# THE ABSORPTION OF OXYGEN BY THE LUNGS.

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FROM our observations, by the carbonic oxide method, on the oxygen tension of the blood as it leaves the lungs in man, we were led to the conclusion that the exchange of oxygen which takes place between the atmosphere and the blood cannot be adequately explained by diffusion alone. The evidence of physiological activity disclosed by these experiments and the previous ones of Bohr by the aerotonometer method, seemed to require further investigation; and in the following paper we propose to give an account of experiments on some of the conditions which affect the absorption of oxygen in normal animals.

Observations by the aerotonometer method on the oxygen tension in the arterial blood have hitherto been made on the dog only. The results we obtained in the case of man, which are described in our former paper, gave an oxygen tension considerably above that of air, and therefore a good deal higher than the tension observed in the dog's blood by means of the aerotonometer.

In order to have the means of directly comparing the results given by the two methods we have made two experiments on dogs by the carbonic oxide method. The oxygen tensions found were 17·6 and 24·4 % of an atmosphere (see Table I.). These results are only a little higher than Bohr's. The maximum oxygen percentage to which the air in the aerotonometer *rose* in his experiments was 20·67; and the minimum to which it *fell* was 16·05. It thus appears that the carbonic oxide method gives results which are nearly the same as those of the improved aerotonometer method introduced by Bohr.

The greater number of our observations have been made on mice and small birds, and we found it necessary to modify slightly the

original method of procedure. The animal was placed in a bottle (or air-tight chamber in the case of dogs, cats and rabbits), through which a current of air containing a known percentage of carbonic oxide was aspirated. The apparatus used was the same as that described at p. 202, Vol. XVIII., of this Journal. The animal was allowed to breathe the mixture of gases supplied in this way, till the hæmoglobin of its blood became saturated with carbonic oxide to the maximum extent for the percentage of this gas present. The bottle was then disconnected, and rapidly plunged into water, so that the animal was drowned whilst still in the atmosphere established by the current passing through the apparatus. The blood was then received from the heart into a small test tube, which was filled up with water. This solution was corked up in the tube, and one or more samples from it were taken to determine colorimetrically the degree to which the hæmoglobin had become saturated by the carbonic oxide. In the case of birds, it was found necessary, after adding the water, to centrifugalise the solution, as the nucleated red corpuscles do not completely dissolve. At the conclusion of each experiment a sample of the gas in the burette was analysed to ascertain how much impurity was present in the carbonic oxide.

In measuring the percentage of carboxyhæmoglobin present in the solution of blood we proceeded as follows. Two narrow test tubes of equal bore were obtained, and in the one (*A*) were placed 5 c.c. of a 1 °/₀ solution of normal ox blood. In the other (*B*) a small quantity of the solution of blood partially saturated with carbonic oxide, from the animal under observation, was placed, and this was diluted with water till it had a concentration equal to the normal solution in tube (*A*). To bring the colour of (*A*), which is more or less yellow by transmitted light, up to the degree of pink observed in (*B*), a solution of carmine of suitable strength (previously adjusted carefully to the blood solution) was added from a burette till the two tubes corresponded exactly in tint. The amount of carmine solution added was noted. The solution of blood in tube (*B*) was now completely saturated with carbonic oxide by shaking it for a few seconds with coal gas, and again the tint of (*A*) was made equal to it by the further addition of carmine solution from the burette. The ratio of the partial to complete saturation was then calculated as in our former experiments (this Journal, XX. p. 503 and p. 519), the result obtained being the percentage saturation with carbonic oxide of the hæmoglobin present in the blood of the animal. In carrying out the titrations we avoided

bright light, which, from the experiments given in our previous paper, might have appreciably affected the results.

For the purpose of calculating the oxygen tension from the percentage saturation of the hæmoglobin we made a new series of experiments (see Table VIII.) to determine with greater accuracy than before the form of the dissociation curve of carboxyhæmoglobin in presence of mixtures of carbonic oxide and air. The curve which we previously obtained was not quite symmetrical, deviating appreciably at certain points from the form of a rectangular hyperbola. It turned out that the reason for this deviation was that, particularly with less than $0.1\%$ of carbonic oxide in the air, the amount of shaking formerly employed (ten minutes' gentle shaking) had not been sufficient. With twenty minutes' pretty vigorous shaking the



FIG. I
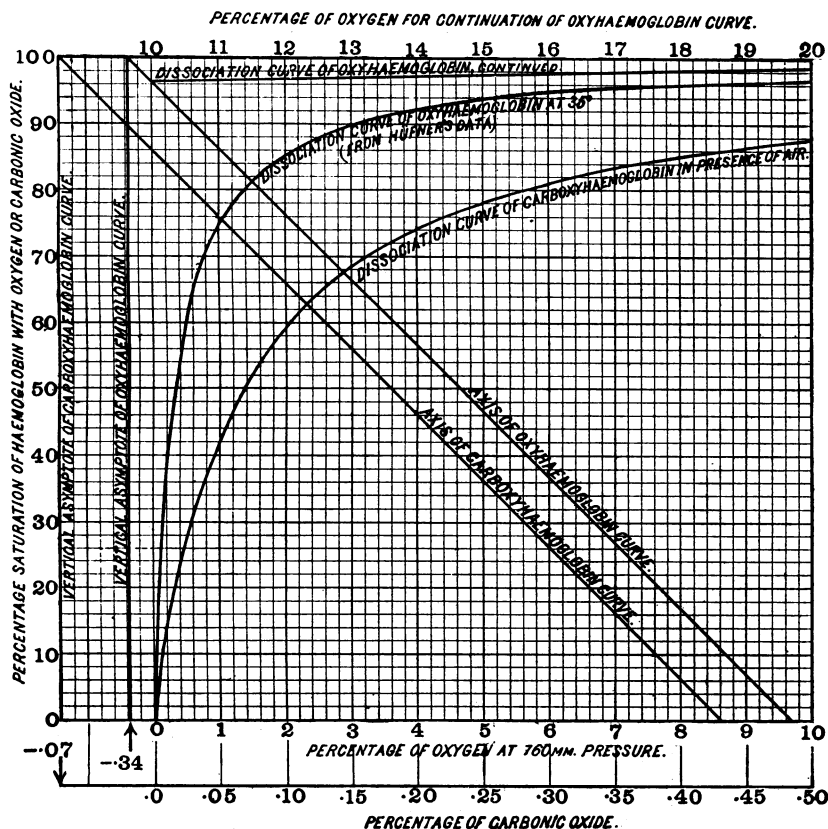
results corresponded very closely to the rectangular hyperbola shown in Fig. 1, and we have used this curve in calculating the oxygen tensions. The calculation of the oxygen tension is made by finding on the curve the percentage of carbonic oxide in air to which the actually observed saturation of the blood corresponds, dividing 20·9 by the former value, and multiplying by the actual percentage of carbonic oxide in the air breathed. Thus, supposing that the blood was found to be 46 % saturated (corresponding to ·060 % of carbonic oxide in air) and the actual percentage of carbonic oxide breathed was ·080, then the oxygen tension of the blood would be $20·9 \times \dfrac{·8}{·6} = 27·9$.

As the alveolar air contains about 6 % of aqueous vapour this result has to be reduced to 26·2. All the results given below are corrected for aqueous vapour. This correction becomes important in the case of experiments at low pressures.

### Experiments on normal oxygen tension.

In Table I. we have placed observations on the tension which exists in the blood as it leaves the lungs when the animal is in approximately normal conditions. It will be seen from the table that the saturation of the hæmoglobin was as a rule under 50 % and that the animal breathed ordinary air to which carbonic oxide was added.

