Elliott (John B.)

PREVENTION OF DISEASE:

PROPHYLAXIS IN PERSON.

By JOHN B. ELLIOTT, M. D.,

Professor of Materia Medica and Therapeutics and Clinical Medicine, Medical Department, University of Louisiana.

Reprinted from the New Orleans Medical and Surgical Journal.

NEW ORLEANS:
L. Graham, Print, 127 Gravier street.
1880.

Prevention of Disease—Prophylaxis in Person.

By JOHN B. ELLIOTT, M.D.,

Professor Materia Medica and Therapeutics and Clinical Medicine, Medical Department, University of Louisiana.

Reprinted from the New Orleans Medical and Surgical Journal.

To touch upon this subject at the present time needs no apology. The question of our ability to prevent epidemic disease has grown to be in the last two years one of national importance, and has become a matter of vital interest to the great commercial centres of the Mississippi valley and the Atlantic coast. When we realize that during the past summer at least one-third of the commonwealths of the Union were more or less apprehensive of an epidemic invasion of yellow fever, and that, thereby, their commercial highways were obstructed and their populations held ready for flight, we may form some feeble estimate of the terrible cost of such apprehensions, and by it may measure with approximate accuracy the responsibility that rests upon the shoulders of the medical profession touching the prevention of disease. The appointment of State boards of health tells that the people demand some help at the hands of the profession, while the higher creation by Congress of a National Board of Health, with powers so broad as to cause alarm through its invasion of political precedent, gives evidence that the representatives of the people feel and sympathize with the demand.

On the other hand, the work that has been done during the past year by the various medical bodies shows that the responsibility has been fully realized by them, and teaches that where means and power are given to the guardians of health they will be used with honest intent and good results.

To discuss what has been done is not, however, the purpose of this paper. The question that presses now is, what may we do for the future? The general methods in vogue for the prevention of epidemic disease are the offspring of common sense rather than of professional knowledge, and it would seem that the public have a right to expect more than this at our hands. More than this every conscientious worker in medicine must hope to bestow, or else must lose that faith in the future progress of his science which will sap the foundations of his energy and arrest endeavor.

To sum up briefly the available methods of prevention, we may class them as follows:

Prophylaxis { External { Quarantine. / Prophylaxis in Place. / Internal { Prophylaxis in Person.

Upon the first the medical profession *is* at variance: it has at times signally succeeded; at others it has signally failed. The laity, according to their relation to the centre of infection, are divided. The populace of an infected district are apt to think that the quarantine which closes their channels of commerce is a useless imposition, while those communities in commercial neighborhood with the diseased centre regard quarantine as the only hope left them for escape. Granting, however, the theoretical efficacy of quarantine, disease will at times penetrate its lines, and the community so reached becomes its prey with no other means of protection than local sanitary measures, or prophylaxis in place. As this measure is most often resorted to after disease has made its appearance—is used to arrest rather than to prevent—its utility is in great measure lost. As a matter of fact, however, the two methods mentioned are civil rather than medical methods. Common sense dictates them, and the civil arm is quite competent to inaugurate and perfect them. The only

purely medical method is prophylaxis in person, or the use of agents that will destroy the poison of the disease in the blood before the poison destroys the person. Patients attacked by disease are sick long before they take to bed or see a physician, and the period preceding the technical sickness has long been recognized as the period of "incubation." So clearly is it accepted as a fact that disease poisons enter the system and then require time for the accomplishment of their effects, that most diseases have their definite periods of incubation assigned them, and all quarantine laws tacitly express this conviction by prescribing a time of probation for persons from infected districts. To combat and destroy disease in the person during this preliminary stage, or rather, to prevent the formation of this stage, is a problem left for the medical profession, and offers the only true medical method of preventing disease. Setting aside, at present, the nature of disease poisons, a perfect prophylatic against a given disease, is an agent that is harmless to the individual taking it, while destructive of the poison in the blood.

