was being actively extruded from E and G. Myelin fragments (from early nerve degeneration stages) are actively ingested by forms I and G, and their subsequent intracellular digestion has been followed under the microscope.

Transformation of Schwann cells to macrophages can also be seen inside the explanted nerve fiber tubes themselves. Removal of blood from the nerves prior to explantation (Ringer's perfusion of the donor) and Trypan Blue injections indicate that the contribution of hematogenous and preformed histiocytes to the macrophage population of our cultures was negligible. Most of the macrophages present were transformed Schwann cells, and all cultures exhibited some transformation. Fibroblasts (endoneurial cells) also turned into macrophages, but less readily; moreover, phagocytes from Schwann cells and those from fibroblasts each retain distinguishing features of their strain. The observed conversions thus belong clearly in the class of cell "modulations".[5,6]

Conclusions. (1) The adult Schwann cell is capable of a wide range of modulation in the course of which it can assume numerous shapes and characters often associated in neuropathology with distinct cell types. (2) Schwann cells presumably are a major source of macrophages during Wallerian nerve degeneration, and their control becomes a prime consideration in nerve regeneration.[7] (3) The active role of the Schwann cell in removing myelin by phagocytosis and digestion has been experimentally verified. (4) The filamentous shape of the spindle-type Schwann cell makes it a superb guide for axons.[8] Its dimensions and staining properties are very close to those of axon sprouts, which suggests one source of error in past unfounded claims of "autogenous" nerve regeneration. (5) The results place increased emphasis on the great versatility of even the adult cell, within the limited potentialities of its strain, in response to the composition and microstructural organization of its environment.[5]

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[7] Weiss, P., *J. Neurosurg.*, 1944, **1**, 400.

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14921

III. Mechanism of Stomal Ulcer Is Related to Length of Afferent Duodenojejunal Loop.*

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The two preceding papers (I and II)[1,2] in this series of experiments suggest definitely that the length of the afferent duodenojejunal loop is an item of real importance in determining whether or not stomal ulcer will follow the Schmilinsky operation or gastric

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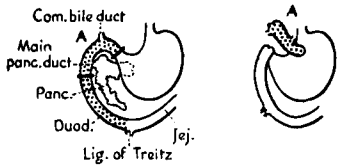
[1] Merendino, K. A., Varco, R. L., Litow, S. S., Kolouch, Fred, Jr., Baronofsky, Ivan, and Wangensteen, O. H., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 222.

[2] Merendino, K. A., Lannin, B. G., Kolouch, Fred, Jr., Baronofsky, Ivan, Litow, S. S., and Wangensteen, O. H., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 226.

[3] Kolouch, Fred, Jr., *Surgery*, in press.

Experiment 1

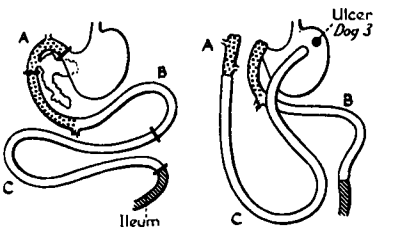
SHORT AFFERENT LOOP and EFFERENT GASTRODUODENOSTOMY



Dog No.	Length of Seg. A	Survival period	Cause of death	Ulcer at autopsy	Theoretic secretin produc.
1	8 cm.	72 da.	Sacrif.	No	Good
2	9 cm.	88 da.	Sacrif.	No	Good

Experiment 2

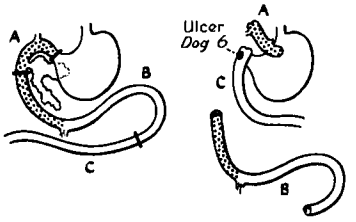
LONG AFFERENT LOOP (segment of lower jejunum interposed between afferent duodenum and stomach) and EFFERENT GASTRODUODENOSTOMY



Dog No.	Length of Seg. A + Seg. C	Survival period	Cause of death	Ulcer at autopsy	Theoretic secretin produc.
3	85 cm.	150 da.	Perit.	Yes	Good
4	85 cm.	185 da.	Sacrif.	No	Good

