PROPOSAL OF A NEW METHOD OF TREATING

THE BLUE EPIDEMIC CHOLERA

BY THE INJECTION OF HIGHLY-OXYGENISED SALTS INTO THE VENOUS SYSTEM.

Read before the Westminster Medical Society, Saturday, Dec. 3rd.

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It is with feelings of no ordinary hesitation that I venture to solicit the patient consideration of the Westminster Medical Society, while I lay before them in the briefest terms I can employ, an outline of some suggestions regarding the treatment of the Indian cholera. I say that it is not without much hesitation that I do so, because on every previous occasion on which I offered any contribution to this Society, or to the general profession through the medium of the medical press, the subjects I treated of were of that obviously experimental kind that I scarcely dreaded contradiction in the inferences I deduced or the arguments I brought forward. In the present instance, it is true, that the foundation of the subsequent observations is also strictly experimental and demonstrable in its nature. Nevertheless the conclusions I may draw are, I feel, rather more calculated to admit of discussion than was the case with any of the previous topics to which I have invited your notice.

From all the statements and histories yet published on the *treatment* of *the* cholera, it is evident that notwithstanding the numerous therapeutic methods hitherto prescribed, the disease still retains so much of its appalling virulence that under certain hygeienic imperfections, in peculiar states of crowded populations, of public moral depression, &c., it sometimes bursts forth with such extraordinary fury that medical aid, however instant, fails in arresting its deadly progress. Of the truth of this assertion sufficient evidence is borne by the history of the Warsaw epidemic, during which eventful period, when the loss of the battle of Ostrolenka threatened the Poles with the immediate fall of their capital, the pestilence assumed so frightful a pitch of violence that we learn from MM. Foy, Brierre de Boismont, and others, that medical assistance, however speedy, however skilful, fell powerless beneath the onset of the disease. Yet in Warsaw there was a combination of the most talented, experienced, and devoted men whom medicine ever furnished to the succour of mankind.

Again, to approach nearer home, we find that in Sunderland the mortality in the cases once termed "*malignant*" is still so great that the experience of the past seems almost valueless for present or future protection. That medicine, as at present administered, prevails in many cases, I do not deny, but that on the other hand cases still occur so violent as to defy its powers is equally manifest. Hence, doubtless, has it arisen that up to the moment in which I address you, the most *practical* men in our profession are occupying themselves assiduously in the search for some more specific remedy than has yet been discovered. I need, indeed, no stronger proof of the legitimacy of these efforts than to point out the distinguished, and above all, *experienced* individuals engaged in their prosecution.

The habits of practical chemistry which I have occasionally pursued, naturally led me, as well as others, to inquire whether in the remote causes, the pathology or physiology of this disease, any data could be discovered which might lead to the application of chemistry to its cure.

Looking to the *remote* causes of cholera, it was quickly evident that though admitted by the majority of deliberate writers on the disease, to be *a poison* (an idea in which I fully coincide), yet so utterly unknown is the chemical nature of this agent, so ignorant are we even of its physical characters (some terming it "animal," some "vegetable," some "aërial" or "terrestrial," and others even endowing it with life); in such utter darkness, I repeat, are we regarding its true constitution, that to attempt to supply an antidote *on the recognised chemical* principles which toxicologists have determined, could possibly be attended with no beneficial or even encouraging results.

Looking then to the stages in the malady consecutive on the operation of the remote cause, what are the cognisable circumstances which may rationally fix our consideration? What, in other words, are the physical changes, if any—what the chemical alterations, if such there be, which the operation of this cause has effected, either in the fluids of the human organisation, or in the solid vessels, &c., in which these fluids are contained?

To answer this question correctly, we must be cautious to take the disease into consideration only in its abstract, *essential* forms, divesting it of all *accidental* phenomena of symptoms and pathology, &c. In the case, then, of abstract cholera, in the "cholera foudroyant" of the French writers from Warsaw, what are the first effects of the remote cause?

