

other objection is that this theory does not consider those autacoids, especially estrin and progestin, which have been shown to play a major rôle in changes in uterine motility.

Second, the inverse relationship of placental histaminase to efficiency of labor pains may be due to the unknown factor or factors which initiate and promote the continuance of labor. That is, the observed changes may be an effect and not a cause.

Third, and most likely, the histaminase content of the placenta is in no way *directly* related to uterine contractions, but may be thought of rather as an index of the amount of active, functioning parenchymatous tissue in the placenta. If this interpretation is accepted, then the rôle of the placenta in the onset and maintenance of parturition becomes more apparent, and physiologic senescence is indicated as a salient, if not causal, factor in the onset and maintenance of labor.

Summary. Although the amount of histaminase in the placenta shows some correlation with the efficiency of uterine contractions, the evidence is not sufficiently definite to warrant such a conclusion.

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The Relation of Bile and Pancreatic Juice to Duodenal Ulcer in Dogs.

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Among the numerous investigators who have worked with complete external biliary fistulas in dogs, the majority¹⁻⁶ have reported a high incidence of duodenal ulcer. Puestow⁷ makes no mention of ulceration in a series of dogs with a segment of the duodenum containing the orifice of the common duct exteriorized, but he is quoted by Blanck⁵ as having stated that several of his animals died rather

¹ Berg, Johnston and Jobling *Proc. Soc. Exp. Biol. and Med.*, 1927, **25**, 334.

² Berg and Jobling, *Arch. Surg.*, 1930, **20**, 997.

³ Kim and Ivy, *J. A. M. A.*, 1931, **97**, 1511.

⁴ Hawkins and Whipple, *J. Exp. Med.*, 1935, **62**, 599.

⁵ Blanck, *Surg. Gyn. and Obst.*, 1935, **61**, 480.

⁶ Hanke, *Arch. f. klin. chir.*, 1937, **187**, 675.

⁷ Puestow, *Arch. Surg.*, 1931, **23**, 1013.

suddenly with perforated peptic ulcers. Rous and McMaster⁸ and Kocour and Ivy⁹ are silent on the occurrence of ulcer in their dogs, and one assumes that they did not find any. Brunschwig, Bissell and Andrews¹⁰ state definitely that in their chronic biliary fistula dogs they found no changes in the gastric or intestinal mucosa.

It is interesting that no ulcers were noted by those two groups of investigators^{8, 9} who developed a good method for the return of bile. This phase of the problem was approached by Blanck⁵ who reported experiments in biliary fistula dogs which he interpreted as proving that the loss of bile results in peptic ulceration, and that the formation of these ulcers is prevented by adding dog bile to the diet of such animals. However, we believe that one cannot accept the author's conclusions on the basis of his data, because obviously, the series of dogs is small, the observation time is very short, and the difference between the control and bile-fed groups is too slight to be significant.

In the present communication, we wish to present a summary of our observations on the incidence of duodenal ulcer in (a) 15 dogs with complete external biliary fistulas prepared according to the method of Rous and McMaster as modified by Kocour and Ivy, and (b) 19 dogs with exclusion of pancreatic juice by separation of the pancreas from the duodenum.

A. *Incidence of ulcer in biliary fistula dogs.* Our 15 dogs to which bile was returned survived from 16 to 175 days after preparation of the bile fistula, only one dog surviving less than 4 weeks. The longest survival recorded by Blanck was 24 days. In our series, chronic ulcers of the duodenum occurred in only 2 dogs; in both of these the ulcer was directly responsible for death by perforation into the peritoneal cavity. The ulcers came as a surprise finding at autopsy because of the excellent general condition of the animals up to a day or two preceding death.

It is interesting that in the 2 dogs which died with chronic ulcers, the bile was returned via a long rubber tube passing through the common duct and terminating in the small intestine about 50 cm distal to the papilla of Vater. This raises the question whether the absence of bile from the upper intestine, rather than bile loss *per se*, is the important factor in protecting the duodenal mucosa from ulceration. The literature bearing on this point is too extensive to be discussed here. We feel justified at the present time in concluding

⁸ Rous and McMaster, *J. Exp. Med.*, 1923, **37**, 11.

⁹ Kocour and Ivy, *Am. J. Physiol.*, 1938, **122**, 325.

¹⁰ Brunschwig, Bissell, and Andrews, *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 41.

that the return of bile to the upper gastrointestinal tract, either by mouth or by an indwelling tube, prevents the formation of duodenal ulcers.

B. *Incidence of ulcer following pancreatic exclusion.* With regard to the question of pancreatic exclusion, we have observed 19 dogs in which the pancreas was separated from the duodenum; in this preparation there is, of course, no entrance of pancreatic juice into the intestine.

The dogs survived from 21 to 720 days after the operation, with malnutrition varying from slight to severe (50% of body weight); in only one instance was a duodenal ulcer observed at autopsy. These findings agree with those of Ivy,¹¹ who reported one case of true ulceration in 24 dogs with ligated pancreatic ducts. The problem of ulcer formation following external drainage of pancreatic juice involves not only exclusion of the juice from the duodenum, but also the very serious matter of fluid and salt loss, and our present report is not concerned with this aspect of the problem. It may be accepted as an established fact that duodenal ulcer only rarely results from absence *per se* of pancreatic juice from the upper intestine.

Summary. Of 15 dogs with complete external drainage of bile, all being supplied with bile by mouth or by a tube entering the upper intestine, duodenal ulcer was observed in 2 cases; only one instance of ulcer was noted in 19 dogs with exclusion of the pancreatic juice by separation of the pancreas from the duodenum.

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Development of Refractoriness to Enterogastrone Preparations.*

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It has been established that after prolonged administration animals may become refractory to crude hormone preparations, particularly to those of hypophyseal origin, which are water-soluble and protein-like in nature. It has not been demonstrated that animals may become

¹¹ Ivy, *Arch. Int. Med.*, 1920, **25**, 6.

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