morning they were given their habitual medication together with 5 mg of Valium® (diazepam), and the catheterization, performed in the supine posture, was started at 8 a.m.

After insertion of a polyethylene catheter (PP 160) into the brachial artery (BA), right heart catheterization was performed in the usual manner through an exposed ante-cubital vein, using a dacron woven Cournand end-hole catheter

(Nos. 6–8, 5500 USCI). With the mid-thoracic level as the zero pressure reference level, the pressures in the superior vena cava (SVC) and right atrium (RA) were usually measured during insertion of the catheter. The right ventricle (RV) pressures, on the other hand, were measured, as a rule, at the end of the catheterization procedure. The pulmonary capillary venous (PCV) pressure was measured, whenever possible, immediately before or after each pulmonary artery (PA) pressure measurement which was performed at rest in the middle of the Fick measurement. During work the PCV pressure was measured during the first 3 min and the catheter was then withdrawn to PA, where, as in BA, the pressure was measured both before and after blood sampling. In patients R1 and R16 a satisfactory PCV pressure measurement was made only at rest at the end of the catheterization. No satisfactory PCV pressure was recorded in patient C 9. This was also the case in patients R1, 2, 3, 5, 14, 15 and 16 during physical work. The expiratory gas for pulmonary gas exchange and cardiac output (direct Fick; $\dot{Q}$, l/min) measurements was collected during ambient air breathing both at rest and at work, and also at work when a mixture of air and carbon monoxide ($F_{ICO} \sim 0.0005$) was breathed in order to measure the diffusing capacity for carbon monoxide (D_{LCO}, ml/mmHg · min) with the CO-steady state method. The arterio-venous oxygen difference ($a\bar{v}_{O_2}$, ml/l) obtained as described by Bäcklund and Tammivaara-Hilty (10) from arterial (Sa_{O_2}, %) and mixed venous (PA) saturation ($S\bar{v}_{O_2}$) was measured in the middle of the gas collection periods, which were as follows: at rest 10 min, at work 3 min (from the 3rd to the 6th min) and, in cases where the patient was able to continue further on the same work load 2 min (from the 8th to the 10th min) during D_{LCO} measurements. In cases where the test had to be terminated earlier, sampling was performed during the last minutes. This had to be done in patients R4 and R12 at rest. Though it was intended that the investigations should be performed under submaximum work load conditions with the guidance of a work test carried out on the previous day the work loads chosen were maximum or near maximum in five R-group (R1, 6, 7, 11 and 16) and in two C-group (C6 and 8) patients, as no lower work loads were possible on the bicycle ergometers used. In a few patients (R6, 7 and 16) the work test was performed without the use of a respiratory valve, as on the previous day the test with a valve had to be terminated early and the measurements of pressure and $a\bar{v}_{O_2}$ during work were considered now of more importance. In patient R2 these measurements could not be made as the test with the lowest work load of 100 kpm/min had to be interrupted after 2 min 20 sec. Because of errors in the gas analyses, the cardiac output measurement was unsuccessful in patient R14 during work (air breathing) and in patients C5 and C7 during diffusion capacity measurements.

The pressures given are mean values, drawn by hand from the mean pressure ($\bar{P}$) variations, caused by breathing. The systolic (e.g. P_{PA_S}), diastolic (e.g. P_{PA_d}) and right ventricular end-diastolic (RV_{ED}) pressures given are arithmetic mean values of the highest and lowest pressures, representative of the period, caused by inspiratory and expiratory intrathoracic pressure variations. All pressures are given in mmHg. The pulmonary vascular resistance, PVR, (mmHg/l)·min, was calculated as $(\bar{P}_{PA}-\bar{P}_{PCV})/\dot{Q}$. In cases where the PCV pressure measurement was unsuccessful, this value was supposed, under resting conditions, to be the same as the mean pressure in the whole material. During work it was calculated by adding the mean percentage increase in PCV pressure in the whole material from rest to work, to the value obtained under resting conditions. The systemic vascular resistance, SVR, (mmHg/l)·min, was calculated as $\bar{P}_{BA}/\dot{Q}$ and at rest also as $(\bar{P}_{BA}-\bar{P}_{SVC})/\dot{Q}$.

RESULTS

The *total haemoglobin* (THb/kg) and *blood volume* (BV/kg) in the individual patients and as group mean values (±S.E.M.) are presented in Table I. The normal mean values (±S.D.) for total haemoglobin obtained in our laboratory for 58–71-year old subjects were 9.3 ±1.3 and 8.1 ±1.3 g/kg for males and females, respectively; the corresponding values for blood volume were 77.2 ±11.3 and 70.6 ±10.6 ml/kg (9). The mean THb/kg was the same in the male and female patients of group R, but compared with the normal values it was decreased to a greater extent in the male than in the female patients. The corresponding value lay nearer to normal in the male patients of group C and exceeded the normal group mean values in the only female patient of this group. The mean value for BV/kg was 1–2 S.D. below the normal values in both the male and female patients of group R and in the male patients of group C, but was normal in the only female patient of group C. In group R the BV/kg value was normal only in patient R3, who still had compensatory metabolic alkalosis, probably because of chloride depletion, as described by Robin 1963 (34)—even though he appeared clinically to be in his habitual state—and in R12, who was the most hypoxaemic patient in group R. Among the male patients of group C the BV/kg value lay within one S.D. around the normal blood volume only in patients C2, 7 and 9.

The mean values for the central haemodynamic factors studied at rest in groups R and C are presented in Table II and the individual findings, both at rest and during work in Tables III and IV.

