

TABLE I.
Phenosulfazole in the Treatment of Mice Infected with EMC or with MM Viruses.

Virus	Therapy		Dilution of infectious material				MLD 50%
	Initial dose (hr)	mg/day	10-5.0	10-6.0	10-7.0	10-8.0	
EMC	0 (control)		30/30*	21/29	17/30	5/30	10-7.0
	17 post infection	12.5	30/30	29/30	23/30	—	10-7.3†
MM	0 (control)		16/16	12/16	12/16	11/16	10-7.9†
	2 pre inf.	12.5‡	13/14	14/15	11/14	—	10-7.3†
	2 post inf.	12.5‡	14/14	14/16	10/14	—	10-7.2†
	19 post inf.	12.5‡	16/16	15/16	9/16	—	10-7.1†

* Numerator = No. of mice dying; denominator = No. of mice in group.

† These figures represent minimal values. The exact titers are at least this great.

‡ Initial dose 8.33 mg/mouse. These mice received 16.7 mg drug per day during the first 24 hours and 12.5 mg per day subsequently. See text.

fact that this same preparation of frozen stored virus when titrated five days later had a titer of $10^{-7.5}$.

The results of the two experiments are summarized in Table I. These data indicate

that treatment with phenosulfazole produced no reduction in mortality among the mice infected with either EMC or MM viruses. Furthermore, there was no indication that it delayed the onset or duration of the disease.

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Evaluation of the Effect of Darvisul upon Infection with SK Strain of Virus in Mice.*

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Darvisul, N-(2-thiazolyl)-phenol sulfonamide, or phenosulfazole was reported by Sanders, SubbaRow, and Alexander¹ to be effective against as many as 100 LD₅₀ of a mouse virus, SK, when administration was begun 24 hours after intraperitoneal infection.

Through the courtesy of Dr. Sanders the virus was received in the form of two infected mouse brains in glycerine. The drug was received in ampules of 25% solution of lot No. 7-8522, through the kindness of Dr. Sanders and Dr. Leo Rane of the Lederle Laboratories. The plan of testing the drug was that outlined by Dr. Sanders and was rigidly observed.

The original brain material was made into a 10% suspension in 10% horse serum physiological salt solution. A titration was done by intraperitoneal inoculations of groups of 5 mice and found to be approximately 2×10^{-7} . A pool was made from the brains of mice sacrificed when moribund and the 10% suspension of this material served as the material with which the therapeutic effects of the compound were tested.

Albino mice of 20 g weight of a single strain were used. As shown in the table 50 mice were inoculated intraperitoneally with the respective concentrations of virus and 24 hours later administration of the chemical was begun by the same route. The stock solutions of compound were diluted 1:31 in physiological salt solution so that each ml contained 8 mg. The material was given

* Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

¹ Sanders, M., SubbaRow, Y., and Alexander, R. C., *Texas Rep. Biol. and Med.*, 1948, **6**, 385.

TABLE I.
Evaluation of Effect of Darvisul on SK Virus in Mice.

Dilution of virus	Treated No. survivors		Controls No. survivors	
	5th day	14th day	5th day	14th day
2×10^{-4}	0/25	0/25	0/25	0/25
2×10^{-5}	1/25	0/25	1/25	0/25
2×10^{-6}	7/25	2/25	7/25	2/25
2×10^{-7}	21/25	18/25	23/25	18/25

Date of Experiment = October 3, 1948.

Numerator = survivors. Denominator = total number inoculated.

intraperitoneally to 25 mice in amounts of 0.5 ml at 9 a.m., 0.25 ml at 1 p.m., 0.25 ml at 4 p.m., and 1.0 ml at 7 p.m. so that the total daily dosage was 16 mg. Control mice, 25 in number, received equivalent volumes of salt solution intraperitoneally.

The results are presented in Table I. It

is apparent that no difference between treated and control mice was observed. It is concluded, therefore, that under the conditions of the experiment Darvisul had no therapeutic effect upon the infection of mice with the SK strain of murine encephalomyelitis virus.

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Behavior of the Thyroid toward Elements of the Seventh Periodic Group.

I. Halogens and Thiocyanates.*

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It will perhaps surprise many readers of this report to learn that the thyroid will filter from the blood not only iodine but the other halogens as well. Further, while it is generally known that feeding thiocyanates to man and other animals will cause the development of goiter, thyroid hyperplasia and goiter have also been produced by feeding relatively large amounts of any of the halogens other than iodine. The evidence for these statements will be assembled, much of it from the literature, and an hypothesis offered that attempts to show that bromides, chlorides, fluorides, as well as thiocyanates all bring about thyroid enlargement by the same means, and to explain why the responses of the thyroid to all of these substances are similar.

Filtration of Halogens and Thiocyanates

* A report of this work was made before the American Society of Biological Chemists at Chicago, May 14, 1947, *Fed. Proc.*, 1947, **6**, 237.

by the Thyroid. The first step in formation of thyroxine consists in filtering iodide from the blood. This filtration by the thyroid is remarkably effective, its concentrating power being of the order of 10,000. In an early experiment of Marine and Feiss¹ nearly 90% of a dose of 5 mg of KI was found in the goitrous thyroid of a dog in 10 minutes. In many more recent experiments with radioactive iodine similar results have been noted. Even when the synthesis of thyroxine is prevented by administration of thiourea and related substances, the thyroid can still filter iodine from the blood, first shown by Baumann, Metzger, and Marine² and subsequently by others. Selective filtration by the thyroid is not limited to iodine; in fact the

¹ Marine, D., and Feiss, H. O., *J. Pharm. Exp. Therap.*, 1915, **7**, 557.

² Baumann, E. J., Metzger, N., and Marine, D., *Endocrinol.*, 1944, **34**, 44.