The all-but-unanimous evidence of those who have witnessed the disease in this its most appalling, though its simplest shape, teaches us that universal stagnation of the venous system, and rapid cessation of the arterialisation of the blood, are the earliest, as well as the most characteristic effects. Hence the skin becomes blue—hence animal heat is no longer generated—hence the secretions are suspended; the *arteries* contain black blood, no carbonic acid is evolved from the lungs, and the returned air of expiration is as cold as when it enters these organs. Such are the primitive effects of the remote cause, and these again constitute the causes of a third set of phenomena, to which it is unnecessary for me to advert on this occasion.

The questions then naturally suggest themselves, Will the alteration of this black and thickened condition of the blood to the state of arterialisation, prevent the sequelæ of exhaustion, impeded secretion, &c., by which the fatal event is induced? and, secondly, What is the best mode by which this artificial arterialisation can be effected, if we admit the probable benefits of the change?

In commenting on the first question, we must at once admit, that in all diseases it would be desirable to counteract the remote cause, if that were possible, according to rational principles, or had experience, no matter though empiric, lent encouragement to the attempt. Experience, however, having fully shown its frequent impracticability in the present instance, we may, I believe, without discussion, confess the justice of attacking the effects. Such a proceeding, moreover, is not without precedent in the treatment of several other affections, in which the produced effect reacts upon, and favours the fatal influence of the primary cause.

So generally acknowledged is this principle in the present case, that in the treatment of the disease now before us, we find a great majority of practitioners earnestly recommending *venesection*, not as a sedative, not as an antiphlogistic, not as a blind empirical specific, but as a means of diminishing the venous congestion, of thus restoring the suspended circulation, and of again recovering the arterial qualities of the blood of which a bright scarlet hue is an outward and visible sign. Such are the principles of Dr. Johnson; such of Mr. Bell, one of the most philosophical writers who has discussed this subject; such are the views of the eminently experienced Annesley, such of Dr. Kennedy, the practical part of whose volume must at least receive our warm approbation; such, in short, are the opinions of a vast majority, if not of all of the writers who have *reasoned* on the essential phenomena of this affection.

Again, another class of physicians embracing the same views, propose by different means to attain the desired object, and in order to remedy the absence of arterialisation, they recommend the inhalation of oxygen gas, or of a mixture of oxygen and atmospheric air, or of the protoxide of azote, that singular aërial compound, to which the name of the "laughing gas" has been applied.

Now it might rationally be imagined, that the success or failure of these methods should afford us a touchstone of some authority, in deciding on the rationality of the principles on which they are practised; and accordingly we find it established by numerical returns of the most convincing kind, that the depletion of blood, whenever *practicable*, whenever performed in *sufficient time*, and when not contravened by peculiar circumstances, of idiosyncracy, particular debility, &c., has effectually removed the effect, and remedied the operation, of the remote cause; in other terms, has cured the disease.

Before proceeding any further, therefore, it is necessary to examine briefly into the causes which interfere with the universality of this remedy; and these I apprehend may be found to reside *in the debilitating influence*, whether transient or permanent, which the detraction of blood sometimes occasions, and which, when added to the debilitating effects of the remote cause, becomes sufficient to overwhelm irremediably whatever vital power still clings to the system. Again, for strictly mechanical reasons, blood may not be procurable; and when we consider that the forces which the venous circulation obeys, are almost completely suspended in the violent cholera, it can scarcely be a matter of surprise that detraction of blood by venesection should frequently be found an impossible operation.

That the inhalation of oxygen gas has failed remarkably in achieving the desired end, is unhappily too notorious. To those however who examine closely into the cause of the failure, the want of success will not be found in the least degree to invalidate the principle that rearterialisation of the blood should tend powerfully to the cure of the disease. Many causes, indeed, conspire to prevent effectually the entrance of the gas into the circulation. The lungs in numerous cases, as proved by the dissections in Warsaw, are thickly invested with the same pultaceous matter which is of familiar occurrence in the intestines; again, the suspended motion of the heart permits but an insignificant stratum of blood to be exposed to the aërial medication, even though the mucous membrane was free from this peculiar excretion.

