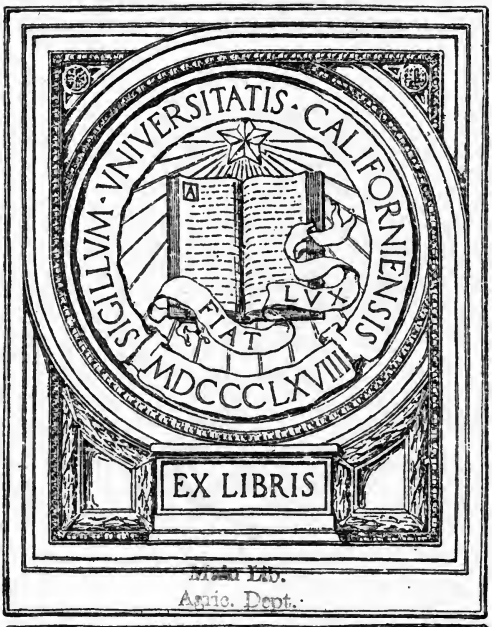

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GENERAL RESULTS OF THE INVESTIGATIONS SHOWING THE EFFECT OF SULPHUROUS ACID AND SULPHITES UPON DIGESTION AND HEALTH.[a]

INTRODUCTION.

The relations of sulphurous acid to health are perhaps of greater importance than those of the preservatives already studied—namely, boron compounds and salicylic acid and its salts. The reason of this is found in the fact that the use of sulphurous acid at the present time is more general, and in certain classes of food products, according to the statements of manufacturers, more nearly approaches a necessity than is the case with boron or salicylic acid compounds.

Sulphurous acid in some form is extensively employed in many technical operations in the preparation of foods. This is especially true in the production of wine, in the preparation of evaporated or desiccated fruits, and in the manufacture of molasses. The problem presents itself under two aspects—namely, the use of sulphurous acid or its compounds for technical purposes in the preparation of foods and its application to the finished products as a preservative.

In the preparation of foods, sulphurous acid is chiefly employed in the form of the fumes of burning sulphur, applied either to the food products themselves in the course of manufacture or to the containers in which the food products are held. In the ripening of the wines in cellars it is customary to fumigate the barrels with burning sulphur each time the wines are racked. In this manner it often happens that the wine before it is finally ready for sale on the market may have been placed in five or more freshly sulphured containers. By this treatment the wine absorbs a varying quantity of the sulphur-

[a] By reason of the restrictions placed by law upon the printing and distribution of bulletins exceeding 100 pages, it is not possible to supply the demand for Bulletin 84, Influence of Food Preservatives and Artificial Colors on Digestion and Health, from the regular edition. In order to give as wide a circulation as possible to the results of the experimental work, it has been deemed advisable, in the case of Part III, on Sulphurous Acid and Sulphites, as in the case of Part I, on Boric Acid and Borates, and Part II, on Salicylic Acid and Salicylates (Circulars 15 and 31), to publish the results in the form of a circular for general distribution.

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ous acid, depending to some extent upon the amount of sulphur used in fumigating.

When sulphurous acid is used as a preservative for food products after the manufacture has been completed, it is usually employed in the form of bisulphite of lime or some similar preparation. Sulphurous acid has the property of uniting with certain organic radicals, such as aldehydes and some sugars, to form compounds which are more or less stable, and in this form it is known as combined sulphurous acid. When it exists in the form of an absorbed gas or in combination with an ordinary metallic base, such as soda, potash, or lime, it is said to be in a free state. Combined sulphurous acid is set free from the organic combination by treatment with an acid with the aid of heat or with a dilute alkali in the cold.

In the accompanying report the effects of the combined sulphurous acid are not to be considered, except in so far as the combination takes place with the foods with which the sulphurous acid may be mixed after entering the stomach. The purpose of the investigation is, therefore, to determine practically the effect of free sulphurous acid—that is, sulphurous acid in a gaseous state absorbed by water or united with a base—rather than the effects of combined sulphurous acid. In no case has any question been considered in these investigations relating to the food value of the organic sulphur existing in proteids and other foods.

It is true that probably in the process of digestion complete saponification of the combined sulphur compounds takes place, so that finally they appear in the small intestines in a free state—that is, as sulphurous acid or sulphites—and are then oxidized to sulphuric acid, as is the free sulphurous acid, during the metabolic processes.

