On the physiological action of nitrous oxide gas / by Dudley Wilmot Buxton.

(2)

ON THE PHYSIOLOGICAL ACTION OF NITROUS OXIDE GAS.

BY

DUDLEY WILMOT BUXTON, M.D. AND B.S.LOND., M.R.C.P.,

Administrator of Anæsthetics in University College Hospital, the Hospital for Women, Soho Square, and the Dental Hospital of London.

[REPRINTED FROM THE TRANSACTIONS OF THE ODONTOLOGICAL SOCIETY OF GREAT BRITAIN, MARCH, 1887.]

LONDON:
HARRISON AND SONS, ST. MARTIN'S LANE,
Printers in Ordinary to Her Majesty.

1887.

LONDON :
HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY,
ST. MARTIN'S LANE.

On the Physiological Action of Nitrous Oxide Gas.

By Dudley Wilmot Buxton, M.D. and B.S.Lond., M.R.C.P.,

Administrator of Anæsthetics in University College Hospital, the Hospital for Women, Soho Square, and the Dental Hospital of London.

In a preliminary communication made before this Society* I attempted to review some of the more authoritative views which have from time to time been advanced with regard to the physiological action of nitrous oxide upon the organism. It remains for me to consider the evidence which experimental research has placed in our hands, and to attempt as briefly as may be to formulate what conclusions are warranted by the results of such researches; and further, to adduce from these conclusions practical rules such as may guide us in the employment of nitrous oxide gas as an anæsthetising agent.

Aeriform bodies can only obtain ingress into the vital system of warm-blooded animals by absorption and diffusion through mucous membranes; practically this absorption is in the higher mammalia confined to the vast expansion of surface afforded by the acini of the lungs. Passing through the sinuous nasal meatuses, aeriform bodies are

* See Trans., Vol. XVIII, N.S. (March, 1886), p. 133.

warmed, and sifted, so to speak, of floating solid particles; they then traverse the guardian portals formed by the larynx, and so enter the lungs. Usually the constrictors of the pharynx maintain a closure of the œsophagus; however, timid persons, whilst inhaling nitrous oxide, make efforts at swallowing, which, by partly inflating the stomach, may give rise to unpleasant effects, nausea or mechanical interference with the action of the heart, and so leading to syncope. This should of course be avoided.

So thin is the wall of the acini and air-cells, that the lungs may be considered as consisting of aeriform matter, separated from liquid matter by an exceedingly tenuous animal membrane, which is capable of the active interchange of gases from the aeriform matter to the liquid matter, and *vice versâ*. Whatever aeriform body is inhaled into the lungs, provided it does not impede the mechanical acts of respiration, can diffuse into the blood, while the gases in the blood can diffuse out into the free air space of the lungs. Gaseous bodies we know exist in at least two conditions in the blood—(1) in mere solution, (2) in combination with the albuminoids found in the corpuscles and serum. The essential conditions of life for the organism are that in proportion as the bodily tissues are split up for the production of movement, or force, heat, electricity, and so on, so should the blood

obtain organic material from the alimentary tract, and oxygen wherewith to build it into the tissues; and secondly, that the blood shall be also depurated of organic and saline refuse, and of aeriform impurities through mechanism supplied by the lungs. This, I need hardly remind you, consists in the diffusion of carbonic acid gas and other obnoxious materials from the blood into the residual air in the air space, and the diffusion into the blood of oxygen from the residual air. So long as the oxygen tension is higher and the carbonic acid tension is lower in the residual air, so long will interchange between blood gases and atmospheric gases take place. When, however, other aeriform bodies than atmospheric air find their way into the air space of the lungs, other conditions are imposed upon the organism. Let us consider these. If the gas be respirable, and actually enters the lung space, it will obey the laws of diffusion, and in course of time displace the residual air. Then, being brought into close contact with the blood, it will either simply allow of diffusion out of blood gases, and, provided its tension in the lungs is above that in the blood, diffuse into the circulation and so reach the tissues, there to be rejected or built into their substance according as it is available or not for their metabolism; and if it is able to link itself into chemical union with some constituents of the blood it will travel so

combined to the tissues, and more or less profoundly influence their behaviour according to its own vital peculiarities.

Let us consider to what class nitrous oxide gas belongs, and what is the *rôle* it plays in the blood. Priestley found nitrous oxide was readily absorbed by water, in a proportion of one-half its bulk. When carbonic acid gas is present in the water no absorption of nitrous oxide takes place; but according to the careful experiments of Davy, when water saturated with nitrous oxide is brought into contact with carbonic acid, the latter ousts the nitrous oxide, becoming absorbed while the nitrous oxide is liberated. According to the same authority nitrous oxide will displace oxygen and air from water. When we remember that blood consists of 78 per cent. of water, we see these researches have a very important bearing. Neutral saline solutions, further, possess very feeble attraction for nitrous oxide. None of the older observers investigated the behaviour of nitrous oxide toward water in which albuminous material was present, and my investigations in this direction are not, I think, sufficiently definite for me to venture upon *ex cathedrâ* utterances; but it seems probable that albuminous solutions of various strengths are possessed of powers of absorbing nitrous oxide other than those inherent in pure water.

The presence of nitrous oxide in the air space of the lungs is of importance in the following relations:—(1) By methods in use in this country oxygen is practically excluded, and, were oxygen admitted together with nitrous oxide, it is probable, our present knowledge tells us, that the oxygen would not be ousted by the nitrogen compound; and (2) the effect nitrous oxide has upon the elimination of carbonic acid gas from the lungs.

1. The deprivation of oxygen leads to asphyxia pure and simple; for example, if a person inhales in an atmosphere of nitrogen, although all carbonic acid (dioxide) diffuses out, yet asphyxial symptoms, hyperpnœa, dyspnœa, and convulsions, appear.

