ON SOME
NEW DOUBLE SALTS OF CARBOLIC ACID,
PARTICULARLY CONSIDERED
AS AGENTS FOR THE TREATMENT OF DISEASE.

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1. THE progress of scientific inquiry has tended greatly to establish the doctrine that many of the diseases which afflict the animal body are due to the influence of organized particles, and that these germs of disease transmitted “*ab extrâ*” to the living organism, grow and multiply, and by their growth and multiplication inaugurate the various phenomena of disease. That this morbid process bore a striking analogy with fermentation had long ago been taught. This analogy, however, is established with a much greater completeness now that Pasteur has demonstrated the true nature of fermentation, viz. that it depends upon the presence, development, and multiplication of specific organized bodies of extreme minuteness, The same kind of observations which

established this fact in regard to ordinary fermentation is now in course of application to the investigation of the changes in the body induced by communicable disease; and some of the conclusions which have been arrived at are deserving of rank amongst the best-established truths in biology. Thus, the researches of Beale and Chaveau have shown that the manifestations of the vaccine disease are due to the operation of minute organized particles which float in the fluid of the inoculable vaccine.

2. Concerning the physical qualities of these organized germs, it is known that, though they vary in size in the cases of different diseases, they are almost incalculably minute; in some instances they cannot be removed from the fluid in which they float by the most careful filtration; they, for the most part, manifest phenomena of active movement, which is sufficient to prove that, minute as they are, they are composed of segments of still more extreme minuteness; they have a long-persistent vitality, and can resist the influence of high temperatures, though a heat of 100° C. is usually sufficient to destroy them.

3. These germs are readily capable of destruction by certain influences. Some chemical agents kill them by effecting their decomposition; other agents render them inert by robbing them of their vital endowments. Before their nature was understood, processes of "disinfection" for the prevention of the communication of transmissible diseases were largely practised. It is now generally admitted that the efficacy of measures of "disinfection" is due to their influence in destroying the organized germs of disease. This destruction disinfecting agents can accomplish in three modes—*First*, by altering the chemical constitution of the organic matter composing the germs; they may, like chlorine or iodine, superinduce an oxidation of the organic bodies, or, like tannic acid, they may cause a deoxidation thereof, or, as in the case of some metalline salts, they may unite with them and form a definite chemical compound. *Secondly*, by destroying the life of the germs without inducing any manifest chemical change; it is by this mode that carbolie acid has

been shown to operate. Or, *thirdly*, by a combination of these two modes, as in the case of sulphurous acid and the sulphites, which, when they act chemically, act as deoxidizers.

4. Although chemical and other means had long been adopted to arrest the vitality of germs of disease external to the organisms of those subject to their influence, it was not until recently that any plan of treatment was adopted with the avowed object of destroying the germs when once they have entered the living body, and when they are, by their growth and multiplication within the organism, actually causing the manifestation of the phenomena of disease. In 1861 Professor Polli, of Milan, instituted a plan of treating zymotic diseases by the internal administration of the sulphites and hyposulphites of the alkalis and alkaline earths, and the plan, according to the testimony of a large number of observers, has borne fruit in a large amount of success. Professor Polli, however, did not claim for these agents that they actually destroyed the vitality of morbid germs within the body, but he considered that, diffusing throughout the constituent tissues of the body, they rendered the latter an unsuitable soil for the growth and propagation of the germs; the sulphites, he said, operated, not upon the fermenting agents, but upon the "fermentible stuff" of the economy. I have carefully traced the operation of the sulphites both experimentally and practically in the treatment of disease, and I am convinced that their action is upon the organized germs themselves.

5. It is found that *traces* of sulphurous acid are sufficient to prevent the fermentation of a large mass of saccharine material. I have myself found that five grains of sulphite of soda completely prevent the fermentation of fifty grains of cane sugar mixed with an equal bulk of yeast; while the presence of two and a half grains under similar conditions restrained fermentation in the proportion of 38 to 11. It is obvious, from the small amount of the agent required to produce the effect, that the result cannot be due to any chemical power of deoxidation that the sulphite possesses. Furthermore, if the sulphite of soda be administered to an

animal, in the tissues of the latter after death the salt is proved to exist as undecomposed sulphite ; as sulphite, also, it for the most part appears in the urine. Although, however, it is thus shown that the salt exercises a very slightly appreciable chemical change upon the organism, it is ascertained that it almost totally prevents post-mortem decomposition. From a large series of observations it may be concluded that the sulphites arrest and prevent the development of organized germs, and there is great reason to infer that they do so by reason of no chemical influence, but by reason of a faculty which they possess of arresting the vitality of low organisms. The lesson taught by the results of the treatment instituted by Professor Polli appears to me to be that a soluble salt which has the action of a poison towards organized particles such as the germs of disease are believed to be can be administered, absorbed and retained within the animal body, without producing any deleterious effects ; that it creates a manifest change upon the body, enabling it to resist the processes of ordinary putrefaction ; and that in diseases which have been ascribed to the influence of morbid germs its administration has been of signal service.

