compounds were not effective cell-division inhibitors, the structures of the effective compounds are so dissimilar that the activity of these compounds as inhibitors appears to be due to a functional group specificity rather than a total structural specificity. Such an hypothesis would indicate that the activity of diazouracil is due to the diazo portion of the molecule rather than to the uracil moiety. Additional work is being conducted in an attempt to determine whether diazo groups at positions other than the 5-position of the pyrimidine molecule are as effective in inhibiting cell division.

Investigation of the relationship between cell-division inhibition by diazouracil and tyrosine antagonism is being continued in an attempt to determine the role of tyrosine in cell division. It is apparent that inhibition of cell division in these experiments was not a result of a block in reactions dependent on high-energy phosphate. Other work in this laboratory has shown that there are no significant changes in the phosphorus fractions of these inhibited *E. coli* systems(3). It may be that tyrosine and/or aromatic amino acid metabolism are involved in the inhibition of cell division.

Summary. Studies were made to determine the specificity of the chemical inhibition of division of *Escherichia coli* and to determine the relationship of division inhibition to important biochemical metabolites. It was found that the cell-division process of *E. coli* could be specifically inhibited, without an accompanying inhibition of culture growth, by diazouracil and by other diazonium compounds, and it is suggested that the diazo group on the compounds is responsible for the inhibition. The inhibition of division by diazouracil was antagonized by tyrosine, and it was shown that the antagonism can not be attributed to a destruction of the inhibitor by tyrosine. Other amino acids, intermediate in the glycolytic and tricarboxylic acid cycles, and energy-rich phosphorus compounds were incapable of antagonizing diazouracil-inhibited cultures.

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Role of Antral Exclusion in Development of Peptic Stomal Ulcer.* (21072)

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The importance of the chemical phase of gastric secretion is well known. This phase is mediated through the production of the hormone gastrin in the antrum of the stomach when food or its digestion products come in contact with the antrum. Dragstedt *et al.* (1,2) have shown that transplantation of the antrum to the colon produces a profound and sustained increase in the secretion of hydrochloric acid from an isolated gastric pouch and also that it causes the development of peptic stomal ulcers in a high proportion of dogs. More than 30 years ago Koennecke(3) had shown that placement of the antrum upon the distal ileum of dogs invited stomal peptic ulcers. Recently, Sauvage *et al.*(4) reported a series of experiments which suggested that the antrum was the most important single factor in the control of gastric secretion. However, all of the experiments reported by Sauv-

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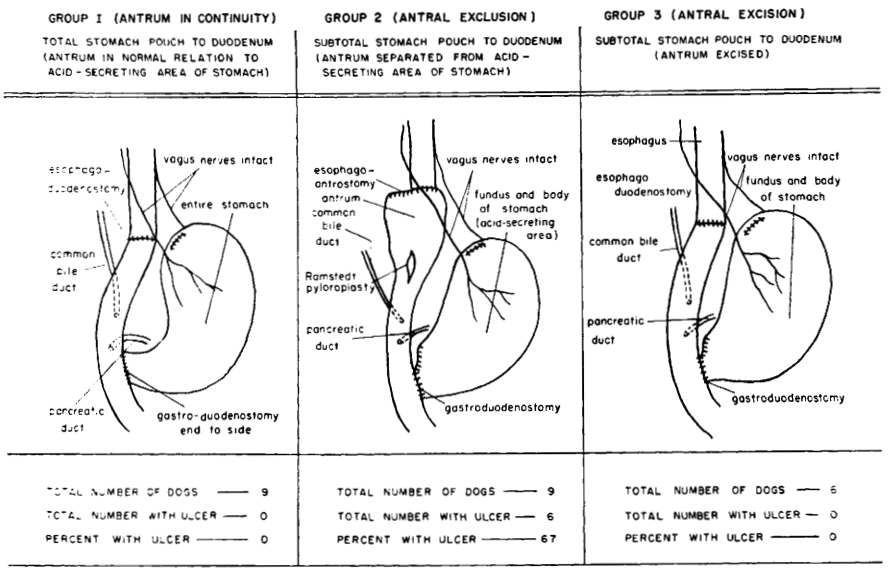

FIG. 1.

age involved operations in which the antrum was either excluded from contact with the acid-secreting segment of the stomach or completely excised. In none of his experiments was the stomach left intact.