Admitting then, according to the practice of the venesectionists, that the detraction of blood is successful under favourable circumstances, by obviating the primitive effects of the remote cause—viz. by re-exciting the current of the blood, and, consequently, permitting new strata of that fluid to be acted upon by the inspired air—admitting this, and further recollecting the manifest causes which occasionally preclude the success of this mode of arterialising the blood, let us next inquire whether there does not exist some certain method of inducing this apparent arterialisation, and that free from the incidental objections to which venesection and gaseous medication are liable. That such a method can be followed, I trust I shall be able to render probable.

It is previously necessary to understand what authority there is for assuming that arterialisation is a chemical process, and that it is legitimate for us to derive therapeutic conclusions from experiments on blood apart from the living body. On this point I deem it unnecessary to dwell any further than by quoting the opinions of Dr. Christison, whose distinguished reputation as an accurate chemist, a *rational* physiologist, and an able practitioner, entitles him to our most unlimited confidence. I quote from his excellent paper on "the mutual action of blood and air," published in the *Edinburgh Medical and Surgical Journal*, and as I have mislaid the number of that journal, I am obliged to re-translate his expressions from the version which appears in the *Archives Générales de Médecine* for October of the present year.

"It is then thus clearly proved that when venous blood assumes the scarlet colour of arterial blood by agitation with atmospheric air, that a considerable proportion of the oxygen of this air disappears. *Carbonic acid is formed*, a much larger quantity of which would be found on analysis, did not the serum possess the property of absorbing a large quantity of this gas. Thus all the essential phenomena of the arterialisation of the blood in the lungs *during life*, at least as regards the change of colour of the liquid *and the alteration of the air*, take place equally in the blood out of the vessels, and consequently these phenomena are *independent of vital action*."

Arterialisation and oxygenation being then used as synonymous terms (and did time or space permit, I could adduce ample additional proofs of their identity), is the oxygenation of the blood *only* to be effected by the decomposition of oxygenated *gases*? The supposition would be absurd, and we have the arguments of the most unbounded though precise analogy, and of actual experimental facts, to convince us, that highly oxygenised *solids* or *fluids* can work the same effect; that as nitrates and chlorates (salts at the maximum of oxidation) can oxygenise the metals and other simple substances with which they are brought in contact, so can these salts, and many others of similar constitution, enter upon the same play of affinity with the blood that occurs between it and the atmospheric air. Oxygenation of the blood, or arterialisation, may, I repeat, be accomplished by other oxydising agents besides those of the gaseous class. Time does not permit me to narrate the experimental proof of this position, but I am for the present perfectly satisfied to maintain its validity by a reference to the well-known laws of oxygenation in the several departments of inorganic and *organic* matter.

It seems to me, then, that, if we could bring certain salts of a highly oxygenated constitution fairly into contact with the black blood of cholera, we would certainly restore its arterial properties, and most probably terminate the bad symptoms of the case. It is however obvious, that in a disease so electric-like in its rapidity, and one moreover in which circulation is almost suspended, and the intestines generally covered with a thick pultaceous paste, it would be a vain expectation were we to imagine that, as in the more protracted yellow fever of *Santa Cruz*, alluded to by Dr. Stevens, time would permit of the absorption of the saline oxygenating materials from the alimentary canal. I therefore conceived the idea of injecting into the veins such substances as an examination of the blood in cases of cholera would show to be most capable of restoring it to the arterial qualities. Before so novel, and apparently startling, a practice as the injection of such remedies into the veins of the human subject could be prudently put into execution, it is necessary to have distinct notions of the effects of the individual salts on the blood without the body, and also while still circulating in the living frame.

Of the salts which contain the greatest quantity of oxygen, and possess most powerfully the action of oxidizing venous blood, may be mentioned the nitrate and chlorate of potash. A very few grains of either of these salts are amply sufficient for effecting this change in a larger quantity of blood than the pulmonic circulation usually contains. Again, we know by clinical experience of the most extensive kind, that nitrate of potash and chlorate of potash enter the circulation from the stomach and alimentary canal, and pass off in the urine, wherein they may be detected without offering any injury to the organisation of the blood through which they passed. From these two facts, it is evident that the injection of the nitrate of potash or chlorate of potash at the veins could possibly do no mischief, and might effect much good, when carried into effect with the precautions to be presently pointed out. In corroboration of the probable efficacy of this mode of treatment, I will briefly allude to two experiments which, in the prosecution of some toxicological inquiries, I availed myself of the opportunity to perform, about three months after Dr. Stevens's researches and experience were laid before the profession.

