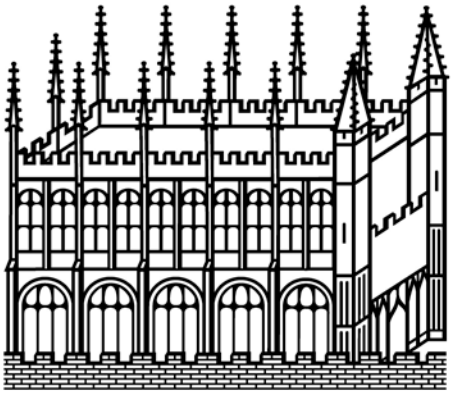

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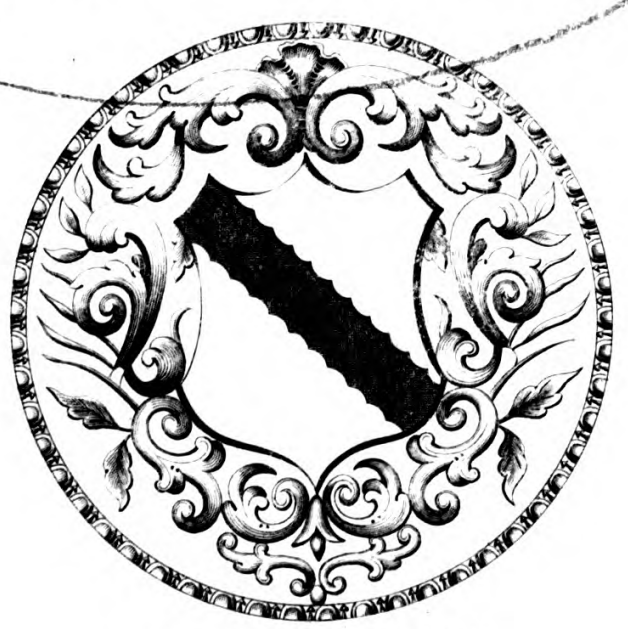

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AN ESSAY

ON

THE OPERATION

OF

POISONOUS AGENTS

UPON

THE LIVING BODY.

BY THOMAS ADDISON, M.D.

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TO

THE MEDICAL AND SURGICAL

STUDENTS

OF

GUY'S HOSPITAL,

FOR WHOSE INSTRUCTION IT WAS PRINCIPALLY INTENDED,

THIS ESSAY IS DEDICATED,

BY

THEIR VERY SINCERE FRIENDS,

THE AUTHORS.

PREFACE.

THE Experiments detailed in this brief Essay were undertaken without any intention of publication. The subject they were intended to elucidate coming within the scope of their duties as public Teachers at Guy's Hospital, the Authors could not but attach to it a lively interest, and were induced to institute the following enquiry, with a view to promote the instruction of their respective Pupils.

The results, however, of their investigations, have otherwise determined them; for they discover, or imagine they discover, in those results, that which is well worthy the attention of the medical philosopher; and which, they are willing to hope, is calculated to throw additional light upon a subject which must ever deeply concern

the physiological, the pathological, and therapeutical Student.

They are not ignorant of the public clamour that has been raised against all experiments on the lower animals, or of the reproaches that have been so gratuitously and indiscriminately levelled at the experimental physiologists both of this country and of France. But whilst they are inclined to disregard the squeamishness of those who have thus included in one sweeping censure all the most celebrated and most zealous cultivators of medical science, they indulge the hope that the more enlightened and more reasonable portion of the community will acquit them of any wish or attempt to practise unnecessary cruelty. They with sincerity declare, that nothing but an ardent desire to advance the cause of their profession, and a well-founded hope of its ultimately tending to diminish the sum of human suffering, could have induced them to institute a mode of investigation so painful to every man of correct feeling.

Whilst they are willing to rest their justification on the tendency and object of their researches, it will, nevertheless, be acceded, by every candid reader, that the Authors of this Essay have been extremely reserved in subjecting the lower creatures even to that degree of suffering inseparable from such experiments. Indeed, they are not without some apprehension, that by the cautious physiologist they may be charged with having been carried too far by this feeling, and with having, consequently, drawn conclusions from too scanty premises. They, however, are not ashamed to avow, that feelings of humanity have prompted them to economise suffering by varying experiments tending to establish the same position, instead of practising a frequent repetition of such as appeared to them reasonably conclusive in themselves. Neither have they, for similar reasons, deemed it necessary to confirm by experiment what seemed to them satisfactorily established by others. Mr. Brodie has shown, that

tying or dividing the lymphatic trunks does not interfere with the operation of poisons on the system; the Authors, therefore, have not considered it expedient to repeat the experiments of that distinguished physiologist, but have confined themselves to the question, whether the absorption of a poison and its subsequent application to the brain are essential to the production of its specific effects upon the body. In conclusion, it may be observed, that if prejudice or preconceived opinion can invalidate testimony, it may probably enhance, in some measure, the confidence of the reader to be told, that, at the commencement of these experiments, the Authors entertained diametrically opposite opinions respecting the question at issue.

To their friend Dr. Hodgkin they take this opportunity of offering their grateful acknowledgments for his valuable assistance in conducting some of the most difficult and delicate experiments.

ON THE

OPERATION OF POISONS

UPON THE

LIVING BODY.

In order to render the object and bearing of the following Essay clear and intelligible, it will be proper to premise some general but concise remarks, as to the nature and influence of those agents usually included under the comprehensive, but very indefinite term of poisons.

By a poison is understood any substance which, taken in a small quantity into the alimentary canal, or introduced into a wound, or even applied to the unbroken and healthy surface of the body, is capable of producing effects deleterious or fatal to animal life. The ideas attached to the

term poison are connected altogether with the extremely minute proportions in which these substances act upon living matter, without regard to the mode in which they produce their effects upon the organs of the body which are essential to health and to life.

Thus every powerful medicine which we make use of may, under this comprehensive but correct definition, be considered as a poisonous agent, which is only rendered beneficial as a remedy for disease, by the diminished quantity in which it is administered, and, consequently, by the diminished influence which it exerts upon the system. For we know that many of the most useful articles in our pharmacopœia will, in comparatively small quantities, produce the most injurious and occasionally fatal effects, when improperly administered; whilst the same obscurity attends our investigations respecting the causes which give rise to the operation of ordinary medicines, — as upon the immediate mode in which the more active specific agents which

are commonly called poisons produce their fatal effects upon animal life.

The distinction, therefore, between our most active and useful medicines and poisons is an arbitrary one; every powerful medicine being, strictly speaking, a poison, when given in sufficient quantity; and most of our poisons being useful and powerful remedies for disease, when administered in regulated quantities. Every substance, then, whether solid, fluid, or aerial, which produces morbid action in the system, is, strictly speaking, a poison: the term, however, is commonly applied to those only of the most active kind.

Now with regard to the immediate impression stamped upon the living powers of the system by poisons, it is a matter which must probably for ever remain involved in impenetrable darkness.

Until we can explain the manner in which a ray of light thrown upon the retina conveys, through the medium of the optic nerve and brain, the sense of vision,

— or the precise mode in which divers causes produce mental emotions, — we shall in vain seek to discover the immediate agency by which a poison produces an influence upon the vital organs of the living body.

This question, therefore, can involve no dispute, for its solution is far beyond the reach of our comprehension.

With respect to the *local* and *visible* consequences which result from the action of poisons, they, on the other hand, are so readily ascertained by experiment and observation, and are so generally known, that they have rarely afforded a reasonable ground either for discussion or controversy. There is still, however, one accessible point connected with the operation of a poison which continues to be disputed, and obscure.

The question alluded to is simply this:—

Through what medium does a poison convey a morbid impression to the system?

Now we know that before any sensible effect can be made upon the general system by the application of a local agent, it is essentially necessary that an impression should be carried to the brain by some intervening medium. It has, therefore, become a point at issue amongst former, as well as modern, physiologists, whether the actual contact of the poison with the brain is necessary for its operation, or whether sympathy between the nerves of the poisoned part and the brain is sufficient to establish a communication through which that organ may become affected.

To bring a poison into actual contact with the brain, it is necessary that the substance should be carried to that organ from the poisoned part through the circulation, either by the medium of the veins, or by the absorbent vessels; — that it should either be conveyed indirectly into the circulating blood, by entering and passing through the absorbents to the subclavian veins; or that it should, on the other hand, directly enter the veins of the poisoned surfaces, and thus be carried im-

mediately into the circulation by passing through those veins into the heart; in which latter case, the poison is said to influence the brain by the medium of venous absorption.

The advocates for the theory of venous absorption, therefore, suppose that every substance which produces a specific action upon the system, must necessarily enter the veins of the poisoned part, either by what they call an imbibition or soaking through of their coats, or by the capillary suctions of their extreme branches; that having thus fairly penetrated the venous tube, the poison is conveyed in the usual course of the circulation to the heart, and thence to the lungs, where, the blood having undergone a chemical change in other respects, returns, still impregnated with poison, to the centre of circulation, the heart, from the cavity of which organ it is sent by the arteries to the brain; and then, but not till then, does the poison meet with a part of the living solids upon which it is capable of producing a specific influence; and that, therefore, actual contact

with the brain by the medium of venous absorption is essentially necessary for the production of those consequences which result from the application of poisons to any part of the living body.

On the other hand, those who support the theory of nervous communication between the poisoned part and the brain, assert, that the constitutional disturbance arising from the application of a local agent, is adequately accounted for by the connexion or sympathy naturally existing between the extremities of the injured or poisoned nerves, and the sensorium.