### TABLE I.

*Experiments on the normal oxygen tension of various animals.*

| Animal | % of CO | Temp. of Bath | Rate of ventilation in litres per minute | Duration of experiment in minutes | Corrected saturation of hæmoglobin with CO per cent. | Oxygen tension of arterial blood in % of an atmosphere | Probable alveolar oxygen tension in % of an atmosphere |
|---|---|---|---|---|---|---|---|
| Mouse | ·062 | — | ·58 | 19 | 39·1 | 27·6 | 13 |
| ,, | ·056 | — | 1·15 | 21 | 43·9 | 20·4 | 13 |
| ,, | ·065 | — | 1·14 | 21 | 38·3 | 32·7 | 13 |
| ,, | ·042 | — | 1·12 | 15 | 39·9 | 17·6 | 13 |
| ,, | ·035 | — | 1·24 | 30 | 32·5 | 20·9 | 13 |
| ,, | ·058 | — | ·90 | 21 | 45·4 | 19·7 | 13 |
| ,, | ·047 | — | 1·12 | 30 | 31·0 | 28·9 | 13 |
| ,, | ·060 | — | ·89 | 40 | 40·0 | 25·5 | 13 |
| ,, | ·056 | — | ·93 | 30 | 40·0 | 23·4 | 13 |
| ,, | ·074 | — | ·84 | 18 | 48·7 | 21·7 | 13 |
| Average | | | | | | 23·8 | 13 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Mouse | ·062 | 30° | ·42 | 20 | 46·5 | 20·3 | 13 |
| ,, | ·079 | 25° | ·80 | 16 | 50·3 | 21·8 | 13 |
| ,, | ·078 | 25° | ·81 | 20 | 49·6 | 22·3 | 13 |
| ,, | ·088 | 35° | ·52 | 37 | 49·4 | 25·1 | 13 |
| ,, | ·119 | 30° | ·44 | 41 | 59·7 | 22·8 | 13 |
| ,, | ·107 | 35° | ·41 | 50 | 53·5 | 26·3 | 13 |
| ,, | ·061 | 28° | ·38 | 27 | 44·7 | 21·5 | 13 |
| ,, | ·079 | 25° | ·86 | 38 | 42·8 | 29·9 | 13 |
| Wild mouse | ·077 | 25° | ·78 | 35 | 54·7 | 18·1 | 13 |
| ,, | ·142 | 28° | ·54 | 57 | 68·8 | 18·3 | 13 |
| Average | | | | | | 22·6 | 13 |
| Man No. 1 | ·043 | — | — | 205 | 24·7 | 37·7 | 13 |
| ,, | ·061 | — | — | 183 | 29·1 | 42·9 | 13 |
| ,, | ·067 | — | — | 190 | 30·2 | 44·0 | 13 |
| ,, | ·078 | — | — | 143 | 35·2 | 39·4 | 13 |
| Man No. 2 | ·067 | — | — | 174 | 34·1 | 36·6 | 13 |
| ,, | ·0476 | — | — | 238 | 27·4 | 36·1 | 13 |
| ,, | ·025 | — | — | 210 | 14·7 | 39·4 | 13 |
| ,, | ·019 | — | — | 240 | 13·0 | 34·0 | 13 |
| Man No. 3 | ·059 | — | — | 158 | 31·1 | 36·3 | 13 |
| Average | | | | | | 38·5 | 13 |
| Dog | ·077 | — | 7·1 | 120 | 55·3 | 17·6 | 13 |
| ,, | ·052 | — | 6·6 | 120 | 37·2 | 24·4 | 13 |
| Average | | | | | | 21·0 | 13 |
| Cat | ·064 | — | 2·78 | 70 | 37·7 | 35·3 | 13 |
| Rabbit | ·061 | — | 5·10 | 130 | 41·5 | 24·5 | 13 |
| ,, | ·077 | — | 2·28 | 60 | 34·5 | 41·0 | 13 |
| Young rabbit | ·053 | — | 6·4 | 110 | 36·7 | 25·5 | 13 |
| ,, | ·090 | — | 4·6 | 110 | 56·7 | 19·5 | 13 |
| Average | | | | | | 27·6 | 13 |
| Bullfinch | ·0715 | — | ·81 | 28 | 33·8 | 36·4 | 13 |
| ,, | ·0725 | 22° | ·77 | 50 | 31·1 | 41·2 | 13 |
| Grey linnet | ·068 | 25° | ·79 | 18 | 24·4 | 57·6 | 13 |
| ,, | ·074 | 27° | ·75 | 30 | 32·3 | 43·1 | 13 |
| Canary* | ·083 | 28° | ·75 | 32 | 49·5 | 23·1 | 13 |
| Frog | ·082 | — | — | 960 | 57·0 | 18·4 | ? |

\* Animal unhealthy.

The temperature of the air current in the earlier experiments was that of the laboratory in December, and therefore varied somewhat. We found, however, after making several experiments, that it was

necessary to be careful to keep up the body temperature of the mouse, and in the present series we have grouped together the experiments made with this precaution. In these latter experiments we kept the lower part of the bottle containing the mouse in a bath of warm water (25° C.—30° C.).

We have not attempted to determine experimentally the oxygen tension of the air in the alveoli of the lungs of the different animals. The percentage value of 13, given in the tables, is about that calculated by Loewy for the human lung. It seems probable that this value holds approximately for animals under normal conditions. The rate of respiration in a mouse, for instance, is, roughly speaking, 150—200 per minute, and its oxygen consumption per unit of its body weight in a bath at about 25° to 30° is about 12 times as great as that in man. Thus the increase in the frequency of respiration in small animals, as compared with man, seems to correspond approximately to the increase in metabolism, and hence probably suffices to keep the alveolar tension of oxygen at about the same value as that of the human lung. To determine the exact value of the alveolar tension, however, is not essential to the question under consideration.

The average oxygen tension in the case of mice is 23·2 : of birds (bullfinches and grey linnets) about 44: of rabbits 27·6. One observation on the cat gave 35·3, and two observations on the dog gave an average of 21·0. Of the results observed in the experiments on the dog by previous investigators, those obtained originally by Bohr are, as already mentioned, nearly in agreement with the values given by the carbonic oxide method, whilst those of Fredericq[1] (=about 12·5 to 7·5, corrected for aqueous vapour) are decidedly lower, possibly for the reasons suggested in our former paper. Finally we made an observation on the frog. To escape the difficulties due to the slow rate of absorption of gases in the frog we placed it in a 6 litre bottle, inverted over water, and containing air to which a small percentage of carbonic oxide had been added. After 16 hours the blood was examined colorimetrically, and a sample of the air in the bottle was at the same time analysed, particularly for oxygen and carbonic oxide. The oxygen percentage present was 20·07, and the carbonic oxide percentage was ·082, which was exactly that calculated, allowing for what had combined with the frog's blood. To determine the time requisite for the maximum saturation of the blood with carbonic oxide

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[1] *Arch. de Biologie,* xiv. p. 105. 1896.

in the air breathed we made observations on mice with about ·06 %
of carbonic oxide and found that after 5 minutes the value observed was
distinctly too low. After 7 minutes the value was still slightly below
the average. After 10 minutes average values were obtained, and
the duration of the experiment had no further influence on the satu-
ration. It should be noted that during these observations the bottle
containing the mouse was placed in a bath at 30° C., and that in air at
this temperature the rate of exchange in the lungs, and doubtless also
of absorption of carbonic oxide, is much less than that which obtains
at ordinary room temperatures.

It was shown in the previous paper that the time required in man
for maximum saturation of the blood (with about ·06 % of carbonic
oxide in the inspired air) was about 90 to 100 minutes. This is about
ten times as long as in the case of the mouse in air at 30°, and as the
metabolism of the mouse is also about ten times as great per unit of
body weight as that of the man the result is just what might be
expected. The time required for other animals may be calculated
on the same principle, the time varying inversely as the rate of
respiratory exchange per unit of body weight. We have, however,
always allowed a considerable margin of time beyond that required,
so as to leave no room for doubt as to the blood being saturated to
its maximum extent.

Along with our results on animals we have included those previously
obtained on man. As the dissociation curve formerly used in calculating
the oxygen tension in man was not correct we have recalculated the
results of the former experiments. The correction thus introduced
brings up the human arterial oxygen tension to an average of 38·5 %
of an atmosphere.

Table I. shows that in all the animals observed the oxygen tension
of the arterial blood as it leaves the lungs is considerably higher than
the alveolar oxygen tension, while in man and small birds, and often
in other animals, it is very much higher than that of inspired air
(19·7 %, allowing for aqueous vapour).

*Experiments on the effects of cold.*

The animals used for this series of experiments (Table II.) were
mice, since they are so readily sensible to cold. After exposure to a
cold atmosphere for a short time, their body temperature begins to fall,
particularly if they are exposed to a somewhat high percentage of

carbonic oxide, and they become torpid. It was easy to cool down the surroundings of the mouse by placing the bottle containing it in cold water. The result invariably was that the oxygen tension went down to about 15 %. The uniformity of the values observed here

TABLE II.

