Respiratory gas exchange in patients with spontaneous pneumothorax

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Pulmonary gas exchange was studied in 12 patients with spontaneous pneumothorax by measuring the partial pressure of oxygen and carbon dioxide in arterial blood and expired gas when breathing air and 100% oxygen. The arterial oxygen tension was below 80 mm. Hg in nine patients, and the alveolar–arterial difference in oxygen tension was abnormally large in 10, but the physiological dead space was generally normal. There was a positive correlation between the size of the anatomical shunt and the extent of the pneumothorax as measured from the chest radiograph. Calculations indicated that the fall in arterial oxygen tension when breathing air could be fully accounted for by the increased anatomical shunt. After the air had been removed ventilation–perfusion relationships appeared to become more uneven, and the anatomical shunt was greater than would have been expected from the size of the lung. Observations during infusions of acetylcholine suggested that active vasoconstriction in poorly ventilated regions may have occurred to a slight or moderate degree in four out of eight patients.

In view of the dramatic nature of a spontaneous pneumothorax it is surprising that so little still is known about the effects it produces on the exchange of respiratory gases in the lung. During the early part of the century, when artificial pneumothorax was widely used as a therapeutic measure, there was considerable interest in its physiological effects. Studies in animals (Bruns, 1913 ; Adams and Morris, 1921 ; Weiss, 1926 ; and Moore, 1931) showed that shortly after induction of a pneumothorax there was a considerable fall in arterial oxygen saturation which returned to normal a few hours later. This, in the absence of a change in total ventilation, was thought to be due to an initial shunt of blood through the collapsed lung which gradually lessened due to pulmonary vasoconstriction. More recently, Simmons and Hemingway (1959) have shown that pneumothorax in the dog produces both a fall in arterial oxygen saturation and a rise in pulmonary vascular resistance.

In man the results were somewhat conflicting. Meakins and Davies (1925) found a rise in oxygen saturation and a fall in carbon dioxide tension following artificial pneumothorax in patients with tuberculosis. Richards, Riley, and Hiscock (1932) found a fall in oxygen saturation following pneumothorax in similar patients, and Stewart and

Bailey (1940) noticed a similar fall in arterial oxygen saturation in patients with spontaneous pneumothorax.

Berglund, Simonsson, and Birath (1961) described a patient with absorption atelectasis in one lung associated with a large anatomical shunt. This shunt was diminished by inducing a pneumothorax on the same side. They mentioned one other patient (Birath, 1945) in whom absorption of air from an artificial pneumothorax was associated with dyspnoea and a fall in arterial oxygen saturation. Both dyspnoea and desaturation were relieved by refilling the pneumothorax with air. It was suggested that the raised intrapleural pressure in pneumothorax might favour restriction of the circulation to the collapsed lung. A further experiment was described in which induction of pneumothorax in a normal subject produced no measurable effect on arterial oxygen saturation.

The abandonment of artificial pneumothorax as a treatment for pulmonary tuberculosis lessened interest in the problem, and there appear to be no studies using modern methods of measuring pulmonary blood flow or gas exchange following spontaneous pneumothorax in man. The purpose of the present study was to measure pulmonary gas exchange when breathing air and oxygen in patients with spontaneous pneumothorax, to study the effect of re-expansion of the lung, and, by infusing a pulmonary vasodilator substance

(acetylcholine) before and after re-expansion, to test the possibility that pulmonary vasoconstriction might be present in poorly ventilated lung units.

METHODS AND PROCEDURE

Technical methods Arterial blood was collected anaerobically from an indwelling polythene catheter into 10-ml. glass syringes, whose dead space was filled with a solution of heparin, and analysed immediately. Arterial oxygen tension (Pao_2) was measured with a Clark electrode (Bishop, Pincock, Hollyhock, Raine, and Cole, 1966) and arterial carbon dioxide tension ($Paco_2$) with a membrane-covered pH electrode (Severinghaus and Bradley, 1958). Expired gas was collected in a Tissot spirometer and was analysed by the Scholander micro method. Alveolar oxygen tension (Pao_2) was calculated from the alveolar air equation assuming alveolar and arterial Pco_2 to be equal. The alveolar arterial difference in oxygen tension ($A-aDo_2$) was obtained by subtraction. Physiological dead space was calculated from the Bohr equation, making the same assumption concerning alveolar Pco_2, and was expressed as a fraction of tidal volume (VD/VT). Anatomical shunt was calculated as a percentage of the cardiac output, from the shunt equation (Berggren, 1942) when the patients breathed 100% oxygen. In the absence of measurements of the oxygen content of mixed venous blood, a value of 4·5 vol.% was assumed for the arteriovenous oxygen content difference.

