Physiological essays on the action of poisons, and on the introduction of saline substances into the veins / by James Blake.

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PHYSIOLOGICAL ESSAYS

ON THE

ACTION OF POISONS,

AND ON THE

INTRODUCTION OF SALINE SUBSTANCES INTO THE VEINS.

By JAMES BLAKE, M.R.C.S.L.

OBSERVATIONS AND EXPERIMENTS

ON THE

MODE IN WHICH VARIOUS POISONOUS AGENTS ACT ON THE ANIMAL BODY.

By Mr JAMES BLAKE.

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The subject of the following researches is one, the importance of which is fully attested by the attention it has received from physiologists. The action of poisons on organized beings has always been considered as a valuable means for elucidating some of the more important phenomena they present; and the facilities which this class of substances affords us of destroying or modifying some of the more complex functions of animals, renders them valuable agents in attempting an analysis of these functions. These circumstances have invested with so much interest the question as to the manner in which poisons produce their effects; and although many researches have been undertaken with the view of elucidating this question, the conflicting opinions still entertained on this point, afford sufficient proof that much still remains to be discovered in this branch of physiology.

Of the many opinions that have been entertained on the manner in which poisons produce their effects, there are only two which it is now necessary to notice, as they express the views of by far the greater number of physiologists of the present day.*

* In using the word poison in these researches, I would be understood as apply-

According to one of these opinions, before a poison can produce any general effects, it is essential that it should be mixed with the blood circulating over the body, and thus brought into contact with the nervous tissue, or, at least, that the poison should, in some manner, be strictly applied to the nervous centres.

The other opinion to which I have alluded is, that these poisons modify or destroy the functions of the nervous system, by an impression made on the nerves of the part, to which they are directly applied, and which, being transmitted to the nervous centres, may destroy these functions independently of any contact of the substance with the nervous tissue generally.

In bringing forward a series of experiments in order to elucidate this question, I would not be understood as laying claim to any credit for originality in these experiments, as most of them have been performed by former physiologists. My only reason for here detailing them is, that in these researches they have been observed with a definite object in view, and in order to furnish data which are not to found in those already published. The same remark will apply to the conclusions I have drawn from those experiments which are in accordance with the opinions entertained by many distinguished physiologists, although opposed by some of our highest toxicological authorities, and also I think by the greater number of physiologists in this country. As the opinion which would ascribe the general effects of a poison to an impression made on the part to which it is directly applied, is in opposition to the conclusions to which a careful investigation of the subject has led me, I shall take a short review of the evidence adduced in support of this opinion. This is of two kinds; that afforded by direct experiment, and that deduced from the consideration of certain pathological and physiological facts.

I. I shall at once proceed to notice the latter, leaving any remarks on the experimental evidence until I shall have related those experiments which I have performed on the subject.

The most important pathological facts brought forward are;—1*st*, the sudden manner in which certain morbid effluvia have been stated to affect the human body; 2*dly*, cases of sudden death taking place after the receipt of a slight wound; and 3*dly*, the production of tetanus by the mere local irritation of a nerve. 1*st*, The facts brought forward in support of the first statement are derived from the sudden effects which are stated to have been produced by the effluvia proceeding from certain fomites of plague. Instances are reported in which persons have fallen down, and instantaneously expired, whilst conveying these supposed fomites from the ships. The validity of these statements cannot, I think, be allowed, after

ing it exclusively to those substances which appear to destroy life by their effects on the nervous system.

the valuable information which has lately been communicated to the public on this subject by Dr Bowring, who has been an eye-witness of the disease in its worst forms, and who has been led to conclude that it is not infectious. Should the report in question have any foundation, it will probably be owing to mere coincidence of sudden death taking place at a moment when the person was so employed. *2dly*, The same remark will apply to cases brought forward of sudden death produced after the receipt of a slight injury. Such cases must be exceedingly rare, as Professor Cooper, a gentleman who has had most extended opportunities of observing such cases, did they really exist, informs me that he has never met with an instance of death suddenly following a slight injury. *3dly*, In regard to tetanus I would observe, that we are not justified in concluding, that the whole of the morbid phenomena are the result of the mere local irritation of a nerve. It is highly probable, that some pathological state has been propagated from the injured nerve to the nervous centres, before the violent symptoms which characterize this disease manifest themselves. Were the symptoms the mere result of the local irritation of a nerve, we might expect to produce them at pleasure, by merely irritating the nerve; but it is well known that this is not the case. In every instance it is necessary that a certain time shall elapse between the local injury and the appearance of the disease, which time is probably required, in order that the pathological condition above alluded to may be produced. It would thus appear that we have no pathological facts which lead to the conclusion, that poisons act by an impression made on the nerves of the part to which they are directly applied.

The principal physiological facts which have been supposed to support the opinion, that poisons may produce their effects on the system, without being generally applied to those tissues, the function of which they appear to destroy, are derived from the instantaneous manner in which some poisons have been stated to act. The support derived from this fact, however, has been founded on erroneous views which have been taken, of the time required for the blood to circulate from one part of the system to another; and also from the statements of the instantaneous action of the more powerful poisons, being deduced from incorrect observations. The following facts will, I trust, substantiate the correctness of these remarks, by showing that a sufficient time always elapses between the application of a poison and the appearance of its first effects, to allow it to enter the circulation, and to be directly applied to the tissue, the functions of which are affected.

II. In order fairly to enter on the investigation of the question which is the more immediate object of these researches, it is necessary that correct ideas should be entertained of the time re-

quired for the blood to circulate from one part of the system to another. I shall therefore commence by relating some experiments which tend to elucidate this important point, more particularly as the conclusions to which they lead are not in accordance with the opinions generally entertained on the subject.

As the introduction of a poison into the circulation is the first phenomenon that follows its application to a part, the following experiment, by affording a proof of the permeability of the tissues, shows how readily this may take place : it also offers a striking example of the rapidity with which the blood circulates.

(Exp. 1.) A drachm of the strongest *Liquor Ammoniæ*, mixed with five drachms of water, was injected into the jugular vein of a dog. A glass rod which had been dipped in hydrochloric acid was held immediately under the nostrils, in order to detect any ammonia that might escape from the lungs. Four seconds after the introduction of the first drop of the solution of ammonia into the veins, it was plainly detected in the air expired from the lungs by the white vapours that were formed on its coming into contact with the vapour of the hydrochloric acid. It would thus appear that in four seconds, this substance must have passed from the jugular vein through the right side of the heart, and reached the capillaries in the lungs; have permeated the parietes of these vessels, and escaped through the whole length of the air tubes.* Analogous experiments have been recorded by Magendie, and other physiologists, in which oil holding phosphorus in solution was injected into the veins, phosphoric acid being detected in the breath a few seconds after its injection.†

Having shown the facility with which the tissues are permeated, I shall now endeavour to elucidate the question as to the rapidity of the circulation, by tracing various substances, from one part of the vascular system to another. My experiments on this point have been much facilitated by the manner in which certain substances have been found to act on different parts of the vascular system.‡ The effects of these substances have been detected

* As the principal interest attached to these experiments depended on the accuracy with which the time of the occurrence of the phenomena was observed, I would remark, that every precaution was taken in order to obtain correct data on this point. I would also state that Dr Sharpey, Professor of Physiology in the London University, sanctioned by his presence the most important of these experiments; and I with pleasure avail myself of this opportunity to return him my thanks for the valuable assistance and advice he has on all occasions so kindly afforded me.

† These observations are confirmed by experiments performed on delicate membranes when removed from the body. The rapidity with which these are permeated by different solutions, affords a decisive proof of the facility with which this process may go on, particularly when we consider that the most delicate membranes that can be used for these experiments are probably many hundred times thicker than the parietes of the capillary vessels.

‡ The proofs of the local action of these substances has been derived from an extensive series of researches on the subject, which will shortly be brought before the

the instant they take place, by the use of the hemadynamometer, an instrument which indicates, by means of a column of mercury, the pressure sustained by the parietes of the blood-vessels, and which immediately becomes modified on any change being produced, either in the action of the heart, or in the capillary circulation.

(Exp. 2.) The following experiment furnishes an example of the time required for a substance to pass from the jugular vein to the capillaries of the pulmonary artery. It had been ascertained that soda and its salts possess the property of arresting the capillary circulation in the lungs. When this effect is produced, no more blood is sent into the left side of the heart and arterial system, and it follows, that the pressure sustained by the parietes of the arteries must be instantly diminished. Fifteen grains of soda dissolved in six drachms of water were injected into the jugular vein of a dog. Six seconds after the first portion of the injection was introduced, the pressure in the arterial system began to diminish, and the mercury in the hemadynamometer speedily sank to zero, although the pulsations of the heart still continued.*

(Exp. 3.) An experiment the reverse of the former was performed by connecting the hemadynamometer with the venous system. When the passage of the blood through the lungs is arrested, it is evident that the venous system must become congested, and thus the pressure supported by the parietes of these vessels will be increased. In this instance six seconds elapsed between the introduction of the substance into the veins, and any perceptible increase in the pressure.

It would appear from these experiments that soda when introduced into the jugular vein affects the capillaries in the lungs in from four to six seconds; a space of time rather greater than that required by ammonia to traverse this distance. This might arise from two causes; either that the diffusive power of some substances is much greater than that of others, and that they thus may be transmitted from one part of the column of blood to another, independently of its progressive motion; or that in some animals the circulation is going on much more rapidly than in others. The

public.—Since the above was written, the experiments in question have been published in a memoir read at the Institute of France.

* The time at which marked effects are produced might not be the moment at which the substance is applied to the tissue affected; a slight interval probably elapses between the arrest of the capillary circulation in the lungs and the diminished pressure in the arterial system. The time, therefore, in which these effects were observed is probably a second or two later than that on which the soda reached the capillaries. The importance of taking into consideration even these apparently trifling circumstances will be acknowledged, when it is shown that an interval of two or three seconds forms a considerable fraction of the whole of the time required for the circulation to be completed in.

next points between which I shall endeavour to trace the passage of a substance are the jugular vein and carotid artery.

(Exp. 4.) The following experiment, although it does not afford a direct proof of the time occupied by a substance in passing from one of these vessels to the other, yet shows that it cannot, in this instance, have exceeded seven seconds. A tube, furnished with a stop-cock, was inserted into the carotid artery of a dog, the point of the tube looking towards the heart. A solution, containing seventy-five grains of chloride of barium in six drachms of water, was introduced into the jugular. Blood was allowed to escape from the carotid artery three seconds after the introduction of the salt into the vein, and was received into a vessel (No. 1) for four seconds. Another vessel (No. 2) was then substituted, but as the action of the heart was already arrested, a small quantity of blood only escaped from the arteries into it; the blood from the left side of the heart was afterwards added to it. The blood from the right cavities of the heart was collected in another vessel, (No. 3.) The quantities of blood contained in these different specimens were as follows: No. 1. contained four fluid drachms; No. 2. twelve drachms; and No. 3. twenty drachms. Each specimen was evaporated, carefully incinerated in platinum vessels, treated with hydrochloric acid, filtered, precipitated with sulphate of soda; the precipitate was collected, washed with diluted nitric acid, dried and weighed.

The following are the results: The quantity of sulphate of baryta furnished by No. 1 weighed 3.33 grains; that from No. 2, weighed 4.62 grains; and from No. 3, 0.90 grain. If from these data we calculate the quantity contained in equal quantities of blood in the different specimens, it appears that No. 1 contained 3.33 grains in four fluid drachms; No. 2 contained 1.54 grains in an equal quantity; and No 3 but 0.18 grain in the four drachms. This proves that the blood which contained the greatest proportion of the salt had already passed through the arch of the aorta before the action of the heart was arrested, or in less than seven seconds after the introduction of the salt into the jugular vein. If we consider that when the first vessel was removed, a considerable quantity of the salt had already entered it, we must conclude that the moment of its first escape from the carotid could not have been later than five seconds after its introduction into the jugular vein. The very slight trace of the salt found in the blood from the right cavities shows how completely the blood had been renewed.

The following observations will show the time required for a substance to pass from the jugular vein to the termination of the coronary arteries. This may be ascertained by availing ourselves

of a property which some substances possess of suddenly paralyzing the heart when mixed with the blood circulating over its parietes.

Examples of such substances are found in infusion of tobacco, oil of tobacco, the *Upas antiar*, arsenic, oxalic acid, nitrate of potass, and hydrocyanate of potass, all of which, whether they act on other textures or not, have the property of speedily destroying the irritability of the heart, and thereby rendering it unable to contract in its contents.

(Exp. 5.) On injecting a solution of these substances into the veins, an interval varying from seven to fourteen seconds has been found to elapse between their introduction and the arrest of the heart's action. The cessation of the action of the heart has generally been ascertained by the use of the hemadynamometer, but in one experiment, in which the thorax was opened, artificial respiration being performed, the motion of the heart was seen to be suddenly stopped, seven seconds after the introduction of the first portion of a solution of nitrate of potash (one of those substances which exert this affect on the heart) into the jugular vein.

I shall now relate an example illustrating the space of time required for a substance to pass from the commencement of the aorta and to be generally diffused into the systemic capillaries. The manner in which this can be observed, is by injecting a substance, which had been ascertained to arrest the capillary circulation, into the axillary artery of the right side, the point of the syringe looking towards the heart: when pushed with force, the injection is thrown back into the aorta, and thus becomes distributed over the body. The hemadynamometer furnishes an index of the moment in which the capillary circulation becomes affected, for the pressure in the arteries becomes instantly increased. When a substance capable of exerting such an action on the capillaries is injected, it is found that these vessels become affected in an interval varying from four to seven seconds after its first introduction. It has already been shown in Exp. 3, that the interval which elapses between the introduction of a substance into the jugular vein, and its appearance in the carotid artery, may not be more than five seconds. From this point four seconds may be required before it is distributed to the systemic capillaries; thus giving an interval of nine seconds, which may intervene between the introduction of a substance into the jugular vein, and its general diffusion throughout the body.

(Exp. 6.) I shall conclude the observations I have to bring forward on this part of the subject, by relating one experiment which shows the time required for a substance to pass from the aorta through the whole of the vascular system, back into that vessel, and thence through the coronary arteries over the parietes of the heart. A substance capable of paralyzing the action of the heart was injected into

the axillary artery, so as to pass into the aorta. Under these circumstances, a space of time, varying from thirty-five to forty-five seconds, has been found to elapse between the introduction of the substance and the cessation of heart's action. I would remark, however, that all those substances which act in this manner on the heart also possess the property of impeding the passage of the blood through the capillaries for a time varying from fifteen to twenty-five seconds, so that these experiments furnish no exact indication of the time in which a substance which does not possess this property may pass between the points above alluded to. From those experiments in which the phenomena would be observed with the greatest accuracy, I conclude, that the time required for a substance which does not act on the capillary tissue, to pass from any part of the vascular system back to the same point again, varies in dogs from twelve seconds to twenty seconds. These conclusions are in perfect accordance with those arrived at by Hering from a series of carefully conducted experiments on horses, in which he found that the whole round of the circulation was completed in about twenty-five seconds.

Having now the requisite date by which to determine the time in which a substance can be circulated over the body, I shall proceed to relate some experiments which have been performed with a view of discovering if a sufficient interval elapses between the application of those poisons which have been shown to act on the nervous system, and the first symptom of their effects, to allow them to be brought into contact with the nervous tissue throughout the body. Experiments have been tried with concentrated hydrocyanic acid, woorara, nicotine, conia, and strychnia,—poisons which have been shown to produce the most rapid effects on the animal economy.

(Exp. 7.) Half a drachm of concentrated hydrocyanic acid was prepared by passing sulphuretted hydrogen over the bicyanide of mercury. The gas being previously dried by passing it over chloride of calcium, the acid was collected in a receiver surrounded by a freezing mixture. It was used immediately after its preparation. In order to insure a marked effect being produced, the whole of the acid was poured, on the tongue of a strong dog, weighing about eighteen pounds, the head being kept elevated. Eleven seconds elapsed between the application of the poison and the appearance of any morbid symptom. The respiration then became affected. The animal was dead thirty-three seconds after the administration of the poison. If a tube be introduced into the trachea, through which the animal can breathe, a longer interval elapses between the application of the poison and the appearance of its effects. This is probably owing to the acid not being inhaled with the breath ; for on account of the extreme volatility of

the strong acid, it is converted into vapour the instant it comes into contact with so warm a surface as the mouth, and in this state it is applied to the capillaries in the lungs, and rapidly absorbed. It thus has a shorter distance to pass through before reaching the nervous centres than when it enters the capillaries of the mouth, and circulates through the right side of the heart.

(Exp. 8.) A tube being introduced into the trachea of a dog, a drachm of the strong acid was poured on the tongue of the animal. Sixteen seconds elapsed before any symptom of the action of the poison manifested itself, and the animal died about forty-five seconds after the application of the poison. These experiments have been repeated twice, and always with the same results. They show that, in these instances at least, a sufficient interval has always elapsed between the application of the acid, and the moment when its first effects were produced, to allow of its being brought into contact with those tissues on which it appears to act.

(Exp. 9.) The woorara is a poison which has been stated to produce instantaneous effects when introduced into the circulation. As it is not very rapidly absorbed, the readiest way of testing its action was by injecting it into the veins. Five grains of the poison dissolved in five drachms of water were injected into the jugular vein of a dog. Twenty seconds elapsed before any symptom of the action of the poison could be observed. Violent convulsions were then produced, and the animal was dead about forty-five seconds after the introduction of the poison. This experiment has been repeated three times, and has constantly furnished analogous results; the time required for the poison to produce its first effects varying from sixteen to twenty-three seconds. *

(*Exp.* 10.)—The active principle of the hemlock, or conia, is a poison which has been stated by Dr Christison to produce effects so rapid, that an appreciable interval did not elapse between the introduction of the poison and the death of the animal.—(See Transactions of the Royal Society of Edinburgh.)

Having obtained a considerable quantity of conia from an alcoholic extract of the seeds of *Conium maculatum*, and which exactly resembled in physical and chemical characters that described by Dr Christison, I proceeded to try the following experiment, using a large dose of the poison, in order to insure a marked effect the moment it should begin to act.

Ten drops of conia, neutralized with a small portion of diluted hydrochloric acid, were injected into the femoral vein of a dog by

* The poison was procured for me by my respected Professor, Dr A. T. Thompson, whom I have to thank for the valuable assistance he has afforded me whilst conducting these experiments.

means of a finely pointed glass syringe.* Fifteen seconds elapsed between the introduction of the poison and the appearance of any symptoms of its action. The respiration was then violently affected, and the animal was dead thirty seconds after the injection of the poison;—thus affording a proof of its virulence; for by no other substance that I have used has death been produced in so short a time. This experiment has been repeated four times, and in no instance have any symptoms manifested themselves in less than fifteen seconds.

(*Exp.* 11.) The next substance whose action I have tried is nicotina, or the active principal of tobacco. Two drops were injected into the jugular vein of a dog. The first symptoms of its action manifested appeared fifteen seconds after the injection. The animal was dead in about one minute and a half after the administration of the poison.

When this substance was applied to the tongue, an interval of twenty seconds elapsed before any marked symptoms manifested themselves.

(*Exp.* 12.) The striking effects produced by nux vomica are such as enable it, the moment on which these are first produced, to be carefully appreciated. A solution containing twelve grains of the alcoholic extract was introduced into the jugular vein of a dog. Convulsive movements were observed twelve seconds after the introduction of the first portion of the injection. The animal died in about a minute and a half.

