Exercise Limitation Following Extensive Pulmonary Resection *

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Cardiac output imposes the principal limit to maximal oxygen intake in the normal exercising subject (1, 2). After pulmonary resection reduction in the ventilatory capacity, the diffusing capacity, or the maximal cardiac output might impose a lower limit to maximal oxygen intake. The relative importance of each of these factors in limiting oxygen intake might depend on the amount of lung resected. This study was undertaken to determine the primary factor limiting oxygen intake in each of a group of eight patients whose lung remaining following resection varied from 33% to 55%.

Methods

Patients. Table I describes the patients. Resectional surgery was performed because of far advanced tuberculosis. Two of the eight patients had simple pneumonectomy; the remaining six had pneumonectomy with contralateral segmental resection or lobectomy. In calculating the amount of lung remaining, each segment was assumed equal to $\frac{1}{8}$ of the initial total lung tissue.

Methods. The following measurements were made: 1) maximal oxygen intake for treadmill exercise; 2) lung volumes sitting; 3) membrane diffusing capacity for carbon monoxide, lung capillary volume, and pulmonary blood flow at rest sitting and during treadmill exercise; 4) arterial oxygen saturation, oxygen and carbon dioxide partial pressures, and pH standing at rest and during treadmill exercise; 5) right ventricular pressures and pulmonary vascular resistances supine at rest and during exercise.

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Maximal oxygen intake (MOI) was determined according to the method of Mitchell, Sproule, and Chapman (1) on a motor driven treadmill; oxygen intake was measured during the last minute of a 2½-minute exercise period. Expired air was collected in a Douglas bag; volume of expirate was measured in a Tissot spirometer after a known volume had been removed for gas analysis. Oxygen and CO₂ concentrations were measured by a Beckman paramagnetic oxygen analyzer and by a gas chromatograph, respectively. Each patient was studied on successive days until the MOI was determined; treadmill speed was increased at ½ mile per hour increments until further increments in work load produced no greater than 54 ml per minute increments in the patient's oxygen intake, or until the patient could not sustain further increments of work load for the required time.

Vital capacities and timed expiratory volumes were measured with a Stead-Wells spirometer. Functional residual capacity was measured by the closed-circuit helium method (3).

Apparent CO diffusing capacity (DL_{CO}) was measured during breath holding, both at a high and at a low alveolar oxygen tension so that pulmonary membrane diffusing capacity (DM_{CO}) and capillary blood volume (V_c) could be calculated by the method of Roughton and Forster (4). Measurements were made at rest and at MOI. Change in pulmonary blood flow may alter pulmonary capillary blood volume (5, 6) and apparent CO diffusing capacity (DL_{CO}). Hence, in order to calculate DM_{CO} and V_c, it is essential that blood flow be the same when DL_{CO} is measured at high and low alveolar oxygen tensions. Pulmonary capillary blood flow and DL_{CO} were measured simultaneously as described by Johnson, Spicer, Bishop, and Forster (5), and measurements of DL_{CO} made at high oxygen tensions were required to have a blood flow (Q_c) within 10% of that measured under corresponding conditions at a low oxygen tension. In measurement of DL_{CO} and Q_c, test gas mixtures containing 0.5% Ne, 0.3% CO, and 0.3% C₂H₂ in a balance of oxygen and nitrogen were used. For measurements at rest, the test gases contained 20% and 98% oxygen; for measurements during exercise, the test gas mixtures contained 30% and 98% oxygen. The subjects breathed an oxygen-nitrogen mixture of similar oxygen concentration to that in the test gas to be inspired for 2 to 3 minutes before measurements of DL_{CO} to insure uniform alveolar oxygen

tension during breath holding. Analysis of expired air was made with a gas chromatograph (7). Normal ranges for $\dot{V}_{\text{MCO}}$, V_c , and $\dot{Q}_c$ at rest and exercise are from measurements made in 12 young normal subjects in our laboratory. These data have been previously reported in part (8).