*Experiments on the effects of fall of temperature on the oxygen tension of arterial blood.*

| Animal | % of CO | Temp. of bath | Rate of ventilation in litres per minute | Duration of experiment in minutes | Corrected saturation of hæmoglobin with CO per cent. | Oxygen tension of arterial blood |
|---|---|---|---|---|---|---|
| Mouse* | ·200 | 7·5° | ·417 | 45 | 79·5 | 15·0 |
| ,, | ·078 | 5·0° | ·500 | 30 | 61·6 | 14·2 |
| ,, | ·103 | 5·5° | ·500 | 45 | 65·5 | 15·7 |
| ,, | ·101 | 6·0° | ·505 | 52 | 65·8 | 15·6 |
| Average | | | | | | 15·1 |

* Animal died. Rectal temperature just after death = 19·5°.

suggests that the cold had nearly paralysed the "mechanism" of absorption, and that the tension observed was approximately that due to diffusion from the alveolar air. This series of observations would seem to afford ground for grave objections to any experiments on the oxygen tension of the blood in which the fallacies arising from fall in body temperature or other abnormal conditions are not carefully avoided. The actual fall of temperature in these experiments of course could not be accurately measured, but in the first experiment the rectal temperature just after death was measured with a very fine thermometer, and found to be 19·5°.

It is not unlikely that in some of the experiments recorded below, particularly in those with high percentages of carbonic oxide and low atmospheric pressures, an appreciable fall in body temperature had occurred, in spite of the precautions we took to avoid this.

### Experiments with high percentages of carbonic oxide.

In this series of experiments, which were made on mice, we investigated the effect of the lack of oxygen which must arise in the body when a large portion of the hæmoglobin is saturated with carbonic oxide. The results (Table III.) show that when more than 60 % of the hæmoglobin is saturated, and the other respiratory conditions are normal, the tension of oxygen begins to rise very markedly. In certain

TABLE III.

*Experiments with high percentages of carbonic oxide.*

| Animal | % of CO | Temp. of bath | Ventilation in litres per minute | Duration of experiment in minutes | Corrected saturation of hæmoglobin with CO per cent. | Oxygen tension of arterial blood |
|---|---|---|---|---|---|---|
| Mouse | ·189 | 25° | ·372 | 72 | 64·8 | 29·1 |
| ,, | ·212 | 25° | ·435 | 31 | 61·0 | 38·7 |
| ,, | ·204 | 30° | ·520 | 35 | 66·5 | 28·9 |
| ,, | ·190 | 30° | ·536 | 40 | 63·3 | 31·5 |
| ,, | ·178 | 30° | ·577 | 31 | 68·2 | 24·0 |
| ,, | ·215 | 28° | ·566 | 37 | 66·7 | 30·2 |
| ,, | ·356 | 30° | ·441 | 30 | 75·5 | 32·8 |
| ,, | ·298 | 28° | ·320 | 45 | 72·0 | 33·5 |
| ,, | ·337 | 25° | ·268 | 64 | 78·9 | 25·5 |
| ,, | ·237 | 25° | ·380 | 38 | 77·8 | [19·4] |
| ,, | ·264 | 26° | ·366 | 45 | 84·5 | [13·5] |
| ,, | ·407 | 27° | ·240 | 43 | 72·7 | 46·2 |
| ,, | ·532 | 26° | ·192 | 60 | 83·1 | 30·4 |
| ,,* | ·526 | 26° | ·188 | 13 | 87·0 | 21·8 |
| ,, | ·438 | 26° | ·227 | 47 | 77·6 | 36·0 |
| ,, | ·428 | 26° | ·226 | 48 | 82·2 | 26·3 |
| ,, | ·232 | 30° | ·435 | 32 | 75·3 | 21·3 |
| ,, | ·171 | 30° | ·273 | 33 | 63·1 | 28·5 |
| Average | | | | | | 30·3 |
| Grey linnet | ·194 | 25° | ·415 | 33 | 63·1 | 32·4 |
| Bullfinch | ·119 | 25° | ·387 | 40 | 51·6 | 45·0 |
| Grey linnet * | ·232 | — | ·845 | 7 | 55·6 | 53·0 |

* Animal died.

instances the tension observed was twice as high as that of the inspired air. Another very remarkable fact brought out by these experiments is that, provided the natural fall of body temperature is avoided, the mouse can still live and retain consciousness and the power of creeping about after as much as 84 % of its hæmoglobin has been thrown out of action by saturation with carbonic oxide. It is important to bear this fact in mind in studying the experiments with atmospheres at diminished pressures which are described below.

On the other hand we found that birds were unable to survive after about 60 % of their hæmoglobin had been saturated. They usually became restless, and died suddenly just after some unusual exertion.

In the case of men poisoned by gradual absorption of carbonic oxide after explosions in coal mines, the highest saturation observed was 83 % (v. Haldane, Report on the causes of death in Colliery Explosions, 1896, p. 40), but in many cases the saturation found was considerably less.

In two of the experiments the oxygen tensions found were ab-
normally low. These experiments were made on a cold day, when
several of the mice were observed to have become torpid in their cage.
It therefore seems probable that the mice used in these experiments
were suffering from cold before they were put into the bottle.

### *Experiments with mixtures of carbonic acid and air.*

In order to ascertain whether the hyperpnœa produced by air
containing carbonic acid is associated with increased absorptive activity
for oxygen on the part of the lungs, we made several experiments with
air containing about 6 % of carbonic acid. The carbonic acid was
passed into the air-current in a steady stream from a cylinder, and
the percentage present determined by an analysis of a sample of the
mixture from a bottle placed in the air-current beyond the animal.
Table IV. shows that no definite rise in the oxygen tension of the blood

### TABLE IV.

*Experiments with air containing carbonic acid.*

| Animal | % of CO | % of $CO_2$ | Duration of experiment in minutes | Corrected saturation of hæmoglobin with CO per cent. | Oxygen tension of arterial blood | Oxygen tension of inspired air | Temp. of room |
|---|---|---|---|---|---|---|---|
| Mouse | ·087 | 6·1 | 16 | 51·6 | 23·7 | 18·5 | 12° |
| ,, | ·092 | 6·8 | 22 | 61·8 | 16·6 | 18·4 | 12°* |
| ,, | ·048 | 3·5? | 40 | 40·8 | 19·7 | 15·7? | ?† |
| ,, | ·058 | 3·5? | 30 | 36·3 | 28·6 | 15·7? | ?† |
| Lark | ·090 | 7·3 | 18 | 40·2 | 37·0 | 18·1 | 12° |

* Mouse looked cold.
† Expired air used for ventilation.

was observed. Carbonic acid does not, therefore, appear to act as a
stimulus to the absorption of oxygen by the lungs.

### *Experiments with mixtures of oxygen and air.*

In this series of experiments the oxygen was supplied from a cylinder
by means of a T tube inserted into the rubber tubing conveying the air
to the apparatus. In cases where oxygen alone was given, the supply
from the cylinder was made larger in volume than the current which
was being aspirated through the apparatus, and the excess was allowed
to escape from the open end of the T tube. In each experiment a
sample from the current was taken for analysis. It is apparent from
this table of results that in these conditions, *i.e.* where the blood is

TABLE V.

*Experiments with mixtures of oxygen and air.*

| Animal | % of CO | Temp. of bath | Ventilation in litres per minute | Duration of experiment in minutes | Corrected saturation of hæmoglobin with CO per cent. | Oxygen tension of arterial blood in % of an atmosphere | Oxygen percentage of air | Probable alveolar oxygen tension in % of an atmosphere |
|---|---|---|---|---|---|---|---|---|
| Mouse | ·580 | 25° | ·71 | 15 | 56·5 | 128 | 86·5 | 75 |
| ,, | ·614 | 25° | ·72 | 10 | 58·1 | 124 | 87·3 | 76 |
| ,, | ·296 | 25° | ·74 | 15 | 60·6 | 54·4 | 47·5 | 39 |
| ,, | ·142 | 25° | ·74 | 20 | 37·2 | 66·6 | 47·7 | 39 |
| Grey linnet | ·118 | — | ·75 | 18 | 28·0 | 89·0 | 45·5 | 37 |
| ,, | ·434 | — | ·73 | 11 | 41·5 | 170 | 87·4 | 76 |

partially saturated with carbonic oxide and where the air breathed contains a much higher percentage of oxygen than that of the atmosphere, there is still active absorption by the lungs. The tension of oxygen in the blood is always much higher than that of the alveoli. The absolute difference between alveolar and arterial oxygen tension increases, but the relative difference remains about the same. In connection with these experiments it must of course be kept in mind that the amount of available oxygen in the arterial blood is less than normal, in spite of the great increase in the oxygen tension.

