THE INFLUENCE OF SHORT PERIODS OF INDUCED ACUTE ANOXIA UPON PULMONARY ARTERY PRESSURES IN MAN[1]

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The effects of acute anoxia on pulmonary artery blood pressure, induced by breathing low oxygen (10 per cent O_2 in N_2) for short periods of time, have not been reported in man. Since acute anoxia is used extensively as a cardiac test and is frequently encountered in anesthesia, changes resulting in the pulmonary artery blood pressure should be of interest.

METHODS. The influence of breathing 10 per cent oxygen in nitrogen has been studied on 5 unanesthetized, conscious white males in a resting basal condition. Their age ranged from 23 to 47 years. Four of the subjects had essentially normal cardiac function without pulmonary involvement. In the fifth subject a diagnosis of aortic insufficiency had been made; his brachial artery blood pressure values were within normal limits except for a slight lowering of the diastolic pressure. In table 1 appear data on the average blood pressure values, including systolic, diastolic and mean pressures, in the brachial artery, pulmonary artery and right ventricle of the five subjects. All individual measurements were within normal limits. Right heart pressures and cardiac output were determined by using the right heart catheterization technique (1, 2, 3, 4). Arterial, pulmonary artery and right ventricle blood pressures were measured using the Hamilton manometer (5). In two cases pulmonary artery and right ventricle pressures were taken simultaneously using a double lumen catheter (6); the arterial blood was obtained from the brachial artery and the mixed venous blood from the pulmonary artery. A demand type valve (Army Air Forces A-16) was used to supply the compressed air or the 10 per cent oxygen mixture to the subject. The expired gas was collected in a calibrated Tissot spirometer. Measurements of cardiac output and blood pressures were determined first while breathing ambient air (21 per cent oxygen). Then the subjects breathed the 10 per cent oxygen mixture for a period of approximately 10 minutes, at the end of which the cardiac output was measured and the blood pressures recorded from the brachial artery, pulmonary artery and right ventricle. A second series of control measurements, while breathing ambient air, was taken 30 minutes after the end of the period of low oxygen breathing.

RESULTS. The average data obtained on the 5 subjects appear in table 1.

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TABLE I

Influence of breathing 10 per cent oxygen on the respiratory gas exchange and hemodynamics in 5 subjects at ambient pressure

	AVERAGE BREATHING AIR	AVERAGE BREATHING 10% O_2
1. *Arterial blood* (brachial artery)		
CO_2 content, vol. %	48.1	45.9
O_2 saturation, %	94.5	73.4
pCO_2, mm. Hg	39.5	32.6
pHs	7.42	7.49
2. *Mixed venous blood* (pulmonary artery)		
CO_2 content, vol. %	50.3	49.0
O_2 saturation, %	69.5	50.0
pCO_2, mm. Hg	42.8	36.4
pHs	7.40	7.47
3. *Pulmonary ventilation*		
Liters per min	7.2	11.0
Rate per min	16	20
CO_2 output cc. per min	207	273
O_2 consumption, cc. per min	241	193
4. *Cardiac output determination*		
Heart rate per min	67	80
Arterio-venous diff., cc. per l	42	37
Blood flow, liters per min	5.74	5.20
Stroke volume, cc	82	65
5. *Arterial blood pressure*, mm. Hg		
Systolic	121	128
Diastolic	67	68
Mean	90	93
6. *Pulmonary artery blood pressure*, mm. Hg		
Systolic	21.9	35.1
Diastolic	6.0	13.0
Mean	13.1	23.0
7. *Right ventricle blood pressure*, mm. Hg		
Systolic	22.0	35.0
Diastolic	4.2	7.0
Mean	7.9	14.0
8. *Resistance, dynes sec. Cm^{-5}*		
Pulmonary	130	255
Peripheral	1216	1407

The values are recorded in the first column while breathing air and in the second column while breathing 10 per cent oxygen.

1. *Respiratory gases in the blood.* The oxygen saturation decreased 21.1 per

cent in the arterial blood and 19.5 per cent in the mixed venous blood while breathing the 10 per cent oxygen. There was a small decrease in the CO_2 content (1.3–2.2 vol. per cent). The pCO_2 decreased 6.9 mm. Hg in the arterial blood and 6.4 mm. Hg in the mixed venous blood, with a corresponding increase of 0.07 of the pHs. This was undoubtedly due to hyperventilation.

