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## Action of Sodium Thiosulfate in Treatment of Metallic Intoxications and Lesions of the Skin.

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Since sodium thiosulfate therapy was first introduced clinically by Dennie and McBride,[1] much interest has centered about its use in metallic toxemias. Given intravenously it has proven efficacious in relieving dermatitis due to heavy metals, especially arsenic and mercury. Myers and Groehl[2] have studied the excretion of arsenic when sodium thiosulfate was given in cases of post-arsphenamine dermatitis. Its use in diagnostic procedure[3] has, in many instances, shown arsenic to be the etiological factor in skin lesions of obscure origin.

The object of this investigation was to study the effect of salvarsan and sodium thiosulfate on the blood chemistry of experimental animals. Chloride and sugar determinations were made, these two substances being chosen as representatives of two main groups of blood constituents, namely electrolytes and nonelectrolytes, and also because they represent the abnormalities in the production of skin lesions as found in eczema in arsenical and mercurial poisoning. In a succeeding publication the action of sodium chloride on the sugar and chlorides will be given, as well as the effect on other blood constituents such are urea, uric acid and the calcium-phosphorus balance.

Whitehorn's[4] method was used for the chlorides, and Hastings and Hopping's[5] modification of McLean's[6] method for sugars. Examination of the blood was always made previous to the injection. The animals were subjected to handling and were made accustomed to their surroundings so that conditions of shock can hardly be considered as playing any part in the taking of the specimens. The blood was obtained from the ear vein.

Salvarsan, in the form of a 0.5 per cent solution of the disodium salt in freshly distilled water, was given intravenously by gravity to rabbits, in doses of 50 mg. per kg. body weight. Table I gives the average values for 7 rabbits for the sugars and chlorides at different intervals after the salvarsan injection.

TABLE I.

*Changes in the blood sugar and chlorides after the administration of Salvarsan.*

0.5 per cent aqueous solution — Dose: 50 mg. per kg. body weight.
Intravenous injection.

| | Initial blood | Blood after intervals of minutes | | | | | |
|---|---|---|---|---|---|---|---|
| | | 0+ | 10 | 20 | 40 | 90 | 180 |
| Sugar—mg./100 cc. | 117.4 | 131.8 | 126.1 | 136.0 | 143.3 | 125.1 | 131.6 |
| NaCl—mg./100 cc. | 536.9 | 529.1 | 539.4 | 547.7 | 563.1 | 592.5 | 586.8 |

Sodium thiosulfate was administered intravenously in the form of a 25 per cent freshly prepared aqueous solution. The dose was 700 mg. per kg. body weight. The average blood changes for a group of 9 rabbits are shown in Table II.

TABLE II.

*Changes in the Blood Sugar and Chlorides after the Administration of Sodium Thiosulfate.*

25 per cent solution — Dose: 700 mg. per kg. body weight.
Intravenous injection.

| | Initial blood | Blood after interval of minutes | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 0+ | 15 | 30 | 60 | 90 | 180 | 300 |
| Sugar—mg./100 cc. | 129.0 | 169.0 | 151.7 | 152.68 | 144.46 | 120.2 | 130.4 | 123.6 |
| NaCl—mg./100 cc. | 529.9 | 510.2 | 539.4 | 540.74 | 529.50 | 539.9 | 567.7 | 554.0 |

