Nerve inhibition and its relation to the practice of medicine / by H.O. Thomas.

Part VIII. *January 1883.*

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SURGERY AND MEDICINE.

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AND ITS RELATION TO THE

PRACTICE OF MEDICINE

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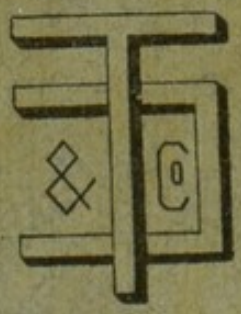
H. O. THOMAS.



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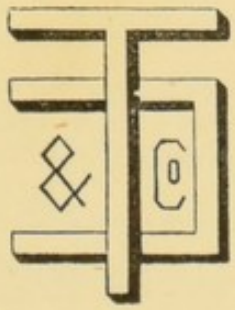

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ON THE

INHIBITION OF NERVES.

THE THEORY OF THE ACTION OF REMEDIES AND ITS VALUE TOWARDS ELUCIDATING THE QUESTION OF THE EXISTENCE OF INHIBITORY NERVES.

For many years, I have carefully noted the effect which followed the administration of certain drugs used in medical practice, which have been favourites with physicians for many centuries, and have observed in common with others a peculiarity, viz., that during their action symptoms at times appear which are apparently inconsistent with those to be expected, from their attributed quality, the exception occurring nearly as frequently as signs of action consistent with their classification in therapeutics. A search in the records given us by authorities in therapeutics for an explanation of this anomaly, only informed me, that a drug with a given quality might, in special doses or under special circumstances, act as though it were a drug of another quality, or a drug at times might so act that symptoms indicative of opposite causes would follow the use of one drug, —a sort of dual action. This theory appeared to me

preposterously unreasonable, and being based upon no exact data, I was unable to accept it. After giving this matter long consideration, and at the same time, happening to take some interest in, and perusing the contributions of investigators, regarding the open question of the existence of nerves of inhibition, this led me to the conclusion, that the question of inhibition was one which would throw some light upon the action of drugs, and conversely the action of drugs would also clear away much of the haze that surrounded the unsettled question of the existence of inhibitory nerves. Any drug prescribed during the treatment of disease, must belong to one of the two classes known as sedatives and stimulants. There is no remedy that can act without the induction of retardation or acceleration of vital action, if we except tonics, which in latter times have very properly been termed "chemical food," and, if they are of any use at all, must act as aliments do, by supplying certain elements essential to the attainment or maintainance of the normal standard of vigour in the body.

To explain my views in relation to the action of remedies, and give my quota towards the elucidating of the subject of inhibition, the action of a few of those sedatives and stimulants, best known to me, will be discussed in the following pages.

SEDATIVES.

THE action of physiological doses and the probable effect of therapeutic doses of many remedies have, in most instances, been deduced from observing the effect of lethal or toxic doses. Such conclusions are not trustworthy evidence of the remedial qualities of drugs, inasmuch as when the lethal condition is approached the distinguishing signs of special poisoning begin to merge, so that their identity is nearly lost. For instance, the differences between a fatal dose of belladonna and one of opium, or strychnia, are less than the variations of symptoms to be noticed when the subject is under a safe or physiological dose of either of these. The effect of a fall of a balk of timber on one person, would give no information to a witness as to what would follow if there descended on another person a portion of timber too light to kill. Again, conclusions arrived at, after witnessing the action of toxic doses, have been tinged by our previous opinion of their qualities. This antecedent bias has caused even recent investigators to assert the possibility of certain medicines possessing, in varied doses, diverse properties,—stimulating one and depressing at the same time another structure.* This error has arisen from insufficient attention to the fact, *that each drug has a special affinity for certain structures, thus causing a temporary defect of co-ordination.*

* Royle's Materia Medica, page 754,—Article, Morphia

Some writers on therapeutics have made a class distinction between drugs of similar quality, sedatives and narcotics,* this classification being based upon the varying degree of affinities of drugs with like quality for particular structures. I fail to see that this is any justification for separating those drugs which have been termed sedatives and narcotics. To me the terms are synonymous. To place various drugs in diverse classes because they may vary in affinity for separate structures is as unreasonable, as to vary the species of the different members of the human race, on account of the quality of the food they *incline* to. Sedatives or narcotics retard life, and their effect upon the structures, which they primarily operate upon, *is to inhibit more or less their function which causes in other structures, unaffected by the sedative, the signs of defective inhibition, or want of co-ordination.*

In experiments performed upon the vagus nerve, all mechanical interference, such as section, ligature, and electric shock, has been termed stimulation or excitation of the nerve.† This is, in my opinion, incorrect, as it is evident to me that in the majority of recorded experiments, these generally give rise to a shock to the nerve, arresting its action.‡ These

* Royle, Headland, and J. Harley.

† Foster's Physiology, page 119.

‡ Surgeons frequently observe instances which illustrate the variable effect following mechanical interference with life. For example, a person falls from the top of a flight ot steps, and immediately he suffers from faintness, palor of skin, sickness, and all the signs of shock. Again, another individual descends from a height of fifty feet, and suffers from simple excitement, and perhaps immediately ascends to the same position and continues his labour.

experiments have also shown that nerves are capable of acquiring some degree of habituation, so that the shock from mechanical interference loses its effect, just what we observe to follow in the use of drugs.* In proof that mechanical irritation of this nerve induces a condition of shock, we have the accepted fact that atropia (true stimulant)† protects the nerve from the shock consequent upon mechanical disturbance.‡ I have not as yet met with any evidence which proves the existence of any inhibitory nerve fibres in this or any other nerve.

Again, diverse qualities have been attributed to drugs from observing their mode of action varied upon the lower animals as regards symptoms, in comparison with the signs of their action on man; but this fact does not inform us that any drug varies in its properties, whether given to man or any of the lower animals.§ It only demonstrates that drugs vary in their affinity for analogous structures in the various types of animals experimented on; and that one drug may give rise to varied degrees of intensity of symptoms in special tissues of the several types of animals tested; yet, in all, the qualifying drug effect will be found to be identical.

* Preliminary account of an inquiry into the Functions of the Visceral Nerves, by J. Lister. Pages 376-7.—Pro-Royal Society, 1859.

† See Stimulants.

‡ Foster's Physiology, page 171.

§ Harley—Vegetable Neurotics, pages 105-6 and 191-2.

Do sedatives act as direct stimulants? I believe they do not; but during their action there may be simulated stimulation, and in those instances where this simulation appears, it is during their primary sedative action, — then also the sedative is exerting a minimum or sectional effect only. To illustrate my views, I will discuss the action of opium and alcohol, remedies that properly belong to the class of pure sedatives, and which by their action upon the several organs of the body prove it. Their effects can be best observed by noticing their physiological influence upon the iris, heart, blood-vessels, and viscera. If a full dose of opium, short of being a rapidly fatal dose, be given, the diameter of the pupil becomes diminished. This is caused by the drug having a primary sedative or paralysing action upon the radiating muscular fibres of the iris, through its primary affinity for the sympathetic system of nerves specially controlling the radiating muscular fibres. But if a fatal dose be administered, then the cerebro-spinal nerves, hitherto less affected by by the opium, show signs of its full toxic effect, and the circular muscular fibres of the iris also become paralysed, as evidenced by the increased diameter of the pupil. The effect of opium upon the heart and blood-vessels is to act first upon the blood-vessels, but, secondarily on the heart. Hence we have at first an increased volume in the pulse from diminished tonicity, and finally a slower rate of beat when the dose has been sufficient and has had time to influence the heart. There is also to be observed a diminution of the solid

constituents in the liquid secretions of the body and a fall of temperature. All these are signs of retardation of vital changes—sedative action. The exception to these general signs of the physiological effect of opium is to be met with when small initial doses of opium are given; then may be noticed acceleration of pulse and vomiting, which may be thought to indicate stimulation rather than retardation.