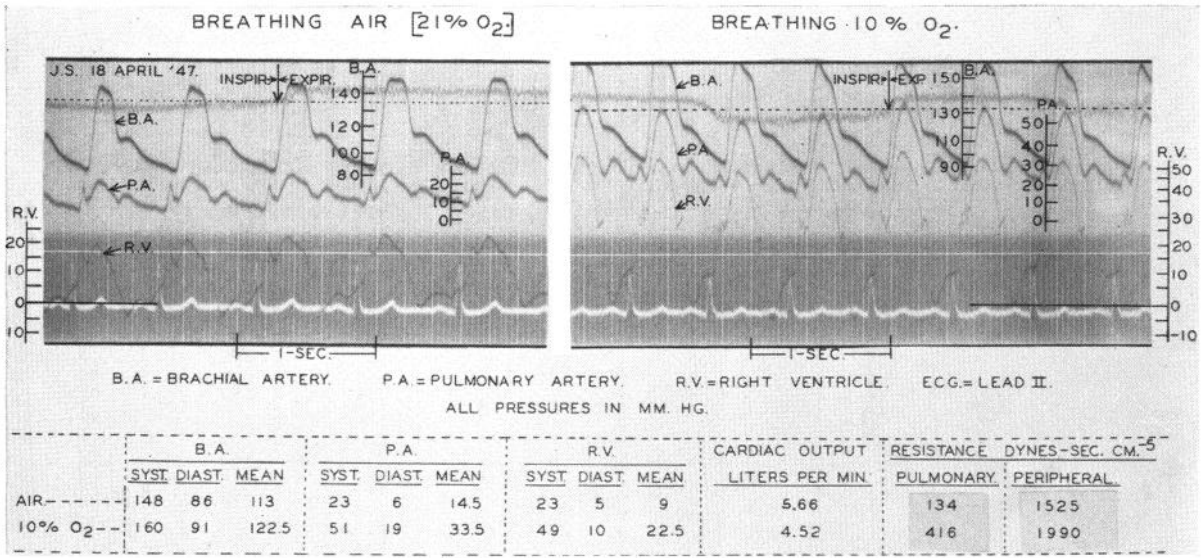
2. *Pulmonary ventilation.* The volume of expired gas was greatly increased on the 10 per cent oxygen (3.8 liters per min. or 52.7 per cent). The CO_2 output showed a considerable increase (31.9 per cent) on low oxygen breathing. This change is consistent with the hyperventilation and with the lowering of the pCO_2 in the blood. The oxygen consumption was reduced 20.0 per cent and the rate of breathing increased 25.0 per cent on the low oxygen mixture.

3. *Pulmonary artery blood pressure.* A very significant degree of pulmonary hypertension was produced by the anoxia, resulting from breathing the 10 per cent oxygen mixture as shown by the large rise in pulmonary artery blood pressure (table 1 and fig. 1). The diastolic pressure rise was the greatest, from 6 mm. Hg on ambient air to 13 mm. Hg on low oxygen. The systolic pressure rose from 21.9 to 35.1 mm. Hg on an average, and the mean pressure from 13.1 to 23 mm. Hg. The pressure rise in the pulmonary artery occurred rapidly after the breathing of 10 per cent oxygen started, with maximal increase in pressure being reached within 2 to 4 minutes. The elevated pressure persisted as long as the subject breathed the low oxygen mixture (average 15 to 20 min.). After switching from low oxygen to ambient air breathing, the pulmonary artery pressure returned rapidly back to normal, with readily measurable changes after one minute on ambient air breathing. The systolic pressure rise was of the same magnitude in the right ventricle as in the pulmonary artery; the end diastolic pressure in the right ventricle rose somewhat.

4. *Cardiac output.* There was a slight decrease in arterio-venous oxygen difference (5 cc. per liter) on the low oxygen breathing. Since consumption was reduced 20.0 per cent, the calculated blood flow was decreased from 5.74 to 5.20 liters per minute (a 9.4 per cent reduction). In general the greater the decrease in cardiac output on low oxygen, the higher the corresponding pulmonary artery pressure. Pressure tracings are shown in figure 1 from a subject in which the cardiac output was decreased 20.3 per cent while breathing 10 per cent oxygen, and these tracings were taken immediately after the cardiac output determination. In the above case the decrease in cardiac output was the greatest and the pulmonary hypertension was the largest observed. The average stroke volume for the 5 cases was reduced from 82 to 65 cc. as a result of the small reduction in cardiac output, and of the 19.4 per cent increase in heart rate. The calculated pulmonary resistance was increased almost 100 per cent (130 to 255 dynes sec. cm.$^{-5}$) on low oxygen.

5. *Peripheral blood pressure.* The arterial pressure showed only a slight average rise on low oxygen breathing, an increase of 7.0 mm. Hg systolic, 1 mm. Hg diastolic and 3 mm. Hg. mean. The calculated peripheral resistance increased insignificantly from 1216 to 1407 dynes sec. cm.$^{-5}$ or 15.7 per cent.

