XIX. *Observations on the Theory of Respiration.* *By* William Stevens, *M.D. D.C.L. Fellow of the Royal College of Physicians in Copenhagen, Fellow of the Royal College of Surgeons in London, &c. &c.* *Communicated by* W. T. Brande, *Esq. V.P.R.S.*

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The cause of the dark colour of the blood in the venous circulation has long been a subject of discussion; but even at the present moment the question has not been satisfactorily decided.

It is universally admitted that the expired air contains carbonic acid, but it is still doubtful in what part of the system this acid is formed. Lavoisier maintained that carbon was the cause of the dark colour of the venous blood, and that the acid was formed in the pulmonary organs, by the combination of that carbon with the oxygen of the air. At one period this theory was generally adopted, though the evidence in its favour is almost entirely hypothetical; for hitherto there has not been even one well-conducted experiment which proves the existence of any form of free carbon in the venous blood.

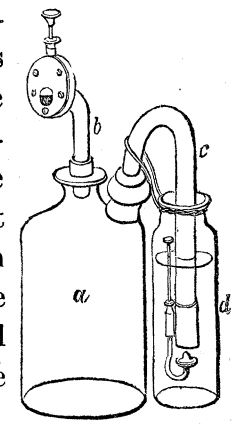
Another class of physiologists maintain that the carbonic acid is formed, not in the lungs, but in the general round of the great circulation; in proof of which some experimentalists have asserted that they had obtained carbonic acid from venous blood; but others, of equal respectability, who have repeated the same experiments, deny the existence of this acid in the venous current. The air-pump has hitherto been almost exclusively used for the purpose of deciding this question; but the positive proofs which have been brought forward by the one class of physiologists have been so completely contradicted by the negative proofs of the other, that a great majority remains still in favour of the old theory. In fact, Tiedemann and Gmelin, the latest writers on this subject, are decidedly of opinion that venous blood does not contain carbonic acid. As this is a very important question, the following experiments were made in reference to it.

1. A glass vessel containing a small quantity of warm and fluid venous blood was put under the receiver of an air-pump. In proportion as the air was exhausted, a number of globules appeared to escape from the blood, which were at first small, but in proportion as the air was removed they became larger in size.

2. A small quantity of venous blood, contained in a glass vessel, was covered with a layer of barytic water. This was put under the receiver of an air-pump. When the

pump was used, globules were observed to escape from the blood, which passed through the barytic water, but the transparency of the latter was not affected.

The annexed sketch is a representation of an apparatus which was invented by Mr. Squire, of Duke Street, Grosvenor Square, and used in the following experiments. To a double-necked pint bottle, *a*, two glass tubes were fitted, one, *b*, ascending, the other, *c*, descending. The ascending tube is terminated by an air-tight box, having an aperture, over which a slide is moved by means of a strong wire. The descending tube is terminated by a brass orifice, which is closed at pleasure by a brass cap, having a cone in the centre surrounded with leather, and moved with a sliding wire. *d* represents a four-ounce phial with a loop of wire round the neck, by which it is connected with the descending tube. The phial was filled to the double line with distilled water.



3. The pint bottle and both tubes being filled with pure hydrogen gas, the orifice of the upper tube was placed on the skin, near the bend of the arm; a vein was then opened, and the orifice slid carefully along until it included the incision which had been made by the lancet. The valve was opened, and as the blood passed into the bottle, hydrogen was expelled through the descending tube, the orifice of which was immersed in distilled water. As soon as five or six ounces of blood had entered the bottle, both the orifices were carefully closed. The orifice of the descending tube was then immersed in barytic water, and the valve being opened, the whole was placed under the receiver of an air-pump. In proportion as the air was removed, the hydrogen, as well as any gas that might escape from the blood, passed through the barytic water, without, however, producing the slightest change in its transparency.

