

ated. This synergistic effect of plant growth regulators on antibiotic inhibition of disease may have an important practical application in the economic use of antibiotics in plant disease control.

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Received December 21, 1953.

Effect of Piromen on Survival Following Severe Thermal Injury in Rats¹

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A series of experiments conducted by McCarthy *et al.* (1-4) leads us to conclude that rather large volumes of various parenteral solutions were necessary to promote survival of rats following severe thermal injuries of 32 percent or more of the total body surface. Hence, we were very much interested in the experiments reported by Greene, Stuart, and Joralemon (5) in which they showed that significantly increased survival rates over control survival rates of thermally injured rats were obtained following treatment with the drug Piromen.² We were most anxious to learn whether rats receiving severe thermal injuries of 50 ± 2 percent of the body surface would survive if treated by single intraperitoneal injections of Piromen postburn. Recent work (3) with this extent of injury demonstrated that survival of more than 60 percent of rats burned in this way necessitated continuous intravenous infusions, begun immediately postburn, and continued for 10 hr, during which time a total of 18 percent of the body weight of sodium lactate, sodium chloride, whole blood, and plasma was infused. Consequently, we treated a number of rats receiving 50 ± 2 percent burns with single, postburn intraperitoneal injections of 1 µg of Piromen per rat. All these animals died. During a discussion of this experiment with Greene and Stuart, one of us was advised that our dosage was excessive. Hence, we treated a second group of rats receiving 50 ± 2 percent burns with 0.1 µg of Piromen per rat. These animals also died. We have subsequently reduced the percentage area burned

and varied the dosage of Piromen to conform to that which Stuart (6) considered optimum, that is, 0.65 µg/kg. We have been unable to confirm the findings of Greene *et al.* (5).

Material and Methods. Unshaved male Wistar rats under ether anesthesia were subjected to back burns in water at 90° C for 35 sec according to the procedure reported by McCarthy (7). In those experimental groups that included simultaneous controls, the animals were segregated for test or control treatment by lot prior to burning. Therapy in all cases was administered intraperitoneally immediately following burning according to the method reported by Greene *et al.* (5). The Piromen,³ lot number N-P-68, was diluted with pyrogen-free distilled water just prior to use. A new stock bottle of Piromen was used for each experiment. All syringes and needles were autoclaved and rinsed thoroughly with pyrogen-free distilled water. The control treatment consisted of intraperitoneal injections of 0.9 percent NaCl solution given in volumes equivalent to those which the Piromen-treated animals received. Following the burning and treatment, all animals were returned to individual wire-mesh cages where they had free access to water and Purina Laboratory Chow. The animals were checked every 3 hr for the first 12 hr following the burn and twice daily for the remainder of a 10-day postburn interval, at which time any living animals were sacrificed. Each animal listed in these experiments was skinned upon its death or sacrifice and a planimeter measurement made of the burned area. Any animals found to have injured areas outside of the range designated for a particular group were not included in such a group but were discarded. The weight variations of the animals in the various experimental groups in no case exceeded 20 g. In experiments A and B, all rats received 50 ± 2 percent burns. In A, each animal received 1 µg of Piromen (P), and in B, each animal received 0.1 µg of P. In experiment C, each animal received a 37 ± 2 percent burn and 1 µg of P. In experiment D, all rats received a 36 ± 2 percent burn; half of these animals each received 1.0 µg of P and the other half received no therapy. In experiment E, all rats received a 32 ± 2 percent burn; half of these received 0.1 µg of P, a fourth of them each received a volume of 0.9 percent NaCl solution equivalent to that which the Piromen-treated group received, and a fourth of them received no treatment. All Piromen-treated animals in experiments A to E inclusive received their respective P concentrations in 0.1 cc of diluent. In the experiments F, G, and H, 10 rats in each, selected by lot, received P and 10 rats in each received placebo therapy. The dosage of P was calculated individually so that each rat received 0.65 µg/kg; the placebo therapy of 0.9 percent NaCl solution was given in volumes calculated individually so that each rat received a volume equivalent to that which an animal of similar weight would have received of the P solution.

