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Lysozyme Content of the Stomach and Its Possible Relationship to Peptic Ulcer.*

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The bacteriolytic enzyme lysozyme has been shown to depolymerize and hydrolyze a mucopolysaccharide obtained from lysozyme-susceptible organisms.[1] The depolymerization of this substrate as measured viscosimetrically has been used as an accurate and speedy test for the assay of the enzyme.

Acetone desiccated mucosa of horse and hog stomachs were found by this method to contain 15.2 and 714 units of lysozyme per gram respectively (samples were obtained through the courtesy of Dr. R. H. Barnes of Sharp and Dohme, Philadelphia). Mucosa of the fundus, antrum, pylorus and duodenum of human stomachs resected for peptic ulcer were found to contain mean lysozyme titers of 12, 120, 316, and 213 units per gram of wet weight respectively. One case of ulcer of the duodenum showed the following lysozyme titers: fundus: 2, antrum: 200, pylorus: 224, and duodenum: 400 units per gram.

Assays of the gastric juice of 30 normal individuals and 29 unoperated ulcer cases showed mean lysozyme values of 7.69 and 14.3 units per cc respectively. The difference of the means is statistically significant. All cases with obstruction, as evidenced by intractable vomiting, had a mean lysozyme titer of 1.7 units per cc. This low value is probably explained by peptic destruction of lysozyme. Approximately 50 γ of crystalline pepsin inactivated (at 37°C) 81% of an equivalent amount of lysozyme in one hour and 92% in 2 hours. The mean lysozyme titers of the unoperated ulcer cases without the 7 obstructed individuals was 18.3 units per cc. This figure is statistically highly significant.

The mean lysozyme titers of the gastric juice on other groups of cases were: postgastrectomy (for ulcer), 7 cases—30.7; gastroduodenitis, 2 cases—23.8; marginal ulcers, 3 cases—33.1; postgastroenterostomy (for obstruction), 2 cases—9.1 units per cc.

It seems significant that in the 7 postgastrectomy cases no instance of hyperacidity was found, while 6 of the 7 individuals had a high lysozyme titer. The gastric juice of the 2 marginal ulcer cases which followed gastrectomy showed low or normal acid levels but high lysozyme titers (62.9-32.6 units per cc).

Because of the known beneficial effect of vagectomy on peptic ulcer, 5 cases were studied before and after operation. The mean fall in titer was 44.4%, ranging from 16.7 to 74.4%. This indicates that lysozyme production is, at least in part, influenced by nervous control.

Pure eggwhite lysozyme, in high concentrations, completely removed the surface mucus of the Pavlov pouch of an anesthetized dog when instilled over a period of 4 hours. The lysozyme was dissolved in pooled normal human gastric juice. A small ulcerated lesion resulted in the antral portion of this pouch, characterized by a destruction of the mucous cells within the gastric pits in the lamina propria. In another living dog, almost complete removal of the surface mucus was accomplished by instillation of eggwhite lysozyme dissolved in saline through a Levine tube into the functioning stomach. These observations were based on histological study of sections of the mucosa taken at the conclusion of the experiments.

Furthermore, a mucopolysaccharide frac-

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1 Meyer, K., and Hahnel, E., *J. B. C.*, 1946, **163**, 723.

tion was isolated from hog gastric mucosa which, on incubation with eggwhite or *ficus* lysozyme,[2] was hydrolyzed, yielding reducing sugars. The 2 known (neutral and acid) polysaccharides of gastric mucin[3] are not attacked by lysozyme.

Dodecyl sulfate, which has been reported to influence mucin production,[4] strongly inhibits eggwhite and gastric lysozyme. The latter, in extracts of human mucosa, is completely inactivated by M/1000 dodecyl sulfate.

The facts reported in this paper strongly suggest a role for lysozyme in the etiology of peptic ulcer.

[2] Meyer, K., Hahnel, E., and Steinberg, A., *J. B. C.*, 1946, **163**, 733.

[3] Meyer, K., Smyth, E. M., and Palmer, J. W., *J. B. C.*, 1937, **119**, 73.

[4] Shay, H., Komarov, S. A., and Siplet, H., *Science*, 1947, **105**, 128.

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Lysozyme in Chronic Ulcerative Colitis.*

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It has been previously shown in experimental animals that there is a low lysozyme content of the colonic mucosa in contrast to that of the stomach and in assays of apparently normal segments of 3 human large intestines, surgically removed for carcinoma, the lysozyme concentration was similarly low (mean = 3.5 units/g tissue). However, following the observation that lysozyme was able to remove the surface mucus from the dog stomach,[1] the present investigation was undertaken to determine whether abnormal concentrations of this mucolytic enzyme were present in the feces of patients with chronic nonspecific ulcerative colitis.

Table I summarizes the results of the stool lysozyme determinations. It is to be noted that the concentration of the enzyme in the feces of the control individuals was low whether the determinations were made on specimens obtained following a normal bowel movement or after purging with magnesium sulfate or castor oil. Similarly, in 3 chronic ulcerative colitis patients whose disease necessitated ileostomy and colectomy, the lysozyme concentration of the ileal stools was uniformly low. Also, in the single patient with idiopathic diarrhea who failed to show any organic change in the mucosa of the gastro-intestinal tract, there was little lysozyme present in the stool. In marked contrast to the above noted findings was the elevated lysozyme concentrations in the fecal excretions of 12 patients in whom the diagnosis of nonspecific chronic ulcerative colitis was established by roentgen and proctoscopic examination and in whom exhaustive search for pathogenic bacteria and/or parasites was negative. Even more striking was the high titer of lysozyme found in specimens of mucus obtained from the rectosigmoid region of patients with this disease.

In some instances it was possible to collect 24-hour stool specimens so that the total lysozyme excreted per day could be determined. The highest total lysozyme content noted in the feces of the control group was 528 units in 24 hours, whereas lysozyme excretion in the colitis patients was as high

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[1] Meyer, K., Prudden, J. F., Lehman, W. L., and Steinberg, A., PROC. SOC. EXP. BIOL. AND MED., 1947, **65**, 220.