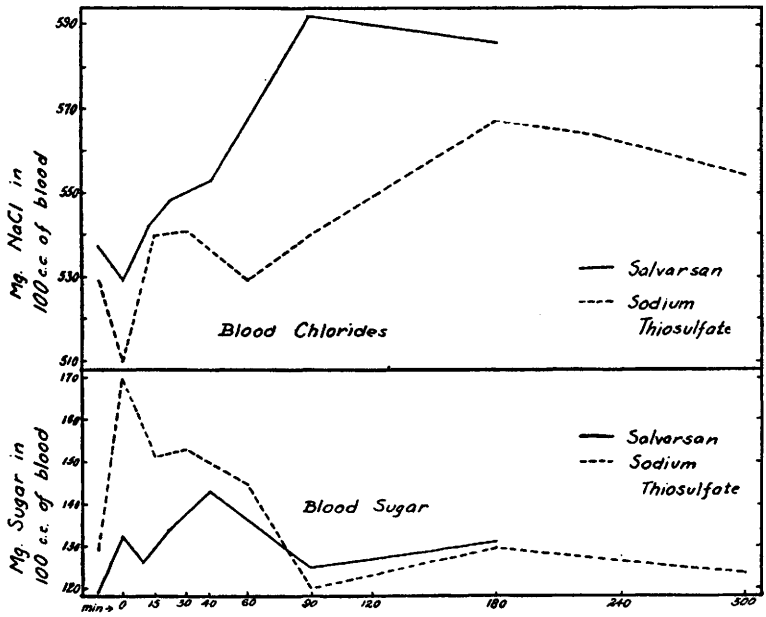


CHART 1.

Chart 1 shows graphically the results of the two types of treatment.

It will be seen that salvarsan and sodium thiosulfate have a parallel effect which exists quite uniformly over a period of 3 to 5 hours. The blood sugar is increased immediately after the injection, and later decreases to the original level or lower. The chlorides, on the other hand, drop first, followed by an increase and then a very slow decrease. A comparison between the blood chlorides and the leucocyte count as carried out by Mueller and Myers[7] shows that for both there is a period of pronounced drop over the same interval. The leucocytes return to normal gradually, but the increase in chlorides extends over a considerably longer period. These results have been checked up clinically, confirming the experimental findings on rabbits.

It may be reasonably assumed that the reason for the effectiveness of sodium thiosulfate in cases of arsenic intoxication is due to a stimulation of the processes which normally take care of arsenic but which have become sluggish on account of the toxic action of the metal. Thiosulfate passes through the same channels as salvarsan, but where the latter intoxicates the cells and retards their action, the former is tonic, rather than toxic, and stimulates the processes by which it, and also the arsenic, may be eliminated.

Mention must be made here of the work done by Mueller and Myers[8] on the mechanism of arsenic lesions. They have demonstrated that skin and liver are both controlled by the autonomic nervous system. All salvarsan injections, with the exception of silver salvarsan, are accompanied by a shock of the involuntary nervous system as evidenced by a decrease in the leucocyte count. In some cases, more susceptible than others to reactions after salvarsan, this leads to an intoxication of the involuntary nervous system. There are two types of skin and liver function to be considered here: first, the prevention of too great quantities of arsenic from entering the cells from the blood stream, and second, the excretion of arsenic that has been deposited in the cells. Intoxication of the autonomic nervous system and consequent slacking of the nerve control of the cells of the skin and liver leads to the following vicious circle: 1. Arsenic from the blood enters the cells in unduly large quantities due to the interruption of the "barrier" function. 2. *Cellular activity is so impaired that*

*the organs are unable to excrete arsenic in sufficient quantities.* 3. Excessive loading of arsenic in the skin and liver causes injury and even destruction of the cells, producing dermatitis and jaundice. The work of Throne, Van Dyck, Marples and Myers[9] has shown that arsenic may produce lesions of the skin which are only manifest in many instances several years after the initial intoxication. The same authors have demonstrated that arsenic may be an etiological factor in the genesis of eczema.

Sodium thiosulfate, when given intravenously, causes increased arsenic excretion as shown by the urine analyses before and after thiosulfate reported by Groehl and Myers.[2] When this load is removed from the cells and the factor so irritating to the involuntary nervous system is lessened it is probable that this latter is able to resume its normal function of maintaining a barrier and excreting arsenic normally.

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## The Hydrogen Ion Concentration of the Nucleus and Cytoplasm of the Egg Cell.

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By means of the microinjection apparatus the series of acid dye indicators of Clark and Lub and the basic dye Neutral Red