2. Now does nitrous oxide in any way interfere with the elimination of carbonic acid (dioxide) from the lungs? Careful experiments have shown that nitrous oxide affects carbonic acid elimination in only an indirect way.* During the cutting off of oxygen supplies, the tissue metabolism, whereby carbonic acid and water are thrown into the circulation, is greatly lessened, and as a consequence the production of carbonic acid is decreased, so that in this case the diminished elimination is merely an indication of lessened production. We find a marked similarity between the tissues rendered stagnant by nitrous oxide,

* Amongst others I may mention those of Davy, Frankland, and the careful and painstaking researches of Coleman, published by this Society.

and the sluggish behaviour of organic matter in animals during hibernation. At the same time there is a fairly active carbonic acid elimination, as much in fact as represents the tissue waste during the period of anæsthesia; and this carbonic acid, in the absence of recuperative oxygenation, is, I submit, an important matter requiring our attention when we have to take into consideration the practical lessons the physiology of nitrous oxide narcosis teaches. Here I will briefly say it seems consonant with these lessons that we should ensure the removal of this carbonic acid so that the patient may not breathe and re-breathe nitrous oxide polluted by it.

We may then take it that the blood is capable of acquiring nitrous oxide by simple absorption, and probably by the union of that gas with the albuminous materials found in the liquor sanguinis and corpuscles. No attempt has as yet succeeded in demonstrating the conjunction of nitrous oxide with hæmoglobin—at least no crystallised forms have been found, such for example as we are cognisant with in the case of nitric oxide hæmoglobin. However, in the last case we have to bear in mind the fact which was pointed out long ago by Davy, that nitric oxide possesses a strong affinity for the salts of iron, so that it is perhaps not unwarrantable to suppose the iron-containing hæmoglobin should readily unite itself in actual

chemical union with nitric oxide. But nitrous oxide can, as we have pointed out above, actually oust oxygen from its condition of absorption, and must with great rapidity become intimately associated with some of the blood constituents in order that it may be wafted, with the extraordinary rapidity we all are aware of, to the nervous centres, there to bring about that profound change in the nerve tissue which is evidenced externally by the anæsthetic coma of nitrous oxide narcosis. Researches made by means of the spectroscope upon blood when it is impregnated with nitrous oxide, do not, at least to my mind, afford us evidence of value. MacMunn, whom I have before quoted, failed to obtain any characteristic spectrum from the blood of animals poisoned with nitrous oxide. I have repeatedly made the attempt to obtain a spectrum peculiar to this agent, but have also met with want of success, the only bands discernible being the broad one between Fraunhofer's D and E lines, which of course merely represents the spectrum of reduced hæmoglobin. My friend Dr. Halliburton, Assistant Professor of Physiology in University College, was good enough to examine some blood for me, and he concurs in the results given above. Now this negative evidence cannot, I submit, be taken as sufficient for us to base conclusions upon which deserve to be reckoned final. The present methods

at my disposal preclude me from ascertaining the condition of the blood when nitrous oxide in quantity sufficient to induce anæsthesia is given along with oxygen. I hope to be able to conduct this research later on; but as it necessitates a Fontaine's chamber I can only prosecute it in Paris. Under the present circumstances, *pari passu* with the introduction of nitrous oxide we have the reduction of the hæmoglobin by the tissues, hence the spectrum of reduced hæmoglobin which is found.

In all experiments upon Mammalia with nitrous oxide gas, methods have been adopted which not only ensure a supply of the gas entering the lungs, but at the same time cut off the ingress of oxygen, so that there must in these cases always be a danger of confounding the symptoms due on the one hand to nitrous oxide, with those upon the other which arise solely from the deprivation of oxygen. And further, in some experiments which we shall shortly have to consider, a third set of symptoms intrude themselves, namely, those dependent upon re-breathing noxious exhalations from the lungs. It is incumbent then upon us to make allowance for these sources of confusion.

It has been my endeavour in my own researches to eliminate as far as possible those conditions giving rise to serious fallacies in deducing conclusions, by conducting control experiments in

which asphyxial phenomena were brought about. Further, by the use of an expiration valve in my tracheal canulæ, I have attempted to obviate accumulation in the lungs of mephitic material. I am quite sure that much of the erroneous teaching which even now is rampant, and which regards nitrous oxide narcosis as merely asphyxia, arises from neglect of the above precautions.

Among experimental researches I think we must place Sir Humphry Davy's first, not only in priority, but in excellence; for considering the limited means at his disposal, and the imperfect knowledge of physiology which existed in his day, we must admit his research was worthy of so great a philosopher.

In one series of experiments Davy placed cats, dogs, guinea-pigs, rabbits, mice, and birds under bell-jars filled with nitrous oxide by displacement over water, and allowed them to respire the gas. In some cases he noted much excitement, followed by loss of sensation, and final death through cessation of respiration. He removed certain of his animals from beneath the bell-jar, and placing them before a fire watched their recovery. Curiously enough, he observed that in many instances the animals were more or less paralysed, some being hemiplegic and some paraplegic—at least such appears from his statements to have been their condition.

In his second research Davy compared the behaviour of animals immersed in nitrous oxide with those placed in hydrogen and others kept below water. Reasoning from these experiments he says, "there was every reason to suppose that their (the animals') death in nitrous oxide could not depend upon the simple privation of atmospheric air; but that it was owing to some peculiar changes effected in the blood by the gas."*

But these experiments, like those of many subsequent observers, are open to the criticism that the method employed confounded asphyxial with nitrous oxide effects.