No argument is necessary to prove that certain chemical compounds are believed to be destructive to the poisons of epidemic diseases. The annual use of this class of compounds has enlarged to such an extent as to have generated a new branch of commerce. Vast amonnts of money are annually expended in attempts to destroy the disease poisons in the streets of our cities, and the public mind has become so familiar with the fact of disinfection, as to regard its omission as a civic delinquency. The general recognition, therefore, both by the professional mind and by the mind of the laity, of true material poisons, as the causes of epidemic disease—which poisons can be met and destroyed externally to the body—leaves no ground for argument against attempts to meet and destroy those same poisons after they have entered into the body of the individual. Furthermore, it is but rational to conclude that it is a much more hopeful task to prevent the breaking down of a system by killing a poison before its work is accomplished, than to remedy at last the physiological damage which is manifested in the complete collapse of the incipient

chill and the subsequent reaction of the febrile state. Too often the period for medical aid has passed before the physician is sent for, and the blame of the fatal issue has to be borne by the practitioner who has no room for his skill. In such an issue the blame does not belong to the individual practitioner so much as it does to the profession at large, who have failed so far to furnish sufficient methods of prophylaxis in person.

To this branch of medical inquiry the present paper is a contribution, the following experiments and results being offered with the hope that they may stimulate research and lead to some results in this direction:

In 1867 and 1868, the attention of the writer was fixed by the experiments of Polli (from 1855 to 1861) upon the Sulphites and hyposulphites of the alkalies and the alkaline earths. To state briefly, from memory, in these experiments it was claimed that the sulphites administered to dogs could be detected in the tissues of the dead animal (still in the form of sulphite) twenty-four hours or more after the administration of the salt. From the known effect of sulphurous acid as an antiseptic and antizymotic, it followed naturally, from these experiments, that the use of the sulphites should be essayed with hope in that class of diseases recognized as zymotic; and Polli claimed to have achieved success in the treatment of the major exanthemata with the sulphites and hyposulphites of sodium and magnesium. It would naturally suggest itself, from these reputed successes, that if the sulphites are potent to arrest this class of diseases after the patient has become technically "sick," they would be still more potent to prevent them, provided the salts could be taken without harm to the individual.

As the results of Polli's experiments upon dogs have been controverted by subsequent experimenters, and as the success claimed by him in the treatment of zymotic diseases has not been experienced by later therapeutists, the administration of the sulphites has fallen into disuse, and they are now regarded as a class of remedies possessing valuable powers, but as inferior in any given direction to other agents at our disposal.

An opportunity was afforded the writer for testing the

powers of the sulphite of sodium, as a prophylactic, in 1876, in an epidemic of scarlet fever. In this test, the sulphite, having achieved all that could be expected of it by the most earnest advocate of its power, subsequent experiments upon men and animals were undertaken to explain the mode of its action, and account for the results. In order to present the subject in logical sequence, the chronological order of the therapeutical and physiological experiments will be reversed in stating them.

In seeking to learn the mode of action of sodium sulphite, the first question that presents itself for solution is: Does the sulphite of sodium remain in the blood as sulphite for any length of time after its absorption into the circulation?

This was claimed by Polli, while it was denied by Rabuteau; Polli, as has been stated, claiming that the sulphite could be found still as sulphite in the tissues of animals who had taken the salt. Rabuteau did not accept the results of Polli, as he could find no sulphite in the urine of patients taking sulphite (in therapeutic doses); his inference from this failure being that the sulphite was rapidly transformed into sulphate as soon as it entered the circulation.

To answer this first query, the following experiments were tried:

The first experiment was made upon a healthy dog whose estimated weight was 40 pounds. The salt used was the normal sodium sulphite, $Na_2\ SO_3,\ 7OH_2$. The reaction relied upon for the detection of the sulphite was its decomposition by nascent hydrogen liberated from hydrochloric acid (HCl.) by chemically pure zinc. The reaction may be stated as follows:

1st. $3Zn + 6HCl = 3Zn\ Cl_2 + H_6$;

and, 2nd, $Na_2\ SO_3 + H_6 = SH_2 + OH_2 + 2\ Na.OH$.