Blood was collected for analysis from an indwelling catheter placed in the brachial artery during upright exercise at loads varying from rest to MOI. Arterial oxygen saturation was measured by a Van Slyke apparatus; pH, arterial Po_2 , and PCO_2 by an Instrumentation Laboratories physiologic blood gas analyzer.

Right heart catheterization was performed with the subject in the supine position. A portable bicycle generator was pedaled at a constant rate for the 5 minutes of supine exercise. Cardiac output was measured by the Fick method at rest and during the last 3 minutes of exercise.

Results

Maximal oxygen intake (MOI). Six of the eight patients reached a maximal oxygen intake as defined in the Methods. Two, one of whom

TABLE I
Description of patients

Patient	Sex	Age	Height	Body surface area	Lung re- main- ing	Time after surgery
			cm	m ²	%	months
MS	F	27	166	1.52	55	2
BW	F	29	163	1.57	45	3
MG	F	41	150	1.29	42	36
CY	M	32	170	1.72	39	29
MC	F	29	159	1.55	39	26
RT	M	36	172	1.63	36	24
AB	F	29	167	1.42	36	46
RH	F	47	153	1.57	33	47

was trained for 3 weeks, were unable to achieve MOI. Oxygen intakes at graded exercise loads are illustrated in Figure 1. The highest oxygen consumption achieved is listed in Table II.

Ventilation. Lung volumes are presented in Table III. Half-second forced expiratory volume

FIG. 1. OXYGEN INTAKE ($\dot{V}_{\text{O}_2}$) VS. TREADMILL SPEED. Each discrete point represents a single measurement of oxygen intake. Definite plateaus in oxygen intake with increases in treadmill speed indicate valid estimates of maximal oxygen intake (MOI) in six of the eight patients.

TABLE II
Maximal oxygen intake

Patient	Work load*	Maximal oxygen intake	
		ml/min	% Pred.†
MS	4.0	957	55
BW	5.5	1,246	65
MG	6.5	984	70
CY	4.5	1,318	51
MC	4.5	1,047	52
RT	4.0	898	40
AB	4.25	724	50
RH	3.5	796	43
Average	4.6	996	53

* All patients exercised at the speed indicated, no grade for 2.5 minutes.

† Maximal oxygen intake in milliliters per minute per kilogram body weight was predicted from the following regression formulas derived from Andersen (9, 10): women $\dot{V}O_2 = 42.7 - 0.248 \times \text{age}$; men $\dot{V}O_2 = 50.1 - 0.247 \times \text{age}$.

(FEV_{0.5}) was low with respect to the amount of lung remaining. This suggests some degree of partial airway obstruction. The maximal breathing capacity (MBC) can be roughly predicted from the FEV_{0.5} (13). The comparison between predicted MBC and minute ventilation during maximal exercise illustrated in Figure 2 suggests that most patients were operating at or near their ventilatory capacities during maximal exercise.

Diffusion. Average capillary blood volume (Vc) was normal at rest with respect to blood flow and amount of lung remaining, but it increased less than would be expected from the increase in blood flow during exercise (Figure 3).

FIG. 2. COMPARISON OF VENTILATION DURING MAXIMAL EFFORT ($\dot{V}_E$) WITH MAXIMAL BREATHING CAPACITY (MBC). $\dot{V}_E$ is plotted against MBC predicted from the half-second forced expiratory volume. In all but two patients, ventilation during maximal effort equals or approaches the diagonal line of identity, indicating that at maximal exercise the patients were breathing at or near their MBC.

Average membrane diffusing capacity for carbon monoxide (DM_{CO}) at rest and exercise was less than predicted for the amount of lung remaining, but the difference was not statistically significant (Table IV). DM_{CO} was reduced most with respect to lung remaining in the two patients who had the least remaining lung. MOI was reduced much more than would be predicted from the reduction in DM_{CO} in all but two patients, AB and RH (Figure 4).