Practically, in the technical use of sulphurous acid in the manufacture of food products only the fumes of burning sulphur are employed. Desiccated fruits, pared or unpared, are subjected, after the removal of the pit or core, to the fumes of burning sulphur in what is known as a "sulphur box." In the manufacture of wines a piece of so-called "sulphur candle"—that is, a piece of cloth which has been dipped in melted sulphur—is burned. This candle is attached to a wire, ignited, placed in the barrel, the bung inserted, and the candle allowed to burn until the whole of the sulphur is consumed. Previous to the sulphuring it is the custom to thoroughly wash the barrel so that the interior thereof at the time of sulphuring is moist. The moist surface of the wood absorbs the sulphurous acid more freely than does the dry wood. The ostensible object of the sulphuring is to keep the barrels sweet; in other words, to destroy any yeasts or other ferments which may adhere to the surface of the

wood or be present within it. The barrels are often sulphured some days, or even weeks, before they are filled; at other times the filling of the barrel with wine takes place immediately after the sulphuring. In both cases notable quantities of sulphurous acid become diffused throughout the wine itself. It is evident that some care must be exercised in the use of sulphur in wine making for two very important reasons. In the first place, if too much sulphur be used, red wines would to a certain extent be bleached. In the second place, if the wines become entirely saturated with sulphurous acid the secondary fermentations which produce the ripening of the wine would not take place. In such cases the wines apparently appear to be perfectly mature within one or two years, whereas the proper maturation of a wine requires a much longer time. In the manufacture of nonfortified sweet wines much larger amounts of sulphur are used than in the manufacture of dry wines. This is an important fact, since it shows that the large quantities of sulphur are not necessary for the preservation of dry wines, because it is well known that red wines, which are generally very dry, are quite as well preserved as white, although containing much less sulphurous acid. It is claimed that in the manufacture of sweet wines—that is, those in which the natural sugars coming from the juice of the grape are not entirely fermented—larger quantities of sulphur are necessary to prevent fermentation after the wine is mature. If the sweet wine be made from a suitable kind of grape—that is, one which is so rich in sugar that it gives a certain maximum quantity of alcohol and still leaves some unfermented sugar—it is evident that no excess of sulphurous acid will be necessary. In such a case the wine would be preserved by its natural alcoholic content. If, on the other hand, a sweet wine be made from a must so poor in sugar that it is necessary to add an additional quantity, the product can not be regarded as a natural wine, and hence there seems to be no necessity for providing for its manufacture.

In the manufacture of sirups and molasses it is quite customary to expose the freshly expressed juices of the cane to the fumes of burning sulphur. The "sulphur box" used in this case is so constructed that the juice, falling over shelves by gravity, absorbs the fumes of the burning sulphur rising from the box, which to this extent serves as a chimney. The sulphur dioxid becomes incorporated with the components of the juice, forming more or less stable compounds which are not entirely broken up by subsequent boiling. The sulphur in this form, as well as that which may still be present in the free state—that is, either as an absorbed gas or in combination with metallic bases—passes into the finished product. When sugar is made the sulphur compounds are concentrated in the molasses and this con-

centration becomes greater in proportion to the number of crops of sugar crystals removed. In very low grade molasses the sulphur naturally occurs in extraordinarily large quantities.

In the preparation of evaporated apricots, peaches, pears, and mandarins sulphuring is practiced for the following reasons:

1. To produce as clear and intense a yellow color as possible.
2. To conceal decayed portions of the fruit which have been overlooked in trimming.
3. To prevent fermentation and decay during the drying of the fruit.
4. To protect the fruit during drying from flies and other insects the larvæ of which would otherwise develop after the fruit was stored.
5. To kill the cells of the fruit and thus make the texture more porous, which expedites drying.

In the application of the fumes of burning sulphur in the preparation of evaporated apples the principal object appears to be the preservation of the color of the finished product. Fruits which have been sulphured before evaporation seem to have a lighter color than those which are dried without sulphuring. At the same time it is well known that highly sulphured fruits are preserved with a lower degree of desiccation than those not sulphured, and for this reason a greater weight of fruit is produced from a given weight of the raw material when sulphur is used. It is not difficult to preserve a water content of 30 per cent or over in the finished product when liberal sulphuring is practiced. The use of sulphurous acid also makes it easier to protect the finished product from mold and fungous growths in general after manufacture. That excessive quantities of sulphur are not necessary for the production of evaporated fruits of pleasing appearance is well attested by analytical data obtained by the examination of fruits purchased in the open market having a light and pleasing color and at the same time containing only a small quantity of sulphurous acid. On the other hand, it is quite easy by certain forms of treatment during the process of manufacture to obtain a product in which sulphurous acid is present in excessively large quantities. The analytical data also show that a portion of the sulphurous acid used in the preparation of such products becomes oxidized into sulphuric acid after a certain time, thus artificially increasing the small amount of sulphates naturally present in some food products, which does not appear to be a desirable practice.

As sulphurous acid in some form is almost universally employed in the manufacture of wines, molasses, and sirups, and in the prepara-

tion of desiccated fruits, it is evident that the prohibition of its use would necessitate a radical change in methods of manufacture. This fact, however, it might be stated, has nothing whatever to do with the purposes of the present investigation. Assuming that in the manufacturing processes certain added bodies are used which are found on investigation to be injurious to health, the rational conclusion of such an investigation would be not to excuse or overlook the use of such bodies, but to institute investigations looking to their suppression. If, therefore, the results of the present study indicate that sulphurous acid, even in small quantities, is a deleterious substance when added to foods, it would be reasonable to expect that manufacturers, as well as investigators, would immediately take steps looking to the early suppression of the injurious substance. While it is not likely that such an event could be accomplished within a year or two, it is reasonable to suppose that it could be eventually brought about without any disturbance to manufacture and without any diminution in the output of the article.