These experiments, I think, furnish sufficient proof that the opinion of the instantaneous action of poisons must be founded on incorrect observations. An interval, never less than twelve seconds, has been shown to elapse between the application of a poison and the first symptom of its action; an interval in itself so short as might almost justify its being neglected, particularly in the present state of opinion of physiologists on the rapidity with which the organic processes are carried on; but which becomes of importance when compared with the time actually occupied for the performance of these processes, as it is quite sufficient for a poison to be brought into general contact with those tissues it affects. This being the case, it is unphilosophical to suppose that these effects on the nervous centres are owing to an impression communicated to them by the nerves, and not the result of the direct application of the poison to them.

The following experiment supports these conclusions, by show-

* In order to prevent the contact of the poison with the blood until the moment when the injection was pushed, a small portion of oil was drawn into the point of the syringe, which could thus be introduced into the vein in readiness to push the injection on a signal being given, without any danger of the poison becoming mixed with blood.

ing that the nearer to the nervous centres is the part of the vascular system into which the poison is introduced, the more rapid is its action.

By injecting a poison which acts on the nervous system into the aorta, the distance it has to traverse before reaching the nervous centres is much less than when it is introduced into the venous system. We should thus have an appreciable difference in the interval elapsing between its introduction and the appearance of the first symptom of its effects, whether it be introduced into the artery or the vein.

(*Exp.* 13.) A tube was introduced into the axillary artery of a dog. Five grains of woorara, dissolved in two drachms of water, were injected, so that it should pass into the aorta. The first symptoms of the action of the poison manifested themselves seven seconds after the injection, and the animal was dead in thirty seconds after the introduction of the poison.

On comparing this experiment with Experiment 7, we find a difference of some seconds elapsing in the first appearance of the action of the same poison, according as it is introduced into the nervous or arterial system. Analogous experiments have been performed with other substances, and constantly with the same results.

As the evidence derived from these experiments in support of the theory of general diffusion being necessary for the action of a poison is only presumptive, the present state of our knowledge not allowing us to detect their presence in the nervous tissue, I have endeavoured to strengthen it, by showing that the mere contact of a poison with a large extent of surface is not sufficient to produce any general effects, as long as it is prevented entering the general circulation. The only parts available for these researches are the abdominal viscera, on account of the facility with which they can be insulated from the general circulation, their connection with the nervous system remaining unimpaired.*

(*Exp.* 14.) The abdomen of a dog was laid open. A ligature was passed under the vessels entering the liver, and tied. Three drachms of hydrocyanic acid of Scheele's strength, containing 3.3 per cent. of acid, were introduced into the stomach through an opening made in its parietes. The poison was thus brought into contact with a large surface, freely supplied with nerves, at least with those nerves on which poisons are supposed more particularly to produce these impressions. (See Addison and Morgan on Poisons, page 35.) Under these circumstances, the poison remained in the stomach ten minutes, without producing the slightest general effect. The ligature on the *vena portæ* was then re-

* I am aware that analogous experiments have been performed by Magendie, Segalas, and other physiologists, but as those I have to bring forward differ from theirs, and afford a more complete proof of the fact I wish to establish, I have thought it advisable to relate them.

moved, so as to restore the circulation over the viscera. One minute after the removal of the ligature, the animal began to experience the effects of the poison. The ligature was again replaced; but before this could be effected, a sufficient quantity of the poison had been absorbed to arrest the respiratory movements, and the animal must have speedily perished, had not artificial respiration been had recourse to. After this had been continued eight minutes, the animal was sufficiently recovered to continue the respiratory movements itself. After a short interval the ligature from the *vena portæ* was again removed. The animal was dead in two minutes.

This experiment affords a strong proof of the non-action of poisons when merely applied to the extremities of nerves, for not only did the poison produce no effects before it entered the circulation, but we find the animal recovering from the effects of the poison, with three drachms of hydrocyanic acid still in its stomach.*

(*Exp.* 15.) As it might be objected to this last experiment that the nerves to which the poison was applied were not in their natural condition, on account of the circulation not going on over them; and that they were thus rendered incapable of transmitting any impression that might be made on them, the following modification of the experiment was devised.

The abdominal aorta of a dog was exposed, and a ligature passed around it, immediately above the origin of the cœliac axis and mesenteric arteries. A tube was then introduced into the aorta, directly below the origin of these vessls, so that any injection introduced through the tube must pass into them. A ligature was passed round the vessels entering the liver, and an opening was made in the *vena portæ*, so as to allow the blood to circulate over the viscera, when the ligature was removed from the aorta. Five grains of woorara, dissolved in four drachms of water, were now introduced through the tube, and passed into the cœliac axis and mesenteric arteries. The ligature from the aorta was then removed, and thus the blood containing the poison was circulated over the whole of the abdominal viscera, and applied to the extremities of the nerves, in circumstances favourable for the transmission of any impression that might be made on them by this large dose of poison. Seven minutes, however, elapsed be-

* The explanation that has been brought forward of the sudden action of some poisons by Muller and those physiologists, who consider that the circulation requires one or two minutes to be completed in, and yet who allow that poisons only act when applied to the nervous centres, is shown by this experiment to be incorrect. They state that the poison becomes applied to the brain and spinal chord by diffusion and imbibition through the tissues, independently of its being transmitted by the blood. Yet, in this instance, we have the poison they bring forward as possessing this power of expansion in the highest degree in contact with a large surface of the body without giving any proof of its having reached the nervous centres, independently of its transmission by the blood.—(See Muller's Physiology, translated by Baly, p. 247.)

fore the slightest symptom of the action of the poison manifested itself, and the animal did not die until fifteen minutes after the introduction of the poison; even then it is probable death was produced by the blood containing the poison having escaped from the *vena portæ* into the cavity of the abdomen, from whence a portion of the poison was again absorbed and carried into the general circulation.

Any remarks on these experiments would be perfectly superfluous, the striking nature of the facts clearly showing the point they were intended to illustrate. I would only observe that they are in perfect accordance with a number of facts brought forward by other physiologists.

III. It now only remains for me to notice some experiments that have been brought forward by Messrs Addison and Morgan, in their Essay on the operation of poisonous agents, (Lond. 1829,) and which, if free from fallacy, would prove that some poisons can produce general effects from an impression made on the nerves of the part to which they are directly applied. The most important experiment adduced by these gentlemen in support of the local action of a poison is that in which the jugular vein of a dog was exposed in a considerable part of its course. Two ligatures were applied to it, three inches apart; a portion of woorara was introduced into that part of the vessel, comprised between the ligatures, and the upper ligature was then removed. The blood was thus brought into contact with the poison which became applied to the parietes of the vein. In these circumstances, it is stated that the poison rapidly produced its effects; and it is concluded that these effects were owing to an impression made on the nerves of the insulated portion of the vein.

I would observe, however, that there must evidently be some fallacy in this experiment, for had the vein been perfectly insulated in the space comprised between the two ligatures, the only parts by which it still remained connected with the system were at those parts of the vessel beyond the ligatures, and thus, as far as nervous communication was concerned, it was in the same condition as if it had been removed entirely from the body, for a ligature still was around the lower part of the vessel, and one had previously been placed around the upper portion; an assertion quite sufficient to incapacitate the nerves which had been included in it, from performing their functions, and thus there remained no means by which an impression made on the nerves in the insulated portion of the vessel would be transmitted to the nervous centres. As this obvious source of fallacy must have struck the authors of the experiment did it really exist, I conclude that the vein could only have been partially separated from the surrounding tissues. In this case we have a ready explanation of the action of the poi-

son, the free anastomoses which exist between the veins of opposite sides readily permitting the poison to become mixed with blood circulating through the body. Even supposing the complete insulation of the vein, the ready manner in which solutions become diffused through fluids, would forbid the conclusion that the solution of the poison in the blood could be confined to the insulated portion of the vessel. It must speedily become mixed with the blood in the upper part of the vessel, above the point at which it was insulated, and thus could readily enter the general circulation.

Another experiment brought forward by these gentlemen to prove that a poison does not exert its effects by being taken into the blood, and thus applied to the nervous centres, is one in which they connect the carotid arteries of two dogs in such a manner, that they suppose the blood from the heart of the one dog is sent to the brain of the other. This supposition, however, is entirely opposed to the physical arrangement of the vessels that supply the brain. Were the carotids the only vessels going to this organ the experiment would be a fair one; but in the dog the vertebral arteries are so large as readily to furnish a sufficient supply of blood to the brain, even when the carotids are tied. The only condition in which the blood could pass from one animal to the other is by the pressure of the blood on the parietes of the superior end of the carotid of each dog being less than the pressure on the inferior portion of the carotid of the dog with which it was connected, and the quantity of blood that passed would be in proportion to the difference of pressure on the two ends of the tube connecting the vessels. I have ascertained by direct experiment with the hemadynamometer, that the pressure exerted on the parietes of a tube, inserted into the distant extremity of the carotid, is less by a column of mercury of not more than two or three-tenths of an inch, than the pressure on a tube inserted into the end nearer the heart. If we suppose, therefore, that the pressure in the arterial system of each animal was originally equal, (a fact by no means probable,) it is evident that but a very small quantity of blood can pass from the arteries of one animal to those of the other, and this only whilst both are in the same state. As soon as the poison begins to exert its influence on either animal, the pressure in its arterial system will be diminished, and thus, far from blood containing the poison being sent to the brain of the sound animal, the only effect of this arrangement will be to cause a reflux of pure blood from the arteries of the sound dog into those of the poisoned one. It is not surprising that, under these circumstances, the experiment furnished a negative result. It is evident that from neither of these experiments can any argument be deduced in favour of the local action of poisons.

I shall now draw up a short abstract of the facts which these ex-

periments have been intended to illustrate, observing, that in using the word poisons, I would only now allude to those which appear to act on the nervous system.

1. That the time required* by a substance to permeate the capillary vessels may be considered as inappreciable.

2. That the interval elapsing between the absorption of a substance by the capillaries and its general diffusion through the body may not exceed nine seconds.

3. That an interval always more than nine seconds elapses between the introduction of a poison into the capillaries or veins and the appearance of its first effects.

4. That, if a poison be introduced into a part of the vascular system nearer the brain, its effects are produced more rapidly.

5. That the contact of a poison with a large surface of the body is not sufficient to give rise to general symptoms, as long as its general diffusion through the body is prevented.

* In regard to the statement as to the time required for substances to be diffused through the body I would observe that all my experiments have been performed on full grown dogs. It is probable that these observations might require to be slightly modified in applying them to other animals. It is also evident that a difference must exist in the time occupied by a substance in reaching the capillaries in different parts of the body. The time here given, or nine seconds, is that in which I conclude a substance may be applied over the greater part of the body, more particularly to the central parts of the nervous system. It would appear that seven seconds may suffice for its being conveyed to the capillary terminations of the coronary arteries.

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ON THE ACTION OF POISONS.

In directing the attention of the Society to a point, which, during the past century, has been so fully discussed by physiologists, it might be supposed that I should find a difficulty in bringing forward anything which may be worthy of its notice. But, far from being exhausted from the labour that has been bestowed upon it, the subject of the action of poisons on the animal economy, still presents to us one of the richest fields, from which we may obtain facts for the advancement of that branch of knowledge, on which medicine, as an inductive science, must be founded. The effects produced by poisons are, in fact, but the most striking instances—the extreme cases, in a series of phenomena, which comprehends not only the entire destruction of the functions of an organ, but even the slightest modifications which these functions may receive. It is not the mere explanation of a few isolated phenomena that is embraced by this part of physiology, for the prospects that its pursuit presents to us are, perhaps, as unbounded as any that ever excited the imagination of a Paracelsus, the vista it opens to our view, promises apparently to conduct us farther into the arcana of nature, than the daring of Prometheus would have led him.

But if such are the fruits that are to be obtained from the cultivation of this branch of science, how is it, it may be justly asked, that the labour which has been already bestowed on it, has produced such slight results? and to what must we attribute the want of success that has hitherto attended its investigation? Fortunately for the future prospects of science, this sterility can be proved to be owing to the unphilosophical manner in which the subject has been pursued, rather than to any inherent barrenness of the soil. If, after two centuries of research, physiologists are not yet agreed on the most fundamental, and apparently the most simple questions connected with this subject, it is not that it presents to us problems which are above our reason to solve, or phenomena which are not amenable to those laws which govern the universe; but it is in the method by which these researches have been conducted, that we shall find an explanation of the want of success that has attended them. Instead of proceeding with the utmost circumspection in the investigation of phenomena so complicated as are those offered by the animal economy, the physiologist has neglected the most simple and fundamental rules of philosophizing, in a science where these rules are most necessary; he has cast aside the chart which should guide him in the research of truth, at a moment when he is about to enter on a course, surrounded by rocks and quicksands.

In proof of these assertions, I have but to refer to the unphilosophical attempts which were made towards the end of the last century, to explain the action of poisons on chemical grounds, although physiologists possessed not the slighest knowledge, either of the chemical composition of the substance they experimented with, or of the fluid they supposed changed by it. Were I to select an instance from our own times, I have but to mention the fact of memoirs having been written to prove, that poisons do not act by their direct contact with the nervous centres, because sufficient time did not elapse after their application, to allow of their reaching these centres, before symptoms of the action were manifested; and yet this argument was brought forward with an utter ignorance of the most important data on which it could be founded, namely, the time required for the blood to circulate from one part of the system to another. Another instance connected with this subject of the unphilosophical mode of advancing hypotheses is furnished us by Müller, (See Müller's Physiology, by Bayley, p. 247, Vol. i.) who, admitting that poisons act only when applied to the nervous centres, yet, finding that effects are produced more rapidly than the erroneous views he entertains of the rapidity of the circulation would render possible, supposing they were only conveyed by the blood, advances the explanation, that it is by permeating the animal tissues that they arrive at the brain. The most simple experiment, or the slightest consideration of the physical properties of these tissues, would have been sufficient to convince him that such could not be the case.

When such has been the spirit in which this branch of physiology has been pursued, can we be astonished that but little light has been thrown upon it? It is, indeed, a curious fact, that two hundred years after the promulgation of the system of Bacon, a spot is to be found on the field of science, from which the dark shadows of the scholastic philosophy have not yet been dispersed. It is only within the last few years, that physiological investigations have been undertaken in a truly scientific spirit; or in the aim of becoming acquainted with the more simple and tangible phenomena connected with organized beings, before attempting to elucidate those of a greater degree of complexity. The success that has attended the researches of Magendie on the physical properties of the tissues, of Poiseuille on the circulation, and of Müller on the structure of the glands, is but a striking proof of how great was our ignorance on the simplest and most elementary facts. But to return to the subject of this memoir.

The action of poisons presents to us, as does every physiological problem, a dynamical and chemical question. The former is evidently the first to be solved, as attaching itself to a branch of science more simple, and of a higher degree of generality than

chemistry. In the question before us, the dynamical problem relates to the determination of the part of the animal economy on which the poison produces its effects. This may be either on the part to which it is directly applied, or after it has entered the blood-vessels, or only when it is brought into contact with the brain and nervous centres. This question, it will be perceived, is quite independent of the other or chemical one, which involves the molecular changes produced in the blood, or in the tissue on which the poison acts, and must be solved before the latter can be entered on with any chance of success. It is the former or dynamical question which I now propose to investigate, having lately published some observations relating to the chemical part of the subject, in a memoir read before the Royal Society in February last. In a paper which was read before the Royal Society in August 1839, (See Edin. Med. and Surg. Journal, No. 142,) I have already treated this subject under its dynamical point of view, and before proceeding, I shall take the liberty of transcribing a short summary of the result of the experiments contained in that memoir.

"1*st*, That the time required* by a substance to permeate the capillary vessels may be considered as inappreciable.

"2*d*, That the interval elapsing between the absorption of a substance by the capillaries, and its general diffusion through the body, may not exceed nine seconds.

"3*d*, That an interval always more than nine seconds, elapses between the introduction of a poison into the capillaries or veins, and the appearance of its first effects.

"4*th*, That if a poison be introduced into a part of the vascular system nearer the brain, its effects are produced more rapidly.

"5*th*, That the contact of a poison with a large surface of the body, is not sufficient to give rise to general symptoms, as long as its general diffusion through the body is prevented."

Notwithstanding the proofs I then brought forward, to show that the application of a poison to the nervous centres was necessary before it produced any general symptoms, still there was one class of experiments which I had not then tried, but which were calculated to furnish the strongest evidence, for or against the position I had supported. It is evident, that, if a poison acts only when applied to the nervous centres, in different sorts of ani-

* In regard to the statement as to the time required for substances to be diffused through the body, I would observe that all my experiments have been performed on full grown dogs. It is probable that these observations might require to be slightly modified in applying them to other animals. It is also evident that a difference must exist in the time occupied by a substance in reaching the capillaries in different parts of the body. The time here given, or nine seconds, is that in which I conclude a substance may be applied over the greater part of the body, more particularly to the central parts of the nervous system. It would appear that seven seconds may suffice for its being conveyed to the capillary terminations of the coronary arteries.

mals, it must require a longer or shorter time before it shows any symptoms of its action, according as the circulation is more or less rapid, or as the course it has to run before arriving at these centres, is longer or shorter. As my former experiments had been performed only on dogs, I was, at the time of the publication of the memoir above alluded to, unable to furnish any data on this point. In the present communication, however, I hope to add this important link which was wanting in the chain of evidence on which my position was founded. The experiments I have now the honour to lay before the Society, have been performed on horses, rabbits, and fowls,—animals offering us the extremes as to rapidity of circulation, at least of those animals which are readily available for these researches. As the time required for the blood to circulate from one part of the body to another, had not been determined for any of these animals, with the exception of the horse, (on the circulation of which, however, the experiments of Hering are not of the most conclusive nature), I have, in every instance, endeavoured to ascertain this important element in the investigation. My experiments on horses have not been numerous, but they were such as I could place full confidence in, and supported, as they are by the previous researches of Hering, I can, without hesitation, lay them before the public.

Expt. 1. A tube was inserted into the jugular vein of a horse, and another into the carotid artery; with the latter, the hæmadynamometer was connected, in order to ascertain the pressure in the arterial system, and thus to have a direct indication of any change that might take place in the action of the heart.*

A solution, containing half an ounce of nitrate of potass, a salt which possesses the property of arresting the action of the heart,† dissolved in five ounces of warm water, was injected into the jugular vein. In sixteen seconds after the introduction of the salt into the vein, the action of the heart was arrested, as was shown by the rapid descent of the mercury in the hæmadynamometer; no pulsation took place after this. The animal struggled violently some time after the action of the heart had been arrested, and respiratory movements continued three minutes and a half after the injection of the poison. The interval that elapsed between the introduction of the poison into the vein, and the arrest of the action of the heart, furnishes the time required for the blood to pass from the jugular vein to the capillary terminations of the coronary arteries; or, at least, for a solution mixed with the blood, to pass over this space, it being necessary probably to make a slight al-

* Immediately before the injection, the pressure in the arterial system was equal to a column of mercury of from 6.5 to 7.5 inches; a pressure which Poiseuille generally found to exist in the animal.

† See Archives Generales de Medecine, Nov. 1839.

lowance for the diffusion of the fluid, independently of the onward motion of the blood.

Analogous experiments have been performed three times. In one instance in which the animal had lost a great deal of blood, the action of the heart was not arrested until twenty seconds after the injection of the poison. In another instance it was again sixteen seconds.