Experiment 3

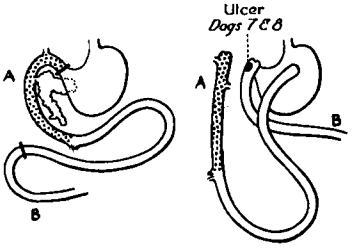
SHORT AFFERENT LOOP, partial duodenojejunectomy, and EFFERENT GASTROJEJUNOSTOMY



Dog No.	Length of Seg. A	Length of Exc. seg. B	Survival period	Cause of death	Ulcer at autopsy	Theoretic secretin produc.
5	10 cm.	75 cm.	81 da.	Sacrif.	No	Poor
6	8 cm.	75 cm.	77 da.	Obs. aff. l.	Yes	Poor

Experiment 4

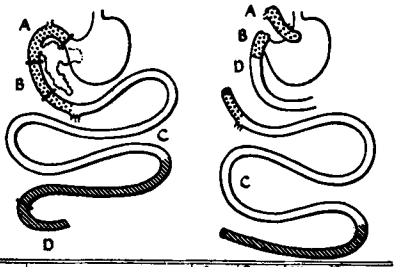
LONG AFFERENT LOOP and GASTROJEJUNOSTOMY



Dog No.	Length of Seg. A	Survival period	Cause of death	Ulcer at autopsy	Theoretic secretin produc.
7	75 cm.	150 da.	Perf. ulc.	Yes	Poor
8	90 cm.	55 da.	Perf. ulc.	Yes	Poor

Experiment 5

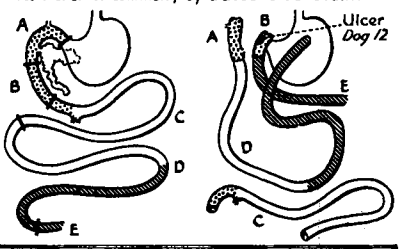
SHORT AFFERENT LOOP, partial duodenojejunectomy, EFFERENT GASTRODUODENOSTOMY, and restoration of continuity by DUODENOILEOSTOMY



Dog No.	Length of Seg. A	Length of Seg. B	Length of Exc. seg. C	Survival period	Cause of death	Ulcer at autopsy	Theoretic secretin produc.
9	12 cm.	7.5 cm.	135 cm.	85 da.	Sacrif.	No	Satis., ?
10	7 cm.	4 cm.	135 cm.	53 da.	Sacrif.	No	Satis., ?

Experiment 6

LONG AFFERENT LOOP (interposition of lower jejunoileal segment between afferent duodenum and stomach), partial duodenojejunectomy, EFFERENT GASTRODUODENOSTOMY, and restoration of continuity by DUODENOILEOSTOMY



Dog No.	Length of Seg. A + D	Length of Seg. B	Length of Exc. seg. C	Survival period	Cause of death	Ulcer at autopsy	Theoretic secretin produc.
11	90 cm.	12 cm.	60 cm.	81 da.	Sacrif.	No	Good
12	90 cm.	3 cm.	60 cm.	75 da.	Perf. ulc.	Yes	Satis., ?

FIG. 1.

Master chart indicating the 6 types of operative procedures invoked to study the "secretin, distance and sensitivity" factors in 12 dogs. The results of the experiments also are shown.

TABLE I.
Data Relating to Experiments Carried Out to Test Importance of Secretin, Distance and Sensitivity Factors

Dog	Length of afferent loop cm	Position of efferent stoma	Theoretic secretin production	Length of postoperative life days	Cause of death	Ulcer at efferent stoma
1	short (8)	Duodenum	Good	72	Sacrificed	No
2	" (9)	"	"	88	"	"
3	long (85)	"	"	150	Died; peritonitis due to perforated gastric fundal ulcer	
4	" (85)	"	"	185	Sacrificed	"
5	short (10)	Jejunum	Poor	81	"	"
6	" (8)	"	"	77	Died of obstructed afferent loop	Yes
7	long (75)	"	"	150	Died; perforated stomal ulcer	"
8	" (90)	"	"	55	" " "	"
9	short (12)	Duodenum, short segment (7.5 cm)	Questionably satisfactory	85	Sacrificed	No
10	" (7)	Duodenum (4 cm)	Questionably satisfactory	53	"	"
11	long (90)	Duodenum (12 cm)	Good	81	"	"
12	" (90)	Duodenum (3 cm)	Questionably satisfactory	75	Died of perforated stomal ulcer	Yes