From the first of these experiments it might be inferred that a gas is capable of being removed from venous blood by the air-pump: but this supposition may possibly be erroneous; for similar globules appear to arise when we use water, even after it has been boiled and then cooled in a close vessel to 98°. The second experiment shows that this appearance is not due to the escape of carbonic acid; and from the third experiment it is very obvious that carbonic acid cannot be so obtained from venous blood which has not been exposed to air.

4. About four ounces of serum were put into a Hope's eudiometer, the upper division of which contained four tenths of a cubic inch of carbonic acid: they were agitated together, and after a few minutes the serum had absorbed the whole of the acid. This impregnated serum, without being exposed to the air, was transferred into the double-necked pint bottle, which had previously been filled with hydrogen, and which was immediately put under the receiver of the air-pump. When the pump was used, the hydrogen, as well as the gas which appeared to escape from the serum, passed through the barytic water; but its transparency was not affected.

From this experiment it is obvious that serum (consequently blood or other albuminous fluid,) may absorb carbonic acid, and so retain it as not to be separable by the mere removal of the pressure of the air.

The air-pump has hitherto been used almost exclusively by the experimenters on venous blood; and those who deny the existence of carbonic acid in it, do so almost entirely on such evidence. The fact of their not having thus obtained this gas is correct; but there is an error in the conclusion drawn from it, which is the chief cause of the difference of opinion on this subject; for such experiments only afford a positive proof that carbonic acid cannot always be obtained from blood placed under the exhausted receiver of the air-pump: but, with respect to the existence or non-existence of such acid in the blood, the proof is merely negative; for in experiment 4. the pump did not separate carbonic acid from serum previously impregnated with it: consequently such experiments are inconclusive.

5. Carbonic acid was introduced into an empty bladder that had been previously well moistened with warm water. When the bladder was distended about one third, its neck was firmly tied with a waxed thread, by which it was suspended in the centre of a receiver of an air-pump. When the pump was worked, the bladder increased in volume, and in a few seconds was much distended. Nearly the whole of the atmospheric air was exhausted from the receiver, but the bladder, though apparently very tense, did not burst, neither did it decrease in size. A shallow glass vessel containing barytic water had been placed under the same receiver, but the transparency of this was not affected. Hydrogen was then transmitted into the receiver, and the bladder was reduced to the same size as when first suspended under it; but, after an interval of four hours, it had become perfectly flaccid. In fact, there was scarcely a particle of carbonic acid left in it, and the barytic water within the receiver contained a quantity of carbonate of baryta.

6. The double-necked bottle was carefully filled with pure hydrogen, and about five ounces of blood were drawn into it from a vein in the arm, in the same manner as in experiment 3. Both the orifices of the bottle were then closed, and the blood and the hydrogen well agitated together. After this the lower orifice was immersed in distilled water, and the bottle left undisturbed for nearly an hour, to allow the hydrogen to act on the blood. The orifice of the descending tube was then immersed in barytic water, the lower valve was opened, and the whole apparatus put under the receiver of the air-pump. When the pump was used, the gas which was over the blood passed through the barytic water, and immediately rendered it turbid. This experiment seems to prove that venous blood does contain carbonic acid; and as the only difference between experiments 3 and 6 was, that in the former the pump was used *immediately*, and before the hydrogen had time to act on the blood, whilst in the latter the hydrogen was allowed to act nearly an hour, it would appear that the hydrogen has some power of removing the carbonic acid, and that this removal may even take place through a membrane. In the last experiment, the blood which was

used had been carefully excluded from atmospheric air, and the hydrogen was pure; consequently the carbonic acid could have been derived from no other source than the venous blood itself.

7. A few ounces of venous blood were drawn into a double-necked bottle previously filled with hydrogen. After having been gently heated, the hydrogen was found to contain carbonic acid. This experiment was made at Copenhagen in the beginning of 1833, by Professor FORCHAMMER and myself; but the conclusion which *we drew from it respecting the existence of carbonic acid* in the blood was by some objected to, in consequence of the interference of *heat*: the air-pump experiments, however, remove all such objections.

