In addition, the effects of nitroethane and 2-nitropropane on the blood pressure of rabbits were compared with those induced by glycerol trinitrate, erythrityl tetranitrate and sodium nitrite. The results are shown in Fig. 1. The nitrates and sodium nitrite had very much more effect in much smaller doses than did the nitroparaffins.

14178

Occlusion of the External Pancreatic Secretion in Man.

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Recent experience has shown that survival for at least many months is possible in man following apparent occlusion of the external pancreatic secretion. This situation obtains after pancreatoduodenectomy is performed for carcinoma of the head of the pancreas or ampulla of Vater. While an anatomic "cure" of such lesions might now be envisaged, it is not known if man can survive *indefinitely* without external pancreatic secretion. Data bearing on this question can only be obtained from a study of operated patients to observe evidence of impaired physiologic activity which itself may not permit of indefinite survival. In this connection it may be pointed out that where only a portion of the head of the pancreas and a portion of the duodenum have been resected, the patients are not suitable subjects for such studies since there is considerable variation in the pancreatic duct system and accessory ducts, anastomosing with the main pancreatic ducts, may enter the first or the terminal segments of duodenum.

The data recorded below were obtained upon 3 male patients, all subjected to a one-stage resection of the head and neck of pancreas, lower 4 to 6 cm of stomach, entire duodenum, and first 2 to 4 cm of jejunum (Fig. 1). Continuity of the alimentary tract was re-established by choledochojejunostomy, and gastro-jejunostomy. Two patients, Fl. and H, had large carcinomas of the head of the pancreas. Patient W. had a large carcinoma of the ampulla of Vater extending upward in the common bile duct. Postoperatively, none exhibited pancreatic or biliary fistulæ.

Patients Fl. and H. survived operation for 5½ and 5 months respectively dying of carcinomatosis. The latter condition was the cause of general deterioration which became most pronounced during the last 2½ and 2 months respectively. Patient W. remains well, has gained 25 pounds in weight and is engaged in physical labor 11 months after operation.

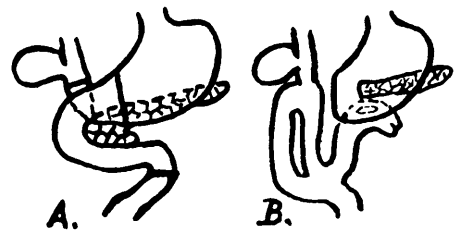

FIG. 1.

Diagram of one-stage pancreatoduodenectomy for excision of lower portion of stomach, entire duodenum and head of pancreas for carcinoma of the latter. A, showing levels of transection of dilated common bile duct, in lower portion of stomach, and in upper portion of jejunum. B, showing reconstitution of continuity of upper alimentary tract by gastrojejunostomy, choledochojejunostomy, and jejunostomy. The transected neck of pancreas is closed by mass ligature and sutures, thus resulting in occlusion of external pancreatic secretion.

Character of Stool. Patients Fl. and H. both had one or 2 daily large, bulky, soft, light tan or clay-colored foul stools following operation and during their survival period. Actual steatorrhea was present for a period in patient Fl., who had as many as 6 stools a day. Patient W. had steatorrhea prior to operation, but afterward, when bile alone was returned to the alimentary tract, the stools were normal.

TABLE I.
Blood Chemistry in 3 Patients with Occluded Pancreatic Ducts.

Patient	Plasma proteins, g %		N.P.N., mg %		Fasting dextrose, mg %		Blood amylase, Somogyi units	
	Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.	Pre-op.	Post-op.
Fl.	6.57	6.18 (14 wks)	20	18.6 (14 wks)	111	92 (6 days)	—	31 (14 wks)
H.	6.34	6.06 (12 wks)	16	23 (4 wks)	81	65 (12 wks)	45	21 (8 wks)
W.	6.25	6.00 (13 wks)	32	30 (13 wks)	—	88 (13 wks)	266	105 (12 wks)

TABLE II.
Fat Absorption in 3 Patients with Excised Head of Pancreas and Duodenum Occluding Pancreatic Secretion.

Patient	Post-operative weeks	Fat intake g in days	Fat in stools g	% fat absorbed
Fl.	14	280 5	248	8.8
		219 3 (+ pancreatin)	142	35
H.	5	344 8	330	4
W.	12	450 8	37	91.6

TABLE III.
Blood Lipids and Cholesterol in 3 Patients with Occluded Pancreatic Secretion.