In matters of this kind it is advisable to proceed when possible with conservative steps and to avoid any attempt at sudden and revolutionary changes in methods of manufacture. In all such cases, however, it will be found not only possible and desirable to make the food product in question without the use of the deleterious substance, but there is evidence to show that the products thus manufactured will be more palatable, more wholesome, and more valuable than those made according to the methods commonly used at present. Practical experiments have shown, for instance, the possibility of producing a high grade sirup from cane juice and other saccharine saps without the use of the fumes of burning sulphur. Analytical data show the presence on the market of considerable quantities of desiccated fruits of good appearance in which the quantity of sulphur is so small as to be ascribed rather to the conversion of the natural sulphur content of the product than to the addition of the sulphur in its manufacture. At the present time considerable quantities of wine are made without the addition of sulphur of any description, and these wines are of fine appearance, excellent flavor, and of noted purity and wholesomeness.

In so far as the mere tint of the food product is concerned, it is not a difficult matter to familiarize the public with a tint of a different kind from that which would be produced by the use of sulphur. The only arguments of any force favoring the use of sulphurous acid in food products are those which relate either to the preservation of the food product or to its color. As the preservation of the product can be easily secured, and a slight change in color

rendered familiar without working any hardship, these arguments seem to have no force whatever in justifying the continuation of the use of sulphurous acid in foods. It may be the part of wisdom in the administration of food laws to tolerate existing methods of manufacture for a certain length of time looking to their amelioration or change, but that is a question with which this investigation is not concerned.

There is reason to believe, therefore, as a result of the present studies, which have shown that the use of sulphurous acid in foods is deleterious, that a rapid change will be made in the processes of manufacture, looking to the complete and somewhat speedy suppression of its employment. The use of sulphurous acid and sulphites never adds anything to the flavor or quality of a food, but renders it both less palatable and less healthful. Every fact which has been brought out, therefore, in the investigation tends to accentuate the justness of the conclusion, namely, that the use of sulphurous acid in foods should be suppressed.

ORGANIZATION OF THE EXPERIMENT.

The organization of the work in general was practically identical with that of the previous investigations as reported in Parts I and II of Bulletin 84 and summarized in Circulars 15 and 31.

The experiments were conducted on twelve young men from the Department of Agriculture and a local medical school, who voluntarily assumed the obligations imposed by work of this kind. They pledged themselves to abide by the rules and regulations guiding their conduct during the period of the observation, to indulge in no unusual exercise or study, to pursue the ordinary tenor of their daily lives without any more variation than is incident to regular habits. They further undertook to eat only the food which was given them at the hygienic table, to collect and deliver for analysis the excreta of their bodies, to observe regular hours respecting sleep and work, and to report the quantity of water which was drunk away from the hygienic table. The young men were not placed under surveillance, but simply were trusted with their pledge that they would not violate any of the rules of conduct prescribed. The diet was varied so as to give a choice of meats, vegetables, fruits, and cereals, with bread, butter, milk, and coffee. Food of the best quality was purchased, free of any added preservative or coloring matter and in a perfect state of preservation, and every precaution was used to have the food and all the appurtenances of the table perfectly sanitary.

ADMINISTRATION OF THE PRESERVATIVE.

SCHEDULE OF ADMINISTRATION.

The fore period in Series VII began on February 1, 1904, and the after period closed on March 11. The fore period extended over a period of ten days, the preservative period lasted twenty days, and the after period ten days, a total of forty days under observation. The divisions of the periods are shown in Table I.

TABLE I.—*Dates of periods and subperiods, Series VII.*

Periods and subperiods.	Date of beginning.	Date of ending.
	1904.	1904.
Fore period	Feb. 1	Feb. 10
First subperiod	....do...	Feb. 5
Second subperiod	Feb. 6	Feb. 10
Preservative period	Feb. 11	Mar. 1
First subperiod	....do...	Feb. 15
Second subperiod	Feb. 16	Feb. 20
Third subperiod	Feb. 21	Feb. 25
Fourth subperiod	Feb. 26	Mar. 1
After period	Mar. 2	Mar. 11
First subperiod	....do...	Mar. 6
Second subperiod	Mar. 7	Mar. 11

Series XI and XIII, mentioned in the following pages, are special studies conducted at a later date. The purpose of these studies was to develop certain points in regard to the effect of the preservative on the blood and the distribution of the nitrogenous elements of the urine, to which the results obtained in Series VII had pointed as being of special interest and calling for further elaboration.

The salt used for the administration of the sulphurous acid was sodium sulphite, and the quantity of SO_2 contained therein was calculated. About one-fourth of the weight of crystallized sulphite (Na_2SO_3 7 H_2O) is composed of sulphurous acid (SO_2). The total and average amounts of the preservative administered and all individual variations in the quantities taken may be found in Table II.