Expt. 2. The following experiments strikingly confirm the above result. The object of it is, to ascertain the time in which a substance injected into the jugular vein, will make its appearance in the blood from the carotid artery.* A tube was inserted into the jugular vein of a horse, another into the carotid artery of the opposite side. In order to avoid any of the injections becoming directly mixed with the blood, the animal was thrown on the side on which the tube was introduced into the jugular, so that the side from which the blood escaped was the highest, the poison being injected into the vein. A solution, containing one ounce of nitrate of baryta, dissolved in five ounces of warm water, was injected into the jugular vein. Ten seconds after the commencement of the injection, blood was allowed to escape from the carotid, and received into a vessel, No. 1. during five seconds; another vessel was then substituted, No. 2. and received the blood escaping from the carotid, from fifteen to twenty seconds after the introduction of the substance into the jugular vein. What escaped from the artery after this, was received in a third vessel, No. 3. The heart, however, had already stopped when the last vessel was applied. These different specimens were carefully analysed; no trace of baryta could be obtained from the blood in No. 1. or that which escaped from the artery, between ten and fifteen seconds after the injection of the poison. In the blood from No 2, baryta was readily detected; and although an accident during the analysis led to the loss of a portion of it, it still yielded a much greater quantity in proportion to the quantity of blood, than did the contents of No. 3, or the blood obtained from the carotid subsequent to twenty seconds after the injection of the salt into the veins, thus proving that the blood which was most strongly impregnated with the poison, escaped from the carotid between fifteen and twenty seconds after the introduction of the salt into the vein. From the large proportion of the salt in the blood that escaped during this interval, we must conclude, that the moment at which blood containing the salt, first began to escape from the artery, must have been about sixteen seconds after its introduction into the

* The same thing has been already done by Hering as regards the time for blood to pass from the jugular vein of one side to that of the other, after having gone the round of circulation. The modifications which I have introduced into his experiment renders it, I think, more accurate.

veins. On account of the tube in the carotid being rather small, I think it probable that a second or two might have been lost, from this cause, the blood not being able to escape with sufficient freedom.

It will be seen that these experiments agree very closely with those performed by Hering, who found, that in the horse, the round of the circulation was completed in twenty-five seconds. Having thus clearly determined the velocity of the circulation, it remained to ascertain the time required for a poison which acts on the nervous system, to produce its effects. It is evident, that, should its action be due to an impression produced on the nerves of the part to which it is directly applied, no appreciable interval should elapse between its application, and the appearance of symptoms of its action. If, on the contrary, a poison affecting the nervous system, only acts when applied directly to the nervous centres, it is equally evident, that no symptoms of its action should manifest themselves until, at least, sixteen seconds after its application, this being the shortest period in which blood with which it has been mixed, (supposing the poison injected into the jugular vein,) can be brought into contact with any part of the nervous centres. The substance I made use of was strychnia, as I have found it to act more rapidly than any other poison, not excepting woorara and conia.

Expt. 3. A tube was inserted into the jugular vein of a healthy horse, the animal being ordered to be killed on account of some disease of the foot, which had not at all affected its general health. Immediately before the injection, the pulse was about 50. The animal was not confined, so that the slightest symptoms of the action of the poison might be immediately recognized. A solution containing six grains of crystallized strychnia, dissolved in three ounces of warm water acidulated with nitric acid, was injected into the jugular vein; sixteen seconds after the injection of the poison, the first symptoms of its action showed themselves by a slight convulsive movement of the superficial muscles of the thorax; seventeen seconds after the injection, the animal fell as if it had been a dead mass; every muscle in the body was in a violent state of spasm; the animal lay in this state for about a minute and a-half; convulsive movements then came on, and lasted until death, which took place about four minutes after the injection of the poison.*

In this experiment, the poison, although administered in a very large dose, did not produce the slightest effect on the animal, un-

* I with pleasure avail myself of this opportunity of publicly thanking M. Boulay fils, of the Royal Veterinary College of Alfort, for the kindness with which he afforded me opportunities of conducting some experiments on horses, at that establishment. I have also to express my sincere thanks to Drs Kemp and Gilbert for their valuable assistance whilst conducting many of these experiments.

til sixteen seconds had elapsed after its introduction into the vein, and it required seventeen seconds before any marked symptoms of its action manifested themselves. It will be seen that this is the time required for the blood to pass from the jugular vein to the termination of the coronary arteries; and may also suffice for it to reach the arteries distributed to those parts of the spinal chord, nearest the heart. I know not if the earlier occurrence of convulsive movements in the muscles of the thorax, can be connected with the poison having first reached that part of the chord from which these muscles receive their nerves.

I shall now notice experiments that have been performed upon dogs in connection with this subject. As a full account of these experiments will be found in the 142d No. of the Edinburgh Medical and Surgical Journal, I shall merely allude to the more important results they furnish, referring to my former paper for details. It appears that in dogs, the time required for the blood to pass from the jugular vein to the termination of the coronary arteries, varies from seven to fourteen seconds; in full-grown, middle-sized animals, the shortest time in which a poison, acting on the nervous system, has shown symptoms of its action, after it had been introduced in the jugular vein, is twelve seconds.

The following experiments, which have been performed on birds, furnish us with interesting data, on the connection which exists between the rapidity of the circulation, and the time required for a poison to act.

Expt. 4. As the velocity of the circulation in this class of animals is a point which has not yet been determined, I shall relate an experiment undertaken with the view of ascertaining this fact. The means I employed were the same as those I generally use, viz., the injection of a substance into the jugular vein, which possesses the property of arresting the action of the heart when circulated over its parietes, the hæmadynamometer being connected with the arterial system. On injecting a drachm and a-half of a solution of nitrate of baryta, into the jugular vein of a fowl, the action of the heart became arrested in six seconds, as was proved by the rapid descent of the mercury in the hæmadynamometer.*

Having thus ascertained the time required for the blood to pass

* On opening the thorax immediately after death, the heart was found motionless with scarlet blood in the left cavities, showing that in this class of animals the salts of baryta exert the same effect on the heart as in quadrupeds. Another interesting phenomenon noticed in this experiment, was the continuation of muscular movements for some minutes after death; a phenomenon which is characteristic of the salts of baryta and those substances which are isomorphous with it in their action on quadrupeds. In performing this experiment, I had also an opportunity of observing the pressure of the blood in the arterial system of the bird; a fact which has not, as I am aware of, been previously ascertained. It was found equal to a column of mercury of from four to five inches. In the goose the pressure was equal to a column of mercury of six inches, the circulation being rather slower, as ten seconds were required for a substance to pass from the jugular vein to the heart.

from the jugular vein, to the capillary terminations of the coronary arteries, the following experiment was performed, to show the time in which a poison when introduced into the vein, gives rise to any symptoms of its action.

Expt. 5. A solution containing one grain and a-half of nitrate of strychnia, dissolved in a drachm and a-half of warm water, was injected into the jugular vein of a fowl. In six seconds and a-half after the introduction of the poison into the vein, the animal became convulsed, and so rapid was the action of the poison, that in eight seconds after its introduction, the animal lay apparently dead, the only sign of life being a movement of the tail, which continued for some seconds after every other motion had ceased.

The next experiment I have to relate had been performed on a quadruped (the rabbit), in which animal I find the circulation much quicker than in the fowl.

Expt. 6. A tube was inserted into the jugular vein of a full-grown rabbit; by which to inject the poison, the hæmadynamometer was connected with the femoral artery. A solution containing three grains of chloride of barium, in a drachm and a-half of warm water, was introduced into the vein; in four seconds, the action of the heart was arrested; violent spasm came on, and the animal died about a minute and a-half after the arresting of the heart's action.*

Expt. 7. In another full-grown rabbit, a solution containing half a grain of nitrate of strychnia was injected into the jugular vein; in four seconds and a-half, the first symptoms of the action of the poison showed themselves; the animal fell on its side, and respiration was immediately arrested; in seven seconds after the introduction of the poison into the vein, the animal lay apparently dead. Before proceeding to offer any remarks on the above experiments, I shall endeavour to present the data they furnish us in a tabular form.

	Time required for the blood to pass from the jugular vein to the capillary terminations of the coronary arteries.	Time that elapses between the introduction of a poison into the jugular vein, and the first symptoms of its action.
In the horse,	16 seconds.	16 seconds.
„ dog,	11 to 12	12
„ fowl,	6	6½
„ rabbit,	4	4½

These are the facts which I have now the honour to lay before

* The pressure in the arterial system immediately before the injection of the poison was equal to a column of mercury of from four to 4.4 inches, the oscillations not exceeding a tenth of an inch at each pulsation of the heart. When the thorax was opened immediately after death, the heart was found motionless, with the exception of slight contraction of the right auricle. The descending cava was contracting vigorously, and continued to do so when all communication between it and the heart was cut off. Muscular movements were observed to continue ten minutes after death.

the society. Derived as they are from direct experiments which have been performed with the utmost care, and solely in the desire of throwing some light on the much disputed question as to the action of poisons, I trust they will be considered as accomplishing the end for which they were undertaken.

Before offering any remarks on them, I shall draw up a short summary of the facts contained in this memoir, the interest of which, I think, will be increased, when viewed in connection with the result to which former experiments had led me.

It would appear from the facts above stated, 1*st*, That a constant ratio exists between the time required for a poison to act, and the rapidity of the circulation.

2*d*, That in those animals on which experiments have been made, a sufficient interval always elapses between the introduction of a poison into the vascular system, and the symptoms of its action, to allow of the blood with which the poison has been mixed, reaching the capillaries of the tissue on which the poison exerts its deleterious effects.

To these conclusions I would add, as proved by my former memoirs, that with those poisons which act on the nervous system, the closer the part of the vascular system at which a poison is introduced, is to the nervous centres, the more rapid is its action; and also, " that the contact of a poison with a large surface of the body does not give rise to general symptoms, as long as its diffusion through the body is prevented."

On these facts I now offer a few remarks, although it is far from my intention to intrude on the science any new theories or hypotheses, which, unfortunately for the progress of physiology, are but too easily manufactured; and which, when once formed, are far too dear to their fabricators to be submitted to the rude test of experiment. Had not such been the case, we should not at the present day, 200 years after the immortal discovery of Harvey, be seeking for data on the simplest and most readily ascertained phenomenon connected with the circulation. But to return from this digression.

The first, and perhaps the most interesting inference that results from these experiments, is, that poisons only act when applied directly to the tissues they affect. I am aware that, in making these assertions, I am stamping as erroneous, views which have received the sanction of physiologists of the highest eminence, and which are supported by experiments apparently of indubitable character. In opposition to these experiments, I should be sorry to place my own researches, were not my confidence shaken in observations, which, connected as they intimately are with the circulation, have yet been undertaken without a preliminary knowledge of some of the most important points connected with that function. Had my experiments even been of a nature to call for the assistance of

any nervous fluid, or vital force for their explanation, I should have looked with much suspicion on the results they furnished me. But when I find that a careful investigation of facts leads to the rejection of these unphilosophical hypotheses,—when I see a substance producing its effects only where it is present, affecting the heart, only when brought into contact with its parietes, deranging or destroying the functions of the nervous tissue, only when it impregnates it; when, in fact, my experiments tend to cast down some of those barriers which would separate physiological phenomena, from the dominion of laws which govern inorganic bodies, I cannot but hope, that the facts which lead to these views, are simply the expression of truths, destined to receive a further confirmation by the progress of science. That our being able thus to localize the action of a poison is a step made towards the explanation of physiological phenomena, is evident; for when we see that a substance introduced into the blood, primarily affects the functions of an organ by its direct contact with that organ, we naturally conclude that these effects are the result of changes produced in the organ in question, from causes more or less analogous to those which we are accustomed to see acting on other matter; and we are immediately led to seek out what these changes are, as a farther step towards the solution of this important problem. If, on the contrary, we suppose the nervous system primarily affected by an impression made on the nerves of the part to which the poison is directly applied, the solution of the problem becomes removed to a much greater distance, and it even presents itself under a form, which, in the present state of physiology, it would be useless to attempt.

Having thus localized the action of a poison, I shall take a short review of some facts which would tend to throw a still farther light on this important subject, by offering a few observations on the connection which exists between the chemical composition of a poison, and its physiological action. On this subject I can scarcely enter, without incurring the charge of egotism; for I am not aware that any experiments bearing directly on this point have been published by other observers. At the same time it is evident, that, on a field so vast, the labours of a single individual, who is but just entering on the path of physiological inquiry, can have thrown but little light; such, in fact, is the case. The connection above alluded to between the chemical composition of a poison and its physiological action, is but as yet dimly shadowed forth, rather than demonstrated, by the experiments I have undertaken. At the same time, I hope to bring forward sufficient evidence, to prove that in many cases this connection really exists.

In a paper read at the meeting of the British Association at Newcastle, in 1838, I arrived at the conclusion, from some expe-

riments I had performed on the injection of substances into the veins, that those substances which arrested the action of the heart, appeared to agree in one respect, viz. that they all modified considerably the chemical composition of the blood. In a memoir, "Sur l'action de substances salines introduites dans le systeme circulatoire," read at the Academie des Sciences at Paris, in June 1839, (see Archives Generales de Medecine, November 1839,) I stated another interesting fact, tending to connect the physiological action of substances, with their chemical composition, viz. "that, when introduced into the veins, all the salts of the same base exert an analogous effect on the animal tissues, this effect being but slightly modified by the combination of the base, even with the most powerful acids." This fact, however curious in itself, is rendered much more interesting by its forming a corollary to an important law, which subsequent experiments have led me to discover, viz. that, when introduced into the blood, isomorphous substances appear to exert an analogous action on the animal tissues.* Connected as isomorphism is already known to be, with many common chemical properties, and probably with others which yet remain to be discovered, it is interesting to find, that the physiological action of every inorganic compound, is so closely related to certain chemical properties it possesses. There is still another fact to which I would call attention, which is the difference in the general effects produced by poisons on the animal economy, according as they are derived from organic or inorganic compounds. In the numerous experiments I have performed on poisons, derived both from the vegetable and mineral kingdom, I have constantly seen this difference strikingly marked; and it is an interesting fact, that ammonia, which, by its chemical composition, stands, as it were, between the organic and inorganic compounds, should agree with some of the former in its action on the nervous system, whilst its action on the heart and general capillaries, approaches it to potash, with which it is isomorphous.

Such are the facts that would tend to point out a connection between the chemical composition of a substance and its physiological action. I am fully aware that they are at present but few, and form a very imperfect body of evidence on which to establish so important a point; and it is only with the view of directing the attention of physiologists to so interesting a subject, that I have been induced thus to bring them forward. As a physiologist, it has been only under a physiological point of view that I have investigated these phenomena; but I am convinced that they are not destined to receive their full application, until chemistry shall be

* The evidence on which this law is founded has been lately laid before the public in a memoir read before the Royal Society in January last, and published in the last number of this Journal.

sufficiently advanced, to throw a light over those complicated reactions which result from the contact of the blood and the tissues, with the various organic and inorganic compounds. I am afraid that this would be a consummation of our hopes, which, in the present age, we are not destined to arrive at; for, however rapid the progress of chemistry has been during the last few years, it is still very far from being able to grapple with those questions, the elucidation of which so much interests the physiologist. For the present, therefore, we must content ourselves with collecting facts on this important subject, confident that we are thus laying the foundation for generalizations, which shall sooner or later place physiology far above the position which it now occupies.

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OBSERVATIONS

ON THE

PHYSIOLOGICAL EFFECTS

OF

VARIOUS AGENTS INTRODUCED INTO THE CIRCULATION, AS INDICATED BY THE HAEMADYNAMOMETER.

By Mr JAMES BLAKE, London.

(From the Edin. Med. and Surg. Journal, No. 139.)

The subject which has given rise to these researches is, "The action of various substances on the animal economy when introduced into the veins, more particularly as regards the influence they exert in modifying the circulation."

My attention was first directed to this subject by a remark of Professor Sharpey, in his Physiological Lectures, on the extensive field of inquiry which was opened to us in this branch of physiology, by the invention of the haemadynamometer. As it is by the aid of this instrument that the results at which I have arrived have been obtained, it will perhaps render the description of the experiments more intelligible, if, before proceeding, I give a short explanation of it.

I. *Description of the Haemadynamometer.*—It consists of a glass tube, so bent as to form two vertical branches and a horizontal one. To the horizontal branch is adapted a brass cap, which

serves to connect it with a tube, which is inserted into the artery. The glass tube is fixed to a graduated scale. When used mercury is poured into it, until it attains in the vertical arms, a height corresponding to the zero of the scale. It is then connected with the tube inserted into the artery, and on turning a stop-cock, with which the tube is provided, the blood enters the instrument, and the pressure in the arteries is instantly indicated, by the difference in the height of the surface of the mercury in the vertical branches. The great advantages offered by this instrument are; that it enables us to detect any change in the action of the heart the instant it takes place, and also affords us a means of substituting the accurate expression of so many inches of mercury for the undefined terms, more or less strong.

Cause of Pressure in the Arteries.—Before entering into a detail of the experiments I have to bring forward, I shall offer a few remarks on the cause of the pressure in the arterial system, and how this pressure can be modified. As we are now treating a subject which is entirely under the dominion of physical laws, I shall consider the arterial system as composed of a set of elastic tubes, into which a constant supply of fluid is sent by the action of the heart, and from which a corresponding quantity is discharged by a number of small orifices, the capillaries. It is evident, that, in order that there should be any amount of pressure sustained by the parietes of these tubes, the quantity of fluid sent into them must be more than can be freely discharged by the discharging orifices, and that, in fact, the amount of pressure which they sustain will be in proportion to the quantity sent in, above that which can be freely discharged. It also follows, that any variation in the pressure which may be supported by the parietes of these tubes, may depend either on the quantity of fluid sent into them in a given time being increased or diminished, or an alteration in the discharging orifices. From these remarks, it is evident that the pressure in the arterial system, as shown by the haemadynamometer, is nothing but an expression of the force required to cause a certain quantity of blood to pass through the capillaries in a given time.

I have been thus particular in describing the manner in which the pressure in the arteries may be modified, as our inquiries as to the manner in which certain substances act will be much facilitated by keeping these simple hydraulical laws in view.

The changes in the physical properties of the blood must also be an important element in modifying its passage through the capillaries, but it is one which the present limited state of our knowledge, as regards these changes, does not enable us fully to estimate.

Effect of Respiration on the Heart.—With these remarks I

shall close the preliminary observations which I have to offer, and shall now proceed to a detail of the experiments which I have performed, in order to elucidate the manner in which various substances act, when taken into the circulation. Many of these, although speedily causing death, seem to exert no immediate effect on the heart,—this organ remaining apparently unaffected, until its supply of arterial blood is cut off, owing to the respiratory movements being stopped. I shall, therefore, commence by relating an experiment which was performed to ascertain the effects of respiration on the action of the heart.