This is, perhaps, one of the most important questions to which a physiologist can direct his attention: it is not confined to the phenomena produced by the action of poisons, — to the operation of arsenic upon the stomach, — to the effects of opium upon the brain, — nor to the deadly consequences which result from the wounds inflicted by venomous reptiles; but it involves a theory which has reference to

every morbid action that takes place in a living animal, from the operation of local irritation upon the functions of the brain and nervous system: for whether constitutional disturbance shall be produced by the imperceptible operation of noxious miasmata, or whether it shall arise from a visible and local cause, as in the inoculation of small-pox, syphilis, or hydrophobia, still we find no distinct line of demarcation separating the essential characters of what is strictly called a poison, from those produced by more general and more ordinary causes of disease.

No distinction can be made in reference to the interval which elapses between the application of the cause and the developement of the effect; for no distinction can be established which has reference to the periods that shall elapse between the application of a poison or of an ordinary cause of disease, and the appearance of the effects produced by them on the brain, as we find in both cases an endless variety in this respect. The poison of Prussic acid, applied to the mouth or nose, will destroy

life in a few seconds. The contagion of the plague has been known to produce death in a few minutes; for, during the time at which this pestilence was raging at Marseilles, it is recorded, that the men who were employed by the merchants to carry the infected goods from the ship to the warehouses, fell down and suddenly expired, from the first impression made upon the system by effluvia arising from the burdens which they were carrying.

The poison of hydrophobia is usually from two to three months before it affects the system; but an ordinary cause of disease has been nearly as long a time in producing constitutional disturbance; for individuals have been exposed to the effluvia of marsh miasmata, and after that exposure more than six weeks have elapsed before the constitution has manifested any consequent sympathetic derangement.

We do not mean to deny that some poisons will operate upon the system more quickly, and others more slowly, than any

known and ordinary cause of disease; for this fact is fully established by the instantaneous effect of hydrocyanic acid, and by the lengthened period (nearly a twelvemonth) which has been known to elapse between the inoculation of the poison of hydrophobia, and the developement of its sensible effect upon the body; but we contend, that these exceptions do not affect the correctness of the analogy, which indisputably exists relative to the period of time which may elapse before a poison, or an ordinary cause of disease, shall affect the system.

But analogy may be carried still farther.

Without regarding analogy as to *time*, let us look for analogy in reference to *effect;* and here, again, we find a perfect similarity between the sensible consequences of poisons, and those of other morbific agents.

We have only to mark with attention the symptoms of tetanus, and compare them with those which result from the

action of the poison of nux vomica, and the most perfect resemblance will be found to exist between the two; yet the symptoms of tetanus are produced by an ordinary cause of disease; and the symptoms which indicate the operation of nux vomica upon the system are produced by what is usually called a specific agent, or, in other words, by a poison.

In both cases, however, we find the same spasmodic contractions of the voluntary muscles, increased at intervals by paroxysms; and in both cases the morbid action commences at the same point, viz. in the muscles of the lower jaw. More of this hereafter.

A still more remarkable instance may be adduced to illustrate the similarity of effects arising from an injury from mechanical violence, from an ordinary cause of disease, and from the inoculation of a poison. We allude to those effects which are produced by gunshot wounds, by exposure to the contagion of fever, and by the poisoned wound of a venomous reptile.

It is well known to military men, that a slight and superficial wound, received on the field of battle from a musket-ball, is occasionally followed by a very extraordinary and alarming train of symptoms. An injury of this kind occurring to persons whose courage is undoubted, and in whose mind no apprehension has existed respecting the consequences of the wound,—it has been found that, to the brave as well as to the coward, a trifling injury of this nature is now and then followed by the most serious indications of constitutional disturbance; that immediately a deadly paleness appears, — that respiration becomes laborious, — extreme prostration of strength is produced, — that the pulse becomes feeble, irregular, and depressed, — and that these alarming symptoms, have, in some instances, ended in the death of the individual. Here, then, we have a total and rapid destruction of life from the trivial local injury of a superficial contused wound; and death is evidently produced by depression of the vital powers of the nervous system, from sympathy with the injured part.

Let us compare these with the effects produced by an ordinary cause of disease — plague for example — and we find in the aggravated forms of this disease, that the first impression made upon the system is precisely the same in many respects; for it sometimes happens that before reaction takes place, the system sinks at once, overpowered by the shock it has received from the influence of the pestilential effluvia.

We find that the same prostration of strength, and the same depression of energy in the vital organs of the system, will indicate that the constitution is by these two different causes affected in a nearly similar manner.

Compare with these again the constitutional disturbance produced by the bite of the rattle-snake, — and we shall find that the poisoned wound inflicted by this reptile will produce destruction of life in nearly the same way; for before any local suffering shall occur, the powers of life will be depressed by the action of the poison, and before reaction can take place, those powers

will be annihilated by the first overwhelming impression made upon the brain and nervous system.

Analogy, therefore, as regards *effect*, can be perfectly established between the consequences of a local injury, those which are produced by the poisoned wound of the more venomous reptiles, and those which arise from the influence of an ordinary cause of disease. Therefore the analogy between poisons and other agents capable of exciting morbid action in the system is complete, as well as it regards their sensible effects, as in reference to the interval of time which may elapse between the application of their causes, and the developement of their effects.

Theory founded upon hypothesis may perhaps oppose this assertion; but reasoning deduced from facts will be found, we believe, to confirm the truth of the parallel.

All fair analogy forbids the conclusion, that a poison or an ordinary cause of disease shall at one time produce constitutional disturbance through the medium of one system of organs, and at another time

through the medium of another system of organs: that, under certain circumstances, a poison or any other cause of disease shall affect the functions of the brain and nervous system, at one time through the medium of the nerves, at another time by the circulation, and at another by the action of the absorbent vessels: that at one time a poison shall be taken up by the veins, and carried through the circulation to the brain, before it produces any sensible effect: that at another time the absorbent vessels shall take up the substance, and, by their communication with the subclavian veins, be thus instrumental in carrying the specific agent into the circulation, and thence to the brain: and that again at another time the impression made upon the extremities of the nerves of the poisoned part shall at once, by the medium of those poisoned nerves, be conveyed to the brain, independently of absorption either by the veins or absorbent vessels. It is contrary to all fair analogy to suppose that any variety observed in the *effect* of a local agent can

essentially depend upon the medium by which it is carried into the system.

As reasonably might it be presumed that at one time the sense of taste was communicated by a branch of the fifth pair of nerves, and at another time by the salivary ducts, as to entertain a belief that veins, absorbents, and nerves individually performed a function of precisely a similar nature.

On the contrary, every organ in the living system is destined to perform its proper functions, and, as far as our physiological researches have yet extended, we are justified in assuming that no two organs in the human body are capable of performing the same function, neither can two functions be performed by the same organ.

It will not, for instance, be said that the sympathy between the brain and stomach is conveyed along the eighth pair of nerves at one time, and by the circulating system at another: that when vomiting occurs as a consequence of concussion of the brain, it is occasioned by nervous sympathy; and that when morbid sensibility of the brain is

produced by derangement in the digestive organs, that morbid sympathy is the result of absorption: that there are two roads between these two organs, by which sympathy is established; the one leading from the head to the stomach, and the other from the stomach to the head.

Since, then, the various phenomena resulting from the effects of poisons upon the system are too intimately connected with those produced by other causes of morbid excitement to admit of any distinct line of separation; since we are led by analogy to believe, that the medium by which an impression is made upon the brain and nervous system is the same in both cases, it must be manifest that the question, which has arisen amongst physiologists in every age, respecting the medium through which poisons influence the general system, is one that has reference also to the mode in which all morbid phenomena are produced in the living system; and, therefore, it involves a theory of the highest importance to the

physiologist, to the physician, and to the surgeon; a theory, indeed, intimately and inseparably connected with every branch of science which has for its object the elucidation of those phenomena produced by local agents of every description upon the living body.

It is unnecessary to dwell upon the opinions and experiments of the earlier physiologists with regard to the medium through which poisons produce their effects upon the body: their opinions were hypothetical, and their experiments were instituted principally with a view to explain the visible and sensible effects of these substances. And although we find in the works of Fontana and others, and in the later productions of Orfila, much valuable information respecting the morbid appearances which indicate the effects of different poisons, yet the most interesting question relating to the medium by which those effects are produced, is left as they found it, involved in doubt and obscurity.

Physiologists, however, both abroad and in this country, have of late years paid very great attention to this subject; and by the publication of their experiments, and the ingenuity of their reasoning, have endeavoured to establish a theory which would associate the operation of almost every poison with the process of venous absorption.

There are some poisons, however, that destroy life too quickly to admit of this explanation; and these were by our former, and are by the common consent of our present physiologists, supposed to operate immediately upon the nerves. It is, nevertheless, generally believed, that, with a few such exceptions, the medium by which a communication between a poisoned part and the brain is established, consists in the process of absorption; and that until the substance of the poison is brought into contact with the brain by the course of circulation, no specific effect will be produced in the system. Popular opinion, therefore, and modern publications, favour the theory of venous absorption.

In the Philosophical Transactions of the Royal Society we find an account of certain experiments instituted by Mr. Brodie, for the purpose of ascertaining on which of the vital organs a poison exerts its primary influence, and through what medium that organ becomes affected.

The experiments, and the inferences which have been drawn from them, are as follow : —

In the first experiment, the essential oil of bitter almonds was applied to the tongue of a cat, in consequence of which the life of the animal was instantly destroyed.