6. There is another agent, however, which has been proved to manifest a similar and probably a higher power in extinguishing the life of low organisms ; this agent is carbolic acid. For its introduction and for the investigation of its properties we are greatly indebted to Mr. Calvert in this country, and to M. Lemaire in France. It is known to have a powerful influence in killing fungi, microzoa, insects, and their ova—in fact, all the lowest forms of animal and vegetable life. It arrests fermentation and putrefaction, not by inducing any perceptible chemical change—for M. Lemaire and Mr. Crookes have separately proved that it neither interferes with any chemical change nor itself suffers any change—but simply by extinguishing the vitality of ferments. It is ascertained that a quantity of carbolic acid sufficient to destroy myriads of lowly endowed organisms may be administered to mammalia without inducing any deleterious effect upon the latter. But there are certain difficulties and incon-

veniences in the administration. The following points are ascertained from observations upon the lower mammalia:—That if carbolic acid be administered pure or but slightly diluted, it acts as a violent irritant and caustic; that in doses somewhat feebler it causes agitation, convulsion, partial or complete loss of sensibility, narcotism; that it tends to induce congestion of the vessels of the brain, the stomach, the intestines, and the lungs. In small doses, however, it is absorbed into the system and finally exhaled by the lungs, producing only, occasionally, such symptoms of slight narcotism as are produced by alcohol, which in its chemical constitution it much resembles.

7. Carbolic acid has now been employed as an internal remedy in many cases of disease, especially those in which, as there are good grounds for believing, the system is embarrassed by the presence and multiplication of organized poisons. The records indicate that much success has attended its employment. In the treatment of cholera it was found to be valuable. In few diseases is the evidence of causation by organized germs greater than in cholera; no agent has been discovered more potent than carbolic acid to destroy the vitality of organized particles; if, therefore, it be possible to administer to the living body a sufficient quantity to prove fatal to the contained organisms, there are good grounds for expecting a successful treatment.

8. The difficulty, however, has been the administration of carbolic acid in sufficient quantities without the production of its irritant and caustic effects, and its absorption with due rapidity. It is at all times necessary to dilute it with a large quantity of water, and in this way it is nauseous, so that children and delicate persons refuse to swallow it. It has been proposed to substitute for carbolic acid its soluble salts—the carbolates—but these are themselves objectionable from their nauseous taste, and M. Lemaire advances against them the all-sufficient objection that they are very unstable compounds.

9. The double salts which I am about to describe present none of the practical difficulties before mentioned. Containing in each equivalent one equivalent of carbolic acid,

they manifest the same effects as the agent itself, and, as I shall presently show, they are capable of the most ready administration and complete absorption. It had been known that equivalent weights of carbolic acid and sulphuric acid combined to form a stable sulpho-carbolic acid, which presented some analogies with sulpho-vinic acid. My friend Mr. Crookes succeeded, by neutralizing this acid with potash, in producing a crystalline salt—sulpho-carbolate of potassium. To Mr. Crookes, undoubtedly, belongs any merit that may attach to the inauguration of this inquiry. From the ready solubility and not unpleasant taste of the sulpho-carbolate of potassium, I thought with him that it afforded an indication towards the discovery of a valuable practical antiseptic for internal administration.

10. I then devoted myself to the preparation and investigation of the various sulpho-carbolates of the alkaline and metallic bases, and I have now succeeded in producing a series of definite double salts. In the prosecution of the inquiry I have to acknowledge the valuable aid which I have received from Messrs. Balmer and Child. We prepared the sulpho-carbolates of the alkalis in September, 1867. The sulpho-carbolate of zinc was obtained by us in a state of great purity in July, 1868, and we have recently succeeded in preparing the sulpho-carbolates of copper and of iron.

Sulpho-carbolate of sodium ($C_6H_5, NaSO_4 + Aq$) may be obtained in fine rhombic prisms, colourless, having a slight taste of creosote. The crystals have a characteristic tendency to cohere in the form of minute rosettes. The salt is very soluble in alcohol and in water; it is immediately dissolved by six times its bulk of cold distilled water.

Sulpho-carbolate of potassium crystallizes in oblique rhombs.

Sulpho-carbolate of ammonium is obtained in the form of rectangular plates.

Sulpho-carbolate of magnesium is in appearance an amorphous powder; under a lens it is seen to be a congeries of acicular crystals.