resection carried out on the Billroth II plan of operation. The purpose of this paper is to attempt to determine, if possible, the relative importance in the occurrence of stomal ulcer of the 3 factors suggested in the first presentation. It is believed by varying the conditions of the experiment that, the significance of each of these 3 factors may be subjected to experimental scrutiny. The 3 items to be examined with respect to their importance in the genesis of stomal ulcer are: (1) The secretin factor (2) The factor of spatial separation of alkaline and acid digestive secretions (3) The sensitivity factor, implying an increased susceptibility of the mucosa of successively lower segments of the small intestine to injury by the acid gastric secretions.

Method. Six modifications of the total intragastric duodenal drainage operation of Schmilinsky and McCann were carried out in a series of 12 dogs. The operations were devised to study the influence of both short and long afferent duodenojejunal loops on the development of stomal ulcer just beyond the efferent gastric outlet with special reference to an attempt to evaluate the significance of the 3 factors enumerated above. In other words, in addition to varying the length of the afferent loop, the site of the efferent outlet of the stomach was varied, permitting testing of the importance of the secretin factor and the item of mucosal susceptibility to corrosion by the acid gastric secretions. These latter objectives of the study necessitated the making of some rather complicated operative procedures. By transsection of the duodenum just beyond the major pancreatic duct and interposing a loop of jejunum between the proximal portion of the duodenum and the stomach, (or by excision of a portion of the duodenum and the upper jejunum in other experiments), it became possible to vary all the factors which we wished to scrutinize. In some experiments the afferent loop was long, yet the requirements of a functional secretin mechanism were met satisfactorily by placement of the entire length of the duodenojejunal segment (beyond the major pancreatic duct), at the efferent gastric outlet. By interposition of a short segment of duodenal mucosa between a high ileal segment and the gastric outlet, it was possible to note when stomal ulcer followed, whether it occurred in the short duodenal segment or in the more susceptible high ileal mucosa beyond.

Results. The results of the experiments are shown in Table I and in the graphic record of the operations. (Fig. 1). Five of

TABLE II.
Incidence of Occurrence of Efferent Stomal Ulcer as Related to Theoretic Efficiency of Secretin Mechanism.

Theoretic quality of secretin mechanism	No. of dogs	No. of dogs developing ulcer	Incidence in %	Anticipated incidence in % if correlation was perfect
Good	5	1	20	0
Questionably satisfactory	3	1	33.3	
Poor	4	3	75	100

TABLE III.
Incidence of Efferent Stomal Ulcer as Related to Spatial Separation of Source of Alkaline Duodenal Juice from the Gastrojejunostomy Stoma.

Length of afferent duodenojejunal loop	No. of dogs	No. of dogs developing ulcer	Incidence in %	Anticipated incidence in % if correlation was perfect
Short	6	1	16.2	0
Long	6	4	66.6	100

TABLE IV.
Incidence of Occurrence of Efferent Stomal Ulcer as Related to Position of Efferent Stoma.

Position of stoma	No. of dogs	No. of dogs developing ulcer	Incidence in %	Anticipated incidence in % if correlation was perfect
Duodenum	8	2	25	0
Jejunum	4	3	75	100

the 12 dogs died of ulcer; in 4 of these, perforation was present. All ulcers were stomal in character, that is, just beyond the gastric outlet on the efferent loop, save one which occurred in the fundus of the stomach (Dog 3).

In Dog No. 6, the ulcer was not perforated, death being due apparently to obstruction of the short afferent loop—an item which probably had something to do with the occurrence of the ulcer. The dogs which did not succumb to ulcer were sacrificed at intervals of from 53 to 185 days.