Dr. EDWARDS confined some animals in an atmosphere of hydrogen, and they continued to live for a considerable period, during which it was found that the hydrogen had acquired a portion of carbonic acid, which in some cases was equal in bulk to the size of the animals. By some these experiments were considered as conclusive of the evolution of carbonic acid from venous blood; but others maintained that there might have been a sufficient quantity of oxygen in the pulmonary cells to account for the formation of the carbonic acid. This objection is also removed by the above experiment.

Dr. MITCHELL of Philadelphia made an experiment in 1830 with hydrogen and venous blood, but without obtaining any carbonic acid. Mr. G. H. HOFFMAN of Margate made a similar experiment in 1832, and obtained a sufficient quantity of carnic acid, not merely to render lime water turbid, but even to render the hydrogen uninflammable. These contrary results seem to me to have arisen from Dr. MITCHELL having used the air-pump *immediately*, and before the hydrogen had time to act on the blood so as to displace its carbonic acid; whereas Mr. HOFFMAN agitated the hydrogen with the blood, and probably allowed a sufficient time for their mutual action.

8. A small quantity of venous blood was drawn into the double-necked bottle, containing atmospheric air, the valve at the orifice of the ascending tube was closed, and the orifice of the descending tube was immersed in barytic water. The bottle was put under the receiver and the pump immediately used. But in this experiment the barytic water was not more affected than it would have been by a similar quantity of common air. This proves that when the blood is exposed even to common air, carbonic acid cannot be obtained, when the pump is used immediately, and before any change of colour in the blood has taken place; that is, before the air has had time to act upon it.

9. A small quantity of blood was drawn into the double-necked bottle containing atmospheric air, as in the last experiment. Both of the valves were closed, and *after agitation, the bottle was allowed to stand about an hour, during which the colour of the blood changed from venous to arterial.* The lower orifice was then immersed in barytic water, the apparatus was put under the receiver of the air-pump, and when the pump was used, the gas which escaped *gave a milky appearance to the barytic*

water. In the eighth experiment the pump was used immediately, and before the air had time to act on the blood, or the blood on the air. In the last, one hour was allowed for the action of these agents upon each other; during which the blood on the surface changed from venous to arterial, and the air over the blood received the addition of carbonic acid.

Those who maintain that carbonic acid is *formed* in the lungs will say, that in the last experiment the carbon of the blood attracted the oxygen of the air, and that the carbonic acid so formed was then evolved. But there is one circumstance which is I think fatal to such an explanation, for all the acids blacken the blood, and carbonic acid possesses this blackening property in a remarkable degree. When we agitate a small quantity of carbonic acid gas with arterial blood, the colour immediately changes to venous, and when we add carbonic acid to venous blood it becomes almost black. Now, if the carbon of the blood attracted the oxygen of the air, and if the carbonic acid were thus formed in the blood itself, it is evident that the *first* effect of the air on the blood would be to make this fluid blacker than it had been before; but the opposite of this is the fact, for the *first* effect of the air is, not to blacken, but to brighten the blood; consequently, from this alone, we may infer, that the acid is not formed during the experiment, but that it exists ready formed in the blood, and that it is only removed, and not produced or formed, by the atmospheric air.

I have already observed that one class of experimenters have obtained results by means of the air-pump which are in direct opposition to those obtained by others. May we not now, from the above experiments, explain this difference by supposing that those who could not obtain carbonic acid made their experiments before the air had had time to act on the blood, whilst the others had allowed some time to elapse?

From the preceding statement we may, I think, conclude,

1st, That venous blood contains carbonic acid;

2nd, That the mere effect of diminished pressure upon the surface of the blood is not necessarily followed by the escape of its carbonic acid*.

We have seen in some of the above experiments that atmospheric air possesses a property of removing carbonic acid from venous blood; it becomes therefore a question how this effect is produced. I have ascertained that nitrogen is ineffective; we may therefore infer that the oxygen is the principal agent; and that such is the fact is proved by the following experiments.