TABLE III
Ventilatory function

Patient	Total lung capacity		Residual volume Total lung capacity $\times 100$		Forced vital capacity		0.5-sec forced expiratory volume	
	Meas.	% Pred.*	Meas.	Pred.*	Meas.	% Pred.*	Meas.	% Pred.†
	ml				ml		ml	
MS	2,678	58	37.7	31.6	1,667	45	997	39
BW	3,088	69	38.4	32.3	1,902	53	1,109	45
MG	2,761	71	30.5	36.2	1,918	65	663	33
CY	3,883	64	39.2	30.1	2,360	50	896	28
MC	1,920	45	29.2	32.3	1,359	40	672	29
RT	2,460	40	36.2	31.8	1,570	33	750	23
AB	2,142	46	53.9‡	32.3	986	26	520	22
RH	1,939	48	32.3	38.2	1,313	44	643	32

* Predicted values from Needham, Rogan, and McDonald (11).

† Predicted from Miller, Johnson, and Wu (12).

‡ Difference between measured and predicted significant at .05 level.

Blood pH and gas analyses and alveolar ventilation. The results of blood pH and gas analyses are contained in Table V.

Resting measurements of arterial pH and P_{CO_2} did not, in any instance, suggest hypoventilation; on the contrary, patients BW and RH appear to have been hyperventilating, as indicated by alkalosis and low arterial P_{CO_2} . During treadmill exercise at previously determined maximal loads, average alveolar partial pressure of CO_2 (P_{ACO_2}) rose minimally, with the highest individual maximal P_{ACO_2} when breathing room air being 48 mm Hg. However, except for MS, whose volume of expired air ($\dot{V}_E$) was 29 L per minute with predicted MBC 53 L per minute, alveolar oxygen tension did not fall with exercise, and average arterial pH fell to only 7.35 (normal 7.19 ± 0.09) (1).

Resting arterial oxygen saturation when breathing room air was above 94% in all patients except AB and RH. At rest, most of the difference between the oxygen saturation of blood in equilibrium with alveolar oxygen tension and the oxy-

FIG. 3. PULMONARY CAPILLARY VOLUME VS. CARDIAC OUTPUT. Pulmonary capillary volume (V_c) is expressed in milliliters per body surface area per fraction of lung remaining (F_{lung}), cardiac output in terms of cardiac index per fraction of lung remaining. The normal range of capillary volume with increasing blood flow ($\dot{Q}_c$) is indicated by the heavy lines, resting and exercise points for the patients indicated by the closed and open circles, respectively. Regression line constants for patient and normal data are indicated in the upper left panel: α = intercept, β = slope, σ_e = standard error of estimate at mean. The rate of increase of capillary volume with increasing blood flow is significantly less than normal, and despite greater than normal blood flow per unit lung during exercise, capillary volumes per unit lung do not exceed the normal maximum.

TABLE IV
Lung capillary volume, membrane diffusing capacity, and blood flow

Patient	Work load	Cardiac index	Heart rate	Lung capillary blood volume	Lung membrane diffusing capacity for CO	
					Meas.	% Pred.*
	<i>mph†</i>	<i>L/min</i> <i>×BSA</i>	<i>beats</i> <i>min</i>	<i>ml</i>	<i>ml/min</i> <i>mm Hg</i>	
MS	Rest	2.6	100	42	30	52
	1.5	3.4	109	54	26	
	2.5	3.4	112	50	28	
	4.0	4.0	156	59	25	
	5.0	4.3	156 + PVC	56	36	51
BW Trained	Rest	2.8	116	54	25	45
	5.5	6.9	170	67	31	45
MG Trained	Rest	2.4	95	54	14	29
	4.0	7.2	127	46	28	49
CY	Rest	2.8	80	62	32	42
	4.5	5.0	176	83	30	32
MC	Rest	2.2	88	50	28	52
	1.5	3.2	111			
	4.0	4.9	175	71	27	44
RT	Rest	1.0	124	29	24	31
	4.0	3.3	128	55	27	28
AB	Rest	4.8	102	48	18	30
	4.0	6.1	163	56	16	22
RH Trained	Rest	2.1	72	17	12	25
	3.0	4.1	128	39	10	
	3.5	5.0	118 + many PVC	29	13	21