The animal on which the experiment was performed was a dog. A tube was introduced into the trachea, and an opening made in the parietes of the thorax, so as to prevent air from entering the lungs by the action of the respiratory muscles. Artificial respiration was had recourse to. The pressure in the arterial system was taken by the haemadynamometer, (which, for the sake of brevity, I shall in future designate as the instrument,) being connected with a tube, which was inserted into the femoral artery. It was found to be equal to a column of mercury of six inches and a-half. All access of air to the lungs was now cut off; the pressure in the arterial system gradually diminished. In two minutes, the column of mercury supported was only three inches and a-half, the pulsations of the heart having become much slower. The lungs were now inflated with air; this was instantly followed by a quickened action of the heart, and an increase of the pressure in the arteries, which was indicated by the mercury in the instrument rising about 25 seconds after the injection of the air. Air was again prevented from entering the lungs during a space of three minutes and a-half. The column of mercury had now diminished to two and a-half inches, the heart pulsating very slowly. Air was now injected into the lungs with exactly the same effect as before. After three respirations had been performed, the column of mercury had again attained its former level of six inches and a-half. After the supply of air had been cut off for eight minutes and a half, the column of mercury had diminished to one inch; the heart was still observed pulsating. Air was again injected into the lungs, but this was not followed by any action on the heart, although it was observed pulsating for three and a-half minutes after this time.

Effects of Transfusion of Blood.—The effect of the transfusion of blood on the pressure in the arteries is a subject which has already been fully investigated by Magendie. He found that the injection of eighteen ounces of blood in the veins of a dog produced no increase of the pressure in the arterial system. But it appears, that the pressure in the arteries of the animal from which it had been abstracted, had become diminished; and I think it highly probable that its reinjection into the veins of this animal

would have caused the pressure in the arteries to have been again increased. The detail of these experiments will be found in the third volume of his "Leçons sur les Phénomènes Physiques de la Vie."

Injection of Water.—The injection of water into the veins is a subject which has also been investigated by this able physiologist; but on this point the experiments which I have performed do not agree with those which he has related. He states that the injection of about a pint of warm water into the jugular vein was followed by the sudden diminution of the pressure in the arterial system. On repeating this experiment, I have, on two occasions, found that an opposite effect was produced, or that the introduction of a considerable quantity of water into the veins is followed by an increase in the pressure in the arteries. Two pints of water, at a temperature of 102° Fah., were gradually injected into the veins of a dog, and it was found that the column of mercury supported by the blood in the arteries was full an inch and a half higher than it was before the operation. This result receives support from the effects produced by the injection of warm water into the veins in cases of cholera, which are evidently not such as would indicate that the action of the heart is diminished. I think it probable that the animal operated on by Magendie was in a sinking state before the injection of the water, as it had already served for one or two experiments.

II. *Classification of Substances.*—I shall now proceed to investigate the action of those substances, which, when injected into the veins, exert a marked influence on the animal economy. For reasons, which will be obvious as we proceed, it will be advisable to divide these substances into three classes. The first class will comprehend those which by acting directly on the contractility of the heart, and which, when injected into the veins, produce death, by suddenly stopping the contractions of that organ. The second class will contain those substances, which, although causing death quite as rapidly or even more so than the former, yet leave the heart to all appearance unaffected, the action of the poison being directly on the nervous system. The third class will include those, which, though acting directly on the nervous system, yet agree in exerting a powerful influence in modifying the capillary circulation. In a fourth class I shall advert to the action of several substances which cannot be referred to either of the three foregoing heads. Imperfect as the first investigations in so comprehensive a subject must necessarily be, I think that these researches, in so far as they have been conducted, will enable me to localize the action of the greater number of the substances experimented on, so as to justify my placing them in one or the other of these classes.

1. *Substances acting on the contractility of the heart.*—

The substances which will come under the first class, and of which the action on the heart has been experimentally investigated are the following :—the nitrate, arsenite, and carbonate of potass, carbonate of soda, ammonia, iodide of arsenic, oxalic acid and galls.

Injection of Nitre.—A description of the manner in which nitrate of potass acts when injected into the veins will furnish us with a good example of the action of this class of substances ; and by giving a detail of an experiment with this salt, I shall be enabled to dismiss the others, with a few remarks on their action, in so far as they may differ from it. The animal operated on was a dog. A tube was inserted into the jugular vein, by which to inject the poison ; another tube was inserted into the femoral artery, by which to connect the arterial system with the instrument, in order to ascertain the pressure. Immediately before the injection of the poison, the column of mercury was found equal to six inches.

Action of Nitre.—A solution containing fifteen grains of nitrate of potass, dissolved in six drachms of water, was injected into the vein. Ten seconds after the injection, the column of mercury in the instrument began to sink, the pressure in the arteries rapidly diminishing, owing to the action of the heart being suddenly stopped. Thirty seconds after the injection of the salt, the column of mercury supported was only equal to an inch and a half. The animal continued struggling for some time after the heart had stopped beating ; and the respiratory movements continued 20 seconds after the cessation of the circulation. The struggles were evidently not convulsive, and the animal appeared quite sensible until death took place, which happened about 45 seconds after the injection of the poison. The thorax was opened immediately after death ; the heart was exposed within a minute and a half after the injection of the poison. The right auricle was observed to be still pulsating, but not the slightest contraction could be produced on any other part of the heart, even by the galvanic stimulus. The left side of the heart was opened, and found to contain a considerable quantity of blood of a bright scarlet colour. The right side of the heart contained a quantity of dark blood.

When a very weak solution of this salt is used, its immediate effect is to cause dyspnœa, the action of the heart being rendered irregular ; the pulsations after a short time become quicker, and the pressure in the arterial system increased. A solution containing a grain of the salt produced these effects when injected into the veins, the height of the column of mercury being increased half an inch. Two grains, when injected, produced an increase of pressure in the arteries equal to two inches of mercury. Three grains were then injected into the veins of the same dog. In 25 seconds after the injection, the pulsations of

the heart were suddenly stopped, and were not again renewed. The thorax was immediately opened, the state of the heart was exactly the same as in the last experiment; the right auricle still contracting, but all the other parts being insensible to stimuli.

Action of Arsenite of Potassa.—Arsenite of potass, when injected into the veins, much resembles nitre in its action on the heart. It does not appear, however, to exert so powerful an influence in destroying the irritability of this organ as nitre. The injection of a solution containing 15 grains of this salt was followed by dyspnœa in about 10 seconds; and the sudden cessation of the action of the heart, 20 seconds after its introduction into the veins. On opening the thorax the right auricle contracted on being irritated, but the left ventricle could not be made to contract, even when galvanism was applied. The left sides of the heart contained a considerable quantity of scarlet blood.

Action of Carbonate of Potass.—Carbonate of potass is analogous in its action to nitre, although it does not appear to be so deleterious an agent. A solution containing five grains, when injected into the veins, gave rise to the same phenomena as were produced by the injection of a grain of nitre. A solution containing twelve grains of this salt suddenly arrested the action of the heart in 15 seconds after its injection; a few slight and apparently partial pulsations again took place, but these soon ceased, and the animal was dead in about a minute and a half after the introduction of the poison. The necroscopic appearances were the same as those described in the last experiment, the heart retaining after death a slight degree of irritability. The blood in its cavities was firmly coagulated.

Action of Subcarbonate of Soda.—I have not myself investigated the action of subcarbonate of soda; but I find in an experiment recorded by Magendie, that its injection into the veins in a concentrated state was almost instantly fatal. He attributes the deleterious action of this substance, to the effect it has in preventing the coagulation of the blood, and thus causing effusion into the surrounding tissues; but I consider there can be but little doubt, that it was by affecting the irritability of the heart that it so suddenly caused death.

The action of subcarbonate of soda on the heart is a subject which has been experimentally investigated since writing the above paragraph; and the results of the experiments, certainly, do not bear out the explanation which has there been given of Magendie's experiment. In the experiments performed by me the heart retained in a marked degree its irritability, after death had been caused by the injection of a strong solution of subcarbonate of soda into the veins. Extensive ecchymosis had also taken place in the lungs; but at the same time the right side of the heart was not distended

with blood, nor was the left side in so empty a state as would have been the case, had death been caused by an arrest of the pulmonary circulation.

Action of Ammonia.—The action of the ammonia also is a subject, which I have not experimentally investigated; but from a case related, with a rare degree of professional candour, in the Medical Gazette for December 30, 1837, I think it is evident, that its introduction into the blood is followed by results precisely analogous to those produced by the substances whose action we have been considering. It is there stated that the injection of a solution of ammonia into a nævus was followed by the sudden death of the subject of the operation, and which, from the symptoms described, I consider was owing to the action of the heart being stopped by some of the injection having entered the veins.

The supposition now advanced as to the power of ammonia in arresting the pulsations of the heart has since been confirmed by direct experiment. It was found that a drachm of a strong solution of ammonia, mixed with six drachms of water, stopped the action of the heart twenty-five seconds after its injection. The heart retained a slight degree of irritability after death.

Action of Iodide of Arsenic.—Iodide of arsenic, although so poisonous a substance, does not appear to exert so strong an action on the heart as might be expected. Solutions, containing each six grains of this substance, were twice injected into the jugular of a dog, without producing the slightest appreciable effect on the heart. On injecting a solution, containing fifteen grains of this substance, the action of the heart was immediately stopped. Only the right auricle retained its irritability after death.

Action of Oxalic Acid.—Oxalic acid, when introduced into the veins in small quantities, does not appear to exert any direct action on the heart. The injection of half a drachm into the jugular vein was followed by the sudden cessation of the action of the heart. The blood in the left ventricle was scarlet.

Action of Infusion of Galls.—The effect of the injection of a weak solution of galls was to cause the pulsations of the heart to become slower, the pressure in the arterial system being diminished. Six drachms of a concentrated infusion caused the heart to stop 15 seconds after its injection. On opening the thorax the heart contracted on exposure to the air, the left ventricle contracting apparently more readily than the right. Dark blood was found in both sides of the heart, although respiration did not cease until the action of the heart had been arrested for some seconds. I think it probable that the presence of dark blood in the left side might be accounted for by the previous injection of a considerable quantity of the substance having altered the physical properties of the blood.

Remarks on the Action of Nitre, &c.—Before proceeding to the investigation of the mode of operation presented by those substances which act directly on the nervous system, I shall offer a few remarks on the experiments already related.

The first fact that strikes us on a review of these experiments is the sudden manner in which the action of the heart is stopped, and the almost total absence of irritability in that organ after death. In all the experiments also, we have the absence of those symptoms which are usually considered as indicating an affection of the nervous system, the time and manner in which death occurred corresponding to that which would result had excision of the heart been performed. I think these facts are sufficient to justify the arrangements I have made of these substances, as proving fatal by acting locally on the heart.

Having attempted thus far to localize the action of these substances, the next question which presents itself is, do they act by being applied to the internal surface of the heart, or is it by circulating over its parietes? There are many reasons which would lead us to conclude that it is the circulation of these substances, when mixed with the blood, over the parietes of the heart, that produces the affection of that organ. The principal of these are, the absence of any immediate effect on the heart when the substance is injected, although it is then applied in its most concentrated state to the lining membrane of the right side;—the great dyspnœa produced before the heart is affected, indicating that the substance is passing through the lungs;—and the right side retaining its irritability after death, although it was to this part of the heart that the substance was applied in its most concentrated state. These, I think, are sufficient reasons for concluding that it is through the medium of the blood circulating over the parietes of the heart that these sudden effects are produced.

But the most important consideration connected with these experiments, is the endeavour to ascertain on what common property possessed by these substances, their similarity of action depends.

There is one property, however unlike these may be in other respects, in which they all agree, and this is, in effecting considerable changes in the chemical composition of the blood.

The change of colour produced by the presence of the various salts in the blood, the marked action on organic substances by the iodides, the dark colour imparted by the acids, and the important combinations formed by tannin and gallic acid with the constitution of the blood, are sufficient proofs that we are employing substances which exert a considerable influence in modifying the composition of this fluid. The present state of our knowledge in organic chemistry, unfortunately, is such, that we are unable even to form an idea of the nature of the changes which take place in the

blood, so that all speculation on this point must be useless. There is one part, however, with which that science furnishes us, which will account for the small quantity of some of these substances necessary to prove fatal. This is the formation of definite compounds between organic substances and inorganic bases, containing not more than two or three per cent. of the inorganic base, so that the presence of a few grains of a salt in the blood may give rise to an alteration in a considerable portion of that fluid.

Amongst the substances whose action we have been considering, are some which are daily taken into the stomach in considerable doses, and which are undoubtedly rapidly absorbed ; and yet their action on the animal economy, when taken in this manner, is certainly not such as might be supposed to result from the absorption of substances, the presence of which in the blood in any quantity must be productive of such serious consequences.

It is an interesting fact, however, that the therapeutical action of these substances (nitre and the carbonates of potass and soda) is to increase the secretion of the kidnies, by which they are again rapidly eliminated from the system, thus affording an effectual means of preventing their accumulation in the blood to any amount.

2. *Substances acting on the Nervous System.*—I shall now proceed to investigate the action of those substances on the circulation, which appear to produce death by destroying the functions of the nervous system.

The substances the operation of which I have experimentally investigated in this class are strychnia, conia, and hydrocyanic acid. The manner in which these substances act will be illustrated by the following experiment.

Action of Strychnia.—A grain of strychnia, dissolved in a small quantity of acetic acid, was injected into the veins of a dog. The first effect of the poison was to produce general convulsions about 30 seconds after its injection, the action of the heart being at the same time rendered irregular; but I think this can be fully accounted for by the convulsive struggles of the animal. All external signs of life ceased about a minute and a-half after the injection of the poison ; the heart still continued beating. A minute after the apparent death of the animal, the column of mercury in the instrument indicated that the pressure in the arterial system was about equal to what it was before the introduction of the poison. The pressure in the arteries gradually became diminished, as in the experiment in which the effect of respiration on the heart was ascertained. Five minutes after death, the column of mercury supported was only equal to one inch and a-half. No farther diminution was observed, owing to the blood in the tubes having coagulated. The thorax was not opened for a quarter of an hour after death. The right sides of the heart then contracted on

being exposed to the air. They contained a considerable quantity of dark-coloured blood. The left ventricle contained a small quantity of blood, which was as dark as that in the right.

Strychnia when introduced into the circulation in so small a quantity as not to produce any general symptoms, does not appear to exert the least influence on the heart.

Action of Hydrocyanic Acid.—Hydrocyanic acid when injected into the veins, although analogous to strychnine in its sudden action on the nervous system, yet appears also to exert a decided effect on the heart, not apparently by destroying in any degree its property of contracting, but by rendering the contractions irregular, and causing considerable variations in the pressure in the arterial system.

Five drops of hydrocyanic acid in six drachms of water were injected into the jugular vein of a dog, the instrument being connected with the femoral artery. In fifteen seconds the action of the heart became irregular. The column of mercury, which was before equal to about six inches and a-half, now oscillated between six and twelve inches, the greatest elevation being attained after two or three quickened pulsations. These great variations in pressure were in part due to the respiration being considerably affected, and to the struggles of the animal. But this cause certainly is not sufficient entirely to account for it. Forty-five seconds after the injection of the poison all respiratory movements ceased, and in a few seconds the animal appeared quite dead. The action of the heart, however, still continued. Immediately after the death of the animal, the column of mercury indicating the pressure in the arteries was about eight inches, or fully an inch higher than it was before the injection of the poison. The action of the heart became more regular a short time after death, the pressure in the arterial system gradually diminishing. Four minutes after death the column of mercury was only one inch and eight-tenths, the pulsations being still 100 in a minute. The thorax was opened about seven minutes after the apparent death of the animal. The right side was found to be still contracting occasionally. The left ventricle did not contract on the application of mechanical stimuli. Both sides of the heart were distended with dark blood, which was firmly coagulated.

The injection of half a drachm of hydrocyanic acid into the veins was followed by analogous results as regards the heart; in this instance, however, only ten seconds elapsed before it was affected, and the animal was killed more quickly.

Action of Conia.—The action of conia when injected into the veins is very analogous to that of hydrocyanic acid, except that the action of the heart was rendered more regular by its injection.

A single drop introduced into the veins began to produce its effects in about thirty seconds. These were first manifested by the respiration being stopped, and by the occurrence of general convulsions. The animal was apparently dead in about a minute. The heart still continued pulsating, and was ultimately stopped by asphyxia. On opening the thorax and pericardium the stimulus of the air was sufficient to produce general contractions of the heart. Both sides were distended with blood, which was dark and coagulated.

Remarks on Strychnia, &c.—The action of these substances, strychnia, hydrocyanic acid, and conia, affords a striking contrast with that of those contained in the former class.

In the one instance the action of the heart is suddenly arrested, the functions of the nervous system being destroyed on account of the circulation being stopped; in the other class of substances we find those, whose action is first on the nervous system, the heart remaining comparatively unaffected, carrying on the circulation as if independent of the inanimate mass which surrounds it.

3. *Action of the third class of Substances.*—I shall now proceed to consider the action of the third class of substances, or those which appear to exert a decided effect in modifying the capillary circulation. The property here taken as a ground of classification is certainly not of such primary importance as that which has served for the formation of the other classes, which are distinguished by the manner in which the substances placed in them produce death.

But in the class now under consideration it is not this property which has been taken as the ground of arrangement, for they all apparently prove fatal by acting on the nervous centres; but as I find they all agree in exerting a considerable influence in modifying the capillary circulation, even when not given in any sufficient quantity to produce any marked effect on the nervous system, I have taken this quality as that which serves for their classification.

Action of Tobacco.—The first of these substances which I shall consider is tobacco. The pressure in the arterial system, before the injection of the poison, was equal to a column of mercury of six inches and a-half. An infusion from about ten grains of tobacco was injected into the jugular vein; in about 10 seconds the respiration was affected, it becoming very laborious and blowing. Twenty seconds after the injection of the poison the action of the heart suddenly stopped, and in a few seconds the column of mercury had diminished to two inches. After the heart had stopped for a few seconds it again began pulsating, the pressure in the arterial system becoming considerably increased, and being irregular, the column of mercury oscillating between six and twelve inches, the oscillations often amounting to four or five inches at each pulsation. In three or four minutes the pressure was again reduced,

the oscillations not being so great. The introduction of another injection of the same strength was attended with exactly analogous results. On injecting an infusion from two scruples of tobacco the heart was stopped in about 20 seconds, and remained arrested for 30 seconds; the column of mercury had diminished to one inch; but, on the heart again commencing to pulsate, the pressure in the arterial system suddenly became increased, and in the course of four or five pulsations was equal to a column of mercury of from ten to twelve inches. The mercury oscillated for some time between seven and twelve inches; it gradually, however, became more regular, and sank to about six inches and a-half. The animal did not appear much affected by the tobacco; the respiration was rather deep, but there were no convulsive movements or loss of consciousness.

An infusion from three drachms of tobacco injected into the veins of another dog was followed, as before, by the cessation of the action of the heart for some seconds; it then again commenced beating, and the pressure in the arterial system was much increased. The animal died about two minutes after the introduction of the poison much convulsed. The heart continued beating some time after death, and was finally stopped by asphyxia.

Action of Euphorbium.—Euphorbium when injected into the veins appears to act in a manner analogous to tobacco.

A solution when injected caused the heart to stop in about 20 seconds. The pressure in the arterial system immediately before its injection was equal to about four inches of mercury, but it suddenly became diminished, the column of mercury supported being only an inch and a-half. After the action of the heart had been suspended for 30 seconds it again commenced, and in ten or twelve pulsations the pressure in the arterial system had become so considerably increased, that the column of mercury after attained the height of fifteen inches, the parietes of the arteries thus being submitted to a pressure nearly four times as great as they sustained before the injection of the poison. The oscillations in the column of mercury were very considerable, often amounting to four or five inches at a single pulsation.