In explanation of this clinical fact, which appears to disprove my contention, I advance the following reasons:—(1) This simulated stimulation is only temporary, and is evidence that the drug has affected only those structures for which it has a primary affinity—the time being too short or the dose too small for its full physiological action to have been developed: and thus the phenomena of the so-called defective inhibition or want of co-ordination appear,—this is often interpreted as indicating stimulation. (2) That by the use of any remedy there is introduced into the system a foreign body, which may give rise to some temporary constitutional disturbance until some amount of habituation has been acquired. We have many familiar examples of this,—as change of air, diet, pleasure, relief of pain, sea voyage,—yet no physician would advise a trip to sea in place of prescribing an emetic, the latter being nearer at hand and more certain of action. So with opium, its indirect effect in simulating stimulation is not so ready or safe as employing a genuine stimulant, when the effect is desired. (3) The most

probable explanation of the non-occurrence of vomiting, in some instances, after the administration of opium I believe is this, that in some subjects, especially children, it rapidly affects the pneumogastric nerve and its branches, so that defective co-ordination is avoided, and thus the stomach and intestines remain quiescent. The proof of this are the observed clinical facts that only large doses produce vomiting at the commencement of their action, or at the termination of their action, *i.e.*, when the pneumogastric nerve has not been yet reached by the drug or its influence on the nerve is waning,—this nerve being affected later and recovering earlier from the drug than the sympathetic nerves. There is further proof in the fact that when opium is given by the skin method its action is rapidly operative all round, and the period of possible and isolated excitement of the pneumogastric nerve and its branches is bridged over so that vomiting is avoided. This explanation of the phenomena of vomiting after the use of a sedative is quite consistent with what we observe of the effect from doses of belladonna, which also induces vomiting occasionally.

Many of the prevailing errors regarding the therapeutic effects of both opium and alcohol have arisen from misrepresentation of the signs of their action, and of the symptoms of the disease which they were required to correct.

Alcohol in its various forms, as in popular use, I maintain to be a drug possessing purely sedative properties, and in its

method of action is allied to opium. It primarily affects the sympathetic nerves, then the vagus, and finally the cerebro-spinal system. When the nerves become subject to a full non-toxic dose, the pupil contracts; but after a fatal dose has been taken, the pupil dilates some time before death.* The action of alcohol upon the heart and blood-vessels, through the vagus and sympathetic system, is also analagous to that of opium. Primarily it attacks the blood-vessels through the sympathetic nerves, diminishing their tonicity,—thus relieving the heart from blood pressure,—so that the initial signs of its action may be a temporary acceleration of the pulse, as well as an increase of its volume, simulating stimulation; but if the dose is sufficiently increased, then the heart is affected, and the pulse also becomes reduced in rate.

Again, by alcohol, the solid constituent of the liquids secreted are diminished, and the normal quantity of carbonic acid exhaled by the lungs is reduced; and in corroboration of these ascertained data there is to be observed a fall of temperature. All these signs point to a purely sedative result—retardation of life, not acceleration or stimulation. The simulated signs of stimulation by alcohol arise from the primary affinity that certain doses of alcohol have for certain nerve structures, and a misinterpretation of the signs of its primary action has engendered the belief that true stimulation is gained; and though sometimes this mistake in practice may

* Anstie, on Stimulants and Narcotics.

do no harm, yet when true stimulation is required its administration may be a serious error. Its primary effect cannot be trusted, as a safe substitute, when stimulation is urgently demanded and requires to be continued. It may be argued that contraction of the pupil, when influenced by alcohol, may be brought about by stimulation of the circular muscular fibres of the iris, and not by paralysis of the radiating muscles. But the only explanation admissible regarding the mechanism of the increased volume of the arteries when influenced by alcohol, enables us to check our deduction regarding the mechanism of the action of the iris under its influence. If this drug could stimulate, then the diameter of the blood-vessels would be lessened from contraction of their circular muscular coat. Again, if alcohol could stimulate, then its primary affinity for structures specially under the control of the sympathetic nerves would cause this stimulating property to influence first the radiating fibres of the iris, and dilatation would be the first alteration observed in the pupil during its first stage of action.

Other neurotic sedatives act, after introduction into the human frame, much like opium and alcohol. I have observed the action of Calabar Bean frequently during later years, when prescribing it for chorea, tetanus, and the muscular spasm attendant upon fractures of bones. I have observed that its action has many signs in common with opium and alcohol. In the early stage of its action the sympathetic nerves first

begin to feel its effect, and we have vomiting and purging, from its delayed effect upon the pneumogastric branches of nerves supplying the muscles of the intestinal muscular coat; but as soon as the sympathetic nerves succumb to its influence, then the cerebro-spinal nerves are inhibited also, and the striated muscles relax. The heart is not as much inhibited by this drug as it is by digitalis, but its sedative action upon the heart is greater than that of opium or alcohol.

During the physiological action of Calabar Bean, the pupil becomes contracted from palsy of the radiating muscle of the iris, but as soon as a lethal dose is operative the pupil dilates before death, showing that the other nerve centres have been influenced.* Henbane, another drug of the sedative class, during its primary action dilates the pupil, and this is explicable by the fact that Henbane possesses a primary affinity for the cerebro-spinal nervous system.† Experiments have shown that the striated muscles are first controlled by it; secondly, the sympathetic; and finally the vagus becomes inhibited, so that the pulse, accelerated during its primary action is finally reduced below the normal rate.

Digitalis again, is a sedative that possesses a primary affinity for the vagus, and is practically useful in influencing the important organs to which the nerve is distributed. Its sedative property, negatives its being prescribed in

* Anstie, on Stimulants and Narcotics, page 481.

† Experiments of Harley, and the Clinical Observations of Dr. T. Browne.—British Medical Journal, Nov. 25th, 1882.

those cases of heart disease, where there exists degeneration of its motor structure. During its primary or physiological action it has no effect upon the muscles of the iris, and the anatomy of the nerve, which Digitalis primarily affects, excludes the probability of the iris being influenced until a lethal dose of the drug has been taken and other nerve centres have become poisoned by it, then the pupil dilates before death. When the merits of various anæsthetics are discussed, æther is frequently incorrectly referred to as a heart stimulant, when the proper explanation of its merit should be, that its affinity for the heart, probably through the vagus, is less than that of chloroform, and thus it becomes a safer anæsthetic. In the action of septic poisons there are examples of special affinity for various structures, these so operating, that the so-called signs of defective inhibition or want of co-ordination become the distinctive signs of special diseases.

I feel some confidence in predicting that in the medical practice of the future, this affinity for certain structures, possessed by contagious and infective poisons, will become a basis for the selection of aids in treating the diseases which these poisons cause, instead of the present tendency at attempting to neutralise the original evil by a general antiseptic saturation of the blood and tissues, we shall in future have more of physiology and pathology with our chemistry to guide the physician.

STIMULANTS.