Krishaber's researches, made chiefly with rabbits, may be considered under two categories: those in which nitrous oxide with small undetermined quantities of air was employed, and secondly, when, the animal being tracheotomised, nitrous oxide only was breathed. His conclusions are that nitrous oxide narcosis differs wholly from the asphyxial state, for, as he justly points out, no true anæsthesia is brought about in asphyxia, whereas entire loss of sensation and voluntary movement come about in a minute when nitrous oxide is employed. With Krishaber's subsequent attempt to institute a comparison between nitrous oxide narcosis and the anæsthetic sleep of chloroform we have in the present connection nothing to do.

* Collected Works, vol. iii, p. 204.

Amory of New York has done some very valuable work upon the physiology of nitrous oxide; he investigated the gas expired during the inhalation of nitrous oxide, and further repeated Davy's experiments by placing pigeons under bell-jars filled with nitrous oxide by forcing in that gas above and letting out the atmospheric air below. Dr. Amory's researches, both those quoted and those which I have for the present passed by, are altogether admirable, and throw much light on the difficult question under review.

It appeared evident to me that nitrous oxide gas exerted a very considerable effect upon the nervous system, and I was anxious to undertake experiment in the direction of the ascertainment whether or not it produced physical changes in the condition of the brain. One way in which it was possible to investigate this point was to examine the actual changes, if any, in the brain whilst the animal was placed under nitrous oxide.

Accordingly the experiments were made, by the kindness of Professor Victor Horsley, at the Brown Institution.

The skull of a medium-sized dog was trephined, and nitrous oxide gas given through a tracheal tube fitted with a very freely acting expiration valve. The trephine hole exposed the outer third of the sigmoid gyrus on the right side. Under normal conditions the brain was seen some mea-

surable distance beneath the bone, pulsating quietly and synchronously with the respiration. The colour of the brain covered with pia mater was pinky red, or, more exactly, vermilion.

As soon as the animal began to breathe nitrous oxide, the respiratory rhythm being interfered with, the brain pulsations became more notable and somewhat hurried. When the gas was pushed, and the animal made to take it in freely, the brain substance was seen to swell up and gradually reach the trephine hole. The colour now began to change, and a dark, blue-red shade appeared to creep over the exposed brain, robbing the brightness of the vermilion and replacing it by a laky purple. The brain undulations were at this stage found to lessen in frequency and amplitude. The brain substance still increased in volume, and even protruded without the trephine hole, almost motionless, and of a pearly, glistening lustre of bluish hue. The vessels, examined with a strong lens, presented the well-known look of commencing stasis. At this stage the nitrous oxide was stopped and the animal allowed to inspire air freely. Quietly and gradually with each successive breath of air the brain receded, the undulations returning and resuming their normal rhythm and range. With these changes came a return of the vermilion tinge which characterises the healthy brain substance. This experiment was repeated; in some

cases the animal was anæsthetised by means of a face piece with an expiration valve, and in others a tracheal tube was introduced, but the phenomena observed were strikingly uniform. It was next determined to conduct a control experiment, first pushing the nitrous oxide to the verge of death, and subsequently producing asphyxia by deprivation of all air.

In the experiment in which nitrous oxide was given, the brain being exposed as in the last research, the gas was pushed until respiratory movements completely ceased. In a little over a minute (1 min. 10 secs.) the brain substance had become livid and swollen to above the calvarial edge; the animal was absolutely insensitive to painful sensation; his limbs showed marked jactitations. In about 1 min. 30 secs. normal respiratory movements had ceased. Artificial respiration was promptly had resort to, and speedily the natural thoracic movements were resumed. The trachea was then occluded and the brain observed. In about a minute the brain substance assumed a deep purple dull hue, which in another half minute became very intense; the brain then began to recede, sinking deeply from the trephine hole. In two minutes the sphincters became relaxed and further sinking of the brain took place. In three minutes the respiration movements were very profoundly interfered with, only manifest-

ing themselves by long-drawn gasps which were separated by long intervals. In five minutes, although all respiratory movements had ceased, the heart still beat. In six minutes access of air was allowed, but artificial respiration failed to effect recovery.

These experiments appear peculiarly instructive, firstly, as showing in a very marked way the difference between the brain condition when fed with nitrous oxide-laden blood, and when supplied with deoxidised blood containing tissue refuse; and secondly, when viewed in relation with the clinical phenomena of nitrous oxide narcosis. As I pointed out in my last communication to this Society, there is a zone of hyperæsthesia which separates the normal consciousness from the absolute loss of sensation on the one hand, and on the other which unites the stage of oblivion, or sleep, with the return to full mental activity. It is presumably at this epoch that the dreams of mental exaltation and physical joy occur, and it is then that slight external physical stimuli—*e.g.*, a flash of light, a noise, a movement—will become a thousandfold magnified and perverted in the patient's brain. The peculiar filling of the brain would seem to offer a physical counterpart for these mental conditions, and apparently rapidly so modifies the brain cells that they are incapable of further reception or ideation: an initial increased

exaltation gives way to a complete abeyance of function.

Experiments in the same lines were also made with regard to the action of nitrous oxide upon the spinal cord.* The animal being under the influence of chloroform and curare, the laminæ of the lower dorsal and lumbar vertebræ were removed and the cord exposed lying in the spinal canal. The animal was then made to respire nitrous oxide, only expiring through a slit in the canula. A very marked effect soon showed itself: the cord gradually enlarged and cerebro-spinal fluid began to well out, showing the enlargement of the whole length of the cord. This experiment was repeated, and the same result was always obtained. However, as will readily occur to you, two causes might have conceivably produced this effect, namely—(1) the exclusion of oxygen, *i.e.*, the asphyxia, or (2) the presence of nitrous oxide. To test which of these possible factors was really responsible for the swelling up of the cord, the animal was deprived of air, and no nitrous oxide given. At first the cord remained unchanged—at least no swelling took place, and no escape of cerebro-spinal fluid occurred. Soon, however, as the blood became more and more deoxygenised, the cord grew smaller, shrinking below its former level in the spinal canal.

