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Gas Exchange in Severe Chronic Obstructive Lung Disease in Relation to Inspired Oxygen and Increased Carbon Dioxide Fraction, Physical Exercise and Body Posture

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ABSTRACT

Pulmonary gas exchange (Douglas bag), arterial blood gas tensions and acid–base balance (electrode technique), were studied in 25 patients with severe chronic obstructive lung disease and a ventilatory capacity (MVV_F) ≤35% of predicted normal values. Comparisons were made, in the habitual state, between patients with earlier periods of manifest respiratory insufficiency (R-group) and a group of patients (C = comparison) with the same ventilatory impairment, but no such periods of insufficiency.

During ambient air breathing at rest, in the supine posture, the means and ranges of arterial blood gas tensions were not significantly different in the R- and C-groups, but standard bicarbonate and base excess were more elevated in the R-group. $P_{a_{O_2}}$ ranged from 37 to 73 and $P_{a_{CO_2}}$ from 36 to 63 mmHg. The elevated V_D/V_T was not consistently different at rest in the supine and sitting body postures, but in the supine posture most of the ventilatory variables were lower in both groups and $P_{a_{CO_2}}$ was higher in the R-group. In the C-group some of the ventilatory variables remained lower during exercise in the supine posture. During supine exercise V_D/V_T decreased in the C-, but not in the R-group.

The habitual $P_{a_{CO_2}}$ level and acid–base status were important factors for ventilatory changes during hypoxia, hyperoxia and induced hypercapnoea. Also the habitual $P_{a_{O_2}}$ influenced these changes. R-group female patients and two C-group male patients with secondary polycythemia seemed to be most adapted to chronic hypercapnoea.

INTRODUCTION

The pulmonary gas exchange, arterial blood gas tensions and acid–base balance in the habitual state of patients with severe chronic obstructive lung disease and with maximal voluntary ventilation (MVV_F) ≤35% of predicted normal values, were investigated to find out whether any differences existed between patients known to have had periods of manifest respiratory insufficiency (R-group) and patients who had had no such periods (C = comparison-group). The patients were studied during ambient air breathing at rest and during work in order that knowledge might be gained of the conditions during their daily activities. These studies were performed in two body postures in order to find out whether the common clinical opinion that patients with pulmonary dyspnoea are not orthopnoeic could be confirmed and is true also in patients with earlier periods of manifest respiratory insufficiency.

Studies during hypoxia and hyperoxia were also conducted, with the aim of obtaining a picture of the components of the alveolo-arterial oxygen tension difference in these patients. By increasing the hypoxaemia and the carbon dioxide retention, in certain respects induced hypoxia and hypercapnoea simulate an acute exacerbation of the airway disease, and induced hyperoxia corresponds to a therapeutic situation in connection with an acute exacerbation. The ventilatory reaction and the changes in arterial blood gas tensions were also studied in these patients in order to find out if differences in these variables could be the reason for differences in the clinical course of the disease in these two groups of patients.

MATERIAL

The material consisted of 25 patients, selected among persons treated in 1968–1970 at the Department of Pulmonary Diseases, University Hospital, Uppsala, for chronic obstructive lung disease and with a maximal voluntary ventilation (MVV_F) ≤35% of predicted normal values. The principles for selection of the patients have been described and the material presented in detail by Brundin & Tammivaara-Hilty (3, 26, 28).

The material was divided into two groups according to the

clinical development of the disease: 1) a respiratory insufficiency (R) group of 14 patients (8 male, 6 female), who had had periods of manifest respiratory insufficiency on one or more occasions and 2) a comparison (C) group of 11 patients (10 male, one female), who had never had respiratory symptoms of the same degree of severity.

The average age, height and weight of the R-group male patients was 62 (50–69) years, 61 (52–82) kg and 174 (162–186) cm and of the female patients 64 (57–72) years, 53 (39–73) kg and 161 (158–165) cm. The corresponding values of the C-group male patients were 59 (39–70) years, 62 (53–83) kg and 172 (162–180) cm and of the one female patient 56 years, 46 kg and 158 cm.

METHODS

The gas exchange studies were performed on two separate days: all the gas exchange studies in the sitting posture were done on the first day after a light lunch and all those in the supine posture the day after, in connection with the right heart catheterization (started at 8 a.m.) In patient R4 all gas exchange studies were performed on the same day, the studies in the supine posture (ambient air breathing and hyperoxia) preceding study at rest sitting on an ergometer bicycle.

The principles for arterial blood sampling and gas exchange studies during ambient air breathing, at rest and during exercise on an electrically braked bicycle ergometer, induction of hypoxia and hyperoxia at rest, right heart catheterization and laboratory methods have been described by the author elsewhere (5, 26, 27). For calculation of the veno-arterial shunting ($\dot{Q}_{sh}/\dot{Q}$, %) in this material, however, the $a\bar{v}_{O_2}$ difference measured during hyperoxia was used. In measuring the $a\bar{v}_{O_2}$ difference it was taken for granted that $S_{a_{O_2}}$ was 100%, and the pulmonary arterial saturation was measured. In calculating the arterial oxygen content consideration was also taken of the $P_{a_{O_2}}$ value measured during hyperoxia.

Hypercapnoea ($F_{I_{CO_2}}$ 0.0542–0.0604 in air) was induced at rest in the supine posture in connection with the right heart catheterization in 22 patients and in connection with gas exchange studies, after a ½–1 year long period of physiotherapeutic breathing exercises and circulatory training, in 2 patients (R8 and R12). The study was postponed in patient R8 for technical reasons and in patient R12 because she was too unwell to tolerate the test at that time. In patient R4 no hypercapnoea was induced. The hypercapnoic test was performed more than 10 min after hyperoxia in all patients, except in 5 from group R (R1, 3, 5, 8 and 14) and 3 from group C (C2, 3 and 7), in whom it was performed more than 10 min after the work test. The intention was to collect the expiratory gas during the last 5 min of a 10-min period of induced hypercapnoea and to perform blood sampling in the middle of the gas collection period. As several of the patients became so distressed that the test had to be terminated earlier, however, gas collection and blood sampling had to be performed during a few minutes before termination in these patients; further details are given elsewhere (27). Gas analyses from collection periods of ≤ 1 min were not included in the calculations. The values for patients R8 and 12 are not included in the group mean values presented in Table V. The gas exchange calculations were made according to the same principles as described earlier (5), except that they were modified in regard to the $F_{I_{O_2}}$ and $F_{I_{CO_2}}$ concerned. The calculations were performed by computer.

Voluntary hyperventilation was induced at the end of the right heart catheterization, in the supine posture, for 1 min and during the last 20 sec of this 1-minute period arterial blood was sampled for measurements of arterial blood gas tensions and acid–base balance.

Pulmonary gas exchange studies were performed during exercise at a conventional exercise test up to maximum work load (28) and also from min 12 to 15 and 27 to 30 at a submaximum work load (or maximum in a few cases) in the sitting posture in patients who were not too incapacitated. This test was started more than 10 min after the maximum work test, which enabled the submaximum work load to be chosen. In a few cases (R6, R11 and C8) the chosen work loads were maximum for the patient, but the lowest available. The patient cycled in the conventional way without breathing through a respiratory valve during the first 10 min, and also from the 15th–25th min, and the respiratory valve was then connected to the patient for flushing of the Douglas bag with expiratory gas before gas collection, which was performed between the 12th and 15th and 27th and 30th min. These investigations had to be excluded in patients R4, 7, 12 and 16, as they were too incapacitated to perform any exercise test or terminated the test after only a few minutes. In patients R6 and R11 no gas collection could be performed in connection with the "long-term" work test as the patients were too dyspnoeic to tolerate breathing through a respiratory valve. In patients R6 and R15 the test was terminated after 11.5 and 16.5 min, respectively, because of dyspnoea and fatigue. The arterial blood sampling was performed in the middle of the gas collection periods.

Arterial blood gases and acid–base balance were also measured, in the supine posture during ambient air breathing and 10 min after the short-term and long-term exercise tests in the sitting posture, on the first day of the gas exchange tests.

RESULTS

1. *Pulmonary gas exchange, arterial blood gas tension, acid–base balance and arterial oxygen saturation findings during ambient air breathing*, in the supine posture at rest, are presented in Table I for male and female patients of groups R and C.

Among the R- and C-group patients the range in arterial blood gas tensions was wide. In the R-group $P_{a_{O_2}}$ varied from 37 to 73 mmHg and $P_{a_{CO_2}}$ from

Table I. *Pulmonary gas exchange, arterial blood gas tensions, acid–base balance and oxygen saturation during ambient air breathing in supine posture at rest in respiratory insufficiency (R) and comparison (C) group patients*

Mean values and S.E.M. are given

	R-group			C-group		
	Male	Female	All	Male	Female	All
	$n=8$	$n=6$	$n=14$	$n=10$	$n=1$	$n=11$
$\dot{V}_E$, 1 BTPS/min	8.7±0.6	6.8±0.3		9.1±0.5	8.3	
$\dot{V}_{O_2}$, ml STPD/min	227±9	204±6		234±8	200	
Vent. equiv.	38.5±2.0	33.8±1.9	36.3±1.5	38.9±2.3	41.5	39.1±2.1
R	0.79±0.02	0.74±0.00	0.77±0.01	0.75±0.02	0.76	0.75±0.02
f (breaths/min)	20±2	17±2	18±1	18±1	20	18±1
$\dot{V}_A$, 1 BTPS/min	3.3±0.3	2.6±1.2		3.3±0.2	2.9	
V_D, ml BTPS	240±22	223±30		282±23	225	
V_D/V_T	0.51±0.03	0.55±0.03	0.53±0.02	0.54±0.01	0.54	0.54±0.01
P_{A-aO_2}, mmHg	28.9±3.5	27.3±3.3	28.2±2.4	28.0±1.3	23	27.6±1.3
P_{aO_2}, mmHg	58.4±3.5	52.7±3.9	55.9±2.6	60.4±2.7	71	61.4±2.6
P_{aCO_2}, mmHg	50.6±3.0	54.8±2.5	52.4±2.0	46.3±2.8	46	46.3±2.5
pH	7.42±0.02	7.38±0.00	7.40±0.01	7.40±0.01	7.42	7.40±0.01
HCO_3^-, mEq/l	30.4±0.9	29.0±1.6	29.8±0.9	26.8±0.7	28	26.9±0.6
BE, mEq/l	6.5±1.0	4.8±1.7	5.8±0.9	2.6±0.7	4	2.7±0.7
S_{aO_2} calc., %	88.6±2.3	84.2±3.4	86.7±2.0	90.1±1.5	94	90.5±1.4
S_{aO_2}, %	88.4±2.2	83.2±4.2	86.2±2.2	90.1±1.5	92.6	90.4±1.4

36 to 63 mmHg. In the C-group P_{aO_2} varied from 49 to 72 mmHg and P_{aCO_2} from 36 to 63 mmHg. Two of the most hypoxaemic C-group patients (C2 and 6) had secondary polycythemia, the highest P_{aCO_2} levels (58 and 63 mmHg) and the lowest arterial pH values (7.35 and 7.34).