I SHALL only discuss the physiological effect and medicinal results that follow the use, either experimentally or therapeutically, of belladonna, this drug being selected in consequence of its value, in my opinion, as a pure stimulant of nerve centres controlling organs essential to life.

Difference of opinion prevails among therapeutic authorities, as to whether certain drugs are endowed with sedative or stimulant properties.

By the term "stimulant" I mean any matter which, after its introduction into or absorption by vital tissues, increases the activity of the condition antecedent to its introduction, without supplying the source of force for maintaining this increase of power or function—as food can do. *i.e.*, a stimulant draws upon a reserve, which can only be renewed by food. How therapeutists could have come to the conclusion that belladonna

"Possesses powerful anodyne and hypnotic properties." "Valuable antispasmodic."*

At the same time

"Stimulant effect on the circulation,"—"potent diuretic"—*

* Harley, Vegetable Neurotics, page 244. Headland, Actions of Medicines, page 275. Royle, Materia Medica. page 493.

is to me explicable only by the supposition that investigators have not made the physiological doses of belladonna the basis for their deduction in prescribing, and its toxic effects their basis for antidotal treatment.

If the symptoms which follow the physiological doses of belladonna, are analysed, there always remains evidence of stimulation, and during its action the phenomenon of special affinity for certain structures is demonstrable, just as may be observed during the action of sedatives. Its effect in full physiological doses is to stimulate the radiating fibres of the iris by its special affinity for the sympathetic nerves, a branch of which aids in regulating the radiating muscle of the iris; but it may be said that this dilatation of the pupil by belladonna arises by the same mode of action as that which causes Henbane to dilate the pupil. But this objection is inconsistent with the fact, that the blood-vessels are diminished in calibre when under the influence of belladonna, from the contraction of their muscular coat (necessarily a stimulative result), so that the pulse is less perceptible, but increased in tone, and the temperature becomes elevated. Further, the heart's action is always accelerated by belladonna from its secondary affinity for and stimulating effect on the vagus nerve, which nerve this drug can protect from the collapse arising from mechanical irritation,* provided the use of the drug be such as not to approach too near the

* Foster's Physiology, page 171.

toxic area. During the action of belladonna the solid constituents of the liquids excreted are increased—another phase of stimulation. Hitherto no evidence has been made known which shows that belladonna retards life so long as its action does not overstep the area of physiological action—that of safety; and this area of perfect safety in a healthy subject is exceeded as soon as the drug, whether sedative or stimulant, begins to act beyond the structures, for which it has a primary or special affinity. A remarkable discord of opinion exists in explanation of how belladonna can benefit in medical practice. With some of these views I coincide, from most of them I must dissent. For instance—

"Belladonna allays pain . . . . the attendant spasm . . . it relaxes muscular fibre" . . . . "in spasms the expulsive effects moderated" . . . . Belladonna relaxes the hollow viscera, and it is to this effect that we must attribute its antispasmodic as well as expulsive action.—Harley, Vegetable Neurotics, page 230.

"By relieving spasm arising from irritation of the air tubes, gall ducts, and ureters in bladder, belladonna is serviceable."—Royle, Materia Medica, page 495.

These quotations, all from recognised authorities, are a collection of contradictions. If it allays pain, relieves spasm, relaxes muscles, how can it possibly have an expulsive action?

"The constricting fibres of the intestines and of the ducts of glands are, in like manner, relaxed by belladonna, and of this we may take dilatation of the pupil as the outward sign. The dilatation of the pupil under the influence of belladonna is active and due to a stimulant effect on the sympathetic nerve."—Royle, Materia Medica, page 492.

If the constricting fibres of the intestines are relaxed by belladonna, how the dilation of the pupil by the same drug, can be an active change, I fail to perceive. This inconsistent teaching appears to have arisen from a misinterpretation of the mechanism of stimulation on the non-striated muscle. For instance, the effect that stimulation has upon the pupils, and upon the muscular coat of the blood-vessels, as an example—

"The sympathetic has, it will be observed, an effect on the iris, the opposite of that which it exercises on the blood-vessels. When it is stimulated the pupils are dilated while the blood-vessels are contracted." —Foster's Physiology, page 466.

"It is probable that these fibres are under the control of the sympathetic system of nerves. If so, it must be observed that the sympathetic nerves have an effect upon the iris directly opposite to that which it exercises upon the blood-vessels, since when it is stimulated the pupils are dilated, while the blood-vessels are contracted." — Ranney, Applied Anatomy of the Nervous System, page 133.

The sympathetic has not an opposite effect on the iris to which it has upon the blood-vessels. Stimulation of the sympathetic nerve excites the circular muscular coat of the blood-vessels to contract, and this contraction can only take place in the direction of diminishing the area of a circle. The iris being a radiating muscle, if stimulated through the sympathetic nerve, can only contract in the direction of its largest circumference, as the iris is a radiating muscle attached at its greatest or external circumference, so it can only contract in the direction of its outer circumference, its base of

resistance, and so dilatation must occur when the radiating muscle of the iris is in action; theoretically, dilatation of the pupil corresponds to contraction in a blood-vessel, when either is under sympathetic stimulation.

"Retention of urine is a frequent result of a full medicinal dose of belladonna."—Royle, Materia Medica, page 492.

In this quotation we have, with regard to the action of belladonna, another out of many errors that are to be found in standard works written on therapeutics; it is an example of the toxic action being selected as evidence of the medicinal result of a drug. Retention of urine is not a result that follows a medicinal dose of belladonna; but it may be urged. as evidence, that it relaxes the muscular coat of the bladder and points to a sedative effect. This I deny. It is excellent evidence that belladonna is a stimulant, and its toxic effect upon the bladder is quite consistent with its effect upon other structures, and in support of this contention my reasons are the following :--

If the anatomy of the nerve supply to the bladder be considered, it will be found that the upper part of the bladder is supplied from the hypogastric plexus of the sympathetic, while the spinal nerves can be traced directly to its neck and base.*

* Quain's Anatomy, vol ii., page 426-7. Eighth Edition.

The most reliable authority on the action of the vegetable neurotics has conclusively established that large doses only have the effect of causing retention of urine, and I hold that causation of this act arises in this manner.* As soon as a toxic dose of belladonna has crossed its area of physiological action (sympathetic and vagus), the store of nerve energy, within the area upon which it has primarily drawn is much diminished,† but further forward in the toxic area which

* We have proof of this in the observation made by Dr. J. Harley, at page 205-7 of his excellent contribution to therapeutics, "Vegetable Neurotics,"—"I have occasionally injected 1-20th of a grain of atropia; and agreeably with what I have observed after the use of larger doses than 1-30th, the effect upon the pulse has been less apparent than after an ordinary full dose of 1-48th of a grain." As contributions to the elucidation of the properties of drugs, we have the labours of the Edinburgh Committee, presided over by the late Prof. J. H. Bennett, and Dr. J. Harley's volume on the Vegetable Neurotics. These two volumes, in my opinion are, incomparably, the most able and trustworthy contributions to therapeutics; they present the reader with data from which he can glean much practical information, though he may dissent from some of their deductions. As for instance, in regard to belladonna Dr. Harley at page 230 of his volume, asserts the probability of this drug possessing relaxing and stimulating power. This I hold, is just half of a fact; a toxic dose which appears to relax circular fibres under the control of the sympathetic nerves, and stimulate longitudinal ones under the control of the spinal nerves, does not actually so operate, but the phenomenon is properly explained, only upon the supposition that when the muscles under the control of the spinal nerves are affected by belladonna, those under the control of the sympathetic have been previously exhausted by primary stimulation. This is also the explanation of the observation that belladonna is a better antidote to opium than opium is to belladonna. In belladonna poisoning the nerves having been "run down," opium cannot reasonably be expected to awaken nerve force; but in opium poisoning the nerve force may be arrested (held), and it might be expected that the stimulus of belladonna would gain relieve."