* These experiments were made at the University College Physiological Laboratory, and I am indebted to Mr. John Rose Bradford, B.Sc., for their execution and to Professor Schäfer for the use of the Laboratory.

There was no doubt but that while in nitrous oxide administration the cord, like the brain, grew larger, in asphyxia it shrank. To test this effect further, the following crucial experiment was tried. The animal was subjected to asphyxia, and the cord was watched until it had perceptibly shrunk, when nitrous oxide was allowed to enter the lungs. If, as we assumed, nitrous oxide was capable of dilating the vessels of the cord when acting upon them in a normal condition, it was thought that it should produce a like effect when the cord vessels were contracted by asphyxia. The experiment confirmed this supposition, for as soon as the animal had its lungs well saturated with nitrous oxide, the cord was seen to expand and the cerebro-spinal fluid began to escape.

We may now briefly consider the conclusions these experiments upon the brain and spinal cord appear to justify. In brain and cord alike, we meet with dilatation of the vessels, with of course an increased blood supply to the nerve-centres. Such a condition would indicate a condition favourable to the dissociation of nervous energy, but this would soon be followed by a condition of over-distension and interference with due regularity of the cerebral and cerebellar circulation subversive of ideation and the performance of adjusted muscular action. The interference to the cord circulation must also interfere with the due con-

duction along its paths as well as with the correlation between its parts and the higher brain centres. At present we may not be in a position to theorise beyond the broad general statements given above, but I think we may justly recognise in the interference with the circulation of the brain and spinal cord, produced by the inhalation of nitrous oxide, a phenomenon which accounts for not only the everyday experience we meet with in giving the gas to human beings, but also to those aberrant cases which occur more rarely, and evince marked nervous exhaustion or irregular outbursts of nervous energy. But of these states I will speak again later on.

The development of nervous symptoms certainly varies largely with the initial state of the nerve protoplasm, for while in some persons nitrous oxide induces marked nerve disturbance, in others it brings about none whatever. I may here be allowed to introduce a brief note upon ankle clonus as revealed under nitrous oxide. This phenomenon is in a certain percentage of cases produced when the patient is deeply under the gas.

Among reflexes it is usual to consider two classes, skin or superficial reflexes, of which a familiar example is found in the conjunctival reflex, and deep, of which we have examples in ankle clonus and the patellar jerk and front tap reaction. In

health, and under normal functional conditions, the superficial and the patellar reflex are present; certain pathological conditions lessen or exaggerate these reflexes, and cause the development of ankle clonus. I think, however, we may take it that the presence of ankle clonus points always to disease or functional derangement of the spinal cord. Now nitrous oxide produces very marked derangement of the reflexes. In October, 1883, Professor Horsley* drew attention to the persistence of the patellar phenomena under profound anæsthesia, and long after the disappearance of the superficial reflexes. Clonus I have found to be developed in a number of cases, although it is not a constant phenomenon of nitrous oxide narcosis; hence this gas not only abrogates the function of the brain centres, but also produces marked disturbance in the cord, while it blunts or obliterates peripheral sense. What is the exact nature of this derangement of the cord functions we cannot, I think, venture at present to offer an opinion; we can only study it by means of the phenomena it reveals. These also are various, differing, it would appear, according to the stability of the nervous centres of the individual subjected to observation. Nor is this surprising when we remember that the effects are very transitory, and must be largely influenced by

* "Brain," vol. vi, p. 369 *et seq.*

collateral circumstances. The more constant cord phenomena are—rigidity of the muscles, which passes into complete flaccidity; jactitations which appear rhythmic and general; loss of superficial reflexes; persistence of knee jerk. Among the occasional phenomena we may reckon—ankle clonus; opisthotonus and emprosthotonus; paralysis of the bladder and defæcation centres, and involuntary and unconscious passage of urine and fæces; probably, excitation of the sexual centres, and abolition of the normal checks imposed upon the production of orgasm. Further, we must reckon the secondary results apparently due to a more lasting cord effect, as seen in paresis or even paraplegia following nitrous oxide inhalation. Many of these phenomena are confessedly rare, and are perhaps only elicited in nervous systems predisposed to take on the condition, whatever it may be, which nitrous oxide induces. In some respects nitrous oxide would appear to hold comparison with strychnine. The rigidity, with the occasional liberation of irregular and disorderly explosions of nerve energy, occur, although with different degrees of persistence, alike with one and the other drug. This would perhaps give a clue, and suggest that under nitrous oxide the higher ideomotor centres lose control, the resistances throughout the cord are lessened, and the cells, deprived of the normal restraints imposed by habitual

and associated action, tend to irregular explosive outbursts. It seems at least probable that under nitrous oxide not only do we meet with a stage of preliminary exaltation of function, misdirected indeed, and unconstrained by judgment, in the brain centres, exemplified by the stage of hyperæsthesia spoken of above, but that in the lower cord centres we recognise a similar initial heightening of activity, also irregular and disorderly, followed by cessation of their functionation. Indeed, I venture to think the same sequence of events happens in the vital centres, and that this explains much of what follows in the remarks made upon blood pressure, cardiac, and respiratory rhythm. But although we may not as yet go far enough to dogmatise upon what is the nature of this action upon the cerebro-spinal axis, yet it seems consonant with our facts to regard it as a sedative, which, while provoking an initial exaltation of function, eventually plunges the tissues into a sleep, or state like the long dose of hibernation. Certain it is in some cases one meets with a quiet prolongation of nitrous oxide narcosis, unaccompanied by the wild convulsions of asphyxia, when the breathing absolutely stops while the heart still beats on. In this state presumably the cord centres have gradually yielded, and, the medulla reached, the respiratory centre has also peacefully ceased from work, and the patient is entranced alike in his mental and vegetative

functions. In these cases artificial respiration, conducted for one or two admissions of air, restores the patient to animation, and all goes well. No danger is, in fact, incurred unless the anæsthetist is either incompetent or negligent of his solemn charge. It seems hardly worth while to do more than to beg you to compare mentally these phenomena with those afforded when asphyxia terminates life. To contrast what has just been described with the mental activity persisting almost to the last gasp, the purposeful struggles, the wild chaotic respiratory efforts, the frantic writhings of the voluntary muscles, and at length the general massive convulsions passing into a false quiet marked by an occasional gathering together of the failing nervous energy to effect a spasmodic explosion of muscular force.