Most patients of both group R and group C were hypoxaemic and hypercapnoic in spite of hyperventilation, as the alveolar ventilation was decreased and the dead space ventilation increased. P_{aO_2} showed only a tendency to be lower ($p<0.20$) and P_{aCO_2} to be higher ($p<0.10$) in the R-group. Standard bicarbonate (HCO_3^-, $p<0.02$) and base excess (BE, $p<0.01$) were higher in the R-group due to metabolic compensation of the respiratory acidosis. There were no statistically significant differences between male and female patients of group R. The alveolo-arterial oxygen tension differences were equally high in all groups except in the only C-group female patient, in whom it was lower. This patient was less hypoxaemic but hypercapnoic to the same extent as the male patients of the same group.

2. The same *pulmonary gas exchange, arterial blood gas tension, acid–base balance and saturation* findings *during ambient air breathing* as in Table I are presented in Table II for different sub-groups of groups R and C classified according to whether hypoxia was induced or not and to whether it was terminated at the higher or the lower F_{IO_2} level.

Hypoxia was not induced in patients R4, 12 and 16. Patient R4 was the most tachypneic, hypercapnic and acidotic patient and he had the lowest alveolar ventilation and highest V_D/V_T ratio of the male patients. The moderate increase of BE indicated that the patients carbon dioxide retention was more severe than in his habitual state. This probably was due to the respiratory valve and tachypnoea, as the patient was less hypoxaemic and hypercapnic when breathing without the valve (26). It may be mentioned, however, that this patient, in spite of using the same respiratory valve and having the same breathing frequency, was considerably less hypercapnic in the sitting posture when his ventilation had increased because of change of body posture. Both female patients (R12 and 16) also had high V_D/V_T ratios, they were hypercapnic and were two of the most metabolically compensated of the female patients. The high BE values indicate that these patients were chronically hypercapnic. Patient R12 was the most hypoxamic patient of the whole material.

Table II. *Pulmonary gas exchange, arterial blood gas tensions, acid–base balance and oxygen saturation at rest in supine posture during ambient air breathing in different sub-groups of groups R and C classified according to whether hypoxia was induced or not, and to whether hypoxia was terminated at the higher (F_{IO_2} 0.1395–0.1530) or thelower (F_{IO_2} 0.1035–0.1260) F_{IO_2} level*

Mean values and S.E.M. and/or range are given

	R-group						C-group			
	Male				Female		Male			Female
			Terminated at					Terminated at		
Induced hypoxia ...	−	+	~15% O_2	~11% O_2	−	+ and termin. at ~15% O_2	+	~15% O_2	~11% O_2	~11% O_2
	$n=1$	$n=7$	$n=4$	$n=3$	$n=2$	$n=4$	$n=10$	$n=2$	$n=7$	$n=1$
$\dot{V}_E$, 1 BTPS/min	8.4	8.8±0.6 7.2–12.3	8.2±0.5 7.2–9.2	9.6±1.4 8.0–12.3	7.5	6.4±0.4 5.8–7.4	9.1±0.5 7.9–12.6	8.7 8.0–9.3	9.3±0.6 8.0–12.6	8.3
$\dot{V}_{O_2}$, ml STPD/min	204	230±10 201–262	233±12 207–262	226±18 201–262	203 201–204	204±9 184–225	234±8 202–266	243 223–263	232±10 202–266	200
Vent. equiv.	40.9	38.2±2.3 27.3–47.0	35.3±2.9 27.3–41.1	42.0±2.9 37.1–47.0	37.2 36.8–37.5	31.6±2.3 27.2–37.9	38.9±2.3 30.3–53.5	35.9 30.3–41.5	40.3±2.9 30.7–53.5	41.5
R	0.72	0.80±0.02 0.74–0.92	0.76±0.00 0.74–0.78	0.83±0.04 0.79–0.92	0.75 0.74–0.75	0.74±0.00 0.72–0.75	0.75±0.02 0.61–0.86	0.74 0.73–0.74	0.77±0.02 0.70–0.86	0.76
f (breaths/min)	30	18±2 10–24	18±3 10–24	18±1 17–20	23 19–27	15±1 14–18	18±1 12–24	17 12–21	19±1 12–24	20
$\dot{V}_A$, 1 BTPS/min	1.9	3.5±0.3 2.5–4.6	3.0±0.3 2.5–3.7	4.1±0.4 3.4–4.6	2.2 2.1–2.3	2.7±0.2 2.2–3.2	3.3±0.2 2.4–4.3	3.1 2.7–3.4	3.5±0.2 2.8–4.3	2.9
V_D, ml BTPS	192	246±25 174–351	245±27 184–300	248±53 174–351	192 155–229	238±42 176–363	282±23 206–436	322 207–436	277±20 206–364	225
V_D/V_T	0.62	0.49±0.03 0.35±0.57	0.52±0.03 0.42–0.57	0.46±0.06 0.35–0.57	0.57 0.55–0.58	0.54±0.05 0.47–0.69	0.54±0.01 0.43–0.61	0.55 0.54–0.56	0.53±0.02 0.43–0.61	0.54
P_{A-aO_2}, mmHg	7	32.0±1.7 27–40	32.8±2.6 28–40	31.0±2.7 27–36	32.0 26–37	25.3±4.2 16–36	28.0±1.3 18–33	25.5 18–33	29.1±0.6 26–31	23
P_{aO_2}, mmHg	58	58.4±4.1 43–73	51.8±4.4 43–62	67.3±2.9 64–73	44.0 37–51	57.0±3.3 48–64	60.4±2.7 49–72	55.0 50–60	63.1±3.1 49–72	71
P_{aCO_2}, mmHg	66	48.4±2.3 43–60	51.3±3.3 45–60	44.7±1.7 43–48	59.0 57–61	52.8±3.2 44–59	46.3±2.3 36–63	49.5 36–63	45.0±2.7 38–58	46
pH	7.32	7.43±0.01 7.39–7.50	7.43±0.02 7.39–7.50	7.44±0.00 7.43–7.44	7.40	7.37±0.00 7.35–7.38	7.40±0.01 7.34–7.46	7.39 7.34–7.43	7.40±0.01 7.35–7.46	7.42
HCO_3^-, mEq/l	29	30.6±1.1 28–36	31.5±1.7 28–36	29.3±0.9 28–31	33.5 32–35	26.8±1.0 25–29	26.8±0.7 24–30	26.5 24–29	26.7±0.8 25–30	28
BE, mEq/l	+5	6.7±1.1 4–12	7.8±1.8 4–12	5.3±0.9 4–7	9.5 8–11	2.5±1.2 0–5	2.6±0.7 −1–6	2.0 −1–5	2.7±0.8 0–6	4
S_{aO_2} calc., %	87	88.9±2.6 79–96	85.0±3.5 79–92	94.0±1.0 93–96	77.5 70–85	87.5±3.0 79–93	90.1±1.5 82–95	87.5 83–92	91.4±1.7 82–95	94
S_{aO_2}, %	87.5	88.6±2.5 78.2–95.8	84.4±2.9 78.2–91.5	94.2±0.8 93.3–95.8	74.6 64.3–84.9	87.5±3.0 79.1–92.8	90.1±1.5 80.9–95.7	86.7 80.9–92.5	91.7±1.5 83.4–95.7	92.6

The only significant differences during ambient air breathing at rest between all R- and C-group patients and between R- and C-group male patients, in whom hypoxia was induced, were a higher standard bicarbonate (HCO_3^-, $p < 0.01$) and BE ($p < 0.05$) in the R-group. The 4 R-group and the only C-group female patient differed in several respects. The C-group female patient had a higher $\dot{V}_E$, ventilatory equivalent for oxygen, respiratory quotient (R), breathing frequency, $P_{a_{O_2}}$, $S_{a_{O_2}}$ calc. and arterial pH. There was a possible tendency to higher R ($p < 0.20$), $P_{A-a_{O_2}}$ ($p < 0.10$) and V_D/V_T ($p < 0.20$) values in the R-group male patients, but these differences were not statistically significant.

Between the R-group male patients who terminated the hypoxia at the higher $F_{I_{O_2}}$ level ($n = 4$) and those who continued at the lower level ($n = 3$) the only significant difference during ambient air breathing was a lower $P_{a_{O_2}}$ ($p < 0.05$) in the former patients. The ventilatory equivalent, R and $P_{a_{O_2}}$ were probably significantly lower ($p < 0.05$) in the 8 R-group patients (4 male, 4 female) who terminated the induced hypoxia on breathing 15% O_2 than in the 3 R-group patients (all men) who continued at the lower level. No significant differences were found between the C-group male patients who terminated the induced hypoxia on breathing ~15% O_2 and ~11% O_2 ($n = 2$ and $n = 7$, respectively) or between the 2 C-group male patients and the 8 C-group patients (7 male, 1 female) who terminated the hypoxia at these respective levels. This was probably due to the fact that the 2 C-group male patients were different in most respects both in regard to pulmonary gas exchange, arterial blood gases, acid–base balance (see Table I) and to central haemodynamics including haemoglobin (27).

3. *Pulmonary gas exchange, arterial blood gas tensions, acid–base balance and arterial oxygen saturation during induced hypoxia* in groups of patients corresponding to those in Table II are presented in Table III.