Patient	Time post-operative, weeks	Total lipids, mg %	Total cholesterol, mg %	Free cholesterol, mg %
Fl.	11	963	137.7	93.6
	16	630	42.4	27
	20	573	100	82.4
H.	3	1066	151.5	217.2
	6	577	54.5	36
	18	653	92.5	80
W.	7	576	84	48.4
	35	785	92	77.5

Meat Digestion. Raw ground beef was fed to each patient, 2 pounds, during a 24-hour period and subsequent stools inspected for undigested fragments. These were present in small quantities in patients Fl. and H., not in patient W.

Blood Chemistry. The observations on blood chemistry are summarized in Table I. No abnormalities are noted except for an elevated blood amylase in patient W preoperatively which became normal 3 months after operation.

Fat Absorption. For these studies the patients were afforded a uniform diet including 60 cc of olive oil, 12.5 g of butter fat, and 1.8 g of fat in milk a day. A capsule of carmine was administered and passage of carmine stools marked the beginning of a period during which all stools were collected; 5 to 8 days later a similar capsule was given and the appearance of the carmine in the stools marked the end of the period. The stools were emulsified in a mechanical mixer, extracted with alcohol-ether and petroleum ether, and the recovered fat weighed. The results of these studies are summarized in Table II. The 2 patients with fatty stools apparently absorbed only 8.8 and 4% respectively of fat ingested, whereas the patient with normal stools absorbed 91.6%. The increased

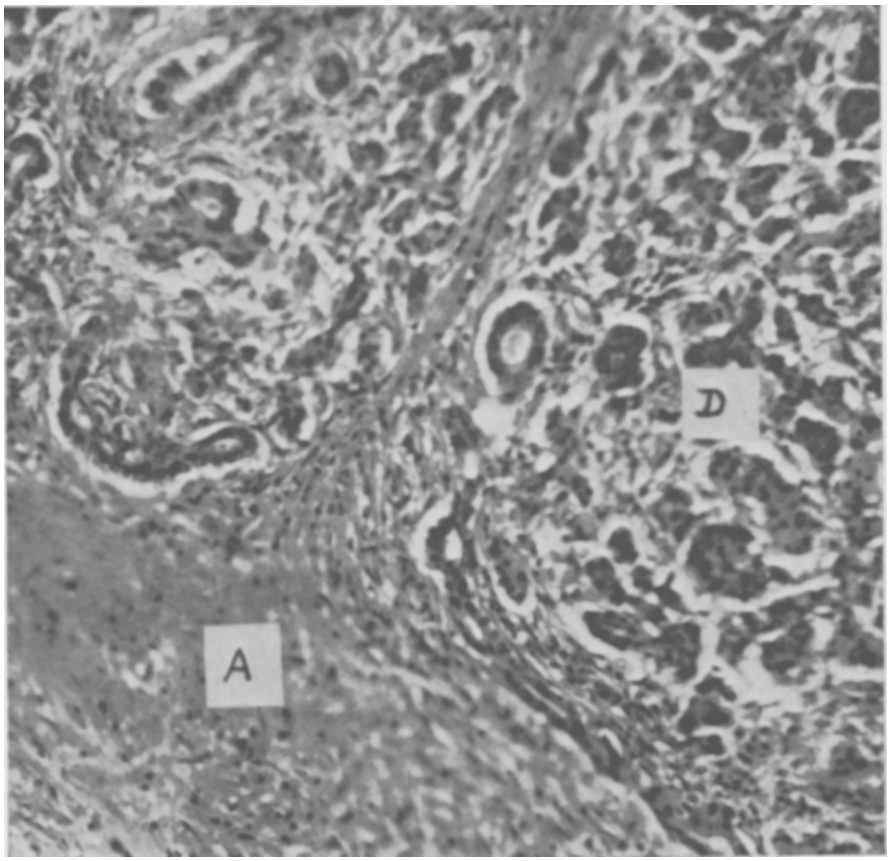

FIG. 2.
Photomicrographs × 200 of the remaining pancreas obtained at necropsy from patient Fl., 5 months after excision of the head of the pancreas and duodenum (occlusion of external pancreatic secretion). A. Fibrosis. D. Persisting acinar tissue, the cells of which are shrunken. Interacinar edema and fibrosis.

absorption of fat when pancreatin was administered is shown in patient Fl. Whipple and Bauman[1] observed 97% fat absorption in 2 patients from whom part of the duodenum and part of the head of the pancreas were resected, but in one instance there was considerable variation from 33% to 98% from day to day. In a third patient in whom the entire duodenum and head of pancreas were removed fat absorption varied daily from 0 to 92%.