The experiments reported here were devised to determine the effect of changes in the position of the antrum (relative to the parietal cell portion of the stomach) on gastric secretion of hydrochloric acid and on ulcer genesis. It was our thesis that the separation of the antrum from the remainder of the stomach caused the marked ulcerogenic effect of Sauvage's operation.

Methods. Adult mongrel dogs were anesthetised with pentobarbital sodium, 30 mg per kg of body weight. Intermittent positive pressure artificial respiration with compressed air was used. An incision was made in the tenth left intercostal space and the stomach and duodenum were exposed by opening the esophageal hiatus and drawing them into the chest. The esophagus was divided just above the esophagogastric junction, care being given to leave the vagus nerve trunks intact. The distal end of the divided esophagus was inverted with interrupted silk, leaving the stomach as a blind pouch. An end-to-end anastomosis was then accomplished between the proximal esophagus and either the duodenum or the gastric antrum. The blind vagally-innervated stomach pouch was then anastomosed end to side to the duodenum just below the papilla of the pancreatic duct. The esophageal hiatus was closed by suturing the esophageal curura of the diaphragm to the esophagus. In those dogs where the antrum was left in normal continuity with the duodenum, either a Ramstedt pyloromyotomy or a Heinecke-Mikulicz pyloroplasty was done to prevent any obstruction from pylorospasm which might attend division of the stomach with its consequent division of the vagal innervation of the pylorus. The study involved 3 different groups of dogs. In the dogs in Group I (Antrum in Continuity) the total gastric pouch was anastomosed to the duodenum end-to-side. In the dogs in Group II (Antral Exclusion) the antrum was divided from the parietal cell portion of the stomach. The proximal parietal cell pouch was anastomosed to the side of the duodenum, and intestinal continuity was established by anastomosing the esophagus to the antrum which retained its normal attachment to the duodenum. In the dogs in Group III (Antral Excision) the antrum was excised and the parietal cell pouch was anastomosed to the duodenum end-to-side. Three additional dogs having the Group I operation (Total Gastric

TABLE I. Heidenhain Pouch Data on Gastric Secretion in B Dogs in Groups I and II. (Values are milliequivalents of hydrochloric acid secreted during 8 hr collection period.)

Group I—Operation (total gastric pouch with antrum in continuity)						
	Dog #C-1		Dog #C-2		Dog #C-3	
Stand	Pre Op	Post Op	Pre Op	Post Op	Pre Op	Post Op
1	7.86 mEq	1.00 mEq	1.04 mEq	.06 mEq	2.01 mEq	1.38 mEq
2	5.15	2.03	1.22	.19	.55	.14
3	6.34	.71	2.83	.19	.34	3.22
4	13.52	1.13	4.34	.45	2.22	1.93
5	9.01	1.17	1.92	1.61	1.82	1.46
6	16.32	2.63	2.56	.45	1.85	.98
7	11.07	1.01	1.33	.0	1.52	.65
8	9.09	.44	3.50	.14	1.50	1.73
9	9.69	1.76	3.97	.0	1.89	.46
10	2.81	1.95	3.01	.36	.67	
11	2.16	1.71	5.86	.44		
12	6.45	1.51	3.67	.0		
13		.42				
14		.65				
15		3.64				
Avg	8.29 mEq	1.45 mEq	2.94 mEq	0.32 mEq	1.37 mEq	1.33 mEq
Change	Down 82%		Down 89%		Down 3%	

