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The Influence of the Vegetative Nerves Upon the Distribution of Arsenic After Salvarsan Injections.

ERNST F. MÜLLER, C. N. MYERS AND E. MARPLES.

From the Department of Dermatology and Syphilology, College of Physicians and Surgeons, Columbia University, New York.

The present investigation gives a comparison between the distribution of arsenic in normal animals[1] and animals which were under the influence of epinephrin. Epinephrin was given subcutaneously twenty minutes before the salvarsan was injected intravenously. In Table I the figures in column (A) indicate the arsenic content in mg. per 100 gms. dried specimen of the various organs after an intravenous injection of 80 mg. salvarsan per kilo body weight, preceded by the subcutaneous injection of 5 mg. per kilo body weight of epinephrin. The figures under (B) are given for comparison and represent arsenic determinations in rats which received intravenous injections of 160 mg. of salvarsan per kilo of body weight without epinephrin. A dose of 80 mg. of salvarsan is equivalent to 25 mg. of metallic arsenic and a dose of 160 mg. of salvarsan contains 50 mg. of metallic arsenic.

TABLE I.
Average arsenic content of organs.

Interval	Blood		Liver		Spleen		Brain	
	A.	B.	A.	B.	A.	B.	A.	B.
Immediate	71.17	14.76	71.05	9.33	18.39	42.53	1.230	39.12
5 min.	90.96	42.21	96.48	33.84	30.59	32.84	0.911	5.51
10 min.	72.63	15.96	109.04	17.47	27.12	66.49	0.880	3.85
20 min.	77.39	13.72	102.33	96.02	20.36	61.16	0.215	1.90

Table II shows the percentage of the arsenic, actually injected, that is present in the organs at the given intervals. Here again the

TABLE II.
Percentage of arsenic remaining in tissues of rats.

Interval	Blood		Liver		Spleen		Brain	
	A.	B.	A.	B.	A.	B.	A.	B.
Immediate	53.62	5.12	35.52	2.66	3.67	4.25	0.07	1.20
5 min.	68.08	15.80	48.24	8.46	6.12	3.28	0.06	0.18
10 min.	54.36	5.97	54.52	4.37	5.42	6.65	0.05	0.12
20 min.	57.92	5.12	51.12	24.00	4.07	6.12	0.02	0.09

figures in column (A) represent salvarsan preceded by epinephrin and those under (B) salvarsan alone.

The results of these studies can be briefly summarized as follows: Under normal conditions arsenic injected in the form of the disodium salt of salvarsan intravenously into the mammalian body is immediately distributed to the various organs. Only 5.12 per cent of the amount actually injected remains in the blood stream immediately after the injection while 94.88 per cent must either be distributed in the tissues or be excreted. Shortly after this general distribution a reorientation of all organs sets in. As demonstrated in former work,[2] there is an increase in the action of the liver and other abdominal organs accompanied by a dilation of their vessels. At the same time, the activities as well as the vascular capacity of the peripheral organs are diminished. Simultaneously with this typical rearrangement of almost all organs, arsenic disappears from the peripheral organs, of which the brain represents one part. Arsenic reappears in the blood stream and is gradually accumulated in the liver with a corresponding decrease of the arsenic findings in blood and other organs. Fig. 1 shows the arsenic content in mg. per 100 gm. dry specimen in the organs at different intervals after the injection of salvarsan alone and salvarsan preceded by epinephrin.

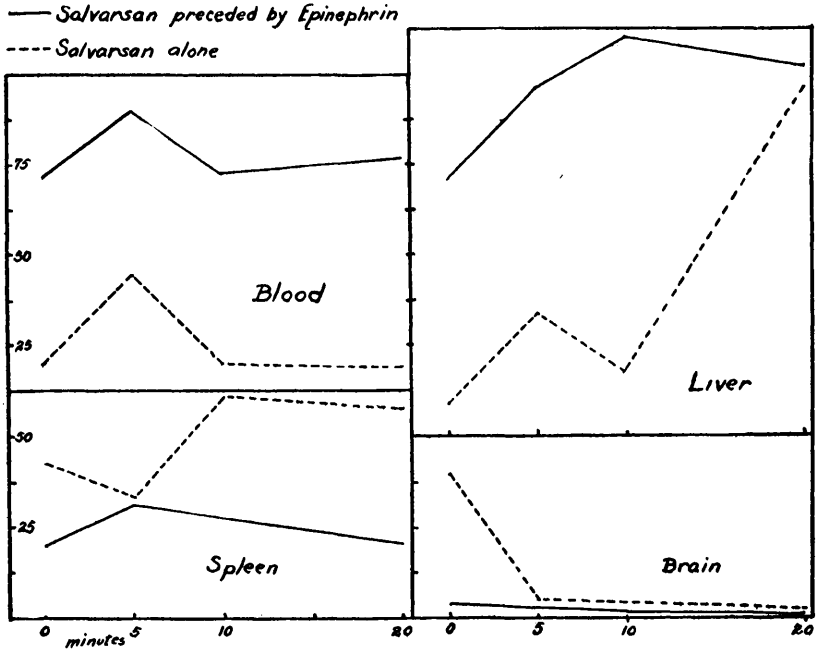

FIG. 1.

If epinephrine is given previous to the injection of salvarsan the distribution of arsenic is markedly changed as far as the actual values are concerned. Instead of 5 per cent of the amount of arsenic actually injected 53.62 per cent remains in the circulation immediately after the injection, so that only 46.38 per cent (minus the excreted portion) can be distributed into the organs. These figures parallel the arsenic content of the brain which is 39.12 mg. per 100 gms. dry specimen in normal rats and only 1.22 mg. in epinephrinized animals. The percentage of the total dose of arsenic actually injected which finds its way to the brain is 1.2 per cent under normal conditions as compared with 0.07 per cent in epinephrinized animals.

The discussion of the individual figures and their significance will be left to a more detailed publication. However, it may be stated that, if the involuntary nervous system is under the influence of epinephrin, almost five times as much arsenic is retained in the blood stream and only a small percentage of that normally distributed into the brain reaches that organ. It is also evident that the second phase of the arsenic distribution, namely the reappearance of arsenic in the blood and its gradual accumulation in the liver, is similarly altered. However, it is interesting to note that even although the percentages are much lower, for both phases of the arsenic distribution in the epinephrinized animals, still they are very similar to those in normal rats. The remarkably low figures for the arsenic in the brain show how much its penetration into the tissues is inhibited as compared with the normal control animals.

Studies with arsenic distribution in rats under the influence of epinephrin show how essential a normal state and a normal undisturbed activity of the vegetative nerves are for the distribution of arsenic, therapeutically administered, in a mammalian body.

This is a preliminary report.

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[1] Fordyce, John A., Rosen, I., and Myers, C. N., *Am. J. Syph.*, 1924, viii, 377.

[2] Müller, E. F., *Munch. med. Woch.*, 1926, lxxiii, 9.

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