† Preparations of Belladonna, Henbane, Conium and Digitalis, usually sold are not so uniform in quality as some of the other vegetable neurotics. Whether a dose of atropia be a small or large dose depends upon the care expended upon its preparation. The Medical Press during late years, has recorded the administratron of large doses of this alkaloid, with only moderate action. I have myself experienced the same disappointment after the giving of atropia, but have also seen potent action result after procuring a supply of the alkaloid from another source.

includes the vagus, the sympathetic and spinal nerves, the store of energy within the spinal nerve is in full force, until this area is crossed and death supervenes. These toxic doses of belladonna, having exhausted the nerve supply of the body of the bladder, at a time when it is commencing to stimulate the base and neck, must necessarily give rise to retention of urine.

As regards the doses of atropia, it is my opinion, that when administered by the subcutaneous method, any quantity exceeding 1-48th of a grain becomes a toxic dose, and that, provided the drug be of good quality, it is always advisable to commence with much less, say 1-60th, and increase gradually until the physiological effect is attained.

Belladonna is now admitted to be an antidote to opium poisoning, but it has also been noticed that opium will not act as an antidote to belladonna. This is further evidence that belladonna possesses genuine stimulant properties only, as over-stimulation (poisoning by a stimulant drug), must lead to exhaustion, a condition which would certainly not be benefited by any drug that tended to arrest vital action.

The efficacy of belladonna as an antidote to opium is explicable by the fact that it possesses an earlier affinity for the vagus than opium possesses. Thus, if a toxic dose of opium be taken, and an antidotal dose of belladonna be also given, ere the opium has affected the vagus, the other drug precedes

it in affecting the vagus, and thus protects the nerve rather than neutralises the coming action of the opiate. The prescribing of a combination of opium and belladonna is evidence, I maintain of ignorance, for which at the present day, no trained practitioner has good excuse.

In the selection of drugs for the treatment of maladies, it is my opinion that more attention ought to be given to their physiological action on the healthy portion of the body, as it is the indirect or secondary effect of remedies, acting upon the healthy portions of the body, which in many instances brings about relief to the diseased area, the latter not being susceptible to direct drug action.

Of this we have an example in the acute pain attendant on pneumonia, as when opium in doses much too small to soothe pain by its toxic effect upon the nerves, gives much relief. This it may do, by partially paralyzing the vascular system, and thus by enlarging the blood area, relieving pressure at the inflamed area. This is also the explanation of the action of opium, when given as a remedy for internal hemorrhage, pressure is taken from the clot plugging the ruptured vessel. This explanation of the beneficial action, following the use of opium in cases of hemorrhage, is not generally accepted, otherwise the prevailing practice of resorting to the administration of ergot in cases of hemorrhage would be seen to be erroneous practice; inasmuch as this drug excites the blood-vessels generally to contract, and the blood pres-

sure is increased at the point of leakage, a locality which is, in most instances, in an abnormal state and cannot respond to the drug. Consequently, the liability to leakage is much increased by giving ergot, hemorrhage from the uterus excepted; for here the physical and physiological conditions are very different, though in this instance, the beneficial action of the drug is brought about by indirect action, the excitement of the muscular structure of the uterus. The use of belladonna during a time when the recurrence of hemorrhage is dreaded, is also incorrect. My clinical experience has fully confirmed what appears to me, in these cases, a reasonable explanation of the action of sedatives.

The theory here advanced in explanation of the apparent divergent action of drugs will, if used as a guide to the interpretation of the data given by experimental and clinical observers, enable us to harmonise the signs that follow the action of drugs, which otherwise would appear contradictory. It is my opinion that this theory will also be of some assistance towards the settling of the open question as to the existence of "nerves of inhibition."

My explanation of the phenomena which have led physiologists to believe in the existence of inhibitory nerves is as follows:—That each animal contains, stored in certain nerve-centres a quantity of nerve force, the total quantity of

which, for the sake of illustrating my argument, may be reckoned as represented by a unit, this being originated by the nervous system and stored in several nerve-centres, here supposed to be represented by five, component of the total (unit), and to contain the nerve force in as many parts. There exists evidence which makes it not an unreasonable supposition, that if, by a drug or mechanical influence, any one of these five nerve-centres is inhibited, then there remains one-fifth more available source of force for service elsewhere, which could only be utilized by deflection along the remaining unaffected four-fifths of nerve structure. This economy of nerve force, in one direction, would raise the fractional energy of the remaining untouched nerve-centres so that their force would be represented by a fractional power of one-fourth of the total unit. Such a transposition of nerve energy, would cause, for a time, those parts to which the remaining nerve-centres (four fractions) habitually conveyed energy to show signs of excitement. And there are fair grounds for believing that such inhibition can be induced or prevented by drug influence, as it is patent that the simulated signs of stimulation follow the action of narcotics, from certain drugs producing isolated action upon certain nerves only; and the question naturally arises, Why, during the action of sedatives, should there be a temporary excitement of the nerve-centres when no stimulation had been exercised nor extra force introduced? This excitement cannot exist without extra source of power, and as the

excited nerve-centres had already their usual store, it is reasonable to suppose that this sign of increased energy-excitement can have been derived by deflection of the store usually expended in the inhibited area, or that the remaining unaffected nerve-centres, by the inhibition of one area, can and do at once draw from the common source the greater force left at their service.

Experimental physiology and clinical observation both are in favour of the probability that nerve force can be distributed collaterally; and Why should not the store of nerve energy within a special centre if arrested from being distributed to its usual points of expenditure,* be deflected into another centre, all being known to be connected.

It is from observation of the signs that follow the administration of drugs belonging to the class known by the terms sedatives and narcotics—inhibitory drugs—that we must seek for physiological and clinical information which may enlighten us in regard to the debatable question of the existence of nerves of inhibition, rather than to the effects that result from mechanical interference with vital structures †; though I

* Dr. Marshall Hall inclined to this opinion, see Meryon's Rational Therapeutics and Functions of Sympathetic Nerves, page 31, edition 1872.

† Experimental investigation has shown that mechanical interference with nerve-centres and trunks sometimes produces shock, and at other times excitement. This makes observations, taken during direct interference with the parts experimented upon, indecisive. Again, in very many instances, observation of the effect of direct interference is made while the subject of experiment is under the influence of an anæsthetic, the toxic action of which introduces another source of error.

would not totally ignore information from such a source. If we select opium and alcohol, both narcotics, in illustration of the views upheld in this contribution, after a physiological dose of either of these, if a careful watch is kept upon its progress across their area of physiological action, what do we observe; first, one system of nerves—the sympathetic — is inhibited and the remaining ones are excited, but as soon as another nerve-centre is reached by the narcotic and becomes also inhibited, all the other nerve-centres show further excitement and when these have succumbed to the drug action, we have the total narcotic effect. Those, who are accustomed to the habitual use either of alcohol in any of its various popular forms, or of opium, or indeed of any narcotic, tell us of the pleasures they enjoy from the extra activity of the sensorium. Some even profess that with the aid of what is mistermed alcoholic stimulation and the sedative action of other narcotics, they are, whilst under its influence, mentally and physically superior; this might be found to be true, if it could be proved that temporary drug inhibition of nerve-centres, not necessary to mental or physical exertion, did increase the nerve force available for use by the remaining unaffected nerve-centres.