In patients who terminated the hypoxic test on breathing ~15% O_2, the following changes were seen from air breathing to termination of the hypoxia: In the 4 R-group male patients $\dot{V}_E$ increased by 63%, $\dot{V}_A$ by 25% and V_D/V_T by +0.09, in the 4 R-group female patients $\dot{V}_E$ increased by 31% and $\dot{V}_A$ by 22%; V_D/V_T was unchanged (+0.01). In the 2 C-group male patients (C6 and 8) $\dot{V}_E$ increased by 16 and 27% and $\dot{V}_A$ by 44 and 15%; V_D/V_T was unchanged (- 0.01) in patient C6 and increased by 0.06 in C8. A decrease of the breathing frequency in patient C6 contributed to the fact that V_D/V_T remained unchanged during hypoxia. $\dot{V}_E$ increased most in patient R1 (192%), who had the severest pulmonary hypertension of the whole material. This increase was twice as great as in patients R2 and 7, who were equally hypoxaemic during the acute exposure to hypoxia: all had carbon dioxide retention and an arterial pH over 7.42. The different ventilatory reactions may be due either to the fact that patients R2 and R7 were chronically more hypoxaemic ($P_{a_{O_2}}$ about 45 mmHg) or to differences in the degree of pulmonary hypertension or in the cardiac compensation against the increased pressure in the pulmonary circulation.

The mean decrease of $P_{a_{CO_2}}$ was about 4 mmHg in the R-group male and female patients, but in the 2 C-group male patients the changes were extremely different: In C6 $P_{a_{CO_2}}$ decreased from 63 to 56 mmHg and in C8 it remained unchanged at 36 mmHg. In the R-group male patients $P_{A-a_{O_2}}$ decreased to 22 mmHg and in the female patients to 16 mmHg; in C6 it was unchanged (18 mmHg) and in C8 it decreased to 20 mmHg.

In the 3 R-group male patients who terminated the induced hypoxia with breathing ~11% O_2 (R3, 6 and 8) there was no increase of the mean $\dot{V}_E$ or $\dot{V}_A$ from ambient air breathing to the higher $F_{I_{O_2}}$ level, as $\dot{V}_E$ decreased in R3 and increased in the two others. V_D/V_T decreased in R3 and increased in the two others. $P_{A-a_{O_2}}$ decreased to 15 mmHg. In the 7 corresponding C-group male patients $\dot{V}_E$ and $\dot{V}_A$ increased by 19 and 22%, V_D/V_T remained unchanged and $P_{A-a_{O_2}}$ decreased to 16 mmHg. In the only C-group female patient $\dot{V}_E$ and $\dot{V}_A$ increased by 20% and 34%, V_D/V_T decreased by 0.03 and $P_{A-a_{O_2}}$ decreased to 8 mmHg.

From *ambient air breathing to the lower* $F_{I_{O_2}}$ *level*, $\dot{V}_E$ increased by 36%, $\dot{V}_A$ by 20% and V_D/V_T by 0.10, and $P_{A-a_{O_2}}$ decreased to 15 mmHg in the 3 R-group male patients. In the C-group male patients under corresponding conditions $\dot{V}_E$ and $\dot{V}_A$ increased by 60 and 66%, V_D/V_T remained unchanged (+0.01) and $P_{A-a_{O_2}}$ decreased to 13 mmHg. In the only C-group female patient $\dot{V}_E$ and $\dot{V}_A$ increased by 53% and 79%, V_D/V_T decreased by 0.04 and $P_{A-a_{O_2}}$ remained unchanged at 10 mmHg. $P_{a_{CO_2}}$ decreased by 6, 7 and 10 mmHg in the groups mentioned.

Table III. *Pulmonary gas exchange at rest in supine posture during hypoxia in groups of patients corresponding to those in Table II*

Mean values and S.E.M. and/or range at the higher $F_{I_{O_2}}$ level are given for patients who terminated the hypoxic test at this level ($F_{I_{O_2}}$ in 4 R-group male patients 0.1496±0.0033, in 4 R-group female and 2 C-group male patients 0.1395) and for patients who continued at the lower $F_{I_{O_2}}$ level ($F_{I_{O_2}}$ in 3 R-group male patients 0.1514±0.0014 and 0.1179±0.0041, in 7 C-group male patients 0.1465±0.0024 and 0.1073±0.0017, and in the C-group female patient 0.1395 and 0.1038). ^{z} = mean value of 2 patients

	R-group				C-group				
	Male			Female	Male			Female	
Induced hypoxia terminated at ...	~15% O_2 $n=4$	~11% O_2 $n=3$		~15% O_2 $n=4$	~15% O_2 $n=2$	~11% O_2 $n=7$		~11% O_2 $n=1$	
		~15% O_2	~11% O_2			~15% O_2	~11% O_2	~15% O_2	~11% O_2
$\dot{V}_E$, 1 BTPS/min	13.5±2.5 10.6–21.0	9.5±0.5 8.7–10.3	13.1±0.7 11.7–14.0	8.4±0.3 7.8–9.0	10.6 9.3–11.8	11.1±0.6 9.4–13.8	14.9±0.8 12.9–18.5	10.0	12.7
$\dot{V}_{O_2}$, ml STPD/min	222±13 195–259	203±4 197–212	153±38 82–213	176±10 149–192	177 168–186	221±12 196–282	221±15 169–291	188	186
Vent. equiv.	59.5±7.3 48.9–80.9	46.9±1.7 43.5–48.6	102.4±1.7 63.7–171.5	48.6±4.6 41.2–60.5	60.3 50.2–70.4	51.1±3.5 38.2–67.0	69.1±5.5 53.3–95.6	53.1	69.6
R	0.98±0.05 0.89–1.11	0.97±0.01 0.95–1.00	1.72±0.54 1.07–2.80	1.06±0.03 1.02–1.14	1.17 0.97–1.36	0.95±0.02 0.86–1.02	1.15±0.05 1.01–1.42	0.99	1.16
f, breaths/min	20±3 10–25	18±1 16–20	18±2 15–20	17±1 15–19	15 13–16	19±2 11–25	20±1 14–25	22	22
$\dot{V}_A$, 1 BTPS/min	4.0±0.2 3.5–4.2	4.0	4.9±0.1 4.8–5.0	3.3±0.1 3.0–3.5	3.9	4.4±0.3 3.5–5.9	5.8±0.3 4.3–6.7	3.9	5.2
V_D, ml BTPS	601±344 227–1632	259±7 248–271	418±66 299–528	267±28 187–316	450 378–523	339±44 252–593	418±59 306–750	231	290
V_D/V_T	0.61±0.06 0.51–0.78	0.50±0.02 0.47–0.53	0.56±0.02 0.51–0.59	0.53±0.02 0.46–0.58	0.58 0.53–0.62	0.53±0.01 0.48–0.60	0.54±0.03 0.47–0.73	0.51	0.50
$P_{A-a_{O_2}}$, mmHg	21.8±1.7 18–25	16.0±2.1 12–20	15.0±4.0 8–22	15.8±1.6 13–20	19.0 18–20	16.0±0.9 12–18	12.9±1.1 8–16	9	10
$P_{a_{O_2}}$, mmHg	35.5±3.5 31–46	47.0±2.7 43–52	36.3±0.9 35–38	36.5±1.3 33–39	41.0 38–44	43.4±2.4 33–51	29.1±3.5 20–35	50	35
$P_{a_{CO_2}}$, mmHg	47.0±2.7 41–54	42.7±1.8 40–46	38.3±0.7 37–39	49.3±2.3 44–55	46 36–56	41.7±2.3 34–52	37.9±2.4 32–50	41	36
pH	7.44±0.01 7.42–7.48	^{z}7.46 7.45–7.46	7.49±0.01 7.47–7.51	7.40±0.00 7.38–7.42	7.42 7.38–7.45	7.44±0.01 7.40–7.49	7.47±0.00 7.42–7.49	7.43	7.37
HCO_3^-, mEq/l	30.8±1.7 27–34	^{z}29.0	30.0±1.2 28–32	28.8±0.8 28–29	27.0 25–29	27.9±0.6 26–30	27.6±0.7 26–30	27	22
BE, mEq/l	6.8±1.7 3–10	^{z}5.0	6.0±1.2 4–8	4.5±0.5 3–5	3.0 1–5	3.7±0.7 1–6	3.4±0.8 1–6	3	−4
$S_{a_{O_2}}$ calc., %	68.5±4.9 66–83	^{z}84.5 80–89	73.0±2.5 70–78	67.8±2.3 61–71	75.5 70–81	79.6±2.9 65–87	58.4±4.7 32–70	87	66
$S_{a_{O_2}}$, %	66.3±5.7 54.7–81.9	86.8±1.7 85.0–90.1	69.9±2.8 64.3–73.3	67.2±2.7 59.3–70.3	72.6 68.0–77.1	78.4±2.8 63.6–85.3	54.8±3.7 37.7–71.0	81.6	66.5

Table IV. *Minute ventilation ($\dot{V}_E$) and lung clearance index (LCI) during lung N_2 wash-out period of pure oxygen breathing ($F_{IO_2} \sim 0.99$); $\dot{V}_E$, alveolo-arterial oxygen tension difference (P_{A-aO_2}), arterial blood gas tensions, acid–base balance and veno-arterial shunting as per cent of cardiac output ($\dot{Q}_{sh}/\dot{Q}$, %) after at least 15 and at most 25 min of pure oxygen breathing in supine posture*