10. A piece of moist bladder was tied firmly over the mouth of a tumbler containing pure oxygen gas. This was introduced into a large bell glass filled with carbonic acid. In a short period the membrane which had been tied over the glass became convex, and so tense that it appeared to be on the point of bursting. On examining the air contained in the tumbler, it was found that the oxygen had drawn in a large

* In performing the above experiments I was assisted by Mr. Squire, to whom I feel under great obligation for the zealous and able manner in which he aided me in the whole of the present investigation.

quantity of the carbonic acid; but no oxygen appeared to have passed out of the tumbler.

11. A piece of moist bladder was tied over the mouth of a tumbler containing carbonic acid; this was introduced into a bell glass filled with pure oxygen. In a short period the membrane became concave, and the oxygen in the larger vessel was found to be mixed with carbonic acid.

These two experiments prove that oxygen possesses the power of attracting carbonic acid, even through the medium of a membrane which is much denser than that interposed in the lungs betwixt the air and the blood; consequently, the extreme delicacy of the pulmonary membrane can be little impediment to the transmission of carbonic acid in the process of respiration.

I have ascertained that such transmission, or, in other words, the peculiar power by which oxygen abstracts carbonic acid from the blood, is more energetic in a high than in a low temperature. Hence venous blood drawn in a warm room changes colour more rapidly than blood drawn in a cold atmosphere.

12. A few ounces of venous blood were drawn into the double-necked bottle which had been previously filled with pure oxygen; the valves were closed, the blood was well agitated with the gas, and the colour immediately changed from venous to arterial. The bottle was allowed to stand about half an hour, and was then placed under the receiver of an air-pump. When the pump was used the oxygen was found to be strongly impregnated with carbonic acid; in fact, the first bubbles of air which passed through the barytic water rendered it milky.

From the rapidity of the change of colour from venous to arterial, or from dark to florid, in this experiment, it seems very improbable that any carbonic acid should have been *formed* in the blood, but that, on the contrary, it had previously existed in the blood, and that the whole of this blackening gas had been instantly removed by the oxygen.

13. A piece of the intestine of a rabbit that had been recently killed was filled with *carbonic acid*, and suspended in a bell glass containing *oxygen*. In a short period the acid escaped, and the intestine became quite flaccid.

14. A piece of intestine, similar to that used in the last experiment, was filled with *oxygen*, and suspended in a bell glass of *carbonic acid*; the intestine began to swell almost immediately, and in three minutes it burst.

15. The *lung* of a rabbit was filled with oxygen, and suspended in a bell glass of carbonic acid; it began to swell almost instantly, and in one minute it burst.

16. The *lung* of a rabbit was carefully inflated with carbonic acid, and was then suspended in a bell glass of oxygen. In a very short period it became flaccid, and the external oxygen was impregnated with carbonic acid.

These experiments show how admirably the structure of the lungs is adapted for the action of oxygen on carbonic acid. Vitality may have some share in accelerating this process in the pulmonary organs, but we know that by the agency of oxygen dead blood may be changed from venous to arterial, even through a dead membrane.

This power which gases possess of acting on each other is in some respects similar to that which takes place in fluids, and which has been described by DUTROCHET under the name of *endosmosis* and *exosmosis*. In the experiments detailed by this philosopher the intervening septum is supposed to contribute materially to the phenomena. In the experiments with gases the intervening membrane does not prevent, but it does not contribute to, the change. But independent of this, the existence of this power in gases was not known to DUTROCHET until after the fact had been fully ascertained by others. Mr. DALTON many years ago proved that hydrogen possessed the power of penetrating or mixing with carbonic acid in opposition to gravity; that oxygen possesses the same property, but in a higher degree, I ascertained in the island of St. Thomas in 1827. I afterwards made experiments on a larger scale, in 1830, at the high rock of Saratoga, where there is an atmosphere of natural carbonic acid; and the result was communicated to many physicians in America previously to any of the American publications on the subject.

