prophylaxis and treatment of experimental vaccinia of rabbits, have shown that they are completely ineffective. Under the circumstances any value that the compounds may possess in the treatment of severe generalized vaccinia or variola of human beings would probably depend upon the prevention or control of secondary staphylococcal or streptococcal infections of the lesions.

In these experiments the prepared abdominal skins of adult rabbits were scarified and the areas inoculated with 1:500 dilutions of stock crude vaccinia virus in 50% glycerin.*

Immediately after inoculation 4 rabbits were given an intravenous injection of 1000 units of penicillin† per kg of weight, followed by a second injection 4 hours later. Thereafter, injections were given at 9 a.m., 1 p.m. and 4 p.m. daily for 5 days in succession, totalling 17 doses or 17,000 units per kg. Four additional rabbits were treated in the same manner with 10,000 units of streptomycin‡ in saline solution by intramuscular injection, totalling 17 doses or 170,000 units per kg. All animals, including 4 untreated controls, developed vaccinal lesions on or about the 5th day after inoculation and were kept under observation for a total of 15 days following inoculation. None of the treated animals showed the slightest activity on the part of penicillin and streptomycin in the prophylaxis of vaccinia as compared with the untreated controls.

Twelve additional rabbits were inoculated in the same manner. Four were kept as untreated controls. Treatment of the others was instituted on the 5th to 6th days after inoculation at which time vaccinal lesions were present. Four rabbits were given penicillin and 4 streptomycin in exactly the same manner and in the same dosages as described above. All animals were kept under observation for a total of 20 days following inoculation. None of the treated animals showed the slightest clinical improvement or suppression of developing lesions, as compared with the untreated controls.

Summary. Penicillin in dose of 1000 units per kg by intravenous injection for a total of 17 doses (17,000 units per kg) was completely ineffective in the prophylaxis and treatment of experimental vaccinia of rabbits. Streptomycin in dose of 10,000 units per kg by intramuscular injection for a total of 17 doses (170,000 units per kg) was likewise completely ineffective in the prophylaxis and treatment of experimental vaccinia of rabbits.

* Kindly supplied by Dr. B. Hampil of the Sharp and Dohme Co., Glenolden, Pa.

† Commercial penicillin (Lot No. 45072102) kindly supplied by the Commercial Solvents Corp.

‡ Kindly supplied by the Abbott Laboratories, North Chicago, Ill.

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Survival of Rats Given Methionine* Before and After Thermal Injury.

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The beneficial action of *dl*-methionine in combating selenium poisoning[1] and various types of hepatic injury[2-4] has been well established. Methionine has also been shown to have a protein-sparing action when fed to normal dogs on a low protein diet[5] and following thermal burns in rats.[6] We have

* The methionine used in these experiments was supplied by Wyeth, Incorporated.

1 Lewis, H. B., Schultz, J., and Gortner, R. A., *J. Pharm. and Exp. Therap.*, 1940, **68**, 292.

2 György, P., *Am. J. Clin. Path.*, 1944, **14**, 67.

3 Miller, L. L., Ross, J. F., and Whipple, G. H., *Am. J. Med. Sc.*, 1940, **200**, 739.

4 Beattie, J., *Lancet*, 1944, **2**, 787.

5 Miller, L. L., *J. Biol. Chem.*, 1944, **152**, 603.

6 Croft, P. B., and Peters, R. A., *Lancet*, 1945, **1**, 266.

TABLE I.
The 48-Hour Survival of Burned Rats Given 160 mg of Methionine in Aqueous Solution 2 Hours Pre-burn.

Exp. No.	Date	Methionine treated		Water controls		Untreated		Surface burned %
		Burned	Survived	Burned	Survived	Burned	Survived	
62	9-26-45	3	3	4	0	4	2	30-33
68	10-13	4	4	3	2	4	2	26-30
72	26	4	4	4	4	4	3	25-29
74	27	2	1	3	2	4	1	25-29
78	11-17	6	6	3	2	4	3	28-31
80	16	2	1	4	2	2	2	25-29
82	21	3	3	1	0	1	0	30-34
84	24	2	2	4	1	4	1	28-30
108	6-11-46	8	7	8	1	8	2	29-31
Totals		34	31	34	14	35	16	
% survival			91		41		46	

TABLE II.
The 48-Hour Survival of Burned Rats Given 320 mg of Methionine in Aqueous Solution Post-burn.

