THE EFFECTS OF RESPIRATION OF OXYGEN ON BREATHING AND CIRCULATION.

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It was shown by Paul Bert(1) that exposure of living organisms to an abnormally increased partial pressure of oxygen has, in general, a detrimental effect. In the case of warm-blooded animals, however, the effect which he discovered was only shown at oxygen pressures exceeding about three atmospheres. At pressures considerably higher than this the central nervous system was soon damaged irreparably, so that the animals did not recover. When removed from the atmosphere they remained comatose, and displayed symptoms similar in many respects to those of strychnine poisoning, and resembling also the after-effects of prolonged exposure to want of oxygen, as in CO poisoning. His description of the spastic condition of the limbs and easily induced opisthotonus in the animals experimented on corresponds rather strikingly with the similar symptoms recorded by one of us in miners who had been rescued alive after prolonged unconsciousness from CO produced in colliery explosions(2).

Lorrain Smith(3) discovered that though oxygen at less than three atmospheres' pressure produces in warm-blooded animals no evident nervous symptoms, yet prolonged exposure to even as little as 70 p.c. of an atmosphere of oxygen (or 60 p.c. in the alveolar air) may produce fatal pneumonia. The lung epithelium is of course exposed to the full effects of the oxygen; and it can hardly be doubted that if the far more sensitive tissues of the central nervous system were really exposed to a considerably increased oxygen-pressure very evident nervous symptoms would be produced. As will be shown in a paper shortly to be published by Douglas and Haldane, the blood passing through the brain of man loses under normal conditions probably not more than about 2 c.c. of oxygen per 100 c.c. of blood, and the CO_2-pressure of the blood does not rise more than about 3 or 4 mm. The co-efficient of absorption of oxygen in blood at body-temperature is ·022. Hence when pure oxygen is breathed at two atmospheres pressure there will be in simple solution in the arterial blood, allowing for the presence of about 6 p.c. of

$CO_2 + H_2O$ in the alveolar air, about 4·14 c.c. of oxygen per 100 c.c., or 3·9 c.c. in excess of what is normally present. Hence if the circulation rate remained normal, there would be about 2 c.c. of free oxygen per 100 c.c. of the venous blood returning from the brain, and the oxygen-pressure in the brain would therefore be extremely high.

The experiments now to be described were undertaken for the purpose of seeing whether any evidence could be obtained that the tissues of the nervous system are defended against the influence of the oxygen by diminution of the circulation through them, so that the excess of free oxygen in the arterial blood is used up as it passes through the capillaries, and thus cannot, except at extremely high pressures of oxygen, reach the tissues. The diminution in the circulation through the brain capillaries might easily be brought about by contraction of capillaries in the manner recently described by Krogh(4). If the circulation is diminished when oxygen is breathed it is evident that the pressure of CO_2 in the tissues must rise; and in the respiratory centre this rise of CO_2-pressure will, other things being equal, imply rise of hydrogen ion concentration and consequent increase in breathing and fall of alveolar CO_2-pressure. A very slight fall in alveolar CO_2-pressure will, however, suffice to compensate for the rise in CO_2-pressure in the tissues in consequence of a sufficient slowing down of the circulation to reduce the oxygen-pressure of the venous blood to normal. Complete compensation could not, however, be expected, since otherwise there would be no stimulus left to account for the slowing down of circulation.

The problem which we set ourselves to investigate, therefore, was whether there is any fall in alveolar CO_2-pressure when oxygen at increased partial pressure is breathed. We also watched the pulse carefully, as any diminution in pulse-rate would serve as an index of slowing of the circulation. It was already known from the careful experiments of Parkinson(5), that an appreciable, though small, diminution in pulse-rate is produced by breathing pure oxygen. Most of our experiments were carried out at ordinary atmospheric pressure; but one series was at increased atmospheric pressure in the large steel chamber of the Lister Institute. We are much indebted to Professor C. J. Martin for personal help and facilities afforded to us for this series.

The experiments were made as follows: two large Douglas bags were filled respectively with pure oxygen and air. The subject then sat quietly and breathed from one of the bags through Rosling valves and a comfortable mouthpiece (with a nose-clip on the nose) for at least five minutes. Towards the end of this period the pulse was repeatedly counted, and

finally a sample of alveolar air, obtained about one second after the completion of an inspiration, was taken by the ordinary Haldane-Priestley method, and the CO_2 determined.

The mean results at ordinary atmospheric pressure were as follows:

	Alveolar CO_2 percentage		Pulse		Number of pairs of observations
	oxygen	air	oxygen	air	
L. D.	6·04	6·25	75·1	81·0	36
J. S. H.	5·25	5·42	78·0	82·7	3

The following results were obtained in a very careful series made on one day in the steel chamber at a total pressure of 2·08 atmospheres or 1580 mm.

	Alveolar CO_2 percentage		Pulse		Number of pairs of observations
	oxygen	air	oxygen	air	
L. D.	2·46	2·69	76·5	87·7	4

If we convert CO_2 percentages into pressures of CO_2 the results are as follows:

		Alveolar CO_2-pressure in mm. of Hg.		
		Oxygen	Air	Fall with oxygen
At ordinary atmospheric pressure ...	L. D.	42·8	44·3	1·5
	J. S. H.	37·2	38·4	1·2
At 2·08 atmospheres	L. D.	37·7	41·2	3·5

Out of the 43 pairs of observations the CO_2-pressure was only in six cases lower with air than with oxygen; and only in four cases was the pulse-rate higher with oxygen.

It is clear from these observations that when oxygen is breathed at normal barometric pressure there is a drop of about 1·5 mm. in alveolar CO_2-pressure, and about five beats per minute in the pulse during rest sitting. At 2·08 atmospheres the drop is about 3·5 mm. in alveolar CO_2-pressure, and eleven beats per minute. The experiments therefore confirm the theory (which is in itself probable from many considerations into which we need not enter here) that excess of free oxygen in the arterial blood causes slowing of the circulation. The result of this slowing down will be that in accordance with the conception running through so much of Claude Bernard's work, the "internal environment" of the tissues tends to be kept approximately constant in spite of great variations in the external environment. We can thus understand why it is that so high a pressure of oxygen is needed before the central nervous system is affected. The observed drop of 3·5 mm. in the alveolar CO_2-pressure when oxygen at 2·08 atmospheres pressure was breathed would

correspond to a slowing in the brain circulation sufficient to reduce the oxygen-pressure in the blood leaving the brain to normal. An oxygen-pressure such as we tested in the steel chamber is sufficient to cause fatal pneumonia within two or three hours. Neither of us, however, could detect any definite subjective symptoms of psychical disturbance on breathing the oxygen for a few minutes. On the other hand distinct symptoms of irritation of the air-passages were produced in L. D., and did not pass off for several hours.

Our attention was directed to a paper by Yamada(6) in which his alveolar CO_2-pressure was carefully measured in order to investigate the effects of breathing mixtures of oxygen, air, and CO_2. These experiments showed that whether or not CO_2 was present in the inspired air the alveolar CO_2-pressure was distinctly lower with oxygen than with air. He concluded that the oxygen increased the excitability of the respiratory centre to CO_2. This is, of course, a possible explanation, but is not probable in view of the evidence that want of oxygen increases the excitability of the centre to CO_2, or contributes towards exciting it(8). In any case the experimental results of Yamada are in complete harmony with our own.

Conclusion.

Respiration of oxygen, particularly at increased barometric pressure, increases the breathing and diminishes the pulse-rate. These effects are presumably brought about by slowing of the blood-flow through the tissues, which protects them against the poisonous action of the high oxygen-pressure.

REFERENCES.

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