The second experiment consisted in the injection of the same poison into the rectum of another animal of the same species, by which death was occasioned in two minutes.

In neither case were any morbid appearances found on dissection.

From these experiments a conclusion has been drawn, that the poison acted upon the brain by the medium of the nerves, and for the following reasons; viz. that as the tongue is more plentifully supplied with nerves than the mucous coat of the intestine, a poison which produced a first impression upon the nerves would operate more powerfully and quickly when applied to the tongue than when injected into the rectum; whilst, on the other hand, as the inner coat of an intestine affords a more extended surface for absorption than the membrane covering the tongue, it is supposed that a poison which produced an impression upon the system by venous absorption would operate more forcibly and quickly when thrown into the gut than when applied to the mouth. Now as the poison applied to the tongue destroyed life more speedily than when administered in the form of an enema, a conclusion has been drawn by Mr. Brodie, that the brain was in both cases affected by the medium of the nerves.

Whether Mr. Brodie's theory be true respecting the intermediate mode by which, in the foregoing experiments, an impression was conveyed to the sensorium, — whether the essential oil of almonds produces its specific effect upon the system through the medium of the nerves, or by the medium of other organs,—is a question which we shall leave for the present. But we must protest against the train of reasoning by which the theory of nervous communication has, in this instance, been supported; for in support of that theory it is assumed, that the susceptibility of any part of the human body to a morbid impression may be correctly estimated by a dissection of its nerves, and that in proportion to the greater size and number of those nerves will be the rapidity with which such morbid impression is conveyed to the brain. We must also dispute the assumption, that the extreme irritability of the nerves of the tongue, under one proper cause of excitement, is to be considered as a proof of their increased excitability to action under the impression of a morbid agent.

Each assumption appears to us to be equally untenable, and to involve a theory respecting the multiplied functions of a single nerve, which is not only unsupported by analogical reasoning, but which is in many instances directly contradicted by fact.

Analogy teaches us, that to each fibril of a nerve a separate office is assigned; for we have not a single instance to prove that any one nervous filament in the living system is capable of essentially performing a double function.

It may be objected to this assertion, that the sciatic nerve is an organ by which the sense of touch is conveyed from the skin to the brain on the one hand, and by which the action of the voluntary muscles is excited by a communication from the brain to the extreme branches on the other; whilst it is also true, that by dividing the trunk of the nerve, the sense of feeling, and the power of voluntary motion, are suspended in that part of the limb to which the branches of the nerve are distributed: but it must be recollected, that a single nerve is not divided

in this case; for we have every reason to believe, that each filament which is distributed to a muscular fibre is separately given off from the medulla spinalis, and that those branches which terminate upon the skin are as distinct in their origin and course as in their distribution; and it will be found, that every nerve which apparently performs a double function is composed of a double order of fibres, each of which is destined to perform its proper and separate office.

By the functions of a nerve we of course mean the functions performed by its extreme branches, as unconnected with the effect produced upon the brain by a local stimulus applied to its main trunk; for it is well known that the *trunk* of a nerve may, under the action of very different stimuli, convey a similar impression to the brain, the effect of which is recognised under the general term of *sensation*, whilst its *extreme terminations* only receive and convey to the sensorium those peculiar impressions, for the production of which the organ was first called into existence; and, as it is proved

that the same stimulus applied to the extremities of a nerve, which is highly susceptible of its influence, and which consequently produces an immediate and powerful effect upon the system, may be applied without producing any sensible effect upon the extreme branches of another nerve, which, from the operation of a different exciting cause, may evince an equal degree of excitability ; — as, in short, it has been shown that the functions of a nerve cannot be determined by its comparative sensibility, we are at a loss to conjecture what has induced Mr. Brodie to support an opinion, in which he is neither borne out by fair reasoning nor by sound analogy ; whilst, to prove that he is directly contradicted by fact, the following experiment was instituted : —

The spinal marrow of a half-grown rabbit was divided ; the leg was inoculated with strong Prussic acid : the animal died in three minutes after the introduction of the poison, this being the usual period of time in which that poison was found to

operate upon these animals under common circumstances when introduced into the same part.

Now, if the impression produced upon the brain by the application of Prussic acid to a distant part be the consequence of its action upon nerves of sensation and voluntary motion, as has been supposed to be the case by Mr. Brodie in his experiment, we should be happy to receive from the advocates of that gentleman's theory a satisfactory explanation of the result of the experiment just related.

If, on the other hand, the impression of the poison be carried to the brain by other organs, we, for the present, leave the advocates of venous absorption and infiltration to account for its instantaneous effect upon the system when applied to the mouth, and shall in the mean time proceed with Mr. Brodie in his experiments.

The effect produced upon the system by the juice of aconite thrown into an intestine is made the next subject of that gen-

tleman's enquiries; and he finds, that the functions of the brain are destroyed before those of the heart; and as confirmatory of the opinion that this poison acts upon the sensorium through the medium of the nerves, Mr. Brodie mentions, that *numbness of the lips and gums is produced for two or three hours* after chewing the leaf of *aconite.* We entirely agree with Mr. Brodie in the deduction which he has drawn from the last-mentioned fact; and as we shall have occasion to employ the same mode of argument in refutation of a theory which is afterwards advanced by that gentleman, we beg our readers to bear in mind the admission, that the partial paralysis produced upon the gums by the local application of a poison is a proof of that poison acting upon the brain through the medium of the nerves.

After detailing some other experiments, made for the purpose of ascertaining on which of the vital organs the poison of tobacco exerts its primary influence, &c. Mr. Brodie proceeds to enquire into the

effects produced by the application of poisons to a wounded surface, and starts the following question: —

How do poisons inserted into wounds act upon the brain?

1. By means of nerves, *like poisons taken internally?*

2. By passing through the absorbent vessels?

3. By passing directly through the divided veins?

To set this question at rest, the following experiments were made by Mr. Brodie: —

The thoracic duct being tied, the leg of the animal is inoculated with ticunas, and it is found that the poison produces its fatal effect in the usual time. It may fairly be concluded, therefore, that the poison did not, in this case, act upon the system through the medium of the absorbent vessels.

The axillary plexus of a rabbit is next divided, and the same poison is inserted into the limb, which produces death after the usual period of time.

Mr. Brodie concludes, that in this experiment he had deprived the limb of nervous communication with the body, and therefore presumes, that the poison acted upon the brain by entering the circulation through the divided veins.

As a further proof of the correctness of his views upon this subject, we are informed, that a tape half an inch wide was tied round the thigh of a rabbit, excluding the sciatic nerve, and that although the leg was wounded and poisoned with ticunas, yet no sensible effect was produced at the end of an hour from the operation : after this interval of time had elapsed, the ligature was removed, and in twenty minutes the animal was found motionless and insensible.

From this experiment Mr. Brodie concludes, that there can be little doubt that this poison affects the brain by passing into

the circulation through the divided vessels. Mr. Brodie further considers it probable, that the poison does not produce its effects until it enters the substance of the brain along with the blood in which it is dissolved; and from analogy infers, that other poisons may affect the system in a similar way.

In drawing this conclusion, Mr. Brodie again assumes, that the nerves of sensation and volition are the organs by which, in the case of nervous communication, a morbid impression is carried into the system. If Mr. Brodie had reversed his experiment, he would have been at once convinced that his theory was, according to his own hypothesis, founded in error; for if, instead of applying the poison of woorara to a limb, around which (excluding the principal nerve) a tight ligature had been applied; if, instead of using that poison, he had applied Prussic acid under similar circumstances, he would have met with nearly the same result. To prove this fact we made the following experiment: —

Four drops of Prussic acid were applied to the wounded foot of a full-grown rabbit, by which death was produced in two minutes and a half.

In another rabbit of the same age a ligature was tied round the leg, to the careful exclusion of the sciatic nerve; six drops of the same poison were then applied to a wound in the foot of the strangulated limb, and without producing the slightest sensible effect.

Mr. Brodie is satisfied that the poison of Prussic acid acts upon the brain by the medium of nervous communication; it is manifest, however, from the foregoing experiment, that, according to the view which he has taken of the subject, the same argument by which the theory of venous absorption is supported in reference to the poison of woorara, holds equally good in this case as applied to the poison of Prussic acid.

Either, therefore (according to Mr. Brodie's train of reasoning), we have a direct

proof that Prussic acid does not act upon the brain by the medium of the nerves, or we must consider his theory respecting the venous absorption of other poisons to be entirely unsupported by the result of the experiment upon which that theory was principally founded; for, according to the position which Mr. Brodie has taken, the application of Prussic acid to the strangulated limb ought to have produced its usual effect upon the system; whilst the division of the spinal marrow, according to his views of the subject, ought to have precluded the possibility of any nervous communication between the brain and any part of the lower extremity to which that poison had been applied; yet, in both cases, we find that such a supposition is directly opposed to the evidence of fact.

Whether, therefore, the poison of woorara affects the system through the medium of nerves, or whether it be carried to the brain by the circulation, is a question which cannot be satisfactorily settled by the experiment which Mr. Brodie has in-

stituted, for the purpose of settling that disputed point, since the explanation he has given of their results is directly contradicted by the other experiments mentioned.