In other words, the nascent hydrogen liberates sulphide of hydrogen, and the presence of the latter is then easily demonstrated by bringing it into contact with lead acetate in solution, when lead sulphide is deposited. By this reaction, one grain of sodium sulphite can be readily detected in thirty thousand grains of water.

Before administering the sodium sulphite to the dog an ounce of blood was drawn from its hind leg and submitted to the identical chemical process intended for the blood after the administration of the salt. This was done to be assured that there was no compound in the blood that could produce the hydrogen sulphide expected from the decomposition of the sulphite.

To simplify the experiment and avoid all possible change in the blood from manipulation or contact with the air, the blood was drawn from the leg into the vessel, (a large sized glass beaker), in which the test was to be made, and a little water was added to dilute the blood. A piece of chemically pure zinc was then dropped into the blood, enough hydrochloric acid was poured in upon it to cause brisk evolution of hydrogen, and the mouth of the beaker closed with a piece of filtering paper wetted with a solution of lead acetate.

This simplification of the experiment was arrived at after one or two failures in the effort to perform the experiment in a closed vessel and to force the gas (SH_2) through a solution of lead acetate by bubbling.

The failures arose from the fact that the heat of the chemical reaction, together with the direct effect of the acid caused a coagulation of the albuminoid constituents of the blood and a consequent swelling up of the contents of the vessel into a frothy mass which prevented the escape of the gas. The frothy mass would pass over through the delivery tube into the solution of lead acetate and seriously complicate the results. In the simplified form the same frothy mass resulted, but before filling the large beaker the distended bubbles would burst and set the SH_2 free directly in the presence of the lead acetate in solution on the filtering paper closing the mouth of the beaker. In the preliminary experiment upon the blood of the dog, before the sodium sulphite was administered, no SH_2 was generated. No trace of lead sulphide could be seen upon the filtering paper.

Pre-assurance against this fallacy being had, thirty grains of sodium sulphite was given to the dog between two slices of fresh meat. In an half hour afterwards an ounce of blood.

was drawn from the hind leg and immediately submitted to the same test as the first specimen.

In this case the surface of the filtering paper became completely covered with a heavy deposit of lead sulphide. After this experiment the dog was kept confined, and six hours subsequent to the administration of the sulphite another ounce of blood was drawn and again tested with like results. The precipitate of lead sulphide was, in the second case, not so heavy as in the first, but was sufficiently heavy to be prominently visible. These results support the conclusions of Polli, and warrant the conclusion that the sulphite of sodium remained still as sulphite in the blood of the dog six hours after its administration.

The second experiment was tried upon a robust and healthy man, who submitted himself for the trial, A. J. Short, 27 years of age; weight, 166 pounds; height, 5 feet, 7 inches. As in the former experiment, a half ounce of blood was drawn by means of cups from the left shoulder, and submitted to the test of Hcl. and Zn. before the administration of the sulphite, and with the same negative result. Upon the prepared filtering paper there was no trace of lead sulphide. Twenty grains of sodium sulphite was then administered in aqueous solution. Estimating that the body of the patient contained 12 pounds of blood, the quantity of sulphite administered would give a solution in the blood of 1-4200. An half hour after the sulphite was administered, a second half ounce of blood was drawn from the same shoulder and immediately submitted to the same test. A plentiful precipitate of lead sulphide was formed upon the filtering paper. Four hours after the administration of the sulphite, a third half ounce of blood was drawn from the same shoulder and tested, when a clearly perceptible precipitate of lead sulphide was formed.

As a fallacy might underlie the above experiment in the fact that hydrochloric acid will liberate hydrogen sulphide from a *sulphide*, an experiment was tried to cover this point. A patient suffering from chronic bronchitis was given 20 grains of sodium sulphite and in fifteen minutes a half ounce of blood was drawn and tested with hydrochloric without the addition

of zinc, no sulphide was formed. The same blood was then tested with the zinc and hydrochloric acid and a copious precipitate of sulphide formed.