Exp. No.	Date	Methionine treated		Water controls		"Tubed" controls		Untreated		Surface burned %
		Burned	Survived	Burned	Survived	Burned	Survived	Burned	Survived	
		Time of therapy post-burn—1 and 5 hr.								
104	12-13-45	8	7	8	4					29-32
105	14	8	8	8	3					28-32
106	17	4	1	4	2	6	1	2	0	28-32
107	18	10	3	9	9	4	1			28-32
Totals		30	19	29	18	10	2	2	0	
% survival			63		62		20		0	
		Time of therapy post-burn—0.5 and 4 hr.								
110	6-11-46	4	1	4	2			6	2	29-31
		Time of therapy post-burn—immediately and 3 hr.								
111	6-14-46	8	5	8	8	8	1			28-31
114	13	8	3	8	2			6	1	30-34
Total of exper. 104-114		50	28	49	30	18	3	14	3	
% survival			56		61		17		21	

tested the effect of the preburn and post-burn administration of methionine on the survival rate of rats subjected to a standard burn.

Methods and Results. Normal stock Wistar rats weighing between 190 and 210 g and maintained on an *ad libitum* diet of Purina Dog Checkers supplemented with whole milk were used in these experiments.

In all experiments a group of healthy rats was selected from the stock cages. In the experiments of Series I, the animals were divided into 3 groups. One group was given 160 mg of methionine in 5.0 cc of distilled water orally through a No. 8 French catheter. A second group was given 5.0 cc of distilled water by the same technic. The third group received no treatment. Two hours after the administration of the methionine solution or water all rats in each of the 3 groups were anesthetized with ether and subjected to a standardized back burn[7] in water at 90°C ±0.5° for 23 seconds. The extent of the burned areas of the rats in each experiment

[7] McCarthy, M. D., *J. Lab. and Clin. Med.*, 1945, **30**, 1027.

was determined by planimetric measurements, as has been previously described.† A 91% survival for the methionine-treated rats (Table I) as compared to 41% survival for the water controls and 46% for the untreated controls was obtained. The increased survival of the methionine group compared to either of the control groups is statistically significant. A P value of less than 0.01 was obtained by calculating the X^2 value from the formula of Fisher[8] for 4-fold tables.

As a consequence of the beneficial results obtained in this series of experiments, several experiments were done in which a single dose of 160 mg of methionine in 5.0 cc of distilled water was given to rats one hour following the burn. These experiments showed no difference in survival between the methionine-treated and water-treated animals. Four experiments were then performed in each of which all rats of one group received 2 doses of 160 mg each of methionine in 5.0 cc of distilled water at one and 5 hours following the burn. A second group in each experiment received 5.0 cc of distilled water at the same postburn intervals. In the third and fourth experiments "tubed" control groups were included. The rats in these groups were subjected to the passage of the moistened catheter at the same time intervals postburn that the treated animals received therapy.

Survival percentages from the summarized data of these experiments No. 104, 105, 106 and 107 (Table II) showed no difference in survival between the methionine-treated and the water-treated rats.

Three further experiments were done, No. 110, 111 and 114, in which the same quantities of methionine were given at shorter time intervals postburn. In experiment No. 110, 160 mg of methionine was given at a half-hour and at 4 hours following the burn. No beneficial results from the methionine were obtained. In experiment No. 111, in which "tubed" as well as water controls were used, similar quantities of methionine were given immediately postburn and at 3 hours postburn. In experiment No. 114, 160 mg of methionine in 5.0 cc of distilled water was given intraperitoneally immediately postburn and at 3 hours postburn. Beneficial results were not obtained from the methionine therapy in these latter 2 experiments. The survival percentages of the methionine-treated rats, calculated from the totals of all experiments in which methionine was administered postburn (Table II), was not significantly different from that of the simultaneous water-control rats. However, the difference in the survival rates of both the water and methionine-treated animals compared with either the moistened tube controls or the untreated controls is significant, P = less than 0.01 for the tubed controls and 0.02 for the untreated controls.

Summary. One hundred and sixty mg of methionine administered orally to rats 2 hours before subjecting them to a standardized thermal injury significantly increased the 48-hour survival rate. One hundred and sixty mg of methionine administered to rats orally following thermal injury did not increase their survival rate. Three hundred and twenty mg of methionine administered either orally or intraperitoneally following thermal injury failed to increase the 48-hour survival rate.

Ten cc of distilled water administered orally following thermal injury significantly increased the 48-hour survival rate.

† *Ibid.*

8 Fisher, R. A., *Statistical Method for Research Workers*, London, 1938, Oliver and Boyd, Ltd.