* $DM_{rest} = 12.13 \times \text{height}^4 \times K - 2.16$ [$K = 1.18$ for males, 1.10 for females (14)], and $DM_{max} = DM_{rest} + 0.2 \times DM_{rest}$.
† No grade.

gen saturation of arterial blood can be explained by the venous admixture caused by anatomical shunts (Table V), but during exercise, arterial oxygen saturation fell more than can be explained by the measured anatomical shunt. Even in the presence of pulmonary disease, ventilation probably becomes more uniform with respect to perfusion during exercise (18), and hence this discrepancy between measured and calculated saturation probably results from impaired diffusion (15). The fall in arterial oxygen saturation with exercise was most pronounced in AB and RH, the patients who had the least remaining lung.

Hemodynamics. Blood flow and heart rate during treadmill exercise are presented in Table IV. The average resting heart rate of 96 beats per minute rose to 156 beats per minute at maximal exercise (normal 187 ± 10) (1). Although cardiac output was low at rest, it was not reduced in pro-

TABLE V
Blood gas and pH, and alveolar air during rest and exercise*

Patient	Exercise	$\dot{V}O_2$	F_{IO_2}	O_{2cap}	$PaCO_2$	pH	PAO_2	$Sc'O_2$ †	PaO_2	$Sc'O_2 - \Delta Sc'O_2$ ‡	SAO_2
	<i>mph/grade/min</i>										
MS	Rest	192	0.21	0.180	40	7.42	99	97	85	96.1	96.1
	Rest		1.00		36	7.42	657		605		
	3.5/0/3.5	865	0.21	0.180	43	7.34	89	95.4	66	94.4	89.8
	4/0/2.5	982	0.21	0.190	47	7.28	94	95.3	80	94.3	90.8
	4/0/2.5		1.00		45	7.28	648		585		
	Cath rest	174	0.21	0.154							95.8
BW	Cath exercise	792	0.21	0.171							94.1
	Rest	197	0.21	0.170	23	7.50	117	98.5	89	96.7	94.5
	Rest		1.00		24	7.51	671		570		
	5.5/0/2.5	1,246§	0.21	0.176	24	7.41	124	98.4	72	97.2	94.4
	5.5/0/2.5		1.00		26	7.38	669		595		
	Cath rest	198	0.21	0.136							96.0
MG	Cath exercise	590	0.21	0.139							95.8
	Rest	224§	0.21	0.200	42	7.42	96	96.9	90	96.5	94.4
	Rest		1.00		43	7.45	652		625		
	7/0/2.5	965§	0.21		48	7.29	102	96.5	75	94.3	90.5
	7/0/2.5		1.00		58	7.27	637		560		
	Cath rest	171	0.21	0.151							90.9
CY	Cath exercise	818	0.21	0.165							91.7
	Cath exercise	750	1.00								
	Rest	267	0.21	0.210	33	7.42	108	97.7	97	95.7	96.6
	Rest		1.00		26	7.42	667		529		
	1.5/0/2.5	405	0.21			7.42	113	98.0	92	96.7	96.0
	1.5/0/2.5		1.00		36	7.40	656		566		
MC	4.5/0/2.5	1,318§	0.21		36	7.28	106	96.5	86	95.9	97.1
	4.5/0/2.5		1.00		43	7.28	649		539		
	Cath rest	196	0.21	0.183							96.0
	Cath exercise	739	0.21	0.189							95.4
	Rest	198	0.21	0.175	39	7.39	97	96.7	72	96.3	96.3
	Rest		1.00		36	7.40	662		637		
RT	4/0/2.5	1,021	0.21	0.188	41	7.33	101	96.5	63	95.6	88.7
	4/0/2.5		1.00		44	7.29	654		595		
	Cath rest	171	0.21	0.159							97.5
	Cath exercise	489	0.21	0.168							94.2
	Cath exercise	872	0.21	0.172							91.7
	Cath exercise										
AB	Rest	240	0.21	0.174	42	7.40	88	96.0		95.3	93.9
RH	Rest		1.00		46	7.38	649		606		
	2.5/0/2.5	530	0.21	0.171	40	7.38	94	96.4			88.6
	4/0/2.5	632	0.21	0.183	44	7.40	98	96.9		94.3	82.2
	4/0/2.5		1.00		53	7.24	642		479		
	Cath rest	201	0.21		41	7.41	94	96.6		95.7	
	Cath rest	203	0.21	0.160	37	7.42	100	97.1		96.2	90.4
	Cath rest		1.00		44	7.40	651		605		
	Cath exercise	607	0.21	0.169	47	7.30	100	96.3		95.2	82.5
	Cath exercise	609	0.21		45	7.28	101	96.1		95.0	
	Cath exercise	530	1.00		51	7.28	644		580		
RH	Rest	223	0.21		36	7.48	96	97.3	80	95.6	93.0
	Rest	237	0.21	0.203	35	7.48	97	97.4	80	95.7	93.8
	Rest		1.00		38	7.48	654		540		
	1.5/0/1.5	580	0.21			7.48	97	97.4	53		86.9
	3/0/2.5	514	0.21	0.213	38	7.45	100	97.4	58	95.8	86.9
	3/0/2.5		1.00		42	7.41	650		535		
	3.5/0/2.5	673	0.21		36	7.48	103	97.9	55	96.3	84.0
	Cath rest	188	0.21	0.181							93.9
	Cath exercise	369	0.21								90.1
	Cath exercise	590	0.21	0.194							90.3