All external signs of life ceased about two minutes after the injection of the poison, but the action of the heart still continued. Artificial respiration was had recourse to three minutes after all signs of life had ceased, the pressure in the arteries being still equal to a column of mercury of nine inches. No immediate effect was produced by the inflation of the lungs. The pressure in the arteries gradually sank.

Ten minutes after the apparent death of the animal a most curious phenomenon presented itself. The column of mercury had by this time become diminished to two inches and a half, when

in a few pulsations it again attained the height of eight inches, although not the slightest sign of life had been evinced for full ten minutes. Slight convulsive movements took place on this increase of pressure in the arteries, and continued for a few seconds. Artificial respiration was still continued, the pressure again gradually becoming diminished. At twenty-eight minutes after the apparent death of the animal the column of mercury was only about one inch and a half. The same extraordinary increase in the pressure again took place, the column of mercury in the course of a few pulsations attaining the height of four inches. This was not accompanied by the slightest perceptible movement of the animal, eighteen minutes having now elapsed since any had been observed. The motion of the heart was finally stopped by injecting a solution of euphorbium into the veins, after artificial respiration had been kept up for thirty-six minutes. After death extensive ecchymosis was found in all the viscera, particularly on the internal surface of the heart, and in the lungs.

This, I think, must have been the result of the great pressure, to which the parietes of the blood-vessels must have been subjected.

Action of Digitalis.—Digitalis agrees with tobacco and euphorbium in modifying the capillary circulation, but it appears also to exert a decided action on the heart, by rendering its pulsations much slower. On injecting an infusion from about a drachm of the leaves, the respiration was affected in five seconds; and ten seconds after the injection of the substance into the veins, the heart was affected, its pulsations being rendered so slow, that, in five seconds, the column of mercury indicating the pressure in the arterial system had diminished from five to two inches. After a few seconds the pressure in the arterial system again became increased, the column of mercury being as high as eight inches, the pulsations of the heart again becoming quickened. When an infusion from three drachms of the leaves was introduced into the jugular vein, the action of the heart was arrested five seconds after the injection of the poison, and no pulsation was indicated after this. The pressure in the arterial system diminished very slowly. One minute after the heart had stopped, it was still equal to two inches and a-half of mercury. Respiratory movements were observed fully a minute and a half after the heart had ceased beating. On opening the thorax the heart was found distended with blood and motionless, general contractions were produced on exposing it to the air. The left cavities contained scarlet-coloured blood.

The short time (only five seconds) which occurred between the injection of this substance, and the cessation of the action of the heart, led me to suspect that it might possibly affect that organ, by acting in the nervous system even before it could be circulated over its parietes. I endeavoured to ascertain if this were really the

case, by injecting a solution of it directly into the arteries, when the phenomena observed fully proved the unfounded nature of this opinion. In order that the substance might be brought into immediate contact with the brain, and also to avoid the possibility of its finding its way directly to the heart, I inserted a tube into the carotid of a dog, the orifice looking towards the brain. The instrument, as in former experiments, was connected with the femoral artery. Another reason which led me to fix on the carotid for introducing the injection was, that the free anastomoses of this vessel would allow a portion of the injected fluid to pass into the general circulation, if the injection were pushed with some force. An ounce of an infusion of digitalis, of the same strength as that last used, was now quickly injected. The immediate effect of the injection appeared to be the production of great pain to the animal. Ten seconds after the injection had been introduced, the pressure in the arterial system became suddenly increased, the column of mercury rising from five inches, at which it before stood, up to twelve and fourteen inches, considerable oscillations taking place. It was not until forty-five seconds after the introduction of the poison that the heart appeared at all affected. The pulsations were then rendered very slow, ten or twelve seconds elapsing between each pulsation, the pressure in the arteries was soon diminished, the mercury standing at about three inches. The nervous system was evidently much affected, but respiratory movements still occasionally took place. About four minutes after the injection of the poison the heart suddenly stopped beating. The heart retained its irritability after death, contracting readily on being stimulated. I think the increase of pressure in the arterial system, taking place so soon after the injection of the poison, was owing to a portion of it having passed from the carotids into the aorta, and being thus distributed over the body; for supposing it to exert on the capillaries that action, which I think we are fully justified in attributing to it, the circulation of the poison through the brain could not have taken place to any amount.

Remarks on Tobacco, &c.—The only remark I have to offer on this class of substances is the impossibility of accounting for the great increase of pressure in the arteries, caused by their introduction into the circulation, without allowing them to possess that property which has been selected as the ground of classification, viz. that of modifying the capillary circulation.

Remarks on Euphorbium, &c.—This increase of pressure evidently cannot depend on any change effected in the action of the heart, as we find it taking place before that organ is affected. The sudden cessation of the action of the heart, when these substances were applied to it in at all a concentrated state, also admits of an explanation, by supposing the capillary circulation over the pa-

rietes of this organ to become so obstructed, that, for a short space of time at least, sufficient blood was not sent over its parietes to keep up its irritability. In endeavouring to localize the action of these substances, two propositions present themselves; viz. is their action on the capillary circulation the result of their direct application to the inner surface of these vessels, or does it follow from some peculiar action they exert on the nervous system? From a review of the above experiments, I am inclined to believe that these substances act directly on the capillaries themselves; and from the great oscillations observed in the pressure in the arteries, it appears that they also exert a power of modifying the elasticity of the larger vessels. It would be useless to attempt to enter into any explanation of the manner in which the two last classes of substances produce their effects. I shall merely remark, that, though differing considerably in their physical and therapeutical properties, yet none of them, as far as I am aware of, exert any marked effect on the composition of the blood. Should they act by producing such changes, these must be widely different from those caused by the first class of substances, and are such as our present knowledge of organic chemistry does not enable us to detect.

4. I have still a few remarks to offer on the action of one or two substances, which I have not been able to arrange in either of the above divisions. These are morphia, cantharides, and nitric acid.

Action of Morphia.—Morphia when introduced into the veins shows its effects on the heart, by rendering its pulsations slower, the pressure in the arterial system becoming diminished. The injection of ten grains of acetate of morphia into the jugular of a dog was followed by a diminished action of the heart.

Action of Cantharides.—Cantharides, although so different from morphia in its therapeutical properties, yet, when introduced into the blood, has the same effect on the heart, in rendering its pulsations slower, and causing a diminution of pressure in the arteries, which is not followed by any sudden increase of pressure, as in the last class of substances.

An infusion from two drachms of the flies was introduced into the veins, without apparently causing much inconvenience to the animal. It produced some dyspnœa when passing through the lungs, and slight irregularity in the action of the heart for a few seconds.

Action of Nitric Acid.—The following experiment with nitric acid affords us an instance of death, produced apparently by obstruction to the passage of the blood through the lungs.

A drachm of nitric acid, mixed with an ounce of water, was injected into the jugular vein of a dog. Twenty seconds after the injection, violent struggles were produced, and all respiratory movements soon

ceased. A minute after the introduction of the acid, the column of mercury indicating the pressure in the arterial system had diminished from seven inches to one inch and a-half. The animal was now apparently dead, but partial efforts to vomit were observed two minutes later. The thorax was opened four minutes after the injection of the poison. The left side of the heart was still pulsating. The right side was distended with blood to the greatest extent possible. On opening it, its contents were found to be quite solid, resembling blood which had been boiled. This solid blood would be traced as far as the second divisions of the pulmonary artery in one direction, and extended the whole length of the descending cava, and a short distance into the iliacs. The left side of the heart contained a small clot of scarlet blood, of the natural colour and consistency.

Action of the Nervous System.—I shall now conclude the detail of these experiments by a short notice of one or two which I have performed, in order to ascertain the direct influence of the nervous system on the heart. I am sorry that, from the many sources of fallacy which the severity of the operation introduces in the performance of these experiments, I am unable to bring the subject forward in a more complete state. In those experiments in which I have obtained positive results, I find that the sudden destruction of the lower part of the spinal chord (from the lower part of the dorsal portion to the end) is not followed by any direct action on the heart, or diminution of the pressure in the arteries. I have also destroyed the portion extending from the lower part of the dorsal to the upper part of the cervical region, without producing any direct effect on the heart, that organ gradually stopping from the asphyxia which was produced by the operation.

I have now brought to a conclusion the detail of the experiments performed by me with a view to ascertain the mode in which various agents, chemical and pharmaceutical, act, when introduced into the veins. I shall not presume to occupy your time by attempting to enter into any theoretical deductions from them, which would come with a bad grace from one who is still engaged in studying the elementary branches of his profession. My aim has been to render these notices as strictly experimental as possible, and to bring forward a few facts which might serve to call the attention of more able inquirers than myself to a subject, the investigation of which is, I think, likely to throw much light on many interesting questions in physiology. And it is this which must serve as my apology for bringing the subject forward in so unfinished a form.

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MÉMOIRE

SUR LES

EFFETS DE DIVERSES SUBSTANCES SALINES

INJECTÉES

DANS LE SYSTÈME CIRCULATOIRE,

Lu à l'Académie des Sciences le 3 juin 1839.

PAR JAMES BLAKE.

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1839.

MÉMOIRE

SUR LES

EFFETS DE DIVERSES SUBSTANCES SALINES

INJECTÉES

DANS LE SYSTÈME RESPIRATOIRE.

Le mémoire que j'ai l'honneur de présenter à l'Académie contient des expériences faites dans le but d'examiner les phénomènes produits par l'introduction de certains sels dans les voies de la circulation.

Les physiologistes du siècle dernier s'occupèrent de ce sujet sous le point de vue des applications qu'on en peut faire à la thérapeutique : mais aucun n'en fit l'objet d'une étude purement physiologique, leurs recherches n'étant pas faites dans le but d'éclairer les phénomènes compliqués de réaction du sang, empoisonné, pour ainsi dire, par la présence de quelques sels, sur les divers tissus de l'organisme. Pourtant il est clair que la propriété que possèdent certaines substances du règne minéral de produire dans le sang des altérations bien constantes, les rend de précieux réactifs pour le physiologiste, et qu'une observation attentive des effets qu'elles produisent sur l'économie, accompagnée d'une exacte analyse des changements qu'elles opèrent dans le sang, ne peuvent manquer de jeter un jour éclatant sur quelques unes des plus importantes questions de la physiologie.

L'état actuel de la chimie organique ne permet malheureusement pas au physiologiste de recueillir encore de ses expériences tout le fruit qu'il en obtiendrait, si cette science, plus parfaite dans ses procédés, lui fournissait les moyens d'apprécier d'une manière rigoureuse les changements que subit le sang par

son contact avec les sels. Naturellement arrêté par cette considération, l'auteur de ce mémoire a dû se borner au simple récit des faits qu'il a observés, dans l'espoir que cette savante assemblée ne les jugera pas indignes de son attention.

Un écrit de la nature de celui-ci ne saurait comprendre le récit des expériences faites jusqu'à ce jour sur le sujet qui nous occupe : Il en existe d'ailleurs une volumineuse histoire dans un ouvrage publié par Scheele. Il paraîtrait, d'après les détails que donne cet auteur, que quelques uns des faits que je vais rapporter avaient été déjà notés par plusieurs observateurs; mais leurs recherches se rapportaient exclusivement à l'action thérapeutique de ces substances salines introduites dans le torrent de la circulation ; et absorbés par la question médicale, ils négligèrent la question physiologique. D'intéressantes expériences sur ce sujet ont aussi été publiées par M. Magendie dans ses *Leçons sur les phénomènes physiques de la vie*, ouvrage auquel j'aurai d'ailleurs occasion de revenir. Dans un mémoire que je lus en 1838, à l'*Association anglaise pour les progrès des sciences*, mémoire qui depuis fut publié par le journal médical et chirurgical d'Edimbourg (avril 1839), je fis allusion aux effets que certains sels paraissent produire sur l'économie; mais à cette époque j'avais encore besoin de quelques recherches pour arriver à ces conclusions générales qu'une plus complète série d'expériences me permet d'adopter aujourd'hui.

Ce mémoire contient le résultat d'expériences faites avec les sels de potasse, de soude, d'ammoniaque, de baryte, de chaux et de magnésie.

Les différences et les rapports que présentent entre elles ces substances, dans leurs effets sur l'organisme, en font deux classes distinctes, ce qui rendrait inutile le récit des expériences faites sur chaque sel en particulier. Je me bornerai donc à la narration d'expériences qui jettent quelque clarté sur les points les plus importants de l'action de deux sels choisis dans l'une et dans l'autre classe.

Ces deux classes de substances diffèrent dans leur action physiologique, en ce que les unes donnent la mort en anéantissant l'irritabilité du cœur lorsque les parois de ce viscère sont arrosées par le sang empoisonné, tandis que le cœur ne paraît en rien affecté par le contact des autres qui font cesser la vie en entravant la circulation pulmonaire. Cette différence d'action peut se rattacher à une différence de composition chimique, la soude et les sels qu'elle forme apportant un obstacle au passage du sang dans les capillaires du poumon, tandis que tous les sels de potasse, d'ammonique, de baryte, de chaux et de magnésie, tuent en paralysant le cœur.

L'expérience suivante fera connaître les effets qui suivent l'injection dans les veines de la soude et de ses composés.

Exp. I. Un tube fut inséré dans la veine jugulair d'un chien fort, du poids de 14 livres. Un autre tube introduit dans l'artère crurale, mettait le système à sang rouge en rapport avec l'hémadynamomètre, instrument d'une valeur inappréciable dans toutes les recherches sur la circulation. Un soluté de quinze grains de soude pure, dans six gros d'eau, ayant été alors injecté dans la veine jugulaire, on observa, après six secondes, une notable diminution de la pression exercée sur le système artériel. Cette pression, égale au commencement de l'expérience à une colonne de mercure de 0 110 m. à 0,140 m. de hauteur, était tombée à 0, 030 m. Les oscillations continuant dans la colonne mercurielle après sa diminution, prouvaient cependant jusqu'à l'évidence, que les contractions du cœur continuaient encore; de sorte qu'on ne peut se rendre compte de la diminution de la colonne de mercure, qu'en admettant que l'arrivée du sang au ventricule gauche avait été empêchée. 45 secondes après l'injection du poison, l'animal avait cessé de vivre. Après avoir étudié l'effet local de la substance injectée, nous ferons l'énumération des symptômes généraux qu'elle produisit.

Le thorax ayant été ouvert immédiatement après la mort, le ventricule et l'oreillette gauches se contractaient encore. Les cavités droites étaient tellement distendues par le sang, que toute contraction de leurs parois était impossible : mais, en tirant un peu de sang de leur cavité, toutes deux recommencèrent à se contracter Le sang renfermé dans le cœur droit était noirâtre et ne se coagula qu'imparfaitement. Le ventricule gauche contenait un petit caillot

de sang écarlate, parfaitement coagulé. (Il arrive quelquefois que tout le sang qui contient l'alcali, est chassé du cœur droit avant que la circulation pulmonaire soit arrêtée, et on en trouve même alors parfois dans le ventricule gauche, mais toujours en quantité trop minime pour être lancé dans les artères.) Tout le système veineux était gorgé de sang. Peu de congestion dans les poumons dont la consistance est normale; aucun empêchement sanguin dans leur tissu.

Dans une expérience rapportée par M. Magendie, dans ses *Leçons sur les phénomènes physiques de la vie*, on lit qu'une solution de sous-carbonate de soude ayant été injectée dans les veines, ce célèbre physiologiste attribua l'arrêt de la circulation pulmonaire à la liquéfaction du sang. Il me semble cependant que la formation d'épanchements sanguins dans le tissu pulmonaire, est plutôt le résultat de l'action de cette classe de substances sur les capillaires, action qui s'exerce soit qu'il y ait, soit qu'il n'y ait pas d'épanchement.

La cessation de l'arrivée du sang au cœur gauche, l'absence de sang alcalin dans ses cavités, et l'état de congestion des cavités droites ainsi que de tout le système veineux, ne tendent-elles pas à prouver que les effets de ces substances sur l'économie sont tous dus à l'obstacle qu'elles apportent à la circulation pulmonaire ?

L'expérience suivante donne une preuve plus forte encore de l'action de cette classe de substances sur les capillaires du poumon.

Exp. II. Un gros de nitrate de soude, dissous dans six gros d'eau, et injecté dans la veine jugulaire sembla suffire à l'arrêt de la circulation pulmonaire. Cependant, le ventricule droit parut à la longue surmonter l'obstacle. Comme dans la précédente expérience la colonne mercurielle dans l'hémadynamomètre tomba peu après l'injection faite; la respiration s'arrêta complètement, et l'animal pendant deux minutes ne donna aucun signe de vie. Après deux minutes, cependant, la respiration se rétablit, la pression artérielle augmenta, et l'animal parut revenir à la vie. La dypsnée se montra de nouveau, et, au bout de cinq autres minutes, la respiration s'arrêta encore et l'animal mourut asphyxié, l'hématose étant sans doute empêchée par la grande

quantité de liquide écumeux qui se forma dans les bronches et qui s'échappa même par les narines.

A la nécropsie on trouva les voies aériennes complètement remplies de ce liquide spumeux et les poumons un peu congestionnés, sans qu'aucun épanchement apoplectique se fût fait dans leur tissu. Le sang recueilli après la mort fournit un caillot solide. L'abondante sécrétion formée dans les voies aériennes, est une preuve de l'action spéciale que le nitrate de soude exerça sur les capillaires du poumon. Une solution plus concentrée de nitrate arrête complètement la circulation pulmonaire.

Il nous semble que ces expériences suffisent pour démontrer l'exactitude de l'opinion ci-dessus énoncée sur l'action de ces substances sur les vaisseaux capillaires du poumon.

Étudions maintenant les symptômes généraux qui suivent leur introduction dans le sang veineux. Ces symptômes, qui nous engageraient au premier abord à ranger ces substances parmi les poisons les plus rapidement mortels, trouvent cependant une complète explication dans l'effet local produit sur les capillaires du poumon.

Dans la première expérience rapportée, quinze grains de soude ayant été injectés dans la veine jugulaire d'un chien, les phénomènes généraux furent les suivants : dix secondes après l'injection, suspension des mouvements respiratoires, opisthotonos violent ; trente secondes après l'injection, le spasme était à son maximum. Il diminua alors peu à peu, et quarante-cinq secondes après le commencement de l'expérience, l'animal parut avoir cessé de vivre. Environ une minute et demie après que tous les signes de la vie eurent cessé, il fit une ou deux profondes inspirations et ne bougea plus.

Les nombreuses expériences que j'ai faites avec cette classe de substances, m'ont appris que ces mouvements respiratoires ont généralement lieu de une à deux minutes après la mort apparente de l'animal. Dans certains cas, ils ont été le prélude d'un retour momentané à la vie, si la quantité de poison injecté n'avait pas été trop considérable. Dans le cas contraire, ils eu-

rent lieu après que tous les autres muscles du corps eurent perdu leur contractilité.

Tels sont les phénomènes généraux qui suivent toujours l'injection des sels de soude en quantité notable dans les veines. Je vais chercher à rattacher ces phénomènes, tout nerveux, à l'action locale que ces substances exercent sur la circulation pulmonaire.

L'explication à laquelle ces phénomènes se prêtent le mieux, consisterait à les attribuer à la compression que doit éprouver l'encéphale par l'accumulation du sang dans le système à sang noir, accumulation due à l'arrêt de la circulation pulmonaire. L'expérience suivante est destinée à prouver que cette cause peut donner la clef de tous les phénomènes observés.