A second experiment was performed (in this case) six hours after the administration of the sulphite when no sulphite could be found.

This series of experiments serves to show that sodium sulphite remains as sulphite in the blood of man somewhat longer than four hours, but not so long as six hours, after the administration of a 20 grain dose.

An experiment was also tried after the method of Rabuteau in order to test the action of the sulphite of sodium upon the processes of combustion in the body, and also to note the effect upon the quantity of sulphate in the urine. A young physician kindly offered himself for this experiment. The direct object of the experiment, was to determine, 1st, the effect upon the quantity of urine excreted; 2d, the effect upon the urea excreted; 3d, the effect upon the sulphates in the urine.

In order to arrive at a normal mean of these excreta the patient was placed upon a regulated diet, containing but little nitrogenous food, and the urine for each twenty-four hours was carefully collected and measured for four days before the administration of the sulphite was begun. The results of this preliminary test were as follows:

Days.	Urine in grains.	Urea in grains.
1st day	16403	293.76
2d day	14492	273.81
3d day	13669	285.04
4th day	23694	364.60
Mean	17064.5	304.3

The experiment was performed in May. The weather from the beginning of the experiment continued increasing in warmth until the third day, as is well indicated by the diminishing quantity of urine. On the third day there was a sudden change to very cool weather. Means were not available for the careful measurement of the sulphates by proper drying and weighing. They could only be approximately esti-

mated by precipitation with barium chloride, filtering, washing and air drying. As this could give only approximate results, the record is not entered, as the temperature of the day and the aqueous vapor present made the results vary.

On the fifth day the patient began taking 20 grains of sodium sulphite in aqueous solution three times a day. The urine was collected and tested as upon the previous days; the diet being the same as during the first four days:

Days.	Urine in grains.	Urea in grains.
5th day	14581.	293.83
6th day	8201.	232.70
7th day	10024.	268.53
8th day	11391.	255.53
9th day	16759.	295.29
Mean	12191.	269.17

The sulphites were estimated as in the first period and were largely increased—apparently doubled. On the fifth day there was a warm change in the weather, and on the sixth day the weather was very warm, as the urine and urea indicate. The urine was collected on the two days following the 9th, the diet being continued, but the sulphite stopped.

Days.	Urine in grains.	Urea in grains.
10th day	8657	202.00
11th day	7746	187.34

The eleventh day was noted as weather hot, temperature F. 87°.

A comparison of the two periods gives the following:

	Urine.	Urea.
1st period	17064.5	304.30
2d period	12101.6	269.17

The comparison of the means for the two periods shows diminution of urine and urea for the period of medication. A careful comparison of the tables, with the notes of temperature of the dates, will show, however, that the weather seems to have had a greater effect than the sulphite. The excess of

urine in the first period is due to the cool change on the fourth day, while during the period of medication the quantity of urine and urea increased from the sixth day to the ninth. The results are rather negative in regard to the excretion of urine and urea, while the sulphates were, as above stated, apparently nearly doubled.

During the period of medication, the urine was tested for sodium sulphite, but none could be detected. This accords with the experience of M. Rabuteau when therapeutic doses were administered.

The inferences to be drawn from the above series of experiments are the following:

1st, Experiments on man. The sulphite of sodium can be detected in the blood as sulphite four hours after the administration of a twenty grain dose.

2d, Upon its entrance into the circulation, it begins to undergo oxidation to sulphate, which process is apparently completed before the lapse of six hours after the administration of a twenty grain dose.

3d. The sulphites in the urine, are largely increased during the administration of sodium sulphite.

4th. The effect of the salt upon the excretion of urine and urea cannot be pronounced from the single experiment tried.

From the fact that it is an alkaline salt it may be judged that it would slightly diminish combustion upon long continued use. From practical experience, to be submitted immediately, I feel safe in the assertion that its continued use in therapeutic doses does no harm to the individual.