That the kind of venous absorption for which Mr. Brodie has contended can, under any circumstances, take place in a living animal, appears to us to be extremely problematical, if not physically impossible; we mean an absorption into the venous circulation through the mouth of a divided vessel. When a vein is divided, it is well known, that unless some branch be interposed between the truncated extremity and the next valve in its course towards the heart, unless the current of blood be driven through the cut extremity of the tube by collateral branches, we find that the sides of the vessel as far as the next valvular interruption will collapse and remain inactive: supposing the poison, then, to enter this flaccid tube, it is completely prevented from mixing with the circulating blood which fills the vessel above the valve by the

pressure made by that circulating blood upon the opposite side of the valve, and, consequently, under such circumstances, unless it can be proved that a poison has the property of propelling itself, it requires no argument to prove that the substance, instead of passing into the circulation, will remain stationary in that part of the vessel through which no circulation is carried on. If, on the other hand, circulation be carried on by collateral branches through that part of the tube which lies between the nearest valve and the mouth of the divided vein, the effect will be still more unfavourable to Mr. Brodie's hypothesis; for the circulation in that part of the vessel will be reversed, and, consequently, instead of being carried towards the heart, the poison will be washed out of the wound: in either case, therefore, it seems highly improbable that the poison can pass through the circulation to the brain by the medium of a divided vein. We do not dispute that foreign substances may be taken into the system by means of absorption; but we very much question the *possibility*

of that absorption taking place, as Mr. Brodie has supposed it does, through the truncated extremity of a divided vessel.

If the term *divided* had, in reference to this subject, occurred but once in the publication to which we allude, we should have concluded that the printer had committed a typographical error; but the word is too frequently used to admit of this explanation.

With regard to the general theory of venous absorption, as supported by Mr. Brodie's experiment of applying a ligature to a limb which has been poisoned, we have to observe, that the experiment will admit of a different explanation from that with which he has furnished us; for since it is proved that the nerves of sensation and volition are not necessarily concerned in carrying to the brain the impression of a certain poison, which he admits must affect the system by nervous communication with the sensorium; since it is therefore obvious that other nerves, performing different

functions, must be concerned in the operation of that poison upon the brain; since we have proved that a ligature placed around a limb, to the exclusion of the sciatic nerve, in the manner above stated, produces the double effect of paralysing the nerves upon which one poison operates, as well as of stopping the circulation through the part, it may be fairly inferred, that if the other poison should happen to act upon the brain by the medium of the same set of nerves, the operation of that poison during the period of strangulation would be suspended from a similar cause, and that, consequently, this experiment relative to the absorption of woorara is quite inconclusive as supporting the truth of either theory.

Having now endeavoured to show that the theory of nervous communication, as well as that of venous absorption, as applied to the operation of specific agents upon the system, have been both supported by Mr. Brodie, either upon untenable assumptions, on the one hand, or by un-

satisfactory experiments on the other, we shall for the present refrain from entering further into an analysis of that part of his paper which relates to the modus operandi of poisons, and proceed to notice the opinions of another toxicological philosopher, Professor Magendie.

This celebrated physiologist has long been known to the scientific world as a strenuous supporter of that theory which supposes actual circulation of a poison through the blood-vessels as essentially necessary to its operation upon the system; and, to establish the truth of this theory, we have been furnished with a detailed account of numerous experiments which would at first sight appear confirmatory of the correctness of that gentleman's opinions upon this subject; and if his theory had related solely to the *possibility* of a poison entering the circulation, and producing, in that way, an impression upon the brain and nervous system, no possible objection could have been offered to the proof which his experiments would have furnished; but

when we find that the object of the learned Professor's experiments, relative to the operation of poisons, has been to establish the fact, that the admixture of *all poisons* with the blood, which circulates through the veins of the poisoned part, is *absolutely* necessary to their operation on the body; when we find the following experiment adduced as a proof of the correctness of the view which M. Magendie has taken of this subject, we feel called upon to urge, in the strongest possible manner, our objections both to the theory and to the slender foundation upon which it has been supported.

Let our unprejudiced readers judge for themselves. The experiment was as follows: —

A dog having, from motives of humanity, been stupified by a dose of opium, was, during the action of the narcotic upon the system, made the subject of the following operation.

The femoral artery and vein of the animal having been divided on one side, the continuity of the canals was re-established by the intervening connecting medium of small cylinders of quill, to which the truncated extremities of the vessels were attached, and through which quills, consequently, the blood passed in the usual course of the circulation. With the exception of the femoral artery and vein thus divided and reconnected by quills, the limb was then amputated from the body, so that in this case the separated member was deprived of all nervous connection with the body at the same time that circulation was allowed to continue through its main vessels.

The poison of upas was then applied to a wound in the severed limb, which produced its effects upon the system after the lapse of the interval of time usual under common circumstances.

By compressing the vein, and thus obstructing the circulation of blood from the

poisoned part to the body, the symptoms indicating the action of the poison upon the system ceased, and returned immediately upon the removal of this mechanical obstruction to the circulation through the limb; so that the experiment appeared conclusive respecting the absolute necessity for venous absorption, as the medium of conveying an impression from a poisoned part to the brain.

To us, however, the following objections offer themselves: —

In the first place, as regards the experiment itself, we have to observe, that unless the canine race in France differs in some extraordinary manner from that which inhabits other parts of the known world, and unless the chemical discoveries of M. Magendie or his countrymen have produced some preparation of opium, of which the peculiar properties are unknown in this country, we must contend that the preliminary steps to the operation were calculated to render all further investigations

upon the body of the animal altogether useless; for we are borne out by well-known and established facts in asserting, that when a sufficient quantity of opium is thrown into the stomach of a dog to make a sensible impression upon the organs of voluntary motion, and to produce from that cause those indications of disturbance in the functions of the brain and nervous system which are known by the general term of stupefaction; when, in short, the animal has been stupified by opium, we find that this effect of the powerful operation of the poison upon the system will interfere so materially with the action of any other specific agent as to render it altogether impossible in many cases to determine, by external evidence, whether, in the event of a fatal termination, the animal has been destroyed by opium or by the other poison (upas, for instance), or by the combined action of the two. We are told, however, that this compound application of poisons was intended solely to diminish the sufferings of the animal which was the subject of the experiment. Without en-

tering, however, into M. Magendie's motives respecting the performance of the operation of double poisoning, to which we have to offer our objections, and without calling in question that gentleman's professions of humanity, we shall proceed to notice the subsequent steps of the operation: these consisting, as we have before said, in the application of a poison to a limb deprived of all nervous connection with the trunk, whilst the circulation in that limb was naturally performed, and the consequent death of the remaining three quarters of the animal. If the result of this experiment had been adduced in proof only of the possibility of the actual entrance of a poison into the veins, we should have been the last to offer our objections to the conclusions which others could have drawn from it; but when we find that the necessity for the contact of that poison with the brain, as a cause of its operation upon the system, is considered as equally established by that experiment, we have to express our dissent *in toto* from the opinions of those who have drawn such a conclusion, and for the following reasons:—In the first

place, it will be admitted, that the blood which circulated from the poisoned limb, through the femoral vein, must have brought the poison with which it was mixed into contact with the inner coats of the veins of the body, in the course of circulation through those veins towards the heart, and that, consequently, a highly irritable and widely-extended surface of membrane was exposed to the action of that poison long before it could have reached the brain. The inner coats of veins, of the heart, and of arteries, were, therefore, prior to the possible contact of the poison with the brain, placed in precisely the same condition, as regards their exposure to the action of that poison, as the cellular tissue of a superficial wound made in any part of the body, for we cannot suppose that *divided* vessels can take up a poison, for reasons already stated; and, consequently, the *undivided* and *uninjured* capillaries must, in the case of *venous absorption*, be considered as the agents by which that poison is conveyed into the circulation, whether that absorption be supposed to take place from the inner coat

of the veins, or from an exposed surface of cellular membrane: whilst, in the instance of *nervous* communication, we must conclude that the impression of a poison is only received and conveyed by the *uninjured* extremities of nerves; for divided or truncated nerves are incapable of performing their proper functions, or, in other words, are incapable of conveying either natural or morbid impressions in the same manner as their sound extremities are found to do. A wound, therefore, presents a more favourable condition of parts for the action of poison than the unbroken skin, simply because it exposes beneath that skin the naked or less protected sentient extremities of nerves; for although, undoubtedly, in every wound, many of the extremities both of nerves and veins are lacerated, yet it must of necessity happen, that many will remain entire although exposed. It is then to this exposure, either of nervous or venous extremities, under such circumstances, that the more prompt action of a poison is to be ascribed, and not to any division or truncation of either nerves or

blood-vessels; such truncated nerves and vessels being alike incapable of performing their natural and proper functions; and hence the sentient extremities of the nerves, as well as the capillary vessels of the inner coat of the vein above the amputated limb, were, in M. Magendie's experiment, as much exposed to the action of the circulating poison as the nerves and capillaries of those structures upon which a poison acts when inserted into a wound in any other part of the body.

If, instead of acting upon the inner coat of a vein, or upon any other highly susceptible surface, in the first instance, a poison be necessarily conveyed to the brain by venous absorption before a sensible effect is produced upon the body, we ought to have met with a different result from the experiment under consideration; for, as the rapidity of the operation of the poison used upon this occasion is, under common circumstances, found to be greatly increased by an increase in the quantity applied to any part of the body,

we must attribute the circumstance to the larger supply of poison with which the vessels are furnished, and, consequently, to the increased quantity which comes into contact with the brain. Now when a ligature is applied around the femoral vein of any animal, and the lower extremity of that animal on the same side is inoculated with upas, we know, that under such circumstances the poison will exert its ordinary influence upon the system; we consequently are led to conclude, if the poison be in such a case carried into contact with the brain, through the veins of the limb, that there must be other vessels sufficiently active and numerous to effect this purpose, without any absolute necessity for a continued circulation through the main trunk of the principal vessel.

