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ACTION OF ANÆSTHETICS ON THE BLOOD CORPUSCLES.

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In the October number of the Dental Cosmos a report was presented of a series of experiments performed by me, on a number of animals, with the view of ascertaining whether the assertion made by a distinguished experimentalist and scientist of England, that nitrous oxide, even under the most delicate manipulation, would prove destructive to life, could be possible. These experiments, which clearly demonstrated the assertion to be unfounded, were not performed in private, but in the presence of a number of gentlemen whose experience in the use of anæsthetics and whose scientific knowledge made them competent judges. First performed before the members of the Odontographic Society of Pennsylvania, they were repeated, after an interval of three weeks, on the same animals, in the presence of the members of the Biological and Microscopical Department of the Academy of Natural Sciences.

A month subsequent to the last-named occasion, one of *these animals*, a rabbit, in the presence of a number of gentlemen, was placed under the influence of nitrous oxide, and kept in a profound state of narcosis for *one hour and five minutes*, by alternating atmospheric air and nitrous oxide, removing the inhaler ever and anon for that purpose. Without question the animal could have been kept in the same condition double or treble the time without injury to it, for in a few minutes after removing the anæsthetic entirely, the animal was restored to consciousness, and leaped from the table to the floor, and for a number of weeks after this ran about my premises in a healthy and lively condition, and no doubt would have been still alive had I not demonstrated on him before the students of the Philadelphia Dental College the absorption

of fats by the lacteals of the villi of the intestines, below the duct of the pancreas, and also the action of the heart and lungs; necessitating as this did opening into the abdomen and thorax, life of course became extinct.

When under the prolonged influence of nitrous oxide referred to, one of the blood-vessels of this animal was opened for the purpose of examining the blood corpuscles under the microscope, and ascertaining whether they had become disintegrated or any change had taken place in their form. On examination no perceptible difference was observable even after this lengthened exposure to the anæsthetic, when compared with the blood of another rabbit, which was not under its influence. This result induced me to examine into the statements made by Dr. Sansom, relative to the action of anæsthetics on the blood corpuscles in his highly interesting and able work on chloroform.*

Prior to giving a description of my experiments in this direction, it may be proper to briefly refer to the prevalent theories on the physiological action of anæsthetics; also to the experiments performed and conclusions arrived at by Dr. Sansom. The view generally entertained is that first suggested by Flourens, that these agents act directly upon the nerve centres, producing regular and progressive modifications in the functions of the brain and spinal axis, first affecting the cerebral hemisphere, then the power of co-ordination in the cerebellum, then the conduction of sensation and motion in the spinal cord, and lastly, if the agent is pushed so far as to decidedly impress the medulla oblongata, suspension of respiration and circulation.

Dr. John Snow, regarding this theory as an erroneous one, and recognizing ether, chloroform, and other anæsthetics as non-supporters of combustion, advanced the theory that these agents interfering with the introduction of oxygen into the system, induced their effect by the suspension of oxygenation, he therefore asserted that "narcotism is suspended oxygenation." This view is embraced and strongly advocated by Dr B. Ward Richardson (the friend, biographer, and editor of his work on "Chloroform and other Anæsthetics"), and in England, apparently, is being very generally adopted by writers on this subject; Dr. Kidd, who has devoted much attention to the study of the action of chloroform, is, however, a prominent exception.

Dr. Sansom, accepting this theory, and knowing that nitrous oxide is not only an anæsthetic but a supporter of combustion, recognized the necessity of presenting something more conclusive in the support of the view, than had heretofore been offered. He therefore in a paper read before the Royal Medical and Chirurgical Society, in 1861, as the result

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* Chloroform, its Actions and Administrations. By Arthur Ernest Sansom, M.B., London: Lindsay & Blakiston, Philadelphia.

of certain experiments performed on the blood corpuscles of man and animals out of the body, attributed the influence exerted by anæsthetics on the nervous system to their acting directly upon the blood corpuscles, by modifying their form and integrity, and indirectly upon the nervous system through this altered condition of the blood, by interfering with its oxygenation. In his work he describes a series of six experiments; placing on glass slides, under a quarter-inch object-glass, human and frog's blood, and subjecting them to the *direct contact* of alcohol, ether, and chloroform, which resulted quickly in the disintegration of the blood corpuscles, leaving nothing but their nuclei and débris of the walls of the corpuscles. From these experiments on blood *out of the body*, he states in the work referred to: "The effect therefore of these agents upon the blood is solution — destruction. At first there is a change induced in the cell itself and upon the nucleus (in the case of frog's blood). The globuline of the blood is acted upon as it were by a caustic. Finally the old corpuscle is destroyed and its coloring matter set free." * * * From the foregoing facts and other considerations, the author considers that certain conclusions in regard to the action of anæsthetics are warrantable. Anæsthetics are agents which when absorbed into the circulation exert an influence upon the blood. They are shown to have the power of altering its *physical character* and *physical properties*. By an action upon its constituent (proteinous) elements, they tend to alter and by a profounder action to destroy its organic molecules. Its physical perfection being interfered with, its function is held in abeyance; the changes which contribute to constitute perfect life are retarded. Narcosis ensues; and is due, not to the influence of a circulating poison, but to the influence of an altered blood. Further on he adds: "Narcotism (or to speak more particularly, chloroform narcotism) is due not to a special poison that 'mounts up to the brain,' but to an altered blood. Then 'narcotism is a suspended oxygenation' Whatever produces to a certain extent insufficient aeration of the blood, produces narcosis; and whatever produces narcosis, produces by some means or other imperfect aeration of the blood."

