PHYSIOLOGICAL ACTION

OF

NITROUS OXIDE,

AS SHOWN BY

EXPERIMENTS ON MAN AND LOWER ANIMALS.

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ANÆSTHESIA.

The term Anæsthesia, strictly speaking, means the absence of all sensation.

This state may be general or local, and may arise from cessation of the functional activity of any part of the nervous apparatus, concerned in the reception of sensory impressions; and this may be owing to causes acting upon the periphery of the sensitive nerves, or on the centres which originate the sensation, or by an interruption of the chain of communication between these extremes.

Now, it is evident that the peripheral extremities may cease their activity from three reasons, viz.:

1. Paralysis or temporary death of the nerve-substance;

2. Deprivation of the vitalizing power of the blood ;

3. Or from both of these causes.

¹ Read before the Boston Society for the Promotion of the Sciences connected with Medicine. April 5, 1870.

The first of these causes may be brought about by the local contact of some drug which interferes with the vitality of the nerve. Such a drug Dr. Richardson supposes ether.

The second cause is often seen in persons, in a limb in which the circulation of blood has been prevented, accidentally or from disease. Such, for instance, when the tourniquet has been applied for some time for the benefit of an aneurism, or when the artery has been occluded by embolism.

Anæsthesia may be, also, caused by a stagnation ' in the capillary circulation.

Cold, or refrigeration, may cause anæsthesia by producing stagnation of the blood in the small vessels, or by depriving the capillaries of blood. This is the explanation of muscular stiffness, caused by bathing in very cold water; on the contrary, when there are increased capillary circulation and enlargement of the blood-vessels, we obtain "pain, heat, redness, and swelling" of the so-called inflammation. I think it not at all improbable that reflex paralysis, caused by exposure to cold, is due to a partial obstruction to capillary circulation; and death by exposure to extreme cold causes loss of sensation, sleep, coma, and death.

Ligature, or severance of a nerve of sensation, destroys its function below the point of contact. Yet the lower portion will conduct a stimulus to the muscular tissue, and sensation, if the recurrent sensory fibres are intact. It is easy to understand that a tumor may so press upon a nerve as to prevent that nerve from conveying nervous impressions.

Cl. Bernard² has shown in some lectures, delivered a year ago, on the Physiological Action of Chloroform, that though a nerve appears to die from periphery to its centre, yet that the death occurs in the nervous centres, and from the trunk extends to the periphery. This he attempted to prove by preventing one portion of the body of frogs from communication except by lumbar nerves, and by tying the aorta high up, leaving the communication of the lower and upper half of the body merely by the nerves. Then the immersion of the lower or the upper half in chloroform and water $(\frac{1}{100})$ showed that

¹ Vide Todd's Cyclopædia of Anat. and Physiology. Anæsthesia.

² Gazette Hebdomadaire, 1869, p. 167 et seq.

the nervous centres had lost their functions, when the trunks could respond to a stimulus, while subsequently the peripheral branches would respond when the trunks could not perform their duties.

Bromide of potassium causes, by its influence upon the vaso-motor nerves, a diminution in the size of the capillaries, thus depriving the tissue of its proper supply of blood. In this way sensation is somewhat diminished, and as this occurs as well in the nervous centres, their functions are impaired to so great a degree as to cause sleep.¹ For a further proof that this is the effect of this drug, I would refer those interested to a paper² containing some experiments on this subject by myself a short time ago. It can easily be understood why this diminution of calibre in the capillary vessels may retard the circulation, so as to impair reflex action and sensibility.

I have not the space sufficient to a further examination into the conditions of the capillary system requisite to produce anæsthesia. I am now engaged in investigating these causes of anæsthesia, and in hopes of obtaining more positive knowledge with regard to them. I simply will call attention to the fact that this point of investigation has been rather neglected by experimenters.

Analgesia is a name given by M. Beau to the effect of insensibility to pain, which may exist without anæsthesia. This may be caused in the state of imperfect etherization or of chloroformization, without the loss of tactile sensation. This author considers that in Saturnine poisoning there is this insensibility to pain and also to tickling. In other words, the lead has so poisoned the nervous system that this will not convey sensory impressions.

We will pass to the consideration of the reflex properties of the nervous system, which is entirely different from muscular contraction and from pain. We may have analgesia, and yet preservation of reflex power. We may have muscular con-

¹ It is to be remembered, however, that wakefulness caused by continued anæmia of the brain would not be benefited by this drug; in fact, the wakefulness would be increased.

² Bromide of potassium and of ammonium. Publications of the Mass. Medical Society for 1869. tractions without necessarily reflex action. Simply stated, it is this:

When an irritation is applied to the periphery of the nervous system in a healthy body, the member irritated will be withdrawn. Sulphate of morphia will deprive an animal of *conscious* sensibility. If the foot be then tickled or pinched, the animal withdraws this member.

When a nerve is laid bare in a living animal, and a mechanical or electrical stimulus is applied to it, we cannot see any visible change in that nerve, as we do in an irritated muscular fibre; but, if this nerve is sensory, we obtain evidence of pain in the animal; if it is motory, we obtain muscular contraction in those muscles supplied by this nerve. If, however, we pass a ligature around this nerve, causing a solution of its continuity, we get no effect, by irritation of the nerve, in the muscles supplied by that portion of the nerve beyond the ligature. Now, if we examine the ordinary method of developing nerve force, we find that it originates in the nerve centre, and is conducted outward to the tissues supplied by the nerve branches. This is true of sensory as well as motory nerves. If we stimulate near its origin the optic nerve, flashes of light are seen. If the auditory nerve is stimulated in like manner, sounds are heard. The same is true with those nerves supplying sensation or motion to certain tissues. It is important to a consideration of this subject, that, wherever the stimulus is applied, to centre, middle, or periphery of the same nerve, the same effects are produced. For instance, a person who has suffered amputation of an arm, often complains of sensations in his fingers. If, however, the nerve has lost its vitality in the trunk as well as periphery, these sensations are not preserved. On the other hand, in certain diseases of the nervous trunks or centres, the limbs have no sensation, and the patient feels as if his limb may be wanting. Such an effect has been experienced when the circulation in my arm has been temporarily suspended, either from laying upon it when asleep, or by pressure upon the nerves. During the first confused moments of wakefulness, I have had to feel for that arm with the other hand.