Mean values and S.E.M. are given

	R-group Male	Female	All	C-group Male	Female	All
	$n=8$	$n=6$	$n=14$	$n=10$	$n=1$	$n=11$
$\dot{V}_E$, l BTPS/min (N_2 wash-out)	7.5±0.8	5.8±0.6		7.4±0.4	5.4	
LCI	12.0±1.1	13.7±0.8	12.7±0.7	13.7±1.1	7.6	13.2±1.1
$\dot{V}_E$, l BTPS/min	8.5±0.8	6.0±0.5		8.7±0.5	6.7	
P_{A-aO_2}, mmHg	103±20	153±30	124±18	95±10	123	98±9
P_{aO_2}, mmHg	547±21	492±32	523±19	556±12	541	554±11
P_{aCO_2}, mmHg	51.1±3.5	59.2±3.9	54.6±2.7	48.4±2.8	47	48.3±2.5
pH	7.41±0.01	7.34±0.01	7.38±0.01	7.39±0.01	7.38	7.39±0.00
HCO_3^-, mEq/l	29.6±0.8	28.7±1.0	29.2±0.6	27.1±0.8	27	27.1±0.7
BE, mEq/l	5.6±0.8	4.5±1.1	5.1±0.7	2.9±0.8	2	2.8±0.8
$\dot{Q}_{sh}/\dot{Q}$, %	5.7±1.3	10.1±2.6	7.6±1.4	5.1±0.6	6.1	5.2±0.6

4. *The pulmonary gas exchange, arterial blood gas tension and acid–base balance* findings *during hyperoxia* ($F_{IO_2} \sim 0.99$) are presented in Table IV. In all subgroups of groups R and C, but not in all individual patients (exception R 12), there was an initial decrease of the minute ventilation ($\dot{V}_E$) during the lung N_2 wash-out period. In the R- and C-group male, but not female patients, after 15–25 min of oxygen breathing the ventilation had returned to (or near to) the original $\dot{V}_E$ levels noted during ambient air breathing. In the R-group female patients P_{aCO_2} was, on the average, 4.4 mmHg higher during hyperoxia than during ambient air breathing ($p < 0.20$). At the same time the P_{aO_2} mean values showed a tendency to be lowest ($p < 0.20$) in the R-group female patients among the different groups. This was due to veno-arterial shunting, which might have been both anatomical and functional, caused by an uneven ventilation/perfusion relationship. It was about 5–6% of the cardiac output in both male groups and the only C-group female patient, and about 10% in the R-group female patients.

The relationship between P_{aCO_2} during pure oxygen breathing and (*a*) arterial oxygen tension (P_{aO_2}) and (*b*) carbon dioxide tension (P_{aCO_2}) during ambient air breathing at rest in the supine posture is presented in Fig. 1. P_{aCO_2} during hyperoxia is influenced by both the habitual P_{aO_2} and P_{aCO_2} level during ambient air breathing in this type of patient.

5. *The pulmonary gas exchange, arterial blood gas tension, acid–base balance* and *saturation* findings *during induced hypercapnoea* (F_{ICO_2} 0.0542–0.0604) at rest in the supine posture are presented in Table V.

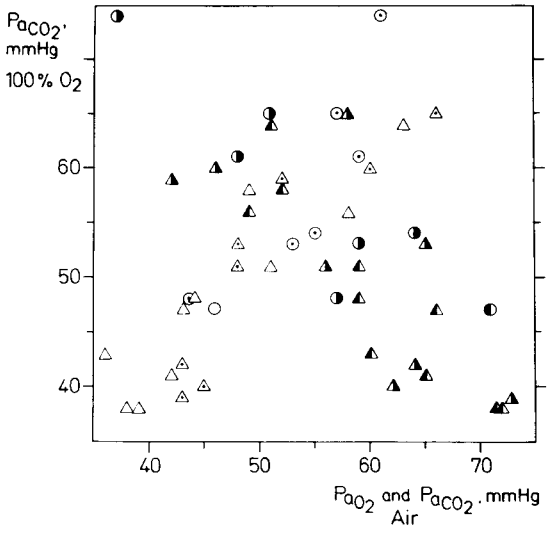

Fig. 1. The relationship between P_{aCO_2} during pure oxygen breathing and (*a*) arterial oxygen tension (P_{aO_2}, mmHg) and (*b*) carbon dioxide (P_{aCO_2}, mmHg) tension during ambient air breathing in supine posture, at rest in R- and C-group patients. Symbols: P_{aO_2}–P_{aCO_2} in R-group male ▲ and female ◑ and in C-group male ◭ and female ◐ patients; P_{aCO_2}–P_{aCO_2} in R-group male △ and female ⊙ and in C-group male △ and female ○ patients.

Table V. *Pulmonary gas exchange, arterial blood gas tensions, acid–base balance and oxygen saturation during induced hypercapnoea (F_{ICO_2} 0.0542 ± 0.0604) in supine posture at rest in R- and C-group patients*

F_{ICO_2} in the R-group male patients was 0.0581 ± 0.0080, in the C-group male patients 0.0562 ± 0.0080 and in all female patients 0.0542. Mean values and S.E.M. are given. ^{z} = mean value of one patient fewer than indicated in the heading

	R-group			C-group		
	Male $n=6$	Female $n=5$	All $n=11$	Male $n=9$	Female $n=1$	All $n=10$
$\dot{V}_E$, l BTPS/min	23.6 ± 2.1	11.5 ± 0.5		19.7 ± 1.6	21.1	
$\dot{V}_{O_2}$, ml STPD/min	^{z}274 ± 9	216 ± 10		270 ± 10	234	
Vent. equiv.	^{z}84.3 ± 10.3	53.6 ± 2.9	^{z}69.0 ± 7.2	73.8 ± 6.4	90.3	75.4 ± 5.9
R	^{z}0.52 ± 0.05	0.55 ± 0.04	^{z}0.54 ± 0.03	0.51 ± 0.05	0.60	0.52 ± 0.04
f (breaths/min)	21 ± 3	17 ± 2	19 ± 2	21 ± 1	24	22 ± 1
$\dot{V}_A$, l BTPS/min	^{z}6.8 ± 1.3	4.2 ± 0.3		7.2 ± 0.6	7.0	
V_D, ml BTPS	^{z}791 ± 179	399 ± 65		522 ± 39	532	
V_D/V_T	^{z}0.64 ± 0.05	0.54 ± 0.01	^{z}0.59 ± 0.03	0.56 ± 0.01	0.60	0.57 ± 0.01
P_{A-aO_2}, mmHg	^{z}16.8 ± 3.8	20.6 ± 2.8	^{z}18.7 ± 2.3	22.9 ± 3.5	10	21.6 ± 3.4
P_{aO_2}, mmHg	83.7 ± 7.7	76.8 ± 1.8	80.6 ± 4.3	87.0 ± 2.8	101	88.4 ± 2.9
P_{aCO_2}, mmHg	61.3 ± 2.3	62.8 ± 1.3	62.0 ± 1.3	57.6 ± 2.6	56	57.4 ± 2.3
pH	7.35 ± 0.00	7.31 ± 0.00	7.33 ± 0.00	7.33 ± 0.00	7.33	7.33 ± 0.00
HCO_3^-, mEq/l	29.5 ± 1.2	28.0 ± 0.6	28.8 ± 0.7	26.4 ± 0.8	27	26.5 ± 0.7
BE, mEq/l	5.5 ± 1.3	3.8 ± 0.6	4.7 ± 0.8	2.0 ± 0.9	2	2.0 ± 0.8
S_{aO_2} calc., %	94.3 ± 1.3	93.8 ± 0.4	94.1 ± 0.7	95.7 ± 0.5	97	95.8 ± 0.4
S_{aO_2}, %	94.0 ± 1.3	94.3 ± 0.4	94.1 ± 0.7	94.7 ± 0.8	96.1	94.8 ± 0.7

The ventilation increased by 0.5 l/min/P_{aCO_2} mmHg in the R-group female patients and in the other groups by about 1.0–1.2 l/min/P_{aCO_2} mmHg. The mean arterial saturation increased in most patients to normal saturation levels. Standard bicarbonate (HCO_3^-) and BE were higher in the R- than the C-group ($p < 0.05$). There was a possible tendency to a lower S_{aO_2} ($p < 0.10$) and P_{aO_2} ($p < 0.20$) and a higher P_{aCO_2} ($p < 0.10$) in the R-group, but these variables were not significantly different in the two groups. Also, pH was higher in the R- than in the C-group male patients ($p < 0.02$). There was also a possible tendency to a higher V_D ($p < 0.10$) and V_D/V_T ($p < 0.20$) in the R-group male patients, but these differences were not significant. The ventilatory variables, P_{aO_2} and pH were higher and P_{aCO_2} lower in the only C-group female patient than in the 5 R-group female patients during induced hypercapnoea.

6. *The pulmonary gas exchange, arterial blood gas tension, acid–base balance and saturation* findings during exercise in the supine posture are presented in Table VI for patients who were able to perform the exercise for at least 6 min in combination with gas exchange studies. It should be noted that 4 of the most incapacitated of 8 R-group male patients and 2 of the most incapacitated of 6 R-group female patients did not participate in this comparative study.

Patients R4 and 12 did not perform a work test and in patient R2 it was terminated after 2 min 20 sec. Patients R6, 7 and 16 performed the work test without breathing through a respiratory valve and the test was terminated after 6, 5 and 4 min, respectively. With the exception of patient R6 (P_{aO_2} 64 and P_{aCO_2} 43 mmHg), these patients had lower P_{aO_2} and higher P_{aCO_2} levels at rest during ambient air breathing than the patients who were able to perform the exercise test in combination with gas exchange studies. In the 4 R-group male patients (R1, 3, 5 and 8) P_{aO_2} was 64 ± 4 and P_{aCO_2} 46 ± 1 mmHg, pH 7.45 ± 0.02 and BE + 7 ± 2 mEq/l at rest during ambient air breathing. In corresponding conditions P_{aO_2} was 57 ± 3 and P_{aCO_2} 53 ± 3 mmHg, pH 7.37 ± 0 and BE + 3 ± 1 mEq/l in the 4 R-group female patients. Corresponding values in the C-group male and female patients are given in Table I as all patients in the C-group were able to perform an exercise test.