Patients studied Twelve patients with spontaneous pneumothorax were studied, nine having no previous history of respiratory disease and three giving a history of chronic bronchitis. All were men, and their ages ranged from 18 to 63 years. The pneumothorax had been present for from two days to six weeks before the study. Clinical details of the patients are given in Table I.

TABLE I

DETAILS OF PATIENTS STUDIED WITH EXTENT OF PNEUMOTHORAX EXPRESSED AS LUNG AREA INDEX

Patient	Age/Sex		Previous Lung Disease	Duration of Pneumothorax	Lung Area Index (%)
1	31	M	None	2 days	64
2	45	M	None	> 3 weeks	59
3	41	M	None	> 3 weeks	76
	59	M	Chronic bronchitis	2 weeks	69
5	21	M	None	1 week	49
6	19	M	None	12 days	74
7	63	M	Chronic bronchitis	10 days	69
8	42	M	None	6 weeks	68
9	57	M	Chronic bronchitis	5 days	50
10	18	M	None	2 weeks	31
11	20	M	None	1 week	76
12	20	M	None	1 week	27

Procedure The patients were studied seated, with a catheter in the brachial artery. In the patients given acetylcholine a venous catheter had previously been passed percutaneously into the right atrium or superior vena cava, under radiological control.

While the patient was breathing air, arterial blood and expired gas were collected over a period of three minutes, two 10-ml. samples of blood being obtained. The same procedure was followed after the patient had breathed 99·5% oxygen for 15 to 20 minutes, this period being extended to 30 minutes in the patients with chronic bronchitis. In order to minimize the effects of any small inspiratory leaks when breathing oxygen, the mouth and nose were enclosed by a loose-fitting plastic mask, through which 99·5% oxygen from another cylinder was passed.

In nine patients acetylcholine was delivered by an infusion pump at a rate of 2 or 5 mg./min. for periods of eight minutes while the patient continued to breathe either air or oxygen. Similar collections of expired gas and blood were made during the last three minutes of this infusion period.

In nine patients the study was repeated 30 to 90 minutes after aspiration of air. Air was removed with a pneumothorax box which was a simple syphoning device. Aspiration continued until the lung impinged on the chest needle or fine chest catheter. A needle was used for the first three patients and a catheter subsequently. In seven of these patients acetylcholine infusion was then repeated.

Standard six-feet postero-anterior chest radiographs in full inspiration were taken before removing the air, and as soon as possible after removing the air. In most patients the time interval after aspiration was about two hours, but one patient did not have a repeat radiograph until the following day.

The size of the lung in the presence of the pneumothorax was estimated approximately from the chest radiograph. The boundaries of the intrapleural space and the border of the collapsed lung were traced on to paper, and areas of intrapleural space and lung were measured by planimetry. The area of the lung was expressed as a percentage of the intrapleural area, and this provides a rough measure of the degree of inflation, the index being termed the lung area index. Since the chest wall might expand with a positive intrapleural pressure the area of intrapleural space after removing the air was used where this figure was available.

RESULTS

MEASUREMENTS BEFORE REMOVING AIR The results are given in Table II. Arterial oxygen tension (Pao_2) was below 80 mm. in nine patients, but there was no correlation with the lung area index.

$A-aDo_2$ when breathing air exceeded two standard deviations above the predicted value (Raine and Bishop, 1963) in 10 of the 12 patients, while VD/VT was raised in four patients. Patients 4, 7,

TABLE II

ARTERIAL BLOOD GAS TENSIONS AND VALUES DERIVED FROM THESE MEASUREMENTS WHEN BREATHING AIR AND 100% OXYGEN BEFORE AND AFTER INFUSIONS OF ACETYLCHOLINE IN PATIENTS WITH SPONTANEOUS PNEUMO-THORAX, BEFORE ASPIRATION OF AIR