In Tables II, III and IV is set forth the incidence of ulcer with reference to an examination of the factors under scrutiny in this study.

Comment. It is apparent from an analysis of the data in Tables II, III and IV that, it is difficult to separate out the eventual role of any single factor. This is especially true of the secretin and distance factors. Experiments 10 and 12 constitute an excellent example of the difficulty. In dog No. 10, the afferent loop was short; in dog No. 12 it was long. In dog No. 10, only 4 cm of duodenal mucosa remained at the efferent outlet for the gastric secretions to glide over in provoking the usual secretin effect; in dog No. 12, only 3 cm of duodenal mucosa remained at the efferent gastric outlet. Spontaneous perforation of a stomal ulcer killed dog No. 12 75 days after the operation. No ulcer was present in dog No. 10, when he was sacrificed at 53 days. In dog No. 10, however, with the short afferent loop (7 cm) containing good secretin containing duodenal mucosa, regurgitation of gastric secretions into the short afferent loop may have sufficed to augment the secretin effect of the 4 cm duodenal mucosal segment at the efferent gastric outlet. In dog No. 12, on the contrary, retrograde regurgitation of gastric secretions into the long 90 cm afferent loop could not reach the rich secretin bearing area of the duodenal segment. This same dog No. 12 provides a striking lesson in another respect. The stomal ulcer occurred in the short (3 cm) duodenal segment (Fig. 2) at the efferent gastric outlet and not in the ileal mucosa just beyond.