1. *Haemodynamics at rest*

The mean *cardiac output* at rest was the same in the male and female patients of group R and the male

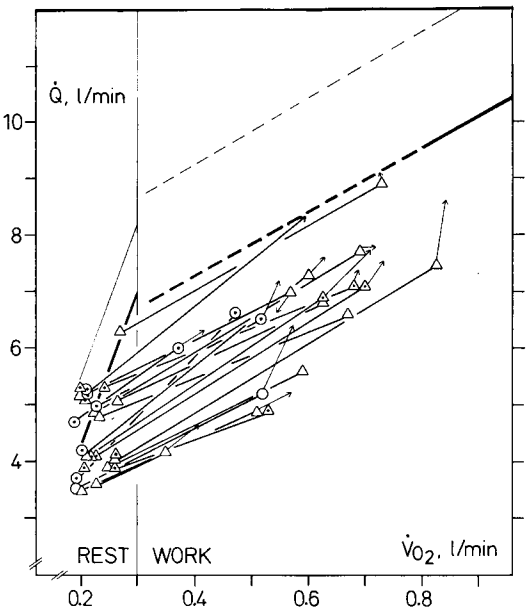


Fig. 1. The cardiac output ($\dot{Q}$, l/min) in relation to oxygen uptake ($\dot{V}_{O_2}$, l STPD) during ambient air breathing in the supine posture at rest and during exercise in group R (△ males, ○ females) and group C (▲ males, ● female) patients. The measurements during exercise continued at the same work load, but breathing of a mixture of CO ($F_{I_{CO}} \sim 0.0005$) in air, are indicated by →. The thin lines are regression lines in 16–41-year old normal subjects (Bevegård et al., 1960; Holmgren et al., 1960). The thick lines are regression lines in 63–81-year old normal subjects (Granath et al., 1964). The broken lines are linear extrapolations from the regression lines.

patients of group C (Table II). On comparing the cardiac output, expressed as cardiac index ($\dot{Q}/m^2$), with the normal cardiac index values summarized by Guyton (17) from findings of several authors, it was found that the values were normal in 4 male patients of group R and one male patient of group C, high in 2 male patients of group R and 4 of group C and 5 female patients of group R, and low in the rest of the patients (two R- and 4 C- group male patients and one female patient from each group).

In relation to the *oxygen uptake* (Fig. 1) the *cardiac output* tended to be low in several of the male patients, especially in group C, and high in several of the female patients in group R. Therefore the combined differences in oxygen uptake as absolute values and $a\bar{v}_{O_2}$ values between the male and female groups can explain the fact that the group mean values for cardiac output were the same. The arterio-venous oxygen difference was lowest in the female patients of group R as they had the most severe arterial hypoxaemia. The mean oxygen uptake, expressed as RMR (Table I) was about + 20–25% and approximately the same in the different groups. Some of the individual differences in cardiac output could have been due to differences in the oxygen uptake.

The tendency to lower *arterio-venous oxygen differences* with decreasing $P_{a_{O_2}}$ is evident in Fig. 2. Which one of these two factors is the dependent variable is impossible to know as a high flow rate through the lung capillaries and consequent reduction of the oxygenation time might cause arterial desaturation.

The basal resting cardiac output might have been different from the cardiac output measured, as the pressures in the systemic circulation and pulmonary artery were not the same before and during the Fick measurement in all patients. The increase of the PA pressure during the Fick measurement increased with the original level of this pressure. Before the Fick measurement the systolic PA pressure (mean ± S.E.M., range) was 39.4 ± 2.2 (29–51) and the diastolic pressure 22.4 ± 1.6 (15–34) mmHg in group R. In group C the corresponding values were 33.7 ± 1.8 (24–56) and 19.1 ± 1.2 (14–27) mmHg. The increase

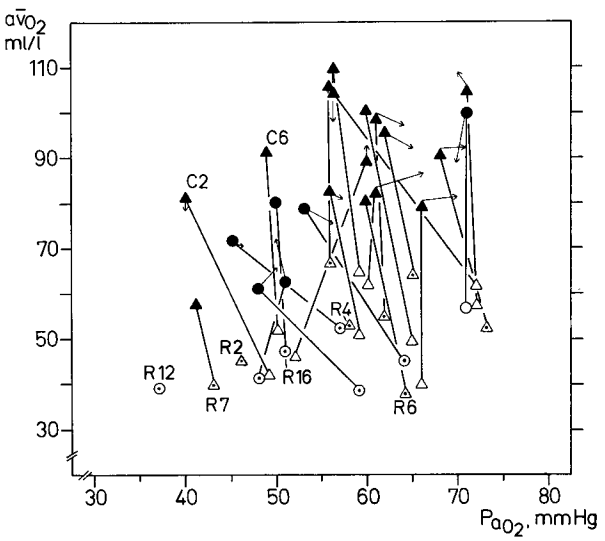


Fig. 2. The arterio-venous oxygen difference ($a\bar{v}_{O_2}$, ml/l) in relation to the arterial oxygen tension ($P_{a_{O_2}}$, mmHg) at rest and during exercise in the patients of groups R and C. At rest the symbols are the same as in Fig. 1 and at exercise: ▲ males; ● females. Patients C2 and C6 are the only patients with secondary polycythemia.

Table II. *The central haemodynamic findings during ambient air breathing in the supine posture at rest in groups R and C, as mean values and S.E.M.*

All measurements are from the Fick estimation, except the pressures in the superior vena cava ($\bar{P}_{SVC}$), the pressures in the right atrium ($\bar{P}_{RA}$)—mostly from the beginning of the catheterization—and the right ventricular systolic (RV_s) and end-diastolic (RV_{ED}) pressures, obtained at the end of the catheterization

	R group			C group		
	Male	Female	All	Male	Female	All
HR (beats/min)	88±6	85±4	86±4	83±4	81	83±4
$\dot{V}_{O_2}$, ml/min	227±9	204±6	—	234±8	200	—
R	0.78±0.02	0.74±0.01	0.76±0.01	0.75±0.02	0.76	0.75±0.12
Hb, g/l	125±3	122±5	123±3	135±6	125	134±6
Sa_{O_2}, %	88.4±2.2	83.2±4.2	86.2±2.2	90.1±1.5	92.6	90.4±1.4
$S\bar{v}_{O_2}$, %	59.0±2.8	57.5±3.9	58.4±2.2	61.8±1.7	61.0	61.8±1.5
av_{O_2} ml/l	51.9±3.7	43.9±2.2	48.5±2.5	52.8±2.8	57.0	53.2±2.6
$\dot{Q}$, l/min	4.5±0.2	4.7±0.3	—	4.5±0.3	3.5	—
P_{PA_s}, mmHg	43±5	45±5	44±3	39±4	30	38±4
$\bar{P}_{PA}$, mmHg	31±3	31±4	31±2	26±2	24	26±2
P_{PA_d}, mmHg	25±3	23±2	25±2	21±2	16	21±2
$\bar{P}_{PCV}$, mmHg	10±1	9±2	10±1	11±2	11	11±2
PVR, (mmHg/l)·min	4.8±0.8	4.7±0.5	4.7±0.5	3.2±0.4	3.7	3.2±0.3
P_{BA_s}, mmHg	142±8	157±14	148±7	133±6	166	136±6
$\bar{P}_{BA}$, mmHg	102±4	109±8	105±4	100±4	120	102±4
P_{BA_d}, mmHg	81±3	77±5	79±2	80±4	96	81±13
$\bar{P}_{SVC}$, mmHg	7±1	5±1	6±1	8±1	7	8±1
SVR, (mmHg/l)·min	22.9±1.4	23.5±2.1	23.1±1.2	22.9±1.7	34	23.9±1.8
$\bar{P}_{RA}$, mmHg	7±1	5±1	6±1	8±1	8	8±1
P_{RV_s}, mmHg	37±3	32±3	35±2	32±3	24	31±3
$P_{RV_{ED}}$, mmHg	7±1	3±1	5±1	7±1	3	6±1