Patient	Lung Area Index (%)	ACh (mg./min.)	Breathing Air			V_D/V_T (%)	Breathing Oxygen	
			Pa_{O_2} (mm. Hg)	Pa_{CO_2} (mm. Hg)	$A\text{-}aD_{O_2}$ (mm. Hg)		$A\text{-}aD_{O_2}$ (mm. Hg)	Shunt (%)
1	64	—	72·5	38·9	33·7	32·4	224	13·0
2	59	—	67·6	35·1	44·9	37·7	511	26·8
3	76	—	80·5	41·9	16·1	32·5	26	1·7
		2				35·8	19	1·3
4	69	—	73·8	42·7	28·9	38·8	75	4·9
5	49	—	70·1	38·4	26·5	27·7	195	11·8
		2	66·0	36·0	32·8	26·7	275	15·9
		5				28·3	296	17·0
6	74	—	78·9	44·2	23·1	34·3	53	3·4
		2	73·5	43·3	21·1	33·1	82	5·3
		5				33·6	121	7·8
7	69	—	53·0	53·0	25·9	53·9	55	3·6
		2	50·8	52·7	25·6	55·6	36	2·4
		·5					45	3·0
8	68	—	82·7	32·7	30·2	27·9	65	4·3
		2	82·5	31·9	27·2	26·6	47	3·1
		5				23·7	53	3·5
9	50	—	53·6	31·3	52·1	50·1	252	14·8
		5				48·3	391	21·2
10	31	—	62·5	26·6	55·4	31·9	444	23·4
		5				28·3	455	23·9
11	76	—	89·3	45·4	1·6	27·3	38	2·6
		5				29·6	—	—
12	27	—	71·5	34·8	31·2	34·0	364	20·0
		5			25·3		429	22·8

and 9, however, had chronic bronchitis, so that V_D/V_T was raised in only one of eight subjects without bronchitis.

Anatomical shunt when breathing oxygen was greater than normal (2% of the cardiac output) in 11 of the 12 subjects. There was a negative correlation (Fig. 1) between the size of the anatomical shunt and the lung area index ($r=0.796$; $P<0.01$).
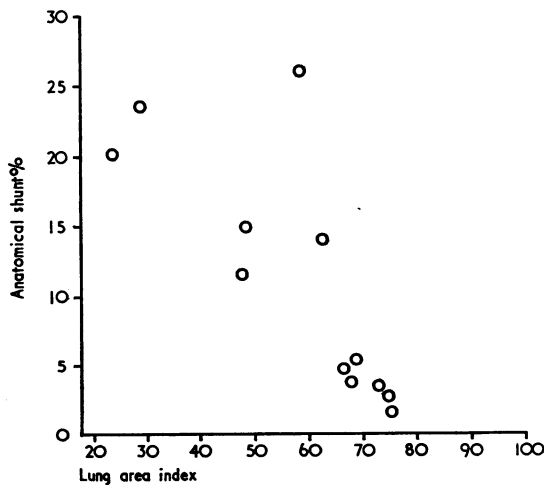

FIG. 1. *Calculated anatomical shunt when breathing 100% oxygen, and extent of pneumothorax expressed as lung area index in 12 patients with spontaneous pneumothorax.*

Although no patients with very small pneumothoraces were studied, Fig. 1 suggests that a pneumothorax with a lung area index greater than 75% would not be associated with an abnormally large shunt.

EFFECT OF REMOVING INTRAPLEURAL AIR Changes in Pa_{O_2}, Pa_{CO_2}, $A\text{-}aD_{O_2}$, V_D/V_T, and anatomical shunt after removing air are shown in Table III and Figure 2. Complete re-expansion of the lung, as judged radiologically, was achieved in four patients, partial expansion in four, but no re-expansion in one. In this patient it is likely that, because of a leak during aspiration, no real change in the size of the pneumothorax had taken place at the time of the study.

$A\text{-}aD_{O_2}$ when breathing air increased after aspiration in four patients, was unchanged in three, and fell in two. The mean change was $+0.4$ mm. Hg, which is not significant. V_D/V_T rose in three patients, fell in two, and was unchanged in four. The mean change, $+0.8\%$, is not significant. However, there was a rise in either $A\text{-}aD_{O_2}$ or V_D/V_T in six of the nine patients from whom intrapleural air was removed. Anatomical shunt decreased after removing the air in four patients and showed no definite change in five (Fig. 3).