Nervous action may be provoked by mental or physical stimulus.

Sensations are generally caused by peripheral irritation, and thence carried to the sensorium.

Sometimes, however, as in hysteria, the sensation may actually arise in the brain without there being any peripheral irritation. This is not merely imagination, but may be real pain in the part referred to by the patient.

A physical stimulus acts upon the motor nerve always through a sensitive nerve. The actions thus produced are called reflex, because they are in appearance reflected by the sensitive to the motor nerve. A good illustration of this is the closure of the glottis when any thing but air touches its sensitive tissue.

It may be in place here to mention the effects of the galvanic current. When an electric current passes along (not across) a nerve, no matter if it be for a distance less than an inch, the whole extent of this nerve is stimulated, as if by an effort of the will. This is the case, whatever be the course of the current, when from the centre to the extremity, or *vice versa*. The nerves are not merely conductors; for, if a drop of ether be placed upon the nerve, the nervous power is temporarily suspended in that nerve below the place of application; but, if strychnia be used, the action is augmented.

HISTORY.1

The following synopsis of what has been advanced in favor of this anæsthetic agent is sufficient to show how slight a knowledge we possess in regard to its physiological action.

Prof. Hermann,² from his personal experiments, thinks that nitrous oxide produces dyspnea (unperceived by the patient on account of anæsthesia). He thinks that its use is very dangerous, because asphyxia may be produced. If mixed with oxygen, the anæsthesia as well as the danger is diminished.

Dr. Krishaber agrees with this statement, and states further, that it can only be respired for four minutes; and that its mode of action is capricious, some patients sinking unexpectedly without asphyxia.

 1 A thorough investigation in regard to the use of this agent has not been attempted.

² Abstract from the Med. Times and Gazette, in the Boston Med. and Surg. Journal, vol. lxxvi., p. 294.

Mr. A. W. Sprague considers it a "reliable anæsthetic and valuable therapeutic." He counsels its use by physicians, and deprecates the use of an impure gas.

Dr. H. J. Bigelow ' comments on the lividity and muscular rigidity attending the use of this gas, and reports the first surgical operation, the excision of a breast in April, 1848, under complete anæsthesia from sixty quarts, the inspired gas being exhaled by a valve. He thinks the lungs cannot procure sufficient oxygen where the latter, as here, is chemically combined, and that the bulk of this gas will practically prohibit its use except for short operations.

Dr. F. A. Ashford² mentions a case of hemiplegia following administration of the gas. The woman had had suppression of the menses. She recovered under the use of the triple phosphates.

Dr. Evans³ says in a note to the French Academy, that the liquid nitrous oxyde has a stronger effect than the gas, and can be used for inhalation, or for local anæsthesia.

M. Preterre⁴ presented through M. Cloquet, to the Academy of Sciences, some results with regard to the action of this gas. One or two moments suffice to produce anæsthesia. There is no nausea or other inconvenience on awaking. M. Dumas spoke of the danger of using impure gas for inhalation, and of the uncertainty of its liquid preparation.

Prof. Hermann,⁶ from a note to M. Chevreul, considers that this gas cannot take the place of oxygen for the support of animal life. Unless mixed with oxygen, it is dangerous to life. This inference he drew from experiments upon himself, in which asphyxia was produced.

On the 7th of December, 1869, Dr. Jeannel read a paper⁶ before the French Academy of Medicine, on the protoxide of nitrogen as an anæsthetic agent. He reports some personal experiments in a very detailed account, giving his experience at the end of each inspiration. He states that there is no record of a fatal case from the use of this drug, notwithstanding its frequent application. I translate a few of his

- ³ Gaz. Hebdomadaire, Sept. 14, 1868, p. 584. ⁴ Ibid., Jan., 1867, p. 10.
- ⁵ Ibid., 1867, p. 103 (Feb. 15). ⁶ Ibid., 1869, p. 786.

¹ Boston Medical and Surgical Journal, N. S., vol. i., p. 17.

² American Journal of Medical Sciences.

words: "The extreme rapidity with which the peculiar protoazotized condition (*engourdissement protoazotique*) disappears to allow the proper exercise of the natural functions, the resistance relative to life in animals plunged into an atmosphere of protoxide of nitrogen, as well as the results of M. Limouzin's experiments, authorize the presumption that this gas is an anæsthetic, less dangerous than ether or chloroform. Whatever may be its nature, anæsthesia is an enterprise against the vital functions."

I have not, as yet, been able to find how the peculiar effects of this so-called anæsthetic agent are explained, nor has any one *directly* stated that the action may be explained by an accumulation of carbonic acid in the blood. A direct proof of this supposition it would be a difficult matter to give. An approximate idea I have attempted to show by a few experiments.

METHOD OF PURIFYING THE GAS.¹

I put some ammonia nitrate (C. P.) in a generating flask, so as to fill it about half full. Into a rubber stopper fitting into the mouth of this flask I fitted a glass tube and a thermometer with a scale running from 54° Fahr. to 600°. I connected this bent glass tube with a wash-bottle containing some crystals of proto-sulphate of iron C. P. (green vitriol). This was then connected with another wash-bottle, containing powdered pumice-stone, saturated with potassa; from these two the gas was passed through two other wash-bottles, containing water, into a gasometer holding about forty-five gallons. The thermometer was never allowed to rise above 400° Fahr. The gas made after this fashion was used in the following experiments.

I could not take one full inspiration of this gas without producing dizziness, and I could not *count* after the sixth inspiration. I shall commence an account of my experiments with this gas with those relating to the elimination of carbonic acid by the lungs. I am led to do so from the fact that my preliminary experiments induced me first to study the phenomena

¹ Gaz. Heb., Dec. 10, 1869, p. 788. Article by M. le Dr. Jeannel, sur le Protoxide de Nitrogen.

connected with respiration, and because it was by so doing that I arrived at a satisfactory explanation of the action of this agent.

DESCRIPTION OF MUZZLE USED IN EXPERIMENTS.