In one series of experiments, a healthy large-sized mongrel dog had, on different occasions, from ten to sixty grains of the chlorate of potash, dissolved in three ounces of tepid water, injected into one of his cervical veins. He seemed to experience no ill effect; the pulse rose in fulness and frequency; he passed urine copiously in a short time, and the urine, when concentrated, gave incontrovertible signs of its containing the chlorate. Blood drawn from the brachial vein had a fine scarlet colour.

In another series of experiments performed on the same animal, he was brought into a state of poisoned asphyxia by the insufflation of prussic acid vapour, or sulphuretted hydrogen gas. While stupified, indeed apparently dead, from the former, the brachial vein was opened and a few drops of excessively dark blood could with difficulty be procured. Half a drachm of the chlorate of potash dissolved in water of the temperature of the blood was injected slowly into the jugular vein; the pulsation of the heart almost immediately began to return, and in the course of eight minutes, scarlet blood issued from the divided brachial vein. In twenty minutes the animal was nearly recovered and passed urine copiously, the secretion affording the usual evidence of its containing the injected salt.

I trust I may not be mistaken, so far as to suppose that I regard the preceding experiments as proofs that the practice of injecting the veins would prove equally successful in the blue cholera of man. The widest inference I wish to derive from them is the evidence they seem to afford, that no disorganization of the blood is thus produced, that the blood in the living animal is thus restored to the arterial tint which the poisonous agents had destroyed, and that the processes of respiration and circulation were thereupon immediately resumed.

On the whole, I conceive that the preceding facts are amply sufficient to warrant us in trying this new method, unless some strong objection be made to its peculiar nature.

The practice of injecting the veins in desperate cases with substances of still more energetic properties than those which the chlorate of potash possesses, is by no means new to medicine. In an extensive and brilliant series of experiments performed on horses at the veterinary school of Alfort, Dupuy demonstrated the extraordinary success attendant on this practice, and the safety with which carbonate of ammonia and many other substances could be injected into the venous system. Again, the records of toxicology afford us examples by no means unique, of the successful injection of tartar emetic into the blood in cases of hopeless narcotic poisoning. In the Journal des Progrés, vol. 3, 1830, MM. Percy and Laurent relate the cases of three Russian soldiers cured of tetanus by injections of opium into the veins. In the same journal, the same writers also mention other cases of tetanus successfully treated by the injection of a decoction of twenty-four grains of the datura stramonium in half an ounce of water.

I trust I have now said enough to induce and justify the trial of this new proposal, at least *in the fearful cases in which venesection is found impossible, and the violence of the malady derides all other means of medication*. Should the method be found to succeed, it will have the advantage of fulfilling all the objects which Messrs. Bell, Kennedy, and Annesley, hold in view when they practise venesection, and that without threatening to induce the debility which the detraction of blood is thought by many to endanger.

In the performance of the operation, the circumstances of the disease must be borne in recollection. When the current of the circulation is impeded, as in the blue cholera, injection from the bend of the elbow can scarcely be efficient. I would, therefore, suggest that the tube, which should be of gold or ivory, be introduced into the external jugular vein immediately as it crosses the sterno-mastoid muscle. I would select this place as the nearest spot to the superior *cava*, free from the danger of the entrance of air caused by the suction force of the right side of the heart, an influence which Berard has shown to be ineffective in the introduction of air, except where the flaccid orifices of a divided vein are kept gaping and stretched by adhesions to adjacent prolongations of fascia or condensed cellular substance; as is remarkably the case with the subclavian and with the jugular in the lower third of its progress. The syringe used in the injection should contain no more than three ounces, the solvent should be distilled water heated to a blood warmth, and the syringe also equally warmed. The tube should not be more than an inch long, and curved gently for the convenience of manipulation, and it should have a marked conical form. In performing the operation, after the vein is exposed, I would make a puncture with a lancet, just sufficient to permit the introduction of the tube, but I would by no means detach the vessel from its connexions. The injection should be deliberately and slowly performed. From ten to thirty grains of the chlorate might, I think, be safely employed. *It would, however, be essentially necessary that before the experiment was tried, a minute analysis of cholera blood should be performed,* and the effects of the oxygenated salts examined, as to the change of colour and their influence on the affinity of that blood for oxygen in its uncombined or its nascent forms. To my mind no satisfactory analysis of the blood in cholera has yet been completed. HERMAN's, the most recent and most minute, is still, I am prepared to prove, far from deserving implicit confidence.*