TABLE II.—*Schedule of administration of preservative, Series VII.*

Period and date.	Sodium sulphite as SO_2 (capsules).						Sulphurous acid as SO_2 (aqueous solution).					
	No. 1.	No. 2.	No. 3.	No. 4.	No. 5.	No. 6.	No. 7.	No. 8.	No. 9.	No. 10.	No. 11.	No. 12.
1904.												
First subperiod:	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*
Feb. 11	0.113	0.113	0.113	0.113	0.113	0.113	0.078	0.078	0.078	0.078	0.078	0.078
12	.240	.240	.240	.240	.240	.240	.178	.178	.178	.178	.178	.178
13	.254	.254	.254	.254	.254	.254	.200	.200	.200	.200	.200	.200
14	.254	.254	.254	.254	.254	.254	.200	.200	.200	.200	.200	.200
15	.254	.254	.254	.254	.254	.254	.200	.200	.200	.200	.200	.200
Total	1.115	1.115	1.115	1.115	1.115	1.115	.856	.856	.856	.856	.856	.856
Average	.223	.223	.223	.223	.223	.223	.171	.171	.171	.171	.171	.171

TABLE II.—*Schedule of administration of preservative, Series VII.*—Cont'd.

Period and date.	Sodium sulphite as SO_2 (capsules).						Sulphurous acid as SO_2 (aqueous solution).					
	No. 1.	No. 2.	No. 3.	No. 4.	No. 5.	No. 6.	No. 7.	No. 8.	No. 9.	No. 10.	No. 11.	No. 12.
1904.												
Second subperiod:	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*
Feb. 16	0.508	0.508	0.508	0.508	0.508	0.508	0.400	0.400	0.400	0.400	0.400	0.400
17	.508	.508	.508	.508	.508	.508	.400	.400	.400	.400	.400	.400
18	.508	.508	.508	.508	.508	.508	.400	.400	.400	.400	.400	.400
19	.508	.508	.508	.508	.508	.508	0	.400	.400	.400	.400	.400
20	.508	.508	.508	.508	.508	.508	.400	.400	.400	.400	.400	.400
Total	2.540	2.540	2.540	2.540	2.540	2.540	1.600	2.000	2.000	2.000	2.000	2.000
Average	.508	.508	.508	.508	.508	.508	.320	.400	.400	.400	.400	.400
Third subperiod:												
Feb. 21	.762	.762	.762	.762	.762	.762	.400	.400	.400	.400	.400	.400
22	.762	.762	.762	.762	.762	.762	.400	.400	.400	.400	.400	.400
23	.762	.762	.762	.762	.762	.762	.400	.400	.400	.400	.400	.400
24	.762	.762	.762	.762	.254	.762	.400	.400	.400	.400	.400	.400
25	.762	.762	.762	.762	0	.762	.200	.400	.400	.400	.400	0
Total	3.810	3.810	3.810	3.810	2.540	3.810	1.800	2.000	2.000	2.000	2.000	1.600
Average	.762	.762	.762	.762	.508	.762	.360	.400	.400	.400	.400	.320
Fourth subperiod:												
Feb. 26	.762	.762	.381	1.020	0	0	0	.400	.400	.400	.400	0
27	.762	.762	0	1.020	0	0	0	.400	.400	.400	.400	0
28	.762	.762	0	1.020	0	0	0	.400	.400	.400	.400	0
29	.762	.762	0	1.020	0	0	0	.400	.400	.400	.400	0
Mar. 1	.762	.762	0	1.020	0	0	0	.400	.400	.400	.400	0
Total	3.810	3.810	.381	5.100	0	0	0	2.000	2.000	2.000	2.000	0
Average	.762	.762	.076	1.020	0	0	0	.400	.400	.400	.400	0
Entire preservative period:												
Total	11.275	11.275	7.846	12.565	6.195	7.465	4.256	6.856	6.856	6.856	6.856	4.456
Average	.564	.564	.392	.628	.310	.373	.213	.343	.343	.343	.343	.223

METHOD OF ADMINISTRATION.

A slight variation in the administration of the preservative was introduced by the fact that it was deemed important that the investigation should include sulphurous acid in a gaseous state as well as in combination as sulphites. The most convenient method for the administration of the gaseous sulphurous acid was found to be by the preparation of an aqueous solution of the acid of standard strength taken, after dilution with water, as an ordinary drink. Water proved to be a more convenient vehicle than milk or other beverages for this purpose.

In the form of sulphites the method of administration in capsules was practiced. This method, as in the previous investigations, was found not only to be the most convenient, but also, all things considered, the most desirable form in which to administer a substance of this kind.

Attention has been called in the previous reports to the distaste which the subject would acquire for a food product in which he knew the preservative had been mixed, and therefore less disturbance of the mental equilibrium was caused by the administration of the capsule, the envelope of which is itself a food product and would be soon

dissolved in the acid digestive juices of the stomach. Moreover, in the solution of this capsule the whole of the preservative is not discharged at once into the contents of the stomach, but the capsule dissolving at different points presents gradually increasing surfaces at which solution of its contents may take place, and this, in connection with the peristaltic action of the stomach, results in a complete incorporation of the preservative with the food in the stomach in a reasonable period of time. Thus, in substances which do not possess any active escharotic action, no possible damage can be done to the walls of the stomach by this method of administration. The objections which have been made to this form of administration are undoubtedly of a merely captious character, for the purpose, if possible, of prejudicing the public against the conclusions reached. Inasmuch as the capsule is a common method of administering solid remedies at the present time the practice of the medical profession approves unanimously this method of exhibition.