Sulpho-carbolate of zinc, $(C_6H_5) Zn'' (SO_4) + Aq$, forms

beautiful clear, colourless, rectangular plates of an unusual brilliancy.

Sulpho-carbolate of copper forms long needle-shaped crystals of a pale green colour, the hue much resembling that of sulphate of iron.

Sulpho-carbolate of iron is apparently a dull red-brown amorphous powder, with here and there lustrous scales which, examined by the microscope, present the form of square plates of a ruby tinge. Its aqueous solution is of a beautiful mauve or purple colour. This appearance affords an excellent test for the presence of sulpho-carbolic acid; a drop of solution of perchloride of iron added to a solution of a salt of sulpho-carbolic acid, developing at once the characteristic colour.

I have been able by this test most readily to detect the presence of one sixtieth of a grain of sulpho-carbolate of sodium.

11. It became my object to determine which of the sulpho-carbolates of the alkalis was most effectual as an antiseptic. As an example of the development and multiplication of organized germs in which a comparative test could be applied I chose fermentation, because its phenomena have been accurately studied and are capable of a close demonstration. I proceeded as follows: I procured a series of glass bottles of exactly the same capacity; the mouth of each was closed by a cork through which passed a narrow glass tube the extremity of which in the interior of the bottle reached nearly to the bottom. Into each of the series were weighed fifty grains of cane sugar and afterwards a bulk of yeast exactly equal in each; one of the bottles was now filled with water; into each of the remaining bottles twenty grains of one of the alkaline sulpho-carbolates were introduced. The corks and tubes being now adapted to each, the bottles were immersed into a vessel of water at 100° Fahr., and kept with no disturbance of the conditions for nine and a half hours. It is obvious that on the occurrence of fermentation, carbonic acid would collect in the upper part of the bottles, and driving out the contained fluid through the tube would

produce a displacement just in proportion to the amount of fermentation. Though this experiment, therefore, could not pretend to a rigid and absolute accuracy, it was, owing to the conditions being identical in each case, a satisfactory comparative test of the power of the different agents in restraining the fermentation. At the end of the time mentioned it was found that from the bottle in which no antiseptic had been introduced the fermentation had displaced the whole of the contained fluid. In each of the others fermentation had occurred imperfectly, but in different degrees; the spaces in each bottle being filled from a graduated burette, a series of comparative results were obtained. Confirmatory experiments agreed in establishing the following as the order of efficiency as regards prevention of fermentation in the various cases:—1. Sulpho-carbolate of sodium; 2. sulpho-carbolate of magnesium; 3. sulpho-carbolate of potassium; 4. sulpho-carbolate of ammonium. It was established that twenty grains of sulpho-carbolate of sodium would completely annul the fermentation of fifty grains of sugar; the last two of the series were far less efficient. The result of this preliminary experiment, therefore, established the superiority of the sodium salt, which also had the advantages of a ready solubility and a taste less unpleasant than that of any of the others; I therefore chose it for internal administration.

12. To test the effects of this salt upon the lower animals, I administered it to two guinea-pigs; it was given in the form of pills made up with a sufficiency of arrowroot; no other food was given. From May 1st to May 5th the two guinea-pigs took 275 grains of sulpho-carbolate of sodium. It produced no obvious effect except a slight looseness of the evacuations. The animals being killed and examined after death, there was found to be no morbid lesion, but the duodenum of one contained an unusual quantity of yellow bile. The bodies were sent to Mr. Henry Child for chemical examination. He reported that the contents of the stomach, the intestines, the substance of the livers, the contents of the bladders, and the whole of the muscular system yielded a

crystalline substance answering to the tests for soda and sulphuric acid, but carbolic acid was not evident to tests. The salt, therefore, was manifest in the economy as sulphate of sodium. Comparing the conditions of the fleshy portion of the leg of one of the guinea-pigs with a piece of freshly-killed lean mutton, the observation being commenced on May 5th, Mr. Child made the following notes :

May 19th.—Piece of meat tainted, damp on outside, and softening in structure.

Leg of guinea-pig, dry on outside, but no other apparent difference.

May 30th.—Piece of meat putrefying, and smelling very badly ; had to throw it away.

Leg of guinea-pig without any smell, but almost dried up.

June 8th.—Leg of guinea-pig quite dry, no other change.

13. Having found that twenty grain doses were taken by the human subject with no ill effect whatever, I increased the dose in several cases to sixty grains, administered every four hours. The only direct effects were a slight tendency to vertigo or dizziness. The odour of carbolic acid could be readily detected in the breath. The urine of a patient who had taken 360 grains of sulpho-carbolate of sodium in twenty-four hours was collected and examined. It gave no evidence of the presence of carbolic acid, but contained a considerable quantity of sulphate of sodium. It showed a marked tendency to resist putrefaction.