* $\dot{V}O_2$ = oxygen intake in milliliters per minute; F_{IO_2} = fractional concentration of inspired oxygen; O_{2cap} = oxygen capacity of arterial blood in milliliters O_2 per milliliter blood; $PaCO_2$ = arterial partial pressure of CO_2 in millimeters Hg; PAO_2 = partial pressure of oxygen in alveolar air; $Sc'O_2$ = end lung capillary blood saturation in per cent calculated from PAO_2 and arterial pH; PaO_2 = partial pressure of oxygen in arterial blood; $Sc'O_2 - \Delta Sc'O_2$ = predicted arterial saturation in per cent; SAO_2 = measured arterial saturation.

† From oxyhemoglobin dissociation curve according to Dill (16), at measured alveolar PO_2 and arterial pH.

‡ Theoretic saturation of mixture of blood in equilibrium with alveolar gas plus shunted blood calculated according to the method of Linderholm (17).

§ Assumed value from previous studies at similar exercise load.

portion to the amount of lung removed, and blood flow per unit lung was high, both at rest and exercise (Figure 4). [Average cardiac index by the acetylene method in 12 normal subjects was: rest $3.5 \text{ L/BSA} \pm 2$; ¹ maximal exercise $12.0 \text{ L/BSA} \pm 2.2$.¹ Normal blood flow per unit lung is then $3.5 \text{ L}/(\text{BSA} \times F_{\text{lung}})$ at rest and $12.0 \text{ L}/(\text{BSA} \times F_{\text{lung}})$ during exercise.²] The results of cardiac catheterization are presented in Table VI. Resting cardiac outputs during cardiac catheterization are of similar magnitude to those measured by the acetylene method. Average maximal supine output was somewhat lower than maximal upright output, probably as a result of the position and the type of exercise. The average mean pulmonary arterial pressure of 19 mm Hg at rest rose to 39 mm Hg during supine exercise. Resting pulmonary vascular resistance (pressure $\times \text{BSA} \times F_{\text{lung}}$ /blood flow) in the remaining lung was normal (Figure 5). Exercise resistance was abnormally high because pulmonary vascular re-

¹ Two $\times$ standard deviation.

² F_{lung} = fraction of lung remaining.

FIG. 4. MEMBRANE DIFFUSING CAPACITY FOR CO (DM_{CO}) VS. MAXIMAL OXYGEN INTAKE. The theoretic reduction in maximal oxygen intake resulting from reduced alveolocapillary membrane diffusing capacity (15) is represented by the curved line. It is most closely approached by the two patients with least lung remaining, who also developed arterial desaturation (Sa_{O_2}) with exercise.

