

This Week's Citation Classic

Davenport H W. Gastric mucosal injury by fatty and acetylsalicylic acids. *Gastroenterology* 46:245-53, 1964. [Section of Physiology, Mayo Clinic and Mayo Foundation, Rochester, MN]

This paper demonstrated that short chain fatty acids and acetylsalicylic acid (aspirin) break the gastric mucosal barrier when they diffuse into the gastric mucosa in fat soluble form. Once the barrier is broken, H⁺ in the lumen diffuses into the mucosa, and Na⁺ in mucosal interstitial fluid diffuses into the lumen. The consequences of back-diffusion of H⁺ into the mucosa include cell destruction, copious output of fluid into the lumen, shedding of plasma proteins, and frank bleeding. These consequences can be prevented or ameliorated by neutralizing the contents of the stomach. [The *SCI*[®] indicates that this paper has been cited over 275 times since 1964.]

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"That this paper should be frequently cited is something of a joke. In 1962, being exhausted by my duties at the University of Michigan and at a dead end in my research, I went on sabbatical leave to the section of physiology at the Mayo Clinic to work under Charles F. Code. I told Code to treat me like a postdoctoral fellow, and he assigned me the problem of explaining why the gastric mucosa, previously irrigated with eugenol, secretes fluid low in H⁺ and high in Na⁺. I proposed that eugenol breaks the gastric mucosal barrier, allowing secreted H⁺ to disappear by back diffusion and Na⁺ to leak into the lumen. Code and I demonstrated that my proposal was correct, and he wrote up the results in what turned out to be, if I

may be truthful as well as immodest, a classic paper.¹

"In the few weeks remaining to me at the Clinic, I tackled the obvious problems: What is the nature of the gastric mucosal barrier, and what happens when it is broken? I studied the effects of fatty acids and their salts for the reason that I knew the barrier must behave like a lipid membrane. Half-way through that work it dawned on me that aspirin should behave the same way.² I thought of aspirin for three reasons. 1. At that time the clinical world was having one of its recurrent spasms about gastric bleeding induced by aspirin, but there were no sensible explanations of the reason. 2. My wife had been junior author of a notorious paper³ demonstrating gastric damage induced by massive parenteral doses of aspirin. 3. Any scientifically sound work on the gastric effects of aspirin would be sure to stir up the animals. I did the work very quickly and wrote up the paper immediately upon my return to Michigan. It was published before the much more important paper,¹ for the reason that it took some time for Code to write the better one and to see it through the Clinic's section of publications.

"As the *Science Citation Index*[®] shows, the aspirin paper did stir up the animals. The work started at the Mayo Clinic occupied me for 16 years and has resulted in a substantial body of new knowledge, provided by many others as well as by myself. That knowledge has, as Morton Grossman predicted, revolutionized the physiology of the stomach, and it has made a considerable contribution to patient care. I am pleased to have participated in that revolution, and I am equally pleased that my work has earned me the William Beaumont Professorship, election to the National Academy of Sciences, and the American Gastroenterological Association's Friedenwald Medal."

1. Davenport H W, Warner H A & Code C F. Functional significance of gastric mucosal barrier to sodium. *Gastroenterology* 47:142-52, 1964.
[The *SCI*[®] indicates that this paper has been cited over 180 times since 1964.]
2. Hogben C A M, Schanker L S, Tocco D J & Brodie B B. Absorption of drugs from the stomach.II. The human. *J. Pharmacol. Exp. Ther.* 120:540-5, 1957.
3. Barbour H G & Dickerson V C. Gastric ulceration produced in rats by oral and subcutaneous aspirin. *Arch. Int. Pharmacodyn. Ther.* 58:78-87, 1938.