SUMMARY OF RESULTS.

MEDICAL AND CLINICAL DATA.

These data clearly show that the administration of sulphites and of sulphurous acid in a free state in the quantities employed produces harmful effects. A tendency is manifested in practically every case to produce headache and digestive disturbances. In some cases these symptoms are not clearly marked, while in others they are extremely well defined. In many cases uneasy sensations and even pain were developed in the stomach and intestines, and there were complaints of "heartburn." The occurrence of this class of symptoms during the administration of the preservative and their gradual disappearance during the after period seem to be conclusive evidence that they could have been due only to the effect of the preservative itself. There were also in some cases attacks of dizziness and palpitation of the heart. In a few cases nausea was developed to the extent of vomiting.

It was recognized, as in previous experiments, that the mental attitude of the subject might play some part in producing these symptoms, or at least might affect the description of them by the man himself. That this, however, does not exercise a dominant influence was more than established by the remarkable effects of the administration of salicylic acid, where, with the same opportunities for mental effects of a depressing character, there was manifested, on the contrary, a persistent demand for more food, the salicylic acid apparently

serving as a stimulant. There is no doubt, therefore, of the fact that the symptoms which are described in the medical history are those actually experienced by the young men, any tendency to exaggeration in the reporting of these symptoms having been carefully considered at the time.

In the case of the men who received sodium sulphite the conclusion is inevitable that the administration of this preservative in the great majority of cases causes headache, sensations of dizziness and occasional nausea, indigestion, pains in the stomach, and other unfavorable symptoms. With the men who received sulphurous acid in an uncombined state, headache was very common, there was a slight tendency to dizziness, accompanied in some cases by nausea, and a feeling of exhaustion and weakness.

In general, it may be said that the most prominent symptom was that of headache, which could hardly have been caused by the imagination. This symptom was very commonly and very persistently experienced at some time during the preservative period.

BODY WEIGHT.

The administration of the sodium sulphite was accompanied by a slight average loss of weight during the preservative period, but the full effect of the preservative in diminishing the weight of the body was shown only toward the end of the preservative period, and there was a continued loss in weight during the after period.

It appears, therefore, that the administration of sulphurous acid in the form of sulphite tends to reduce the weight of the body slowly, and that this tendency is continued for a considerable time after the withdrawal of the preservative. There was a very slight increase in the average weight of the body under the administration of the sulphurous acid in the uncombined form, which increase continued in the after period. The final average effect upon weight for the eleven men shows no change in the preservative period and a slight decrease in the after period.

COMPOSITION OF THE FECES.

The administration of the preservative showed a marked tendency to increase the amount of water in the feces. This was not of sufficient magnitude to warrant classing the preservative as a purgative or cathartic, as the stools were not of a watery consistency. Further, there was no tendency manifested to lessen the secretion of the urine; in fact, in general a diuretic effect was shown. It is of interest to

note this tendency in connection with that of other salts classified as purgatives, and the other disturbances caused by the preservative.

There was a larger quantity of dry matter excreted in the feces under the administration of the preservative, showing a tendency to decrease to this extent the absorption of the food from the intestinal canal. There is thus manifested a tendency on the part of this preservative to derange the metabolic process in so far as these changes in the composition of the feces are concerned.

THE URINE.

Volume and Acidity.

A notable effect of the preservative upon the urine in Series VII was in the increase in volume, thus showing a slight tendency to produce a diuretic effect. This tendency to diuresis is more marked in the cases where sulphurous acid is given in a free state than when it is combined as sulphite. The total solids in the urine were also slightly increased, and there was a marked tendency to increase the acidity, especially in the case of the administration of sodium sulphite. It is evident, therefore, that sulphurous acid has a disturbing effect upon the excretion of the urine, and this effect in general is confirmed by the special Series XIII, in which the sodium sulphite produced a very slight reduction in volume, while sulphurous acid again showed a diuretic effect.

In the special Series XI no diuretic effect is shown. It must be noted, however, that only three subjects took part in this experiment, none of whom was in the original series, and the time of year also may have influenced this result to the slight extent shown, inasmuch as Series XI was conducted in the spring and Series VII in the winter.

Presence of Albumin.

The data which have been recorded for Series VII and XI show unmistakable evidence that the preservative in certain cases produced albuminuria. In the cases in which traces of albumin are present in the fore period, however, there is no proof that the condition was accentuated by the preservative. A further study will be necessary to definitely establish this point.

Microscopic Bodies.

In general, there is shown an increase in the various bodies indicated in the routine examination, particularly in the case of mucous strands and mucous cylindroids. There was no evidence shown which

would indicate any lesions produced, as would be evidenced by a large increased production of the various casts, but the data taken as a whole indicate a strong tendency on the part of the preservative to produce an increased renal activity as evidenced by the general increase of the microscopic bodies.

Distribution of Nitrogenous Bodies.