It is now more than probable that the changes which LAVOISIER believed to occur in the lungs take place in reality in the extreme circulation. Some later writers have assumed that the elements of carbonic acid exist in the blood, and that its formation commenced in the large vessels as they leave the left side of the heart, and was not finally completed until the blood arrives in the right auricle. But that this opinion is erroneous, is evident from the fact, that the blood even in the smallest arteries is as completely *arterial* as that in the left side of the heart, whilst the blood in the smallest veins is equally *venous*.

There is in the capillary system, over the whole body, an intermediate structure which connects the arterial with the venous circulation, and it is in this structure that the blood is changed from arterial to venous. When the arterial blood leaves the minute arteries, it is no longer confined in actual vessels, but in cells that are formed by the surrounding tissue. When this cellular structure is examined in living animals, with the assistance of a good microscope, minute globules are seen to leave the cells and penetrate the surrounding solids, whilst other globules are seen to return and mix with the blood in the cells. Now as we know that it is in these cells that the blood becomes dark and venous, from the addition of carbonic acid, may we not suppose that the globules which leave the blood are minute particles of oxygen, attracted perhaps from the arterial blood by the fixed carbon of the solids, and that the globules which return are minute particles of carbonic acid? This cannot be easily proved; but as carbon is a principal ingredient in the solids when these are converted into fluids, previous to their removal by the lymphatics, it appears to me not improbable that a part of their carbon may be liberated, perhaps for the purpose of evolving heat. We have seen that the blood which receives oxygen in the lungs passes unchanged through the arteries into the capillary system; and it is apparently there that animal heat is evolved. When carbonic acid, which is the result of the above process, is added to the venous blood, it not only blackens the colour, but renders it incapable of supporting life. For this reason warm-blooded animals have a double circulation, one for circulating the arterial, and another for purifying the venous blood*.

When we obtain *hæmatosine*, or the colouring matter of the blood, in a pure state, it is black; but a solution of any neutral salt possesses the peculiar property of striking a beautiful scarlet or arterial colour with it. When we make an incision into a clot of blood which has just coagulated, we find that the clot is then all equally red: when we cut out a thin slice of this red clot, and immerse it in distilled water, the salt serum oozes into the water. In proportion as this takes place the clot becomes darker; and when the whole of the serum is removed, perfectly black. When in this state neither atmospheric air, nor even pure oxygen, is capable of changing its colour; but when we immerse this black clot in a clear saline solution, it instantly changes from jet black to a scarlet, or arterial colour. From these facts we may conclude, that oxygen is a secondary agent in the change of colour from venous to arterial; and that if the scarlet colour of the blood be essential to life, it is produced, not by oxygen, but by another cause. The mere removal of the carbonic acid from venous blood would not produce any change of colour, were it not that there is in the blood itself another agent which produces the arterial tint, the moment that the blackening effect of the carbonic acid is removed: this is effected by the action of the natural saline ingredients of the blood on the colouring matter. When oxygen is added to blood it may have a slight share in brightening the colour, but it can only perfectly effect this when the colouring matter is in contact with a saline fluid. Oxygen is so far from being the sole cause of the arterial colour, that even pure oxygen is *of itself* inert as a colouring agent; whilst a saline fluid changes the colour of the blood from venous to arterial even in an atmosphere of carbonic acid.

Many authors describe the changes which occur in respiration, by asserting "that oxygen disappears, and carbonic acid is emitted." But from some of the experiments which I have detailed, it is evident that the removal of the acid is the first part of the process, and the addition of oxygen the last. Others have maintained that when

* It is well known that cold-blooded animals use very little food. If a rattlesnake gets one good meal in three months, it is all that he requires: but even this is not actually necessary; for I have seen one of these animals that had not tasted food or water for twelve months, as plump, active, and venomous as those in the wild state. On the other hand, all those animals that have warm blood require an immense quantity of food, and if they do not receive this they soon perish; but nineteen twentieths of this appears to be taken into the system for the evolution of animal heat. The carbon is ultimately derived from the nourishment that we use, and the oxygen is directly derived from the arterial blood: a constant supply of nourishment is therefore necessary in warm-blooded animals, but a very small part of the blood which is formed from this is required for nutrition, and if the whole of it were expended in this way, it is very clear that there would be none left to return by the veins.