Knowing that one of the greatest and gravest dangers which beset the induction of anæsthesia is heart failure, it becomes matter of very great importance for us to determine the behaviour of nitrous oxide towards the heart and vascular system in general. My investigations in this direction have been made to ascertain the action of the heart and the variations of blood pressure under nitrous oxide; and further, to determine how far the variations seen when nitrous oxide was exhibited were due to that body, and how far to the coincident deprivation of oxygen.

The animals selected were dogs and cats, but as the results were practically uniform it is unnecessary to particularise the experiments. I must again admit my great indebtedness to my friends Professor Victor Horsley, Mr. Bradford, and Professor Schäfer, through whose kindness alone the research was practicable.

The heart's action does not become much affected under nitrous oxide, and even in cases in which that gas is pushed until complete cessation of respiratory movements occurs, the heart still continues to beat, its action gradually growing weaker. In no case have I seen any tumultuous action of the heart or a sudden cessation, only the gradual sinking to rest noticed above. The attempt at narcotising animals and timid persons produces a temporary acceleration of heart-beat, but as soon as the intellect becomes under the influence of the narcotic this acceleration passes off and the heart-beats become regular and strong and somewhat slowed. It will be remembered that these results are in accord with the statements already published by me, and based upon numerous sphygmographic tracings taken of the human radial pulse.

The blood pressure under nitrous oxide inhalation has the following peculiarities. For the first period it shows little change ; but subsequently a fall of pressure takes place. Upon allowing the

animal to inhale air, the blood pressure recovers itself, but only gradually, and by passing through a phase of somewhat irregular curves. These curves are not respiratory, as they take place even when the animal is completely paralysed with curare, and artificial respiration is maintained. In some cases a slight, but very slight, rise in the blood pressure took place, but a rise of blood pressure which persists for a notable time appears always to follow the nitrous oxide inhalation. Control experiments were conducted to test the effect upon blood pressure when the animal is deprived of air. These were done upon curarised animals in order to avoid the interference caused by dyspnœic convulsions. As soon as the air supply was cut off, the blood pressure began to go up, and rapidly increased until the heart's action, which lessened in force *pari passu* with the heightened blood pressure, became so weak that it was necessary to allow air to enter the lungs. The blood pressure then resumed its normal height very quickly; but the rise which follows after nitrous oxide administration does not appear to ensue after asphyxia.

It seems to me upon reviewing the nitrous oxide experiments, and controlling them by the asphyxia experiments, that nitrous oxide itself has no very marked influence upon the heart or vessels; that what action it has is to steady and slow the heart, and if anything to strengthen it, and that the

action is somewhat prolonged. The vessels, at first almost unaffected, later on undergo a peripheral dilatation leading to a lowering of blood pressure. This, however, is true only when reservation is made; for, as we shall see later on, the splanchnic vascular areas are contracted at first. Upon this last statement I have some additional evidence to offer. A good-sized frog (*Rana temporaria*) was placed beneath a dome-shaped glass vessel, so arranged that the web of one foot was outside the vessel and could be examined under the microscope. The dome was emptied of air and kept full of nitrous oxide, and the frog carefully noted while the web was examined. It was necessary to keep the whole animal in nitrous oxide as cutaneous respiration is very active in the frog. At first the circulation in the web was found to be slowed; at the same time the minute vessels were seen to dilate, and this slowing and dilatation both became more marked as time went on. Changes also appeared to develop in the corpuscles by which they took on a flattened compressed appearance. At length the respirations, which had become slower and slower, became almost extinguished, the capillary circulation in some areas was almost in a condition of stasis, whilst throughout the field extreme slowing had occurred. At this point the frog was allowed free access to air, and at once the respiration

quickened, the blood flow increased in rapidity, becoming many times more rapid than under the gas. The corpuscles resumed this normal aspect. The results of such experiments upon the frog point to a peripheral dilatation of capillaries, and of this further evidence has yet to be adduced. It needs no argument to show that a vascular viscus, like either the kidney or the spleen, must under variations of blood supply undergo variations in size. If, therefore, it were possible to enclose either viscus in an air-tight receiver communicating with an oil manometer, it would give indications of increase or diminution of size according as the blood supply were increased or lessened. Mr. Bradford has kindly enabled me to investigate this point pretty fully.

The experiments made upon the kidney were tolerably numerous, and were singularly uniform in their results. The kidney in an animal narcotised with nitrous oxide speedily undergoes contraction, which corresponds of course with the contraction of the renal arteries. This contraction continues as long as the nitrous oxide is given, but as soon as that is cut off and the animal respires air the kidney speedily recovers its normal size, but no dilatation of vessels beyond normal takes place. With this condition we have to compare the behaviour of the kidney in an animal subjected to asphyxia. Here the kidney undergoes a dilata-

tion as soon as air is cut off. This corresponds with dilatation of the renal arteries, and is probably due to increased heart action called into being by the venosity of the blood. Later on, when the heart fails, the kidney suddenly contracts, a very rapid fall in the kidney curve occurring. Thus a singularly striking contrast in the behaviour of the kidney reveals itself according as that viscus is influenced by nitrous oxide or asphyxia. This effect upon the renal circulation must not be taken as militating against the statements made above with regard to the general blood pressure as shown by the carotid artery and about the circulation in the brain and cord. It is well known that certain sedatives—morphine, for example—dilate the vessels in one area while they contract those of other areas.