Table VI. *Pulmonary gas exchange, arterial blood gases, acid–base balance and oxygen saturation between 3rd and 6th minutes of exercise in supine posture in R- and C-group patients who tolerated breathing through a respiratory valve and performing an exercise test of at least 6 min duration*

Mean values and S.E.M. are given. ^{z} = mean value of 3 patients

	R-group			C-group		
	Male $n=4$	Female $n=4$	All $n=8$	Male $n=10$	Female $n=1$	All $n=11$
Work load, kpm/min	163±13	91±14		151±16	150	
$\dot{V}_E$, 1 BTPS/min	19.6±1.5	^{z}13.1±0.8		19.6±1	17.2	
$\dot{V}_{O_2}$, ml STPD/min	632±39	^{z}452±44		615±41	519	
Vent. equiv.	30.8±0.7	29.1±1.4	30.0±0.8	32.6±1.9	33.2	32.7±1.7
R	0.93±0.04	0.80±0.03	0.87±0.03	0.81±0.02	0.83	0.81±0.01
f (breaths/min)	21±1	23±2	22±1	23±1	24	23±2
$\dot{V}_A$, 1 BTPS/min	10.3±0.8	^{z}5.6±0.7		8.8±0.6	8.2	
V_D, ml BTPS	380±11	^{z}277±43		427±15	327	
V_D/V_T	0.45±0.05	0.48±0.02	0.45±0.01	0.49±0.00	0.46	0.49±0.00
$P_{A-a_{O_2}}$, mmHg	34.3±2.8	32.5±3.2	33.4±2.0	32.8±2.2	27	32.3±2.0
$P_{a_{O_2}}$, mmHg	61.8±2.5	49.3±1.8	55.5±2.8	57.5±2.7	71	58.7±2.8
$P_{a_{CO_2}}$, mmHg	49.8±3.0	56.5±5.5	53.1±2.3	49.1±2.9	45	48.7±2.7
pH	7.41±0.02	7.34±0.01	7.37±0.01	7.36±0.01	7.38	7.36±0.01
HCO_3^-, mEq/l	28.5±1.4	27.0±0.8	27.8±0.8	25.7±0.6	26	25.7±0.6
BE, mEq/l	4.5±1.4	3.0±0.8	3.8±0.8	1.3±0.7	1	1.3±0.7
$S_{a_{O_2}}$ calc., %	90.5±1.7	81.0±1.2	85.8±2.0	87.4±2.3	94	88.0±2.2
$S_{a_{O_2}}$, %	88.9±2.7	79.5±1.6	84.2±2.3	85.7±2.4	91.3	86.2±2.2

The mean work loads were about the same in the male groups, but the only C-group female patient exercised at a higher load than any of the R-group female patients. The mean increase in $\dot{V}_E$ and $\dot{V}_{O_2}$ was about the same in the male groups. The respiratory quotient (R) was higher and V_D/V_T lower ($p<0.02$) in the male patients of the R- than of the C-group. Also BE was probably higher in the R-group male patients ($p<0.05$). In relation to the work load and oxygen uptake both male group patients had a high minute ventilation. There were no consistent changes in arterial blood gas tensions from rest to work in any of the groups. In the R-group male patients the ventilatory equivalent showed a tendency to be lower ($p<0.20$) and the respiratory quotient higher ($p<0.10$) in working conditions. In the R-group female patients the arterial pH was significantly lower ($p<0.05$) during exercise and the respiratory quotient showed a tendency to be higher ($p<0.10$) and $S_{a_{O_2}}$ and $P_{a_{O_2}}$ lower ($p<0.10$) during exercise. In the C-group male patients R was higher ($p<0.05$) and V_D/V_T ($p<0.005$) and pH ($p<0.025$) lower during exercise. $P_{A-a_{O_2}}$ showed a tendency to have increased ($p<0.10$) during exercise in the C-group male patients. In the only C-group female patient there was a marked decrease of V_D/V_T and a slight increase of $P_{A-a_{O_2}}$. If R increases during exercise in patients with chronic obstructive lung disease and carbon dioxide retention at rest, the carbon dioxide retention should be due to hypoventilation because of the adaption of the respiratory apparatus towards $P_{a_{CO_2}}$. Decreasing V_D/V_T during exercise should be due to more equal ventilation/perfusion relationship during work than at rest.

The *diffusing capacity* ($D_{L_{CO}}F$, ml/min·mmHg) according to Filley (10), measured during exercise in the supine posture, was as follows: in 3 R-group male patients (R 3, 5 and 8) 15.6±0.8 ml/min·mmHg at a work load of 167±17 kpm/min, in 4 R-group female patients (R 11, 13, 14 and 15) 16.1±3.4 ml/min·mmHg at a work load of 90±14 kpm/min, in 7 C-group male patients (C 1, 2, 3, 4, 8, 9 and 10) 17.0±2.1 at a work load of 150±22 kpm/min and in the only C-group female patient (C 11) 11.9 ml/min·mmHg at a work load of 150 kpm/min. In corresponding groups and conditions $\dot{V}_E$ and $\dot{V}_{O_2}$ were 23.2±0.9 l/min and 709±13 ml/min,

Table VII. *Comparison of pulmonary gas exchange, arterial blood gas tensions, acid–base balance, oxygen saturation and lactate in two body postures (supine, sitting) during ambient air breathing at rest in all patients and during exercise, at exactly the same work load, in those patients who performed this exercise for at least 6 min and breathed through a respiratory valve*

The mean difference and its standard error ($\bar{d} \pm$S.E.M.) are given. The degrees of statistical significance of the difference are as follows: $P \leqslant 0.001$ ***, $P \leqslant 0.01$ ** and $P \leqslant 0.05$ *. [z] = at rest: 9 patients in both groups and during exercise: 2 patients in the R-group and 6 patients in the C-group

	Supine–Sitting			
	At rest		During exercise	
	R-group $n=14$	C-group $n=11$	R-group $n=3$	C-group $n=7$
$\dot{V}_E$, 1 BTPS/min	-3.2 ± 0.5***	-4.3 ± 0.6***	-0.7 ± 2.3	-4.6 ± 1.3*
$\dot{V}_{O_2}$, ml STPD/min	-62 ± 12***	-66 ± 6***	-39 ± 63	-73 ± 28*
Vent. equiv.	-3.8 ± 1.2**	-5.5 ± 1.5**	0.9 ± 0.6	-2.6 ± 1.6
R	-0.07 ± 0.02**	-0.05 ± 0.02	0.02 ± 0.01	-0.02 ± 0.03
f, breaths/min	-1.1 ± 1.0	-2.5 ± 0.7**	-1.0 ± 1.7	-3.1 ± 0.9*
$\dot{V}_A$, 1 BTPS/min	-1.1 ± 0.2***	-1.4 ± 0.2***	-0.2 ± 0.9	-1.5 ± 0.6*
V_D, ml BTPS	-82 ± 15***	-75 ± 25*	-11 ± 31	-42 ± 28
V_D/V_T	-0.01 ± 0.02	-0.03 ± 0.01**	-0.00 ± 0.01	-0.02 ± 0.01
$P_{A-a_{O_2}}$, mmHg	-6.6 ± 1.3***	-5.8 ± 1.9*	-3.7 ± 3.2	-2.0 ± 1.5
$P_{a_{O_2}}$, mmHg	-1.4 ± 1.8	-0.6 ± 2.2	-3.7 ± 1.9	-0.1 ± 1.8
$P_{a_{CO_2}}$, mmHg	2.6 ± 1.1*	2.0 ± 1.3	0.7 ± 0.9	-0.9 ± 1.6
pH	-0.01 ± 0.01	-0.01 ± 0.01	0.00 ± 0.01	0.01 ± 0.01
HCO_3^-, mEq/l	0.4 ± 1.1	-0.1 ± 0.8	0.3 ± 0.9	-0.4 ± 0.8
BE, mEq/l	0.4 ± 1.2	-0.1 ± 0.6	0.7 ± 0.7	-0.3 ± 0.8
$S_{a_{O_2}}$ calc., %	-1.5 ± 1.4	-0.5 ± 0.8	-1.3 ± 1.2	0.0 ± 1.4
Lact., mmol/l	[z] -0.42 ± 0.20	[z] -0.49 ± 0.26	[z] 0.60 ± 0.30	[z] -1.38 ± 0.50

15.0 ± 0.9 l/min and 507 ± 40 ml/min, 20.9 ± 1.3 l/min and 630 ± 55 ml/min and 20.7 l/min and 572 ml/min.

7. *Body postural differences and degrees of statistical differences in gas exchange during ambient air breathing are presented in Table VII.* Values at rest are given for all R- and C-group patients and during exercise for patients who performed exercise at the same work load for 6 min in the supine and sitting body postures. The exercise tests were performed on two different days and in somewhat different nutritional conditions—the sitting exercise test after a light lunch on the second day after admission to hospital, and the supine test in connection with the right heart catheterization on the day after. At rest most of the ventilatory findings were lower in the supine posture. V_D/V_T, however, was unchanged and $P_{a_{CO_2}}$ higher in the R-group patients. In the C-group patients V_D/V_T was lower, and the $P_{a_{CO_2}}$ unchanged in the supine posture. During exercise only the minute ventilation ($\dot{V}_E$), oxygen uptake ($\dot{V}_{O_2}$), breathing frequency (f) and alveolar ventilation ($\dot{V}_A$) were probably significantly lower during the supine exercise test in the C-group patients. During exercise most of the differences, which were probably caused by the increased dead space ventilation from unequal distribution of ventilation and perfusion along the lung, disappeared during exercise, when the perfusion would have been distributed more uniformly over the whole lung also in the sitting posture.