In the special study (Series XI) made to determine the effects of the preservative on the distribution of the nitrogen-bearing bodies in the urine, there is shown a decrease in the quantity of urea excreted during the preservative period. There is also a decrease in the total nitrogen excreted which is contrary to the tendency shown in Series VII. For the reasons given under the discussion of the volume of the urine the data for Series VII must be given greater weight.

The other bodies remain very constant. There is a tendency to slightly decrease the amounts of uric acid and ammonia, under the influence of the preservative, while kreatinin is slightly increased. This disturbance, the decrease of urea and the increase of kreatinin, shows an interesting relation in so far as the normal processes in regard to the excretion of these bodies is concerned. Urea, which of all the materials excreted contains the largest amount of nitrogen, is believed by some to be an indication of the proteid metabolism. Recently the excretion of kreatinin has received more attention and is regarded by Folin and others as an index to katabolic changes, as during normal metabolism it should remain constant.

The fact that here one is decreased, while the other is increased, is quite significant, and, considered in connection with other disturbances noted, shows that the preservative has exerted a marked influence in deranging the metabolic functions.

Sulphur.

Under the conditions of the experiment the sulphur studies present especially interesting data.

As would be expected, the quantity of inorganic sulphates excreted in the urine is very largely increased by the administration of sulphurous acid and sulphite, this increase, whether sulphite or sulphurous acid was ingested, accounting for the greater part of the preservative sulphur eliminated.

In addition to the increase in inorganic sulphates, an important fact brought out by the data is the increase in the organic combination of sulphur, known as neutral sulphur. This sulphur was uniformly increased in every case during the preservative period, and in some instances, particularly in the subjects receiving sulphurous acid,

where there was no interval between the preservative and after periods, this increase was carried into the after period.

A point worthy of notice here is the fact that the sum of the increase in neutral and inorganic surphur in the preservative period alone more than accounts for the preservative sulphur ingested. This, when the after period is considered, may be derived from an increase in katabolic activities. There does not appear to be any marked effect on the excretion of ethereal sulphates. Half of the subjects show an increase in the excretion of this form of sulphates, which, in the case of these individuals, may indicate a slight increase in the putrefactive changes taking place in the intestines, although, since this increase occurred in the case of the subjects receiving sulphurous acid, it might be attributed to direct combination in the intestines.

There is the same tendency shown throughout by the data, namely, the rapid elimination of practically all of the preservative sulphur in an oxidized form in the urine.

MICROSCOPIC EXAMINATION OF THE BLOOD.

One of the most important conclusions established by the experimental data is that which relates to the comparative number of blood corpuscles and the quantity of hemoglobin as influenced by the action of the sulphurous acid. The data here are of such a character as to admit of no doubt whatever as to their interpretation. Under the influence of the sulphurous acid both the number of red and of white corpuscles in the blood is largely diminished. This is true whether the sulphurous acid is exhibited in the form of sulphites or as free acid. In Series VII the number of red corpuscles in a cubic millimeter of the blood is about one million less in three individual cases, and a uniform decrease is recorded for all but two individuals. In the special study, Series XIII, this effect is confirmed. During the after period the loss in the number of red corpuscles is partially restored and doubtless would have been completely restored had the after period been continued longer. The relative decrease of the white corpuscles is even greater than that of the red blood cells, but is not marked by the same uniformity. This loss is also partially restored during the after period. The data, therefore, are very striking in showing the tendency of the sulphurous acid to diminish the number of both red and white corpuscles, and also to diminish the percentage of hemoglobin. The relation between the decrease in hemoglobin and red blood cells, as expressed by the color index,

shows that the relative decrease of hemoglobin in the blood is not so great as that of the red blood cells. (Fig. 1.)