Group II—Operation (antral exclusion)						
	Dog #E-1		Dog #E-2		Dog #E-3	
Stand	Pre Op	Post Op	Pre Op	Post Op	Pre Op	Post Op
1	.48 mEq	1.28 mEq	1.26 mEq	2.77 mEq	1.59 mEq	13.23 mEq
2	.63	3.06	1.68	2.89	2.92	19.71
3	.67	5.06	2.35	6.30	2.30	17.45
4	1.26	2.16	1.51	1.48	.65	*
5	.69	1.89	.99	5.14	.18	
6	.58	.23	2.21	4.41	1.74	
7	4.38	2.16	3.22	1.84	.49	
8	1.98	7.37	.76	2.93	2.66	
9	2.14	8.38	1.08	3.86	3.41	
10	1.03	5.03	1.82		4.37	
11	1.51	4.00	.89		2.67	
12		3.65	.37		3.16	
13		9.74	.39		1.77	
Avg	1.40 mEq	4.15 mEq	1.43 mEq	3.51 mEq	2.15 mEq	16.80 mEq
Change	Up 197%		Up 146%		Up 681%	

* Dog died with chronic stomal ulcer on 23rd postop day.

Pouch with the Antrum in Continuity) and 3 additional dogs having the Group II operation (Antral Exclusion) had previously had isolated gastric pouches (Heidenhain pouches) made and standardized. Standard pouch collections were made over an 8-hour period 3 times weekly. The dogs were fasted for 16 hours prior to each collection. At the beginning of the 3rd hour of each collection, they were given a standard 200 g cooked horsemeat meal. Specimens were collected hourly and measured for free and total acid and volume. The values reported are the total milliequivalents of free hydrochloric acid secreted during each 8-hour collection period.

Results. The results of the survival experiments are tabulated in Fig. 1 and in Table I.

The 9 dogs in Group I (Antrum in Continuity) survived an average of more than 6 months which was the termination time for the experiment. None of these dogs developed an ulcer, and weight loss following this operation was minimal, the average being 10%.

Similarly, the 6 dogs in Group III (Antral Excision) lived an average of more than 6 months, and none developed an ulcer. The average weight loss in this group too was 10%.

On the other hand, 6 of the 9 dogs in Group II (Antral Exclusion) died with chronic peptic ulcers. The average survival of the 6 dogs with ulcer was 104 days, the range being 49

to 174 days. The weight loss in this group was severe—the average weight loss in the 6 dogs with ulcer being 36%. There was little or no difference in either survival time or ulcer development between those dogs with Ramstedt and those with Heinecke-Mikulicz pyloroplasties.

Most of the dogs in Group I and Group III had a moderately severe chronic esophagitis characterized by hyperemia of the mucosa, marked thickening of the esophageal wall, and moderate dilatation of the esophagus when they were sacrificed. All of the dogs in Group II in which the antrum, retaining its normal attachment to the duodenum, was anastomosed to the esophagus had normal esophagi when they died.

Results of the Heidenhain pouch observations are summarized in Table I.

Following the Group II operation (Antral Exclusion) hydrochloric acid secretion increased markedly. In 2 dogs, the average preoperative 8-hour hydrochloric acid secretion was 1.41 milliequivalents (average of 24 collections). Postoperatively, the average secretion rose to 3.89 milliequivalents (average of 22 collections), an increase of 175%.

On the other hand, following the Group I operation (Antrum in Continuity), the secretion from the Heidenhain Pouch decreased. Preoperatively, the average 8-hour hydrochloric output in 34 collections from 3 dogs was 4.37 milliequivalents, and postoperatively the average of 36 collections from the same dogs was 1.04 milliequivalents—a decrease of 76%.

Discussion. These experiments show the importance of the positioning of the antrum in experimental ulcer genesis. Only those animals with the gastric antrum excluded from the acid-secreting part of the stomach developed ulcers. No ulcers occurred in those dogs in which the antrum remained in continuity with the rest of the stomach, (Group I), nor in those dogs in which the antrum was excised (Group III).