Passing to the effects produced by nitrous oxide upon respiratory rhythm, I will detain you only a few moments.

The chest movement will, as is well known, continue without any air entering if a sufficiently long and small elastic tube be attached to the tracheal canula, so that one can easily compare asphyxia with nitrous oxide narcosis. In the last condition the respirations are at first quickened, but not lessened in depth; later on they grow slower and deeper, and still later they become very slow and somewhat more shallow; finally they

cease. The time in which this cessation comes about varies considerably in animals. I have not seen the dyspnœic struggles under nitrous oxide which asphyxia brings about. In human beings I have seen, especially in children, complete cessation of respiration without the slightest preliminary struggle. Alike in the lower animals and man the breathing recommences if pressure is made on the chest. These changes in respiration are, I am inclined to think, due wholly to the action of nitrous oxide upon the nerve centres presiding over respiration.

In conclusion, there are various practical considerations which I think may well be taken into review while studying the physiology of nitrous oxide narcosis.

If, as I submit, nitrous oxide acts as a sedative in virtue of its own inherent properties, and does not owe its value as an anæsthetic to asphyxial processes called into play by concurrent privation of oxygen, it should be our aim to push the gas and give free vent to expired gas. We should see that our patient changes as freely as possible his residual air during inspiration, and expires as freely as possible the refuse-laden nitrous oxide which has been stationary within the air-spaces during the last respiration. I cannot but think that, whatever may be the saving of gas brought about by employing supplemental bags wherein the nitrous

oxide is collected and re-inspired again and again, the patient suffers by their use from the double evil of breathing diluted and impure nitrous oxide, and further, is not favourably placed for exhaling the refuse of the lungs. I should incline to attribute to this method the cases one occasionally meets with of severe headache, vertigo, dizziness, and other untoward symptoms consecutive upon nitrous oxide inhalation. It is, I believe, a very important point to induce very free inspirations of *pure* nitrous oxide, and to avoid anything like inducing partial asphyxia, and I think in practice this gives the best and the most satisfactory results.

The behaviour of the heart under nitrous oxide should, I take it, encourage us to use this agent freely, and during its administration to watch rather the respiration than the pulse; since it would appear that syncope, if it occurs, occurs secondarily through the lulling to sleep of the respiratory centres. The cases in which nitrous oxide has been said to kill by heart failure are few, and even in these we are not at all sure that the fatal faint was not due to fear or shock incurred by a nervous system already shaken by suffering, and rendered still more obnoxious to shock by an imperfect narcosis. When we remember the period of heightened sensibility which precedes complete restitution of consciousness, we can easily comprehend the terrible jars a debilitated nervous

system must sustain if operative procedure be carried on into this stage. Clover long ago pointed out from his vast clinical experience that patients may be allowed to cease breathing, and yet no fear need be entertained, as a few vigorous pressures upon the thoracic parietes will re-initiate respirations. Now we accept his statement, and explain it under physiological laws.

There are other practical points that are suggested by knowledge of the action of nitrous oxide. Of these not the least important is that the erotism called into existence in a fairly large proportion of patients, and controlled only in a few by the restraints of habitual thought and judgment, should render all persons most careful to avoid possible incrimination through hallucination. For the sake alike of patient and operator a witness should always be within earshot or within sight whenever nitrous oxide is administered.

Again, the decided action this anæsthetic has upon the nerve centres, and its tendency to call forth irregular explosions of nervous energy might by some be taken as contra-indicatory to its employment for patients who are the subjects of epileptiform seizures. I do not, however, think we can with justice say that the giving the gas renders a fit more likely to occur than the operation. We are aware any strong excitant will call forth a seizure, whereas the sedative action

of the nitrous oxide will by lessening stimulation from without, be less inclined to provoke the attack.

There is one further remark I would make, and that is concerning the late M. Paul Bert's method of giving nitrous oxide under pressure. I may say that my reason for giving only a passing notice to what must appear to many of you, as a method, in the last degree important. Fully admitting the immense value in theory of Bert's method, I am bound to confess to myself that it at present needs far too much machinery and elaboration for practical work-a-day men like ourselves. Indeed this view appears to be held even in Paris, where a Fontaine's chamber is accessible, for I hear from a correspondent that no cases of operation have of late been conducted by this method.

In conclusion, I have to thank this Society for its courtesy towards myself. The Odontological Society has done more than any other body to elucidate the action of nitrous oxide, and hence it was but fitting that my research should see the light in that Society, and this has been permitted me through the courtesy of two generations of Secretaries.

EXPLANATION OF PLATES.

These plates represent curves taken in the Physiological Laboratory of University College, London, by kind permission of Professor Schäfer.

No. I shows the pressure of blood in the carotid. As soon as the nitrous oxide gas had fairly replaced the air in the lungs a slight fall of blood pressure took place, which continued until the nitrous oxide was turned off and the animal was permitted to breath air, when a rapid rise of pressure took place.

The lower curve represents the changes of volume occurring in the kidney of an animal under nitrous oxide. The kidney was enclosed in an oncometer and the curve taken with an oil manometer. In this case a decrease in the size of the kidney appeared at the same point as that at which the blood pressure began to fall. This change in the kidney represents a fall of blood pressure in that viscus. Upon access to air complete resumption of normal pressure took place.