FIG. 5. PULMONARY VASCULAR RESISTANCE VS. CARDIAC OUTPUT. Pulmonary vascular resistance is expressed as resistance $\times F_{\text{lung}}$, where resistance = pressure in millimeters Hg/CI; CI = cardiac index; F_{lung} = fraction of lung remaining. Cardiac output is expressed as CI/F_{lung} . The normal 95% confidence limits are indicated by the heavy solid lines and were derived from 175 measurements at various exercise levels reported in the English literature (19-26). The normal mean is indicated by the light line. Closed circles are patients' resting values, open circles measurements during exercise. See text for further discussion.

sistance failed to fall with exercise (Table VI, Figure 5) (19-26). However, the duration of exercise may not have been sufficient to demonstrate a fall in pulmonary vascular resistance, since resistance only begins to fall after 3 to 4 minutes of exercise (24, 27). Resting wedge pressures were normal in two patients. Right ventricular end-diastolic pressure was normal at rest and in two patients after exercise.

Discussion

Ventilation. During maximal exercise, ventilation in seven of the eight patients approached predicted MBC. However, patients who are limited in exercise capacity as a result of impaired ventilation are unable to achieve a maximal oxygen intake (18) as defined by Mitchell, Sproule, and Chapman (1), and hence the six patients who were able to exercise to MOI were not limited in short-term exercise by their reduced ventilatory capaci-

TABLE VI
Hemodynamic data from cardiac catheterization

Patient	State	Heart rate	Blood flow	Oxygen intake	Right ventricular end-diastolic pressure	Wedge pressure	Pulmonary arterial pressure S/D/M*	Total pulmonary resistance	Systemic pressure S/D/M	Total peripheral resistance
			<i>L/min</i>					<i>dyne-sec-cm⁵</i>		<i>dyne-sec-cm⁵</i>
MS	Rest	85	4.4	174			22/ 9/15	253	107/69/85	1,550
	Exercise, air	160	8.5	792			/ /38	358	/ /120	1,130
	Exercise, 100% O ₂	142	8.1	734			/ /27	268	155/77/113	1,120
	Recovery, exercise, 100% O ₂	96			2		34/15/21			
BW	Rest	92	2.9	198	6		22/15/17	352	105/70/88	1,800
	Exercise	131	7.8	590			47/21/30	307	137/90/111	1,142
MG	Rest	85	3.9	171	6		31/14/20	310	105/55/79	1,620
	Exercise, air	155	8.4	818			61/26/43	360	138/80/117	1,110
	Exercise, 100% O ₂	133	7.0	750			/ /25	229	133/76/103	1,180
CY	Rest	78	3.6	196	1		31/ 5/17	373	122/79/96	2,100
	Exercise, air	123	7.5	739			60/18/36	386	157/88/117	1,250
MC	Rest	82	3.7	171			32/10/23	458	116/81/93	2,050
	Exercise, air	143	7.4	489			53/18/30	326	146/91/117	1,270
	Exercise, air	162	9.1	872			54/22/38	335	128/72/90	793
RT						No cardiac catheterization				
AB	Rest	132	5.1	202	5	5	30/15/21	329	116/80/95	1,490
	Exercise, air	179	6.4	607			59/38/49	608	171/95/128	1,580
	Exercise, 100% O ₂	174	6.0	504			54/23/38	511	/ /120	1,610
RH	Rest	83	3.3	188	4	7	28/12/19	462	108/68/94	2,260
	Exercise, air	104	4.2	369			36/17/28	526	126/77/96	1,810
	Recovery, exercise, air	78			3					
	Exercise, air	130	6.0	590			51/14/37	497	154/90/122	1,640
	Recovery, exercise, air	116			7					

* Systolic/Diastolic/Mean.

ties. While the remaining two patients were breathing room air, alveolar oxygen tension rose with peak exercise load while arterial CO₂ tension was not significantly changed from rest, thereby suggesting that, even in these patients, maximal oxygen intake was not limited significantly by the low ventilatory capacity. Although impaired ventilation per se in no instance appeared to limit maximal oxygen intake, increased work of breathing could divert an increased portion of oxygenated blood from muscles of locomotion to muscles of ventilation. This diversion of oxygen to muscles of breathing would not lower the maximal oxygen intake, but could lead to early exhaustion during exercise.

