TABLE I.

Dog No.	Dose of alloxan mg/kg	Clamps removed after minutes	Changes in clamped portion	Changes 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.

A water-insoluble gelatin-base sponge has been obtained by foaming a specially prepared gelatin solution, which is then air dried in Monel metal forms and subsequently sterilized before biologic use.

The dried product is a light, off-white, nonelastic, tough, porous, mold that may be cut into any shape or size. There is no tendency to disintegrate even with relatively rough handling. A piece may be rapidly wet if worked vigorously in the damp fingers or sterile gloves to moisten the cell walls and expel air from the numerous pores; it will then engorge liquid readily and may be squeezed out and used repeatedly.

Physical properties of the material have been reasonably uniform among the several lots which have been studied. A 10 mm cube weighs aproximately 9 mg and will imbibe about 50 times its weight (450 mg) of water, or 45 times its weight (415 mg) of well-agitated, oxalated, whole bovine blood.

The sponge, a gelatin product, was unlikely to be antigenic. This possibility was, however, investigated. Two rabbits were subjected to a series of 5 injections with the bulk solution; two others with a saline extract of the finished product. These rabbits and 2 controls were bled on the 7th day following the last sensitization injection. Serums obtained were layered with dilutions of the antigens and observed for ring formation; later the tubes were agitated and followed for precipitate. All tubes remained clear. Precipitin assays repeated on the 11th and 15th days also were negative. From 3 albino rats, implanted in muscle with sponge 23 days earlier, serums were collected. These were titrated for precipitins, but again the evidence indicated the sponge to be nonantigenic.

Jenkins[7] has shown a relationship between enzymatic digestion of catgut *in vitro* and physiologic absorption *in vivo*.

By use of a standardized technique, which employed a solution of 1% U.S.P. XII pepsin, 100 mg pieces of sponge were digested in about 30 minutes; fibrin foam* yielded similar values.

A preliminary absorption study was made with 21 albino rats weighing approximately 300 g. Into a hind leg muscle of each was implanted a piece of sponge (6 × 8 × 8 mm) which was wet with a solution of bovine thrombin having a potency of 500 units† per cc. At intervals the animals were sacrificed and the implant areas visually examined. Only a small transparent film was in evidence on the 23rd day and no foreign material could be identified 30 days after implantation.

Further absorption data are now being accumulated from 28 albino rats which were implanted with materials in 4 different muscle areas of the two hind extremities. All implanted pieces measured, dry, 5 × 8 × 8 mm. Bovine thrombin solution as described previously was employed. In muscle region A was implanted a piece of fibrin foam soaked in thrombin solution; in region B, a piece of starch sponge‡ soaked in thrombin; in C, gelatin sponge soaked in thrombin; and in D, a piece of gelatin sponge soaked in a solution of penicillin which had a potency of 5,000 Oxford units per cc. Considerable difficulty was experienced in implanting the starch sponge, as in a wet condition it was friable and

[2] Woodhall, B., *J.A.M.A.*, 1944, **126**, 469.

[3] Frantz, V. K., and Clarke, H. T., *Ann. Surg.*, 1944, **120**, 181.

[4] Cronkite, E. P., Deaver, J. M., and Lozner, E. L., *War Med.*, 1944, **5**, 80.

[5] Putnam, T. J., *Ann. Surg.*, 1943, **118**, 127.

[6] Biee, C. W., MacMasters, M. M., and Hilbert, G. E., *Science*, 1944, **100**, 227.

[7] Jenkins, H. P., and Hrdina, L. S., *Arch. Surg.*, 1942, **44**, 984.

* The fibrin foam utilized in this study was prepared by The Upjohn Company in collaboration with Dr. Edwin J. Cohn of the Department of Physical Chemistry, and the Plasma Fractionation Laboratory, Harvard Medical School, from blood collected by the American Red Cross, under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University. The material used came from jars sorted out from a regular production lot because of minor imperfections.

† Clotting activity has been standardized in our laboratory such that if 0.1 cc of a solution clots 0.5 cc of specially oxalated bovine plasma in 15 seconds, that solution is considered to have a potency of 30 units per cc.

‡ Obtained through the courtesy of Dr. M. M. MacMasters, Northern Regional Research Laboratory, Peoria, Ill.

permitted very little manipulation.

Two animals have been sacrificed at regular intervals and specimens taken of each region, for gross inspection and histologic examination. No starch material could be visually identified after the 10th day. Absorption of the gelatin sponges was complete by the 30th day. After 50 days, small yellow nodules of fibrin foam were readily identified; their size indicated considerable but not complete absorption during this period of time. All operative regions appeared normal and well healed.

Details as to techniques, and histologic and experimental results on these and other studies of the gelatin sponge, including a series of neurosurgical investigations with 50 monkeys, are being completed.

The authors wish to express their appreciation to Dr. Glenn C. Bond for the immunologic assays, and to Mr. Stuart L. Long for his assistance in the laboratory and with the animals.

14909

Alleviation of Anaphylactic Shock in Guinea Pigs With Synthetic Benzhydryl Alkamine Ethers.

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Recent studies in this laboratory have shown that synthetic benzhydryl alkamine ethers are capable of preventing fatal asthma induced in guinea pigs by administration of histamine either intravenously or by inhalation of atomized aqueous solutions.[1] The experimental data revealed that the potency of several benzhydryl ethers equalled or exceeded that demonstrated for two Fourneau histamine antagonists, 2-isopropyl-5-methyl-phenoxyethlydiethylamine (929F) and N-phenyl-N-ethyl-N'-diethylethylenediamine (1571F). Staub and Bovet[2-4] and others[5-13] have studied the antihistamine and antispasmodic properties of these Fourneau compounds.

Experiments have been conducted to determine whether benzhydryl ethers are effective in alleviating anaphylaxis in guinea pigs. β-Dimethylaminoethyl benzhydryl ether and β-morpholinoethyl benzhydryl ether, both as hydrochlorides, were selected for this study because of their effectiveness in alleviating histamine-induced asthma.[1]

Methods. Guinea pigs of both sexes weighing 250 to 350 g were passively sensitized by intraperitoneal injection of 0.5 cc of rabbit anti-ovalbumin serum. The rabbits had been

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