It was after great difficulty that I devised the muzzle used in these experiments. I had made tin or copper funnels, shaped so as to fit conveniently over a dog's nose; then a rubber hood fitting tightly to this muzzle and then passing over and around the head, being securely fastened around the neck. This muzzle had two tubes soldered to it, covering each a rubber valve, one for the inlet and the other for the outlet of the gas. It was absolutely necessary to shut off every particle of atmospheric air, or the experiment would fail.

In those experiments where observations were made upon the cerebral circulation, the rubber covering was made to fit tightly over the nose and under the chin, so as to leave exposed the portion of the skull trephined.

After a careful examination of the phenomena induced by the inhalation of this gas, I was led to believe that they were in most part due to some disturbance of the respiratory functions.

What showed this to my mind most conclusively was the fact, that the approach and departure of unconsciousness were so rapid, and that no general disturbance was permanent after a few inspirations of air. Therefore, supposing these effects might be explained by an accumulation of carbonic acid in the blood, I instituted the following experiments. The results of a larger portion are reported, because I am perfectly aware that the elimination of carbonic acid varies very much in the same animal at different times. Therefore, I have endeavored, so far as practicable, to merely make comparative experiments, at the same time, determining the amount of gas given off in natural and in the unnatural conditions of the body. Even these results must be taken with much reserve, on account of the extreme difficulty in drying the carbonic acid gas before its combination with the potassa or soda. This difficulty was much enhanced by the fact that impeding the expiratory function seemed to cause great embarrassment in the inspiratory function.

NITROUS OXIDE.

EXPERIMENT No. I, A.—The muzzle was arranged tightly over a dog's head, and the expired gases conducted through a U-tube containing dry soda-lime.

This tube, empty, weighedAmount of soda used	$\begin{array}{c} 42.000\\ 11.483\end{array}$	grms. "
Actual weight of tube filled with soda After 100 expirations this tube was disconnected and weight	53.483	"
ascertained	54.182	
Previous weight	53.483	"
Gain in weight	.699	
The soda was observed to have gathered moisture during th	ie experi	iment.
B. Now the muzzle was connected by rubber tubing wi	ith gaso	meter
containing nitrous-oxide gas. After 30 or 40 inspirations, th	1e dog h	naving
shown signs of anæsthesia, the outlet tube was connected	with an	nother
U-tube containing soda-lime.		
Weight of this tube empty	29.708	grms.
Amount of soda used	6.315	
Actual weight of tube with soda	36.023	"
After 100 expirations (5 galls. of gas) through the appar	atus, the	e tube
was disconnected.		
Weight of this tube	36.498	grms.
Previous weight	36.023	"
Gain in weight	.475	"
Now 5 galls. of the nitrous-oxide gas was passed		
through a similar apparatus and the weight of soda		
and the U-tube (previous to experiment) ascertained,	36.430	"
Gain in weight by absorption and moisture	.320	"
Actual weight (after the experiment)	36.750	"

EXPERIMENT No. II.—In this experiment I attempted to dry the expired gases by means of a tube containing fragments of chloride of calcium (Ca. Cl.) C. P. The gas was afterward received into a U-tube, containing, as before, soda-lime. Yet the soda gathered moisture in spite of this precaution.

(1.) The U-tube containing soda-lime weighed	35.958	grms.
This same tube, after the reception of 5 galls. of gas from t	he gaso	meter,
(2.) Weighed	36.161	grms.
(3.) After 100 inspirations of gas by a dog	36.675	"
Increase in weight after second experiment	.203	"
" " third "	.514	44

From the leg of the U-tube into which the gas was passed, some of the fragments of soda were removed and dissolved in distilled water. Hydrochloric acid was slowly added in excess, but no effervescence ensued. From the leg of the U-tube into which the expired gases from the dog were passed, some soda was removed and dissolved in water. Hydrochloric acid was here added in excess, and a violent effervescence occurred, showing that some of the increase in weight was due to the absorption of carbonic acid. A lighted match burned with brilliancy at the free outlet of the gas from the U-tube during the experiment.

EXPERIMENT No. III.—Muscular relaxation was caused by 22 inspirations of nitrous oxide gas in a dog who had been subjected to a series of experiments like those detailed above.

Then 50 more inspirations of the gas were taken, and the expired gases conducted through a drying jar containing a large quantity of small fragments of chloride of calcium, and into a U-tube filled with white caustic potassa.

This U-tube weighed with the potassa	32.448	grms.
" " without potassa	24.255	"
Amount of potassa used	8.193	"
After the inspiration of 5 galls. of gas and of 50 expira-		
tions, the-U tube had gained	.022	
EXPERIMENT No. IVTwenty minutes after the preceding	ng exper	riment
the same dog was subjected to a similar experiment with the	gas.	

The U tube with potassa weighs	32.129 24.255	grms. "
Amount of potassa used Twenty-four inspirations of the gas cause muscular re- layation. The part 50 expirations, the dog all the	7.874	66
time inspiring the gas, give a gain in weight of Actual weight of the tube at termination of experiment	.011 32.140	сс сс

In both these experiments the soda was quite dry, and the solution after the experiment gave, on the addition of hydrochloric acid, the effervescence of carbonic acid. A lighted match also burned brilliantly at the free extremity of leg of U-tube during the experiment, thus showing that nitrous oxide or oxygen passed out from the lungs. It was most probably the former.

It will be needless to detail all the experiments of this elimination of carbonic acid, and I will here present a table of the results of all the experiments, giving the amount of carbonic gas exhaled by the lungs. In each case the potassa or soda was carefully examined to detect the amount of moisture ab-

