

Storage of Manganese by Thyroid. Effect on Oxygen Consumption of the Guinea Pig.

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Levine and Sohm¹ observed hyperactivity of rats following the feeding of small amounts of manganese chloride. A similar observation was made by Ray² on mice. Sato,³ working with rabbits, found that the injection of small doses of manganese chloride caused an increase in oxygen consumption whereas large amounts greatly decreased oxygen consumption. These observations suggest that small doses cause hyperfunction of the thyroid gland.

In order to determine whether the increased activity in animals following manganese administration actually results from the element accumulating in the thyroid, guinea pigs were injected subcutaneously with solutions of manganese chloride of different concentrations daily for 6 days and oxygen consumption values were obtained before and after the manganese injections. The manganese content of the thyroid gland as well as of other organs, was determined by the procedure of Ray.⁴ Forty-eight guinea pigs were used in these experiments. All of these experimental animals received a basal diet consisting of 10 parts of rolled oats, 1 part of bran, 0.1 g of sodium chloride, cod-liver oil and cabbage.

It was earlier observed by Ray² that when mice were allowed to drink water containing 0.05 g of manganese chloride per liter, the element readily accumulated in the liver as well as in other tissues of the body. The liver of the normal mouse was found to contain about 3 times as much manganese per unit of weight as the remainder of the body.

However, the concentration in the body per unit of weight equaled that in the liver after the salt was given in the drinking water for 15 days. In 40 days both the body and the liver became completely saturated (1.2 mg of manganese per 100 g of dry tissue). No greater amount could be found in the tissues of animals after 50, 80, or 90 days of manganese administration. When manganese chloride was injected subcutaneously into the guinea pig, however, the element was stored in quantities much greater than that found in mice receiving the salt orally. Table I shows that after injection all tissues of the guinea pig examined stored manganese in varying amounts. The larger the dose injected, the greater was the amount stored. The thyroid appears to be peculiar in that normally it contains relatively little manganese, but it has the property of storing it in amounts out of all proportion to that stored by other organs. It may also be seen from Table I that the dog thyroid exhibits the same property of storing manganese as that of the guinea pig. When manganese chloride was injected subcutaneously into the dog in a dosage of 5.0 mg per kg body weight, the thyroid stored 49 times the amount found in the normal gland. Guinea pigs receiving a like amount of manganese chloride per kg stored 50 times the normal amount.

The data presented in Table II show that when manganese chloride was injected subcutaneously into the guinea pig in dosages ranging from 1.0 mg per kg body weight to 10.0 mg per kg body weight, the amount of oxygen utilized by the animal was markedly reduced (—10.91% to —31.4%). On the other hand, as is also shown in this table, when the small amount of 0.01 mg per kg of manganese chloride was injected, the oxygen consumption was augmented (+8.4%). It is of interest to note that the oxygen con-

¹ Levine, Victor E., and Sohm, Herbert A., *J. Biol. Chem.*, 1924, **59**, Proc. Am. Soc. Biol. Chem., xlviii.

² Ray, T. W., unpublished data.

³ Sato, Juniti, *Arch. int. de Pharmacodyn. et de Therapi*, 1929, **36**, 49.

⁴ Ray, T. W., *J. Biol. Chem.*, 1940, **134**, 677.

TABLE I.
Mg Mn per 100 g Dry Material After Subcutaneous Injection of MnCl_2 for 6 Consecutive Days.

Daily injection MnCl_2 per kilo guinea pig	mg 0.0	mg 1.0	mg 2.5	mg 3.5	mg 5.0	mg 10.0	mg 15.0
Liver	1.16*	1.20	1.40		1.90	6.00	13.00
Testes	0.40	0.41	0.48		0.83	0.69	1.25
Pancreas	0.92	1.60	3.69		—	—	4.86
Salivary gl.	0.75	1.75	2.40		4.05	2.95	4.95
Thyroid	††	3.91	6.94		9.33	12.50	26.50
Daily inj. MnCl_2 /k dog	0.0			3.5	5.0		
Liver	0.84			1.80	2.30		
Thyroid	0.17			4.00	8.52		

*Each figure following an organ in the table is the average for the manganese in mg per 100 g of dried tissue for not less than 5 animals.

††A total of 23 thyroids, 5 from the human being, 6 from the horse, and 4 each from the cow, the calf, and the dog were analyzed. The average of these was 0.19 mg manganese per 100 g of dry thyroid. Since the amount of manganese in the thyroid of the normal guinea pig is too small for accurate quantitative determination, 0.19 mg was assumed to be the average for the normal animal.

sumption values became progressively less as the storage of manganese increased in the thyroid.

Summary. 1. Subcutaneous injection of manganese chloride caused a storage of manganese in all parts of the body but especially in the thyroid gland. 2. Injection of small doses (e.g. 0.01 mg per kg) of this salt pro-

duced an increase in the oxygen consumption of the guinea pig, while large amounts (e.g. 10 mg per kg) reduced the oxygen consumption in this animal. 3. Oxygen consumption values in the guinea pig became progressively less as the storage of manganese increased in the thyroid.

TABLE II.
Effect of Manganese Chloride on Oxygen Consumption of Guinea Pigs.*

Dose MnCl_2 per kg, mg	O_2 used control, cc/kg/hr	O_2 after MnCl_2 , cc/kg/hr	% deviation from control	Mg Mn recovered per 100 g dried thyroid
10	631.41	432.61	—31.4	12.50
5	634.2	535.28	—15.5	9.33
2.5	507.54	442.93	—12.73	6.94
1.0	532.73	474.6	—10.91	3.91
.01	671.0	727.93	+ 8.4	not determined

*All of the oxygen consumption results were obtained by a special metabolism apparatus devised by L. J. Deysach.