the experiment. In ordinary suspensions of activated organisms the serial dilution experiment is not possible because of the high lytic threshold, *i. e.*, the ratio phage/bacteria is so great that the ultimate yield of phage derived from precursor-containing cells is not measurable. The presence of $MnCl_2$ lowers the lytic threshold very considerably and makes it feasible to add relatively large numbers of organisms with the result that significant amounts of phage are released from the lysing bacteria. The phage produced in this way can then be diluted and employed to activate the precursor of a new lot of cells. The original phage used has been diluted to at least 1/1,000,000 without any reduction in activity or plaque count. This we interpret as indicating that the activated bacteria contain some sort of a phage precursor which is transformed into active phage by phage itself. An alternate explanation would postulate the phage to be a living autonomous unit, finding appropriate conditions for multiplication in the successive aliquots of activated organisms. However, there is ample evidence that phage is not a living organism but rather is a protein of high molecular weight possessing the general properties of an enzyme.[9, 10] It seems probable that phage production is not dependent upon bacterial reproduction *per se* but upon environmental conditions adequate for the normal synthesis of phage precursor.

10305

Experimental Pancreatico-Gastrostomy. Method for Conserving External Secretions of Pancreas.

E. COOPER PERSON, JR., AND FRANK GLENN. (Introduced by Bruce Webster.)

From the Department of Surgery, the New York Hospital and Cornell Medical College.

In any work on the pancreas, the well known danger of acute pancreatitis and peritonitis has long invested the gland with the reputation of a surgical *"noli me tangere."* The surgical attack has also been delayed because of the organ's relative inaccessibility, complicated functions and intimate relationship with major abdominal structures. Nevertheless, the need for a surgical procedure to pre-

[9] Northrop, J. H., *J. Gen. Physiol.*, 1938, **21**, 335.

[10] Krueger, A. P., *Physiol. Rev.*, 1936, **16**, 1.

pare a new exit for the external secretions of the pancreas applicable to cases of duct occlusion has long been felt.

The first pancreatic transplant was reported by Biondi who implanted the pancreatic segment into the duodenum. His experiment was unsuccessful; all 6 dogs on which the procedure was attempted died of peritonitis. Stimulated by Desjardins'[1] criticism of Biondi's[2] procedure, Coffey[3] described an original and delicate technic for the successful transplantation of the pancreas into the jejunum. This work was verified, using a simplified technic by Sweet and Simons,[4] and Patrie, Pyle and Vale.[5]

The first successful transplant of the pancreas into the stomach was done by Tripode and Sherwin.[6] They chose this procedure because of the accessibility and size of the organ as well as to eliminate any possible obstruction of the lumen of the bowel. Because this method of blind implantation is not in accordance with modern surgical principles, we felt that a direct visualization of the implanted pancreas constituted an improvement.

The pancreatic transplants were carried out on 25 dogs. The transected end of the pancreas was drawn through an incision in the posterior wall of the stomach by stay sutures visualized through an incision in the anterior wall. The anterior wall incision made possible direct observation of the implanted, transected segment in the lumen of the stomach.

Of the 25 animals subjected to this procedure 9 are still alive. Of 16 only one died of acute pancreatitis due to a technical error. The remaining 15 died as result of further surgical procedures. Autopsy in these cases revealed the transplanted gland to be normal.

In Chart I are presented data of 5 living and 5 expired animals.

All dogs were placed on a standard diet high in vitamins A, B, and C. They remained active and healthy and as shown maintained their weight. At varying intervals following the transplant, analysis of gastric contents, blood sugar and urine were made. Since gastric analyses revealed the presence of pancreatic lipase it must be concluded that pancreatic secretions reached the stomach. The blood sugar varied from 60-90 mg/100 cc and the urine analysis failed to show the presence of sugar. Routine abdominal exploration

1 Desjardins, A., *Revue de Chirurgie*, 1907, **1**, 945.

2 Biondi-Dot, D., *La Clinica Chirurgica*, 1896, **4**, 135.

3 Coffey, R. C., *Ann. Surg.*, 1909, **50**, 1238.

4 Sweet, J. E., and Simons, I. H., *Ann. Surg.*, 1915, —, 309.

5 Patrie, H. H., Pyle, L. A., Vale, C. F., *Surg., Gyn., Obs.*, April, 1917, 479.

6 Tripode, A. M., and Sherwin, C. F., *Arch. Surg.*, 1934, **28**, 345.

CHART I.

Studies upon Dogs in Which a Portion of the Pancreas Was Transplanted into the Posterior Wall of the Stomach and the Remainder of the Pancreas Resected. Gastric lipase positive, blood sugar normal, urine negative, liver micros. fatty infiltration negative.)