Exp. III. Un tube fut introduit dans la veine crurale d'un chien tube assez long pour que son extrémité pénétrât dans la veine cave ascendante. Une injection de soude fut poussée dans la veine jugulaire. Immédiatement auparavant, la pression dans les veines ne produisait pas de différence sensible dans le niveau du mercure de l'hémadynamomètre. Mais, six secondes après l'injection, celui-ci indiquait que les parois des veines étaient soumises à une pression égale à deux pouces de mercure, pression nécessairement supportée par les ventricules du cerveau, et qui dut produire une compression de l'encéphale, plus que suffisante pour rendre compte des phénomènes morbides.

Cette théorie de la cause de la mort subite est appuyée par ce qui se passe après l'introduction de l'acide nitrique dans les veines : cette substance, en solidifiant le sang, l'arrête à sa sortie du cœur droit, et produit ainsi une congestion veineuse d'où naissent des phénomènes exactement semblables à ceux ci-dessus détaillés. Cependant l'action de ces substances ne se borne pas aux capillaires du poumon : l'expérience suivante démontre que les capillaires généraux en éprouvent aussi une action telle, qu'ils nécessitent de la part du ventricule gauche le déploiement d'une force triple de celle qui est nécessaire dans l'état normal de la circulation pour faire passer le sang des artères dans les veines.

Exp. IV. L'hémadynamomètre ayant été mis en rapport avec l'artère fémorale, un tube fut introduit dans l'artère axillaire, sa pointe dirigée vers le cœur, de manière que toute injection poussée dans son calibre dût nécessairement passer dans l'aorte et de là dans les artères. La pression supportée par celles-ci, faisait équilibre à une colonne de mercure de 0m,112 à 0m,150. Une injection d'un gros et demi de nitrate de soude fut poussée dans l'artère axillaire; quatre secondes après, la seringue n'étant pas encore vidée, la pression artérielle commença à augmenter, et en seize secondes, elle égalait une colonne de mercure de 0m,350. Le mercure après être resté stationnaire quelques secondes, descendit graduellement lorsque le cœur eût cessé de battre par l'asphyxie de l'animal, car tout mouvement respiratoire cessa environ dix secondes après l'introduction du sel dans les veines. La présence du sel dans le sang ne parut, en aucune façon, altérer la contractilité du cœur; les pulsations continuèrent au contraire plus longtemps qu'à l'ordinaire après l'arrêt des mouvements respiratoires, la pression artérielle persistant à 0m,150, trois minutes après la mort apparente de l'animal. Les sels de soude dont nous avons étudié l'action par la voie expérimentale, sont le nitrate, le sulfate et le carbonate de cette base. Après l'alcali pur, le nitrate est de beaucoup le plus délétère; injecté à la dose de deux gros dissous dans six gros d'eau, il arrête la circulation pulmonaire, tandis qu'il faut une once à une once et demie d'une solution saturée de sulfate ou de carbonate pour produire le même résultat

Je vais maintenant, Messieurs, mettre devant vos yeux le récit de quelques expériences, à l'aide desquelles je démontrerai l'action de la seconde classe de substances, qui tuent en paralysant le cœur.

Exp. V. Une solution de trois grains de potasse pure dans six gros d'eau fut injectée dans la veine jugulaire d'un chien, après que l'hémadynamomètre eût été mis en rapport avec l'artère fémorale. Le seul effet produit fut une légère accélération du mouvement du cœur, douze secondes après l'injection. Une solution de six grains fut alors poussée dans la jugulaire, et dix secondes après, l'action du cœur cessa tout à coup, comme le prouvèrent la chute rapide de la colonne de mercure et la cessation des oscillations du métal. Quelques secondes après, le mercure était tombé à zéro, sans oscillations dues aux contractions du cœur. (Les mouvements respiratoires continuant quelque temps après que ceux du cœur ont cessé,

on doit prendre garde à ne pas confondre les oscillations dues à la respiration avec celles qui résultent de l'action du cœur.) La poitrine fut ouverte aussitôt après la mort, et le cœur mis à nu moins d'une minute après la dernière expiration. Une légère contraction de l'oreillette droite fut le seul signe d'irritabilité observé. Les parois ventriculaires étaient complètement immobiles, et l'application des deux pôles de la pile ne purent même pas produire de contraction.

Les cavités droites et gauches contenaient une grande quantité de sang noir et bien coagulé à droite, d'un beau rouge et en caillot solide à gauche. (L'état du sang après la mort donne ici un exemple frappant de la différence de l'action des substances étrangères, suivant qu'il circule encore, ou qu'il a été retiré de la veine.)

Indépendamment des indications fournies par l'hémadynamomètre, l'examen anatomique prouve assez que la potasse injectée a agi en détruisant l'irritabilité du cœur. Mais l'injection des sels de cette seconde classe dans les veines d'un animal dont on a préalablement ouvert la poitrine, et chez lequel on pratique la respiration artificielle, fournit la preuve la plus satisfaisante du mode d'action du poison, puisque de sept à dix secondes après l'injection, *on voit* que le cœur est tout à coup paralysé.

L'action des sels de potasse est exactement la même que l'action de la base. Le nitrate, le sulfate et le bi-arséniate ont été tour à tour employés dans nos expériences. De tous ces sels, le nitrate paraît le plus actif : cinq ou six grains suffisent pour arrêter l'action du cœur. L'identité d'action de toutes les substances de cette classe nous permettra de nous borner au récit de la précédente expérience, que nous donnons pour exemple des effets de tous les sels de cette classe injectés dans les veines.

Il nous suffira d'énumérer les substances dont nous avons étudié l'action dans nos expériences ; ce sont le nitrate de baryte, le chlorure de baryum, l'ammoniaque, le nitrate d'ammoniaque, le nitrate de chaux, le chlorure de calcium, le nitrate et le sulfate de magnésie. Introduites dans les artères, ces substances produisent des effets qu'on lira dans l'expérience suivante.

Exp. 6. Comme dans la quatrième expérience, un tube fut introduit dans l'artère axillaire, l'hémadynamomètre ayant été mis en rapport avec l'artère crurale. Une solution d'un gros de nitrate de potasse fut alors injectée dans l'artère axillaire. Quatre secondes après le début de l'injection, la pression artérielle commençaà augmenter, et après sept secondes elle avait atteint $0^m,350$. Pendant quelques secondes, la colonne mercurielle oscilla entre $0m,250$ et $0^m,350$. Vingt-cinq secondes après l'injection, l'action du cœur s'arrêta tout à coup, et la pression artérielle diminua rapidement. Le thorax étant ouvert aussitôt, on voit quelques petits mouvements partiels des oreillettes et des ventricules, mais aucune vraie contraction de ces cavités. Les phénomènes que présente cette expérience prouvent que ce sel, bien qu'il traverse avec la plus grande facilité les capillaires du poumon, exerce cependant sur les capillaires généraux une action analogue à celle des sels de soude. Nous avons aussi une preuve convaincante que l'action de ces substances sur le cœur n'est pas le résultat d'une influence nerveuse quelconque, puisque, dans l'expérience précédente, le poison traverse le cerveau, et cependant le ventricule gauche continue à se contracter sous un poids de six livres pour chaque pouce carré de sa surface, le cœur n'ayant été paralysé qu'après que le sang empoisonné eût fait le tour complet de la circulation et eût été chassé sur ses parois par les artères coronaires. (Les vingt-cinq secondes que met le sang à parcourir le grand et le petit cercle circulatoires, paraîtront peut-être bien peu de temps; et cependant ce sont quelques secondes de plus que ne met le sang à parcourir le même trajet; le délai, sans doute, est causé par la difficulté que le sang altéré éprouve à traverser les capillaires généraux. En preuve de la rapidité de la circulation, je renverrai à un mémoire lu devant la Société royale de Londres, mémoire dans lequel j'ai rapporté un grand nombre d'expériences faites à ce sujet).

Les effets généraux qui suivent l'introduction dans les veines des substances dont il s'agit, sont précisément ceux que le raisonnement serait tenté d'attribuer à priori à la paralysie du cœur. Aussitôt que les pulsations de ce viscère s'arrêtent, l'animal se débat violemment, les inspirations deviennent profondes, la douleur paraît considérable; ce n'est qu'une minute et demie ou deux minutes après la cessation des battements du cœur que l'animal paraît perdre connaissance; et les mouve-

ments respiratoires continuent encore de une à trois minutes après que la circulation s'est interrompue. (Il est un phénomène général que je n'ai remarqué qu'après l'introduction des sels de baryte; je veux parler de la continuation de quelques mouvements convulsifs partiels après la mort : ils durent de vingt minutes à une demi-heure, et sont plus marqués dans la moitié antérieure du corps, peut-être parce que le sel est plus immédiatement répandu dans cette région avant la suspension des battements du cœur.)

Les effets généraux qui suivent l'injection d'une solution de ces substances dans le système artériel, sont les mêmes que ceux que produit l'introduction des sels de soude dans les artères, et sont probablement dus à la compression que doit subir le cerveau par la pression augmentée que supportent les artères.

Résumons en peu de mots les principaux phénomènes de nos expériences. Le premier fait qui frappe l'esprit, c'est le rapport qui existe entre la composition chimique et l'action physiologique des sels employés. Ce rapport n'est pas, il est vrai, tel que l'état actuel de la science des affinités chimiques nous l'eût fait prévoir; car il est évident que les décompositions effectuées dans le sang par ces sels, décompositions sur lesquelles roule toute leur action physiologique; il est évident, dis-je, que ces décompositions dépendent de la base du sel, et ne sont que peu modifiées par la combinaison de cette base avec les acides même les plus puissants. Ce fait est aussi en directe opposition avec les conclusions auxquelles amène naturellement l'étude de l'action de ces substances sur le sang extrait des voies circulatoires; car, en mêlant au sang une solution de différents sels, les réactions produites dans le mélange sont, autant qu'une analyse superficielle permet d'en juger, en relation intime avec la nature de l'acide du sel. Nous en trouvons un frappant exemple dans ce qui se passe lorsque les nitrates de potasse et de soude sont mis en contact avec le sang retiré de la veine. Ces deux sels empêchent la coagulation du sang, et cependant nous avons

vu que leur action physiologique est bien différente. (L'examen microscopique du sang mis en contact avec ces divers sels n'a pas le moins du monde éclairci ce sujet.) C'est donc en vain qu'on tentera d'expliquer l'action physiologique de ces substances par les changements qu'elles produisent dans la composttion du sang, et malgré tout l'intérêt qui s'attache à un semblable problème, sa solution restera toujours impossible, jusqu'au jour où la chimie nous aura fourni les moyens d'apercevoir les changements que subit le sang par son contact avec les matières étrangères. Il est un fait plein d'intérêt, c'est que, de tous les sels dont nous avons étudié l'action, ce sont les sels de soude exclusivement que l'on trouve en quantité considérable dans le sang, qui ne paraissent pas rendre ce fluide incapable de continuer l'irritabilité du cœur.

Quoique nous soyons incapables de surprendre les changements moléculaires survenus dans la composition du sang, il est évident que ces changements doivent intervenir dans les réactions du sang sur les tissus, et que ce liquide est rendu incapable d'entretenir les fonctions des organes avec lesquels il est en contact. Il semble aussi que, devenu inhabile à maintenir les fonctions d'un tissu, il n'ait pas, pour cela, perdu la propriété de conserver les fonctions d'autres tissus; c'est ainsi que la soude dans le sang, malgré son action énergique sur les capillaires du poumon, ne change pas la composition de ce fluide au point de le priver de la propriété de stimuler le cœur. La même remarque s'applique aux changements que produisent les sels de potasse introduits dans le sang, au moyen desquels les capillaires généraux éprouvent une action puissante, sans que les vaisseaux capillaires pulmonaires généraux soient affectés en aucune manière. (Il me semble probable qu'on peut expliquer l'action des poisons qui affectent le système nerveux, en admettant que le sang vicié, sans l'être cependant de manière à affecter les capillaires ou le tissu du cœur, a perdu la propriété de subir les réactions nécessaires à la persistance des fonctions des systèmes nerveux.

A l'appui de cette opinion, je dirai qu'aucun de ces poisons, quelque rapide que soit leur action, ne produisent de symptômes généraux avant que le sang qui les contient n'ait circulé dans le cerveau. J'ai donné des preuves de cette assertion dans un Mémoire lu à la Société royale de Londres.)

L'action de certaines substances sur divers tissus, ou sur différents systèmes de capillaires, est un fait d'une bien plus haute portée que la simple explication du mode d'action des poisons, puisqu'il tend à éclairer l'action locale d'une foule d'agents thérapeutiques, et les phénomènes locaux qui découlent des altérations pathologiques dont le sang devient quelquefois primitivement le siége.

ON THE

ACTION OF CERTAIN INORGANIC COMPOUNDS

WHEN INTRODUCED DIRECTLY INTO THE BLOOD.

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ACTION OF INORGANIC COMPOUNDS, &c.

In a paper on the actions of poison, which I presented to the Royal Society in April 1839, and which was read on the 13th of June in the same year, I incidentally alluded to some experiments I had performed on the action of salts, when injected into the veins. On that occasion I merely noticed these experiments, on account of their having enabled me to determine the time required by the blood, to pass from one part of the system to another.

The results of my experiments on the introduction of saline substances into the vascular system, were communicated to the "Academie des Sciences" at Paris in the same year. (This memoir was published in the "Archives Generales de Medecine," November 1839.) Since this period, a further investigation of the subject has afforded me many new facts, which I now propose to lay before the Society.

At the time I wrote my former memoirs, I had only investigated the actions of the substances I had experimented with, in relation to their action on the heart, and the changes to which they appeared to give rise in the lungs. I had, in fact, divided these substances into two classes, one of which included those which appeared to produce death by destroying the irritability of the heart, whilst the other contained those substances, which prove fatal by arresting the pulmonary circulation. Entirely occupied by these two phenomena, I had noticed but casually the action which the salts of soda and potash appeared to exert on the general capillary circulation. The experiments I have now to bring forward will prove, that the effects that these and some other substances produce on the general capillary circulation, form an important element in the investigation of their general action on the animal economy. But besides those phenomena which depend on the action of these salts on the vascular system, there are others to which I had not at all directed my attention, viz. the effect which these substances appear to give rise to, by their contact with the nervous and muscular tissues. In the present memoir I have carefully recorded the effects produced by each substance on the different tissues to which I have now alluded, at least where these effects have been of a nature to be readily appreciated. I have, in fact, endeavoured to investigate the properties of the living tissues, in the same manner as the chemist would investigate the nature

of an inorganic compound, that is, by observing the phenomena it presents, when brought into relation with other substances.

I am aware that, in the present state of physiology, such a step may appear rash, and not likely to lead to any positive results ; but I know of no surer means that we can command of becoming better acquainted with the complicated phenomena which constitute life, than by introducing certain definite modifications in the circumstances under which these phenomena occur; and I think there can be no question, that the direct introduction of inorganic substances into the blood, affords us one of the most certain means of producing definite and appreciable changes in these circumstances. It is, however, equally true, that the present imperfect state of chemistry leaves us completely in the dark as to the nature of the perturbations which are thus produced, depriving us at the outset of every hope of arriving at any general conclusions, and confining our researches to the mere observation of facts. It is these considerations that have induced me to lay before the Society the following memoir, although I am fully aware that the experiments I have performed, still leave many voids to be filled up. The vast extent of the subject, however, involving, as it does, some of the highest physiological problems, precludes the hope that I should ever have arrived at a point, at which I might consider these researches as complete.

Before proceeding to the detail of the experiments, I shall shortly describe the manner in which they have been performed. The phenomena connected with the vascular system have been observed by the aid of the hæmadynamometer,—an instrument invented by M. Poiseuille, for ascertaining the pressure that the blood exerts on the parietes of the vessels. Had it not been for the almost mathematical precision which this valuable instrument enables us to introduce in researches on the circulation, I certainly should never have ascertained many of the facts which I have now to bring forward. A description of this instrument will be found in Todd's Cyclopædia of Anatomy and Physiology, Art. "Circulation." In ascertaining the pressure of the blood in the arterial system, this instrument has always been connected with the femoral artery. When the substance experimented on has been injected into the veins, it is the external jugular that has always been selected for this operation ; when into the arteries, the injecting tube has been introduced either into the right or left axillary artery, the point of the tube looking towards the heart, so that any fluid injected through it should be forced through the subclavian artery into the aorta, and thus become mixed with the blood circulating through the body. In all operations requiring the use of the hæmadynamometer, it is necessary that the animal should be confined, in order to command the requisite degree of

steadiness. In these circumstances, it is impossible to observe with accuracy the general symptoms that are produced. I have, therefore, always devoted a distinct experiment for the purpose of ascertaining these symptoms, a tube being inserted into the jugular vein, and the animal being placed on the floor, and allowed full liberty, the moment after the substance to be experimented with had been introduced into the vein. In these circumstances, any general symptoms that were produced would be readily detected. The whole of these experiments have been performed on dogs; they have been chosen as nearly as possible of the same size and strength: the general weight was from 12 to 16 pounds. The substances I have used in these experiments have been the sulphate and nitrate of magnesia; sulphate of zinc; sulphate of copper; nitrate of lime, and chloride of calcium; chloride of strontium, and nitrate of strontia; chloride of barium, and nitrate of baryta; acetate of lead; nitrate and acetate of silver; chloride of sodium, and nitrate and sulphate of soda; nitrate and hydrochlorate of ammonia; nitrate, sulphate, biarseniate, and bicarbonate of potassa, and the alkali itself.

The order in which I propose stating the experiments I have performed with these substances, is that in which they are here arranged. This arrangement may be considered in some respects a natural one; for each class of salts, from magnesia to soda, will be found connected by its physiological action more closely with the salt that more immediately precedes and follows it, than with any other.

The fact which I stated in the memoir presented to the Academy of Sciences at Paris, (see Archives Generales de Med. Nov. 1839), that all the salts of the same base exert an analogous action when introduced directly into the blood, a fact, the correctness of which has been proved by a far more extended series of experiments, will dispense with my stating the action of more than one salt of each base.

Magnesia.—When a solution of a salt of this base is injected into the veins, its first effect, if it be not too strong, is to quicken the action of the heart; and it also exerts a powerful influence on the character of the pulse, as is shown by the change which takes place in the oscillations of the column of mercury, indicating the pressure in the arterial system. Six grains of sulphate of magnesia, dissolved in five drachms of water, when injected into the veins, caused the pulsations of the heart to become quicker ten seconds after the injection, or at the moment when the blood containing the salt was circulated over the heart; at the same time, the oscillations of mercury in the hæmadynamometer became much diminished. The pressure in the arterial system was, at the commencement of the experiment, equal to a column of mercury, varying from five to seven inches and a half, at each pulsation of th

heart ; but a few seconds after the injection, the column of mercury was nearly stationary at six inches, the oscillations not being more than two or three-tenths of an inch, instead of two inches and a half, as they were before the injection. Two minutes after the injection, the effects of the salt had quite gone off, the action of the heart being just the same as it was before the introduction of the salt. Five minutes after the former experiment, a solution containing sixteen grains of the salt was injected into the veins, and produced analogous effects on the heart in about ten seconds ; thirty seconds after the injection, the pressure in the arterial system became lower, proving that some change had taken place either in the quantity of blood sent into the arteries, or in the facility with which it was discharged through the systematic capillaries ; for it can only be by a modification of one or the other of these elements that any change can take place in the pressure in the arterial system. When injected in larger quantities, this salt suddenly arrests the action of the heart. A solution containing a drachm of the salt to six drachms of the water, arrested the action of the heart eight seconds after its introduction into the veins. The inspection of the thorax immediately after death, discovered the heart motionless, although exposed half a minute after respiration had ceased. On opening the pericardium, slight movements were observed on that part of the parietes of the ventricle corresponding to the interventricular septum. The auricles were quite motionless. The left cavities of the heart were filled with blood, of a bright scarlet colour ; that in the right cavity was dark. The presence of arterialized blood in the left cavities of the heart, affords a certain proof that the movements of this organ had stopped, before respiration had become arrested.