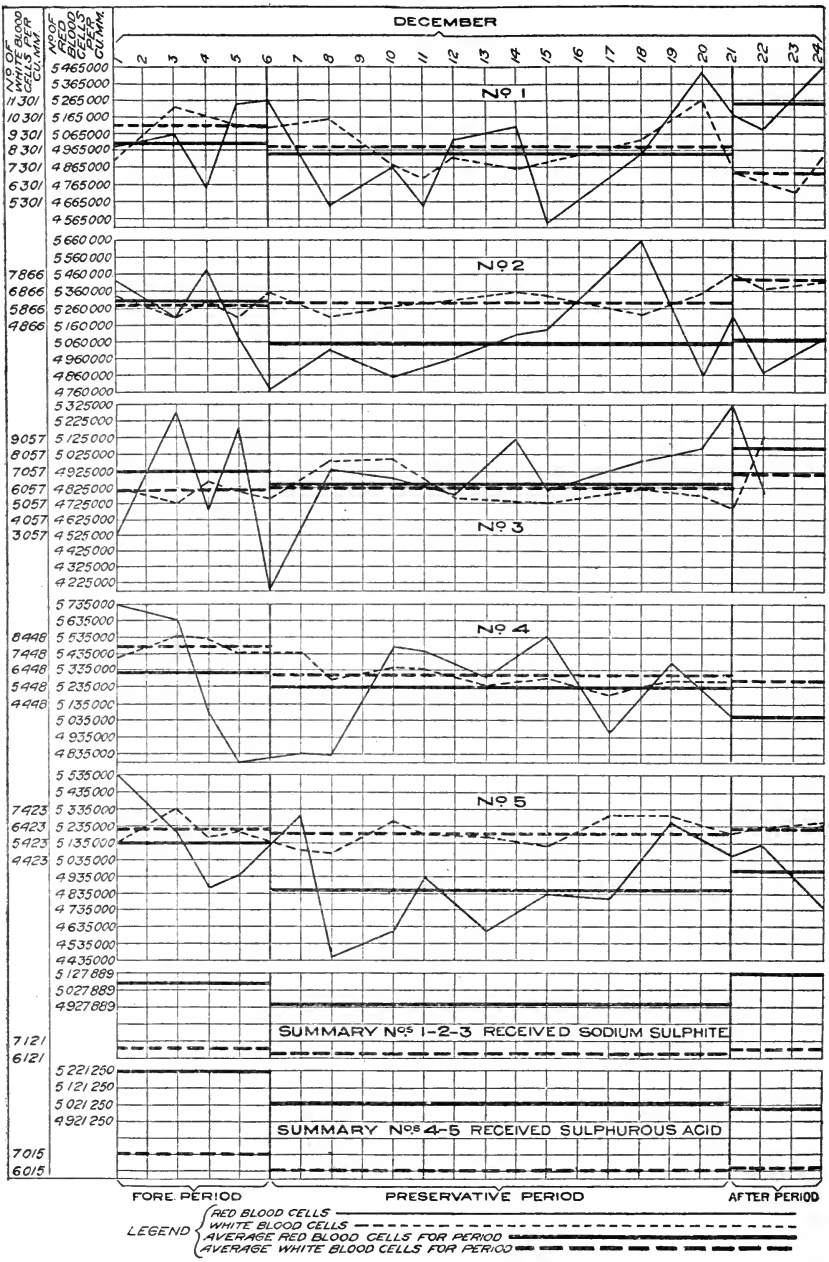

FIG. 1.—Individual and summarized data, showing the effect of the preservative on the red and white blood corpuscles, Series XIII.

METABOLIC PROCESSES.

Nitrogen Metabolism.

The general effect of the preservative upon the assimilation and excretion of nitrogen, as shown by the balance sheets, is not strongly marked. It is evident, however, that there is some disturbance of nitrogen metabolism, especially in inhibiting the absorption of nitrogen in the intestines, inasmuch as both summaries agree in showing an increase of nonmetabolized nitrogen during the preservative period. There was a much more marked disturbance in the case of the subjects receiving sodium sulphite, those receiving sulphurous acid (representing a smaller ingestion of SO_2) showing but little variation from normal conditions.

Phosphoric-Acid Metabolism.

The summaries show that there is quite a marked tendency on the part of the preservative to derange in a measurable degree the metabolism of phosphoric acid. Sulphur both as sulphite and as free sulphurous acid tends to increase the quantity of phosphoric acid excreted in the feces and to decrease the quantity excreted in the urine. It may, therefore, be said to have a decidedly inhibiting effect upon the phosphoric-acid metabolism.

Sulphur Metabolism.

The most important point brought out by an inspection of the sulphur balance sheets is the increased elimination of sulphur over that ingested as preservative. There is an increase in both the urine and feces, the increase in the urine during the preservative period alone, in the case of the subjects receiving sodium sulphite, being greater than the amount of preservative sulphur ingested, while in the case of sulphurous acid the increase corresponds almost exactly to the amount of preservative sulphur ingested.

The increase in the feces, considering the same tendency shown in the nitrogen and phosphoric-acid balances, can hardly be attributed to an elimination of preservative sulphur through this channel, but rather, as is before mentioned, to a decrease in assimilation and absorption from the ingested food. This fact, together with the probable increase in katabolic activities shown as regards the sulphur, indicates that the administration of the preservative produced decidedly unfavorable effects.

These tendencies are more marked in the case of sodium sulphite, though the variations in the conditions of the experiment must be considered in making this statement.

TABLE III.—*Comparative summary of principal determinations made—Series VII.*

Data.	Sodium sulphite (Nos. 1–6).[a]			Sulphurous acid (Nos. 8–11).[b]		
	Fore period.	Preservative period.	After period.	Fore period.	Preservative period.	After period.
Body weight (kilos)	63.71	62.78	62.28	61.87	62.00	62.07
Composition of feces:						
Weight (grams)	82.00	103.00	85.00	87.00	102.00	115.00
Water content (per cent)	72.50	76.15	75.40	74.97	76.60	77.63
Dry matter (grams)	23.00	25.00	21.00	22.00	24.00	26.00
Urine:						
Volume (cc)	1,092.00	1,139.00	1,076.00	1,195.00	1,402.00	1,415.00
Microscopic sediments (per cent of relative occurrence)[c]	54.50	66.70	65.50	.....	.....	.....
Albumin (arbitrary values for relative occurrence)[d]	0	13	7	.....	.....	.....
Sulphur (as SO_3):						
Neutral	.312	.419	.372	.281	.371	.409
Inorganic	2.164	2.729	2.104	1.943	2.249	2.016
Ethereal	.165	.167	.156	.140	.155	.142
Total	2.642	3.316	2.631	2.364	2.774	2.567
Metabolism (percentage results):						
Nitrogen—						
Nonmetabolized (feces)	7.50	8.54	7.47	8.04	8.78	9.26
Metabolized (urine)	85.10	87.17	88.17	80.55	79.10	81.13
Phosphoric acids:						
Nonmetabolized (feces)	29.93	36.34	29.91	32.81	37.13	36.66
Metabolized (urine)	60.03	58.82	57.60	53.66	52.85	51.01
Sulphur:						
Nonmetabolized (feces)—						
Food sulphur only	11.20	12.13	10.05	11.05	11.85	11.73
Including S in preservative	.....	10.16	.....	.....	10.42	.....
Metabolized (urine)—						
Food sulphur only	82.55	106.66	85.32	74.09	89.36	80.31
Including S in preservative	.....	89.30	.....	.....	78.52	.....