Knowing from this circumstance, then, how large a quantity of the poison in M. Magendie's experiment must have been lodged in those veins of the amputated limb which were deprived of their connection with the body, we should have expected

that the length of time which elapsed, in this case, between the inoculation of the poison and the developement of its sensible effect upon the system, would, in some measure, have varied from that which is known to occur under ordinary circumstances.

If, indeed, we had been assured that increased vascular action had been set up in the amputated member, there would have been no difficulty in accounting for the rapid action of the poison upon the theory of the cerebral contact. But we know that circulation, under such circumstances, is necessarily retarded, and that, consequently, the activity of the capillaries is diminished: thus, according to the views of the supporters of the theory of cerebral contact, a poison which, inserted into the sound limb of an animal, would produce the death of that animal in four minutes, ought to have been considerably longer in destroying life when applied to the limb of a similar animal after that limb had been deprived to some extent of its naturally circulating connec-

tion with the body: the reverse of this, however, occurs as a consequence of M. Magendie's experiment; for, in the instance of his experiment no difference in time is observed to indicate the effect of the operation upon the action of the poison.

The objection which thus offers itself to the conclusions of M. Magendie and his followers respecting the difference in time, which (however trifling) ought, according to their own showing, to have accorded with the altered condition of the limb, this objection will not apply to the theory of nervous communication, and for the following reasons: —that, as the nerves of the interior coats of veins are supposed by the supporters of that theory to receive the first impression from a poison which circulates through the cavity of the vessel, and as these nerves are proved by daily observation to possess a high degree of morbid susceptibility; as, moreover, it has been proved by M. Magendie's experiment, according to his *own* showing, that the poison must necessarily pass through

the largest veins in the body in its course through the circulation, it may reasonably be inferred, that any difference in time, which ought, according to the other theory, to have occurred between inoculation and effect, is prevented by the unimpaired functions of those nerves which supply the inner coats of the veins above the amputated limb, as these nerves must, of course, convey, in the usual time, the impression which the circulating poison produces upon their extremities; and as the poison is manifestly brought through the severed limb to the trunk before it can possibly affect the system, it must still remain a point at issue, whether the brain itself, or the nerves of the vein, receive its first impression.

Instead, therefore, of proving the cerebral contact of the poison, we must contend that this celebrated experiment goes no farther than to prove the actual entrance of a poison into the veins.

We must also strongly protest against the assumption that, because a poison has

been found to enter and pass through a vein, it is thence to be inferred that such a process is, under all circumstances, absolutely necessary to its operation.

In the observations which we have now made upon M. Magendie's experiment, it will be seen that we are not opposed to the theory of venous absorption, but to that theory which would associate with it the *absolute necessity* for the admission of a poison into a vein, and the consequent circulation of that poison through the brain, as a cause, and a sole cause, of its effects upon the body.

We contend, then, that M. Magendie has left the question relative to the necessity for venous absorption and cerebral contact, as connected with the operation of poisonous agents, in precisely the same state as he found it. Having, therefore, suggested the probability of a different mode of communication to that which he is anxious to establish between a poisoned part and the sensorium; having also offered our objec-

tions to the fairness of his experiments, and to the soundness of his arguments, we next proceed to notice a more recent publication upon the same subject, from the pen of our ingenious and zealous countryman, Dr. Barry.

The work in question is principally intended to demonstrate the influence of atmospheric pressure upon the circulation of the blood, and of the circulation of the blood upon the action of poisons.

The following description of experiments, instituted by the author and his friends, will make our readers acquainted with his views upon the subject: we begin and continue our extract from page 118.

"Introduction of four grains of Upas tieuté into the thigh of a small dog. The piston and cupping-glass were applied at the same time to a similar wound, on the corresponding part of the opposite thigh. Symptoms of poisoning at the end of eight minutes: these soon acquired such a de-

gree of intensity, that the animal was upon the very point of expiring.

"In this state of extreme suffering, the cupping-glass was removed to the poisoned wound, and the vacuum established. Instantly the symptoms were alleviated. The animal was truly recalled to life; but from time to time he still suffered slight attacks of tetanus. After a quarter of an hour's application, the glass was removed, and the animal appeared restored to health." *

After this account of the performance of the experiment † by Dr. Barry, we are

* *This animal was found dead some hours after the glass had been removed.*

† This experiment appears to us to have been conducted in a somewhat singular manner; or perhaps we ought rather to say, that its description is somewhat imperfect and obscure: for we are informed that after "the introduction of a poison into one thigh of a dog, the cupping-glass was applied to a *similar wound* on the corresponding part of the opposite limb." That this similar wound was *not* poisoned, we may infer from the subsequent description of the operation, from which we learn that after a time the cupping-glass was removed from the *similar wound* to the *poisoned wound*, by which proceeding the symptoms were instantly alleviated. Now it is

furnished with the following remarks by his friend, M. Andral: —

" In this case, the cupping-glass appears to have moderated the symptoms, by arresting all further absorption of the poison; but that which was already in the circulation does not seem to have been recalled to the surface of the wound, because the symptoms continued, although mitigated; unless we choose to suppose that the continuation of the convulsions was owing to the impression already made upon the nervous system. On the other hand, the animal economy does not rid itself of deleterious substances so promptly as is generally thought."

Fifteenth experiment. — With a view to observe whether the cupping-glass acted

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clear from this account that the wound to which the exhausted cupping-glass was, in the first instance, applied, was a simple division of animal matter into which no poison had been introduced: for what purpose, therefore, a vacuum was formed over that part we are at a loss to determine.

by bringing back to the surface any portion of a substance introduced into the cellular tissue by injection, we injected into the subcutaneous tissue of the inside of the thigh of a dog, about two drachms of a saturated solution of the *sulphate of soda.* The wound was carefully wiped, and the glass applied. After working the piston a few times, we found the salt, by means of a proper test, in the reddish liquid which the pressure of the air had forced into the glass."

By this, and by many other experiments of the same kind, Dr. Barry considers that he has *established* one important point in physiology, and *confirmed* another. That he has established the fact, that the circulation through the extreme branches of a vein is kept up by atmospherical pressure upon the surface of the body; and that he has confirmed the formerly disputed point relative to the absolute necessity for venous absorption, as a means of communication between a poisoned surface and the brain.

Respecting the question of venous circulation, as connected with the influence of atmospheric pressure upon the body, we have no present occasion to offer our opinions.

But, with respect to the other point, namely, the confirmation of the theory of venous absorption, and cerebral contact, as established by Dr. Barry's experiments, we beg to offer a few observations.

It will, we think, be admitted by every one, that the soft structures of the surface of the body, which are covered by an exhausted cupping-glass, must necessarily, from the pressure of the edges of that glass, be deprived for a time of all connection, either nervous or vascular, with the surrounding parts. That the nerves mustbe partially or altogether paralysed by compression of their trunks, and that, from the same cause, all circulation through the veins and arteries situated within the area of the glass must cease; this, however, is not the only change which is produced in

a part by the mode in which Dr. Barry has, in his experiments, removed from it the pressure of the atmosphere; for, not contented with merely stopping the circulation, we are informed that the rarification of the air within the glass was still further increased by means of a small air-pump attached to it, so that the fluids contained in the divided extremities of the vessels were forced into the vacuum, and with these fluids, of course, either a part or the whole of the poison which had been introduced.

In such a condition of parts, it will be manifest that the compression on the one hand, and the removal of the poison from the wound on the other, will explain in a very satisfactory manner the result of the experiment, as well to the advocate for nervous communication, as to the supporter of the theory of venous absorption. For if the extreme branches of the nerves of a wounded part be paralysed by the pressure of a cupping-glass, of course no sympathy can be established between those nerves and the brain. Or, if the poison be

entirely removed from its contact with the nerves by the formation of a vacuum over the wound, we may reasonably suppose that the cause of irritation being no longer in operation, the effect will be no longer apparent; and, consequently, whether the impression made upon the system be the effect of the actual contact of that poison with the brain by the medium of venous absorption, or whether it be produced by nervous sympathy, we may in either case expect from Dr. Barry's experiments precisely the same result as he has described to us.

The effects produced by the alternate application and removal of his cupping-glasses to a poisoned wound, in alternately suspending and reproducing the sensible effects of the poison upon the system, may be attributed either to the operation of his apparatus upon the vascular or the nervous systems. We consider, therefore, that in reference to the question respecting the intermediate mode by which a poison produces its effect upon the body, Dr. Barry has proved nothing new; for he has only

shown that an exhausted cupping-glass will suspend the ordinary functions of those organs over which it forms a partial vacuum; and that, consequently, its application to a poisoned wound will suspend the action of the poisonous substance upon the system.

As we have no good reasons for disputing the position which Dr. Barry has thus established, neither have we any further occasion to notice either the grounds upon which it is founded on the reasoning by which it is supported.

On reference to the recent publications of Mayo and others, we find merely a restatement of the opinions of those to whose works we have adverted, founded upon the same, or upon analogous experiments to those we have already detailed.

As it is therefore unnecessary to notice them separately, we may now conclude our preliminary observations upon the opinions of former toxicological writers.

THE OPINIONS OF THE AUTHORS UPON THE SUBJECT OF POISONS.