Dog No.	Initial wt (lb)	Days after procedure	Present wt or at death	General health	Cause of death	Quantitative liver lipid %	Re-exploration post-mortem	
							Gross	Microscopic
251	20	110	18	Good	Animal Alive	3.6		
280	20	88	18.5	"	" "	4.2	Transplant	
244	30	109	28	Fair	" "	5.2	Site Normal	
333	30	30	28	Good	" "			
240	22	118	23.5	"	" "			
254	34	75	28		Pneumonia	6.2		
292	18	45	17		Perforated Jejunal Ulcer	5.2	Patent	
219	20	66	19		Intussusception	5.5	Pancreatic Duct	Pancreas Normal
228	19	38	17		Pneumonia	3.2		
268	17	107	14		"	4.4		

was performed at periods of 10 to 90 days from the time of transplant and revealed consistently firm union between the pancreas and posterior wall of the stomach. There was no evident atrophy of the remaining pancreas. The gross pancreatic tissue within the lumen of the stomach was digested after 20 to 25 days, but the pancreatic duct remained patent and could be cannulated without difficulty. Serial microscopic sections through the site of the implant demonstrated normal pancreatic gland, unulcerated gastric mucosa and a patent duct orifice. Liver biopsy of 3-10 g taken at the time of exploration was studied chemically and microscopically for lipid deposition. Using the Bloor[7] and modifications of the Kaplan and Chaikoff[8] methods, the fat content of the livers was found to vary from 3.6 to 6.7% in the "transplanted animals" as compared to the normal of 3 to 5%. Microscopic studies of the livers, using special stains, failed to reveal the presence of fatty infiltrations.

In order to study the effect of complete exclusion of the external secretions of the pancreas from the intestinal tract, ligation and division of the pancreatic ducts and partial pancreatectomy was carried out in 5 animals. The results are presented in Chart II.

Although the animals were placed on identical diet as those shown in Chart I they lost weight and exhibited syndrome consisting of anorexia, marked exhaustion, intermittent vomiting and foamy stools. They expired following reëxploration or due to intercurrent infections. The pancreatic lipase was never present in the gastric contents of this series of animals. The blood sugar remained normal. Liver analyses disclosed an increase in the ratio of lipid deposition from 8 to 18.4%. Microscopic sections confirmed the presence of fatty infiltration. They also showed beginning degeneration and atrophy of the cell at the periphery of the lobules. Post mortem examination revealed marked pathological changes in the remaining pancreas. Advanced atrophy with chronic pancreatitis was the outstanding picture; however, in 2 instances acute hemorrhagic pancreatitis and pancreatic abscess resulted from the procedure.

Conclusions. 1. By a modification of the Tripode and Sherwin method, the pancreas can be transplanted into the stomach without danger of immediate acute pancreatitis or peritonitis. 2. The intragastric portion of the transplanted pancreas is eventually digested away. 3. The transplanted pancreas retains its external and internal function and shows no sign of atrophy. 4. Complete ex-

[7] Bloor, W. R., *J. Biol. Chem.*, 1929, **82**, 273.

[8] Kaplan, A., and Chaikoff, J. L., *J. Biol. Chem.*, 1935, **108**, 201.

CHART II.

Studies on Dogs with the External Pancreatic Secretion Excluded from the Gastrointestinal Tract by Partial Pancreatectomy and Ligation of the Remaining Pancreatic Duct. (Gastric pancreatic lipase negative, blood sugar normal, sugar in urine negative, liver microscopic fatty infiltration positive.)

Dog No.	Initial wt (lb)	Days after procedure	Wt at death	General health P.O.	Cause of death	Quantitative lipid in liver %	Post-mortem findings	
							Gross	Microscopic
260	33	93	23	Fair	Pneumonia	8.	Pancreatic Abscess Atrophy	Pancreatic Necrosis Chronic Pancreatitis Atrophy
288	28	36	20	Poor	"	11.2	Atrophy	Chronic Pancreatitis
111	18	33	16	Fair	"	11.2	"	Chronic Pancreatitis
295	39	10	36	Poor	Acute Pancreatitis	18.4	Acute Hemorrhagic Pancreatitis	Pancreatic Necrosis
325	32	4	30	"	" "	10	Acute Pancreatitis	Pancreatic Necrosis

clusion of the external secretion of the pancreas by stated methods produces an abnormal deposition of fat in the liver and concomitant degeneration and atrophy of the liver cells. 5. Lipid deposition and degeneration of the liver does not occur in pancreatic transplants.

10306

Absorption, Acetylation, and Excretion of 2 Sulfanilamido Pyridine (Dagenan, M & B 693).*

HERBERT E. STOKINGER. (Introduced by Michael Heidelberger.)

From the Department of Medicine, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York City.

Preliminary reports in English journals[1] on the effectiveness of M & B 693 in pneumonia have been either clinical or bacteriological in nature. Since the administration of this drug will doubtless become widespread in this country, precise knowledge of its absorption and excretion should be made available. Analytical data are herewith presented showing the fate of M & B 693 in both laboratory animals and human patients.

Quantitative estimation of M & B 693 and its conjugated derivative in body fluids is similar to that of sulfanilamide. The original Fuller[2] method was employed using sulfanilamide standards with a factor to account for the difference in molecular weight and color intensity of the pyridine derivative. Determinations of the conjugated form, 2(N-acetylsulfanilamido) pyridine,[3] were similarly made after hydrolysis with p.-toluenesulfonic acid. The percent acetylated values appearing in the tables were calculated from the hydrolyzed values minus the free (unhydrolyzed) times 100.

It was found, as with sulfanilamide, that the rabbit and human detoxify the drug by acetylation; the dog excretes it completely and unchanged in the urine. In all 3 species, the drug is detectable in the blood stream directly after ingestion, and the unchanged, therapeutically active form is completely eliminated from circula-

* Since this was written the name of the drug has been changed officially to sulfapyridine.

1 *Lancet*, 1938, **1**, 1210, 1230, 1305, 1391, 1402.

2 *Lancet*, 1937, **232**, 194.

3 Nomenclature suggested by Crossley, M. L., Northey, E. H., Hultquist, M. E., *J. A. C. S.*, 1938, **60**, 2217.