From these and the immediately preceding experiments it seems to follow that the degree of absorptive activity on the part of the lung depends on the supply of oxygen to the tissues of the body generally and not merely on the oxygen tension already reached by the blood on its way through the lung capillaries.

## Experiments with air partially deprived of oxygen.

In this series of experiments (Table VI.) we have investigated the effect produced on the arterial oxygen tension in mice by diminishing the oxygen percentage of the air breathed.

The bottle containing the mouse was ventilated from a large bag, the air of which had been partially deprived of its oxygen by respiration. The carbonic acid was absorbed by means of potash lime, and a sample of the air passing from the animal chamber was analysed at the end of each experiment. From the composition of this air the oxygen tension of the inspired air was obtained by simply correcting for the aqueous vapour.

TABLE VI.

*Experiments with air partially deprived of oxygen.*

| Animal | % of CO | Temp. of bath when employed | Ventilation in litres per minute | Duration of experiment in minutes | Corrected saturation of hæmoglobin with CO per cent. | Oxygen tension of arterial blood (corrected for aqueous vapour) | Oxygen tension of inspired air | Probable alveolar oxygen tension |
|---|---|---|---|---|---|---|---|---|
| Mouse | ·045 | 25° | ·88 | 33 | 49·1 | 13·2 | 15·9 | 10 |
| ,, | ·014 | 25° | ·82 | 27 | 15·1 | 21·2 | 16·2 | 10 |
| ,, | ·0154 | 25° | ·78 | 27 | 19·0 | 19·7 | 15·5 | 9 |
| ,, | ·0142 | 25° | ·83 | 16 | 21·6 | 14·7 | 9·8 | 6 |
| ,, | ·0131 | — | ·79 | 19 | 22·0 | 13·6 | 13·7 | 8 |
| ,, | ·0124 | — | ·87 | 21 | 23·8 | 11·6 | 9·7 | 6 |
| ,, | ·0117 | — | ·94 | 30 | 30·4 | 7·4 | 8·1 | 5 |
| ,, | ·0413 | 29° | ·53 | 35 | 64·1 | 6·7 | 5·8 | 3·5 |
| ,, | ·0494 | 25° | ·41 | 52 | 64·1 | 7·8 | 6·2 | 4 |
| ,, | ·0382 | 30° | ·48 | 35 | 55·5 | 8·7 | 6·5 | 4 |
| ,,* | ·0170 | 28° | ·70 | 11 | 25·0 | ? | 4·7 | 2·5 |
| ,, | ·0452 | 29° | ·38 | 45 | 60·1 | 8·5 | 5·45 | 3 |

* Animal died.

It had already been shown by one of us[1] that diminution of the oxygen percentage of the air breathed greatly increases the poisonous action of carbonic oxide, and we began these experiments with the expectation that on diminishing the oxygen percentage sufficiently it would be found that as little as ·01 % of carbonic oxide or less would be capable of causing death. To judge from the available blood-gas analyses, which will be discussed below, the arterial blood is not more than half saturated with oxygen when the oxygen tension of the air breathed falls to about a third of an atmosphere. With blood half-saturated with oxygen the oxygen tension is only about ·34 % of an atmosphere according to the dissociation curve of hæmoglobin (Fig. 1), which is constructed from Hüfner's data[2]. As ·34% is only about $\frac{1}{70}$th of the normal arterial oxygen tension one would thus expect that roughly speaking ·01 % of carbonic oxide would, with an oxygen percentage in the air breathed of a third of an atmosphere or less, have as much effect in saturating the blood as ·70 % at normal arterial oxygen tension, and that consequently the blood would, with sufficiently

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[1] This *Journal*, XVIII. p. 201. 1895.

[2] *Arch. f. (Anat. u.) Physiol.* 1890, p. 1. We may remark that this curve is a rectangular hyperbola, like the dissociation curve of carbonic oxide in air. Hüfner's data deviate only slightly from the curve given. Fig. 1 shows the two curves, with their axes and asymptotes.

long exposure, become about 90 % saturated. Table VI. clearly shows, however, that nothing of the sort occurs. With diminishing percentages of oxygen in the inspired air the arterial oxygen tension does, indeed, gradually fall at first almost in proportion to the fall in the oxygen percentage of the air, but at an arterial oxygen tension of about 8 or 9 % there is a distinct limit to the fall, and at the same time to the increase in the action of the carbonic oxide in saturating the blood. This limit seems to be reached when the oxygen percentage of the air breathed falls to a little below 10 %. Further diminution causes no further fall in the arterial oxygen tension until a point is reached (at about 5 % of oxygen in the inspired air) when death ensues so rapidly that the blood has not time to saturate itself to anything approaching its maximum extent with carbonic oxide, the presence of which gas has evidently nothing whatever to do with the cause of death.

The last experiments in the table show that with very low oxygen percentages in the inspired air the arterial oxygen tension may be 50 % above that of the inspired air and about 300 % above that of the alveolar air. The oxygen tension of the alveolar air was calculated on the assumption that the ventilation of the lungs was about thrice as great as usual, the respiratory exchange of the animal remaining about the same. It seems not improbable however that the increase in ventilation of the lungs is over-estimated and that the alveolar oxygen tension was really lower. Thus in the last experiment in the table the frequency of respiration had fallen to 120, and the individual respirations did not appear to be much deeper than usual. Throughout the experiment the animal was very feeble, especially when first placed in the current of vitiated air. The skin was bluish. The fact that the arterial oxygen tension was proportionally so much higher than that of the inspired and alveolar air proves that fall in the arterial oxygen tension beyond a certain point directly or indirectly stimulates the lung to greater absorptive activity. The death of the animal is evidently due in some way to the fall in the oxygen tension of the blood, and not to mere diminution in the percentage of oxygen present in it, since with a tension of 7 or 8 % of oxygen (the minimum observed) the hæmoglobin would still, according to Hüfner, be 96 % saturated with oxygen. The experiments in Table III. show that a mouse can still live and retain consciousness and sufficient power of movement to enable it to creep about, when its hæmoglobin is only 16 % saturated with oxygen, provided the oxygen tension of the blood is at the same time high. In this connection we may also recall the fact that under

a pressure of about two atmospheres of oxygen a mouse can dispense entirely with the oxygen-carrying power of its hæmoglobin, and yet remain quite lively and active[1].

In these experiments and those given in Table VII. we have assumed that the time required to obtain maximum saturation of the hæmoglobin with carbonic oxide would be increased in proportion to the increased saturation of the blood with carbonic oxide for a given tension of the gas in.the atmosphere breathed. We varied the duration of the experiments in order to ascertain whether this assumption was correct, and we have purposely recorded several experiments the duration of which was shorter than the requisite calculated time. In these latter cases it will be seen that the maximum saturation had apparently not been reached, since the oxygen tension, if calculated out, would be higher than in comparable experiments of longer duration. In the rest of the experiments the time was evidently sufficient. Thus in the last experiment in Table VI., in which there was the lowest percentage of oxygen in the inspired air, the calculated oxygen tension is actually less than in two previous experiments of shorter duration. Many of the experiments in Table VII. were, for further certainty, continued for still longer periods.

### Experiments at Low Pressures.

The observations in this series were made on mice and birds. The air current with carbonic oxide supply was arranged as before, the aspirator being attached to a powerful filter-pump, working with water at a pressure of about 40 lbs. per square inch. By this means a current sufficiently large to keep the animal supplied with air could be obtained at very low pressures. The negative pressure was obtained by interposing in the current, before it entered the animal chamber, a stop-cock which was nearly closed. A mercury manometer was used to indicate the pressure. With this arrangement a very steady current at any pressure desired was obtained without difficulty.

The lowest pressure with which we found it possible to work was in the case of mice about 25 % of an atmosphere. Birds suffered much more than mice from low pressures. Even at a pressure of 34 % of an atmosphere one of the birds died after 28 minutes. The results shown in the table entirely confirm the observations given in the section on experiments with air partially deprived of oxygen, since they show

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[1] This *Journal*, XVIII. p. 211. 1895; XXI. p. 161. 1897.

TABLE VII.