Diffusion. The capillary blood volume per unit of remaining lung did not exceed normal maximum, despite the fact that peak blood flow per unit lung during exercise was often much higher

than normal (Figure 4). This observation lends support to the suggestion made by Johnson, Taylor, and Lawson (8) that the maximal potential volume of the pulmonary capillary bed is approached in normal subjects as they exercise to maximal oxygen intakes. An alternative hypothesis is that the lung capillaries in these patients were less compliant than normal capillaries and hence failed to expand further as blood flow increased with exercise.

In a previous paper, Johnson, Taylor, and DeGraff (15) discussed the functional significance of an impaired alveolocapillary diffusing capacity, indicating the manner in which patients with impaired diffusing capacity might be limited in maximal oxygen intake. A prediction curve indicating the diffusion imposed limit to MOI is presented in Figure 4. This limiting curve is approached only by the two patients with the least

lung remaining, and upon exercise, only they developed arterial oxygen desaturation below the normal minimum, 88.5%; hence, oxygen consumption during exercise was probably limited in part by impaired alveolocapillary oxygen transfer in these two patients. Theoretically, if normal ventilation and cardiac output are achieved during exercise, diffusing capacity should become a factor limiting maximal oxygen intake when membrane diffusing capacity is reduced below 50% of normal (15). In our patients, frank alveolar capillary block was not manifest until membrane diffusing capacity was reduced to less than 30% of that predicted at peak exercise. On the other hand, Cournand, Himmelstein, Riley, and Lester have studied two patients who had simple pneumonectomy during childhood (28); they exhibited a fall of arterial oxygen saturation to 85% during exhausting exercise, and hence may have been limited in exercise capacities partly by their reduced diffusing capacities. The difference between Cournand's and our patients may be related to the fact that our patients were unable to achieve normal maximal cardiac outputs during exercise.

Hemodynamics. In five of the eight patients, reduced maximal cardiac output imposed the principal limit to maximal oxygen intake. Linderholm (17) has made a similar observation in patients after pneumonectomy. Although impaired myocardial function is suggested by the low maximal heart rates, the cause of the reduced maximal cardiac output, whether resulting from myocardial failure, reduced pulmonary venous capacity, or obstruction to venous return, was not determined.

Despite chronically increased blood flow per unit lung, pulmonary vascular resistance per unit lung was normal at rest, thereby indicating that even the adult lung has the capacity to accommodate itself to a chronic increase in blood flow. Extended follow-up of these patients will be required to see whether pulmonary vascular resistance ultimately rises, as it does in patients with increased pulmonary blood flow due to congenital heart disease (29-30).

Summary

Factors limiting oxygen intake were studied in eight patients after recovery from resection of from 45 to 67% of their lungs. Maximal oxygen

intake and carbon monoxide diffusion at rest and exercise were measured in all, and arterial blood gases measured at similar exercise loads in seven. Cardiac catheterization was also performed in seven patients with pressure and flow measurements made at rest and exercise. The following conclusions were reached. 1) Maximal oxygen intake was reduced in all patients, although not in proportion to the amount of lung resected. 2) Although some degree of partial airway obstruction was noted in all patients, in no instance could the reduction in maximal oxygen intake be ascribed to impaired ventilation. 3) Reduced diffusing capacity appeared to contribute significantly to the reduction in maximal oxygen intake only in the two patients with least lung remaining. 4) Since maximal oxygen intake in five of seven patients was limited neither by reduced ventilation nor diffusing capacity, it must have been limited by reduced cardiac output.

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