

saline solution, etc., may be injected into the peritoneal cavity a few hours before the operation.

Finally, the exudate is more easily handled after it has been secured than is blood plasma, inasmuch as elaborate precautions are not necessary to prevent its clotting. In cases of the abdominal wall puncture, where the operation is not a clean one, a blood vessel may be pierced, and as a result, varying quantities of blood will be mixed with the exudate. This causes a more rapid clotting than with the exudate alone. The appearance of the exudate varies according to the number of white blood cells present. These may be readily thrown down by centrifuging, and the clear liquid used, or the exudate may be used without centrifuging. The experiments to date show that the white cells in the medium do not prevent the activity of the tissues *in vitro*. Experiments are in progress which, it is hoped, will furnish additional evidence on the use of various exudates as culture media.

2845

Therapeutic activity of sodium thiosulphate.

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Sodium thiosulphate was introduced into therapy several years ago by one of us,¹ in cooperation with Dennie and McBride, as a means of relieving certain types of intoxication, such as the metallic toxemias. The drug, simple as it may seem, has fully met the vital test of yielding prompt relief when administered soon after the development of the toxic symptoms.

Our interest has led us now for several years to a further study of its *modus operandi*. The authors² have previously reported on

¹ McBride, W. L., and Dennie, C. C., Treatment of Arsphenamine Dermatitis and Certain other Metallic Poisonings. *Arch. f. Derm. u. Syphil.*, 1923, i, 63.

² Groehl, M. R., and Myers, C. N., Sodium Thiosulphate in the Treatment of Dermatitis and Jaundice as a Result of Metallic Intoxication. *Therap. Gaz.*, 1924, x, 691.

the excretion of arsenic in cases of arsenic dermatitis. The action of sodium thiosulphate is least marked in cases of inorganic arsenic poisoning; next in order, it is effective after the pentavalent organic preparations; and the greatest efficiency is reached with the trivalent group represented by the arsphenamines. The activity of sodium thiosulphate cannot be judged by the excretion of arsenites. It has been pointed out by Mueller and Myers³ that the skin and the liver are the two main organs involved in intoxication, and on this basis sodium thiosulphate serves as a protective drug in respect to the autonomic nervous system.

The present report offers clinical and experimental evidence in favor of the efficacy of freshly prepared sodium thiosulphate in hastening the excretion of arsenic either in its inorganic or in its organic form. Furthermore, sodium thiosulphate does not disturb the therapeutic action of the arsphenamine compound in its action on *Trypanosome equiperdum*. Prompt results have been noted by leading syphilologists in connection with dermatitis and jaundice following the use of the arsphenamine group. Some clinical data have recently been made available through the investigations of H. H. Dale, of the British Medical Research Committee.⁴

Table I shows the effect of the simultaneous use of salvarsan and sodium thiosulphate, together with the control experiment. Table II shows the action of sodium thiosulphate on the excretion of arsenic in the urine. The clinical history of the case is as follows:*

Male, aged 39, four years ago began to show groups of vesicles on an erythematous base. The vesicles were exceedingly itchy. Diagnosed as *Dermatitis herpetiformis*. These developed the typical pigmentation and scarring of that disease. Two years ago, began taking arsenic in the form of Asiatic pills—nine a day for four months; received solution of potassium arsenite (Fowler's solution) in gradually increasing doses.

³ Mueller, E. F., and Myers, C. N., The Effect on the Involuntary Nervous System of Arsenicals and the Salvarsan Group. *PROC. SOC. EXP. BIOL. AND MED.*, 1924, xxi, 474.

⁴ Harrison, L. W., Effect of Sodium Thiosulphate on the Therapeutic Power of Arsenobenzol Compounds. *Lancet*, 1925, xxii, 1161.

* From the Service of Dr. Throne and Dr. Clark, New York Skin and Cancer Hospital.

TABLE I.

Rat No.	Wgt.	Dose mgm. per kg.	Trypanosome count at time of treatment.	1st day	2nd day	3rd day	5th day	7th day	8th day	9th day	10th day
G-87 (in 20% Na ₂ S ₂ O ₃) G-87 64 mgm. in 40 cc. water. Na ₂ S ₂ O ₃ 8 grams											
5793	166	3.5	136,000	—	+	—	—	D	—	—	—
5794	168	3.5	164,000	—	+	—	—	+	—	—	—
5795	162	3.5	116,000	1000	—	—	—	D	—	—	—
5796	165	5.3	108,000	—	—	—	—	—	—	—	—
5797	160	5.3	172,000	—	—	—	—	—	—	—	—
5798	167	5.3	112,000	—	—	—	—	—	—	—	—
5799	161	8.	136,000	—	—	—	—	—	—	—	—
5800	171	8.	176,000	—	—	—	—	D	—	—	—
5801	164	8.	124,000	—	—	—	—	—	—	—	—
5802	159	12.	188,000	D	—	—	—	—	—	—	—
5803	167	12.	132,000	—	—	—	—	—	—	—	—
5804	160	12.	156,000	—	—	—	—	—	—	—	—
Minimum effective dose = 3.5.											
SALVARSAN G-87 160 mgm. in 100 cc. water.											
5805	162	3.5	164,000	1000	+	—	—	D	—	—	—
5806	167	3.5	136,000	—	—	—	—	—	D	—	—
5807	162	5.3	68,000	—	—	—	—	—	—	—	—
5808	168	5.3	100,000	—	—	—	—	—	—	—	—
5809	156	8.	120,000	—	—	—	—	—	—	—	—
5810	157	8.	168,000	—	—	—	—	—	—	—	—
Minimum effective dose = 3.5.											