Blood Cholesterol and Lipids. Results of these determinations are summarized in Table III. Some variation is observed, but the levels obtained a number of weeks after operation appear to be uniformly within the normal range. No significant changes are apparent. If the normal blood cholesterol is considered to be 100 to 300 mg % the results here obtained are also within normal ranges (with possible non-significant low readings observed in the second determinations in patients Fl. and H.).

Blood Cell Counts. No significance may be attached to the erythrocyte counts in patients Fl. and H., since secondary anemia developed in each case as carcinomatosis progressed; transfusions were given. In patient W. who has remained well the erythrocytes were 4.7 million, leucocytes 5,000, and Hb. 15 g %, 4 months after operation.

Necropsy Findings (Department of

[1] Whipple, A. O., and Bauman, L., *Am. J. M. Sc.*, 1941, **201**, 629.

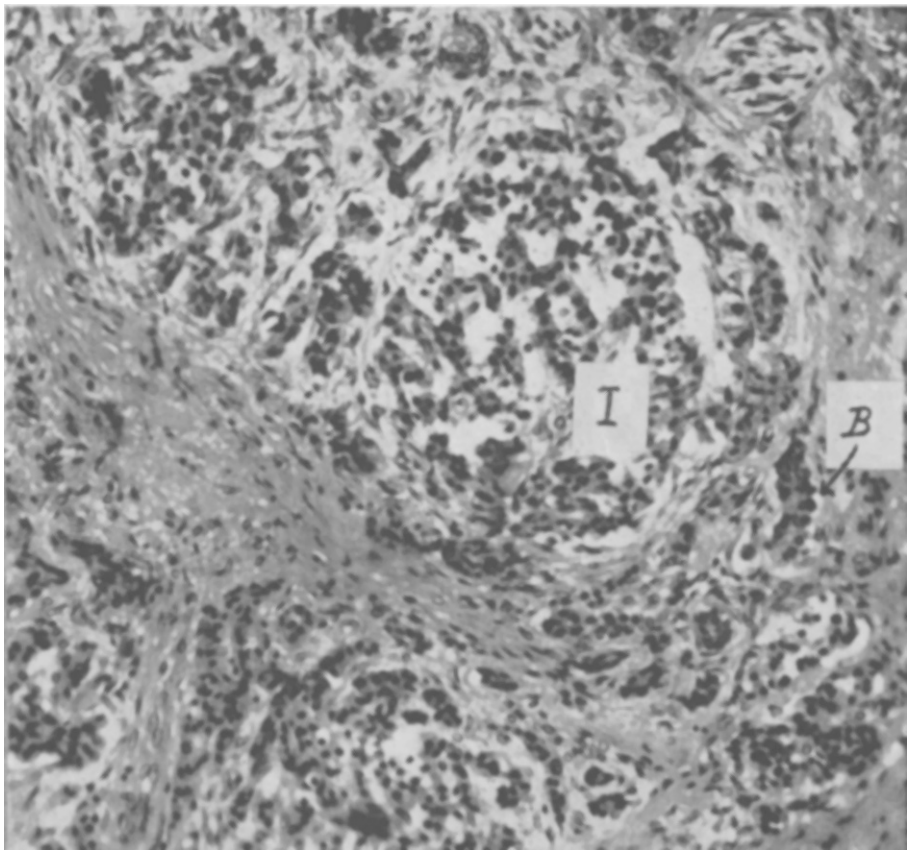

FIG. 3.
Photomicrograph × 225 from remaining portion of pancreas obtained at necropsy in patient H, 5½ months after excision of the pancreas and entire duodenum. Note fibrosis. I. Island of Langerhan's. B. Proliferating ducts. In this field there is little or no recognizable acinar tissue.