Some may suppose that the action here attributed to alcohol is a justification or even an encouragement to its being habitually consumed, but this is certainly not a proper deduction to make from the theory advanced in this paper, as

the habitual use of alcohol or of other narcotics by its inhibitory effect both upon the action and nutrition of the liver, kidney and heart, tends to produce in all persons, and in many produces, a diseased state of these organs. Some may also suppose that the remarks here made in regard to the simulating of stimulation which follows the use of narcotics is also a justification for using them when pure and urgent stimulation is wanted. This would be justifiable only, if no true stimulant was known or near at hand, inasmuch that the administration of a narcotic for this purpose, involves some risk and delay, as simulated stimulation is not so rapidly induced. Again, it may be rapidly followed by the true narcotic action over too large an area, and this in a critical case might put an end to a life previously threatening to ebb—especially if the subcutaneous method of the administration of remedies is practised. For instance, a subcutaneous dose of either opium or belladonna acts rapidly, commencing after a period of fifteen or twenty minutes has elapsed,—one-fourth of the period required when given by the mouth—while after the introduction of alcohol or æther subcutaneously, its action is not as rapid as when given by the mouth. The practice, introduced of late, of injecting æther under the skin in collapse, is certainly wrong, for when thus administered, if its action were not more slowly developed it would be almost certain death to the patient.

Should the explanation tendered by me in illustration of

the mode of the action of remedies, be confirmed by further investigation and accepted as correct, then the difference between simulated and true stimulation will be this, that the first is brought on by inhibition of one or more nerve-centres, leading to an accumulation of nerve force in others not so influenced. True stimulation will be the creation of nerve force in one or more nerve areas, while the remaining nerve-centres of uninfluenced nerve-centres may or may not show signs of diminished energy.*

A dissenting section of therapeutists, among whom are physicians of repute, as clinical observers, have adopted as the basis of their system of medicine, "similia similibus curantur." Their strenuous contention for their accepted dictum is accountable only by the mistake many others have made, which they also have committed, that of not recognising the difference between simulated stimulation and true stimulation.

The order in which remedies elect to affect vital structures, and the varying degrees of intensity with which they act upon them give us the composite phenomenon, which indicates their active presence, and make possible the fact, that every drug

* So many have asserted that they observed relaxation of the striated muscle by the use of belladonna, that it is not possible to ignore their evidence, but this is explicable by the supposition, not an improbable one, that inasmuch, as the common source of nerve power only contains a limited quantity, then hyper-excitement of the non-striated muscle which belladonna primarily affects, may be maintained by abstraction of power from other sources, of which the action of tobacco is rather confirmatory.

when in action has its distinct formula of signs, a mode of influencing organised matter that reminds me of the "lines" and "notes" in music, which, to illustrate my views, I will suppose the "lines" to represent nervous structures, while "notes" of music represent our remedies. In music the position of the notes in relation to the "lines," decide the melody and admit of variations innumerable, so with drugs. The order of primary and secondary and final affinity which the drug may have, gives us a collection of symptoms which, according to the order in which it elects to act presents us with a distinctive trait to each remedy, so that as yet and probably there never will be found a drug with signs of action exactly parallel to those of any other.

All discoveries in physiology must materially increase the efficiency with which we can treat disease, and any information that will show the cause or the effect, in my opinion, of nerve inhibition, will lead to important changes in practical medicine. As yet it has been generally taken for granted that remedies benefit mostly by direct action, whereas, it is their indirect action which often relieves. Stimulants tend to discourage inhibition; whilst sedatives again tend to produce in safe doses partial inhibition, and in toxic doses do produce, complete inhibition. The beneficial action of a sedative may arise by the induction of some degree of inhibition in one area, which would thus increase nerve-store or tension in other areas. An example of this is pre-

sented to us in the success attendant upon the treatment of epilepsy by bromide of potassium. That bromide of potassium is a very valuable remedy in epilepsy is now very generally admitted, and that the cases in which it gives amelioration or cure are those where the causation is from anæmia, not of reflex or centripetal cause, — true epilepsy—which, Dr. Todd, by attributing to an explosion of nerve force, almost anticipated my views of its etiology. To explain the corrective effect of the compounds of bromide in this disease, I must recapitulate some of the well known conditions and symptoms indicative of this ailment. My purpose in limiting myself to true epilepsy is, that epilepsy is a term which is frequently applied to the convulsions symptomatic of uræmia, hemorrhage, poisoning, reflex irritation, worms, introcranial pressure, neuromata, syphilis and other centripetal causes. It is obvious, that in the treatment of any of the foregoing symptoms, the bromides cannot be expected to aid us. During an attack of graver epilepsy—which is only a further stage of the "petit mal"—the most noteworthy phenomena's are loss of consciousness and sensation—the sufferer neither knows nor feels, but there is intense muscular and organic action through the excitement of motor and sympathetic nerve systems. As evidence of excitement of motor nerve-centres, we have the general clonic convulsive action of all parts moved by the intervention of the striated muscles; as evidence of sympathetic excitement we have dilated pupils,—a constant sign in true epilepsy—small

slow pulse, discharge of intestinal excretion and urinary secretion, sexual excitement and increased secretion of urine. The foregoing symptoms are evidence of excitement of the whole motor nerve tract and sympathetic nerve system—the pulse excepted; but this only further shows that the vagus is involved, in what Dr. Todd terms a nerve explosion. From my own opinion in regard to the area of causation—inhibition of the vagus is a probability and points to this nerve being more sensatory than motor in its composition, a matter that as yet remains an open question.

For the purpose of my argument the details of the first stage or onset of the fit, will suffice me, as they must point more directly to the mode of the event, as the signs present during the second stage are modified by the dawn of recovery. Hitherto all investigators of histological evidence, by which they might fix upon the locality, the altered function of which induces epilepsy, have sought for it in centres that show extra activity during its manifestation, and have neglected those nervous centres, the sensorium and posterior roots of spinal nervous tract, that show the remarkable phenomena of intermittent inhibition. Does it not appear a very rational supposition that during the existence of a disease, in which there were signs showing acceleration of life on one side and temporary suspension of life on the other, the region in which life appeared to be arrested ought to be at least

mainly credited with the causation of the ailment? The inhibition of nerve force in the affected area leading to an extra expenditure in unaffected areas.

Most of the experiments performed to elucidate the causation of epilepsy appear to me nearly worthless, as they have been made by interference with the motor centres, notably the pons and medalla oblongata an investigation in these parts being only a search for the cause of the minor or secondary symptoms. The pons and medalla oblongata may be the convulsive centre, but what is wanted is the detection of the locality in which function is intermitted, so that consciousness and sensativeness is temporarily in abeyance, —the initial and major signs of the disease—and which may be very correctly described as an idiopathic intermittent inhibition in one or more nerve areas.