The therapeutical experiment was tried in the fall and winter of 1876, and was undertaken from a conviction of the soundness of Polli's views in regard to the sulphites. The following is a brief outline of the experience:

The epidemic which afforded the opportunity occurred at Sewanee, Tenn., the site of the University of the South. Sewanee is a town that has grown up around the University, and has a population of about eight hundred souls. Added to this population of residents are the University students, about

two hundred in number. A portion of these students are young boys from ten to twelve years of age, attending the grammar school attached to the University. Sewanee is situated upon the Cumberland table land in middle Tennessee, at an elevation of 2000 feet above the sea.

In August, 1876, a case of measles appeared in the person of a servant girl attached as a nurse to one of the resident families. This girl had come from a neighboring town where measles prevailed, and developed the disease one week after she had reached the mountains. The case was fully developed when first seen, and her condition was considered too critical to warrant removal. In a few days all of the children she had been attending, four in number, developed the disease. They were all placed upon sodium sulphite, 7.5 grains three times a day, and little other treatment adopted. The same dose of the sulphite was given to each child, (aged from two to eight years), irrespective of age, and the cases were milder as the age of the patient was less, or as the ratio of the dose to the age increased. The house was quarantined and no further spread occurred. Being in constant contact with my own children, (four in number, from infancy to six years of age), and my residence being just opposite to the infected house, my own children were put upon the sulphite in the same doses. This was the first essay at prophylaxis in person.

About two weeks after this I was summoned to a family in the centre of the community to see two children who had been suffering for some days from the enlargement of all the glands about the throat, accompanied with persistent stiffness of the muscles of the neck. Neither of these children had been sick enough to go to bed or even to be much noticed by those about them. No suspicion of serious disease was entertained. In a few days, however, a summons came to see a case in a neighboring family, and another case in the family of the children with enlarged glands.

Both patients (children) had high fever, and from the fact that measles had already appeared in the community it was expected that these cases would develop as such. The appear-

ance of the eruption, however, accompanied with severe anginose affections showed that a formidable type of scarlet fever had to be dealt with. No history of the infection could be traced.

As soon as fully satisfied of the nature of the disease, an attempt at arrest by prophylaxis in person was determined upon. The conviction was forced that isolation of the houses alone could not prevent the spread of the disease, as there were ten children in the two families who had never had scarlet fever and had already been exposed to infection. There were besides many young people in the neighboring houses who had never had scarlet fever. The children in both of these houses, and also all the young persons and children in the neighborhood were put upon the sulphite in doses from seven to ten grains three times a day. The two sick children were treated with the same salt in double doses, and the following was also used:

℞ Potass. Chlorat, ʒii
Acid. Hydrochlor, gtt. xx
Glycerine, ℥ii
Aquæ, ℥xii

♏ S. Dessertspoonful every 4 hours.*

Both of the cases made good recoveries, and although the children of the respective families were not altogether excluded from the rooms of the patients, no other cases occurred in either family or in the neighborhood.

After this outbreak the disease disappeared for some weeks, and the hope was entertained that the epidemic had been stamped out, when a summons came for me to see a sick child in a family one mile distant from the houses where the last cases had occurred. A child was found sick with a violent case of scarlet fever, the eruption being well out and the case fully developed.

---

*[This prescription was essayed from the great benefit derived from its use by Dr. Baruch, of South Carolina, in an epidemic of diphtheria. It is a modification of the formula of Watson. When the chlorate of potassium is rubbed up in a mortar and the hydrochloric acid added, decomposition takes place with the solution of the *euchlorine* of Davy, now known to be free chlorine and per-oxide of chlorine (ClO_2). The glycerine and water are added quickly while rubbing. The above formula and mode of preparation were found very efficacious. A more complete decomposition would take place by using one drachm of the chlorate to one half drachm of hydrochloric acid, but a smaller dose should then be given.]

No connection could be traced between this and the former cases.