DISCUSSION. The transient pulmonary hypertension induced while breathing



	B.A.			P.A.			R.V.			CARDIAC OUTPUT	RESISTANCE DYNES-SEC. CM.$^{-5}$	
	SYST.	DIAST.	MEAN	SYST.	DIAST.	MEAN	SYST.	DIAST.	MEAN	LITERS PER MIN.	PULMONARY	PERIPHERAL
AIR	148	86	113	23	6	14.5	23	5	9	5.66	134	1525
10% O_2	160	91	122.5	51	19	33.5	49	10	22.5	4.52	416	1990

Fig. 1. Effect of low oxygen (10 per cent) breathing upon pulmonary artery blood pressure.

Tracings in the pulmonary artery and in the right ventricle were taken simultaneously through a double lumen catheter. Note waves during early part of systole in both curves and on the descending part of the right ventricle curve, probably due to movement of catheter at the time of opening and closing of the pulmonary valve.

10 per cent oxygen for short periods of time has been a consistent observation in subjects with essentially normal blood pressures. The average pulmonary blood pressures while breathing air, for the 5 cases reported, are almost identical to the average normal pulmonary artery blood pressures as recorded in this laboratory. The respiratory gas exchange variations are in accord with previous observations on the effects of anoxia of this magnitude. The exact cause of the lowered oxygen consumption is obscure as the gradient across the pulmonary membrane remains essentially unchanged, and the lowering is not observed in chronic anoxia or in acclimatization.

Drinker (7) has demonstrated in dogs that acute anoxia rapidly increased lymph flow from the lungs and that the excessive lymph movement regularly stopped when pure oxygen was given after short periods of anoxia. Capillary permeability was increased by the anoxia resulting in greater filtration of fluid into the alveolar tissue and into the alveoli. In this respect it may be mentioned that preliminary observation in man on vital capacity measurements failed to show any reduction after breathing 10 per cent oxygen for 10 minutes. Von Euler and Liljestrand (8) have very recently reported a rise in pulmonary artery pressure in anesthetized cats with closed thorax, breathing spontaneously or with artificial respiration on low oxygen mixtures. Cardiac output was not determined in the cats, hence the status of the pulmonary blood flow is unknown. According to these authors the vasonconstriction is due to a direct action of the anoxia on the wall of the vessel without intervention of the autonomic nervous system. They have suggested that the distribution of the pulmonary blood flow is regulated through the various parts of the lung according to the efficiency of aeration for each area, a low blood oxygen saturation producing constriction and a high blood oxygen saturation producing dilatation of the respective pulmonary arterioles.

In man, according to Cournand (9), observations made so far tend to indicate that rapid changes in pulmonary arterial pressure are chiefly caused by variations in blood flow, and that clear-cut proof is lacking for autonomic vasomotor regulation of the pulmonary circulation.

The rise in pulmonary artery pressure induced by anoxia in man in this report cannot be attributed to an increase in cardiac output for the latter was slightly decreased, and in the normal subjects the greater the decrease in cardiac output the higher the corresponding pulmonary artery pressure rise. Among the possible mechanisms of increasing pulmonary vascular resistance, the following may be mentioned: 1, stasis in the smaller pulmonary vessels, and 2, pulmonary arteriolar constriction. Drinker (10) has suggested that the altered capillary permeability inaugurates stasis in the smaller pulmonary vessels, a mechanism creating increased vascular resistance which is the main feature of the changes produced by the anoxia. If this mechanism is not operative in man, it may well be that low oxygen tension in the circulating pulmonary blood causes vasconstriction of the pulmonary arterioles or precapillaries by direct action, as postulated by von Euler and Liljestrand in their interpretation of their observations in cats. The question may be raised, however, whether pulmonary

arterioles or precapillary vasoconstriction may not be related to the hyperventilation and mild alkalosis associated with low oxygen breathing. In separate studies of the effects of intermittent positive pressure breathing upon respiration and circulation, hyperventilation and alkalosis of greater magnitude have been observed. These failed to elicit a rise in pulmonary arterial pressure, greater than the expected small increase due to changes in intra-thoracic pressures. On the basis of this experience, it would seem reasonable to doubt that hyperventilation and alkalosis are the cause of the findings reported here.

SUMMARY

1. Pulmonary hypertension was rapidly induced in subjects with normal blood pressures by breathing 10 per cent oxygen for short periods of time with only a very slight rise in systemic blood pressure. The pulmonary pressures rapidly returned to normal when the low oxygen breathing was discontinued.

2. Cardiac output was decreased slightly during anoxia, and the stroke volume markedly reduced, the latter largely the result of an increased heart rate.

3. Pulmonary vascular resistance was almost doubled during anoxia while the systemic peripheral resistance increased only slightly.

4. The possible mechanisms involved in this increased pulmonary vascular resistance during short periods of acute anoxia are discussed.

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