Increase in weight in I gramme and 50 respirations. $\begin{array}{c} .03045\\ .00528\\ .00528\\ .00113\\ .0013\\ .0031\\ .0036\\ .0078\\ .0078\\ .0078\\ .0078\\ .0078\\ .0078\\ .0078\\ .00269\\ .00167\\ .00269\\ .00168\\ .00088\\ .$ Gas not dried Soda absorbed moisture Some moisture absorbed. 6 Soda absorbed moisture Soda dry twenty minutes after recovery Defotasa dry Soda dry after experiment..... Potassa dry after experiment..... 5|Potassa quite dry...... REMARKS Gas not dried..... 3 :10 : 10 é -No. of Galls, used. ຨຨຨຨຨຨຬຬຬຬຬຬຬ 23 anoitaniqani to .oM Gain from respir-ing Nitrous Ox-ide Gas. • .160 * These were taken immediately after recovery from the effects of the gas. mort nist) .riA gai 052* 043 669 250 135 inspir 11.483 grs. 3 3 3 3 3 ÷ 3 3 3 3 ; 3 3 3 3 to sboz to truomA Potasa used. 0.488 8.150 8.193 13.1641.4756.3136.4354.2286.4582.6617.240 11.254 XXVIII Partially relaxed. 20.865 [XXVIII. (A)]Relaxed. 16.298 4.84 Natural.... fion. -ipuon Relaxed 333 3 3 3 3 3 3 3 3 XXII. (B) XXII. (B) XXIII. (B) <u>କ</u>ତି XVIII. XVIII. XXIX IIIVXX XXII. Vo. of Experiment. Myself Dog (19 lbs.). Dog (19 lbs.). Bitch ANIMAL. Bitch (17 lbs.) Uog (19 Jbs.) : 3 3 3 3 3 3 Myself 3 3 3 3 3 3

Table of Elimination of Carbonic Acid by the Lungs.

Leaving out doubtful experiments, in which the { 0.0101 soda had acquired a large amount of moisture. } 0.061

Average gain from inspiring air. Average gain from inspiring gas.

NITROUS OXIDE.

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sorbed from the wet gases, and in every case hydrochloric acid was added to the solution of the alkali after the experiment, and the intensity of effervescence accorded with the determined weight, or, in other words, where the gain in weight was slight, the effervescence was less than where the gain was greater. In the last column the amount of carbonic acid is estimated for one gramme, and considering that the animal had taken fifty inspirations of the gas. These results must of course be compared with each other; and, generally, the amount of carbonic acid exhaled in the natural condition was taken on the same afternoon as when the animal was subjected to the action of the gas, and *always* before inspiring the gas, with the two exceptions which are noted in the table; these exceptions were accidental, and my surprise at the result was at first rather great; until, after further experiments, I thought that I had discovered the cause of this diminished quantity of carbonic acid exhaled. (See table, p. 11.)

Now, if we examine this table carefully, we should merely compare the figures in the last column with each other, as also the effects produced by this agent upon the same animal. If we do so, we shall find that the gas diminishes the amount of carbonic acid exhaled by almost one-half. This then would lead us to suppose that the effects produced by inhaling this gas may be due to the accumulation of carbonic acid in the blood; but a plausible explanation is that the oxygenation of the blood is prevented, and carbonic acid, the result of combustion, is withheld. I was not satisfied with this theory from various reasons. In other cases where carbonic acid is withheld, the effects are by no means so rapid as when this agent is inhaled. Again, I do not yet quite accept a theory, which supposes that an accumulation of carbonic acid in the blood will cause asphyxia and death in twenty minutes. Therefore, the cause of anæsthesia cannot be attributed merely to its accumulation in the blood. This may be the effect of the anæsthetic agent, but not the cause. To show how death may be produced by this gas: I will describe the following experiments:

EXPERIMENT No. V.—*Pigeon in a bell glass containing nitrous oxide.* Pigeon confined in the receiver; the gas let in through an opening at top, into which is fitted a rubber stopper with a glass tube extending twothirds of the way into the jar, while another escape-cock at the top of the jar is left open to let off the atmospheric air. As the sp. gr. of this gas is 1.52, compared with air, the gas would fall to the bottom of the jar and force out the atmospheric air, that is, if the pressure is sufficient to prevent the admixture of air. As soon as a match will burn brilliantly at the escape-cock, this is closed and the animal left to breathe the gas.

4'. The pupils are contracted.

7'. Asleep (eyes closed); more gas let in.

9'. Opens her eyes, if there is any noise in the room.

13'. Eyes are kept closed when there is no noise or movement.

16'. Suddenly awakes and pecks at her tail-feathers; pupils still more contracted; more gas let in.

17'. Eyes closed.

19'. Awakes on rapping the jar. Respiration quiet.

22'. A cart passing along the street awakens her, after which she relapses into sleep.

26'. Repetition of same phenomena from same cause. More gas let in. She opens her eyes, showing the pupil still more contracted. Quiet respiration.

40'. A lighted taper is now introduced into the jar, to see if there may be any great amount of carbonic acid at the bottom. This burns with great brilliancy, when suddenly some loose feathers lying round take fire, and the receiver is filled with dense fumes. The bird is immediately removed, and after one or two gasps dies.

57'. Autopsy. No marks of burning on the body; the tail feathers slighly scorched. An examination of heart and lungs shows death by asphyxia. The blood coagulates on exposure to the air.

EXPERIMENT VI.—A pigeon, confined in a smaller jar containing atmospheric air, both openings closed, lives 1 hour and 24 minutes.

5'. Mouth open, eyes closed.

9'. Still standing in half crouching attitude.

11'. Pupils dilated. Eyes closed unless the jar is shaken.

14'. In a half-comatose condition. Can with great difficulty stand.

17'. Lies on breast-bone, wings hanging down. Is made to sit up by turning the jar, but soon falls over backward, resting on feet and tail.

20'. Distressed respiration. Great muscular trembling.

22'. Comatose.

27'. Lies in any position in which she is placed.

29'. Now is on her back (by laying the jar on its side.) Constrained respiration. Pupils still dilated.

34'. Expiratory movements more rapidly performed.

44'. Respiration almost imperceptible.

1.4'. The receiver is now submerged in a pneumatic trough, to avoid any possibility of the entrance of air.

1.12'. Convulsive movements.

1.24'. Dead.

1.47'. Autopsy. Rigor mortis commencing, muscular tissue very darkcolored. Lungs colapsed, will float on water; they present the marbriform appearance always seen in asphyxia. Heart flaccid and containing fluid blood in right side. Brain pale.

(This pigeon had been subjected, 3 days previous, to the *inhalation* of the gas.)

EXPERIMENT No. VII.—Pigeon confined in the receiver of an airpump, from which the air is rapidly exhausted.

1'. Dead after violent convulsive movements. No change in condition of pupils observed.

4'. Removed from the receiver.

39'. Autopsy. Rigor mortis. Heart firmly contracted, and containing blood.

