

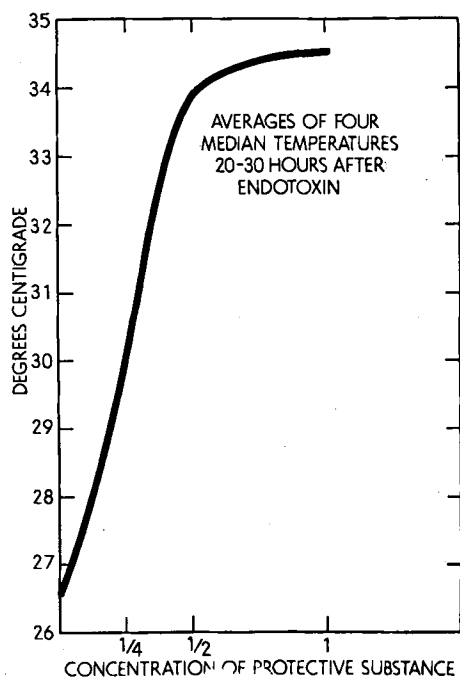


Fig. 5.

Effect of varying doses of impure penicillin.

One can distinguish between the protective effect of penicillin and saline, impure penicillin diluted to $\frac{1}{4}$, and impure penicillin diluted to $\frac{1}{2}$ by using 0.1 ml of endotoxin, as was done in this experiment. In order to distinguish half strength from undiluted material, one must dilute further.

from the insertion of the junction into the mouse.

Hypothermia may be regarded as the physiological response of the mouse to the endotoxin, comparable to fever in most other animals. That it is not merely an ante-mortem phenomenon is evidenced by the fact that less than one-third of the mice die in an experiment. In some instances mice have recovered after their temperatures have been as low as 26°C for 8 to 12 hours.

Summary and Conclusions. The endotoxin of *Salmonella aertrycke* injected intraperitoneally into mice caused a marked fall in body temperature. A certain phase of this hypothermia could be prevented to a significant degree by previous administration of impure penicillin. This phenomenon has been utilized for the quantitative assay of impure penicillin.

A correlation was demonstrated between the antilethal and the anti-hypothermic action of the impure penicillin against bacterial endotoxin in mice.

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Effect of Nicotinic Acid Monoethylamide on the Liver of the Young Rat.

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It has been reported by Brazda and Coulson¹ that a diet containing 1% coramine (nikethamide) produces a rapid and significant increase in the liver weight-body weight ratio of young rats. Nicotinamide, under similar conditions, produces no significant increase.² Inasmuch as coramine is disubstituted

on the amide nitrogen whereas nicotina-
mide is unsubstituted it was decided to determine the effect produced by nicotinic acid monoethylamide in which the amide nitrogen is only monosubstituted. This communication reports the results obtained by use of this compound in the diet.

Experimental. The procedure employed was the same as that used in the study of the effect of coramine.¹ The nicotinic acid monoethylamide was mixed into the basic diet

¹ Brazda, Fred G., and Coulson, R. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1948, **67**, 37.

² Coulson, R. A., and Brazda, Fred G., *PROC. SOC. EXP. BIOL. AND MED.*, 1947, **65**, 1.

TABLE I.*
Effect of the Ingestion of Nicotinic Acid Monoethylamide on the Liver of Young Rats.

No. days	Rat final wt	Liver wt wet	Liver wt dry	Liver wt as % body wt	Liver fat % wet wt	Liver fat % dry wt	Liver % solids	Gain in wt g/day
Control								
5	54.7	2.72	0.80	4.98 ± 0.09†	3.87	13.27	29.21	+3.21
9	70.0	3.36	1.06	4.78 ± 0.09	4.22	13.38	31.47	+3.30
28	148.9	7.74	2.29	5.18 ± 0.13	3.22	10.89	29.60	+3.79
1% nicotinic acid monoethylamide								
5	36.9	2.05	0.61	5.34 ± 0.12	4.28	14.28	29.53	+0.34
9	55.9	3.00	0.93	5.38 ± 0.10	5.14	16.58	30.91	+1.54
28	108.8	5.75	1.87	5.30 ± 0.11	4.50	13.65	32.78	+2.36

* Each figure in the table represents the average value obtained from 5 males and 5 females.

$$\dagger \text{P.E.} = \pm 0.6745 \sqrt{\frac{\sum (v)^2}{n(n-1)}}$$

at a level of 1%. Each of the 3 experimental groups consisted of 10 weanling rats, 5 males and 5 females, each from a different litter. One group was sacrificed for analysis at 5 days, a second at 9 days and the third at 28 days. The analytical procedures were identical with those reported previously.¹ The results appear in Table I.

Microscopic examination of hematoxylin-eosin preparations of sections of livers taken from the experimental animals yielded no unusual pathological findings. Binucleate cells and mitotic figures were seen in slightly greater numbers than in the control series. The difference was not great enough to be of true significance.

Discussion. The ingestion of nicotinic acid monoethylamide at a dietary level of 1% by the young rat failed to produce the significant increase in the liver weight-body weight ratio evoked by coramine.¹ It has been shown by Ellinger and Coulson³ that coramine is con-

verted quite slowly into nicotinamide in the human. Whether this involves de-ethylation or hydrolysis to nicotinic acid and subsequent conversion to nicotinamide is not known. It would appear from the results that the nicotinic acid monoethylamide is possibly more readily converted to nicotinamide than is coramine. That it is thus converted in the human has been demonstrated by Ellinger and Coulson.³ However, since the main purpose of the experiment was to determine the effect of the compound on the liver no evaluations of the rate of conversion to nicotinamide were carried out.

Conclusion. Although the mechanism by which coramine produces its effect on liver size remains unknown it is quite apparent that disubstitution of the amide nitrogen is essential. Monosubstitution of the amide nitrogen with an ethyl group either cannot produce a significant effect or else this compound is so readily converted to nicotinamide, which has no such action, that an effective concentration of the necessary substance cannot be achieved.

³ Ellinger, P., and Coulson, R. A., *Biochem. J.*, 1944, **38**, 265.