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.

TABLE I.
Fat Analysis of Liver Tissue.

Serial No. of animal	Diet	No. days	Vitamin C	No. days	Total wt of liver, g	Body wt	% liver of body wt	% lipids in liver tissue
SIM3	Starved	11	Abund.		10.5	252	4.1	1.4
NM 1	Normal		,,					2.1
NM 3	,,		,,					2.0
NM 2	,,		,,		19.5	366	5.3	2.4
IM 1	No. 1	47	Free	25	30.3	289	10.5	23.9
IM 2	No. 1	50	,,	28	30.5	328	9.3	26.1
IM 4	No. 1	49	,,	27	22.0	275	8.0	10.9
IM 5	No. 1	50	,,	28	26.0	335	7.7	11.8
IM 6	No. 1	52	,,	30	18.0	259	6.9	12.2
HM 1	No. 1	54	Low	54	29.0	339	8.6	20.7
HM 2	No. 1	33	,,	33		286		13.1
HF 3	No. 1	53	,,	53	15.0	316	4.7	6.4
HF 4	No. 1	67	,,	67	8.5	168	5.06	9.1
HF 1	No. 1	117	,,	117	14.0	219	6.8	30.1
GM 2	No. 2	46	Free	21	13.0	172	7.5	11.7
GF 3	No. 2	46	,,	21	13.5	194	6.9	10.4
EF 2	No. 2	100	Abund.		30.5	628	4.8	7.5
EM 1	No. 2	154	,,		44.0	397	11.3	23.8

Diet No. 1—Rolled oats and wheat bran 59 parts, skimmed, dried powdered milk 30 parts, butter fat 8 parts, cod liver oil 2 parts, NaCl 1 part.

Diet No. 2—Rolled oats and wheat bran 48 parts, dextrose 10 parts, desiccated brewer's yeast 1 part, the rest as in diet No. 1.

Five of these were checked chemically by the Van Slyke[3] gasometric method and showed a fat content of 11 to 26%. Another group of 5 guinea pigs placed on this diet but given subminimal amounts of pure ascorbic acid, to prolong the period of survival, showed a fat content of 6 to 30%. The animal having 30% fat in the liver had the longest period of survival (Table). The subcutaneous tissue, mucous membranes, and liver of this animal had a uniform greenish color, showing that jaundice was present before death.

To find out if other factors beside the Vitamin C deficiency were operating in this experiment, we starved 4 animals, giving them only Vitamin C and water. None of these showed gross or microscopic evidence of fatty changes, and the content of fat in the liver of one of those, determined chemically, was 1.4%.

Five other animals were placed on a further modified basal diet enriched with dextrose and desiccated yeast (Diet No. 2, Table). All of these dying from scurvy showed definite fatty changes; in 2 of these this was substantiated by chemical analysis. The degree of fatty changes in this group was probably smaller than in the animals on the unmodified diet No. 1 (Table).

Two animals each were placed on diets No. 1 and No. 2 plus an abundance of ascorbic acid for a minimum of 3 months. These animals seemed to thrive up to about 3 months and then began to lose weight and look ill. Three of these animals were sacrificed at this crucial period and showed moderate degrees of fatty degeneration. EF2 (Table) whose liver was analyzed chemically showed 7.5% fat. The 2 animals on the No. 1 diet showed histologically about the same or slightly greater fatty change. One of these animals (EM1) was permitted to live on. He continued the downhill course and died at the end of 154 days showing a large, firm, nodular liver, ascites with 25 cc of fluid in the peritoneal cavity and edema of the abdominal wall.

Summary and Conclusions. Scurvy produced in guinea pigs by the scorbutogenic diets used is accompanied by severe fatty degeneration of the liver. This process is slightly retarded by additional carbohydrate in the diet. These diets are apparently deficient in some other factor or factors, whose presence is necessary for normal liver physiology and morphology.

[3] Kirk, E., Page, I. H., and Van Slyke, D. D., *J. Biol. Chem.*, 1934, **103**, 203.