We now sum up the attributed physiological effects of bromine, that it is a drug of the sedative class, no person seems to doubt, and that its primary or physiological affinity is exercised upon motor nerves is also very generally admitted; that in toxic doses it also reaches other nerve-centres, is probable, but this does not affect the question which it is my purpose to try and elucidate here, as during its use in the treatment of epilepsy, its efficacy is not dependent upon toxic doses, the patient being generally instructed to either intermit its use or diminish the quantity consumed, if toxic signs follow its use. Bromide of potassium is both a

safe and thorough corrective of the clonic spasm occurring after paralysis affecting the sensitory spinal nerves—it is safe, because of its very obvious unwillingness to extend its sedative action to either the sensorium or any sensitory nerve area, —while opium, alcohol, æther, and chloroform, they first affect the sympathetic, then the sensitory system, and finally the muscular nerve-centres. Bromide commences in the locality in which the former terminates—voluntary motor tracts. Any person who has gained his professional experience in "general practice," but especially a surgeon, must be cognisant of the fact, that the preparations of bromine are worthless as alleviators of pain or excitement in the sympathetic nerves. It is said to "heighten the action of opium;" this it is reasonable to suppose, as a combination of opium and a bromide would produce a more immediate and uniform action, and defective co-ordination would be lessened. The compounds of bromine are now so generally admitted to be sedatives of the voluntary motor tract, that further discussion of their properties is superfluous.

The preceding sketch of true epilepsy and details of the medical qualities of bromide potassium are not suppositions of mine, but authenticated data collected from recognised authorities, and in the absence of contra-evidence must be accepted as true. These facts go to show, that a disease indicated by temporary inhibition in one nerve area, is sometimes controlled, nay cured, by a remedy that induces

inhibition in another area, and the beneficial action of the remedy, must have acted in epilepsy by inducing more or less constant inhibition in the voluntary motor area, and thus thwarting the tendency to deflection of nerve force; or, as Dr. Todd would say of "explosion of nerve force in the sensatory area, towards the motor area, as the inhibition produced by the remedy—figuratively—baring its exit." We have had further evidence in support of this hypothesis, previous to the introduction of the bromides into medical practice.

A very high value was set upon belladonna as a remedy in epilepsy. One of, if not the most able of the French physicians, much extalled its virtues in this disease,—and from what we know now of its mode of action as a preventive of inhibition, we are justified in supposing that it might in many instances have benefited the sufferer. It is most remarkable that the rules which were to be adhered to, during its use, were just those now recommended to be attended to when bromides are employed, that is not to induce toxic action. But as belladonna has a primary affinity for the sympathetic, its anti-inhibitory influence on the sensatory nerve area, would only be very feeble—this direct method of treating epilepsy deservedly fell into disease. For the direct method of medication to benefit, we want a remedy with a primary affinity for the sensorium and its ramifications, granting that the diseased or disturbed area can respond to physiological stimulation. The treatment of epilepsy by the bromides is, I

think, very clear evidence that the deflection of nervous force from one area to other areas, though inhibition as a cause, is no mere supposition; and the deduction, that we are led to from watching the results following the treatment by an indirect method, this idiopathic occurrence of inhibition in true epilepsy, is this, that if we knew of a sedative which possessed a strong primary affinity for the sympathetic nerve system, with little or no affinity for the sensatory nerve system, such a sedative remedy, combined with the bromides, would be a better corrector of the disease than any we have hitherto had; but the curative tendency of this compound, like that of the bromides alone, would be the result of influencing the normal structures — the indirect method of medication; but, indeed, the only way if the pathology of the future demonstrates to us, that the cerebri and posterior columns of the spinal nerve systems are much deteriorated in epilepsy.

From the deportment of the bromides, as correctives of the epileptic state, and the etiology of the disease, there is to be gained information that justifies us in suspecting that alcoholic epilepsy is also caused by temporary surpension of function in the cerebral hemispheres and in the sensatory nerve tracts, it may also be induced from the drunkard having so much and so long indulged in alcohol, that the sympathetic may have acquired an habituation, so that the sensorium and its nerves are acted upon by the drug as though it had a primary affinity

for those structures; thus there would be inhibition of the locality which is also inhibited in true epilepsy, and consequently there would be the simulated signs of that disease.

In the epileptic type of diseases we have illustrations of abnormal states or complaints produced sometimes by inhibition and at other times by stimulation, yet the symptoms, in each instance, very closely approach perfect similarity.

An analysis of the symptoms indicative of the various diseases—contagious, infectious and septic—will show, that in their mode of action, their morbific causes act so as to produce the collective signs characteristic of such complaint by following the same law, which I contend, drugs adhere to, when in operation upon vital structures (drugs which act chemically must obviously be excepted), so that we may even have similar symptoms from opposite causes, just as drugs may induce both simulated stimulation and pure stimulation. In cholera we have an example in which inhibition decides the character of the disease, it commences with all the signs of a morbific cause endowed with the power of inhibiting primarily those sympathetic nerve-centres, which influence the intestinal tract, and during its primary action, we have both the signs of defective co-ordination and excitement of unaffected areas, but if the disease progresses to another stage, other nerve areas show signs of being

inhibited, so that vomiting, purging, and cramps cease,* collapse supervenes, the temperature is characteristically low and the action of all the excretory organs are more or less in abeyance.

The foregoing facts are evidence of inhibition, where the disease similates the action of narcotics, and we have been warned by the latest and best authorities who have written on the treatment of cholera, of the danger of giving sedatives in this disease. To treat cholera in its first stage by sedatives is to run some—justifiable—risk, but if this treatment be persisted in during the second stage it would be injurious.

In typhoid we have an example of true stimulation from a morbid cause, which confines its action principally to those nerve-centres that are essential to life and preside over the organs of nutrition and excretion, these nerves under its influence show exaggeration of normal action, until from overwork they begin to fail. It is not necessary for me here to detail the symptoms of typhoid fever as they must be so well known to my reader—they are the signs of pure stimulation. Although the physiological evidence in cholera points to a cause producing inhibition, the evidence in typhoid points to true stimulation, in both of these diseases we have the same local lesion, a similar result, brought about by causes totally dissimilar; but the

* If I was asked to give to the cramps observed in cholera a designation consistent with the symptoms of the disease, the term "choleraic epilepsy" would be suitable, for the same reasons as induced Brown-Sequard to alter the term "local myelitis" to spinal epilepsy.

physiological evidence which we notice during typhoid informs us that remedies of the sedative class are the proper ones to employ, if medicines are required.

Again, in diseases arising from the action of septic poisons, of which tetanus and hydrophobia are examples, there may be noticed signs similar to those which follow the administration of certain inhibitory drugs, those which cause inhibition and those which cause the so-called defect of inhibition. My reason for selecting these two is the fact, that the signs of each are very well authenticated. An analysis of the symptoms attendant upon true or septic tetanus strongly supports the views here advanced. In tetanus, the most prominent and very obvious signs are excitement of the striated muscles, but by careful attention other signs can be detected, which indicate inhibition of the non-striated muscles and of the visceras. The condition of the striated muscles in this disease is so plainly discernible and generally known that it need not be detailed here. It corresponds with the phenomenon termed defect of inhibition in the nerve-centres controlling the striated muscles. But if the condition of the non-striated muscles is carefully noticed, they appear to be inhibited, through probably their ganglionic nerve-centres. *Evidence of this is presented to us by the tendency, so long as death is not imminent, to constriction of the pupil; this being brought about by the same physio-

* South's Chelius, vol. I, page 377. Wood's Practice of Medicine. vol. II, page 784. Copeland's Dictionary, Tetanus, page 1012.

logical cause which induces diminution of the pupil during the action of some inhibitory drugs. Further, the peristaltic action of the intestine is deteriorated, as shown by constipation and its evils, retention of solid and gaseous gut contents. Along with these there are retention of urine and diminished visceral excretory products. Thus during the action of the poison of tetanus there can be noticed signs of inhibition of certain nerve-centres and the signs of simulated stimulation of other nerve-centres, and there may also be noticed one very distinctive difference between the effect of the poison of tetanus and that of any inhibitory drug, that the action of this virus *never extends beyond the area of nerves distributed to the non-striated muscles.*

This is the probable explanation of the persistent severity of the excitement produced in the striated muscles up to the last moment of life in fatal cases. The patient in very rare cases dies exhausted, but generally from the intense excitement disturbing the co-ordination, of certain important striated muscles, so that life is interrupted ere the vitality of the system has been exhausted. If the poison of tetanus had an affinity for, or could exercise any inhibitory power beyond, the sympathetic nerve area, the excitement of the striated muscles would not be so persistent.