Experiments at low atmospheric pressures.

| Animal | % of CO | Pressure in mm. of mercury | Pressure in % of an atmosphere | Temp. of bath | Ventilation in litres (at normal pressure) per minute | Duration of experiment in minutes | Corrected saturation of haemoglobin with CO | Carbonic oxide tension of alveolar air in % of an atmosphere | Oxygen tension of arterial blood in % of an atmosphere | Oxygen tension of inspired air in % of an atmosphere | Probable oxygen tension of alveolar air |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mouse | ·0054 | 274 | 36·0 | 25° | ·353 | 38 | 5·0 | ·0015 | ? | 6·3 | 4 |
| ,, * | ·0091 | 223 | 29·3 | — | ·417 | 72 | 13·5 | ·00215 | 3·7 | 4·9 | 2·6 |
| ,, | ·0126 | 190 | 25·0 | 25° | ·182 | 64 | 17·3 | ·00242 | 3·6 | 3·95 | 1·7 |
| ,, * | ·0540 | 190 | 25·0 | 25° | ·177 | 94 | 39·5 | ·0102 | 4·7 | 3·95 | 1·7 |
| ,, | ·136 | 198 | 26·1 | 25° | ·143 | 46 | 42·5 | ·027 | 10·8 | 4·2 | 1·9 |
| ,, | ·181 | 198 | 26·1 | 25° | ·129 | 60 | 61·3 | ·036 | 6·8 | 4·2 | 1·9 |
| ,, | ·084 | 195 | 25·7 | 25° | ·214 | 75 | 34·1 | ·017 | 9·9 | 4·1 | 1·9 |
| ,, * | ·0536 | 245 | 32·3 | 28° | ·136 | 30 | 21·7 | ·014 | ? | 5·0 | 2·7 |
| ,, | ·0487 | 296 | 39·0 | 28° | ·222 | 47 | 35·0 | ·0156 | 8·8 | 6·9 | 4·6 |
| ,, | ·134 | 243 | 32·0 | 28° | ·211 | 70 | 57·8 | ·035 | 7·7 | 5·4 | 3·1 |
| ,, | ·028 | 267 | 35·2 | 28° | ·150 | 96 | 29·0 | ·0082 | 6·1 | 6·1 | 3·8 |
| ,, | ·173 | 266 | 35·0 | 28° | ·210 | 57 | 72·3 | ·0502 | 5·8 | 6·1 | 3·8 |
| ,, | ·166 | 266 | 35·0 | 28° | ·200 | 60 | 74·8 | ·048 | 4·8 | 6·1 | 3·8 |
| ,, | ·149 | 215 | 28·3 | 28° | ·222 | 58 | 60·3 | ·031 | 6·1 | 4·7 | 2·4 |
| ,, * | ·055 | 274 | 36·0 | 28° | ·420 | 8 | 8 | ·0158 | ? | 6·2 | 3·9 |
| ,, | ·043 | 197 | 26·0 | 28° | ·234 | 73 | 33·2 | ·0086 | 5·3 | 4·2 | 1·9 |
| ,, | ·0240 | 210 | 27·7 | 28° | ·323 | 94 | 21·7 | ·0052 | 6·0 | 4·5 | 2·2 |
| ,, | ·0935 | 223 | 29·3 | 28° | ·181 | 20 | 24·2 | ·0218 | ? | 4·9 | 2·6 |
| ,, | ·1054 | 223 | 29·3 | 28° | ·294 | 90 | 60·0 | ·0247 | 4·9 | 4·9 | 2·6 |
| ,, | ·158 | 195 | 25·7 | 28° | ·152 | 92 | 56·6 | ·0310 | 7·1 | 4·1 | 1·8 |
| ,, | ·120 | 195 | 25·7 | 28° | ·194 | 45 | 42·4 | ·0236 | 9·6 | 4·1 | 1·8 |
| Bullfinch * | ·136 | 261 | 34·3 | — | ·246 | 28 | 36·6 | ·039 | 19·9 | 5·8 | 3·5 |
| ,, | ·246 | 312 | 41·0 | — | ·570 | 13 | 63·8 | ·086 | 14·7 | 7·3 | 5·0 |
| ,, | ·131 | 375 | 49·3 | 28° | ·500 | 32 | 51·7 | ·0595 | 16·8 | 9·1 | 6·8 |

* Animal died.

again that up to the time of death the tension of oxygen in the arterial blood leaving the lungs is high enough to saturate the hæmoglobin almost completely, and is far above the alveolar tension.

In the second experiment, which gave an unusually low tension, no bath was used, and the body temperature was doubtless low. In the third experiment the animal was comatose for about half-an-hour before death, and one cornea had become opaque. In no other experiment was the animal comatose.

The series includes a case where the mouse died with an oxygen tension just before death of 10 %. In the case of birds the tension was still higher.

Analyses by the blood gas pump of the gases in the arterial blood of animals which have been subjected to these low pressures, seem to show that the hæmoglobin is not nearly saturated with oxygen. The average results of Fraenkel and Geppert[1] are in substantial agreement with those of Paul Bert, and may be quoted here.

*Volume of oxygen obtained from arterial blood (dog).*

α.  From normal animal in air at a pressure of 760 mm. 100 c.c. = 19·47 c.c. of oxygen.
β.  From animal in air at a pressure of 430 mm. 100 c.c. = 18·55 c.c. of oxygen.

α.  From normal animal in air at a pressure of 760 mm. 100 c.c. = 15·45 c.c. of oxygen.
β.  From animal in air at a pressure of 374 mm. 100 c.c. = 11·81 c.c. of oxygen.

α.  From normal animal in air at a pressure of 760 mm. 100 c.c. = 18·08 c.c. of oxygen.
β.  From animal in air at a pressure of 269 mm. 100 c.c. = 9·30 c.c. of oxygen.

From these results it is clear that when the pressure was reduced to $\frac{1}{3}$ of an atmosphere, the blood taken from the arteries was only half saturated with oxygen. According to Hüfner's data this would imply a tension of oxygen in the blood of ·3 % of an atmosphere, whereas the results in the above table show far higher tensions of oxygen in the blood with a pressure of only $\frac{1}{4}$ of an atmosphere.

In considering the apparent contradiction between the blood-pump results and those we now bring forward, we would point out that there is an essential difference in the two methods of observation. In the case of the blood gas pump experiments, the blood had been drawn from the arteries, while by our method we observe the blood as it is in the capillaries of the lungs. Further, our measurements of tension depend on the saturation of the hæmoglobin with carbonic oxide, and the amount of this is determined by the tension of oxygen in the blood

[1] *Ueber die Wirkung der verdünnten Luft auf den Organismus*, 1883.

at the time of its exposure to the two gases in the lungs. The behaviour of carbonic oxide in the body differs from that of oxygen in as much as the latter is withdrawn from the blood to be consumed in the metabolism of the body, whilst the former does not disappear in this way, and therefore cannot be affected by changes in the circulation subsequent to the passage of the blood through the lung capillaries. The explanation of the difference in the results may be found in this difference of method, and there is a considerable amount of evidence to prove that this is the case.

It was originally discovered by Pflüger that blood on leaving the vessel very rapidly undergoes a change which involves the taking up of part of the oxygen contained in its hæmoglobin. We have frequently verified his observation that normal arterial blood becomes distinctly darker immediately on leaving the body. To investigate this change quantitatively he constructed a pump with a specially large vacuum of 8 litres capacity, and compared the amount of oxygen obtained by means of it, with that which could be extracted from the blood by the ordinary much slower method, with a vacuum of 3 litres capacity. The table of results which we here quote indicates that, on the average, he obtained from 100 c.c. of blood by the rapid method 2 c.c. of oxygen more than by the ordinary method.

*Percentages of oxygen obtained from arterial blood (dog).*

Large vacuum (8 litres)  25·4  25·0  24·3  23·7  21·9  21·8  21·7  21·2  21·0  18·7  19·1
= 243·8    Mean = 22·16

Small vacuum (3 litres)  24·7  24·3  22·9  21·6  12·1  20·0  20·9  18·4  20·8  18·0  18·3
= 222    Mean = 20·18

These results point to changes in the blood which lead to a very rapid disappearance of oxygen from the hæmoglobin, and its fixation in some firm combination. As a rule, analyses of the gases from the arterial blood of animals during conditions of asphyxiation show the presence of little or no oxygen. We may quote the summary of these observations which Stroganow has introduced into his paper on the process of oxidation in normal and asphyxia blood.