8. *Differences in pulmonary gas exchange at different time intervals during exercise*, performed in two body postures, and degrees of statistical significance are presented in Table VIII. Note that all patients are not included as not all of them were capable of continuing the work test until the periods concerned

Table VIII. *Comparison of pulmonary gas exchange, arterial blood gas tensions, acid–base balance, oxygen saturation and lactate at the same work load: 1) in the supine posture between the periods 3–6 min and 8–10 min, and 2) in the sitting posture between the periods 3–6 and 12–15 min and between 12–15 and 27–30 min in those R- and C-group patients who breathed through a respiratory valve and thus made gas exchange studies possible*

The mean differences and S.E.M., as well as the degrees of statistical significance are given as in Table VII.
^{z} = one patient fewer than indicated in the heading

	Supine		Sitting			
	(3–6)–(8–10) min		(3–6)–(12–15) min		(12–15)–(27–30) min	
	R-group $n=7$	C-group $n=8$	R-group $n=6$–7	C-group $n=7$	R-group $n=6$	C-group $n=10$
$\dot{V}_E$, l BTPS/min	$^z-1.8\pm0.4$*	-2.2 ± 0.4**	$^z-1.0\pm1.0$	-0.2 ± 0.8	0.1 ± 0.7	-1.0 ± 0.3**
$\dot{V}_{O_2}$, ml STPD/min	$^z-34\pm13$*	-24 ± 9*	$^z-25\pm15$	12 ± 12	-17 ± 23	4 ± 13
Vent. equiv.	-1.0 ± 0.5	-2.3 ± 0.7**	-0.2 ± 0.6	-0.9 ± 0.6	0.9 ± 0.3	-1.9 ± 0.6*
R	-0.02 ± 0.01*	-0.03 ± 0.02	0.00 ± 0.01	0.01 ± 0.01	0.02 ± 0.02	-0.03 ± 0.02
f, breaths/min	-1.1 ± 0.5*	0.3 ± 0.7	-0.1 ± 0.6	-0.6 ± 1.0	-1.5 ± 0.7	-2.7 ± 1.0**
$\dot{V}_A$, l BTPS/min	$^z-0.7\pm0.3$	-0.9 ± 0.2**	$^z-0.6\pm0.2$*	-0.1 ± 0.3	0.0 ± 0.2	-0.4 ± 0.2*
V_D, ml BTPS	$^z-32\pm8$**	-47 ± 22	$^z-13\pm26$	10 ± 18	35 ± 21	18 ± 14
V_D/V_T	-0.01 ± 0.01	-0.01 ± 0.01	0.01 ± 0.01	-0.00 ± 0.00	0.00 ± 0.01	0.00 ± 0.00
$P_{A-a_{O_2}}$, mmHg	-0.3 ± 1.5	-1.9 ± 1.3	0.6 ± 1.3	-0.3 ± 0.4	1.0 ± 1.4	-1.8 ± 0.9
$P_{a_{O_2}}$, mmHg	-2.0 ± 0.6*	-1.0 ± 0.8	-2.4 ± 0.9*	-0.9 ± 1.0	0.0 ± 0.8	-0.1 ± 0.4
$P_{a_{CO_2}}$, mmHg	0.0 ± 0.0	0.4 ± 0.9	1.7 ± 0.6*	0.6 ± 0.8	-0.3 ± 0.3	1.0 ± 0.3**
pH	0.02 ± 0.00**	0.01 ± 0.00	-0.01 ± 0.00	-0.00 ± 0.00	0.01 ± 0.00	0.00 ± 0.01
HCO_3^-, mEq/l	0.9 ± 0.5	0.8 ± 0.4	-0.1 ± 0.3	0.7 ± 0.3*	0.3 ± 0.4	0.2 ± 0.4
BE, mEq/l	1.1 ± 0.6	0.6 ± 0.5	0.0 ± 0.4	0.4 ± 0.4	0.5 ± 0.3	0.8 ± 0.4*
$S_{a_{O_2}}$ calc., %	-0.4 ± 0.5	0.1 ± 0.5	-1.7 ± 0.5*	-1.1 ± 0.4*	0.3 ± 0.6	0.1 ± 0.2
Lact., mmol/l			0.17 ± 0.16	0.90 ± 0.57	0.13 ± 0.16	0.29 ± 0.18

or, in some patients, gas exchange studies could not be combined with exercising.

The work load was 167 ± 17 kpm/min in the R-group male patients and 91 ± 14 kpm/min in the R-group female patients. In the C-group male patients it was 150 ± 22 and in the only female patient 150 kpm/min. *During the supine exercise test* the minute ventilation, oxygen uptake, respiratory quotient, breathing frequency, physiological dead space and arterial oxygen tensions were lower in the 3 to 6 min interval of exercise than at 8 to 10 min in the R-group ($p< 0.05$). In the C-group the minute ventilation, oxygen uptake, ventilation equivalent for oxygen and alveolar ventilation were lower at 3 to 6 min than at 8 to 10 min ($p< 0.05$). The pH value in the R group was significantly higher at 3 to 6 min than at 8 to 10 min ($p< 0.01$). The V_D/V_T ratio showed no consistent change. As the pulmonary gas exchange in this position was not studied during several further intervals of exercise, no conlusions can be drawn on the steady state conditions.

The work loads, which were intended to be submaximum, varied from submaximum to maximum in different patients for the following reasons: 1) in a few cases maximum work loads for the patient had to be chosen as no lower work loads were available on the bicycle ergometers used and 2) in the supine body position the load was experienced differently by the patient than on the previous day in the sitting posture.

In the sitting posture the only differences between the 3 to 6 and the 12 to 15 min intervals in the R-group were that alveolar ventilation was lower and $P_{a_{CO_2}}$ higher in the former. In the C-group corresponding probably significant differences were seen in standard bicarbonate and calculated $S_{a_{O_2}}$. The work load in the 4 R-group male patients was 133 ± 6 and in the 3 female patients 100 kpm/min. The work load in the 7 C-group male patients in this comparison was 147 ± 22 kpm/min. As examples of different reactions in different body postures may by mentioned patients R11 and C1 and 5. Patient

R11 exercised for 3 min in the sitting posture at 50 kpm/min and for 10 min in the supine posture at 50 kpm/min in otherwise equal situations. This patient had less tachycardia and lower ventilation during the supine exercise test. Patients C1 and C5 showed opposite reactions; both had increased PCV pressure and they experienced the same work loads, 100 and 150 kpm/min, as much higher in the supine than in the sitting posture, though the minute ventilation was somewhat lower. This could have been due to increased filling pressures—during exercise PCV was found to have increased from 17 to 26 and from 23 to 36 mmHg, respectively, in the two patients (26).

Between the exercise intervals of 12 to 15 min and 27 to 30 min there were no statistically significant differences in the R-group, but in the C-group $\dot{V}_E$, ventilatory equivalent, f and $\dot{V}_A$ were lower during the first gas collection period. $P_{a_{CO_2}}$ and HCO_3^- were higher during this period in the C-group. These differences might depend on the nearness on the submaximum work load to the maximum physical working capacity. The work load in the R-group male patients was 133 ± 6 and in both female patients 100 kpm/min, and in 9 C-group male patients 136 ± 20 and in the female patient 150 kpm/min. W_{max} in these R-group male patients was 271 ± 64 kpm/min, in the two R-group female patients 200 kpm/min, in the C-group male patients 240 ± 41 and in the C-group female patient 200 kpm/min.

As examples of different reactions may be mentioned the following: Patient R15, who had a W_{max} of 200 kpm/min, but interrupted the long-term exercise test after 16.5 min at 100 kpm/min because of fatigue and dyspnoea. Her ventilation had gradually increased from 22.1 l/min (in the 3 to 6 min period) to 27.8 l/min (12 to 15 min), which was higher than the $\dot{V}_E$ at her maximum work load of 200 kpm/min (24.6 l/min). She was one of the patients who had an equally high lactate concentration during the long-term as the short-term exercise test. Patient C8 had a W_{max} of 50 kpm/min at the conventional exercise test combined with gas exchange studies, but was able to continue for 30 min at the same work load and with the same ventilation, while his arterial lactate was about 2 mmol/l on both occasions. In the previous example the cardiac output was not sufficient for the peripheral oxygen demands and the arterial lactate and ventilation increased—in contrast to the usual decrease of arterial lactate at submaximum work loads during prolonged exercise. There were, however, a few patients (R1, 6 and 14) whose arterial lactate did not decrease during prolonged exercise. R6, who was not able to breathe through a respiratory valve during the prolonged exercise interrupted the test after 11.5 min and at that time point had an arterial lactate concentration of 3.3 mmol/l. R1 and R14 continued the test for 30 min in spite of the fact that had the same arterial lactate level during the conventional and the prolonged exercise test, at the same work load.

9. *Arterial blood gas tensions and acid–base balance* in the supine posture during ambient air breathing are presented in Table IX for the following periods: 1) 10 min after the maximum work test, performed in the sitting posture, 2) 10 min after a submaximum work test of 30 min duration (sometimes maximum and shorter) and 3) during the end phase of 1 min voluntary hyperventilation. In all groups the mean $P_{a_{O_2}}$ values after exercise, both "short- and long-term" exercise were higher than at rest sitting on the ergometer bicycle and breathing through a respiratory valve before the exercise test, or supine at rest the next morning, also breathing through a respiratory valve. The differences in $P_{a_{CO_2}}$ are smaller. In R-group female patients there was a tendency ($p < 0.20$) to lower $P_{a_{CO_2}}$ after both the "short- and long-term" exercise test.

During 1 min of voluntary hyperventilation $P_{a_{O_2}}$ increased and $P_{a_{CO_2}}$ decreased in all groups in relation to the arterial blood gas tension levels at rest. The increase in $P_{a_{O_2}}$ in the R- and C-group male patients reached the same level however, though there was a difference in the $P_{a_{CO_2}}$ levels. The difference in $P_{a_{CO_2}}$ between R-group female and the only C-group female patient increased. In the R-group 3 patients (R5, R8 and R15) and in the C-group 8 patients (exceptions C6 and 10) reached $P_{a_{CO_2}}$ levels $\leqslant 35$ mmHg. Note that the voluntary hyperventilation test was not performed in patients R3 and C2 in connection with this study. $P_{a_{CO_2}}$ during voluntary hyperventilation was significantly negatively correlated to $FEV_{1.0}$ (A), measured 2 days earlier in connection with dynamic spirometry. $P_{a_{CO_2}} = 61.5 - 27.7 \times FEV_{1.0}$ (S.D. 8.1), $r = -0.55$.