during the Fick measurement (see Table II) was probably significant ($p < 0.05$) in group R, but not in group C. The increase in the mean PA pressure was significant ($p < 0.01$) in group R and probably significant ($p < 0.05$) in group C. The difference ($\bar{d} \pm$S.E.M.) in the mean PA pressure before and during the Fick measurement was -3.5 ± 3.3 mmHg in group R and -2.5 ± 2.3 mmHg in group C. The systolic PA pressure increased during the Fick measurement in 6 out of 14 group R patients (R1, 4, 7, 12, 13 and 14) and in 3 out of 11 group C patients (C2, 5 and 9) ≥ 5 mmHg. The same held for the diastolic PA pressure in 3 R-group (R1, 4 and 12) and in two C-group (C2 and C5) patients. As the arterial blood gases were measured only in patient R4 before and during the Fick measurement, no conclusions could be drawn for other patients as to whether changes in arterial blood gas tensions or in acid-base balance were involved in increasing the PA pressure. Only in one patient (C5) was the increase in diastolic PA pressure due mostly to an increase in PCV pressure, which increased by 7 mmHg. Though in a few patients increases or decreases of 2–3 mmHg were noted in the PCV pressure, no significant differences were observed either in the R or the C groups between the PCV pressure recorded before and during the Fick measurement. Neither did the intrathoracic variations of mean PCV pressure change during the Fick measurement. It should be noted, however, that PCV pressure measurement was not successful in all patients in both situations as arrhythmias had to be avoided. The mean PCV pressure variation due to intrathoracic pressure variations was about 11 mmHg in both group R (from 15–4 mmHg) and group C (from 16–5 mmHg). Further, the low blood volumes seen in many patients in this material might have had an effect on the PCV pressures.

As seen from the presentation of the individual data in Tables II and III, several patients were un-

Table III. *The individual central haemodynamic findings in the patients of group R during ambient air breathing in the supine posture at rest and during exercise and, in those cases where the patient was able to continue, at the same work load during breathing of a mixture of CO ($F_{ICO} \sim 0.0005$) in air*

The work loads are given in kpm/min and the duration of the work test periods in min ( ). In patients R 4 and 12 the pressures during the Fick measurement at rest are preceded by resting pressures, when the patients were not breathing through a respiratory valve. The different factors studied are expressed as in Table II
Italics denote measurement performed during ordinary breathing without a respiratory valve. *Value calculated from patient's own resting value with percentage addition according to mean increase for the whole material. **Value at 3 min at the same work load without carbon monoxide ($FI_{CO} \sim 0.0005$). ***Value obtained at end phase of catheterization during ordinary breathing

Pat. Sex	State and load $\frac{kpm}{min}$(min)	HR	$\dot{V}_{O_2}$	R	Hb	Sa_{O_2}	$S\bar{v}_{O_2}$	$a\bar{v}O_2$	$\dot{Q}$	$\bar{P}_{PA}$	$\bar{P}_{PCV}$	PVR	$\bar{P}_{BA}$-$\bar{P}_{SVC}$	SVR
R1 M	rest (10)	124	262	0.78	124	86.5	48.1	66.9	3.9	42	9***	8.5	90–*2*	23–23
	150 (6)	154	524	1.06	126	80.9	21.0	106.1	4.9	89	16*	14.9	102	21
R2 M	rest (10)	97	240	0.75	107	78.2	47.9	45.5	5.3	30	7	4.3	90–*4*	17–16
	100 (2.3)	118	—	—	—	—	—	—	—	45	—	—	120	—
R3 M	rest (10)	77	262	0.92	130	93.4	58.7	63.8	4.1	24	9	3.7	106–*7*	26–24
	200 (6)	96	682	0.88	125	91.4	36.7	96.2	7.1	39	16*	3.2	124	18
	CO+« (5)	101	688	0.91	124	90.3	37.4	92.4	7.4	34	16*	2.4	117	16
R4 M	*rest*	*68*	—	—					—	*27*	*11*	—	*105–9*	—
	rest (3.75)	75	204	0.72	129	87.5	58.4	53.1	3.9	41	11	7.7	114–*9*	29–27
R5 M	rest (10)	80	223	0.76	136	91.5	62.9	55.0	4.1	32	13	4.6	96–*11*	23–21
	150 (6)	130	698	0.91	141	89.9	40.1	98.7	7.1	56	23*	4.6	139	20
	CO+« (5)	134	732	0.90	142	92.0	43.3	97.4	7.5	55	23*	4.3	139	19
R6 M	rest (10)	80	201	0.79	117	93.3	70.5	37.9	5.3	21	7	2.6	110–*6*	21–10
	100 (6)	93	—	—	*121*	*90.4*	*44.2*	*81.2*	—	*31*	*9*	—	*143*	—
R7 M	rest (10)	94	207	0.74	129	81.3	59.2	40.2	5.1	34	*11*	4.5	114–*6*	22–21
	100 (5)	*117*	—	—	*132*	*79.5*	*48.0*	*58.0*	—	*48*	*14*	—	*144*	—
R8 M	rest (10)	75	215	0.79	124	95.8	66.2	52.8	4.1	23	13	2.4	98–*13*	24–21
	150 (6)	108	624	0.88	133	93.3	44.9	91.0	6.9	40	20	2.9	126	18
	CO+« (5)	115	708	0.91	133	94.5	45.5	92.3	7.7	38	20**	2.3	128	17
R11 F	rest (10)	75	184	0.72	112	90.0	65.8	38.8	4.7	35	11	5.1	80–*7*	17–16
	50 (6)	116	368	0.72	122	77.9	42.4	60.9	6.0	54	21	5.5	135	23
	CO+« (3.5)	122	415	0.73	122	76.7	38.6	65.4	6.3	54	21**	5.2	132	21
R12 F	*rest*	*81*	—	—	—			—	—	*34*	*6*	—	*89–4*	—
	rest (7)	89	204	0.74	112	64.3	39.7	38.6	5.3	40	*6*	6.4	97–*4*	18–18
R13 F	rest (10)	74	225	0.75	120	92.8	65.7	45.0	5.0	40	*15*	5.0	141–*7*	28–27
	100 (6)	105	517	0.81	127	83.3	38.9	79.2	6.5	73	25	7.4	182	28
	CO+« (4)	110	548	0.84	128	84.8	43.7	75.8	7.2	66	25**	5.7	182	25
R14 F	rest (10)	97	212	0.74	140	79.1	58.2	41.1	5.2	22	*9*	2.5	112–*4*	22–21
	100 (6)	115	—	0.87	144	80.9	50.1	62.5	—	40	15*	—	141	—
	CO+« (5)	127	594	0.93	149	77.1	42.6	72.0	8.3	43	15*	3.4	145	18
R15 F	rest (10)	97	195	0.75	130	88.0	59.6	52.3	3.7	23	*6*	4.6	108–*4*	29–28
	113 (6)	116	470	0.79	133	76.0	37.6	71.6	6.6	36	10*	3.9	125	19
	CO+« (4)	117	469	0.80	134	75.9	38.3	70.3	6.7	35	10*	3.7	122	18
R16 F	rest (10)	86	201	0.75	117	84.9	56.2	47.4	4.2	25	6***	4.5	114–*4*	27–26
	113 (4)	*102*	—	—	*122*	*82.1*	*35.6*	*80.0*	—	*35*	—	—	*120*	—