HITHERTO we have refrained from declaring any decided opinion whatever as to the *modus operandi* of poisonous agents on the living body; but having assumed it to be unphilosophical to admit a two-fold operation — to admit that such agents may at one time act upon the general system, through the medium of the sentient extremities of nerves, and at another time by the direct application of the poison to the brain, through the medium of the blood; and having attempted to show the fallacy of those experiments upon which the notion of a two-fold operation of poisons has been founded,—we must now venture to acknowledge an attempt to establish the truth of a theory, which we conceive to be supported as well by the experiments of our prede-

cessors, as by those which we have ourselves instituted upon the lower classes of living animals.

The conclusion at which we have arrived is simply this : —

" *That all poisonous agents produce their specific effects upon the brain and general system through the sentient extremities of nerves, and through the sentient extremities of nerves only; and that when introduced into the current of the circulation in any way, their effects result from the impression made upon the sensible structure of the blood-vessels, and not from their direct application to the brain itself.*"

In endeavouring to establish the truth of this our theory respecting the *modus operandi* of *all* poisonous agents, we cannot be insensible to the powerful array of authority which is opposed to us, nor to the influence which that authority has probably exerted upon the minds of all our readers ; we feel, therefore, that we have to contend with

the prejudices as well as with the arguments of our opponents.

Brodie, Magendie, and Barry all appear to be quite satisfied, that in many instances the venous absorption and direct application of a poison to the brain are absolutely necessary to its operation upon the general system; although they are compelled to admit that some poisons act at once through the sentient extremities of nerves. Dr. Barry, however, has particularly laboured to show in how short a time a poison may reach the heart through the medium of venous absorption; a circumstance calculated, if not really intended, to cast a shade of doubt upon the operation of poisons through the nerves in any case.

Now that the humoral pathologists, who ascribed all diseases to a morbid condition of the fluids of the body, and who imagined that all noxious agents producing, and all salutary agents remedying, disease, acted exclusively upon these fluids, that such philosophers should have denied any other

mode of operation upon living matter, it is easy to understand; but that physiologists, since the time of Hoffman, should, with Fontana at their head, have found such extreme reluctance and difficulty in admitting the nervous medium of operation, is not so readily accounted for. The phenomena of sensation and perception, one would have thought, might have taught them that the natural functions of the nerves countenanced a belief in the direct operation of noxious agents upon their sentient extremities. They must have known, that when an impression is made upon any of the external organs of sense, that impression is instantly communicated to the sensorium altogether independently of any thing like absorption; the sentient extremities of the nerves distributed to the individual organ naturally performing the office of conveying the impression to the brain; neither could they have been ignorant that divers active agents exert a direct influence upon the nerves of the part to which they are immediately applied. We see this exemplified in the effects of an application

of opium to a pained part; we see it in the effects of belladonna upon the iris, when rubbed upon the eye-brow, or applied to the surface of the tunica conjunctiva: and it has already been admitted by one of our opponents, that a partial paralysis of the lips and gums is produced by the application of the juice of aconite to the parts. But a still more striking example of the immediate action of a poison upon the part to which it is applied, was afforded during one of our experiments upon a dying Guinea-pig, by the accidental contact of a very minute portion of ticunas with the still living intestine. In this case, the consequence was a complete and instantaneous suspension of peristaltic motion in that part of the bowel to which the poison was immediately applied: and in repeating the application of the poison to other parts of the intestinal canal in the same animal, we found that precisely the same local paralysis was produced.

But if the theory of nervous communication be countenanced by the facts just

enumerated, it is still more strikingly confirmed by certain phenomena, observed to take place in disease. A person receives a slight lacerated wound, a burn, a puncture from a spicula of wood, or a rusty nail; the irritating cause being removed from the part, all shall appear to be going on well, when suddenly symptoms of tetanus supervene, and proceed to the destruction of life: here we have, then, the mere irritation of the nerves of a small portion of the body, so deranging and involving the entire nervous system, as to give rise to one of the most formidable of all diseases, and this, so far as we know, without the slightest evidence of any absorption of morbid matter into the current of the circulation, and with just as little evidence of any thing noxious being directly applied to the brain. If, then, mere irritation, mechanical or otherwise, prove sufficient to derange the whole nervous system in this instance, where, we would ask, is the difficulty of conceiving that morbid irritation, and consequent general derangement, in the system, should result from the application of

a poison, altogether independently of any absorption whatever?

It may, indeed, be said, that admitting the probability, the results of experiments are opposed to the conclusion as an universal principle. This we cannot for a moment admit. We have already pointed out the general fallacy of many of these experiments; and, perhaps, it may now be proper to show, that they are highly objectionable, and altogether insufficient in reference to the question immediately before us. In the first place, it will be recollected, that to disprove the action of a poison upon the system through the nerves, we have been furnished with the account of a certain operation, in which a ligature passed beneath the sciatic nerve was, to the exclusion of the trunk of that nerve, drawn sufficiently tight to produce complete strangulation, and, consequently, total suspension of circulation in the limb below; and because an application of the poison of woorara to a wound in this strangled limb is found to produce no sensible effect

upon the system, we are expected to believe that this poison does not in any case act upon the brain by the medium of a nervous communication; upon the assumption, of course, that if it act through the medium of the nerves at all, it must of necessity act through the medium of the nerves of sensation and volition, or those nerves derived from the medulla spinalis, and not by any possibility through the medium of any other system of nerves.

It will be recollected, that the experiments already detailed in these pages are sufficient to prove, that the projectors of this sweeping conclusion are, according to their own showing, decidedly in error; for if they were correct, the division of the spinal marrow ought, in every instance, to prevent the operation of those poisons, which, according to their own admission, act through a nervous medium; poisons, which produce their effects in too rapid and instantaneous a manner to admit for a moment of the supposition, that their absorption and application to the brain

are necessary: but we know that this is not the case, such poisons producing their effects as certainly and quickly after the spinal marrow has been divided, as in those cases in which that structure is allowed to remain perfect.

This fact we have already established, in an experiment detailed in page 25. of the present essay; in which, after the division of the spinal marrow, the application of Prussic acid to the wounded leg of the rabbit produced the usual effect of that poison upon the brain in the usual time. But, independently of these experiments, even supposing that the woorara did act upon the system through the medium of the nerves of sensation and volition, is it to be supposed that the sciatic nerve could, in the absence of all circulation, perform its functions? Yet, when the ligature was bound tight round the limb, such must have been the condition of that nerve; it must have been placed in a state, such as entirely to unfit it for the performance of its functions, either healthy or

morbid; and, therefore, the experiment must be considered, we think, by every one who reasons fairly and impartially, to be altogether inconclusive.

We have already endeavoured to prove the fallacy of other opposing experiments: we have shown that the pressure of a cupping-glass would act precisely in the same manner as a ligature, and thereby prevent the nerves of the part from conveying either morbid or healthy impressions to the sensorium; we have shown, also, that the vaunted experiment of M. Magendie, even admitting it to have been complete, only proves that certain poisons can and do enter the circulation; whereas, if they do, we contend, that under such circumstances they affect the system at large, not by being carried to the brain by the blood, but by their direct operation upon the internal membrane of the blood-vessels into which they enter, and through which they are carried.

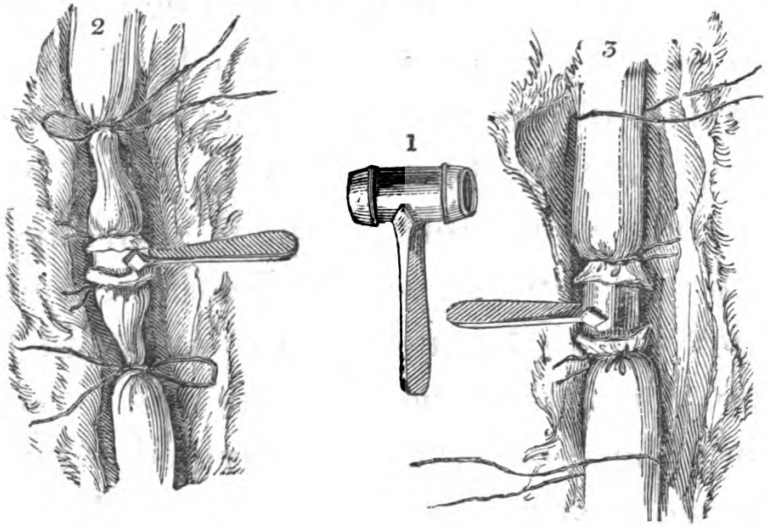
To prove the extreme susceptibility of the inner coat of a vein, when exposed to

the action of a poison, the following experiments were made: —

The jugular vein of a full-grown dog (in size about that of a common harrier) was laid bare to the extent of about two inches; the circulation through the denuded vessel was then completely stopped by the application of two temporary ligatures, one of which was tied round the upper, and the other round the lower, part of the exposed vein; the vessel was then divided between the two ligatures, and the truncated extremities reconnected by means of a short brass cylinder or tube, Plate I. fig. 1., within which was placed a portion of woorara, of the size of a grain of canary seed. In this way the continuity of the canal between the temporary ligatures was preserved entire, the brass tube being inserted and tied within the mouths of the cut extremities, fig. 2., and, consequently, allowing, on the previous impediment to circulation being removed, a free passage of blood from the upper to the lower part of the vein; with which blood, of course, the poison in

the interior of the tube would instantly be mixed, and carried through the circulation.

PLATE I.



Both the temporary ligatures being then removed, fig. 3., the accustomed circulation through the vessel was re-established; and in forty-five seconds the animal dropped on the ground, completely deprived of all power over the muscles of voluntary motion; in two minutes convulsions and respiration had entirely ceased.

