

nicotine and nornicotine. Following the technique employed by Weatherby⁴ and administering intravenously one-sixth LD 50 doses at 2 min intervals to the point of death, we have previously shown³ that the rabbit disposes of nornicotine at a rate comparable to that found for nicotine.⁴ Since repeated intravenous injections into the mouse offer some difficulty, the comparison in this species was carried out as follows:

Employing 2 groups of 40 mice each, each mouse in one group was given $\frac{1}{2}$ the LD 50 dose of nicotine intraperitoneally every 15 min until death, and each mouse in the second group was similarly treated with $\frac{1}{2}$ LD 50 doses of nornicotine. The results are expressed graphically in Fig. 1. From this it is seen that the mouse detoxifies nicotine much more

rapidly than it does nornicotine. In this respect then, the mouse again differs from the rabbit.

Summary. Whereas, the mouse and the rabbit as regards acute toxicity are about equally sensitive to nornicotine, they differ markedly in their sensitivity to nicotine as well as in their ability to detoxify the two substances. In view of such species variation it would seem impractical to evaluate the relative toxicity of nicotine and nornicotine for man on the basis of animal data. Since nicotine and nornicotine are quite closely related structurally, these results again emphasize the hazard of transferring to man toxicity data on related compounds obtained on one species of animal.

14907

Acute Nature of Alloxan Damage.*

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Neutralization of an alloxan solution with NaOH completely abolishes its diabetogenic action.¹ Since alloxan, if injected intravenously, is bound to be neutralized by the buffers of the blood in a very short time, the conclusion that its toxic action must be limited to a few minutes seems to be logical. There are also indications that alloxan is not only neutralized but actually decomposed or disposed of in some way within a few minutes. Leech and Bailey² found that alloxan injected intravenously can be demonstrated in the blood for only 5 min after the injection.

That the toxic effect of alloxan takes place within a few minutes after injection could be

proven by the following experiments:

Thirteen dogs were laparotomized under ether anesthesia, and that part of the pancreas which lies free in the duodenal mesentery was exposed, and its blood supply temporarily interrupted by placing two rubber-protected soft clamps along its both sides. Now a diabetogenic dose (60 to 100 mg/kg) of alloxan was injected rapidly into a leg vein. The clamps were removed one to 6 min after the termination of the injection, and the circulation to the clamped portion was reestablished. The abdominal wound was closed. The animals made a good recovery, and not a single one of them developed any sign of diabetes even temporarily. Ten or 14 days after the first operation the animals were relaparotomized or killed, and biopsies were taken from both the clamped and the untouched splenic portion of the pancreas. Sections were stained with chrome hematoxylin and phloxin,³ and the

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¹ Goldner, M. G., *Bull. N. Y. Acad. Med.*, 1945, **21**, 44.

² Leech, R. S., and Bailey, C. C., *J. Biol. Chem.*, in press.

³ Gomori, G., *Am. J. Path.*, 1941, **17**, 395.

TABLE I.

Dog No.	Dose of alloxan mg/kg	Clamps removed after minutes	Changes	
			in clamped portion	in splenic portion
610	60	6	0	+
608	60	6	0	++
712	75	6	0	+++
714	75	5	0	0
715	75	5	0	++
716	75	3	0	0
411	75	3	0	0
409	75	2	0	+++
410	75	1	0	++
415	75	1	0	0
404	100	3	0	0
614	100	3	+	+++
405	100	2	0	++

0 = normal.

± = questionable or slight changes (predominance of alpha cells in a number of islets).

++ = moderate damage (predominance of alpha cells in the majority of the islets; beta cells scanty).

+++ = severe damage (islets consist of alpha cells only; beta cells absent or only occasional specimens seen).

islets examined for evidences of alloxan damage. Table I. shows the results.

Table I. shows 2 interesting things: First, the unusually high percentage of animals insensitive to the doses of alloxan used in this experiment. Second, whenever changes developed, they were invariably far more severe in that portion of the gland the blood supply of which had not been interfered with. In only one animal did changes of questionable significance develop in the clamped portion of the gland, whereas in all other animals clamping for 1 to 6 min afforded full protection against alloxan damage.

In addition to the changes tabulated, in dogs No. 404 and 405 beta cells were found singly and in very small groups scattered throughout the acinar parenchyma. This very unusual finding may indicate a process of regeneration.

Summary. Clamping of a portion of the dog's pancreas during and for the period of 1 to 6 min after the injection of a diabetogenic dose of alloxan will protect that portion of the gland from alloxan damage while in the unclamped part the beta cells will degenerate. This observation shows that the toxic effect of alloxan is limited to a few minutes immediately following the injection.

14908 P

Certain Properties of a New Physiologically Absorbable Sponge.

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The clinical utility of thrombin for hemostasis is enhanced by its application in a porous matrix which may be left intact and will be physiologically absorbed. For this purpose certain products prepared from human fibrinogen,^{1,2} oxidized cellulose,³⁻⁵ and possibilities for a starch preparation,⁶ have been reported.

Each of these has sufficient limitations to encourage a preliminary report on a substance developed in this laboratory for use as a biologically absorbable sponge.

¹ Ingraham, F. D., and Bailey, O. T., *J.A.M.A.*, 1944, **126**, 680.