In No. II similar curves are taken when the artificial respiration performed mechanically upon a curarised animal was discontinued. In marked contrast to No. I, the kidney curve did not fall, while the blood pressure curve underwent little change. Hence, comparing a brief period of deprivation of air with a similar period during which nitrous oxide is given, both the blood pressure and the kidney curves differ.

No. III shows the effect of a very prolonged period of nitrous oxide administration.

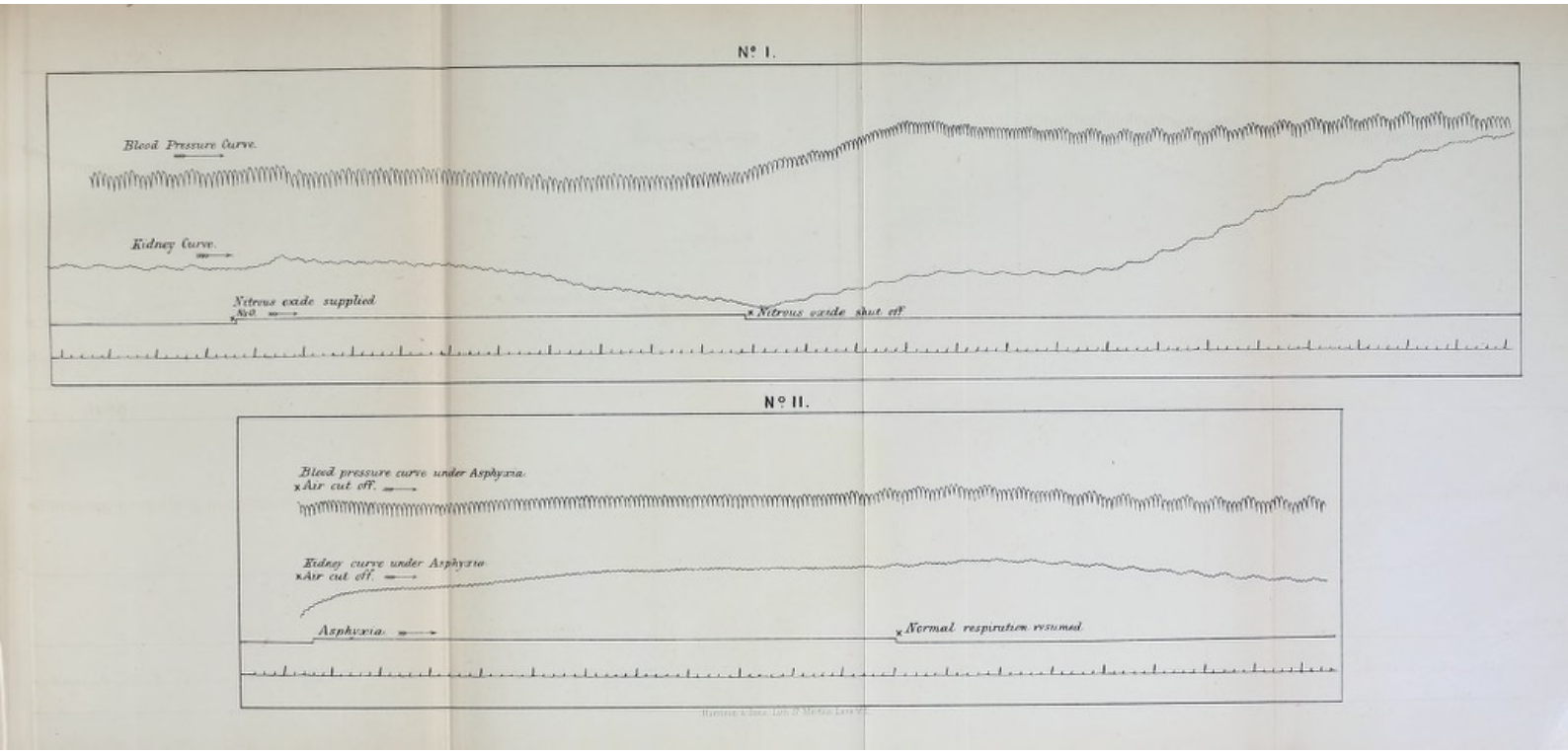
No. IV shows the effect of deprivation of air for a like period. In the first case the blood pressure remains unaltered or falling slightly, but eventually falls rapidly, and finally recovers by passing through a period of vascular excitement marked by leaps and bounds. Under asphyxial