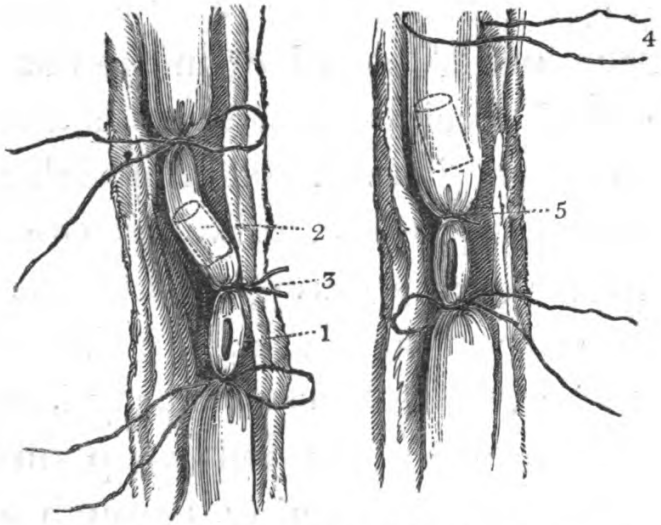
We were perfectly aware, in making this experiment, that the result might be adduced in proof of the truth of the theory of the cerebral contact, as well as of nervous communication of a poison; it was,

therefore, merely made for the purpose of affording a contrast to the following: —

The jugular vein of a dog, of the same size and age with the preceding (both being from the same litter), was exposed, and separated from its surrounding connection, to the extent of three inches; temporary ligatures were then applied, as in the former case. A small opening was then made in the vein, immediately above the lower ligature, Plate II. fig. 1., through which a cylinder of quill, fig. 2., was pushed into the interior of the vessel; within this quill a piece of woorara, of the same size as that used before, had been previously inserted. The vein was now again tied by a permanent ligature above the opening, through which the quill had been thrust, fig. 3., leaving a space of two inches and three quarters between the first upper temporary ligature and the permanent one last mentioned; the interior of the vessel between the two containing the poison which was thus prevented from coming in contact with the sides of the vessel, until washed by blood

out of the quill in which it was contained. The upper temporary ligature was next removed, fig. 4., so as to allow the blood to pass down into the lower part of the vessel as far as the lower permanent ligature, fig. 5., and, consequently, to that part of the vein which contained the poison.

PLATE II.



Now it must be manifest, that the solution of the poison in the blood, under such circumstances, could only act upon the system through the vessels or nerves of the *vein;* for the direct entrance of the poisoned blood into the heart, &c. was prevented by the lower ligature, and we, consequently, ought to have found, in the case of venous absorption, the effect nearly

the same as that which would have occurred from the introduction of the poison to any other part of the body, in which a capillary absorption, and, consequently, a greater length of time, was necessary to its operation; for it will be remembered, that circulation was no longer going on through the trunk of the jugular vein itself.

It was found, however, on the contrary, that in the space of 108 seconds after the removal of the ligature the animal dropped in convulsions, as in the former case, and expired in three minutes and a quarter.

The poison which was used in these two cases has never been known in dogs to produce a sensible effect upon the system, in cases of its insertion into superficial wounds of the body, in less than six minutes, and respiration usually has ceased in from a quarter of an hour to twenty-five minutes.

Now, if we suppose that the poison of woorara produces its effect upon the sys-

tem through the medium of the nerves, we can easily reconcile with that supposition the results of our two experiments: for we may attribute, in that case, the rapid operation of the poison in the last experiment, as compared with its effects upon a superficial wound of the body, to its contact with the acutely susceptible extremities of nerves distributed to the inner coat of the jugular vein itself; and we may also account for the *extreme* rapidity of its action in the first experiment, by its contact with the more extended and equally susceptible surfaces to which it must have been necessarily applied in the course of its direct circulation through the vena cava, the heart and arteries.

To prove that the almost immediate effect of a poison, when circulating through a blood-vessel, is rather to be attributed to its operation upon the sensible structure of the vessel itself than to its conveyance by such means to the brain, we made the following experiments: —

The carotid artery of a middle-sized fox-hound was exposed to the extent of two inches; temporary ligatures were tied round the vessel, as in a former operation upon the jugular vein, vide page 70.; the artery was also divided between them, and reconnected in a similar manner by means of the brass tube, which was charged with the same quantity of the woorara as in the experiment alluded to. The temporary ligatures being removed, the circulation through the vessel must of course have carried the poison from the brass tube instantly to the brain; and we ought, therefore, in the case of venous absorption and cerebral contact, to have produced the instant death of the animal from that cause. It was found, however, that the time which elapsed between the removal of the temporary ligatures and the fatal effects of the poison upon the body, was nearly the same in this as in the former case of its introduction into the jugular vein, for the animal dropped in forty-five seconds, and ceased to respire in two minutes.

The experiment was repeated upon the carotid of a smaller dog, and sixty-eight seconds elapsed before any sensible effect was produced, and in three minutes respiration had ceased.

The femoral artery of a very large and strong bull-dog was then made the subject of a similar operation, viz. the same poison was introduced by the same means, with the view of ascertaining whether any and what difference in the time of operation might be produced by its circulation through a vessel more distant from the heart and brain. In the case of nervous communication, we of course could expect but little variation in symptoms from those produced by the introduction of the poison into the carotid; but in the case of cerebral contact, we, for obvious reasons, might suppose a longer time to elapse between the time of its direct entrance into the circulation and its passage to the head. We found, however, nearly as we expected, that the animal dropped in convulsion in forty seconds after the temporary ligatures

had been removed from the vessel, and that respiration had ceased in less than two minutes: the poison thus producing its effect, in this particular case, even more quickly than when sent directly to the brain through the carotid. The poison used in the five preceding experiments was then applied to a wound in the back of another dog: in six minutes the animal exhibited the effects of its operation, and in sixteen minutes respiration had ceased.

The results of these experiments appear to us completely opposed to the theory which would attribute the action of a poison upon the system solely to its contact with the substance of the brain. They are further strengthened by the following: in which it will be seen, that the mere application of a poisonous agent to the wounded substance of the organ is unattended by those immediate and fatal effects which might be expected by the advocates of the theory alluded to. A portion of woorara, the size of a millet seed, was applied to a wound on the back of a full-grown rabbit:

in four minutes the animal fell paralysed on its side, in which state it remained for the space of three quarters of an hour, when the effect of the poison subsiding, the animal eventually and gradually recovered.

The brain of another rabbit of the same age and condition was then laid bare, and a small portion of the cerebrum sliced off horizontally: in the surface thus exposed, a portion of woorara, of the same size as that used in the experiment on the first rabbit, was inserted, the greatest care being taken to prevent its contact with any part except the brain itself. After the interval of three quarters of an hour had elapsed from the time of the inoculation, the animal was, from motives of humanity, destroyed; but during the whole of that time not the slightest symptom of the effect of the poison upon the system was observed. The animal under excitement leaping about the room as usual.

It may be objected to this experiment, that the divided surfaces of a wounded

brain are incapable of performing healthy functions: this we admit, but at the same time we must contend, that the poison, which was soon dissolved in the moisture of the brain, must have penetrated to a part which, being undivided and uninjured, was still capable of performing its proper offices; and that we ought at all events to have observed some effect from the inoculation, if the theory of cerebral contact had been founded in truth.

Now, whether or not the poison does ever circulate with the blood through the brain, is a question which we do not think it worth while to dispute. We contend, that such is not the cause of its operation upon the system. And whether or not a poison does in all cases enter the circulation, is not the point at issue; for we have contended, that if they do find their way into the veins, they affect the brain and general system by their direct operation upon the nerves of the inner coat of the blood-vessel, and from that cause only.

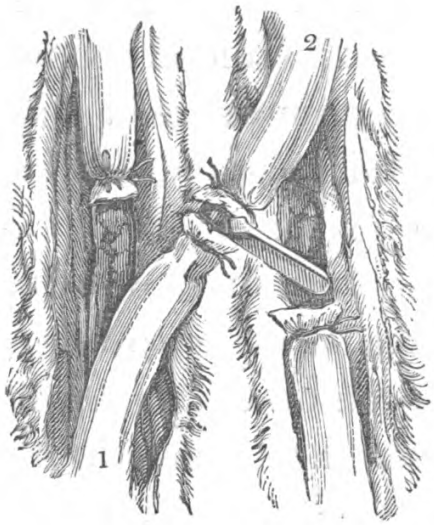
To prove or disprove this position constitutes the grand difficulty, which has at all times baffled the attempts of physiological experimentalists. The nervous and vascular systems are so dependent upon, and so inseparable from, each other, that in performing experiments upon animals, in order to decide the question, each theorist has, in explaining the results, selected that system which most accorded with his peculiar bias. It, therefore, appeared to us a matter of extreme importance to surmount this difficulty, by conducting our experiments, in reference to this question, in such a manner as to avoid the source of ambiguity to which we have alluded. We saw plainly that this was not to be accomplished by any experiment made upon a single animal, as it was utterly impossible to separate nervous and vascular tissue; but it occurred to us, that if we could form a communication between the circulating systems of two animals at once, and maintain a free circulation between them, that we might, per-

haps be able to solve the difficulty and the grand question at once: for if after this communication was freely established, poison introduced into one animal did not affect the other, a reasonable inference might be drawn, that the circulating fluid was not the medium through which the poison operated upon the general system, inasmuch as the blood being poisoned, ought, to a certain degree at least, to affect both. Accordingly, the following experiments were made:—

Two large bull-dogs, of equal size and strength, were held face to face upon a table, embracing each other; so that their breasts and necks were in contact, the animals being placed upon their sides. In this position, it will be seen that the right carotid of one dog and the left of the other were uppermost, and that these vessels, when exposed by operation, might, while the animals were thus held together, be brought into contact. It was therefore our object to establish a connection and a circulation between these two arteries, viz. between the right carotid of one dog, Plate III. fig. 1., and the left of the

other, fig. 2. This was easily accomplished in the manner represented by the accompanying engraving; in which the division and re-connection of the vessels are shown too clearly to need any further description of the operation itself.