EFFECTS OF INFUSION OF ACETYLCHOLINE The effects of acetylcholine in nine patients, with observations both before and after aspirating

TABLE III

ARTERIAL BLOOD GAS TENSION AND VALUES DERIVED FROM THESE MEASUREMENTS WHEN BREATHING AIR AND 100% OXYGEN BEFORE AND AFTER INFUSIONS OF ACETYLCHOLINE IN PATIENTS WITH SPONTANEOUS PNEUMO-THORAX AFTER ASPIRATION OF INTRAPLEURAL AIR

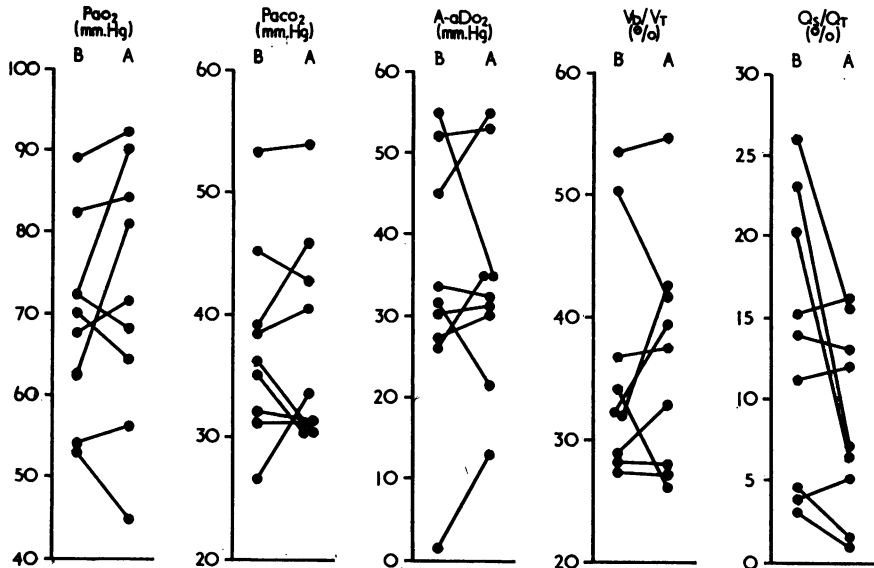| Patient	Volume Removed (ml.)	Lung Area Index (%)	ACh (mg./min.)	Breathing Air			V_D/V_T (%)	Breathing Oxygen	
				Pao_2 (mm. Hg)	$Paco_2$ (mm. Hg)	$A\text{-}aDo_2$ (mm. Hg)		$A\text{-}aDo_2$ (mm. Hg)	Shunt (%)
1	950	73	—	68·1	46·6	32·1	42·8	206	12·5
2	1,300	71	—	71·2	30·3	55·2	38·6	262	15·3
5	3,000	48	—	64·4	40·4	29·8	33·1	210	12·6
			2	59·7	42·7	32·4	37·1	255	14·9
7	1,900	100	—	45·2	53·9	35·3	54·5	71	4·7
			2	44·4	54·5	34·6	56·9	49	3·2
8	2,000	100	—	84·2	31·9	31·1	27·2	22	1·5
			2	85·3	35·7	21·2	23·7		
			5				28·6	25	1·7
9	2,200	100	—	56·6	31·2	52·5	42·2	270	15·7
			5				47·5	302	17·2
10	3,000	100	—	81·0	33·1	34·5	38·5	104	6·7
			5				39·5	—	—
11	1,500	84	—	91·9	43·7	12·8	27·3	16	1·1
			5				27·7	51	3·4
12	3,500	65	—	90·1	30·9	21·6	26·3	94	6·1
			5	28·2			37·3	104	6·7

FIG. 2. *Arterial blood gas tensions, alveolar–arterial difference in oxygen tension ($A\text{-}aDo_2$) and physiological dead space (V_D/V_T) when breathing air, and anatomical shunt (Q_S/Q_T) when breathing oxygen before (B) and after (A) aspiration of air in patients with spontaneous pneumothorax.*

intrapleural air, are shown in Tables II and III and Figure 4. There was no consistent change in $A\text{-}aDo_2$ or V_D/V_T after infusing acetylcholine at 2 mg./minute. Anatomical shunt rose in four patients, and there was a further increase in two of these patients when the rate of infusion was increased from 2 to 5 mg./minute. In the other four patients the shunt was unchanged. In five patients, in whom the infusion of acetylcholine

was repeated after removing the air, the effects were similar.

