PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 145, 967–969 (1974)

The Effect of Aspirin on Duodenal Secretion[1] (37934)

THOMAS R. RUSSELL AND R. SCOTT JONES
(Introduced by R. W. Postlethwait)
Department of Surgery, University of California School of Medicine and Veteran's Administration Hospital, San Francisco, California 94109

Aspirin is undoubtedly the analgesic drug most commonly employed in this country today (1). Although considered sufficiently safe to be administered without a prescription, this drug has deleterious side effects particularly on the gastrointestinal system. The pathogenesis of the adverse effects of aspirin on the gastrointestinal tract is complex. There may be a direct chemical corrosive effect on the gastrointestinal epithelium. In addition, there is evidence that aspirin may produce gastric mucosal damage by enhancing back diffusion of hydrogen ions from gastric lumen into the gastric mucosa (2). Other interesting experiments have demonstrated that salicylates alter the mucus secreted by antral pouches of dogs (3). Aspirin also alters blood coagulation by depression of prothrombin synthesis or by alteration of platelet function decreasing platelet adhesiveness, or by both of these mechanisms (4). In any event, it has been demonstrated clearly that aspirin, ingested in small doses, increases blood loss from the gastrointestinal tract (5). It was the purpose of the present experiment to investigate the effect of aspirin on secretion from duodenal mucosa.

Materials and Methods. Proximal duodenal pouches were prepared in four mongrel dogs weighing 12.3–20 kg by constructing a double mucosal septum at the pylorus and transecting the duodenum proximal to the junction of the common bile duct with the duodenum. The proximal end of the divided duodenum was brought through an abdominal stab wound and sutured to the skin as a mucous fistula draining the duodenal pouch. The distal portion of the cut duodenum was used to re-establish gastrointestinal continuity with a side-to-end gastroduodenostomy. Experiments were begun no sooner than 1 mouth after surgery and were performed by bringing the dogs to the laboratory and placing them in sling harnesses. Secretion from the duodenal pouches was collected using a plastic funnel strapped to the dog's abdomen about the opening of the pouch. The volume of secretion from the pouch was measured to the nearest 0.1 ml. During each experiment, duodenal secretion was collected at 15-min intervals for a 1-hr basal period. Then the dogs were allowed to eat a preparation of canned dog food until they were satiated. Doudenal secretions were collected in 15-min periods for 4 hr subsequent to feeding. After five consecutive daily studies, the dogs were given aspirin, 600 mg by mouth, twice a day for 7 consecutive days. After 2 days of aspirin administration, the dogs were again brought to the laboratory for 5 consecutive days, and duodenal secretion was collected as described. Aspirin was then discontinued; after a period of 2 days, additional feeding studies were performed for the 5 subsequent consecutive days as described previously.

Results. Before aspirin administration, the basal secretion from the duodenal pouches was 0.1 ml/15 min. After feeding duodenal secretion rose to a peak of 0.64 ml/15 min which occurred 1 hour after feeding. Subsequently, duodenal secretion

[1] This work was supported by a Veteran's Administration Clinical Investigator appointment (RSJ). The authors appreciate the expert technical assistance of Benjamin Mitchell.

gradually declined to a value of 0.26 ml/15 min at the end of the 4th hour after feeding. During the period of aspirin administration, basal duodenal secretion was 0.04 ml/15 min and rose to a peak of 0.27 ml/15 min during the sixth 15-min period following feeding. The duodenal secretion subsequently declined to a value of 0.04 ml/15 min at the end of the 4th hour after feeding. During the studies following discontinuing aspirin, basal duodenal secretion was 0.02 ml/15 min and rose to a peak of 0.37 ml/15 min in the fifth 15-min period following feeding, and subsequently declined to a nadir of 0.1 ml/15 min during the sixteenth 15-min period following feeding (Fig. 1). The peak duodenal secretory responses before, during, and after aspirin administration were compared using analysis of variance (6). The variance ratio, F, was 5.13 for the three groups and the Least Significant Difference at the 5% level was 0.24. During administration of aspirin, there was a statistically significant decrease in the peak output of duodenal secretion following feeding. After aspirin had been discontinued, peak feeding responses rose, but did not reach the pre-aspirin level. Figure 2 illustrates the averages of the peak daily secretory responses before, during, and after aspirin administration. These three groups of values were likewise compared using analysis of variance. The variance ratio, F, was 7.97 for the three groups and the Least Significant Difference at the 5% level was