The accepted signs of this disease are the tonic excitement of the striated muscles which, as the disease progresses, are developed in a direction downwards, but at the same time

there is to be observed in the same direction the downwards progress of inhibition of the sympathetic nerves, that takes precedence, if there be any, in relation to time, between interference with the function of the sympathetic system and excitement of the motor nerve-centres. The pathology of tetanus, in my opinion, will have to be sought for in the sympathetic system of nerves—not in the motor nerve area — where search has hitherto generally been made.

In hydrophobia the signs of what has been mistermed defect of inhibition, exist "all round," the septic matter being a true or direct stimulant. To explain all the phenomena characteristic of this disease so as to be consistent with the defect of inhibition theory, we must suppose every nerve in the body to possess inhibitory nerves, and that no nerve is truly automatic, but that each requires a "governor."

Most authors, who have written upon the etiology and treatment of tetanus and hydrophobia, have pointed out that these two distinct diseases have symptoms with similar features, and so close in character, that some authors have suspected them to arise from causes not far allied. But in my opinion there exists not the slightest evidence of relationship beyond the fact that they have each a septic cause of orgination. Tetanus is a disease in which limited inhibition decides the cast of symptoms, while hydrophobia is a disease in which true

stimulation, not co-ordinately acting, gives character to the present signs.*

*The pupil is generally said to be contracted in tetanus and dilated in hydrophobia. Of the last disease I have but little experience, but I have had very many opportunities of observing and treating tetanus, aad have frequently tried both separately and conjointly, the following drugs :—Indian hemp, calabar bean, opium, calomel, and belladonna, but on reviewing my past experience, I am unable to strongly recommend any one of these drugs, though inclined to favour belladonna most, and Indian hemp the least. In tetanus there exists a wonderful tolerance of belladonna or its alkaloid, and my experience of its use in this disease has convinced me that it aids recovery, It has never been used by me in idiopathic cases. In all of the cases in which belladonna was tried the disease had commenced within seven days after the injury, but in most instances at or about the third day. Of those cases which recovered, it was observed that more than forty-eight hours elapsed ere opisthotinos followed after the appearance of trismus. In the rapidly progressive cases drugs of the sedative class relieve the distress, which belladonna or any stimulant can not be expected to do. Some twenty years ago, during a conversation with the late Mr. John Cooper of this town, who had been engaged in surgical practice for about fifty years, he expressed his conviction that tetanus never occurred if the patient, after traumatism, was subjected to a course of opiates. To this opinion I was inclined also, and for many years practised this supposed precautionary measure, but now I am perfectly satisfied, that no opiate will act as a preventative. This is known to me from practical experience, and from what I hold to be the mode of action of drugs of the opiate class, it would not be reasonable to expect it. Indeed, I would prefer to commit myself to the opinion, that opiates would facilitate the incubation of true tetanus rather than tend to prevent it. But the theoretical objections that can be urged against the use of opiates, as preventors of tetanus, do not equally apply against their use in the symptomatic treatment of tetanus when it has become fully developed, as the indirect method of treating tetanus may then benefit. The administration of belladonna is the practice of a direct method of medication and is both rational and theoretically correct, so long as the symptoms are not fully developed; for, as the sympathetic is only invaded gradually by the inhibitory cause, belladonna may diminish the intensity of the coming storm, if not atrest it, by stimulating the sympathetic in front of the advancing inhibition. Theoretically we might expect belladonna to be a preventative of the incubation of tetanus. For some few years I have been trying what belladonna can do, in protecting traumatism from the accession of tetanus, but my experience is too limited to warrant my expressing an opinion of the value of anticipatory stimulation of the sympathetic as a preventative of tetanus. If antidotal treatment can prevail when poison is present,—shorten its duration of action—then certainly preventative medical treatment may hinder or at least mollify a disease should it be incurable. The tendency of medical opinion in our days. in the direction, that no disease, contagious, septic, etc., can be arrested or shortened, has been allowed to influence practice too much—so that even our faith in remedies has been

It is a remarkable confirmation of the reasonableness of the supposition, that inhibition in one area, may lead to deflection or extra accumulation of nerve force in other areas. That we find that nearly all diseased states in which inhibition gives character to the primary signs of the abnormal condition are attended with some degree of excitement outside of the site of the lesion or ground of incubation. Of this we have examples in epilepsy, palsy and tetanus, and again in ague and cholera.

There is another important feature in favour of accepting the opinion "that inhibition is the suspension of life, not the action of special nerves," namely, that it confirms the law laid down by a great surgeon* in regard to septic diseases, that "no two of them can exist in the same part of the body at the same time." This law was again confirmed by another acute clinical observer†, in his "Observations on Morbid Poisons." Although the latter does qualify this axiom by admitting that two septic poisons can sometimes affect the

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thereby weakened. Traumatic tetanus not due to septic influence, that is dependent upon centripetal irritation, we can only hope to successfully aid by sedatives. This rare form of tetanus I have only twice met with, although all the prominent or secondary signs were present in an intense degree in one of them, there were in these cases no evidences of sympathetic inhibition, the patients recovering by the subcutaneous use of morphia in the graver case, and opium by the mouth in the other, the drug acting like a charm. These are the class of cases which we sometimes see reported in the Medical Press, as being relieved by amputation and other surgical interferences.

* John Hunter.

† Dr. Joseph Adams.

same parts, he also adds that such are only exceptions which prove the law. With the conclusion of these two practitioners of our art I fully coincide, and will here try and give my grounds for believing that they were right in their teaching. *

By reconstructing the written axiom relating to the impossibility of the simultaneous, dual incubation and action of septic matter, it is possible to define a law to which there can be no *clinical exception* that is appreciable.

It is this, that no two or more septic poisons can affect the same parts, if singly, they are of contrary properties—one indicating inhibition of life, the other excitement. But septic matters possessed of similar properties may have been seen in dual action,—both inducing excitement or both inducing inhibition.

The dual incubation of typhoid and typhus is a reasonable supposition, which is confirmed by clinical observation, indeed, it is highly probable that they are often in action conjointly, oftener than they are diagnosed. Both the typhus and typhoid poisons indicate true stimulation, though the areas of their several actions are nearly but not exactly identical ; the former

* I am aware that Murchison, Aitken, Brown and others have recorded facts which appear utterly opposed to my views. These facts are certainly indisputable. It is their conclusion that is here maintained to be wrong. During the time I was assistant to my teacher, the late Dr. O. Roberts, at the Workhouse, St. Asaph, he repeatedly showed me instances of dual septic disease, and from my knowledge of his abilities as a clinical observer, I believe his diagnosis was probably correct.

notably affecting the sensorium whilst the latter more affects the sympathetic. Thus, in most instances of dual action of these poisons, this action can be diagnosed, but when single, a differential diagnosis is not so difficult.

