TABLE I.
Toxicity of Tyrothricin for Rabbits by Intravenous Injection.

No.	Dose per kg g	Survival: days 1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	0.0002	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2	0.0002	—	—	—	—	—	—	—	—	—	—	—	—	—	—
3	0.0004	—	—	—	—	—	—	—	—	—	—	—	—	—	—
4	0.0004	—	—	—	—	—	—	—	—	—	—	—	—	—	—
5	0.0006	—	—	—	—	—	—	—	—	—	—	—	—	—	—
6	0.0006	—	—	—	—	—	—	—	—	—	—	—	—	—	—
7	0.0008	—	—	—	—	—	—	D							
8	0.0008	—	—	—	—	—	—	—	—	—	D				
9	0.001	—	—	—	D										
10	0.001	—	—	—	—	D									

water (0.0002 g per cc). Normal adult rabbits were given varying amounts by intravenous injection as shown in Table I; with the tyrothricin employed the maximum tolerated dose was about 0.0006 g per kg of weight.

Sixteen rabbits were inoculated intratesticularly with the Nichols-Hough strain of *T. pallidum*. In from 4 to 6 weeks all developed acute syphilomas with positive darkfield examinations. Four rabbits were kept as untreated controls while the remaining 12 were given daily intravenous injections of 0.5 cc of 1:100 suspensions of tyrothricin per kg of weight over a period of 15 days. This dose corresponded to 0.0001 g per kg, being equivalent to about one-sixth of the maximum single tolerated dose. Clinical records and darkfield examinations for *T. pallidum* were made at daily intervals.

All animals survived with apparently no clinical evidences of toxicity. During and at the end of the period of treatment none showed any clinical evidences of healing of the testicular lesions as compared with the untreated controls and all 16 animals showed persistently positive darkfield examinations. Under the circumstances lymph node transfers were regarded unnecessary.

Summary. The maximum single tolerated dose of tyrothricin for adult rabbits by intravenous injection was about 0.0006 g per kg. Fifteen intravenous injections of 0.0001 g per kg, at daily intervals (totalling 0.0015 g per kg) were completely ineffective in the treatment of acute testicular syphilis of rabbits.

15606

Failure of Penicillin and Streptomycin in the Prophylaxis and Treatment of Experimental Vaccinia of Rabbits.

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Andrews and his colleagues[1] have reported that penicillin is ineffective in the treatment of vaccinia and Parker and Diefendorf[2] have found that the compound was without effect on the multiplication of the virus in the Rivers-Li culture medium and in the intact chick embryo. The activity of streptomycin on the virus has not been reported upon but the results of experiments herein briefly summarized, employing both compounds in the

[1] Andrews, C. H., *et al., J. Path. and Bact.*, 1943, **55**, 173.

[2] Parker, R. F., and Diefendorf, H. W., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 351.

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.

15607

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.