DISCUSSION

These observations demonstrate that the more extensive the pneumothorax the lower was the arterial oxygen tension and the larger the anatomical veno-arterial shunt. It appears that
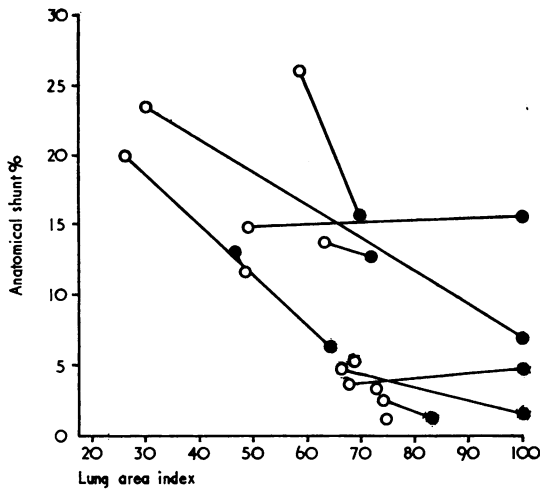
FIG. 3. *Anatomical shunt when breathing* 100% *oxygen, and lung area index, before and after aspiration of air, in nine patients with spontaneous pneumothorax.*
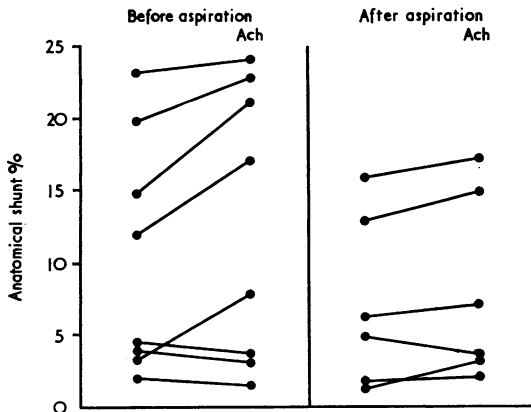

FIG. 4. *Anatomical shunt when breathing* 100% *oxygen, before and after an infusion of acetylcholine* (*Ach*), *in eight patients with spontaneous pneumothorax. In six patients the observations were repeated after aspiration of air from the intrapleural space.*

with a small pneumothorax, when the ratio of lung to intrapleural space area is greater than 75%, the anatomical shunt is not likely to exceed the normal value of 2% of the cardiac output. Assuming symmetrical collapse of the lung, we have calculated that the ratio of lung volume to intrapleural space volume would be of the order of 65% before an increase in anatomical shunt occurs. As the degree of collapse increases anatomical shunt also increases, although insufficient evidence is available to show whether the relationship between shunt and lung volume is rectilinear or curvilinear.

Working with anaesthetized cats, Anthonisen (1964) has shown that a reduction of lung volume to 20% of total lung capacity is not associated with an increase of anatomical shunt, although re-expansion of lung from complete collapse is associated with a much larger shunt for a given lung volume. Similarly, a fall in compliance, due to negative pressure breathing or instillation of water into the airways of anaesthetized animals, is initially associated with a very small increase in anatomical shunt, but as the fall in compliance becomes larger the shunt increases more rapidly (Halmagyi, Colebach, Starzecki and Horner, 1964 ; Collier and Mead, 1964 ; Velasquez and Farhi, 1964). The present findings suggest that complete non-ventilation of alveoli does not occur in man (when sitting) until the lung volume is reduced to about 65% of normal.

Calculations were made in the patients without bronchitis, assuming values for A–V oxygen difference and oxygen capacity, to see whether the degree of shunt found on breathing oxygen could explain the observed A–aDo$_2$ in the same subject breathing air. Patients 1, 2, 5, 10, 11, and 12 had relatively large pneumothoraces (mean lung area index 51%) with large shunts (mean 17%) and in these patients the observed increase above normal in A–aDo$_2$ when breathing air could be accounted for completely in terms of the observed increase in anatomical shunt. Patients 3, 6, and 8 had smaller pneumothoraces (mean lung area index 73%) with smaller shunts (mean 3%). In these patients the increase in A–aDo$_2$ could not be accounted for in terms of the anatomical shunt. It thus seems likely that in the smaller pneumothoraces some alveoli were poorly ventilated, whereas in the larger pneumothoraces they were completely unventilated. The absence of an increase in Vd/Vt in all but one of the patients without bronchitis suggests that there was little ventilation–perfusion disturbance in the direction of areas that were well ventilated but poorly perfused (Severinghaus and Stupfel, 1957).