two gases act upon each other, the one penetrates the membrane at the same moment that the other is removed. But if this were the case, why did the membrane become *convex* in experiment 10, and *concave* in experiment 11? If the action were equal, the membrane would remain unchanged; but this is so far from being the case, that in some experiments the membranes became distended to such an extent that they actually burst.

It was supposed by Spallanzani, and afterwards by Dr. Edwards, that in the process of respiration the carbonic acid was merely exhaled from the lungs. We have seen, however, that venous blood so retains that acid that it cannot be removed, even with the aid of an air-pump; consequently, were there not an active agent for the purpose of removing the carbonic acid from the venous blood as it circulates through the lungs, it would remain unchanged, and almost instantly cause death. It is the power which oxygen possesses of attracting carbonic acid, which renders oxygen essential to life. As hydrogen also possesses this power, it supports life for a longer period than most of the other gases; but hydrogen has a deleterious effect on the blood; and when animals are forced to breathe it, though the carbonic acid is removed, a part of the hydrogen is at the same time absorbed, which blackens the blood, and the animals soon die.

The property which oxygen possesses of attracting carbonic acid, furnishes the following explanation of the process of respiration. When the venous blood arrives in the lungs, the oxygen of the atmosphere is, in the first instance, the active or attracting agent. It removes the carbonic acid, which had been the cause of the dark colour of the blood. When this is removed, or perhaps in proportion as it is removed, the blood becomes the attracting agent, and a portion of oxygen is attracted into the blood, and takes the place of the carbonic acid. From the peculiar structure of the lungs, these changes are rapidly effected, particularly at the high temperature of 98°; and when the process is fully completed, we know from the great discovery of Harvey, that the blood which has received the pure air passes rapidly on to the arterial, and from this again to the capillary system.

If the above theory be correct, it follows that the blood is converted from arterial to venous in the extreme circulation, by the loss of oxygen and the addition of carbonic acid; whilst the venous blood is converted into arterial, by the loss of carbonic acid, and the addition of oxygen; consequently, the essential difference betwixt venous and arterial blood is, that the former contains carbonic acid, and the latter oxygen.

I have said that black is the natural colour of the colouring matter; but when this agent is diffused in a saline fluid, such as the serum, it is of a bright scarlet tint, which is, in fact, the natural colour of arterial blood. When carbonic acid is added to this blood in the extreme circulation, it becomes dark red; but when this acid is removed in the pulmonary organs, the blood then resumes its natural scarlet or arterial colour; and this, as I have said, is produced not directly by oxygen, but chiefly, if not entirely, by the action of the salts of the blood on the colouring matter.

Oxygen, it is true, changes the colour from venous to arterial; this, however, is effected not by any specific action, but by the removal of the carbonic acid, which had been the cause of the dark colour in the venous circulation.

Many objections have been made to the above theory, some of which are frivolous; but there are two which are worthy of notice. The first was made by Mr. PRATER of Edinburgh, who stated, that according to this theory the blood ought to become *arterial* under the exhausted receiver of the air-pump. This objection is removed by the foregoing experiments, which prove that the mere removal of the air's pressure is insufficient to overcome the attraction that subsists between the carbonic acid and the blood. The second objection was made by Dr. GREGORY and Mr. IRVINE of Edinburgh. These gentlemen admit that if the blood were a stronger saline fluid than it is, the salts would be capable of producing all the effects described; but they conceive that the blood is not sufficiently impregnated with saline matter to account for the whole of the phenomena. This objection, even if proved, would only require a modification of the theory; but that there was a fallacy in their experiments which neutralized their conclusion, has been proved by a paper in the Medical Gazette of the 12th of April, 1834.