TABLE II.—URINE SPECIMENS.

Spec. No.	Date	Period	Excreted cc.	Sp. gr.	Moist wt. of spec. gm.	Dry wt. of spec. gm.	Per cent solids	As in mg. per 100 gm. spec.		Notes.
								Moist	Dry	
8569	9/25/24	24 hrs.		1.019	35.4730	0.9395	2.64	0.002	0.10	Sodium thio. 15 gr. daily
8566	9/26/24	A.M.		1.17	36.2010	0.8270	2.28	0.01	0.48	
8570	9/26/24	P.M.		1.010	24.0012	0.3647	1.52	0.03	2.19	
8571	9/29/24	"		1.019	35.7780	1.1400	3.18	0.08	2.63	
8572	10/2/24	"		1.015	34.5480	0.5540	1.60	0.005	0.36	
8579	10/6/24	"	1800	1.020	30.8457	0.6676	2.12	trace	trace	No sod. thio. on this day
8580	10/8/24	A.M.	2500	1.019	22.1320	0.5800	1.80	0.003	0.17	
8578	10/8/24	P.M.	2500	1.017	33.4710	0.5810	1.73	0.005	0.34	
8581	10/10/24	"	1000	1.021	26.1375	0.6575	2.33	0.01	0.61	
8585	10/16/24	"	1000	1.023	31.5030	1.2470	3.96	0.005	0.12	
8582	10/17/24	"	1000	1.020	35.7780	0.0710	2.99	0.006	0.19	No sod. thio. on this day
8583	10/17/24	P.M.	1000	1.022	38.6333	1.5723	3.97	0.05	1.27	
8584	10/21/24	"	1250	1.017	39.3532	1.0842	2.75	0.002	0.05	No sod. thio. on this day
8587	10/27/24	A.M.		1.026	38.2150	1.7850	4.66	0.003	0.05	No sod. thio. on this day
8592	10/27/24	P.M.		1.019	27.0376	1.4176	5.26	0	0	
8593	10/31/24	"	1400	1.019	24.8400	0.7700	3.09	trace	trace	1 gm. sod. thio in 10 cc. water intravenously daily
8591	11/3/24	"	1000	1.015	28.0753	0.6703	2.37	0	0	
8593	11/4/24	"		1.020	43.5071	1.5851	3.64	0.06	1.51	
8596	11/7/24	"		1.022	46.9760	1.8720	3.98	trace	trace	
8597	11/9/24	"	700	1.023	48.1793	1.6043	3.33	0.002	0.06	No sod. thio. on this day
8598	11/11/24	"		1.022	49.9590	2.1020	4.26	0.04	0.95	
8603	11/13/24	"	850	1.025	25.6400	1.1400	4.44	0	0	No sod. thio. on this day
8604	11/15/24	"	800	1.020	27.5377	0.9587	3.44	0.005	0.16	
8670	12/2/24	"	800	1.031	36.0415	1.9420	5.38	0.004	0.08	No sod. thio. on this day
8671	12/4/24	"	900	1.032	39.9013	1.9798	4.99	0.004	0.08	No sod. thio. on this day
8672	12/6/24	"	950	1.027	33.8245	1.5635	4.67	0.11	2.29	
8673	12/8/24	"	600	1.033	39.6360	2.1005	5.30	0.10	1.90	
8676	1/13/25	"		1.010	39.1620	0.6870	1.76	trace	trace	No sod. thio. on this day
Calamine lotion			20		23.5788	7.1003	30.11	0.25	0.84	

Calamine lotion used on skin. The high arsenic content is to be noted.

After entering the hospital a biopsy was done and histological examination made. The patient was immediately given injections of sodium thiosulphate intravenously, 1 gm. every other day, and 15 grains (0.97 gm.) of thiosulphate three times a day after meals. The intestinal bleeding stopped at once, and under continued injections the acute dermatitis of his head, hands and feet slowly subsided, and the peculiar pigmentation with lichenoid papules scattered through it—particularly on the body and on the back of the neck—showed improvement.

Summary. Sodium thiosulphate shows no deleterious action on the trypanocidal activity of the salvarsan groups when the two drugs are given simultaneously. These results are corroborated by clinical observations of other investigators. Sodium thiosulphate plays an important part in the rate of excretion and also the clinical symptoms following an intoxication due to arsenic in (a) inorganic state, (b) pentavalent organic state, and (c) the organic trivalent arsenicals.

Clinical study showed that when the injections of thiosulphate were stopped and the arsenic output in the urine dropped down to about 0.003 to 0.004 mg., the eruption on the head, hands and feet and the peculiar lichenoid eruption on the back, chest, arms and legs regularly became worse. With the renewed administration of the thiosulphate, and when the arsenic output came up to about one decigram of arsenic for each 100 gm. of moist specimen, the eruption regularly improved.

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Hyperglycaemia following experimental cholecystitis.

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A series of fifteen experiments were conducted as follows: A presumably normal mongrel dog was prepared for laparotomy, by administration of morphia and ether, shaving, and cleansing of the abdominal field for operation. Under sterile conditions the abdomen was opened, the gallbladder was identified and incised.