When injected into the arteries, the sulphate of magnesia does not appear to have any influence on the passage of the blood through the general capillaries. A tube being introduced into the right axillary artery, a solution containing sixteen grains of the salt was injected into the artery. No immediate change was observed in the pressure in the arterial system, which could not have been the case, had any change taken place in the passage of the blood through the general capillaries. The immediate effect on the column of mercury in the hæmadynamometer cannot be carefully noted, owing to the violent cries and efforts of the animal, which produce great oscillations in the mercury ; the pressure certainly was not augmented ; and in about a minute, when the struggles of the animal had ceased, the column of mercury was found to have diminished about one inch. Five minutes after the above experiment, a second solution, containing thirty grains of the salt, was introduced into the artery. The phenomena that followed were analogous to those just described, except that the oscillations in the column of mercury were rendered less. When a much

larger quantity of this salt is injected, death appears to follow, owing to its action on the nervous system ; as it appears not to arrive at the heart in a sufficiently concentrated state to arrest its pulsations.

The general symptoms that follow the introduction of this substance into the veins depend, as might be supposed, on the quantities used. A solution, containing eight grains of the salt, when injected into the veins, caused slight dyspnœa ten seconds after its introduction ; in twelve seconds, the animal fell down, as if suddenly paralysed, but soon rose again, and did not appear to suffer any inconvenience. Two minutes after the injection, vomiting took place. After a few minutes, a solution containing fourteen grains was injected ; the animal was evidently affected in ten seconds ; in twelve seconds, it fell on its side ; the legs extended, and appeared totally deprived of all power to move ; the muscles seemed even to have lost their tonicity, as the limbs remained in the position in which they were placed ; there were not the slightest spasms or convulsions, nor did the animal appear to suffer, although perfectly sensible. After lying in this state for ten minutes, the animal got up and walked, but very unsteadily. The action of the heart was arrested on introducing into the veins a solution containing thirty-five grains of the salt ; the heart became paralysed, and the animal fell about twelve seconds after the injection, stretched its legs, and was dead in about thirty seconds,—not more than two or three respiratory movements taking place after the action of the heart had ceased. On opening the thorax, the heart was found in the same state as in the case above related, where this salt was injected into the veins. The presence of this salt in the blood did not interfere with its coagulation. The lungs were rather more scarlet than natural, but their texture was not altered.

Before proceeding to relate the experiments that have been performed with the salts of zinc, I would offer a few remarks on the facts which have been just described. The effect produced by small quantities of the salts of magnesia on the heart, is, as I have stated, to quicken the pulsations of that organ, and also to cause a marked difference in the character of the pulse, as shown by the diminutions of the oscillations of the column of mercury indicating the pressure in the arterial system. This alteration in the character of the pulse may depend on two causes ;—either that the ventricular systole requires a longer time for its completion, the blood being thus forced into the aorta more gradually ;—or it might be due to an increase in the elasticity of the parietes of the arteries. It is to the first of these causes that I am inclined to attribute the phenomenon in question, although the latter may participate in a slight degree in its production. That a longer systole

of the heart is not inconsistent with its quickened pulsation, is evident; for we have only to suppose the period of repose shorter, and we may have the systole much lengthened, whilst the number of the contractions of the organ in a given time are increased.

The Salts of Zinc.—These salts are very closely allied to those of magnesia in their physiological action. When injected into the veins, in fact, the only difference that exists in the action of these two classes of salts is, that those of zinc produce the same effect as those of magnesia, even when exhibited in much smaller doses; the former also acting more powerfully on the nervous system. A solution, containing three grains of sulphate of zinc, when injected into the jugular vein, gave rise to a quickened pulsation of the heart ten seconds after its injection; the oscillations in the column of mercury were also diminished, and the pressure in the arterial system decreased; two minutes after the injection, it being less by a column of mercury equal to two inches; the action of the heart was also slower. Six grains, when injected into the veins, exerted a powerful influence on the heart; the pressure in the arterial system became diminished until it was only equal to a column of mercury of two inches. A solution, containing thirty grains of the salt, arrested the action of the heart eight seconds after it had been introduced into veins. On opening the thorax, the irritability of the heart was found to be more completely destroyed than in the experiments with magnesia.

On injecting a solution of this substance into the arteries, it is found not to exert any influence on the passage of the blood through the systematic capillaries. Sixteen grains introduced through the axillary artery destroyed life by the action it exerted on the nervous system; the heart continued beating for some time after respiratory movements had ceased. In the complete prostration of strength which follows its introduction into the veins, this salt agrees perfectly with the salt of magnesia. This prostration has been noticed by Orfila in his "Traité des Poisons," T. i. p, 576, where he states, that, after the injection of a quantity of this salt into the veins, the animal fell "comme une masse inerte." The sensibility does not seem affected, nor are there any convulsions, the animal lying, according to the expression of the French toxicologist, "dans un etat de calme parfait." The injection of a solution containing six grains of sulphate of zinc into the veins of a dog, weighing about eight pounds, was followed by complete prostration of strength. A solution containing three grains more arrested the action of the heart a few seconds after its introduction into the veins. On opening the thorax, slight movements were still taking place in the ventricles; the blood in the left side of the heart was scarlet; it did not coagulate.* The

* This salt appears to possess the property of dissolving, or at least of preventing

various experiments I have made with this substance would lead me to conclude that it exerts a more marked influence in destroying the irritability of the auricles than of the ventricles. In one case, the ventricles were found contracting rythmically, when the auricles were quite still.

Sulphate of Copper.—This substance, when injected into the veins, exerts a more decided action on the heart, than does the sulphate of zinc. The injection of a solution, containing six grains of the sulphate of copper, gave rise to a quickened and fluttering action of the heart ten seconds after its introduction. This was followed in forty-five seconds by the pulsations of the heart becoming much slower, and a great diminution in the column of mercury, indicating the pressure in the arterial system, which fell full two inches. A solution, containing fifteen grains of the salt, arrested the action of the heart twelve seconds after its introduction into the veins. On opening the thorax, immediately after death, the heart was found motionless, with the exception of slight contractions of the interventricular septum; no movements of the auricles were observed. The right side of the heart contained a considerable quantity of dark blood; the left cavities contained a smaller quantity, which was rather scarlet, but not of so bright a tint as arterial blood; for it appears the sulphate of copper interferes with the change of colour which the blood undergoes in its passage through the lungs, a point in which it differs from the salts of zinc. Injected into the arteries, this salt does not exert any influence on the passage of the blood through the systemic capillaries. Ten grains injected into the axillary artery, produced death by its action on the nervous system, without causing an immediate alteration in the pressure in the arteries.

The general symptoms which follow the introduction of the sulphate of copper into the veins differs from those produced by the salts of magnesia and zinc, by the absence of that complete prostration of muscular power which is so strikingly characteristic of the action of these latter salts. A solution containing three grains of the salt, when injected into the veins, gave rise to efforts to vomit two minutes after its introduction. On injecting a solution containing four grains, into the veins of the same animal, there was dyspnœa produced in fifteen seconds. The animal fell immediately, but continued moving its legs, which were rather

the coagulation of the fibrine of the blood. When blood taken from animals in whose veins this substance has been injected is allowed to stand, a perfectly clear and limpid solution of the fibrine is obtained, the colouring matter being precipitated apparently unaltered. In fact, the sulphate of zinc appears to exert but little influence on the colouring matter of the blood, for when injected into the veins in a sufficiently concentrated state, to completely change the physical character of this fluid, and even of the tissue of the lungs; yet the blood in the left side of the heart is found of a bright scarlet colour.

stiff, although there were no marked spasms or convulsions. After the animal had been lying on its side four minutes, it again rose on its legs, during violent efforts to vomit, but it soon fell down again. The action of the heart was arrested on introducing six grains more into the veins; respiration was suspended in forty-five seconds; the conjunctiva was sensible one minute after the suspension of the respiratory movements. After every respiratory movement had been suspended during two minutes, respiration again commenced, and continued uninterruptedly during a minute and a-half. The animal did not in any degree recover its sensibility, or the power of voluntary motion, during this return of the respiratory movements. In one experiment with this substance, a full respiratory movement took place, on making an incision into the thorax, four minutes after the animal had manifested any sign of sensation, and five minutes after the action of the heart had ceased: this movement was probably reflex; it was not accompanied by any marked irritability of the muscles, which, in fact, did not offer those movements which are generally produced in the muscular fibre, by the contact of air, and the irritation of the scalpel, immediately after death. This absence of irritability in the muscles after death, produced by the injection of sulphate of copper into the veins, as also the absence of irritability in the heart, has been noticed by Orfila. I have also observed that the same effect has been produced on the muscular fibre by the injection of the salts of zinc and magnesia.

The Salts of Lime.—I am not aware that any observations have been published on the action of these salts when introduced into the veins. In their action on the heart they resemble very closely those substances which have been already noticed. When injected into the veins in sufficient quantities, they arrest the action of the heart in from eight to twelve seconds. To produce this effect, a drachm and a-half or two drachms of the chloride of calcium or nitrate of lime are required. When injected in small quantities, the pulsations of the heart are rendered quicker, and the oscillations in the column of mercury are diminished. In their subsequent action on the heart, the salts of lime differ from the salts of magnesia, copper, and zinc, by their tendency to make the action of the heart permanently quicker, the rapidity of the pulsations being increased, until they are introduced in sufficient quantities to paralyse the heart. An examination of the thorax immediately after death discovers the heart more or less deprived of irritability. Sometimes the organ has been found perfectly motionless. The blood in the left cavities is always of a bright scarlet colour. When injected into the arterial system the salts of lime exert no action on the general capillary circulation, the pressure in the arteries not being affected.

On injecting a solution of chloride of calcium through the axillary artery, I have noticed a curious fact, that would tend to prove, that, if there be not regurgitation of blood into the left ventricle during its diastole, there at least cannot be any onward current in the ascending and transverse part of the aorta. The fact to which I allude is, the quickening of the action of the heart four seconds after the introduction of this salt into the axillary arteries, its pulsations being affected in the same manner as when the salt becomes applied to it, after being introduced into the veins; the short interval (only four seconds) elapsing between the injection of the substance into the arteries, and its action on the heart, precludes the idea, that the salt would have been applied to that organ, after traversing the general and pulmonary circulation. The only explanation of the facts that presents itself is, that the injection must have directly reached the origin of the coronary arteries, and was thus applied to the heart. The force with which the injection was pushed would undoubtedly favour this, as the tube inserted into the axillary artery was small; but this would have been readily overcome by any onward movement of the blood in the aorta. I have often observed the same phenomenon when injecting other substances into the axillary artery; but sometimes the heart remains unaffected, until sufficient time has elapsed for the blood containing the substance to go the round of the general and pulmonary circulation.

The general symptoms that follow the introduction of the salts of lime into the veins, differ from those produced by the salts of copper, by the prostration of strength not being so great, and also by the occurrence of spasmodic and convulsive movements. A solution containing six grains of nitrate of lime, merely produced an expression of pain when injected into the veins; the injection of fourteen grains was followed by a spasmodic affection of the diaphragm; this was manifested only during expiration, which was performed by two or three distinct efforts: the same phenomenon has been noticed three times: sometimes the animal appeared to cough two or three times during each expiration. Efforts to vomit are sometimes produced. When a considerable quantity of the salt (from thirty to forty grains) has been injected into the veins, the strength of the animal becomes affected; it either lies down, or walks about very unsteadily; the sensibility does not seem altered. When the salt is introduced into the veins in sufficient quantities to arrest the action of the heart, general spasm is produced in about fourteen seconds. This soon relaxes, and respiration goes on for forty or fifty seconds. The respiratory movements are then suspended, but recommence in about a minute, when eight or ten full inspirations generally take place. A few seconds before respiration ceases, the whole of the muscles of the body are observed to be in motion. These motions appear to be owing to irregular contractions

of the fasciculi of the muscles, not affecting the whole of the muscle at once, for they do not give rise to any general movement. It resembles in fact, a sort of thrill running through the muscles, which is most perceptible in the muscles of the trunk, where it continues some few seconds after respiration has ceased. It will be seen that this phenomenon is much more strongly marked after the injection of the salts of strontia into the veins. In all the experiments I have made with the salts of lime, the lungs have always been found of a bright rosy tint;—in other respects their tissue has appeared unaltered. The colour of the blood in the left cavities of the heart, has always been of a bright scarlet, and very firmly coagulated, the salts of lime evidently favouring the coagulation of the blood.

Strontia.—The salts of strontia, when injected into the veins, destroy the irritability of the heart more readily than the salts of lime. In smaller quantities they render the action of the heart slower, and produce a diminution of pressure in the arterial system, immediately after their injection. After a few seconds, the pressure in the arteries again becomes augmented, and the oscillations in the column of mercury are increased. Ten seconds after the introduction into the veins of a solution containing ten grains of chloride of strontium, the column of mercury in the hæmadynamometer fell one inch and a-half, and appeared to remain stationary for two or three seconds; it then again rose, and fifteen seconds after the injection, it was two inches higher than before the introduction of the salt into the veins. The oscillations in the column were also much increased: before the injection, the systole of the heart only produced an oscillation of an inch in the column of mercury; it now oscillated three inches at each pulsation; the action of the heart was also slower. The introduction of forty grains into the jugular vein, arrested the action of the heart in fifteen seconds. On opening the thorax, both auricles were pulsating regularly; the ventricles were motionless; both the right and left cavities of the heart were full of blood; that in the left side was of a bright scarlet colour. On introducing a solution of chloride of strontium into the arteries, the pressure in the arterial system becomes augmented about four seconds after the introduction of the first portion of the injection. The column of mercury in the hæmadynamometer is rendered about two inches higher, which is sufficient to show, that the passage of the blood through the systemic capillaries is affected. A solution containing thirty-six grains of the salt, arrested the action of the heart twenty seconds after its introduction into the artery. Thirty grains had been previously injected into the arteries of the same animal.

The salts of strontia, when introduced into the blood, appear to act but slightly on the nervous tissue, the action of the heart

being arrested previously to any general symptoms manifesting themselves. Even when injected into the arteries, these salts arrive at the heart in a sufficiently concentrated state to arrest its pulsations, without having given rise to any marked symptoms of their action on the nervous centres. In the experiment above alluded to, in which the heart was arrested by the injection of thirty-six grains into the arteries, the respiration continued uninterruptedly for three minutes after the action of the heart had ceased, and the conjunctiva was still sensible, two minutes after the arrest of the circulation: the animal seemed to suffer a great deal of pain, thirty seconds after the introduction of the salt into the arteries. Ten grains of nitrate of strontia injected into the veins, the animal being at liberty to move about, gave rise to no marked symptom. Sixteen grains of the salt arrested the action of the heart; the animal fell down ten seconds after the introduction of the salt into the veins; there were no convulsions, and the animal remained quite sensible for some time after the heart had stopped. There was expression of pain twenty-five seconds after the injection; the respiration continued for a minute and a-quarter; it then became suspended for a minute, and again commenced, six full inspirations taking place.

But the most interesting phenomenon which is produced by the injection of this salt into the veins, is the continuance of muscular movements after death; these movements last for a quarter of an hour or twenty minutes after death, giving rise to motions of the trunk and limbs. I have observed them to continue for forty minutes in the muscle that had been exposed on opening the thorax, and this, too, with sufficient vigour to move the ribs, although the temperature of the atmosphere was but 42° Fahrenheit. I propose to give a more complete analysis of this phenomenon, when treating of the action of the salts of baryta, which, together with the salts of lead, exert the same action on the muscular fibre.

Baryta.—The salts of baryta are very analogous in their action to those of strontia; in fact, the resemblance that exists between the action of these two classes of salts is quite as marked, if not more so, than that which has been noticed between the salts of magnesia and of zinc. The only difference appears to be, that the salts of baryta are much more poisonous than those of strontia; they are, in fact, the most deleterious substances, as far as regards their action on the heart, that I have experimented with. A solution containing a quarter of a grain of chloride of barium, affected the heart twelve seconds after its introduction into the jugular. The effect on the heart, and on the pressure in the arteries, was precisely the same as that produced by the injection of ten grains of chloride of strontium. On injecting two grains into the veins, the action of the heart was arrested in twelve seconds. On open-

ing the thorax, the state of the heart was the same as in the animal which had been killed by the injection of the chloride of strontium: the auricles were contracting; the ventricles were motionless.

When injected into the arteries, the same effects are produced as when a salt of strontia is used. I shall merely, therefore, refer to the description of the action of this latter salt, without going into any details on the injection of the salts of baryta into the arteries. Their action on the nervous system is so slight, as not to give rise to any marked symptoms. When the heart is paralysed, the animal falls—general spasm comes on, which lasts for a few seconds—respiration is not generally arrested until two minutes after the action of the heart has ceased—the conjunctiva generally retains its sensibility about a minute and a-half after paralysis of the heart—the lungs are found of a bright scarlet colour, but their texture appears unaltered. Neither the salts of strontia or baryta, appear to exert any influence on the coagulation of the blood.

I shall now offer a few observations on one of the most striking phenomenon which follow the introduction of the salts of baryta into the veins. I allude to the continuation of muscular movements after death. I have already noticed this point, when speaking of the action of the salts of strontia; but as this interesting fact has not attracted the attention of previous observers, I have thought it better to give a few details relating to it. In every case in which I have injected the salts of baryta into the veins or arteries, (in all eleven times,) these muscular contractions have been noticed after death. They are never observed to take place with equal force over the whole of the body at the same time, but are always most marked in some particular set of muscles. I have observed them most frequently in the muscles of the thorax and anterior extremity; but I know of no set of muscles in which these movements have not been seen. They do not always take place immediately after death, the animal sometimes remaining quite still for some minutes, after which the muscles may commence contracting. These muscular contractions are sometimes observed at various parts of the body at the same time, or they may be confined almost wholly to one part, or they may affect different parts at different periods. In one instance I have observed them commence a few minutes after death in the muscles attached to the angles of the mouth; from thence they appeared to be propagated to the muscles of the ear, the orbit, and of the side of the face; then to the muscles of the neck, and lastly to those of the thorax and the muscles moving the anterior extremity, in which they did not take place till ten minutes after death. The force with which the muscles contract is sometimes considerable. I have seen the posterior part of the trunk moved by the contractions of

the lumbar muscles, and have on two occasions observed the body pushed away, on furnishing a *point d'appui* to the sole of the foot. This last phenomenon took place ten minutes after the thorax had been opened. The longest period after death at which I have observed these movements take place spontaneously, has been thirty minutes, and this was in the muscles moving the vibricii or whiskers; but in those muscles which had been exposed on opening the thorax, I have seen vivid contractions forty minutes after death, and this when the temperature of the room in which the animal lay was at 42° Fahrenheit. As to the cause of these movements, whether they be owing to an effect produced by the substance on the nervous system, or to its direct contact with the muscles, it would be premature of me to give an opinion. There is one fact, however, which I have observed, which would tend to favour this latter opinion—it is, that when these substances had been injected into the arteries, the contractions are generally most marked in the limb, through the artery of which the injection has been introduced. No other substances that I am aware of, besides the salts of strontia, baryta, and lead, give rise to these movements.*

Lead.—The salts of this metal, in their physiological action, form a link between the salts of strontia and baryta, and those of silver and soda; they agree with the former, in their action on the heart and muscular tissue, and with the latter, by the effects they give rise to in the lungs. When a solution containing three grains of acetate of lead, was injected into the veins, the pressure in the arterial system became diminished in seven seconds; four seconds after this, the column of mercury in the hæmadynamometer regained its former height, and even indicated an increased pressure in the arteries; the action of the heart was rather quickened, and its oscillations less. On injecting a solution containing fourteen grains of the salt, the pressure in the arteries was first diminished, and then became much increased, the column of mercury being from three to four inches higher, about eighteen seconds after the injection; the action of the heart became slower, about two minutes after the injection, and the oscillations at each pulsation of the heart became increased. On injecting a solution containing

* The action of the acetate of lead on the muscles, appears not to have escaped the careful observation of Haller, for I find a passage in Scheele's work—(Ueber die transfusion des Blutes, B. 2, S. 253.) in which he states, when alluding to the experiments performed by Sproegel with this substance, "that the irritability of the other muscles did not appear to have been so completely destroyed as that of the heart, on the irritability of which organ after death, Haller was unable to institute any researches." Unfortunately, I have not been able to find in any of Haller's works the original passage to which Scheele refers. The only other allusion I find to this subject, is in Orfila's work on poisons, where he states, that on opening an animal which had been killed by an injection of chloride of barium into the veins—"les chairs etoient palpitantes."