Setschenow obtained in one analysis 1·16 vols per hundred of blood and in 3 others traces only. Pflüger from two analyses obtained an average of 1·75%, Schmidt from 10 analyses gives ·945%, Afonassjew from 4 analyses gives ·78%. The average of all the observations is ·908%. (Stroganow, *Pflüger's Archiv*, XII. p. 22.)

To test the truth of these results Stroganow used the method, suggested by Hoppe-Seyler, of examining the spectrum of the blood while still circulating in the jugular vein of an animal with the trachea clamped. He never failed by this means to find in the asphyxiated animal's blood the double bands of oxyhæmoglobin, and that for a long time after the cessation of respiration. Even in the veins the bands remained visible up to the point of complete cessation of the heart-beat, although after this they quickly disappeared.

In order to obtain a rough idea of the minimum percentage of oxygen which must have been present even in the venous blood in these experiments we took a test-tube containing a very dilute solution of completely reduced hæmoglobin, and placed between it and a gas-flame another test-tube of equal size containing oxyhæmoglobin in varying dilutions. We found that when the oxyhæmoglobin solution was less than $\frac{1}{6}$th of the strength of the reduced hæmoglobin solution it was no longer possible, even with the most favourable concentrations, to see the oxyhæmoglobin bands through the band of reduced hæmoglobin. It is thus evident that the blood in the veins must be at least 15% saturated with oxygen even in the very last stages of asphyxia. We may therefore assume that at least 4% of oxygen is really present in the arterial blood, although the blood-pump may give no oxygen, even in the earlier stages of asphyxia.

The highest values obtained by the blood-pump are doubtless far too low because the increased quantities of "reducing substances" must cause the oxygen to disappear to a still greater extent than is the case in normal blood. Stroganow after shaking asphyxia blood for a few minutes with oxygen, estimated the amount of this gas which had disappeared into fixed combination per 100 vols (on the assumption that no oxygen was already present in the blood). The following is a table of his results.

Blood from jugular vein of asphyxiated animal  4·926 %.
,,       ,,       ,,       ,,       ,,     2·843 %.
Blood from carotid artery of asphyxiated animal 3·306 %.
,,       ,,       ,,       ,,       ,,     2·344 %.
Average = 3·354 %.

To this must be added the amount of oxygen which as shown above must have been present in the blood within the vessels of the asphyxiated animals. This could not well be less than 4% and may have been much more. We find therefore that at least 7·35% of

oxygen might disappear from the blood in this way before it could be evacuated in the pump.

These considerations show that the results obtained with the blood-pump are altogether untrustworthy in so far as regards their bearing on the present question, since between the time when the blood of an animal suffering from want of oxygen leaves the lung and the time when evacuation in the pump is complete, a large amount of oxygen undoubtedly disappears. This disappearance of oxygen might easily account for the whole difference between the oxygen tensions indicated by the carbonic oxide and those inferred from blood-pump determinations. Even with normal arterial blood Pflüger found in one case that about 10 % of oxygen had disappeared before the blood was evacuated when the ordinary pump was employed.

In connection with this discussion a further possibility must be taken into consideration. Geppert and Zuntz[1] have expressed the opinion, which seems based on good grounds, and has recently been endorsed by Miescher and Jacquet[2], that some parts of the lung may either not be ventilated at all in normal respiration, or are at least much less completely ventilated than others. This, if it be correct, would not only explain the low oxygen tensions sometimes obtained by the acrotonometer method, but would also help to clear up the apparent discrepancy, already referred to, between the blood-pump results and those obtained by the carbonic oxide method. Supposing that in some parts of the lung the blood passed through without being saturated, the small amount of extra carbonic oxide absorbed in these parts owing to the low oxygen tension would always be turned out when the blood again came round to the better ventilated parts of the lung. The carbonic oxide method would thus approximately indicate the oxygen tension of the blood in the better ventilated portions of lung, and not in the worse ventilated.

We have inferred from these experiments and those in the previous section that in asphyxia from atmospheres at low pressures or partially deprived of oxygen the symptoms are due, not to lack of oxygen in the blood, but to the diminution in the oxygen tension. In order to further test this conclusion we have carefully observed what effect on the symptoms was produced by partial saturation of the blood with carbonic oxide, since by partially saturating the blood with carbonic oxide the *amount* of oxygen in the blood can be greatly diminished,

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[1] *Pflüger's Arch.* XLII. p. 229. 1888.

[2] *Archiv f. experim. Pathologie*, XXXIX. p. 470. 1897.

while (other things being equal) the *tension* is not affected. In no case could we observe that the animal became any worse as the saturation of its blood with carbonic oxide increased; and indeed we were at first inclined to think that the carbonic oxide if not in too great excess caused an improvement. The same improvement seemed, however, to occur without the carbonic oxide, and had thus probably nothing to do with it. It seemed to be invariably the case that if the pressure or percentage of oxygen was reduced too rapidly symptoms of asphyxia were apt to appear. Several animals nearly died in this way, although after a time they were able to live perfectly well in the same atmosphere, and the blueness of the skin, which was at first evident, disappeared[1]. After the first experiments we always took the precaution of reducing very gradually the oxygen tension of the air breathed. In one experiment we first exposed the animal for some time to an atmosphere at ordinary pressure containing 16 % of carbonic oxide, so that its blood must have been about two-thirds saturated. On diminishing the pressure we could see no difference between the symptoms of this and other animals. It thus seems evident that the tension, and not the amount of oxygen was what mattered to the animal. If through previous training of the lungs or other means the animal could have increased still further the excess of its arterial oxygen tension over that of the atmosphere it was breathing it could apparently have lived quite comfortably in this atmosphere. That previous training may make a great difference in this respect is, indeed, very probable from the experience of mountaineers.

It seems not unlikely that the importance to the animal of the attainment of a high oxygen tension in the blood passing through the lungs is in some way connected with the large amount of oxidation which, according to the very striking experiments of Bohr and Henriques[2], occurs in the lungs themselves. The experiments of the latter observers[3], showing how very slight an effect on the metabolism is produced by almost completely blocking the circulation, seem also to point in the same direction as our experiments on the effect of very high saturation of the arterial blood with carbonic oxide.

[1] The protocol of an experiment is given in the appendix.
[2] *Arch. de Physiologie*, 1897, p. 590.
[3] *Ibid.* 1897, p. 459.

*Test experiments with Hæmoglobin Solutions.*

In Table VIII. are contained the results of the new experiments we made to determine with greater accuracy than before the dissociation

TABLE VIII.

*Experiments to determine the dissociation curve of carboxyhæmoglobin in presence of air.*

| Temp. °C. | %0 of CO | Saturation of hæmoglobin with CO | | Temp. °C. | %0 of CO | Saturation of hæmoglobin with CO |
|---|---|---|---|---|---|---|
| — | ·376 | 83·4 | | — | ·10 | 58·4† |
| — | ·400 | 85·3 | | 37° | ·085 | 54·8 |
| — | ·382 | 86·3 | | 37° | ·087 | 54·8 |
| — | ·365 | 84·0 | | | | |
| — | ·367 | 84·4 | | Average ·086 | | 54·8 |
| — | ·306 | 82·3 | | | | |
| 37° | ·329 | 83·2 | | 37° | ·069 | 46·4 |
| | | | | — | ·069 | 50·6 |
| Average ·361 | | 84·1 | | | | |
| | | | | Average ·069 | | 48·5 |
| 37° | ·294 | 82·6 | | | | |
| — | ·294 | 80·0 | | — | ·0595 | 42·6 |
| | | | | — | ·0595 | 42·7 |
| Average ·294 | | 81·3 | | | | |
| | | | | | | |
| — | ·252 | 76·0 | | — | ·050 | 38·6 |
| — | ·245 | 76·0 | | | | |
| — | ·248 | 78·9 | | | | |
| | | | | | ·039 | 36·2 |
| Average ·248 | | 77·0 | | | ·0385 | 39·7 |
| | | | | | ·036 | 36·2 |
| 37° | ·195 | 74·2 | | | ·0355 | 38·0 |
| 37° | ·195 | 75·0 | | | ·037 | 34·2 |
| | | | | | ·037 | 34·3 |
| Average ·195 | | 74·6 | | | | |
| | | | | Average ·037 | | 36·4 |
| — | ·125 | 64·6* | | | | |
| — | ·123 | 63·7 | | * Blood of mouse. | | |
| 37° | ·121 | 64·6 | | † Blood of bird. | | |
| 38° | ·132 | 64·2 | | | | |
| | | | | | | |
| Average ·125 | | 64·3 | | | | |

curve of carboxyhæmoglobin in presence of air. These experiments were, when not otherwise stated, made with (about) 1 %0 solutions of ox-blood at the temperature of the room. The method used was the same as that described in our previous paper, but, as already mentioned, the shaking was more vigorous, and was continued for 20 minutes.

