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## *Beta* Cell Changes in Guinea Pig Pancreas in Relation to Blood Sugar Level.*

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The *beta* cells of the pancreatic islets are believed to be the source of insulin,[1] and changes in these cells associated with altered carbohydrate metabolism were described even prior to the discovery of insulin. Experimental procedures reported and designed by several workers to stimulate the carbohydrate-metabolizing activities of the pancreas were found to result in degranulation and vacuolization of the *beta* cells of the islets.

Homans[2] and Allen[3] noted degranulation of the *beta* cells in subtotally depancreatized cats and dogs. Miyairi[4] described atrophic (degranulated?) *beta* cells in dogs and guinea pigs given glucose and adrenalin as compared with the *beta* cells of starved animals. Woerner[5] found "exhaustion" of the *beta* granules in guinea pigs given intravenous glucose over long periods of time.

Several other observers described non-specific granule changes. Ssobolew[6] noted the presence of relatively few fuchsinophile granules in dogs given carbohydrate and intravenous glucose as compared with starved dogs where abundant granules were seen. Marrassini[7] found margination of fuchsinophile granules after administering carbohydrate to rabbits. Poll[8] compared the islet cells of starved frogs and those of frogs given glucose or adrenalin, and in the latter the cell inclusions seen in the starved animals had disappeared.

O'Leary,[9] studying the mouse pancreas *in vivo,* described disap-

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1 Best, C. H., and Taylor, N. B., *The Physiological Basis of Medical Practice,* Baltimore, 1937, William Wood and Company.

2 Homans, J., *J. Med. Research,* 1914, **30**, 49.

3 Allen, F. M., *J. Metab. Research,* 1922, **1**, 5.

4 Miyairi, S., *Proc. Imp. Acad. Jap.,* 1927, **3**, 702.

5 Woerner, C. A., *Anat. Rec.,* 1938, **71**, 1.

6 Ssobolew, L. W., *Virchow Arch. f. path. Anat. u. Physiol. u. f. kl. Med.,* 1902, **168**, 91.

7 Marrassini, A., *Arch. Ital. de Biol.,* 1907, **48**, 369.

8 Poll, H., *Ergäzungsheft z. Anatomischen Anzeiger,* 1931, 71.

9 O'Leary, J. L., *Anat. Rec.,* 1930, **45**, 27.

pearance and presumable emptying of formed vacuoles in islet cells following the administration of glucose.

Vacuolization was noted by Ssobolew,[6] Homans,[2] and Allen[3] in the pancreatic remnants of glycosuric subtotally depancreatized cats and dogs, and these changes were taken to indicate functional overstrain of the islet cells. Kolossow[10] found vacuolization in the *beta* cells of tritons after glucose administration.

The present experiments consisted of observations on the course of degranulation of the *beta* cells following the administration of a single dose of glucose.

Young guinea pigs (not fasted) weighing 300 to 500 g, were given intraperitoneally 2 g per kilo of glucose in a 10% aqueous solution. The blood sugar, determined by the Hagedorn-Jensen method on 0.1 cc of blood obtained from the ear, was followed throughout the experimental period.

Animals were sacrificed at various time intervals from the start of

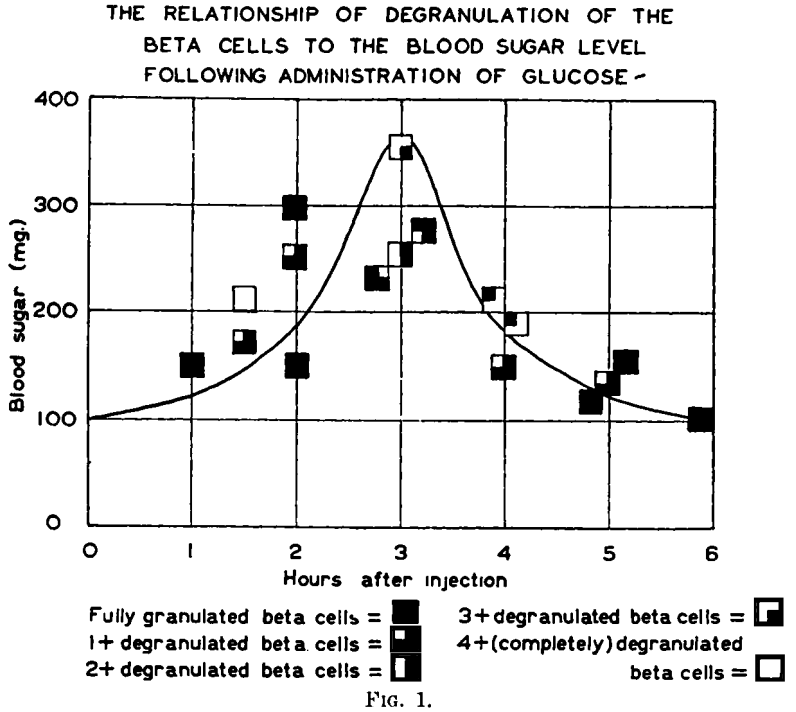


FIG. 1.