14. Taking without selection thirty-five cases of phthisis to whom I administered sulpho-carbolate of sodium in twenty-grain and thirty-grain doses, I endeavoured to ascertain if it possessed any special effect upon general health and nutrition. Of the thirty-five cases, four were in the first stage of the disease, twenty-five in the second stage, and six in the third.

The treatment was for the most part continued for two months, the ordinary dietetic and tonic means being adopted in addition. Concerning these thirty-five patients, the following points were noted :

I. *Evidence of symptoms directly produced by the drug.*—

These were only manifested in four out of the whole number. One stated that the "medicine made him feel nervous," but declared there was improvement, both in breathing and in general strength. A second suffered severe headache, and the treatment was omitted. A third, a young female with disease in the third stage in both lungs, stated that "the medicine made her feel stupid and useless for a few minutes," but her general strength improved. A fourth said that the immediate effect was to make her feel powerless, but she became better and more cheerful.

II. *Influence on general health.*

A. 13 cases manifested great improvement.

B. 15 „ „ considerable improvement.

C. 5 „ „ no advantages.

In class A three patients stated that "they felt quite different men;" all testified to a great improvement, and these assurances were corroborated by signs of obvious improvement and by decadence of the signs of disease.

In class B the effects attested were—1, increase of strength; 2, decrease of cough; 3, arrest of foetid expectoration; 4, improved rest; 5, increased appetite; 6, arrested night perspirations.

In class C one was a case of acute phthisis, in which the medicine was frequently vomited; the second coexisted with great hypochondriasis, and vomiting was a prominent symptom; in the third there was marked hysteria, and no improvement was manifested; in the fourth the disease progressed without any change for the better; and in the fifth the drug was omitted on account of headache.

III. *Influence of nutrition.*—There were in cases of fifteen patients whose weight was recorded—

A. Gain of weight in 9 cases.

B. Loss of weight in 6 cases.

A. The increase of weight was 1 lb. in four cases, $2\frac{1}{2}$ lb. in one, $3\frac{1}{2}$ in two, 4 in one, and $5\frac{1}{2}$ in one; an average gain of $2\frac{1}{2}$ lbs.

B. The decrease of weight was, in three cases, from $\frac{1}{2}$ lb.

to $1\frac{1}{2}$ lb.; in a fourth case 3 lbs. (very extensive disease of both lungs); in a fifth a decrease of 4 lbs. in weight was manifested coincidently with improvement in signs and symptoms; whilst in the sixth case the loss was 6 lbs., and the drug was omitted on account of sickness.

15. After a review of these cases I think it can be scarcely denied by any of those conversant with pulmonary disease that they bear a favorable contrast with similar cases placed under any other circumstances, however favorable. Without claiming for the salts, however, any undue advantages, we are, at least, justified in concluding—that the sulpho-carbolate of sodium, in doses amounting to sixty grains per diem, may be taken in the great majority of cases by patients in delicate health for a period of two months without the production of any deleterious effect whatever.

16. Concerning the operation of the sulpho-carbolate upon the economy, we can conclude that it is absorbed and then decomposed within the body into sulphate of sodium which is voided by the urine and carbolic acid which is exhaled by the lungs. Whether or no the carbolic acid is also in part excreted by the urine is undetermined; but it is certain that a marked influence is produced by the treatment upon that secretion—a fact proved by the extraordinary preservation of the latter from putrefaction. Although the tissues of the animal body do not disclose to tests the presence of carbolic acid, it is certain that they have undergone some potent change whereby they are preserved from decomposition. It is possible that the germs whose development in the dead body gives rise to the phenomena of putrefaction can obtain no vitality in tissues wherein carbolic acid is present.

17. Taking into consideration (1) that, as established by a multitude of observations, carbolic acid is a powerful agent for the destruction of organized germs, (2) as I think the foregoing observations afford sufficient evidence, the sulpho-carbolate of sodium is a practical and efficient vehicle, whereby carbolic acid can be conveyed to the tissues of a living animal. I consider that an *à priori* case is made out for the treatment of zymotic diseases (*i. e.* those diseases whose manifesta-

tions are considered to be due to the operation of organized germs) by the sulpho-carbolate of sodium.

18. As to the success which has hitherto attended the application of these principles, I desire to speak with great reserve. I have myself employed the sulpho-carbolate of sodium as an internal remedy in a large number of diseases of the zymotic class (including diphtheria and very severe scarlet fever) during twelve months. I have had no case which has terminated in death or in any untoward complication. I consider, however, that any individual experience is of the least possible value in the elucidation of the question of the value of the treatment in cases of zymotic disease. Such a question can only be determined by the accumulation of data, and especially by the employment of the remedies in the organized departments of the State.