In bright weather the room was also partially darkened during the titration.

In the previous paper we have given the results of several experiments to show that by means of blood or hæmoglobin solutions the oxygen tension of a gas mixture differing markedly from air can be determined when the carbonic oxide tension is known. In the present series of experiments, however, we were putting a greater strain upon the method, and we have therefore made a number of additional test experiments. We found in the first place that, as shown in Table VIII., a hæmoglobin solution from the blood of birds and mice gave the same saturations on shaking with air containing a given percentage of carbonic oxide, as the hæmoglobin from the blood of an ox, sheep, or man (see our previous paper). This solution however becomes turbid on shaking much more readily than ox-blood[1]. The hæmoglobin is also particularly liable to an alteration which shows itself in the fact that on saturation with carbonic oxide the solution is not so pink as normal blood. To avoid these changes, which may easily cause fallacy, we found that it was of great importance that the bottle employed for shaking the hæmoglobin solution and gas mixture should be perfectly clean and smooth. Any roughness on the glass hastened the coagulation &c. very greatly.

As the dissociation curve which we formerly obtained was distinctly too low on account of insufficient shaking, and the new curve was obtained at room temperatures, we made two experiments specially to see whether the new curve was also true for the temperature of the body. The results, which are given in Table VIII., show that the temperature made no appreciable difference.

Finally, we made several test experiments to see whether, at the very low oxygen tensions employed in many of our experiments, and at the body temperature, the hæmoglobin method still indicated correctly the oxygen tension. These experiments (Table IX.) showed

TABLE IX.

*Experiments on the dissociation curve of carboxyhæmoglobin in presence of air at very low pressures.*

| | Barometric pressure | | | Duration of | |
| %of CO | in mm. of mercury | in % of an atmosphere | Temp. °C. | shaking in minutes | Saturation of hæmoglobin |
|---|---|---|---|---|---|
| ·094 | 194 | 25·5 | 37° | 84 | 56·5 |
| ·067 | 199 | 26·2 | 37° | 95 | 48·2 |

[1] See Ramsden, *Arch. f. (Anat. u.) Physiol*, 1894, p. 517.

that the method still gave perfectly exact results. The period of shaking employed was 1½ hours. The bottle was kept completely immersed in a water bath, and was shaken by a machine. We made several experiments with about 55 minutes' shaking, and found that the saturations obtained were then slightly (about 3 or 4 %) too low. With 30 minutes' shaking the results were markedly too low. It was necessary to allow about 5 times the ordinary period of shaking, since the tension of carbonic oxide corresponding to a given saturation of the hæmoglobin, was in these experiments only about a fifth of the tension in experiments with air at ordinary pressure.

We have not yet determined the dissociation curve of carboxy-hæmoglobin in the absence of oxygen, but we may mention here the results of one or two preliminary experiments in which mixtures of carbonic oxide and hydrogen were employed. Thus we found that at 37°, and with a tension of ·0044 % of carbonic oxide, hæmoglobin solution after 20 minutes' shaking became 80 % saturated. At 15°, and with ·0047 % of carbonic oxide the hæmoglobin became 98 % saturated. The hydrogen employed in these experiments was, however, not quite free from oxygen, and the shaking was probably not continued long enough, so that the saturation obtained at 37° can only be regarded as a minimal one. The experiment however was sufficient to show that the very low carbonic oxide tensions employed in some of our experiments could not appreciably affect the accuracy of our method. The results at the same time show the marvellous delicacy of hæmoglobin solution as a reagent for carbonic oxide. In the absence of oxygen as little as ·0001 %, or one part in a million, of carbonic oxide could certainly be detected colorimetrically with hæmoglobin solution.

## CHIEF CONCLUSIONS.

1. In the animals investigated the normal oxygen tension in the arterial blood is always higher than in the alveolar air, and is in some animals even much higher than in the inspired air. The absorption of oxygen by the lungs thus cannot be explained by diffusion alone.

2. Fall in the body temperature causes a marked fall in the oxygen tension of the arterial blood.

3. Increase in the oxygen percentage of the alveolar air causes an almost proportional increase in the oxygen tension of the arterial

blood, so that active absorption still proceeds in atmospheres richer in oxygen than atmospheric air.

4.  Diminution in the oxygen percentage or tension in the alveolar air causes a fall in the oxygen tension of the arterial blood; but want of oxygen, whether produced by carbonic oxide poisoning, by diminution in the oxygen percentage of the air, or by diminution in atmospheric pressure, causes a marked increase in the *relative* excess of arterial over alveolar oxygen tension: hence want of oxygen acts as a stimulus to absorption of oxygen.

5.  The symptoms caused by diminution in the oxygen tension of the air breathed are due to fall in the oxygen tension reached by the blood in the lungs, and not to diminution in the quantity of oxygen carried by the blood from the lungs.

## APPENDIX.

### PROTOCOLS OF THREE EXPERIMENTS.

No. 1.   *Experiment on mouse with air containing a high percentage of carbonic oxide.*

Full-grown black and white mouse.  In bath at about 27° C.  Ventilation with air containing CO started at 5.7 p.m.  (Meter already filled with the mixture.)  At 5.9 hyperpnœa and loss of power.  Symptoms more marked at 5.10.  Mouse very pink.

| Readings of burette delivering CO. | | | Readings of meter (continuous observations of time required for one revolution, which was equivalent to ·50 litres). |
|---|---|---|---|
| 5.13 | 88·55 | | |
| 5.17 | 84·45 | | 1′ 42″ |
| | | | 1′ 41″ |
| 5.26 | 75·3 | Mouse no worse, and is fairly lively, | 1′ 36″ |
| | | though weak in legs. | 1′ 36″ |
| 5.31 | 70·2 | At 5.30.   Rate of ventilation dimin- | 2′ 10″ |
| | | ished.   Bath 27°. | 2′ 7″ |
| 5.37 | 64·05 | | 2′ 7″ |
| | | | 2′ 5″ |
| 5.41 | 59·95 | Mouse about same. | 2′ 0 |
| | | | 2′ 3″ |
| 5.45 | 55·85 | | 2′ 7″ |
| | | | 2′ 6″ |
| 5.49 | 51·8 | Drowned at 5.50. | 2′ 5″ |
| 36 | 36·75 | | 2′ 5″ |
| | 1·02 | | |

The ventilation was thus ·50 litres in 2′ 5″, or 240 c.c. per minute, and as in each 240 c.c. of air there was 1·02 c.c. of CO, the percentage of CO (uncorrected) was ·425.

*Analysis of sample of CO from the burette.*

Volume taken      18·205
After $CO_2$ absorbed    18·205
$$CO_2 = \overline{\quad\cdot 00}$$
After oxygen absorbed 18·02
$$Oxygen = \overline{\quad\cdot 185} = \cdot 88 \text{ of air} = 4\cdot8\,^0/_0.$$

∴ true percentage of CO was ·407.

The result of the titration of the blood was as follows:

A.   Titration up to tint of animal's blood.

         2·7 c.c. of carmine not quite enough.
         2·9 c.c. right⎫
         3·1 c.c.   ,,   ⎬ = 3·1 c.c.
         3·3 c.c.   ,,   ⎭
         3·5 c.c. slightly too much.

B.   Titration up to tint of same blood saturated with CO.

         5·4 c.c. not quite enough.
         5·7 c.c. right⎫
         6·0 c.c.   ,,   ⎬ = 6·0.
         6·3 c.c.   ,,   ⎭
         6·6 c.c. slightly too much.

$$\therefore \text{ saturation} = \frac{3\cdot1}{8\cdot1} \times \frac{11}{6} = 70\cdot1\,^0/_0.$$

Corrected for dissociation $= 72\cdot1\,^0/_0$.

As $72\cdot1\,^0/_0$ corresponds on the dissociation curve to $\cdot177\,^0/_0$ of CO, the oxygen tension of the blood was $\frac{49\cdot7}{177} \times 20\cdot9 = 48\cdot1\,^0/_0$ of an atmosphere. Corrected for aqueous vapour this becomes $46\cdot2\,^0/_0$.