Experiments that have been performed on birds since this memoir was written, prove that these salts exert the same action on the muscular fibre of this class of animals as they do on that of mammalia.—J. B. April 23.

a drachm of the salt, into the veins, the action of the heart appeared arrested in ten seconds, and the mercury in the instrument fell rapidly. The animal, apparently dead, lay perfectly still a minute and a-half after the injection, and remained so for two minutes; the heart again commenced pulsating, and the pressure in the arterial system was in a few seconds equal to a column of mercury of eight inches; the respiration was also renewed. On injecting another drachm of the salt, (making in the whole three drachms that had been introduced into the veins,) the action of the heart was arrested in ten seconds, but the pulsation of the auricles appeared to have been renewed after about a minute, producing no effect, however, on the pressure in the arterial system, which remained at zero. On opening the thorax, the right auricle was found contracting feebly, but no movements were observed on any other part of the organ; both cavities of the heart contained a great deal of blood; that in the left side was more scarlet than that in the right; but not of that bright colour which arterial blood ought to be. When introduced into the arteries, the acetate of lead is found to influence the passage of the blood through the general capillaries. A solution, containing six grains of the salt, when injected into the axillary artery, produced a sudden increase of pressure in the arterial system; in four seconds, the column of mercury, which, before the injection, was equal to from five to six inches, began rapidly to rise; thirty seconds after the injection, it was up to twelve inches; the respiration was arrested a minute and a-quarter after the injection; yet the pressure in the arteries diminished but slowly. Two minutes after respiration had ceased, the column of mercury was still equal to ten inches; at three minutes, it had fallen to six inches, the contractions of the heart continuing regularly, and producing oscillations of half-an-inch; at five minutes after respiration had ceased, the mercury had sunk to three inches and a-half; and at seven minutes, the pressure in the arteries was only equal to a column of mercury of two inches, the action of the heart being very weak. After having reached this point, it again became increased to six inches, on the animal taking a deep inspiration; the pulsations of the heart were also rendered quicker by this renewed arterialization of the blood. There was but one respiratory movement; and after this, the heart gradually became arrested as in asphyxia.

The general symptoms that this substance produces when introduced into the blood, are owing to two causes, either to its action on the lungs and heart, or on the nervous system; when injected into the veins, it kills by its action on the lungs, or by destroying the irritability of the heart; but when introduced into the arteries, it evidently proves fatal, by its action on the nervous system, with which it is brought into direct contact. Its action on the lungs is shown a few minutes after the introduction of the

salts of lead into the veins, by the escape of a great deal of froth from the mouth ; this froth, having its origin in the air cells, speedily prevents the aeration of the blood, the bronchi and trachea being filled with it, and the animal thus perishes by asphyxia. After death, the lungs present the appearances observed in the first and second stages of pneumonia, their tissue being engorged and hepatized; livid spots were observed on the surface, and the air passages were either impermeable, or filled with a frothy fluid of a whitish colour, but slightly tinged with the colouring matter of the blood.* This secretion is formed in considerable quantities ; for although I have never been able to collect the whole that has been produced, yet I have certainly seen as much as four or five ounces escape at the trachea. In one experiment an animal was suffocated by this secretion, after only three grains of acetate of lead had been introduced into the veins.

The action of this salt on the nervous system is most strikingly shown when it is introduced into the arteries. In an experiment to which I have already alluded, respiration became suspended a minute and a-quarter after the introduction of six grains of acetate of lead into the arteries, (six grains had been previously introduced in divided doses), the animal lay apparently dead, with the exception of occasional movements of the tail during the space of seven minutes ; these movements of the tail were very violent, but were not accompanied by any movements in other parts of the body; at the end of seven minutes, however, the animal gave a deep inspiration, and then lay perfectly lifeless. I have often observed this renewed respiration follow the injection of the acetate of lead into the veins ; but in these cases it took place about two minutes and a-half after respiratory movements had been suspended. When introduced into the veins in sufficient quantity, the acetate of lead arests the action of the heart, by its direct influence on that organ. The quantity required to produce this effect seems to vary in different cases; in the experiment above alluded to, three drachms were injected into the veins, before the action of the heart was stopped, whilst I have in another instance seen the heart lose its irritability, by the introduction of only twelve grains of the salt into the venous system. I would observe, that, in the former experiment, the animal was larger, weighing about twenty pounds ; and also that the salt was dissolved in spring-water, acidulated with a small quantity of acetic acid, distilled water being used in the other experiments. As I have before stated, this salt gives rise to contractions in the muscular fibre after death ; but not in so striking a manner, as do the salts of strontia and baryta. The acetate of lead alters the physical character of the blood, no

* A superficial analysis of this fluid shows that it contains a considerable quantity of albumen, and by incineration lead can be readily detected in it.

perfect coagulation taking place, when it has been injected into the veins.

Silver.—The salts of silver agree with those of lead in their action on the systemic capillaries. They exert a more marked action on the lungs; but do not appear to be so deleterious to the heart. The injection of a solution, containing three grains of nitrate of silver, into the veins, causes at first a diminution, and then an increase in the pressure in the arterial system. After a short time, the pressure in the arteries was again diminished, the blood being no longer aerated, owing to the production of a great quantity of frothy fluid in the air passages. The animal died from asphyxia, about twelve minutes after the introduction of the salt into the veins. On opening the thorax immediately after respiration had ceased, the heart was found pulsating rythmically, and continued contracting for ten minutes. The right auricle was irritable half-an-hour after the thorax had been opened. If the salt is introduced into the veins in larger quantities, the passage of the blood through the lungs is suddenly arrested. On injecting into the veins a solution, containing a drachm of the salt, the column of mercury in the hæmadynamometer began to sink ten seconds after the injection. At thirteen seconds, it was equal to only two inches; nor were any oscillations produced in it, although the heart continued beating strongly. The pressure in the arteries never again rose, no blood being sent into the arterial system, although the heart could be seen to be beating violently, by the movements it produced in the parietes of the thorax. The heart was exposed three minutes after the injection; the left ventricle was still contracting feebly. The right side of the heart was so distended with blood, as to render contraction impossible. The left cavities appeared to have contracted on their contents, as much as the distended state of the right side would allow. There was a small quantity of dark blood in the left ventricle, which was coagulated, though not very firmly, having been evidently slightly affected by the salt, a small portion of which must have found its way to the left side of the heart; on opening the right ventricle, more than seven ounces of dark grumous blood escaped from it, and from the vessels leading to it. I have, on one occasion, seen the action of the heart arrested after this substance had been introduced into the veins. It was, when a solution containing twelve grains of the salt had been used, the jugular veins having been divided immediately after the injection, in order to prevent the brain from being affected, by the great venous congestion that supervenes on the arrest of the passage of the blood through the lungs. By this means, respiratory movements were not immediately arrested, and the blood containing the salt passed into the left side of the heart, and became circulated over its parietes,

giving rise to an arrest of its contractions ; but, even in this case, the ventricles manifested signs of irritability ten minutes after death.

When introduced into the arteries, the salts of silver evidently give rise to a great obstruction in the passage of the blood through the systemic capillaries. A solution containing two grains of the acetate of silver, when introduced into the arterial system, gave rise to an increase of pressure equal to a column of mercury of six inches, two grains more injected into the arteries were sufficient to produce death, giving rise to a pressure equal to fifteen inches of mercury. The heart was stopped by asphyxia about five minutes after the respiration had ceased.

When the salts of silver are injected into the veins, the nervous system appears to be affected solely by the action of these salts on the lungs ; for I have never noticed a symptom which I could attribute to their direct action on the nervous tissue. When the quantity injected is small, the circulation through the lungs is not arrested, but a secretion takes place, which, by obstructing the air-passages, prevents the aeration of the blood, thus indirectly affecting the nervous system. This secretion, however, is not always produced, and yet even then the animal seems to die of asphyxia, owing to extensive changes produced in the tissue of the lungs. When the quantity of the salt is sufficient to arrest the pulmonary circulation, the nervous system becomes violently affected, owing to the congestion which immediately takes place in the veins. In a few seconds, opisthotonos comes on, and the spasm relaxes in a short time by the death of the animal. The effects that follow the introduction of the salts of silver into the arteries closely resemble those produced by the acetate of lead, when injected into these vessels. Respiration was suddenly suspended by the injection of two grains of nitrate of silver into the arteries. This, however, was the second injection ; the respiratory movements were renewed three minutes after they had been suspended, five or six full inspirations taking place. I am inclined to think the symptoms which manifested themselves in this case, as well as those produced by the salts of lead when injected into the arteries, are owing to the great increase of pressure in the arterial system. The influence which the salts of silver exert over the passage of the blood through the lungs, is evidently much greater than that of the salts of lead, for I have never seen the circulation of the blood through these organs totally arrested by any dose of the latter salts.

Soda.—The salts of soda bear a close resemblance in their physiological action to those of silver. In the memoir I read at the Academie des Sciences at Paris, to which I have before alluded, I have related experiments showing the action of these salts when injected into the veins and arteries. As might be expected, the

quantities required to produce the same effects are much greater when the salts of soda are used, than when those of silver are injected. I have nothing to add to what has already been published on this subject, except the following experiment, which I performed at the suggestion of my esteemed friend, Dr Sharpey. It furnishes an additional proof of the correctness of the opinion that I had advanced, as to the cause of the violent nervous symptoms that manifest themselves when the pulmonary circulation is arrested; and it also shows how slight the action of the salts of soda must be on the nervous tissue. The animal was prepared by exposing the two jugular veins. A solution containing three drachms of nitrate of soda was injected into the venous system,—a quantity more than sufficient to arrest the passage of the blood through the lungs. A few seconds after the injection, violent opisthotonos came on. This was instantly relieved by dividing both the jugular veins,—congestion in the brain being thus prevented. The animal lost a great deal of blood, but, notwithstanding this, it survived the experiment two hours. During this time, no nervous symptoms were observed; the respiration continued regular, there were no convulsions, and sensibility was unimpaired; in fact, the animal seemed only to be suffering from loss of blood, the presence of so large a quantity of soda in the blood being apparently in no way injurious, except by the action it exerted on the lungs. At the end of two hours, the animal died asphyxiated, owing to the air-passages becoming filled with a frothy secretion.* Neither the salts of soda or silver exert any marked action on the general muscular tissue. The irritability of the muscles after death appears to be rather increased.

It now remains for me to notice the action of the salts of ammonia and potassa, when injected into the vascular system. The physiological action of these substances, does not allow of their taking a place in that natural arrangement we have hitherto pursued, and by which a substance has always stood in close physiological relation to that which preceded it, and that which followed it. There is undoubtedly a great difference between the action of the salts of magnesia and those of soda, yet have we observed the phenomena which characterize the action of these substances, gradually manifesting themselves, or disappearing; becoming more strongly marked or less perceptible; so that although we find no one phenomenon common to the substances which occupy the extremes of the series, yet we are unable to se-

* It would appear that Orfila has noticed the production of this frothy secretion, both when the salts of lead, and those of silver had been injected into the veins. He, however, seems to have attributed its origin to the stomach, as, he says, the animal vomited some whitish substance, together with a great quantity of frothy fluid.

lect any two substances placed together in the intermediate part of the scale, which, in their physiological action, do not present many striking points of resemblance.

Ammonia.—The salts of ammonia, like most of those substances we have hitherto examined, exert, when injected into the veins, a powerful action on the heart: they differ, however, from the other substances, with which they may agree in this respect, both by their influence on the systemic capillary circulation, and by the general symptoms they give rise to. When a weak solution of the salts of ammonia is injected into the veins, the action of the heart becomes quickened, and the pulse smaller, a few seconds after the injection; the pressure in the arteries soon becomes increased, owing to the passage of the blood through the systemic capillaries being impeded. A solution containing six grains of nitrate of ammonia, caused an increased pressure in the arterial system fifteen seconds after its injection, and at thirty-five seconds, the column of mercury, which, before the injection was from four to six inches, rose to eleven inches:—this pressure soon became reduced, and the action of the heart irregular, great oscillations taking place in the mercury. A solution containing forty grains of the salt, when injected into the jugular vein, caused an augmentation in the pressure in the arterial system, the column of mercury rising as high as fourteen inches a few seconds after the injection. The action of the heart was arrested ten seconds after the introduction into the veins, of a solution, containing two drachms of the salt. On opening the thorax, the auricles were contracting rythmically, the ventricles appeared to have totally lost their irritability; both cavities of the heart were full of blood, that in the left side was scarlet, and firmly coagulated, that in the right was of the ordinary colour of venous blood. The alkali itself in much smaller quantity produces the same effects. A solution containing twenty drops of a saturated solution of ammonia, arrested the action of the heart.

When injected into the arteries, the salts of ammonia caused a great augmentation in the pressure in the arterial system. A solution containing two drachms of the nitrate of ammonia, arrested the action of the heart a minute after it had been injected into the axillary artery, respiratory movements continuing forty-five seconds after the heart had stopped.

The salts of ammonia appear to exert a powerful action on the nervous system, agreeing in this respect much more closely with poisons derived from the organic kingdom, than with any inorganic substances whose action I have yet investigated. Fourteen seconds after the injection into the veins, of a solution containing ten grains of nitrate of ammonia, the animal fell on its side, affected with slight convulsions. After lying on the ground for half-a

minute, it rose, and did not appear to suffer the least from the injection; the introduction of ten grains more into the veins, gave rise to similar symptoms; the animal fell, but was again on its legs thirty seconds after the injection, the action of the salt being apparently due to its contact with the nervous tissue, and passing off as soon as blood which does not contain the salt, becomes again circulated over the nervous centres. Some minutes after the injection, the hind legs appeared to be partially paralysed, and after this had passed off, first one fore leg, and then the other, appeared to suffer in the same manner. Introduced into the veins in larger quantities, these salts appear to deprive the animal of the power of controlling its own movements; the whole body becomes violently convulsed; these convulsions very much resemble those produced by strychnine, and like these, can be called out by the slightest jar or noise; the respiratory movements remain unaffected, and the sensibility appears unimpaired, even in the midst of the strongest convulsions. In two instances, after death produced by the salts of ammonia, I have observed a sort of convulsive movement of the left auricle, which was in violent motion, without, however, causing any regular contraction, the movement seeming to part from many distinct points.*

Potass.—The accounts I have already published of the action of the salts of potass, (see Arch. Gen. de Med. Nov. 1839), will enable me to pass them over, with but a slight notice of their action on the vascular system. In this respect they exactly resemble the salts of ammonia, producing the same action on the general capillaries, and on the heart; both these substances appear also not to exert the least action on the lungs. In their action on the nervous system, there is a marked difference between the salts of potass and those of ammonia,—the violent convulsions which follow the introduction of the latter class of salts into the veins, never being observed when the salts of potass are injected. After the injection of six grains of the bicarbonate of potass into the veins, I have seen the animal fall on its side, the posterior extremities slightly convulsed, and after a few seconds again rise. On introducing an additional quantity of the salt, the heart was arrested, the salts of potass, after those of baryta, being the most fatal to the action of the heart.

Having now related the more important facts that have been observed in my experiments, I shall conclude by offering one or two observations which they appear to suggest.

The most curious fact which a consideration of the above experiments presents to us, is the close connection which appears to exist between the physiological action of these substances and their

* Convulsive movements caused by the injection of hydrochlorate of ammonia into the veins have been noticed by previous observers.

chemical properties. The property to which I more particularly allude is that of isomorphism. The analogy in the physiological action of isomorphous compounds, was first forced on my notice, by the perfect resemblance that exists between the salts of silver and of soda in their action on the animal economy when injected into the veins; differing as these salts do in their sensible chemical properties, but closely connected as being isomorphous. Farther investigation soon proved to me that this fact was of far more importance than I had anticipated, by showing that most striking points of resemblance exist generally beween isomorphous compounds in their action on the animal tissues, when introduced directly into the blood.* In the present state of chemistry, it would be useless to attempt to derive from this fact any farther generalization, for the doctrine of isomorphism itself is still in a very imperfect state.

Before quitting this point, I would recall an observation I made in a memoir read at the Academie des Sciences in June 1839, and which follows as a corollary from the fact of the analogous action of isomorphous compounds, although I had no idea at that time that such was the case. In speaking of the connection between the chemical composition of substances, and their physiological action, I observed—"Ce rapport n'est pas il est vrai tel que l'etat actuel de la science des affinités chimiques nous l'eut fait prevoir, car il est evident, que les decompositions effectuées dans le sang, par ces sels, decompositions sur lesquelles roule toute leur action physiologique, il est evident dis-je, que ces decompositions dependent de la base du sel, et ne sont que peu modifiées par la combinaison de cette base avec les acides, même les plus puissants." Should a more extended series of researches prove, that the identity which I have noticed in the physiological action of isomorphous compounds does not in all cases hold good, yet I think that the facts above related are sufficient to show that there exists some intimate connection between the chemical properties of substances, and their physiological action, the investigation of which promises to furnish a rich field for physiological researches.

* There is apparently an exception to this rule in the salts of lead, which, although agreeing with those of baryta and strontia, in most of the phenomena they present, yet exert an analogous action on the pulmonary tissue with the salts of silver, with which they are not isomorphous, but it has been remarked, that there exists a striking analogy in the combinations which the oxides of these two bases form with organic compounds; an analogy which does not exist between the oxide of silver and any other base. There is also a difference between the action of the salts of potass, and those of ammonia on the nervous tissue; for although these substances exert the same action on the heart and the systemic capillaries, yet the violent nervous symptoms that follow the introduction of the salts of ammonia into the veins are never produced by the salts of potass. The peculiar action of the salts of ammonia on the nervous tissue,—an action which connects it in its physiological relations with organic poisons,—is interesting when we consider the chemical composition of ammonia, standing as it does between organic and inorganic compounds.

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