To restate then, briefly, the suggestions advanced in the preceding observations, I propose to effect by the injection of powerful oxygenating salts, directly into the veins, that change to the arterial state, which Mr. Bell and others attempt by venesection, an operation which, though fraught with the utmost utility in many cases, is in others palpably inadmissible even on the testimony of its warmest and ablest supporters; and in all other cases, when performed after a certain lapse of time, is asserted by some high authorities to be hopeless if not dangerous in the extreme.

2nd. This mode, by injection, I have shown, by the experiments which I myself performed, to be free from the imputation of its being unsupported by analogous facts. I have also shown that in other diseases of imminent peril, venous injection has been boldly and successfully practised with substances, themselves even possessed of virulent energies.

3d. The substances I recommend to be employed are proved by numerous experiments to exert no coagulating, corrosive, or solvent agency on the blood, they passing through the circulation freely in healthy animals and in man.

4th. *I have limited the proposal on its first employment to those awful cases in which all other systems of medication are shown to be inert.*

In conclusion, then, I trust I may be permitted to express my hope, that in appearing before you for once in a speculative character, I have not been guilty of wasting your time with utterly profitless speculations. Were I willing to trespass on it more fully I could derive many additional arguments from the recent admirable analyses of healthy blood performed by Lecanu of Paris, and which prove the errors of M. Herman's experiments; from the consideration of the theories of Herschel and Prout regarding the agency of minute quantities of saline matter in the blood; from the investigations lately published by my eminent friend Dr. Christison, on the mutual action of blood and air; from the researches of Faust and Togno and Mitchell of Philadelphia, and of Graham of Glasgow, on the endosmose and exosmose of gases, and the influence of this extraordinary action on the oxygenation of the blood; from the clinical researches of Reid Clanny of Sunderland, of Cooke of Kentucky, and others. I did intend to draw collateral support from a reference to Dr. Stevens's researches in Santa Cruz; that author, however, being, as I have been since informed, on the eve of publishing full and detailed accounts of his inquiries, I have deemed it imprudent to press his investigations into the present paper. Lastly, I think it right to say that I have designedly avoided any comment on the physiological treatment of the remote cause of the disease.

Before I conclude, I have further to request your attention to the circumstance of a similar recommendation to that I now venture to propose, being published this day in a weekly medical journal,* nearly in the words I uttered last Saturday evening when giving notice of my intention to propose the injection of saline substances into the veins. If the treatment of a disease so afflicting as that which we are now discussing were a legitimate theme for the indulgence of any expressions of disappointment or irritation, I might be apparently justified in complaining of this circumstance. I might appeal to the gentleman who presided on the last evening—to the secretaries—to the meeting itself, whether I did not distinctly make the proposition. I might appeal to Dr. Johnson, who has received a written communication from me on the subject on Tuesday last. I might even appeal to the reporter of the

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* Herman mentions *free acetic* acid as an ingredient in healthy blood. He also states that after coagulation of the cholera blood, the crassamentum was *acid* and the serum *alkaline*! It is unnecessary to dwell on the latter statement, as it involves an impossibility. Concerning the first, it is sufficient to observe that in the best analysis of the blood ever performed—viz. that by M. Lecanu of Paris, and for which he obtained the gold medal from the Academy (vide *Journal de Pharmacie, September and October* 1831), no statement occurs of the detection of acetic acid, though, had it been present, M. Lecanu's process must have revealed its existence.