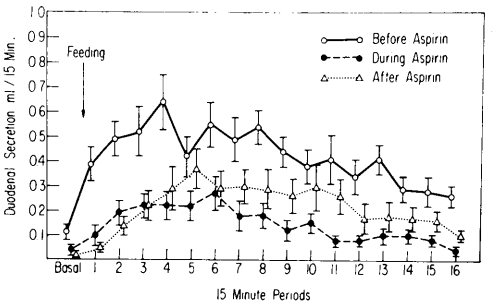

FIG. 1. Volume secretions from duodenal pouches in dogs after feeding, before, during, and after aspirin administration. Each point represents the mean of five observations on each of four dogs ± the standard error of the mean.

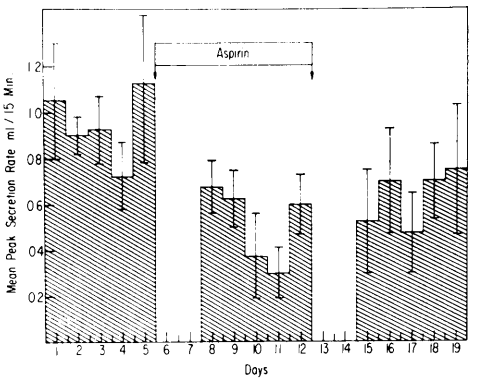

FIG. 2. Peak duodenal secretion before, during, and after aspirin administration. Each bar represents the mean of the peak duodenal secretion stimulated by feeding in each of four dogs ± the standard error of the mean.

0.22. Aspirin administration was associated with a statistically significant decrease in duodenal secretory response to a meal. Following discontinuing aspirin, the duodenal secretory values rose, but were still significantly lower than the pre-aspirin values.

Discussion. The results of this experiment demonstrate clearly that the administration of aspirin markedly reduced the duodenal secretory response to a meal. The secretion from pouches of the portion of the duodenum between the entrance of the common bile duct and the pylorus may come from two sources: Brunner's glands or the duodenal epithelium. It cannot be ascertained with certainty in these experiments whether the increased secretion after feeding was due to secretion of Brunner's glands or of intestinal epithelium or of both. Takeuchi *et al.* (7), however, have recently demonstrated that the administration of aspirin for long periods decreased the number of goblet cells containing mucin droplets in the mucosa of the jejunum and colon. This raises the possibility that the alterations in secretion produced by aspirin may be due to a decreased number of goblet cells in the duodenal mucosa. Some deleterious effects of aspirin on gastrointestinal mucosa are due in part to the direct contact of aspirin with the mucosa. This possibility is excluded in the present experiment, however, since there was no direct contact of aspirin

with the mucosa being studied. The results of the present experiment, therefore, are due to the systemic effect of aspirin. Similar findings were observed by Menguy and Masters (3), who noted that aspirin produced a reduction in the quantity and an alteration in the composition of mucus secreted from antral pouches in dogs when the mucosa under study was excluded from alimentary continuity, so that the test substance did not contact the mucosa being studied. Although aspirin may cause alterations in the secretion from the duodenum in dogs, there is no evidence in this study to relate this observation with the pathophysiology of any disease.

Summary. Duodenal secretion was measured in mongrel dogs prepared with proximal duodenal pouches, and this secretion was observed before, during, and after administration of aspirin. Aspirin produced a marked and statistically significant inhibition in duodenal secretory response to a meal, and recovery was not complete by the end of a week after discontinuing the aspirin.

1. Tainter, M. L., and Ferris, A. J., "Aspirin in Modern Therapy, A Review." Bayer Company, Division of Sterling Drugs, Inc., New York (1969).

2. Davenport, H. W., Gastroenterology **49**, 189 (1965).

3. Menguy, R., and Masters, Y. F., Surg. Gynecol. Obstet. **120**, 92 (1965).

4. Goodman, L. S., and Gilman, A., "The Pharmacological Basis of Therapeutics," 4th Ed. MacMillan, New York (1970).

5. Grossman, M. I., Motsumota, U. K., and Lichter, R. J., Gastroenterology **40**, 383 (1961).

6. Snedecor, G. W., and Cochran, W. G., "Statistical Methods." Iowa, State University Press, Ames (1967).

7. Takeuchi, T., Ensrude, E. R., and Steggerda, E. R., Amer. J. Digest. Dis. **17**, 49 (1972).

Received Oct. 26, 1973. P.S.E.B.M., 1974, Vol. 145.