EXPERIMENT No. VIII.—A pigeon lives in a tight receiver, containing nitrous-oxide gas, but 32 minutes. This pigeon was placed in the same receiver as in Experiment No. V., over an air-pump. A few strokes were first made to rarefy the air; immediately the gas was let in, the bird showing signs of distressed respiration. Some excitement ensued, which was succeeded by quiet and regular respiratory movements.

3'. Eyes are closed, and the bird is apparently fast asleep in a sitting posture.

17'. On rapping the jar, she stands up, but immediately relapses into her former posture and condition.

19'. Repetition of same phenomena.

20'. On exhaustion of a portion of the contained gases, she awakes; and, when the jar is again filled with the gas, she relapses into a sleep. If, on the contrary, the gas is allowed to enter as fast as it is exhausted, she remains asleep.

23'. Again the gases are partially exhausted, and she opens her eyes. Pupils are contracted. As soon as the respiration becomes distressing, the gas is let in.

25'. Respiratory movements become more rapid. She sinks down with eyes half closed.

28'. Respiration spasmodic. Eyes wide open.

30'. One or two respiratory gasps, with mouth wide open.

31'. Respiration imperceptible.

32'. Removed from the receiver. Dead.

50'. Autopsy.—Rigor mortis. Muscular tissue dark colored. On opening the thorax only a few drops of blood could be found, though there was an abundance in the muscular tissue. Heart very flaccid, and will not contract by stimulation. When the heart is removed, very little blood in the thoracic cavity. Lungs marbriform, and float on water. The skull being opened, let out a small quantity of serous fluid, and the brain was very white, and of the same color throughout all portions. No blood in vessels at base of skull. (This pigeon had been subjected to the inhalation of the gas a few days previous.) EXPERIMENT IX.—Rabbit in the same receiver; escape-cock open; lives only 53 minutes.

3'. Veins in ears swollen.

4'. Match burns brilliantly at escape-cock, showing that the jar is full of nitrous oxide. Supply is shut off.

6'. Ears pale; veins not much distended. More gas let in (five gallons in all). Supply shut off.

9'. Cannot stand on her feet. Eyes have remained open up to this time.

11'. Ears livid.

24'. Lying flat on bottom of the jar. Difficult respiration; eyes closed. Is not aroused by tapping on the jar. No abnormal congestion of veins in ears. More gas let in; ears livid; veins dark colored; very anxious respiration. Eyes open; pupil greatly contracted.

26'. More gas let in.

31'. Ears and skin quite livid. Remains quiet for twenty minutes, during which time breathes very slowly. Cries at length, and makes a few feeble movements.

53'. Respiration imperceptible.

1.4'. Autopsy made and now completed. Ventricular contractions occur only when stimulated by movement of the air, or by touching the heart. No electricity used. Right auricle contracts feebly and irregularly for one hour and seven minutes, when I was obliged (it was midnight) to leave off my observations. I kept a wet sponge upon the heart, but the next morning there was no contraction visible. Peristaltis of the bowels continued for half an hour after the body was opened. These last two effects occurred in a few other cases.

EXPERIMENT No. X .- Death by nitrous-oxide inhalation.

A small black-tan bitch (about fifteen pounds). Healthy, and very well nourished.

This dog was muzzled and allowed to respire the pure gas (at first, the air came in under the hood) until she died.

As in all the previous experiments, when muscular relaxation occurred, there was a discharge of soft fæces from the bowels, and of urine from the bladder. After the expiration of about three-quarters of an hour, and fifteen minutes from the time muscular relaxation was observed, the respiration grew more and more feeble, then became more and more imperfectly performed; finally, after three or four convulsive efforts, it ceased. After waiting for a minute or two, the muzzle was removed, and artificial respiration slowly and carefully maintained for ten minutes, by compressing the thorax and drawing forward the tongue; also, by alternately forcing into the lungs pure air, by means of Dr. Richardson's artificial respirator, and by drawing out the air about eighteen times to the minute. The thorax was then opened, and the heart and lungs examined. Both ventricles and the right auricle were relaxed and distended with blood of a dark fluid color. The blood in the thorax was dark colored. The lungs were of a marbriform appearance, and there appeared a number of small air-bubbles (we had used artificial respiration). No more extended examination was made. There was no rigor mortis for one hour after death.

Two or three times it has happened to me, when I had thought an animal dead from asphyxia, after the inhalation of this drug, to be surprised by voluntary respiration recurring, after I had removed the muzzle. In fact, I have now two dogs alive, who have not respired for one whole minute several times when undergoing an experiment. Never has an animal died unexpectedly, and it was always very difficult for me to cause asphyxia, if the smallest modicum of air passed into the lungs.

EXPERIMENT XI.—A rabbit was forced to inhale, by means of a muzzle, fifteen gallons of nitrous oxide, and for three-quarters of an hour, with an occasional inspiration of pure air. When respiration ceased, the muzzle was removed, and the animal placed on the table, apparently lifeless, though cardiac pulsation continued. The trachea was opened and artificial respiration, by Gréhant's apparatus, instituted; but, instead of air, I attempted to force gas into the lungs. The bellows, however, were not air-tight, and air passed into the lungs. Voluntary respiration recommenced after the first blast of air; but finally I succeeded in forcing enough gas to destroy the rabbit, and I then opened the thorax, and the heart pulsated for half an hour after the cessation of respiration. As the apparatus had broken, I could not continue my experiment, as I at first intended.

The object of this experiment was to see if the heart would pulsate after artificial respiration with nitrous oxide was maintained.

These experiments all show that death is caused by asphyxia, and not by paralysis of the central organ of circulation, nor probably by venous congestion. So far I was satisfied; but I was determined to discover, if possible, the cause of anæsthesia.