Each square represents a single animal and the degree of degranulation is indicated by the shading. The squares are plotted against the blood sugar level at varying times after the injection of glucose.

[10] Kolossow, N. G., *Z. f. Mikro. Anat. Forsch.*, 1927, **11**, 43.

the experiment. Pieces of pancreas were fixed in Bouin's fluid with 2.5% sulpho-salicylic acid and in formol-Zenker. Paraffin sections were stained with the Mallory-Heidenhain azan stain and with chromium hematoxylin and phloxin after permanganate oxidation.[11]

The sugar tolerance curves obtained showed a 250-350 mg peak at approximately 3 hours with a return to normal levels of about 100 mg at the 5th and 6th hours.

Some degree of degranulation of the *beta* cells was found in most of the animals whose blood sugar was elevated. This ranged from sparsity of granules in some of the *beta* cells or margination to complete absence of the granules in nearly all of the *beta* cells. The *alpha* cells appeared unaltered. These changes were uniform throughout the pancreas.

The most marked degranulation was present in those animals killed at the 3rd and 4th hours when the blood sugar was at its peak or was falling. Lesser degrees of degranulation were observed at the earlier and later observation periods. In both fed and fasted control animals with normal blood sugars, degranulation was not observed.

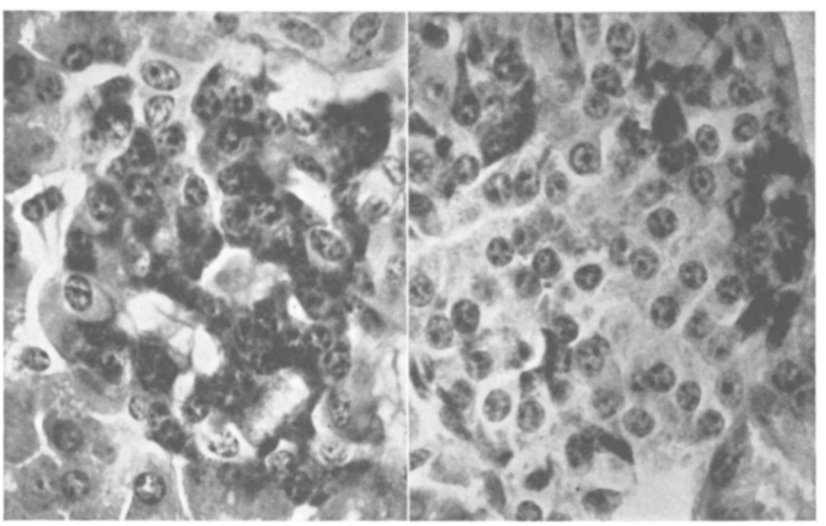

FIG. 2A (Left).
Microphotograph of a normal islet. The dark cells are beta cells laden with granules.

FIG. 2B (Right).
Microphotograph of a considerably degranulated islet. There are normally granulated beta cells along the edges whereas centrally located is a large group of degranulated beta cells.

[11] Gomori, G., *Am. J. Path.*, in press.

The granule changes were graded from 1+ to 4+ and are shown in relation to the blood sugar curve in Fig. 1. Examples of a well granulated islet and of a considerably degranulated islet (graded at 3+) are shown in Fig. 2.

This presumable cycle of disappearance and reappearance of the *beta* granules was confirmed by means of serial pancreatic biopsies in individual animals. These guinea pigs were given glucose subcutaneously and the abdomen opened at intervals under local novocaine anesthesia.

*Conclusions.* Disappearance of the specific granules of the *beta* cells in the pancreatic islets of guinea pigs given intraperitoneal glucose was noted during the subsequent hyperglycemia. The *beta* granules were again in evidence after the blood sugar reached normal levels. These histological changes, suggesting functional activity of the *beta* cells, may be related to the secretion of insulin in response to elevation of the blood sugar.

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## Production of Fatty Livers in Guinea Pigs with Scorbutogenic Diets.

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In the course of observations of Vitamin C deprivation in guinea pigs we noted that these animals showed at post-mortem large fatty livers in addition to the usual findings of scurvy. The pathology of the internal organs in scurvy has apparently not been extensively studied. Bessey, Menten, and King[1] have noted changes in the adrenal glands in which a decrease or disappearance of lipoid material was observed. They also mentioned fatty changes in various organs including the heart, liver and skeletal muscles.

Twenty-five of 27 animals dying from scurvy on a modified Sherman *et al.*[2] scorbutogenic diet showed moderately severe to very severe fatty changes in the liver both grossly and microscopically.

[1] Bessey, O. M., Menten, M. L., King, C. G., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 455.

[2] Sherman, H. C., La Mer, V. K., and Campbell, H. L., *J. Am. Chem. Soc.*, 1922, **44**, 165.