The Heidenhain pouch data clearly explain the difference in ulcer incidence following these operations. A 175% increase in hydrochloric acid secretion followed the Group II operation (Antral Exclusion); a decrease of 76% in secretion followed the Group I operation (Total Gastric Pouch with the Antrum in Continuity).

The increase in gastric secretion in dogs with the antral exclusion operation (Group II) can be explained on the basis of increased production of gastrin by the antrum which is in prolonged contact with food and alkaline secretions such as saliva, and refluxed bile and pancreatic juice. The decrease in gastric secretion attending performance of the Group I operation (Total Gastric Pouch with the Antrum in Continuity) can be explained by the suppression of gastrin formation occasioned by the continuous flow of acid gastric secretion over the antral mucosa. In addition to this factor, there is a lesser degree of contact with food in the antrum in this operation, since the entire gastric pouch was not in the stream of flow of the intestinal contents; undoubtedly however, there is considerable reflux of food and intestinal content into the blind gastric pouch.

These experiments lend support for those operations(5,6) recently introduced in the treatment of peptic ulcer, in which a subtotal resection of the parietal cell segment of the stomach is done and the antrum is anastomosed to the residual parietal cell segment. For apparently the antral phase of gastric secretion is not nearly so great when the antrum retains its normal relation to the remainder of the stomach as when the antrum is excluded from contact with acid gastric juice.

Conclusions. 1. Exclusion of the antrum from continuity with the residual gastric pouch is the chief ulcerogenic factor in the Sauvage operation in which the antrum is anastomosed to the esophagus (Group II dogs). 2. Stomal peptic ulcer was not observed in vagally innervated total gastric pouches when the antrum remained in contact with the residual gastric pouch (Group I dogs). 3. Augmentation of the secretion of acid from an isolated Heidenhain pouch attends antral migration or exclusion (Group II dogs). Diminution of secretion from such a pouch was observed when the vagally innervated entire stomach, with the antrum in its normal position, was attached to the side of

the duodenum as a blind pouch (Group I dogs).

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Propagation in Tissue Cultures of Cytopathogenic Agents from Patients with Measles.*† (21073)

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Numerous attempts have been made in the past to propagate the agent of measles in lower animals, in chick embryos and in tissue cultures(1-3). The results of different investigators were often at variance or directly contradictory. It has been made reasonably clear, however, that monkeys, especially *M. mulatta,* are moderately susceptible to experimental inoculation(3). Furthermore the researches of Rake, Shaffer and their collaborators have provided evidence suggesting that the agent which passed through bacteria-retaining filters could be maintained indefinitely in serial passages in the developing chick embryo(4,5). These workers(5) also confirmed the earlier observations of Plotz(6) who apparently had succeeded in growing the agent in a modified suspended cell culture of chick embryonic tissues. Egg passage in the hands of Shaffer and his coworkers(7,8) regularly appeared to alter the pathogenicity of the agent for man as indicated by the development of a mild and much modified disease following the inoculation of egg adapted materials into susceptible children. In certain cases this modified disease seemed to be followed by resistance to measles as indicated by the results of subsequent natural or artificial exposure to the virulent form of the agent(9). Since 1943 when the last of the communications by Rake and his collaborators appeared, no important progress has been made in the study of the etiology of measles. This fact may in large part be attributed to the lack of a convenient laboratory method for the demonstration of the presence of the agent which induced no recognizable changes in eggs or cultures of chick tissues. Moreover, repeated attempts by Shaffer(10) to demonstrate a serologic reaction, such as complement fixation, using materials from the infected chick embryo failed. Accordingly, the only available technics have consisted in the inoculation of man or the monkey. The former is obviously impractical as routine and the latter tedious, expensive and frequently inconclusive because of variation in individual susceptibility.

With these considerations in mind we have recently attempted to cultivate the agent of measles in cultures of human and monkey cells employing procedures applied successfully to the propagation of the poliomyelitis viruses(11-13).* In blood and throat washings of typical cases of measles agents have been demonstrated that can be maintained in serial

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