In reverting to the various causes of anæsthesia, I reasoned that it could not be caused by paralysis of the nerves of sensation from the contact of a noxious agent, for I could not see how it was possible that so inert a substance in the blood could paralyze these nerves. It is very easy to understand why the contact of ether or chloroform may do so. However, to eliminate this cause, I tried the following experiment:

EXPERIMENT No. XII.-February 15, 1870.-Black puppy.-Experiment to try power of crural nerve.-The puppy inhaled four gallons of the nitrous oxide, and air was occasionally let in through the muzzle after-The skin was incised over right ham, and the muscles divided. ward. The crural (?) nerve was brought out through the cut, and isolated on a glass rod. Occasionally the dog cried hard and kicked slightly, but when the nerve was touched the muscular movements were more violent. The induced current caused several contractions of the limb, and the animal did not express signs of pain. The wound was closed, and the animal set at liberty. An examination of the gasometer showed that twelve gallons of the gas had been used during the whole experiment, which lasted fifteen to twenty minutes. In a moment or two the dog seemed as well as before. Very little blood was lost in the experiment, and from a small artery cut, the blood oozed in a very small jet, but was not thrown with much force. It was easily closed with the tooth forceps, as were two or three little veins which had also been cut. The blood was dark-colored, but the muscles were rather pale. No signs of asphyxia were noticed.

I was satisfied from this experiment that the nerves could conduct, and therefore sought for some other method of investigation.

In order that my readers may understand how I came to think of what seemed to me the probable effect of anæsthesia from inhalation of this agent, I am going to relate my personal experience with its inhalation. It agrees materially with the effects experienced and detailed by Dr. Jeannel, in a paper referred to before this.

I inhaled the gas made as the dentists in Boston make it, and not as I afterward made it. I took twenty inhalations¹ before losing sensation. I could use my hands and was perfectly conscious, for I endeavored to push away from the outlet-valve Dr. N——____'s finger, as he was obstructing the passage of expired air. I then held my nose, and, after three expirations more, I felt as if all my members were, what is commonly called, asleep; especially in the right arm, in which the circulation was accidentally impeded. In two more, I could not see, but could hear Dr. N. counting, and was conscious of my respiration being hurried and blowing, but not troubling me. I then lost all sensation and experienced a most singular feeling of elevation (as if I was in rapid motion

¹ I am afraid I allowed air to enter my nostrils at first, thus delaying the effects.

in the air). I could not now control my pharyngeal muscles, so that air passed through my nostrils. I recovered almost instantly, but had trouble in talking, my words coming thick and *throaty*.

I have since taken the gas several times and experienced the same pleasurable sensations, only occurring more rapidly. Two inspirations of the gas (purified) are sufficient to thicken my voice, and cause dizziness. After the sixth or eighth, I know nothing. Three inspirations cause the peculiar sensations in the periphery, which I supposed due to arrest of capillary circulation. It was not due to arrest of arterial circulation, for that only partially produces the same effect, and, while taking the gas, the pulse can be felt. The veins are not congested, as in ether, and in obstructed respiration.

These facts led me to suppose that I should investigate the condition of the capillary circulation. What induced me still more strongly to attribute its effects to this cause was, that its effects are very rapid both of approach and departure, and, as fortunately we can see its mode of action, we can, by inspiring air, almost immediately restore consciousness and the vital functions. But there is a peculiar condition produced by this gas, which, when seen, requires instant relief.

All animals, so long as they *appear* to respire, can be awakened to consciousness almost immediately. But, at a certain stage, animals appear to stop all attempts at respiring, and lie motionless. If not forced to inhale air, they will die. The gas will not then support life. I have experienced this state (but was unconscious at the time). When the tube dropped from my mouth, I sat as in a trance for half a minute, making no respiratory effort, when all of a sudden I was told that I began to smile and to expire the contents of my lungs at the same instant. I was conscious of smiling, but did not notice whether I expired or inspired air after the tube dropped from my hands.

EXERMENT XIII.—I put some fresh arterial blood in a flask and passed through this one gallon of nitrous-oxide gas, and then agitated the flask; no change of color ensued. I then put some blood from this flask in one test tube and some of the fresh blood in another, and left them to stand for four days, examining from time to time. At the end of this time there

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was no difference in their appearance, except that possibly the serum of the blood submitted to the above experiment was a little more tinged with red than the other. I likewise placed some of the blood under the receiver of an air-pump, exhausted the air, and then filled the receiver with the gas. After twenty-four hours there was no change of color. I then experimented after the method pursued by Dr. W. A. Hammond, with a view of determining in what condition the cerebral circulation stood during the inhalation of this gas.

Dr. J. C. Warren kindly trephined a dog's skull, and into this opening I screwed a brass plate. Some days after the operation, the animal being in good health and spirits, I screwed into this plate a glass tube, on to the bottom of which was fitted a rubber bag containing a colored fluid. The tube was marked off in inches and tenths of an inch. The rubber bag impinged upon the dura mater, and was turned down until the fluid rose to a given point.

EXPERIMENT No. XIV.—This dog, under the effects of ether, was subjected to the following operations:

At 2.30 P. M. a round brass plate was screwed firmly into the hole in his skull made by the trephine ten days ago. The operation was completed at 3 o'clock, and the dog placed in kennel. At 5.15, the cerebrometer was screwed into this plate, and the height of the fluid in the gauge determined $(1\frac{1}{10}$ inch). The cerebral pulsations were carefully noticed, regular and rapid. On sudden movement of the animal the fluid ascended about $\frac{2}{10}$ of an inch, and then remained as at first observed. The gas (N. O.) was now inhaled by the animal, and the first effect noticed was a rise of fluid in the tube $(\frac{5}{10}$ of an inch). Then the cerebral pulsation was less forcible and diminished in rapidity (to one-half number of pulsations) When more gas was inhaled, the muscles relaxed and the fluid mounted $\frac{13}{10}$ of an inch (3 inches $\frac{1}{10}$), and the pulsations imperceptible. Air was then inhaled, and the pulsations came on very rapidly, and the fluid quickly (but gradually) fell to same mark as at first noted (viz., $1\frac{8}{10}$ inch). (See tabular view, next page.)

EXPERIMENT No. XV.—9 o'clock A. M.—The gauge of cerebrometer screwed into its place, at a height of $\frac{9}{10}$ of an inch. The pulsations, according to column of fluid in the gauge, were 150 per minute. After twelve or fourteen respirations with the gas, the pulsations were more feeble and beat 120 per minute. After one or two more, which were of an explosive character, the pulsations could not be distinguished, and the fluid rose to a height of $2\frac{2}{10}$ inches.

Duration of experiment, four minutes.