No. 2.   *Experiment on grey linnet in air containing a high percentage of oxygen.*

The bottle containing the animal was ventilated in the manner already described with a mixture of air and gas from a cylinder of compressed oxygen (Brin's). This gas contained about $88\,^0/_0$ of oxygen. The CO was added in the ordinary way to the current of air, and a sample from a bottle placed between the animal chamber and the meter was taken for analysis.

| Readings of burette delivering CO. | | Readings of meter. |
|---|---|---|
| 1.54 | 69·2 | |
| 1.55 | 68·25 | |
| 1.56 | 67·3 | 1 litre in 81″. |
| 1.57 | 66·4 | |
| 1.58 | 65·45 | |
| 1.59 | 64·5 | 1 ,, ,, 81″ |
| 2.0 | 63·6 | |
| 2.1 | 62·65 | |
| 2.2 | 61·75 | 1 ,, ,, 81″ |
| 2.3 | 60·85 | |

| Readings of burette delivering CO. | | Readings of meter. |
|---|---|---|
| 2.4 | 59·9 | |
| 2.5 | 59·0 | 1 litre in 81″ |
| 2.6 | 58·05 | |
| 2.7 | 57·15 | |
| 2.8 | 56·25 | |
| 2.9 | 55·35 | |
| 2.10 | 54·45 | 1  ,,  ,,  81″ |
| 2.11 | 53·5 | |
| 17 | 15·7 | = ·74 litres per minute. |
| | ·924 | |

$$\therefore \text{ percentage of CO (uncorrected)} = \frac{·924}{7·4} = ·125.$$

*Analysis of sample of CO from the burette.*

Volume taken        17·26
After $CO_2$ absorbed 17·26
$\therefore CO_2 =$    ·00
After $O_2$ absorbed   17·055
$\therefore O_2 =$    ·205 $= 5·7 °/_0$ of air.

$\therefore$ the true percentage of CO was ·118.

Titration of the blood solution (centrifugalised).

A.  Up to tint of animal's blood.

·7 c.c. not quite enough.
·9 c.c. right
1·1 c.c.  ,,  } $=1·0.$
1·3 c.c. slightly too much.

B.  Up to tint of same blood saturated with CO.

7·3 c.c. not quite enough.
7·7 c.c. right
8·1 c.c.  ,,  } $=7·2.$
8·5 c.c. slightly too much.

$\therefore$ saturation $= \frac{1}{6} \times \frac{132}{7·9} = 27·2 °/_0$.

Corrected for dissociation $= 27·5$.

As $27·5 °/_0$ corresponds on the dissociation curve to $·026 °/_0$ of CO the oxygen tension of the blood was $\frac{·118}{·026} \times 20·9 = 94·8 °/_0$ of an atmosphere. Corrected for aqueous vapour (at 42°) in the alveolar air this becomes 87·2.

*Analysis of gas from ventilation current.*

Volume taken        14·21
After $CO_2$ absorbed 14·16
$\therefore CO_2 =$    ·05
After $O_2$ absorbed   7·69
$\therefore O_2 =$    6·47 $= 45·5 °/_0$.

No. 3. *Experiment on mouse in an atmosphere at low pressure.*

During this experiment, which was arranged in the manner already described, a constant negative pressure of 195 mm. of mercury was (after the first few minutes) maintained. The barometer stood at 755 mm., and the pressure gauge at 560 mm. The bath was kept at about 28°. Between 11.20 and 11.30 the pressure was gradually reduced to 210 mm. The delivery of carbonic oxide was begun at 11.32. At this time the animal showed marked loss of power over the limbs. The respirations were 172 per minute, and not very deep. The skin seemed slightly blue.

| Readings of burette delivering CO. | | | Readings of meter (continuous observations of time required for one revolution, which was = ·50 litres). |
|---|---|---|---|
| 11.33 | 95·6 | | |
| 36 | 94·65 | Pressure now reduced to 195 mm. | ·50 in 2′ 50″ |
| 40 | 93·4 | Mouse fairly well: sitting up. Resps. 180. Not blue. | ,, ,, 2′ 48″ |
| 46 | 91·6 | | |
| 49 | 90·72 | | ,, ,, 2′ 56″ |
| 52 | 89·9 | | ,, ,, 2′ 56″ |
| 55 | 89·05 | | ,, ,, 2′ 58″ |
| 58 | 88·2 | | ,, ,, 3′ 0″ |
| 12.4 | 86·55 | Mouse as before. Resp. 160. | ,, ,, 3′ 0″ |
| 10 | 84·95 | | ,, ,, 3′ 0″ |
| 14 | 83·9 | | ,, ,, 3′ 3″ |
| 19 | 82·65 | | ,, ,, 3′ 3″ |
| 23 | 81·65 | As before. Resp. 150. | ,, ,, 3′ 6′ |
| 25 | 81·15 | | ,, ,, 3′ 7′ |
| 28 | 80·35 | | ,, ,, 3′ 9″ |
| 32 | 79·35 | | ,, ,, 3′ 8″ |
| 35 | 78·55 | | ,, ,, 3′ 11″ |
| 39 | 77·6 | | ,, ,, 3′ 12″ |
| 41 | 77·1 | | ,, ,, 3′ 12″ |
| 44 | 76·5 | Skin quite pink, and not blue. | ,, ,, 3′ 15″ |
| 47 | 75·6 | Resp. 150. Hyperpnœa scarcely noticeable, and breathing looks about normal. | ,, ,, 3′ 16″ |
| 52 | 74·3 | | ,, ,, 3′ 18″ |
| 58 | 72·8 | | ,, ,, 3′ 17″ |
| 1·2 | 71·8 | | ,, ,, 3′ 17″ |
| 5 | 71·05 | Creeps about; and seems quite as | ,, ,, 3′ 17″ |
| 30 | ⎰7·5 | lively as at beginning of experiment. | |
| | ·25 | Skin quite pink. | ∴ ventilation = ·152 litres |
| | | Killed at 1.7. | per minute. |

The percentage of CO (uncorrected) was thus $=\dfrac{\cdot 25}{1\cdot 52}=\cdot 164\,^0/_0$.

*Analysis of CO from the burette.*

Volume taken    16·80
After $CO_2$ absorbed 16·80
    ∴ $CO_2=$    ·00
After $O_2$ absorbed    16·67
    ∴ $O=$    ·13 $=6\cdot 2\,^0/_0$ of air.

∴ the true percentage of CO was ·158 $^0/_0$.

Titration of the blood solution.

A.  Up to tint of animal's blood.

<div style="display:flex">

**No. 1.**

2·5 not quite enough.

$\left.\begin{array}{l}2\cdot7 \text{ right} \\ 2\cdot9 \quad ,, \end{array}\right\} = 2\cdot8.$

3·1 slightly too much.

**No. 2.**

2·5 not quite enough.

2·7 right.

2·9 ,,

3·1 slightly too much.

</div>

B.  Up to tint of same blood saturated with CO.

<div style="display:flex">

8·6 not quite enough.

$\left.\begin{array}{l}9\cdot0 \text{ right} \\ 9\cdot4 \quad ,, \end{array}\right\} = 9\cdot2.$

9·8 slightly too much.

8·3 not quite enough.

$\left.\begin{array}{l}8\cdot7 \text{ right} \\ 9\cdot1 \quad ,, \\ 9\cdot4 \quad ,, \end{array}\right\} = 9\cdot1.$

9·9 slightly too much.

</div>

$$\therefore \text{ saturation} = \frac{2\cdot8}{6\cdot8} \times \frac{14\cdot2}{9\cdot2} = 55\cdot4 \,^0/_0. \qquad \therefore \text{ saturation} = \frac{2\cdot8}{7\cdot8} \times \frac{141}{91} = 55\cdot6 \,^0/_0.$$

$$\text{Mean} = 55\cdot5.$$

$$\text{Corrected for dissociation} = 56\cdot6 \,^0/_0.$$

As 56·6 corresponds on the dissociation curve to ·091 $^0/_0$ of CO, and as the pressure was 195 mm., and the tension of aqueous vapour in the alveoli 46 mm., so that the alveolar tension of CO was $\cdot158 \times \dfrac{195 - 46}{760} = \cdot0310$, the arterial oxygen tension was $20\cdot9 \times \dfrac{\cdot031}{\cdot091} = 7\cdot1 \,^0/_0$ of an atmosphere.