In drawing these conclusions, of an altered condition of the blood, from appearances presented by the blood *out of the body*, Dr. Sansom evidently leaves it to be inferred that somewhat if not exactly analogous results are produced on the corpuscles *in the body*, when human beings or animals are under the influence of anæsthetics by inhalation. After a patient, oft-repeated series of experiments performed by me during the past three months, not only on blood out of the body, but also in cases in which human beings and animals have been placed under the influence of ether, chloroform, and nitrous oxide, and the blood drawn from them *prior* to and *after* the administration of these agents has been carefully *examined* and *compared*, the results obtained compel me

to take very decided exceptions to such conclusions being justifiable in the premises.

Fig. 1.

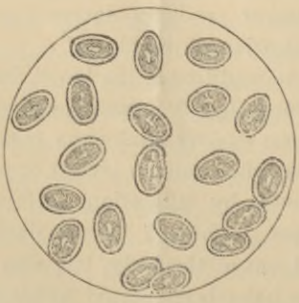
Frog's blood placed upon the slide, and chloroform brought in direct contact with it.

First Series.—The experiments were as follows: In my examinations of the blood of man and animals, when ether and chloroform were brought in direct contact with it out of the body, under a fifth objective, the discharge of the nuclei and the disintegration of the corpuscles have invariably occurred, and in the frog leaving a result similar to that which is presented in the accompanying drawing (Fig. 1), from one of my specimens, wherein it will be observed that the field is occupied by the nuclei, débris of disintegrated globuline and corpuscles, in which the change of form, size, and other characteristics are most striking.

Second Series.—On placing, however, two glass slides containing frog's blood over watch-crystals, one holding chloroform and the other ether, and covering them with glass finger-bowls for half an hour, thus exposing one to an atmosphere of ether, and the other of chloroform, I found, on removing the bowls, and permitting the bloody sides of the slides to remain downward, until all the ether and chloroform had evaporated, that no disintegration or marked change in the form of the corpuscles was observable under the microscope, on comparing them with the blood of a frog unaffected by an anæsthetic. This forcibly demonstrates the difference between exposure to *direct contact* and the *vapor* of chloroform, even out of the body.

Third Series.—Over and again in the presence of a number of gentlemen, I have placed frogs under the influence of ether, chloroform, and nitrous oxide, and examined their blood corpuscles immediately after without finding any disintegration or change in the form of the corpuscle. In one instance, a frog was so completely narcotized by chloroform that it died; the thorax of the animal was opened, the lungs cut out, and the blood obtained directly from that organ, and even here, where, if the inference of an altered blood was correct, there should have been discharge of nuclei, disintegration, or *marked* change in the form of the

Fig. 2.

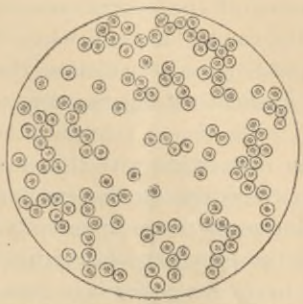


Corpuscles from the lungs of a frog which died under the influence of chloroform.

corpuscle, nothing of the kind was evident, as will be seen by the accompanying illustration, drawn from the slide on which the blood was placed. (Fig. 2.) As already intimated, the experiments in this direction have been prosecuted on every available occasion within the past few months; and I have not confined myself to frogs, but, in the course of vivisections on a large number of animals (rabbits, dogs, cats, and pigeons), to illustrate my course of lectures on physiology this winter, when these animals have been placed under the influence of ether or chloroform, their blood has been examined and no change in the form of the corpuscle has been evident.

Fourth Series.—The examination of the blood of a number of human beings, drawn prior to and after having been under the influence of ether, chloroform, or nitrous oxide, for the extraction of teeth, has yielded similar results, as will be evident from the accompanying illustration of the blood, obtained from a patient (Fig. 3), while under the influence of chloroform. Any one accustomed to microscopical examinations will recognize the normal characters of the corpuscles, so far as it is possible to present them in a wood-cut.

FIG. 3.



Corpuscles of a patient under the influence of chloroform.

The results of these investigations were recently presented to the members of the Microscopical and Biological Department of the Academy of Natural Sciences, illustrated by a large number of microscopical slides, and although some time has elapsed since the blood was placed on many of them, the corpuscles retain their form unchanged.