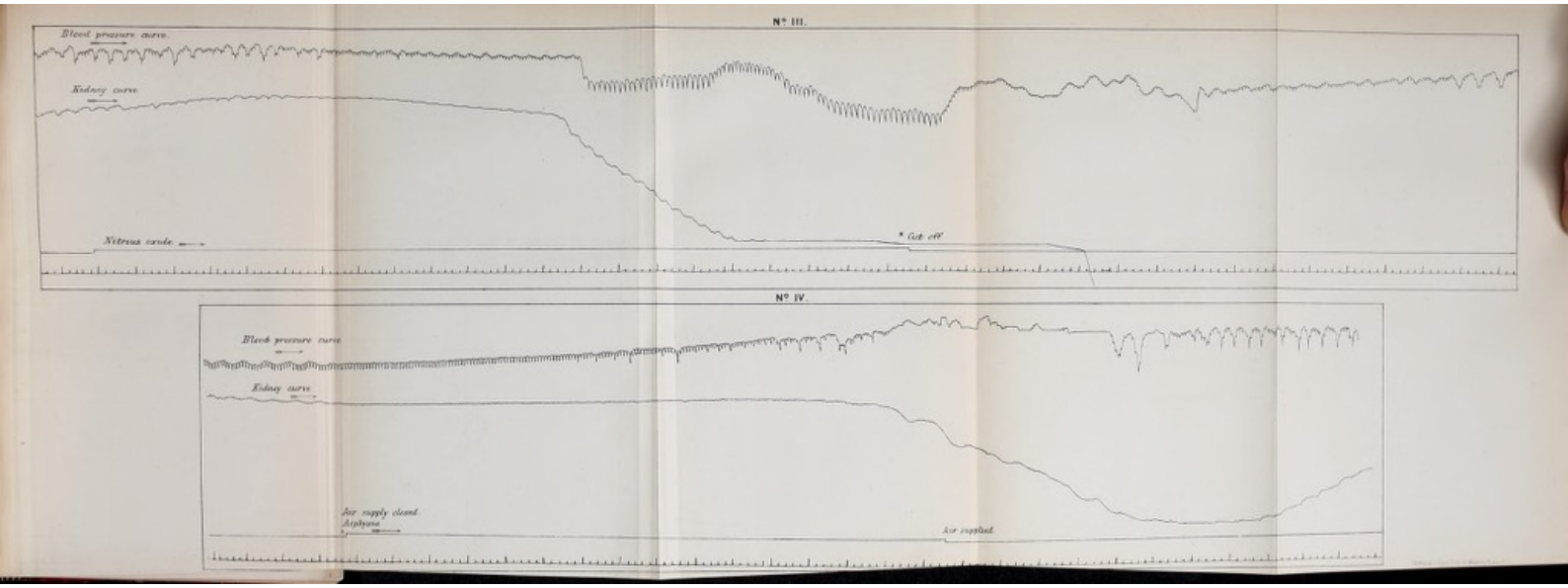
conditions the blood pressure curve is raised almost from the beginning.

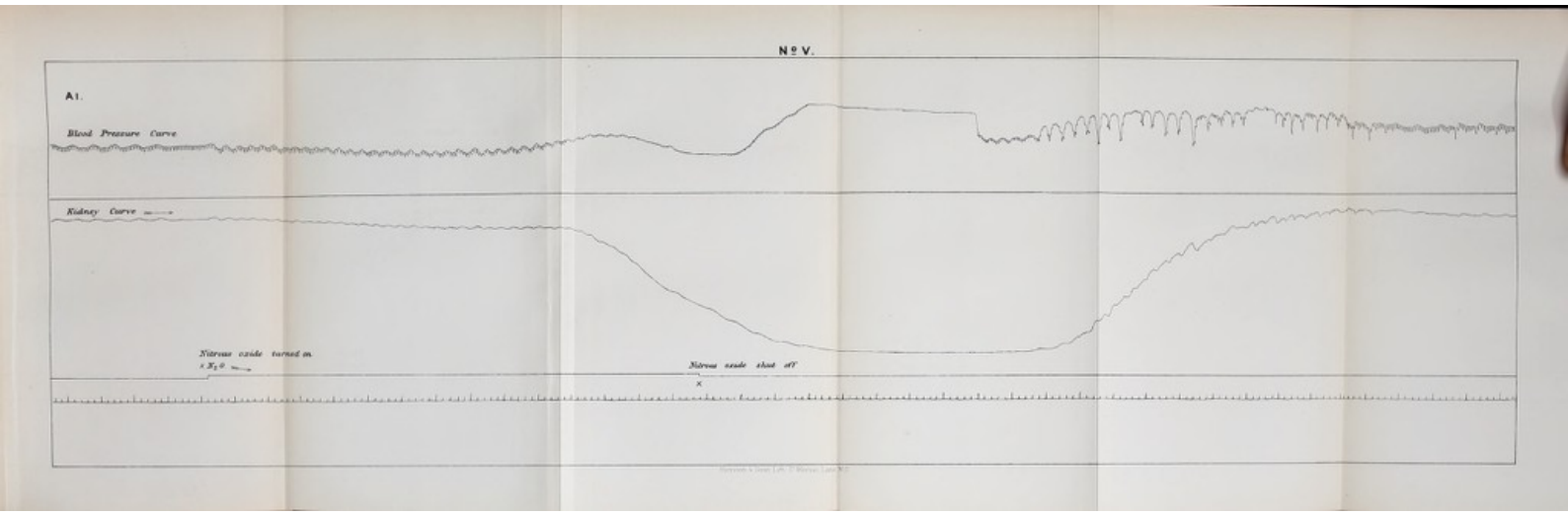
Under nitrous oxide (III) the kidney, as soon as the gas has fairly asserted itself, steadily contracts until simultaneously with the fall of blood pressure it undergoes a very marked and rapid diminution in size. Under asphyxia (IV) the kidney does not contract until the heart has given out as shown by the tumultuous state of the blood pressure curve, then the kidney rapidly contracts. Thus in III the contraction is more gradual and occurs much sooner than in IV, and is wholly independent of heart failure, as in III the heart was beating regularly and well throughout the time occupied in taking the trace.

No. V shows further blood pressure and kidney curves under nitrous oxide.

Harrison and Sons, Printers in Ordinary to Her Majesty, St. Martin's Lane.


N° I.
Blood Pressure Curve.
Kidney Curve.
Nitrous oxide supplied.
N2O
Nitrous oxide shut off.
N° II.
Blood pressure curve under Asphyxia.
Air cut off.
Kidney curve under Asphyxia.
Air cut off.
Asphyxia.
Normal respiration resumed.


N° III.
Blood pressure curve.
Kidney curve.
Nitrous oxide.
* Cut off.
N° IV.
Blood pressure curve.
Kidney curve.
Air supply closed.
Asphyxia
Air supplied.


Nº V.
A1.
Blood Pressure Curve
Kidney Curve
Nitrous oxide turned on.
$\times N_2O$
Nitrous oxide shut off
×