able to complete the planned test periods. The reasons, which were associated with the patients' disease, are given below.

The direct Fick measurement at rest had to be terminated early in patient R 4 because of severe dyspnoea accompanied by a marked increase in BA and PA, but not PCV pressure' and a simultaneous decrease in Pa_{O_2} from 65 to 58 mmHg and in pH from 7.39 to 7.32, and an increase in Pa_{CO_2} from 60 to 66 mmHg; also in patient R12 because of cough, dyspnoea and fatigue, with a simultaneous gradual increase in BA and PA pressure. During the later phase of the Fick measure-

Table IV. *The individual central haemodynamic findings in the patients of group C during ambient air breathing in the supine posture at rest and during exercise, and at the same work load also during breathing of a mixture of CO (F_{ICO} ~0.0005) in air in all patients except C 6, who had to terminate the test after 6 min*

The work loads are given in kpm/min and the duration of the work test periods in min ( ). The different factors studied are expressed as in Table II
Italics denote measurement performed during ordinary breathing without respiratory valve. *Group mean value. **Value at 3 min at the same work load without carbon monoxide (F_{ICO} ~0.0005). ₀, value calculated from $\dot{V}_E$ and re-measured $\dot{V}_{O_2}$ and R the next day.

Pat. Sex	State and load kpm/min (min)	HR	$\dot{V}_{O_2}$	R	Hb	Sa_{O_2}	$S\bar{v}_{O_2}$	$a\bar{v}_{O_2}$	$\dot{Q}$	$\bar{P}_{PA}$	$\bar{P}_{PCV}$	PVR	$\bar{P}_{BA}$-$\bar{P}_{SVC}$	SVR
C1 M	rest (10)	115	202	0.76	141	95.7	67.1	57.6	3.5	23	*17*	1.7	100–*12*	29–25
	100 (6)	144	512	0.73	142	95.0	41.8	105.1	4.9	40	26	2.9	118	24
	CO+« (4)	145	564	0.84	144	95.6	41.9	109.3	5.2	37	26**	2.1	119	23
C2 M	rest (10)	85	266	0.72	155	83.4	64.1	42.1	6.3	42	11	4.9	115–*8*	18–17
	200 (6)	119	727	0.80	165	69.3	34.1	81.4	8.9	69	14	6.2	135	15
	CO+« (5.5)	130	722	0.85	169	64.4	30.9	78.6	9.1	77	14**	6.8	130	15
C3 M	rest (10)	72	206	0.86	131	92.8	71.4	39.7	5.2	23	11	2.3	113–*8*	22–20
	150 (6)	97	565	0.88	133	92.0	49.3	80.3	7.0	29	10	2.7	113	16
	CO+« (5)	98	547	0.95	133	90.0	46.7	81.5	6.7	28	10**	2.7	111	17
C4 M	rest (10)	90	260	0.70	141	91.9	59.3	65.2	4.0	23	8	3.8	112–*7*	28–26
	200 (6)	132	825	0.82	147	86.4	32.9	110.4	7.5	52	12	5.3	127	17
	CO+« (3.75)	142	840	0.86	148	83.4	36.4	97.9	8.6	51	12**	4.5	130	15
C5 M	rest (10)	82	245	0.79	107	93.6	52.7	62.3	3.9	31	23	2.1	94–*11*	24–21
	150 (6)	124	590	0.90	117	82.6	18.6	104.9	5.6	59	36	4.1	91	16
	CO+« (4)	129	—	—	120	—	—	~112.1	—	60	—	—	96	—
C6 M	rest (10)	79	263	0.74	169	80.9	58.9	52.2	5.1	30	*15*	2.9	96–*10*	19–17
	113 (6)	97	625	0.83	170	77.3	38.7	92.0	6.8	48	19	4.3	121	18
C7 M	rest (10)	71	236	0.79	133	91.4	65.1	49.5	4.8	18	6	2.5	90–*5*	19–18
	200 (6)	93	669	0.73	137	90.4	38.4	100.6	6.6	26	8	2.7	104	16
	CO+« (4)	92	—	—	136	—	—	~93,7	—	23	—	—	99	—
C8 M	rest (10)	80	223	0.73	131	92.5	59.0	62.1	3.6	25	*8*	4.7	116–*7*	32–30
	50 (6)	89	348	0.75	137	88.7	45.8	82.6	4.2	32	12	4.8	140	33
	CO+« (4.5)	91	398	0.65	137	89.6	44.6	86.5	4.6	30	12**	3.9	136	30
C9 M	rest (10)	75	225	0.61	137	86.2	62.2	46.1	4.9	24	10*	2.9	78–*9*	16–14
	200 (6)	104	691	0.82	142	89.7	44.7	89.7	7.7	32	18*	1.8	98	13
	CO+« (3.75)	109	717	0.78	143	90.1	43.8	93.2	7.7	30	18*	1.6	96	13
C10 M	rest (10)	77	211	0.78	104	92.8	58.4	50.9	4.1	21	5	3.9	89–*5*	22–20
	150 (6)	103	602	0.85	106	85.2	30.0	82.8	7.3	36	13	3.2	110	15
	CO+« (5.5)	112	623	0.90	106	87.7	33.3	81.5	7.6	30	13**	2.2	111	15
C11 F	rest (10)	81	200	0.76	125	92.6	61.0	57.0	3.5	24	11	3.7	120–*7*	34–32
	150 (6)	106	519	0.83	129	91.3	36.5	99.8	5.2	34	17	3.3	137	26
	CO+« (6.5)	110	572₀	0.91	128	90.8	39.8	89.3	6.4	33	17**	2.5	126	20₀