Five minutes after this last experiment, when the fluid appeared to be at a constant point, viz., $\frac{9}{10}$ of an inch, the gas was again applied. The number of pulsations, about 160 per minute. When muscular relaxation was attained, the fluid stood at a height of $2\frac{6}{10}$ inches. (The dog struggled before this state occurred, and it was then the last $\frac{4}{10}$ were attained; when quiet, however, the same height was preserved.) The gas was now taken of (three minutes), and gradually the pulsations became more distinct and rapid, and the fluid stood as at first, at about one inch.

EXPERIMENT No. XVI.—A. Before inspiring gas, liquid in tube stood at one inch, and pulsations = 152. After ten respirations, liquid mounted two inches, a rise of one inch, and pulsations could not be distinguished. Then, on air being respired for a minute and a quarter, the liquid descended to the one-inch mark, where it stood at first.

SAME DOG.—B. Before inspiring gas, liquid in tube = one inch, pulsations = 128. After partial anæsthesia, the pulsations = 97.

After twenty inspirations, liquid rose $\frac{4}{10}$ inch, and pulsations could not be distinguished.

SAME DOG.— C. Respiration interfered with and the liquid rose $\frac{6}{10}$ inch and pulsations became indistinguishable. This interference was accomplished by closing the inlet-tube of the muzzle. The experiment lasted scarcely a minute, and the animal remained quiet.



At A. First Observation. Respiration of air, normal. Fluid in cerebrometer standing at one and eight-tenths inch.
At B. Second Observation. On sudden muscular effort, fluid rose in gauge two-tenths of an inch.
At C. Third Observation. Partial anæsthesia. Additional rise of fluid in cerebrometer, of five-tenths of an inch.
At D. Fourth Observation. Anæsthesia, with muscular relaxation. Additional rise of fluid, six-tenths of an inch.
At E. Fifth Observation. Respiration of air, normal. Equable but abrupt fall of fluid in gauge, thirteen tenths of an inch to the original level.

I administered the gas in this experiment, and my assistant, Mr. J. T. Boutelle, took the observations. Having had experience in astronomical observations, his figures are very reliable.

I am enabled to confirm these results by accompanying sphygmographic traces, which, by the kindness of Dr. Parker, of the Colton Dental Association, were obtained from sever a NITROUS OXIDE.

persons who were taking the gas at his rooms. I take this occasion of thanking him for his valuable assistance. I took the precaution of testing the purity of his gas upon myself. It is to be noticed in these traces that during the period of anæsthesia the pulse is hurried, though diminished in power. This, I think, is explained from the fact that the capillary stagnation obstructs the arterial circulation, to compensate which the pulsation must be more rapid; for, while the anæsthesia is passing off, the force is very much increased, and the number of pulsations is diminished, owing to the very free passage of the circulation through the capillary system.

If the congestion were very great and long-continued, the relief to the arterial circulation would not occur so soon after the removal of the gas.

TRACE OF NATURAL PULSE.¹ Radial Artery.—March 29th.



¹ To understand the plates, it is necessary to compare a trace marked with a certain letter (say A) with the same letter (A), as each letter corresponds to the name of a certain person. It may be noticed that each letter occurs three times, at least; the trace having been taken *before*, *during*, and *immediately after*, anæsthesia has occurred.



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NITROUS OXIDE.





H. Just after anæsthesia.

Do not these experiments point to the mode of action of this agent? I deem it of the highest importance, in viewing experiments, to compare, as far as practicable, several experiments together, and obtain from these the leading phenomena, and if they are constant there can be no necessity in attempting a very large number of such to prove a certain point. These experiments were very satisfactory, and I could see no use in prolonging the misery of experimenting, not only for the animals, but as well for myself. This was the point which I thought proved by these experiments, that the gas, though perfectly respirable (that is, capable of passing into and out of the lungs), yet would not deliver up its oxygen to the blood, nor cause the elimination of as much carbonic acid from the blood as if atmospheric air or pure oxygen were respired. I should consider this effect upon the capillary system to be caused by the non-aëration of the venous blood in the lungs. This fact, I have since learned, has existed as a theory of the mode of action of nitrous oxide, though I was not aware of this until my investigations were concluded.

The act of respiration in warm-blooded animals consists of an interchange of oxygen and carbonic acid by means of the blood in the lung-tissue. It is also well known that if a gas deficient in oxygen, or which contains oxygen combined with another gas in such proportions as to be with difficulty decomposed, be presented to the pulmonary tissue, oxygenation of the blood is not accomplished, and asphyxia is produced. In the asphyxia caused by protoxide of nitrogen, the process of respiration ceases after inspiration and before expiration. If, now, the heart has not ceased its pulsations, and the thorax be compressed, forcing out the gases contained in the lungs, voluntary respiration, with the act of expiration, will recommence and the vital functions be restored.

I have observed that the cardiac pulsations persist for a long time after the cessation of the respiratory function, and that a rabbit, supposed to be dead fifteen minutes before, was picked up and thrown on to the table before proceeding to an autopsy, and immediately began to respire, and lived several days, until the exigencies of a subsequent experiment demanded the sacrifice of its life.

I do not think that death, following the inhalation of this gas, is due to syncope, though I am well aware that Professor Brown-Séquard states that this condition may be caused by a capillary stasis. The following observations confirm me in this belief. The capillary stasis is only transient, and seems to depend upon the defective respiration; for, as soon as that in restored, the stasis is relieved, as we should naturally expect is the state of asphyxia. Finally, the motions of the heart are not paralyzed till some time after the cessation of respiration.

The anæsthesia is caused by an insufficient oxidation of the tissues by means of the blood. If, now, the lungs be forced to receive this gas, they inspire it without decomposing the oxygen, and death ensues from asphyxia; or, if air be allowed, the animal revives, quickly regaining its consciousness, sight, hearing, sensation, and muscular powers in the same order. Generally, there is a period of three or four minutes after respiring air, that loss of sensation persists. If the gas be reapplied before the expiration of this period, the loss of sensation may be kept up for a longer time, and so on, as in the administration of ether. Now, in order to show that my explanation in regard to this agent is not only plausible but evidently a true one, notice these facts. When a person faints from breathing an impure air, the respiration is imperfectly performed, the face and skin are remarkably pale, and there is loss of sensation. When a person experiences the partial effect of drowning, the same phenomena as are observed after inhaling this gas are noticed, viz., numbress, buzzing in the ears, and a rather agreeable sensation all over the body, resembling, as near as we can express it, that produced by tickling the whole surface of the body.