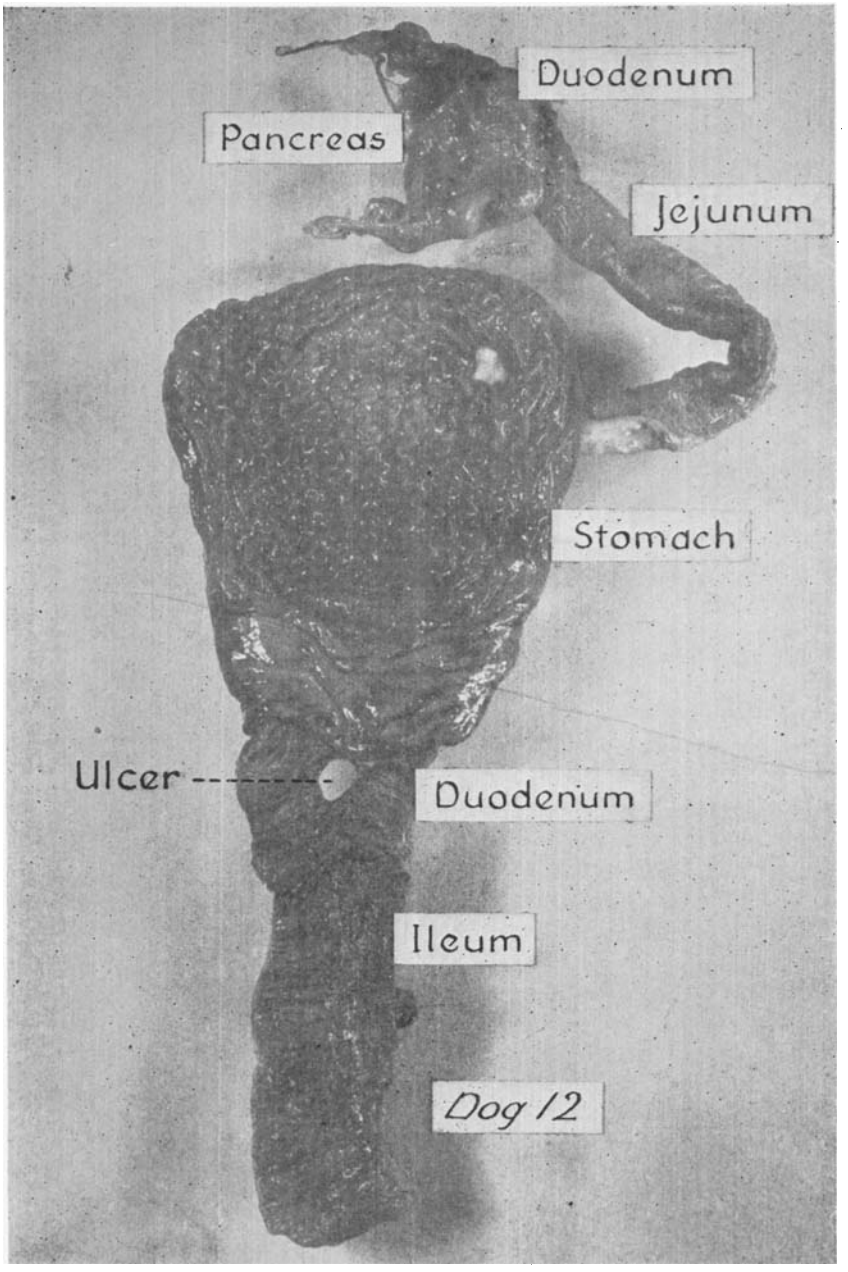


FIG. 2.
Photograph of spontaneous perforation of stomal ulcer in Dog 12. Note the position of the perforated ulcer in the small segment of duodenum interposed between stomach and ileum at the efferent gastric outlet.

In this group of experiments, stomal ulcer occurred only once in a dog with a short afferent loop (dog No. 6); in this instance, however, stenosis of the afferent inlet stoma was present, interfering with delivery of the alkaline secretions from the duodenal loop. Moreover, in long afferent loops, in which extraneous factors might influence the motility of the segment and hence delivery of the content of the loop, it would appear that,

such long afferent loops invite stomal ulcer.

A large number of experiments in each group would undoubtedly be helpful in resolving the importance of each of the factors scrutinized in this study. In addition, the animals not dying of spontaneous perforation of a stomal ulcer should be allowed to survive longer before sacrifice.

It is not unlikely that, employment of additional modes of attack may help to separate out more definitely, the component important parts in the predisposition to stomal ulcer presented by the long afferent duodenojejunal loop. Three such methods are now being applied to the problem in this laboratory: (1) assay of the secretin potency of intestinal mucosa from varying levels of the bowel in both dog and man in dogs with pancreatic fistula. (2) Determination of the loss in titratable alkalinity, if any, of the content of the long afferent duodenojejunal loop as delivered at the afferent gastrojejunal stoma (3) Experiments in which the sensitivity of the mucosa of various segments of the intestine is examined by allowing hydrochloric acid to drip upon isolated surfaces.

Conclusions. It is difficult to separate out with finality the role of the various factors contributing to the development of stomal ulcer attending employment of a long afferent loop in the operation of complete intragastric drainage of the content of the duodenal loop. The secretin factor can not be divorced completely from the considerations of the "distance" factor. Experiment No. 12 suggests rather definitely that, the "sensitivity" factor is not as important as the other two.

The evidence garnered in this study lends strong confirmation to the deductions arrived at in the previous two studies indicating that, a long afferent duodenojejunal loop invites stomal ulcer in any gastric operation carried out on the Billroth II plan of procedure.

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Effect of 2, Methyl Amino Heptane Upon Cardiac Automaticity During Cyclopropane Anesthesia in Dogs.

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Epinephrine and certain related aromatic amines, when used during cyclopropane anesthesia, cause pronounced cardiac irregularities. Ventricular premature beats, ventricular paroxysmal tachycardia, auricular and ventricular fibrillation are the usual manifestations.[1,2] Recently a group of aliphatic amines has been prepared which possess vasopressor activity and other pharmacologic effects of epinephrine. Studies on cardiac automaticity during cyclopropane anesthesia using these aliphatic amines have not been reported. One of these, 2-methyl amino heptane (EA-1) is useful to overcome circulatory disturbances during spinal anesthesia.[3,4] Inasmuch as cyclopropane is frequently used in conjunction with spinal anesthesia and may be used when this amine has been administered, it is essential to determine if it causes disturbances in cardiac rhythm and if these disturbances are similar to and as severe as those caused by epinephrine.

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