ment Pa_{O_2} was 37 mmHg, Pa_{CO_2} 61 mmHg and pH 7.40. The symptoms were relieved by giving oxygen after the termination of the Fick measurement.

2. *Haemodynamics during work*

During work the *cardiac outputs*, when related to *oxygen uptake* (Fig. 1), were usually lower than the extrapolated cardiac output values of the normal material of 61–83-year old normal subjects (16) or 16–41-year old normal subjects (5, 23).

In 5 R-group (R1, 2, 6, 7 and 16) and in one C-group patient (C6) the chosen work loads (see Tables III and IV), which were the lowest available, proved to be maximal, and could be tolerated for only 2 min 20 sec—6 min.

In patients R1 the PA mean pressure increased from 40 mmHg at rest to 80 mmHg at 3 min, and further to 95 mmHg at 6 min; simultaneously Pa_{CO_2} increased from 48 to 56 mmHg and the pH decreased from 7.50 to 7.36, while Pa_{O_2} remained unchanged at 56 mmHg from rest to the last

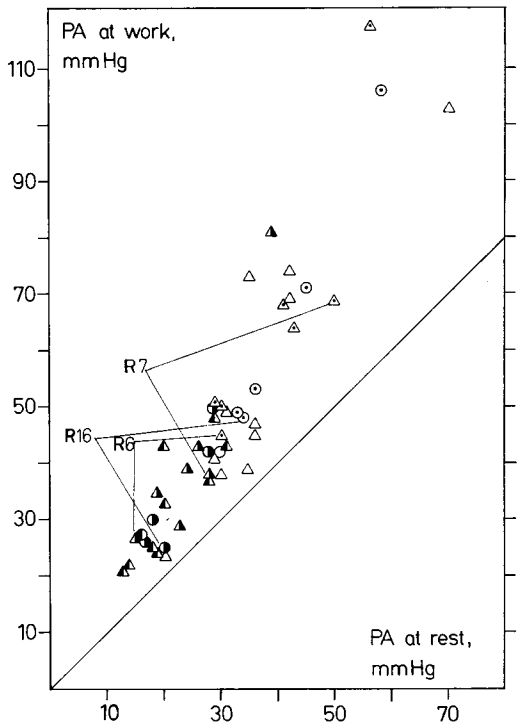


Fig. 3. The relationship between the pulmonary arterial (PA) systolic (Group R: △ males, ⊙ females and group C: △ males, ○ females) and diastolic (Group R: ▲ males, ◑ females and group C: ◭ males, ◐ female) pressures at rest and during exercise during the Fick measurement. In patients R6, 7 and 16 the exercise was performed without breathing through a respiratory valve. In 61–83-year old healthy male subjects (Granath et al., 1964) the upper normal limit (mean+2 S.D.) at rest for the PA systolic pressure was 30 mmHg and for the diastolic pressure 16 mmHg; the corresponding pressures in submaximal working conditions were 62 and 30 mmHg at mean cardiac outputs of 5.8 and 10.3 l/min, respectively.

minutes of exercise. This patient was so dyspnoeic that he had to sit up after termination of the exercise, which he had performed lying in a 30-degree half sitting posture. In this patient the pressure increase in the pulmonary artery was caused both by flow increase during exercise and by pulmonary vasoconstriction—possibly due to P_{aCO_2} or pH, as both the systolic and diastolic pressures increased. The marked systolic PA pressure increase ensuing from a small increase in cardiac output is, however, a sign of a largely reduced capillary bed or vasoconstriction. Patient R2 tolerated the work load of 100 kpm/min only for 2 min 20 sec, and during this time the increase in PA and in BA pressure was marked in relation to the work load, P_{aO_2} decreased from 46 to 35 mmHg and pH from 7.39 to 7.37, and P_{aCO_2} increased from 60 to 65 mmHg. The necessity for early termination of the work test was unexpected, as on the previous day the patient had had a W_{max} of 235 kpm/min in the sitting posture. During the supine work test the heart rate (HR) increased less and the blood pressure more, P_{aO_2} was lower and P_{aCO_2} higher. As, in the supine posture, HR increased less than in the sitting position, it is possible that the right ventricle was unable to respond with an increasing stroke volume to the increased filling of the right ventricle during exercise in this position.

Patients R6 and 7 were able to continue at a work load of 100 kpm/min for 6 and 5 min, respectively, without breathing through a respiratory valve, but showed marked increases in both the pulmonary arterial and systemic blood pressures. In patient R16 who managed a work load of 113 kpm/min for 4 min (also without a respiratory valve), the $a\bar{v}_{O_2}$ and PA pressure were high, but the BA pressure, probably because of an extremely low cardiac output, increased moderately. Two of the above patients (R7 and 16) were severely hypoxaemic (and hypercapnoeic), but showed large differences in $a\bar{v}_{O_2}$. The ECG pattern in all of these patients indicated a possible myocardial disease (8) and all of them had a high systolic blood pressure. The PCV pressure was not pathologically increased in these patients. The low blood volumes should be noted, however (Table I), and may have been responsible for the low resting pressures. During work the PCV pressure increased both in R6 and 7 (not measured in R16), but not with certainty to a pathological extent. During hypercapnoea (40, 41) the BA and PCV (in R7 and 16 only the diastolic PA pressure was measured) increased in these three patients.