PLATE III.



In this way, then, we established a circulation of blood from the heart of one dog to the head of the other; and it was therefore reasonable to suppose, according to the theory of the supporters of venous absorption and cerebral contact, that the dog contributing blood to the other, would, after inoculation with a poison, be supplying his neighbour with poisoned blood, which reaching the substance of the brain, must

necessarily produce the same effects in the one as in the other. This, however, was not the case; for upon introducing the poison of nux vomica into the back of the animal, from whose carotid the blood was passing to the opposite vessel of the other dog, we found that although the usual violent effect was produced in the inoculated animal, and although that effect continued for the space of fourteen minutes, during which period a free circulation was carried on between them in the manner already mentioned, yet that not the slightest indications of the action of the poison upon the system could be observed in the other dog.

Satisfied that the experiment had been continued long enough, the artery was then tied in the neck of the sound dog, the vessel was divided, and the sufferings of the other and expiring animal were terminated. On the following day the surviving dog continued free from all symptoms of poisoning.

It can hardly be supposed in this case, that if the poison had been dissolved in the

blood which circulated through the carotid of the poisoned dog, no portion of it would have reached the brain of the other, since it was repeatedly seen during the operation that a free current constantly passed through the vessels from one animal to the other; indeed if such had not been the case, it must be manifest that coagula would have formed in them, as well as in the brass tube by which they were connected. In the case, therefore, of sanguineous contamination and cerebral contact, we think it fair to infer that both animals ought to have been affected by the poison in nearly the same way, and at the same time, the opposite of which was proved to be the case.

This experiment having satisfied us that the circulation of a poison through the brain was not the cause of its operation upon the body, we next proceeded to ascertain, by a nearly similar mode, whether in all cases the contamination of the blood in the veins, which supplied a poisoned part, was necessary to the operation of the poison upon the system.

Two large hounds were secured neck to neck, as in the former case, and the division and re-connection of the jugular veins effected in a manner precisely similar to that already described in the case of the double circulation through the carotid, so that the venous blood from the head of one dog passed into the heart of the other. The animal contributing blood to the other was then inoculated on the side of the face with nux vomica, and in the usual time exhibited the usual symptoms: these continued without intermission during the space of seven minutes after the animal was first affected, the circulation being freely kept up through the artificially-connected jugulars: at the end of this period the circulation was beginning to become impeded by the formation of a small coagulum in the tube, and we therefore terminated the experiment by destroying the poisoned animal, the other dog never having shown the slightest symptoms of being poisoned. Now, if in this case the poison had been taken by the veins in a sufficient quantity to affect the distant tex-

tures to which it was carried in its course through the circulation, we do not think it possible that either dog could have escaped; at all events, if either had escaped, it would have been the poisoned animal, whose veins were prevented carrying contaminated blood from the part through the system by their connection with those of another.

Having, in the foregoing experiment, encountered considerable difficulty in forming a connection between the cut ends of the two different arteries by means of the single intervening brass tube already described, (page 70. Pl. 1. fig. 1) we have since constructed a different instrument for the purpose, consisting of two short brass cylindrical tubes, (Pl. IV. fig. 1. and 2.) to each of which a long handle is attached (fig. 3.): one end of each tube is furnished with a shoulder to prevent the ligature, by which it is tied to the vessel, from slipping off (fig. 4.), whilst by the opposite ends (fig. 5. and 6.), they are so fitted, one within the other, as to form, when thus connected, one single continuous tube. The advantage

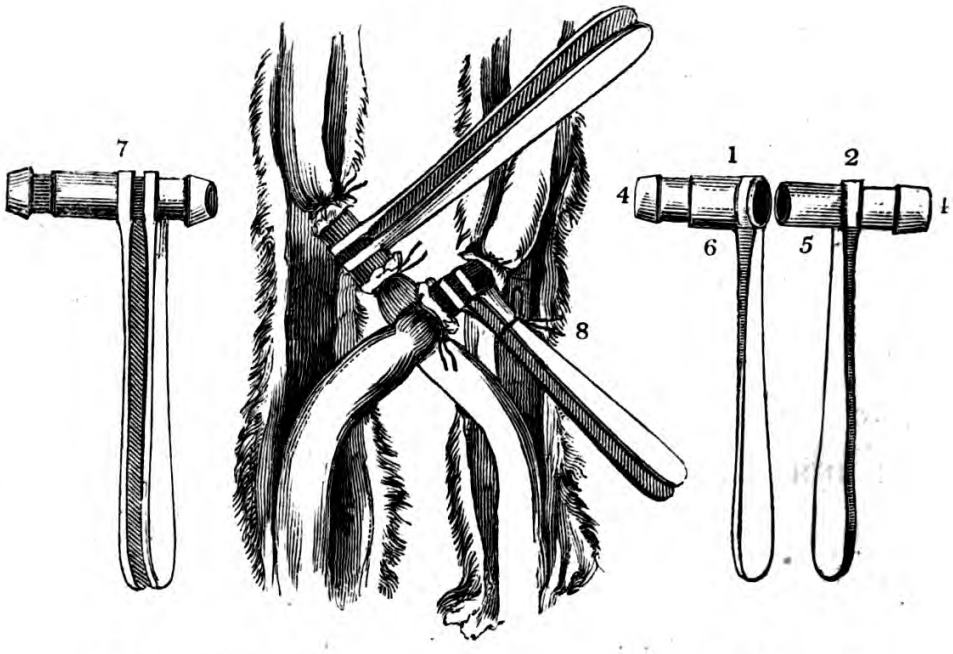
of this instrument consists in the very great facility which it affords in the re-connection of divided vessels, the truncated extremities of which are, from their elasticity, with difficulty brought together and properly adjusted, by means of a single tube in such experiments as those which we have just mentioned. It will be seen, however, that when one end of each tube is tied within the mouth of a divided artery, the continuity of the canal is easily re-established by the junction of those tubes in the centre, as already described (fig. 7.).

By the aid of this double tube we were enabled in a subsequent experiment to establish a *complete* double circulation between the carotids of a poisoned and of a sound dog, by connecting the lower and upper ends of the divided arteries in both animals, so that each supplied the brain of the other with that portion of blood which had before passed through the carotid artery to his own, and, consequently, the poisoned dog in this case received from the unpoisoned animal a supply of arterial

blood equal in quantity to that with which he was parting.

The mode of forming this connection of the two vessels, is shown by the following cut, which will render any further explanation of the instrument unnecessary. The handles are tied together (fig. 8.), to prevent the separation of the tubes.

PLATE IV.



The experiment was conducted in the following manner: —

Two large half-bred bull dogs, each weighing about forty pounds, were the animals selected for the operation. The

carotid artery of each dog having been laid bare on one side, and separated from its connections with surrounding parts to the extent of three inches, temporary ligatures were applied above and below, and the arteries were divided between them, as in a former case; the brass tubes were then attached to the extremities of the vessels, and the necks of the two animals being held and closely bound together, the divided arteries were, without the least difficulty, re-connected, and the circulation reversed, as shown by the foregoing figure.

One of the dogs was then inoculated on the back with a concentrated preparation of strychnine, which had been found upon other occasions to produce death in these animals in about three minutes and a half.

In three minutes and a half the inoculated animal exhibited the usual tetanic symptoms which result from the action of this poison, and died in a little less than four minutes afterwards, viz. about seven minutes from the time at which the poison

was inserted, during the whole of which time a free and mutual interchange of blood between the two was clearly indicated by the strong pulsation of the denuded vessels throughout their whole course.

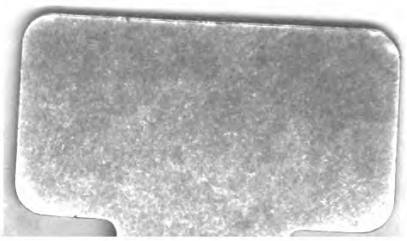
The arteries were next secured by ligature, and the living was separated from the dead animal; but neither during the operation, nor at any subsequent period *, did the survivor show the slightest symptom of the action of the poison upon the system.

From these, then, and from many other similar experiments, which it would be needless to instance, we have been led to the conclusion that all poisons, and, perhaps, indeed, all agents influence the brain and general system, through an impression made upon the sentient extremities of the nerves, and not by absorption and direct application to the brain.

* This animal was killed on the following day.

So far as we are competent to judge, the conclusion is borne out by the experiments detailed in this Essay; but if those experiments be not satisfactory to our readers, we at least indulge the hope, that what has been advanced may lead to the discovery of more satisfactory and more conclusive evidence than has yet been adduced on this truly important question; a question, indeed, of the deepest interest, not as a mere matter of curiosity, but as involving the elucidation of many of the most prominent, and at present the most mysterious phenomena of a living body.

If found to be correct, the principle for which we contend will not be limited to the operation of those noxious agents usually denominated poisons, but it may probably tend to the better understanding both of the causes and cure of diseases in general.

THE END.

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