Pathology) in patients Fl. and H., 5½ and 5 months respectively after operation revealed abdominal carcinomatosis. The livers, riddled with metastases, showed no gross evidence of fatty changes. There was no gross evidence of re-establishment of pancreatic duct communications between the stumps of transected pancreas and adjacent loop of jejunum. Histologic study revealed fatty infiltration in the liver cells of the central portions of the lobules. This type of fatty infiltration is seen regularly in patients dying after a long period of debility characterized by marked reduction in food intake, as obtains in carcinomatosis. Sections of the remaining pancreas in each case showed marked fibrosis and atrophy of acinar tissue as well as invasion by carcinoma. The dense scar tissue capping the transected neck of the pancreas showed nests of carcinoma cells as well as a few small pancreatic ductules. No ulcerations in the gastrointestinal tract were present.

Discussion. The outstanding difference in reactions among the 3 patients subjected to resection of terminal portions of stomach, entire duodenum and head of pancreas, was in the character of the stool and fat absorption. Two patients exhibited fatty stools and very low absorption of ingested fat. The third patient who had typical steatorrhea before operation, had normal stools and normal fat absorption after operation when only increased flow of bile was returned to the alimentary canal (biliary flow was not completely obstructed prior to operation). The presence of an accessory pancreas in this patient could not

account for the normal stools since if this existed there could hardly have been steatorrhea for 3 weeks prior to operation, as was the case. It might be stated that no final evidence of occlusion of pancreatic juice obtains in this patient since he is still alive. However, the operation performed in this case was identical with that performed in the other two patients, namely, removal of the lower 4 cm of the stomach, entire duodenum, upper 3 cm of jejunum with transection of the neck of the pancreas at the level of the superior mesenteric vessels. The upper loop of jejunum was anastomosed to the stomach and farther along with the common duct. It thus appears that re-establishment of pancreatic ducts with the bowel could not be rapidly accomplished, if at all, bearing in mind the anatomical relationships in man. Furthermore, as previously stated, the return of normal appearing stools occurred very promptly after operation, within two weeks. It is hardly probable that under these conditions re-establishment of ducts between transected and ligated neck of pancreas with jejunum, several centimeters away could have occurred so promptly.

The above studies fail to afford a clue to any profound disturbance in the general physiologic economy of man resulting from occlusion of external pancreatic secretion, other than failure of appreciable fat absorption and incomplete digestion of raw meat in some instances. Theoretically inability to absorb fat would in time impair general nutrition if fat is an indispensable food by virtue of essential fatty acids. Furthermore, the absorption of fat soluble vitamins might be prevented and thus eventually lead to some type of avitaminosis. On the other hand, the administration of pancreatin, when necessary, could quite conceivably permit the absorption of sufficient fat, and this provided for, no other significant disturbances might be anticipated.

Conclusion. No general physiologic disturbances are observed in a patient who has survived occlusion of the external pancreatic secretion for 11 months. Previous weight loss was regained. The blood, stools, and fat absorption are normal and heavy physical labor is possible. In 2 other patients with similar occlusion, bulky fatty stools immediately developed and fat absorption was radically reduced. No other general physiologic disturbance was detected during their period of survival (5½ and 5 months respectively) except for some impairment in digestion of raw meat, death resulting from carcinomatosis. The basis for the marked variation in fat absorption following occlusion of the pancreatic juice in man remains obscure.

14179 P

Effect of Calcium Pantothenate and Para-Aminobenzoic Acid on the Gray Hair of Humans.

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It has been reported that a deficiency of the filtrate factors of the vitamin B complex may be accompanied by graying of fur in rats and dogs. The administration of the filtrate factors and, in addition, other vitamin B factors appeared also to darken the fur in some animals.[1-5] Morgan[1,3] was the first to observe that the active substance is in the filtrate fraction of vitamin B_2, *i.e.*, it is found in the water extract of yeast, lime, or rice bran

1 Morgan, A. F., Cook, B. B., and Davison, H. G., *J. Nutrition*, 1938, **15**, 27.

2 Oleson, J. J., Elvehjem, C. A., and Hart, E. B., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 283.

3 Morgan, A. F., and Simms, H. D., *J. Nutrition*, 1940, **19**, 233.

4 Lunde, G., and Kruegstad, H., *J. Nutrition*, 1940, **19**, 321.

5 Morgan, A. F., *Science*, 1941, **93**, 261.