In the only C-group patient (C6) tested in maximum working conditions, the PCV pressure was pathologically elevated already at rest and increased like the PA pressure and $a\bar{v}_{O_2}$ (partly due to the high haemoglobin concentration) at a very low work load. The T-wave changes which had only been seen for a few weeks prior to the investigation (8) and the increased PCV pressure fit well with left ventricular failure. In this patient the right ventricle might also have been in latent failure as the RV_{ED} pressure was high and the increase in both the PCV and PA pressure increased the work of the right ventricle. Further, the carbon dioxide retention might have had an impairing effect on the myocardial contractility and the pH decrease to 7.32 at the low work load of 100 kpm/min could have had a constricting effect on the pulmonary vessels (21).

The relationship between the *PA systolic* and *diastolic pressure at rest* and the corresponding pressures *during work* are presented in Fig. 3. The same tendency as in the pressure changes from complete rest to Fick measurement was seen; namely, the increase in pressure was dependent on the original pulmonary arterial pressure level. Of the patients with high pressures a few more belonged to group R than to group C. In general, however,

these patients were also nearer to their maximum physical working capacity. Granath et al. (16) found that the upper limit (mean +2 S.D.) for normal male subjects 61–83 years old was about 56 mmHg for systolic PA pressure and about 26 mmHg for diastolic and about 41 mmHg for the PA mean pressure, and about 32 mmHg for the PCV mean pressure at flow rates which were, on the average, twice as high as in our patients.

When the *systemic arterial mean pressure* and the *mean pressure gradient* over the *pulmonary peripheral vessels* are presented in relation to cardiac output (Fig. 4), the systemic arterial resistance (SVR) and pulmonary vascular resistance (PVR) can be read along the oblique iso-resistance lines in the figure. In relation to the regression line between cardiac output and arterial mean pressure in the normal material of old healthy subjects mentioned above, the SVR of our patients fell on both sides of the line. There were, however, some patients, who either already at rest had a high mean arterial pressure in relation to their cardiac output, and therefore a high SVR, or who during exercise at a work load which for them was almost maximum (e.g. R11) developed a high arterial pressure while their cardiac output increased very little. The only patients who at rest had a diastolic blood pressure from 95–100 mmHg were R13 and C11. During work the directly measured diastolic pressure was >100 mmHg in patients R5, 6 and 13 and C1, 4, 8 and 11. Patients R6 and 13 and C1 had diastolic arterial pressures of >110 mmHg. In some of these patients the increased arterial pressures might have contributed to the increased PCV pressures. Many of them also had high pulse pressures, even though in some cases the diastolic pressure was normal.

In all patients of this material PVR lay beyond the normal regression line for old healthy male subjects (16), but in some of the patients, however, it lay inside the upper normal limit. These patients were usually those with increased PCV pressures. The work of the right ventricle was therefore in reality greater in these patients than could be concluded from the measured PVR. In 5 out of 8 patients of group *R* in whom PVR was measured during work, the PVR is an approximation as the PCV pressure was not measured, but calculated from the mean PCV pressure increase. In 2 of these patients PVR decreased during work. Out of 11 patients of group C, in only one of whom the PCV pressure was an approximation, the PVR decreased during work in

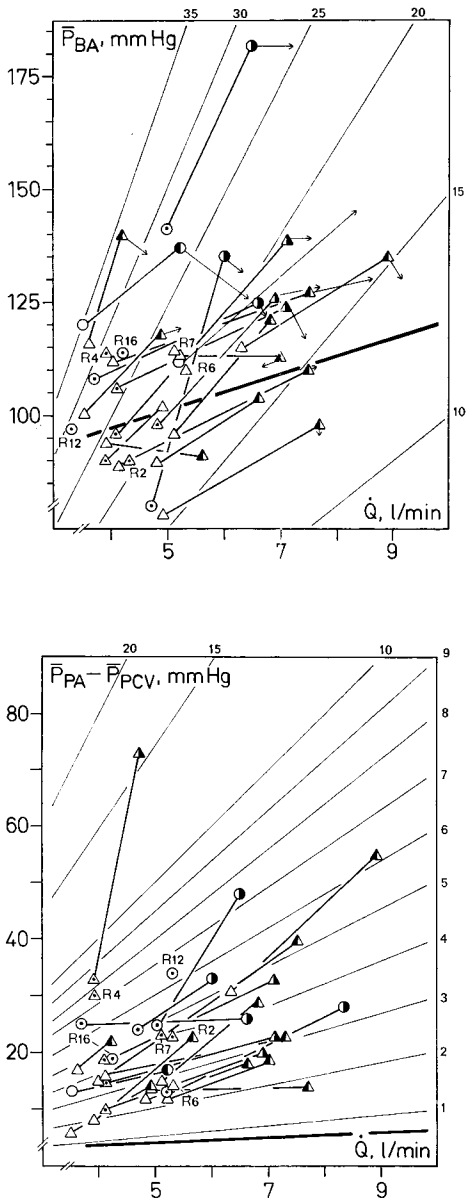


Fig. 4. The mean brachial arterial pressure ($\bar{P}_{BA}$, mmHg) and the pressure drop over the peripheral pulmonary vessels ($\bar{P}_{PA}-\bar{P}_{PCV}$, mmHg) in relation to the cardiac output ($\dot{Q}$, l/min) in the supine posture at rest and during exercise in the patients of groups R and C (same symbols as in Fig. 1). The thin oblique lines are isoresistance lines. The systemic vascular and pulmonary vascular resistance are given in (mmHg/l)·min. The thick oblique lines are the regression lines from the normal material of 61–83-year old healthy male subjects (Granath et al., 1964). The regression equations for the normal material were: $\bar{P}_{BA} = 3.61 \times \dot{Q} + 83.4$, $r = 0.69$ and S.D. $= \pm 13.0$ and $(\bar{P}_{PA}-\bar{P}_{PCV}) = 0.34 \times \dot{Q} + 2.8$, $r = 0.48$ and S.D. $= \pm 3.3$.