[a] Received an average of 0.472 gram per day of SO_2.
[b] Received an average of 0.343 gram per day of SO_2.
[c] Nos. 1 to 12.
[d] Calculated only for subjects who showed no albumin in fore period, including Nos. 1 to 12.

GENERAL CONCLUSIONS.

From a careful consideration of the data in the individual cases, and the summaries of the results, it appears that the administration of sulphurous acid in the food, either in the form of sulphurous-acid gas in solution or in the form of sulphites, is objectionable and produces serious disturbances of the metabolic functions and injury to digestion and health. This injury manifests itself in a number of different ways, both in the production of clinical symptoms which indicate serious disturbances, malaise, or positive suffering, and also by inducing certain changes in the metabolic processes which are not manifested in the way of ordinary clinical symptoms, and are only detected by careful chemical and microscopical study of the excretory products. It can be safely said from the evidence adduced that the administration of sodium sulphite and sulphurous acid, as above indicated, produces a marked influence of an unfavorable character on metabolism. As a result of this action, an assimilation of food materials containing organic phosphorus is retarded, while there is evidence of increased sulphur katabolism. The sulphur balance sheets

show what an immense burden has been added to the already overworked kidneys, which are called upon in this case to remove nearly all, if not quite all, of the added sulphur from the body, previously converted, in great part, to sulphuric acid. It is not possible that placing upon the kidneys this increased work of excreting sulphur can result in anything but injury. The fact that the microscopic crystalline and amorphous bodies in the urine are increased in number under the influence of the added sulphur, is another indication of the extraordinary demands made upon the kidneys in such circumstances.

This increase is interesting in respect of the effect which the continued exhibition of sulphurous acid must eventually have upon the structure of the kidney. It is reasonable to suppose that the continued use of a body which produces such results would cause lesions of a histological character that eventually would develop conditions which would give serious apprehension. In the nature of these experiments it was not possible to examine the organs of the body histologically and hence the above conclusion is only based upon experience of a similar character where the organs in question have been subject to such examinations. While there might be no distinguishable lesion of the kidneys produced during a period of twenty or thirty days, or even longer, it is plain that, sooner or later, lesions of a very serious character, producing organic diseases, possibly of an incurable type, would be induced. The further observation that there is a marked tendency to the production of albuminuria, although of an incipient character, is an indication of the unfavorable results of the administration of the sulphurous acid. It is, therefore, evident that by increasing the burden upon the excretory organs, the administration of sulphur in the form mentioned is highly detrimental to health.

All of these tendencies can not be interpreted as being other than of a decidedly harmful nature. Another effect which the administration of the sulphur produced, and one of a more serious character still, is found in the impoverishment of the blood in respect of the number of red and white corpuscles therein. The administration of a substance which diminishes by a notable percentage these important component particles of the blood must be regarded in every sense as highly prejudicial to health. Some of the most important functions of the blood, as has been well established by careful physiological studies, are intimately connected with the number and activity of both the red and white corpuscles. The bleaching effect of the sulphurous acid upon the color of the blood is a matter of less consequence and no great effect is produced upon the hemoglobin, but the diminution of the number of red and white corpuscles is a matter of serious concern.

The variations of the metabolic processes, from the normal, as indicated in this series of experiments, were never of a character favorable to a more healthy condition of the system, but, on the other hand, all these variations, in so far as the effect of the changes could be distinguished, are of a prejudicial character. There is no evidence whatever that the sulphur added to the foods in the form of sulphurous acid or sulphites takes any part in the nutrition of the tissues of the body containing sulphur, namely, the proteids; hence no claim of food value can be established for these bodies. The evidence all points to the fact that they are purely drugs, devoid of food value, having no favorable effects upon the metabolic processes, but, on the other hand, exerting deleterious and harmful effects. The conclusion, therefore, is inevitable that as a whole the changes produced in metabolic activity by the administration of sulphur in the forms noted above in the comparatively short time covered by the experiments are decidedly injurious. The verdict which must be pronounced in this case is decidedly unfavorable to the use of this preservative in any quantity or for any period of time, and shows the desirability of avoiding the addition of any form of sulphurous acid to products intended for human food.

[Cir. 37]

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