Presenting the statements for what they are worth, and desiring that others may either confirm or disprove them by experiments of their own, as carefully conducted and as frequently repeated, and not merely performing a few experiments and then drawing conclusions which they would not be warranted in doing, I would suggest to such that there are two modes of preparing blood for microscopical examination, each of which has been tried in my investigations. First plan—the blood, placed on a slide, is spread with a knife-blade thinly over the glass, then waving it backward and forward in the air, the blood is dried by evaporation, and can be covered with a thin glass slide, cemented, and kept for a considerable length of time without change. Second plan—a drop of blood is placed on the slide, a thin glass cover is brought in contact with the edge of the drop, and by capillary attraction, a stratum of blood is drawn under it. Although this answers for immediate examination, unless some men-

struum is employed for the preservation of the blood, its characteristics become so completely changed in the process of coagulation that the specimens become useless. In pursuing these investigations, care must be exercised to prevent the *direct contact* of ether and chloroform with the blood corpuscles, as this makes the greatest possible difference.

In conclusion, although it is not my intention in this communication to engage in an extended inquiry relative to how anæsthetics produce their effects, it seems to me that the above experiments demonstrate that we are not warranted in denying that these agents act directly upon the nerve centres. All the phenomena, indeed, attendant upon their administration, the gradual exaltation of the cerebral functions followed by the progressive impairment and temporary suspension of the special senses, the loss of co-ordination on the part of the cerebellum, and when the agent is pushed too far, the arrest of respiration and circulation through the decided impression made upon the medulla oblongata, seem to favor this hypothesis, in contradistinction to the theory that anæsthesia is due to suspension of oxygenation.

In connection with this, I cannot refrain from saying, when taking into consideration the readiness with which fluids absorb gases, that undue prominence apparently has been given by physiologists to the blood corpuscles as *the* carriers of oxygen to the tissues, and carbonic acid gas to the lungs, for it is reasonable *to infer that the liquor sanguinis is actively engaged in this operation.* After the most careful examination under the microscope, I have been unable to observe those modifications in the form of the corpuscles in venous and arterial blood, changing from biconvex to biconcave disks, and attributed to the absorption of the gases, of which so much is said in the books. That anæsthetics, when acting directly upon the nerve centres, may interfere with the oxygenation of the nervous mass, is possible, but it is to be viewed rather as an *effect* than as a *cause* of narcosis. Again, even admitting that such agents as chloroform and ether, by interfering with natural respiration and the oxygenation of the nervous mass, might possibly produce their result in that way, it is difficult to understand how this can be brought to bear upon an agent like nitrous oxide, which contains an excess of oxygen over atmospheric air. To those who may assert that nitrous oxide is a compound (and not a mixture like atmospheric air), and therefore incapable of decomposition and furnishing oxygen to the nervous mass, I would remind them of a law in chemistry, that when two compounds, the elements of which have a stronger affinity for each other than the compounds in which they exist, are brought in contact under favorable circumstances, a mutual decomposition occurs, and new compounds are formed in their place. It may be said that the conditions in the body are not favorable to such results; but who shall have the temerity to assert that, when recalling the incessant compositions and

decompositions of a chemical character taking place in the body, fully recognized and admitted by those who insist most upon the controlling influence of vitality? It is a well-known fact, that nitrous oxide is a supporter of combustion, and that a lighted candle burns with increased brilliancy in it; here the combination of the nitrogen and oxygen in definite proportion is not so strong but that the carbon of the candle is able to seize upon the oxygen, and augment the size of the flame. The function of respiration consists in a mere interchange of gases, of the exhalation of carbonic acid gas and the introduction of oxygen; the latter, absorbed by the blood, is carried to the nervous mass and other tissues, and results in their oxygenation, a slow form of combustion, which is but a difference in degree with the burning of the candle. If, then, the nitrous oxide, as can be readily demonstrated, yields up its oxygen to support the burning of a candle, where is the philosophy in denying that it may also as freely give up its oxygen to a tissue which has such a strong affinity for it as the nervous mass, when they are brought in direct contact with each other?

In addition to these arguments, it should be remembered by the readers of this magazine, that in cases of impending asphyxia from drowning, hanging, inhalation of noxious vapors, etc., on a part of a number of animals experimented upon by my friend and co-laborer, Dr. Geo. J Ziegler, animation was promptly restored in every case by the injection of nitrous oxide water into the intestines of the animals. In these cases the efficacy of this agent in supplying oxygen to the blood and the nervous mass was most satisfactorily demonstrated.

If we assume that the influence of anæsthetics is dependent not upon a direct action on the nerve centres, but to an altered condition of the blood and the suspension of oxygenation, we must apply the same principle to all diffusible stimulants.

In a forthcoming number of the magazine, I shall present a series of experiments of the results obtained from the *direct contact* of anæsthetics with the different portions of the nervous system.