The sick child was put upon the sulphite and the *per-oxide* of chlorine mixture. The only other child in the family was put upon the sulphite of sodium. Two days elapsed before any effect of the medication could be noticed in the sick child, then it began to improve, and afterwards rapidly recovered. The other child, although always in the sick room, escaped infection, while a child from a neighboring family, not taking sulphite, and who had been in the sick room, contracted the disease. The children in the family of this second case, (three in number), were put upon the sulphite and all escaped.

The next case appeared in the body of the town among children who were not taking the sulphite. Later in the epidemic a case occurred in a house near my own, in the person of a young girl who had taken no sulphite. In the same house were five children who had never taken the disease; they were all put upon the sulphite and all escaped. In my own house a case occurred in a young lady who was not taking sulphite; the case was severe; all of my own children who were taking the sulphite escaped, although some of them had access to the sick room. The above enumerated cases are the only ones around whom the opportunity for a trial of prophylaxis was afforded. In reviewing the many cases attended through the epidemic, no one is on record in which the disease was contracted while the sulphite was being taken. The fact that in six different families, aggregating, exclusive of the patients, twenty-three children, the disease was checked with the first case, and that outside of these families none others who were taking the sulphite contracted the disease, seems to point strongly to one conclusion. Whether these results we mere coincidences, or true effects of an efficient cause, remains to be proved by still further trial. The experience was sufficiently invariable to impress upon the mind of the writer the conviction of the relation of cause and effect between the sulphite and exemption from disease. In addition to the recovery of the cases treated through the epidemic, some of which were of the severest form, in no

case was there a single after effect of disease noticed. The recoveries were rapid and convalescence was complete.

It is well to add that in severe cases where the patients were not seen before the third or fourth day, it was some time before any beneficial effects from the sulphites could be noticed, and the certainty was felt that if the experience afforded by these cases had been relied upon for a judgment of the efficacy of the sulphite, great doubts would have been entertained as to its usefulness. This experience *during* the disease has probably caused the discredit that has fallen upon the sulphites. The value of the remedy lies in its power to *prevent*. Just as it will under ordinary atmospheric conditions arrest the process of fermentation by checking the propagation of the organisms which produce that transformation, so in the blood of the animal body, where it still remains as sulphite, the conviction is entertained that it can with equal certainty arrest the propagation of some disease poisons.

When we pass from the particular diseases considered to speculate upon the further usefulness of the sulphites in other forms of epidemic diseases, we pass into a field of conjecture where nothing can be determined save by experiment.

Believing that epidemic diseases are caused by the propagation in the blood of living organisms, it is still a natural conclusion that as these organisms undoubtedly differ, so must they stand in different relations to a given antizymotic. Because a given remedy will arrest the development of one species of germ, we have no valid ground for asserting *a priori* that it will arrest the development of all others. These details must ever remain a matter to be determined by experience. Some interesting notes have been received of experiments with the sulphite during the past two years in yellow fever, but the collection of written data is not yet sufficient to warrant the publication of the favorable notes so far received.

As to the quantity of the sulphite to be taken in experimental prophylaxis, the following considerations will serve as a guide. In the practical experiments in prophylaxis essayed in the epidemic cited above, seven and a half grains of the sul-

phite of sodium was given three times a day to children under ten years of age. This, in the blood of a child of fifty pounds weight would give a solution of about 1-3500, with a steadily diminishing strength of the solution through four hours. This amount was given to my own children for two months consecutively and with a short interval continued through another month with no bad effect and with some supposed benefit to their general health. For adults the corresponding dose would be about twenty grains or more. From such experimental data as are recorded of the effects of sulphurous acid upon low forms of life, it would seem that one large dose would be more efficacious than repeated small ones. One large dose once a day would render the blood, at least once in the twenty-four hours, less fitted for the development of low orders of organisms. Twenty grains morning and night could be safely essayed by an adult under the eye of a physician, and would be a legitimate test of the sodium sulphite as a prophylactic in any given epidemic. Any evil effects of the remedy would be slow, and would probably be evidenced by some loss of the red globules of the blood. This could be easily remedied by some ferruginous preparation.