DISCUSSION

The use of Bohr's formula and the assumption that $P_{AO_2} = P_{a_{CO_2}}$ can be discussed in gas exchange

Table IX. *Arterial blood gas tensions and acid–base balance in R- and C-group patients in supine posture: 1) 10 min after a maximum work test in sitting posture, 2) 10 min after a "long-term" work test (usually 30 min at a submaximum work load) in sitting posture, and 3) during the end phase of a 1-min period of hyperventilation in supine posture*

Mean values and S.E.M. are given. ^{z} = one patient fewer than indicated in the heading

	R-group			C-group		
	Male $n=7$	Female $n=6$	All $n=13$	Male $n=10$	Female $n=1$	All $n=11$
1. $P_{a_{O_2}}$, mmHg	64.0±4.4	64.7±2.1	64.3±2.5	69.3±2.2	75	69.8±2.0
$P_{a_{CO_2}}$, mmHg	49.0±2.1	50.2±2.0	49.5±1.4	45.4±2.2	39	44.8±2.1
pH	7.40±0.00	7.36±0.01	7.38±0.00	7.37±0.00	7.38	7.37±0.00
HCO_3^-, mEq/l	28.6±1.00	25.7±0.8	27.2±0.7	24.7±1.1	23	24.6±1.0
BE, mEq/l	4.6±1.1	1.5±0.7	3.2±0.8	0.10±1.3	−2	−0.1±1.2
$S_{a_{O_2}}$ calc., %	91.1±1.8	90.7±1.1	90.9±1.1	92.8±0.7	95	93.0±0.7
2. $P_{a_{O_2}}$, mmHg	^{z}68.3±4.4	62.8±2.3	^{z}65.7±2.5	66.7±2.2	73	67.3±2.1
$P_{a_{CO_2}}$, mmHg	^{z}47.7±2.1	50.5±2.2	^{z}49.1±1.5	45.8±2.1	39	45.2±2.0
pH	^{z}7.41±0.00	7.37±0.01	^{z}7.39±0.00	7.39±0.00	7.36	7.38±0.00
HCO_3^-, mEq/l	^{z}28.5±0.9	26.3±0.7	^{z}27.4±0.6	26.0±1.0	22	25.6±0.9
BE, mEq/l	^{z}4.5±1.1	2.3±0.8	^{z}3.4±0.7	1.6±1.1	−3	1.2±1.1
$S_{a_{O_2}}$ calc., %	^{z}93.0±1.3	90,3±1.4	^{z}91.7±1.0	92.3±0.8	94	92.5±0.8
3. $P_{a_{O_2}}$, mmHg	71.9±7.5	61,7±4.4	67,2±4.6	72.1±2.9	79	72.8±2.7
$P_{a_{CO_2}}$, mmHg	42.3±3.4	47.5±4.4	44.2±2.7	37.2±2.6	33	36.8±2.4
pH	7.47±0.01	7.41±0.02	7.44±0.01	7.44±0.00	7.47	7.45±0.00
HCO_3^-, mEq/l	29.7±1.1	28.0±1.1	28.9±0.8	25.9±0.8	25	25.8±0.7
BE, mEq/l	5.7±1.1	3.7±1.3	4.8±0.8	1.2±0.9	±0	1.1±0.8

studies of chronic obstructive lung disease, as these patients have an unequal ventilation/perfusion distribution. The alveolar carbon dioxide tension is exactly the same as the arterial carbon dioxide tension only in ideal conditions, which seldom exist even in normal subjects. Difficulties in measuring the correct alveolar carbon dioxide tension are also encountered in other methods, e.g. continuous and rapid analyses of the expiratory gas. The reproducibility of the gas exchange measurement has not been studied under exactly the same conditions in this material. The results of several estimations in the same patient in different test situations support the validity of the method for clinical use, however, as no highly divergent results were obtained.

The visually observed breathing pattern and breathing frequency showed no major fluctuations at rest during air breathing, with the exception of patients R4 and R12. The blood gas values therefore can be expected to be representative for the whole gas collection period though the blood sampling period was shorter. In the mostsev erely ill patients breathing though a respiratory valve influenced the blood gas tension values, however (26).

During hypoxia and induced hypercapnoea steady state conditions were less well fulfilled as these tests often were terminated after only a few minutes breathing of the gas mixtures. As the blood sampling and gas collection in these cases were more simultaneous, the methodological errors caused by non-steady state conditions should have been reduced. The gas collection was not always performed during the same minutes from the start of hypoxia or induced hypercapnoea. This might have given rise to interindividual differences.

The general condition of these patients was variable and the testing conditions during exercise could not always be standardized as in normal subjects. There were very few statistically significant differences in gas exchange between the 3 to 6 min period of exercise and the 12 to 15 min period in the sitting posture. Several of the gas exchange para-

meters ($\dot{V}_E$, $\dot{V}_A$ and V_D) were, however, lower in the 3 to 6 min period than in the 8 to 10 min in the supine posture period. This could be due to non-steady state conditions. Non-steady state conditions were also seen during the prolonged exercise test in a few patients with a low circulatory capacity.

The number of tests omitted or terminated earlier was more frequent in R-group patients. Only very seldom did this happen for precautionary reasons. In patient R5 the lower F_{IO_2} level during hypoxia was, however, omitted as on the day of catheterization the patient had had right bundle branch block, which must have appeared after the submaximum long term exercise test on the previous day as it was not observed in connection with the exercise tests. In none of the patients were tests terminated for lack of motivation. Reasons for termination during hypoxia: dyspnoea, unspecific distress in the chest or low arterial blood pressure, but never typical angina pectoris. A few of the patients were also distressed during hyperoxia (most R12 and R4). These patients had increasing carbon dioxide retention during hyperoxia, which might have caused the feeling of distress. The induced hypercapnoea was experienced as most distressing in patients with low habitual $P_{a_{CO_2}}$ levels and in patients with the highest increase in ventilation, which usually was combined with an increase in arterial blood pressure (27). In some of these patients a failing left ventricle might have accentuated the feeling of dyspnoea, which seemed to be the cause of earlier termination as the ventilation did not usually increase to MVV levels during induced hypercapnoea.

Gas exchange at rest and during exercise

At rest during ambient air breathing in the supine posture the arterial oxygen and carbon dioxide tensions ranged from 37 to 73 and 36 to 63 mmHg, respectively, in different patients. In a few patients the arterial blood gas tensions were within normal limits, in comparison with normal subjects of the same age and studied in the same body posture. Mellemgaard (17), Sorbini et al. (24) and Ward et al. (29), among others, have shown that $P_{a_{O_2}}$ decreases with age and that the decrease per year is greater in the supine posture. Studies performed by the author in normal subjects in two different age groups also showed the same trend (5). There were no significant differences in arterial blood gas tensions in resting conditions between R- and C-group patients. The R-group patients were, however, metabolically more compensated. V_D/V_T ranged from 0.35 to 0.69 in the R- and from 0.43 to 0.61 in the C-group. $P_{A-a_{O_2}}$ ranged from 7 to 37 mmHg in the R- and from 18 to 33 mmHg in the C-group. This ratio was lowest in the most severely ill patient R4.

There was no consistent difference between the supine and sitting postures in regard to $P_{a_{O_2}}$, but $P_{a_{CO_2}}$ was higher in the supine posture among R-group patients. The elevated V_D/V_T ratio was higher in the C-group in the sitting posture. There was a significant increase of most of the ventilatory variables (Table VII) from the supine to the sitting posture. The fact that in the supine posture these patients have a lower minute ventilation and that the diaphragmatic movements probably are somewhat more effective, as the diaphragm is pressed upwards by the abdominal organs, may explain that many of them are less dyspnoeic in this posture. As several of these patients have increased ventricular filling pressures in their habitual state (26), they might be orthopnoeic in association with failure, however. During exercise some of the ventilatory variables remained higher in the sitting posture in the C-group (7 patients), but there was no consistent change in the R-group (3 patients). Two out of 7 C-group and all 3 R-group patients had elevated PCV pressures, which are known to increase ventilation in an increasing number of patients when they exceed about 25 mmHg (12). In some, but not all patients in this comparison, the increased PCV pressure might have increased the minute ventilation to a greater extent in the supine posture.

$P_{a_{O_2}}$ and $P_{a_{CO_2}}$ seemed to be related to the type of underlying lung disease, which has been described in detail by Brundin & Tammivaara-Hilty (3). Patients with mainly emphysema had higher $P_{a_{O_2}}$ and especially lower $P_{a_{CO_2}}$ values than patients with a combined type of disease. In patients with bronchiectasis and emphysema the $P_{a_{O_2}}$ values were, however, lower (R7 and R12). These trends at rest are in agreement with results reported in the literature. The PP (pink puffer) and BB (blue bloater) patients of Filley et al. (9) and the A- and B-group patients of Burrows et al. (4), Marcus et al. (16) and Jones (13) correspond roughly to the patients of the present study with mainly emphysema and mainly chronic bronchitis. The classifications in different materials are, however, not exactly the same. This and the fact that most of our patients had a combination of chronic bronchitis and emphysema makes

exact comparisons impossible. In submaximum supine working conditions there was no consistent decrease of $P_{a_{O_2}}$ in patients with mainly emphysema. Thus the findings are not in agreement with those of Jones (13) who observed that $P_{a_{C_2}}$ decreased in emphysematic and increased in chronic bronchitic patients at submaximum working levels in sitting posture. The only patient with mainly emphysema and a marked $P_{a_{O_2}}$ decrease was patient C5, who was in latent left ventricular failure. As most of the patients of this study had both chronic bronchitis and emphysema (3), no division of the material according to the clinical type of the disease has been made.

A further factor which seemed to have influenced the arterial blood gas tensions was the cardiac function. Slightly or moderately increased PCV pressures (26) did not seem to impair the arterial oxygenation in patients R5, R8, R13 and C1. The reason might be that the increased PCV pressure, transmitted in the retrograde direction, might prevent the lung capillaries from collapsing and make the perfusion more uniform. In patient C5 with a PCV pressure of 36 mmHg at a work load of 150 kpm/min in the supine posture, $P_{a_{O_2}}$ decreased rapidly from rest to this work load. In patient C6, with secondary polycythemia and moderately increased PCV pressure (probably from a recent minor myocardial ischaemic lesion) as described by Brundin & Tammivaara-Hilty (5), it might be speculated that during excercise the ventilation was stimulated by the increased PCV pressure and therefore prevented a further decrease of $P_{a_{O_2}}$. This explanation is supported by the atypical ventilatory reaction during exercise. The hypoventilation has been found to persist also during exercise in patients with a high haemoglobin concentration reported in the literature (13) and also in the other patient of the present study with secondary polycythemia.