Thirty to ninety minutes after removal of intrapleural air the increase in lung volume towards normal was not accompanied by any improvement of ventilation–perfusion abnormalities. In fact the distribution of ventilation–perfusion ratios became more uneven as judged by a rise in either A–aDo$_2$ or Vd/Vt in six of the nine patients in whom air was removed. Anatomical shunt decreased more than 2% in four patients after the air was removed and was unchanged in five. When

anatomical shunt was related to the extent of lung expansion (Fig. 3) it was seen that the points had shifted to the right of the original line, suggesting that approximately one hour after the removal of intrapleural air there was a greater shunt for a given lung volume than before the air was removed.

This finding is comparable to that of Anthonisen (1964), who reported that the anatomical shunt was greater for a given lung volume when the lungs were re-expanded than when they were first collapsed. The most probable explanation for this is that a relatively great pressure is required to open a ventilatory unit which is completely closed (Mead, 1961), so that in the early steps of re-expansion an increase in lung volume from collapse may be achieved mainly by airway dilatation. This is a possible explanation for the increase in V_D/V_T which occurred in three of our patients after aspiration of intrapleural air.

Calculations of the theoretical effect of the observed anatomical shunt on the $A-aD_{O_2}$ when breathing air were repeated for the values obtained after intrapleural air was removed. The observed $A-aD_{O_2}$ when breathing air could still be explained in terms of the shunt in patients 1 and 5 but could no longer be explained in this way in patients 2, 10, 11, and 12. However, in patients 1 and 5 V_D/V_T increased after air aspiration and it appears that in all of these patients the distribution of ventilation–perfusion ratios became more uneven after air aspiration.

Acetylcholine infused centrally in doses of up to 10 mg./minute has been used by a number of workers as a pulmonary vasodilator, freedom from systemic effects being shown by the absence of any changes in cardiac output, heart rate, or blood pressure (Fritts, Harris, Clauss, Odell, and Cournand, 1958; Bishop, Harris, Bateman, and Davidson, 1961). Söderholm and Widimský (1962) have used $A-aD_{O_2}$ derived from oxygen saturation measurements as an index of ventilation–perfusion inequality in patients with diffuse lung disease or diaphragmatic paralysis. $A-aD_{O_2}$ was increased after acetylcholine infusion, suggesting that local vasoconstriction was released in underventilated areas.

In the present study, acetylcholine was used to test the possibility that active vasoconstriction had occurred in lung units rendered hypoxic due to reduction of ventilation. Of the eight patients studied when breathing air, none showed a definite rise in $A-aD_{O_2}$ or V_D/V_T either before or after removal of intrapleural air. This finding is in contrast to our previous report (Norris and Bishop,

1966) of a significant increase in $A-aD_{O_2}$ in a group of seated normal subjects; the reason for this difference is not clear. When $A-aD_{O_2}$ was measured in the same patients when breathing 100% oxygen the calculated anatomical shunt showed an increase after acetylcholine in only four of the patients.

The calculation of anatomical shunt assumes that cardiac output did not change during the infusion of acetylcholine. Most workers have found that acetylcholine in the present dose has no effect on cardiac output (Söderholm and Widimský, 1962) or causes a slight increase (Chidsey, Fritts, Zocche, Himmelstein, and Cournand, 1960). No change in blood pressure or pulse rate occurred with acetylcholine in the present studies. If a rise in cardiac output had occurred the tendency would be to under-estimate anatomical shunt after acetylcholine.

The present observations suggest that active vasoconstriction in poorly ventilated lung units may occur in some subjects with spontaneous pneumothorax. However, it could have been present only to a slight extent in the four patients who responded to acetylcholine, and the positive correlation which was found between the size of the pneumothorax and the degree of shunt shows that full compensation for reduced ventilation by reduced local blood flow was not achieved. Moreover, no consistent effect of acetylcholine on $A-aD_{O_2}$ was present after aspirating air, so that it did not appear that an increase in intrapleural pressure was responsible for the lack of response to acetylcholine. The possibility remains that acetylcholine did not reach vessels which were completely occluded by vasoconstriction or that organic changes had occurred in the walls of the vessels. Since the duration of pneumothorax in the patients who had acetylcholine was not greater than six weeks, the latter possibility seems unlikely.

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