3 patients and remained unchanged in one during the first 6 minutes of exercise. When the work load was continued, PVR—assuming that the PCV pressure was the same as during the first 3 minutes of exercise—decreased in all patients in group R who were able to continue at that load, and in 6 out of 8 patients of group C. In patient C2 PVR increased and in C3 it remained unchanged when the work was continued.

DISCUSSION

Heart catheterization of patients with severe chronic obstructive lung disease, in their habitual state, has to be done with great care in order to avoid complications. Resuscitation of these patients would be more difficult than of patients with normal respiratory function. For safety reasons, repeated PCV pressure measurements had to be omitted in several of the R-group patients, as arrhythmias or right bundle branch block appeared as soon as attempts were made to bring the catheter tip to the wedged position. No acute complications occurred in these patients except that in patient R12 the distress caused by the Fick measurement had to be relieved by immediate administration of oxygen after termination of the test. In patient R16, who had previously had atrioventricular block (8), there was a supraventricular arrhythmia with interference between ectopic atrial and nodal beats the day after the catheterization, but after a period of atrial fibrillation and frequent ventricular ectopic beats there was a return to sinus rhythm one day later. In patient R7, who came to the laboratory with atrial fibrillation, the sinus rhythm returned spontaneously at the beginning of the catheterization.

The oxygen uptake values obtained may have been influenced by an unequal ventilation/perfusion distribution in patients where steady state conditions were not fulfilled (17) and also by decreased alveolar ventilation resulting from the increased dead space ventilation caused by the ventilatory valve. The cardiac output measurement at rest may have been influenced by these factors in the most severely disabled patients, in whom, as mentioned in "Results", the pressures increased in the pulmonary artery and in some patients also in the systemic artery during the Fick estimation. In these patients the increase in dead space ventilation caused impairment of alveolar ventilation and carbon dioxide retention, which in turn influenced the pressures. The alveolar ventilation could not be increased because of the small total ventilatory capacity. The mechanism for the pressure increase may be the same as in induced hypercapnoea (40, 41), as the arterial carbon dioxide tension is increased in both. The Fick measurement at rest corresponds, however, in these patients, to conditions in which CO_2 production is higher than in the fasting state and at total rest, that is to conditions encountered during the patients' daily activities. In the whole material, in relation to the calculated normal values the oxygen uptake at rest was increased to about the same extent as in the old healthy subjects reported by Granath et al. (16). The steady state and basal conditions were thus well fulfilled in most of the patients in this material though many of them were dyspnoeic even at rest.

As several authors (27, 33, 35) have shown the PCV and left ventricular end-diastolic (LV_{ED}) pressures to be equal by simultaneous measurements, in this study the PCV pressure have been considered to correspond to the LV_{ED} pressure, though other authors have previously been uncertain whether the PCV pressure, could be used for this purpose. This hesitation has been based on the view that large intrathoracic pressure variations, alveolar pressures and shunting from the bronchial to the peripheral pulmonary vessels may influence the PCV pressure more than the pressure in the left atrium in patients with chronic obstructive lung disease (19, 24, 26, 29, 43). Sapru et al. (35) found the PCV and LV_{ED} pressures to be equal in patients without valvular or lung disease and the same finding was made by Rao et al. (33) in 3 patients with respiratory insufficiency both during failure, when the pressures were high, and after recovery, when the pressures had normalized. The same was shown by Lockhart et al. (27) in 9 patients with chronic bronchitis. Lockhart et al. showed also, by measuring both the PCV and intra-oesophageal pressure at rest and during exercise, that the PCV pressure was not dependent on the intrathoracic pressure alone, as the PCV pressure, but not the intra-oesophageal pressure increased during exercise. Kitchin et al. (26) also showed that PCV pressure increased more than intrathoracal pressure during exercise.

In this material there were several patients with impaired left ventricular function, if PCV pressure levels of 13 mmHg at rest or 20 mmHg at exercise, as recommended by Enghoff, Nordgren and Ström (12), are regarded as upper normal limits. The upper

limit (mean +2 S.D.) of the resting PCV pressure of the 61–83-year old healthy male subjects (16) was about the same as that used here, but the corresponding exercise PCV level would be 31 mmHg. This limit was considered too high as the mean age of our patients was about 10 years lower and as some of the elderly "normal subjects" with high PCV pressures might have had a myocardial disease.

A suspicion that the left ventricle might also be involved was aroused in some patients from a retrospective study of the ECG changes, ECG reactions, varying blood pressure reactions at different exercise tests and changes in the physical working capacity independently of the ventilatory capacity, as described in detail by Brundin & Tammivaara-Hilty (8). Several of these patients with suspected myocardial disease also had increased PCV pressures. In patients R 5, 8 and 13, and C 5 and 6, the PCV pressure was elevated even at rest and in R 11 the increase was seen during exercise at a very low work load, which was, however, near to maximum for the patient. In some of these patients, as mentioned in "Results" a high arterial blood pressure might have contributed to the increase in PCV pressure. In patient C 1, who showed a normal QRS complex in the scalar ECG the increased PCV pressure, noted both at rest, together with an RV_{ED} pressure, during exercise and during induced hypercapnoea, might have explained the high ventilatory increase during exercise and the lower physical working capacity with tachycardia than was expected from the ventilatory tests. PCV pressures of $\geqslant 25$ mmHg, as were found in this patient and patient C 5, have been shown by Gazetopoulos et al. (15) to stimulate ventilation.

In some patients, such as patient R 6 with a normal PCV pressure at rest and at a low work load in spite of T-wave inversion over the left ventricle—and C 8, with normal QRS complexes and normal PCV pressures at rest and during exercise at a very low work load, the PCV pressure increased during arterial hypertension induced by hypercapnoea. This was probably also the case in patient R 7, in whom, however, the PCV pressure measurement during hypercapnoea was unsuccessful and only the PA pressure was seen to increase—somewhat later than the arterial blood pressure. The changes are described in detail and the mechanism involved is discussed by Tammivaara-Hilty (40, 41). During arterial hypertension produced by an angiotensin infusion in patients with chronic obstructive lung disease Baum et al. (4) found the stroke work index to be lower than in normal subjects.