The diffusing capacity for carbon monoxide ($D_{L_{CO}}F$, ml/min · mmHg) according to Filley et al. (10), measured during exercise, was about equally reduced in the R- and C-groups. It should be noted, however, that as far as the clinical condition was concerned it could be measured only in 3 R-group male (R3, R5 and R8), 4 R-group female (R11, R13, R14 and R15) and 10 C-group patients (all except C 6). (The values for 2 C-group patients have been excluded from the results as these measurements were technically unsatisfactory.)

Gas exchange during hypoxia, hyperoxia and induced hypercapnoea

During ambient air breathing $P_{A-a_{O_2}}$ decreased from about 25 to 32 mmHg to about 9 to 19 mmHg in patients who terminated the hypoxia at the higher $F_{I_{O_2}}$ level. The V_D/V_T ration increased in the 4 R-group male and one of the C-group patients (C8), but not in the 4 R-group female and the second C-group male (C6) patients. This change seems to be correlated to the increase in minute ventilation and probably to pressure increase in the pulmonary artery.

In patients who continued further at the lower $F_{I_{O_2}}$ level, the $P_{A-a_{O_2}}$ difference of about 29–31 mmHg during ambient air breathing decreased to about 15–16 mmHg at the higher and to about 9–13 mmHg at the lower $F_{I_{O_2}}$ level. The changes in V_D/V_T were not consistent at the higher $F_{I_{O_2}}$ level either in the R-group (3 male patients) or in the C-group (7 male and one female), but at the lower $F_{I_{O_2}}$ level this ratio increased in the R-group patients but remained unchanged in the male C-group patients and decreased in the female C-group patient. Though these results have to be regarded with some reservation as the steady state conditions were not fulfilled in all patients, there might be a connection between the ventilatory increase/pulmonary arterial pressure increase ratio and increase of V_D/V_T during hypoxia.

Whether these differences in V_D/V_T changes from ambient air breathing to the lowest hypoxic levels can be compared with "responders and non-responders" of Lindsay & Read (15) during hyperoxic conditions cannot be stated. The "responders" in the present material could be those patients who react with a greater ventilatory and PA pressure increase during hypoxia making the physiologic dead space even greater than during ambient air breathing. Included among "responders" should probably also be those patients who were so disabled that hypoxia was not induced (except R16). Three of the 4 R-group female patients, increased their ventilation less. In general the patients who had only slight or moderate pressure and ventilation increases during hypoxia belonged to the patients who could use best the available ventilatory capacity during exercise (R13, 14, 15 and C3 and 5). The ventilatory and vascular responsiveness should be studied further in larger patient material in order to find out whether some persons are more prone

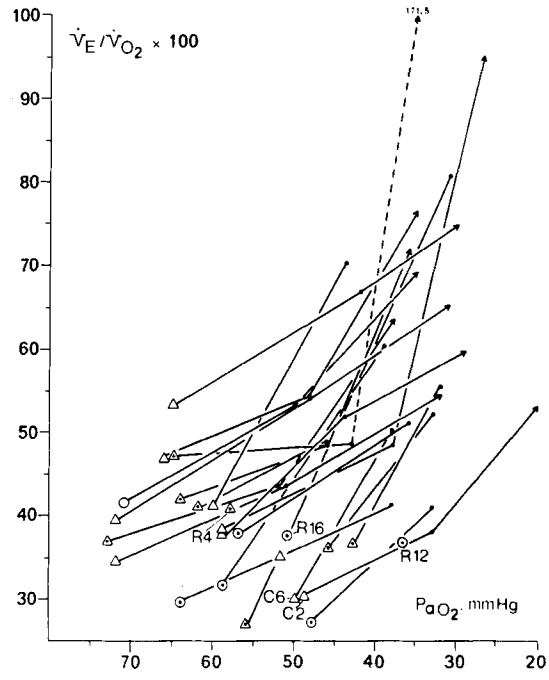

Fig 2. The ventilation equivalent $(\dot{V}_E \times 100)/\dot{V}_{O_2}$, in relation to arterial oxygen tension (P_{aO_2}, mmHg) in the supine posture at rest during ambient air breathing (R-group male △, female ⊙; C-group male △ and female ○ patients) and in most cases one or two induced hypoxic levels (F_{IO_2} 0.1395–0.1530 and 0.1035–0.1260→).

to get chronic lung changes by reason of the above mentioned factors.

The P_{A-aO_2} difference deviated more from values in normal subjects during hypoxia than during ambient air breathing; in 50-year-old normal subjects this value decreased to below 5 mmHg, but remained at a level of about 8–16 mmHg in the present patients.

In only a few patients was veno-arterial shunting, studied during pure oxygen breathing and important component of the increased P_{A-aO_2}. There was a tendency to increased carbon dioxide retention during hyperoxia in patients with decreased habitual P_{aO_2} and increased habitual P_{aCO_2} levels (Fig. 1).

During induced hypercapnoea the arterial oxygenation improved in all patients investigated. In most of the patients the improved alveolar ventilation due to increased tidal volume resulted in normal oxygen saturation levels. The arterial oxygen saturation during induced hypercapnoea was lowest in patients R1, with the severest pulmonary hypertension in the material and C6 with secondary polycythemia, severe arterial hypoxaemia during ambient air breathing and a small ventilatory increase during induced hypercapnoea.

Ventilation in relation to decreased oxygen and increased carbon dioxide concentration in the inspiratory air

The relationship between P_{aO_2} and the ventilatory equivalent for oxygen during ambient air breathing and during hypoxia at one or two levels is presented in Fig. 2. The ventilation equivalent for oxygen during ambient air breathing shows a tendency to decrease with decreasing P_{aO_2}, with the exception of some of the most severely ill patients, in whom the "hypoxic drive" contributes to the ventilation. In patients with somewhat higher P_{aO_2} levels, combined in two patients (C2 and 6) with secondary polycythaemia, the ventilation is low, obviously because of its adaptation to habitually increased P_{aCO_2} levels, as seen in Fig. 3.

That ventilation during CO_2 breathing increases

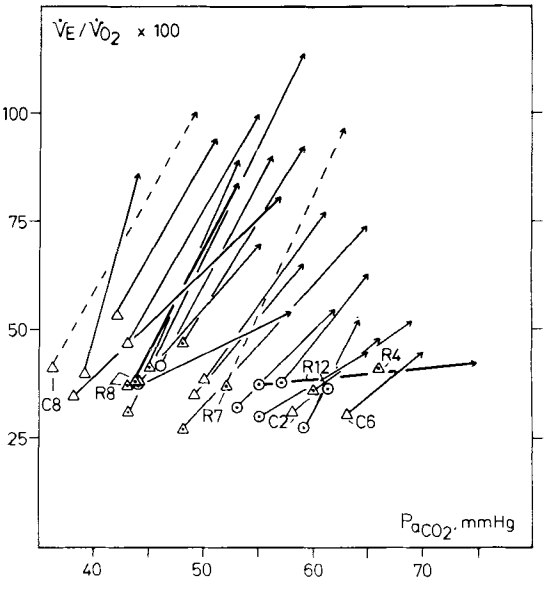

Fig 3. The ventilation equivalent $(\dot{V}_E \times 100)/\dot{V}_{O_2}$, in relation to arterial carbon dioxide tension (P_{aCO_2}, mmHg) at rest in supine posture during ambient air breathing (R-group male △, female ⊙; C-group male △ and female ○ patients) and during induced hypercapnoea (→) with F_{ICO_2} 0.0542–0.604 in air. Thick lines for patients R8 and R12 indicate that hypercapnoea was induced in connection with the follow-up investigation after training. Broken lines indicate that P_{aCO_2} was measured and ventilation equivalent only roughly approximated.

less in emphysematic patients than in normal subjects was found already 1913 by Reinhardt (20). Scott (23) showed 1920 that the ventilation is adapted to the increased carbon dioxide content of arterial blood in patients with chronic obstructive lung disease. The adaptation mechanism has been intensively studied (1, 2, 6, 7, 8, 11, 18, 19, 22, 25). Tenney (24) proposed that the ventilation was decreased in order to reduce the oxygen cost of breathing. As pointed out earlier, not only the $P_{a_{CO_2}}$ level, but also the acid–base status both of the blood and possibly of the cerebrospinal fluid as well as the haemoglobin concentration, seem to be important factors for the ventilatory regulation. This can be seen in findings in patient C2, who in spite of a $P_{a_{O_2}}$ level of 20 mmHg did increase his ventilation only moderately and significantly less than normal persons, in whom Weil et al. (30) have found that ventilation increases at these $P_{a_{O_2}}$ levels very steeply if the $P_{a_{CO_2}}$ is kept constant and on normal levels. In patient C2 the ventilatory capacity was not impaired to such an extent that lung mechanical factors would have been the reason for the moderate ventilatory increase.

Schaefer et al. (22) found thar prolonged exposure of normal subjects to increased CO_2 levels increased their physiological and alveolar dead space. Therefore these authors speculated that increased P_{CO_2} might be an etiologic factor in emphysema. The highest ventilatory equivalent increase during hypoxia took place in patients R3 with the abnormal decrease in oxygen uptake and cardiac output as described by the author elsewhere (26), and in patient C10, who was anaemic (104 g/l).

The role of the haemoglobin concentration in the ventilatory regulation might not in general be as important (1) as in a few cases in this material. The individual findings indicating that deviating haemoglobin concentration (either low or high) are associated with ventilatory changes can hardly be coincidental though the number of these cases is small. In view of the important function of haemoglobin as a transporter of both oxygen and carbon dioxide it is to be expected that it would be involved in the ventilatory regulation. This might take place via the circulatory changes occurring when the cardiac output adapts itself to changes in the haemoglobin concentration and the blood volume. It might also be due to the buffering capacity of the haemoglobin molecule.

Carbon dioxide tension levels during voluntary hyperventilation were better correlated to the degree of airway obstruction than the habitual $P_{a_{CO_2}}$ levels probably because of the mentioned adaptive mechanism. Rotsztain et al. (21) found that the decrease of $P_{a_{CO_2}}$ during voluntary hyperventilation was smaller in patients with chronic obstructive lung disease with carbon dioxide retention than in patients with normal carbon dioxide tension levels.

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