I cannot speak from my own personal experience, but I will relate a fact which very strongly impressed my mind at the time. My brother ' was in a kayak (in which it may be known the body is firmly secured), on Jamaica Pond, when the boat upset, and from its buoyancy, and from the fact that he

¹ I give his letter in reference to the fact; though he does not know for what purpose I desired it, nor what are the effects of this gas upon the system.

"NEW YORK, March 26, 1870.

"I have yours in reference to 'sensations.' The occurrence was so long ago, that all vivid recollection has gone. About all I do remember is, a greenish appearance of every thing, as I seemed to be quietly and gently sinking away. There was no sensation of effort, no struggling at this time; the sensation not unlike settling down gently upon a perfectly soft and yielding feather-bed, only 'more so.' This is about my recollection of it." could not extricate himself, his head was partially immersed for ten or fifteen minutes at least; certainly long enough for some of us, standing on the shore, to go seven-eighths of a mile, unloose a boat, and to his assistance. From his constrained position, he was under great embarrassment in respiring air, which he could do only by stretching his head up so as to take in air by the nose, and, as he became wearied by these attempts, he could do so less and less frequently, and had just given up the attempt when he was rescued in an almost exhausted condition. He always possessed the faculty of holding his breath when swimming *under* water, for a much longer time than any of our companions. I remember, at the time, he expressed to me these same sensations, and I have no doubt they can be explained in the same way that we explain the same sensations produced by the protoxide of nitrogen.

The blood, owing to an insufficient supply of respirable . oxygen, accumulates the preëxisting amount of carbonic acid in the blood, and in this way causes an arrest of capillary circulation. Having proceeded thus far in my writing, I came across, *accidentally*, a lecture of Prof. George Johnson, in the number of the *Medical Times and Gazette* for April 3, 1869. I am exceedingly surprised to see a confirmation of his theory in regard to the anæsthetic action of nitrous oxide. What he has arrived at by careful reasoning, I have been able to obtain by actual experiment.

For example, he says :

"Nitrous oxide is a rapidly-acting anæsthetic, causing complete unconsciousness in less than a minute. At a high temperature it is an oxidizing agent, but at the temperature of the body it gives up no oxygen, and is exhaled again unchanged. When inhaled in place of atmospheric air, it rapidly replaces the oxygen of the blood, and, this being done, the functions of the brain are completely suspended, and there is a state of profound coma, which quickly passes off when air is again allowed to enter the lungs"... "there is no reason' to conclude that the inhalation of either nitrous oxide or nitrogen causes an accumulation of carbonic acid in the blood." Before this he says, "to produce oxidation of the

¹ Vide Experiments, No. I.-IV., etc.

brain, there must be (1) a free current of blood through the capillaries of the brain; (2) the blood must be duly aërated or oxygenized; (3) the blood must be unmixed with any material which prevents or impedes the giving up of oxygen from the blood to the tissues."

If we accept these three rules for the preservation of the nerve-functions, of course, if one be wanting, the nerve-functions are suspended. Now, the Experiments XIV., XV., and XVI., taken in connection with the accompanying sphygmographic traces, show an increase of capillary tension, with, as we should suppose, increased number of arterial pulsations; but, finally, *arrest* of capillary pulsation in the brain. At this stage anæsthesia occurs. When the pulsation recommences and the tension falls, consciousness sets in. This effect, then, is a violation of Rule 1. Again, the blood having no oxygen to give up in the capillary system, there is a violation of Rule 3.

Now, to prove this in a different way, please recall certain experiments undertaken with a view of determining the variation in the quantity of carbonic acid eliminated in the natural state and during anæsthesia from inhalation of the gas.

A fact at one time inexplicable to my mind is now perfectly comprehensible. I noticed that, during anæsthesia from this agent, the carbonic acid eliminated was two-thirds of that during consciousness, before the inhalation; while, immediately after the inhalation and during consciousness, the carbonic acid eliminated was one-third only of that during the anæsthesia.

Now, it seems to me reasonable to consider that during the anæsthesia the free carbonic acid in the lungs is given off, and, until the stagnation in the capillary circulation is attained, there is only a modification of combustion. When this capillary stasis occurs, there is no combustion, and temporary death to the nerve-substance is effected. On the inspiration of air the combustion is resumed and the product of oxygenation or combustion, viz., carbonic acid, does not *immediately* appear in the expired air. The nitrous oxide must be eliminated first.

The interference with the respiratory functions is previous to the stagnation in the capillary system; and, therefore, this latter effect is due to asphyxia, which, if continued, produces death. Now, if this state be prolonged beyond the time that the process of oxygenation in the blood can be resumed, you cannot restore the animal to life. Provided, however, the central organ of circulation, viz., the heart, has sufficient power to overcome the inaction in the capillary system and the lungs receive pure air, or still better, oxygen, life can be restored. There is, in other words, no poisonous agent in the blood. There is simply a functional arrest of capillary circulation.

I will add here, in answer to the numerous inquiries as to the preservation of consciousness after decapitation, that it is simply impossible, for the capillary circulation is stagnant, likewise oxygenation of the blood is prevented, on account of which there is a paralysis of the nerves, or death positive.

I am now occupied in some investigations concerning anæsthesia caused by arrest of capillary circulation through mechanical interference. This will be a difficult matter, and will require much patience and time before any satisfactory result is attained.

In an operation requiring but fifteen to twenty minutes I should prefer to use this gas to ether, provided that the pain of the operation is not to be too severe afterward. If the administrator of the gas has had experience, I can see no objection to its use, in any case where an anæsthetic is indicated, for a few moments.

The different stages of etherization can be easily attained with this as with any other anæsthetic, and the life of the patient is entirely under the control of the person administering the gas. I do not speak as an enthusiast. I commenced these investigations feeling that I was concerned with a dangerous anæsthetic, which was too commonly used by dentists and quacks. I believe^{*}it to be as innocuous as any anæsthetic, provided it be pure and given by an experienced person.