"Virchow has related a case of typhoid, combined with striking symptoms of cholera."* This was only *a case* with *striking* symptoms. No more. The supposition that the poison of typhoid and cholera can jointly manifest their action, so as to be clinically appreciable, is an impossibility.† To teach the possibility of the dual incubation of septic matters with divergent qualities, which the action of the germs of typhoid and cholera indicate, is to maintain a physiological paradox.

It would not be unreasonable to admit the co-presence in one subject of more than two germs productive of diseased states, provided they affect separate areas during incubation,‡ no matter what might be the qualifying action of such germs.

* Aitken, Practice of Medicine, vol. i., page 131.

† There is a remarkable confirmation of this to be found in Aitken's Practice of Medicine, vol. ii.. page 246. Dr. Williams, of St. Thomas's Hospital, reports a case suffering from tertian ague, in which the ague subsided and smallpox appeared, but after the smallpox had run its course the ague reappeared. This is an example of two poisons with divergent qualities, acting antidotically, but not acting conjointly as regards time, the ague poison tending to inhibition, the smallpox virus tending to stimulation.

‡ By acting in separate areas proper combinations of drugs are well known to act more pleasantly and effectively than single drugs, for the very obvious reason that defective co-ordination of action is avoided; thus, for instance an aperient secures a more general permit to pass.

But such an occurrence would give such a compound of symptoms, that their clinical diagnosis could only be made from physical changes rather than physiological ones.* The poisons of typhoid and cholera are diametrically the opposite in action, and limit their action to the "same parts."

The interpretation of the phenomenon of inhibition given in this treatise, points out a reasonable explanation of the mode by which predisposing causes favour the development of the exciting cause in septic diseases. Frequently a morbific disease has seemingly appeared to have resulted from a non-septic causation, such as exposure to cold, fatigue, shock, excitement, panic, hurry, worry or depression of spirit. It has been too generally supposed that the predisposing cause to morbific disease must be one that debilitates or inhibits life, but there are good grounds for believing that a cause which even accelerates life is the more probable predisposing cause to some morbific disease. By considering the phenomena of latency or delayed incubation of septic poisons, some light can be thrown on the question as to the mode of action of predisposing causes. We know that the period of latency, which precedes the development of the signs of any septic disease is never uniform; consequently, the physiological suitableness or unsuitableness of the ground

* Dr. Aitken also mentions a case of triple disease reported by Ring, namely smallpox, measles and whooping cough. This could have been diagnosed from its physical aspect.

for incubation of the poison, must vary in each individual, some being able to escape contagion or infection from this unsuitable condition being a total hinderance to incubation. This immunity, it is reasonable to believe, does not depend upon the excellent standard of health the individual may possess, but probably from the accident that no predisposing cause could exert its action in the direction of the path of the morbific poison. Some of our septic diseases—as typhus and typhoid—select the robust, these are fevers of the sthenic type; other morbific diseases, such as cholera, select the feeble, notably the "old soaker," these are of the asthenic type. In the first, the predisposing cause probably fans the flame of life; in the second, the same cause probably blasts or inhibits the vitality of a frame already enfeebled or depreciated by the popular practice of some degree of continuous inhibition as, for instance, alcoholic drinking.

A septic poison, which favours inhibition, may have its period of latency shortened by any event or action that depresses life, while another such poison possessing qualities that are indicated by vital excitement may have its period of latency shortened by an event which tends in the same direction. That events or predisposing causes are often factors in the development of the excitants of morbific disease, is generally admitted; but, if my interpretation of the mode by which they can favour the development be correct, it follows that the predisposing cause of one septic disease may act as

a preventative of the incubatian of the germ of another septic disease. The evidence upon which we have accepted the possibility of a predisposing cause, as aiding the incubation of germs productive of morbific disease, is mostly from an unprofessional source, as the history of the patient before the medical attendant was called to attend. But by attention to the very same source of evidence, we find a widespread belief, that a coming attack of these diseases has been warded off by the immediate practice of details which are not similar in their effect. It is a popular expression in speech, "I took it in time and worked it off," meaning that success had been gained. The opinion that by prompt recourse to certain methods contagious and infectious disease may be aborted, is not confined to the unprofessional public, as authorities in medicine have recorded their inclination ro this opinion. My purport in discussing this question is to try to show that there is some good foundation for this general opinion. The successful cases of what is also termed "shaking off" the exciting cause of a disease, are no doubt instances in which the artless individuals practised by chance appropriate remedies, as we well know that the unsuccessful cases form the majority; and this is to be expected at all times, as from our experience in the antidotal treatment of toxic poisoning by drugs, that even when the time of poisoning and the remedy is known, a minimum of time is a very important item towards success in saving life.

Some of the most able physicians living in our time have recorded that, they have observed abortive cases of typhus, typhoid, smallpox and of other septic diseases, and this ought to encourage us to hope that, by an early knowledge or suspicion of special contagion or infection, we may be able to prevent incubation.

Physicians, like the surgeons of the early part of this century, are taking for granted that there are more immovable impediments in their front than there actually exist. Many barriers that were thought, forty years ago, to be impassable to successful surgical treatment have been removed, and it is my strong conviction that the art of preventing and prescribing for diseased condition will before long be so completed, that practice of medicine will become as uniform and as effectual as the manipulations of surgery are, and, towards the advent of this great progress in therapeutics, the study of the phenomena termed inhibition will greatly contribute.

The evidence advanced in support of the theory propounded in this pamphlet is certainly not sufficiently extensive to warrant its being accepted as correct. It has been subjected to every test known to me, and in every comparison the result has been satisfactory. I believe that it explains all the phenomena in connection with inhibition and the varied action of drugs, and, should it stand the tests which many others can better apply, it must lead to a greater uniformity in medical practice. During these last thirty years, there has prevailed much

dissent in therapeutics, some accepting those views which are popularly termed the orthodox opinions in regard to drug action, others seceding, and guided by a theory, perhaps true, but not containing the whole truth, others covertly disbelieving in the curative tendency of any medicine; or, after years of scientific and clinical study, like my eminent fellow-townsman Dr. Inman, openly and courageously proclaiming that "men, horses, tigers, monkeys or codfish can do without doctors."

CONTRIBUTIONS TO MEDICINE AND SURGERY.

This Volume will comprise the following Parts:—

PART 1. Intestinal Obstructions. (*Published.*)

PART 2. The Principles of the Treatment of Joint Disease, Inflammation, Anchylosis. Reduction of Joint Deformity, Bone Setting. (*In the Press.*)

PART 3. The Principles of the Treatment of Fractures, Recent, Delayed, and Un-united.

PART 4. On the Reduction of Dislocations.

PART 5. On Fractures of the Lower Jaw. (*Published.*)

PART 6. Fractures, Dislocations, Diseases and Deformities of the Bones of the Upper Extremity.

PART 7. Fractures, Dislocations, Deformities and Diseases of the Lower Extremity.

PART 8. The Inhibition of Nerves by Drugs. Proof that Inhibitory Nerve-Fibres do not exist.

PART 9. Spinal Deformities.

PART 10. Lithotomy.