* The name of the journal was mentioned by Dr. O'SHAUGHNESSY.—ED.

journal in question itself; and, lastly, I might call upon a gentleman to whom, on Saturday evening last, I read the notes of my brief paper. But, Sir, I forego all these feelings, for, on reflection, I think it is extremely unlikely that any member of our profession could be wilfully guilty of the baseness of thus embezzling the ideas and suggestions of another, however valuable or valueless these suggestions might be. I am, therefore, rather inclined to express my great pleasure, that the principle of this proposition should receive support from so respectable a quarter. There is, however, thus much difference between us. The medical journal recommends the injection of common salt, the *chloride* of *sodium*. I, on the other hand, advise that of the nitrate or chlorate of potassa. I would venture to remind the editor that *chloride* of *sodium*, though it does redden venous blood, cannot possibly oxygenate it, as *it contains no oxygen itself*. There are, indeed, many substances capable of reddening blood, which cannot arterialise or oxygenate it. Hydrogen gas, for example, is stated by Dr. Davy to possess this quality. I believe it will, therefore, be conceded, that as far as theory is concerned, the salts I mention are likely to ensure more satisfactory therapeutic results than that which the writer in question has proposed.

LONDON MEDICAL SOCIETY.

December 5, 1831.

Dr. Burne, President, in the Chair.

THE CHOLERA.

The subject of the blue epidemic cholera has obtained its share of attention here, as well as at the Westminster, although this Society has not had the advantage of numerous newspaper paragraphs to secure for its late meetings the "overflowing audiences" of the other institution. Indeed, at this elder and more sedate association, the members would be "frighted from their propriety" by the sieges of two or three hundred visitors which have added to the *eclat* of the more westernly society.

On the present occasion one of the "cholera lions" (Mr Searle will pardon the term*) attended and admixed a share of personal experience with the speculations which necessarily occupy the debates in London. The excitement amongst medical men in London on this subject is very great, and certainly the decimating pestilence will not arrive so far south without meeting with abundance of combatants who have held due preparative discourse respecting it and its horrors.

With a view to reduce points of discussion into as small a compass as possible, the President, on introducing the subject of *the cholera*, divided the text into four heads of discourse, to which he requested all observations might be confined. 1. Its history. 2. Instances in which it could be proved to have been communicated by contagion, whether from personal contact with the affected, or the handling of garments; and whether any party present would feel it as safe to sleep in the wards of a hospital filled with cholera patients, as in a hospital filled with cases of rheumatism or ague. 3. The symptoms of the various stages and their morbid appearances. 4. The treatment of the various stages.

Mr. Searle presented himself to the meeting, and, directing his remarks to the second head, stated that he believed, on the following grounds, that the epidemic cholera was not necessarily contagious. He had had from thirty to fifty patients at a time under his care in a hospital at Warsaw, during two months of which period, not a single case of cholera had occurred in any of the attendants, who had eight or ten of them of a night by turns slept in the unoccupied beds which were mingled promiscuously amongst the sick. These people were always attending the patients, putting bed-pans into their cots, assisting in the dissecting-room, sewing up the dead bodies, which were very numerous, and burying the dead. Throughout his (Mr. Searle's) entire period of residence, only one man attached to the hospital was attacked, and he had nothing more to do with the patients than to assist the apothecary in compounding the medicines. This man had been intoxicated for several days, received a severe beating for it, was afterwards confined two nights in a damp building, where it was said he had his shirt taken from his back, took the cholera, and died. He (Mr. Searle) had himself constantly resided, and slept, in wards in India where there were above a hundred patients whom it was impossible to leave for an hour, and yet, during fourteen years of intercourse with the disease, he had never known a case of what he could consider decided contagion. He certainly imagined, however, it might become contagious under a particular combination of circumstances. Yet every-thing he saw discountenanced the opinion that it was *propagated* by contagion. In Warsaw there were ten professional gentlemen sent thither by the French government, who constantly visited the hospitals, witnessed the *post-mortem* examinations,

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* A Sunderland practitioner might gain a large sum by showing himself in town just now, at half-a-crown a head.