¹Supported in part by the Medical Research and Development Board, Office of the Surgeon General, Department of the Army, Contract DA-49-007-MD-88.

²A bacterial polysaccharide complex.

³The Piromen was made available to us through the courtesy of Dr. William F. Windle of the Travenol Laboratories, Inc., Morton Grove, Ill.

TABLE 1. Survival rates of thermally injured rats receiving single injections of Piromen or placebo immediately postburn.

Expt.	No. of rats	Wt range in g	Percent burn	Therapy	Piromen dose (μg)	Percent survival hours					Days 10
						3	5	8	12	24	
Part I. Varied dosages of Piromen											
A	12	202-210	50 ± 2	P	1	100	0	0	0	0	0
B	10	200-210	50 ± 2	P	0.1	20	0	0	0	0	0
C	5	220-240	37 ± 2	P	1	100	40	0	0	0	0
D	5	190-210	36 ± 2	P	0.1	100	20	0	0	0	0
	5	200-210	36 ± 2	None	—	100	60	0	0	0	0
E	10	190-210	32 ± 2	P	0.1	100	90	70	10	10	10
	5	197-210	32 ± 2	None	—	100	100	80	20	0	0
	5	190-210	32 ± 2	PI	≈	100	100	40	0	0	0
Part II. Piromen dosage calculated individually on basis of 0.65 μg/kg body weight											
F	10	190-210	32 ± 2	P	0.65 μg/kg	100	90	50	20	10	10
	10	190-210	32 ± 2	PI	≈	100	90	50	30	0	0
G	10	215-235	32 ± 2	P	0.65 μg/kg	100	100	50	0	0	0
	10	215-235	32 ± 2	PI	≈	100	100	50	10	10	10
H	10	250-270	32 ± 2	P	0.65 μg/kg	100	100	70	20	0	0
	10	250-270	32 ± 2	PI	≈	100	100	40	30	10	10

Results and Discussion. The results of these experiments are summarized in Table 1. The survival times of the animals in the several groups increased as the percentage of the area burned was reduced from 50 \pm 2 percent to 32 \pm 2 percent. No significant difference in survival percentage of the Piromen-treated rats was observed among the several experimental groups within the dosage ranges given. Since the majority of the animals listed in Table 1, Part I, received burns greater in surface area than those reported by Greene *et al.* (5), it is possible that the dosages of Piromen administered were not sufficient to permit recovery from the injury. However, we are at a loss to explain why those animals in Part II of Table 1, which received burns similar to those reported by the above authors and which received optimum therapy calculated individually for each animal, did not respond to the Piromen therapy as they have reported. We have had no experience regarding the ability of the drug to protect when given prior to burning, although Mefferd, Henkel, and Loefer (8) have reported that Piromen affords protection from x-irradiation when given prior to the radiation. Millican (9) has used Piromen in the treatment of mice following thermal injury and has found it to be ineffective in promoting survival. We have given normal rats the drug within the dosage range given to the thermally injured rats and have found no ill effects. We have also administered the drug intravenously to burned animals and have found it to be of no benefit.

Summary. Single intraperitoneal injections of Piromen given to rats immediately following severe thermal injury were found to be ineffective in promoting survival under the conditions of the experiments reported above.

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Received January 18, 1954.

Prevention of Alloxan Diabetes by 2-Tetrahydroxy Butyl 5-Methyl 4-Carboxy Furan and Its Sodium Salt

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Large doses of cysteine and glutathione injected prior to alloxan, but not after alloxan, have been found by Lazarow (1) to protect animals from diabetes. Patterson, Lazarow, and Levey (2) explained this mechanism by showing that alloxan reacts with cysteine to form dialuric acid and with glutathione to give rise to dialuric acid and an additional compound showing a maximum at 305 m μ , which, it is stated, is formed by a reaction involving alloxan and the

¹ The authors record their grateful thanks to the Ministry of Education, Government of India, for the award of one of the Ministry's Senior Research Scholarships to one of them (V.K.S.).