Some authors (32, 36) have found among their patients with chronic obstructive lung disease and secondary polycythemia an increased right and/or left ventricular filling pressure, which decreased after venesection if the total blood volume remained decreased. Segel & Bishop (36) found a decreased filling pressure of both ventricles, but Rakita et al. (32) noted this on the right side of the heart. Several authors (25, 32, 33, 45, 47) have also observed that the total blood volume is increased in patients with chronic obstructive lung disease in failure and that both the total blood volume and increased filling pressures, noted in several of the patients, return to normal during recovery. Most of these authors have considered that the changes are due to alterations in the red cell volume, but Abraham et al. (1) have also found a decrease in plasma volume during recovery.

As the blood volumes were somewhat low in many of our patients, all of whom were investigated in their habitual state as assessed clinically, this may explain why in some cases the filling pressures were normal even though according to other findings, such as ECG and discrepancies between the ventilatory and physical working capacities (42), myocardial impairment was obvious (R 6, 7 and 16). The validity of the blood volumes obtained by the alveolar CO method can be discussed, for reasons to be mentioned below. However, it seems obvious, even from conventional Hb measurements that these patients with the exception of two had normal or low Hb values. The blood volumes obtained have to be compared with the normal values of our laboratory, as the THb measured by the alveolar CO-method has been reported by Bratteby et al. (7) to give 5–12.5% lower values than THb with the ^{51}Cr technique at the THb levels in question. As the BV of these patients has been calculated from Hb values measured from arterial blood sampled in the sitting posture at rest on an ergometer bicycle, instead of from capillary blood in a semi-recumbent sitting position, the BV's obtained might be systematically somewhat lower than in normal subjects of corresponding age (9). On the other hand the blood volume measurements were performed before arterial blood sampling in connection with gas exchange studies on the previous day. In most of the patients, except R 4 (in whom the gas exchange study during exercise was excluded) and patients

R7, R12 and R16 (in whom gas exchange studies included only studies in resting conditions and on one work load), 150–200 ml of blood was sampled. Therefore the red cell blood volume might have been lower at the time of the catheterization than when measured 1–2 days earlier. A decrease in haematocrit from arterial blood samples taken in the sitting posture on the previous day to those taken in the supine posture during the catheterization depends both on differences in body posture and the amount of blood sampled during gas exchange studies. It can be questioned whether veno-arterial shunting may have influenced the THb measurements. As the lung N_2-washout period during THb measurements was prolonged to 15 min in most of the patients and veno-arterial shunting, as reported in another connection by the author (41), was small after 15–25 pure oxygen breathing, the longer equilibration time at the THb measurement should have been long enough.

The same rise in PCV pressure during exercise as in our patients has also been found by Kitchin et al. (26) and Horsfield et al. (24), but not by Williams et al. (43). As these authors found the increase in cardiac output to be normal in their patients, they considered it improbable that increased PCV pressure would have been caused by left ventricular failure. As the patients in the present material had low cardiac outputs compared with normal healthy subjects of corresponding age, they might have had impaired myocardial function. Low cardiac outputs have also been found by Filley et al. (13) in patients with emphysema, but not to the same extent in chronic bronchitis. As these authors reported no measurements of PCV pressure it is impossible to draw conclusions as to whether some of their patients with emphysema and low cardiac output might have had impaired myocardial function.

The pulmonary arterial hypertension in most of these patients was slight to moderate and corresponded to pressure levels found by most authors (24, 26, 39, 44, 46) when their patients were not in failure or polycythemic; in conditions of failure and polycythemia the pulmonary hypertension has been generally reported to be much more severe (1, 20, 25, 27, 29, 33, 36, 39, 47). Though the mean values for mean PA pressure and the PVR were higher in group R than in group C, only PVR was statistically significantly lower in group C ($p < 0.025$), as the interindividual differences in both groups were large. Though the mean S_{aO_2} and PA pressures did not differ significantly between groups R and C, there might, however, be a causal relationship between them as a negative correlation was found between S_{aO_2} on the one hand and mean PA pressure ($r = -0.43$) and the pressure gradient ($\bar{P}_{PA}-\bar{P}_{PCV}$) over the pulmonary peripheral vessels ($r = -0.59$) on the other. According to my own investigations (40) and Harvey et al. (21) and Stuart-Harris (38), who have reviewed the findings of earlier authors, arterial hypoxaemia is only one of the factors correlated to pulmonary hypertension. This is also evident from the results for the male and female patients of group R of the present study, in whom the same pulmonary hypertension and cardiac output was found, but a tendency to lower S_{aO_2} in the female patients. In this material in resting conditions a correlation was also found between arterial carbon dioxide tension (P_{aCO_2}) and mean PA pressure ($r = 0.54$), on the one hand, and $\bar{P}_{PA}-\bar{P}_{PCV}$ mentioned earlier ($r = 0.63$), on the other. Corresponding correlations were also found at rest between base excess in arterial blood and mean PA pressure ($r = 0.49$) and pressure gradient ($r = 0.61$), but not between pH and the corresponding findings. The better correlation between the base excess than pH with pressures over the pulmonary vessels, may be due to differences in electrolyte concentration as pointed out by Robin (34), among others. The pH in these patients may be alkalotic either because of acute hyperventilation—or because of prolonged metabolic alkalosis after respiratory insufficiency, if there is chloride depletion. Among other factors contributing to pulmonary hypertension may be mentioned the differences in left ventricular filling pressures in the individual patients, though between the groups no significant differences were found. Also, the positive correlation found in this material between PCV and RV_{ED} pressure ($r = 0.56$) might be one of the indications in favour of the idea that pulmonary hypertension often is a disease of the whole heart, as can be concluded from many autopsy studies (14, 30) and as pointed out by Altschule (2). The results obtained by Kitchin et al. (26), Parker et al. (31), Rao et al. (33), Horsfield et al. (24), Lockhart et al. (27), McCredie (28) and Baum et al. (4) can be interpreted in the same way. Furthermore most of the patients with severe chronic obstructive lung disease are at an age where arteriosclerotic changes are common. There is no possibility of excluding arteriosclerosis without autopsy studies. Perhaps even more interest should be paid

to the combination of arteriosclerotic heart diseases and chronic obstructive lung diseases, as smoking, for example, common among both types of patients, might be one of the aetiologic factors. The prevalence of ischaemic ECG changes has been shown by Bhargava & Woolf (6) to be higher among patients with CO_2 retention, though this prevalence was not different in patients with less severe chronic diffuse pulmonary diseases than in a control group.

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