

This Week's Citation Classic

Davenport H W. Destruction of the gastric mucosal barrier by detergents and urea. *Gastroenterology* 54:175-81, 1968.
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This paper demonstrates that bile salts (10, 20, and 40 mM in neutral solution, 40 mM in a liquid meal, and 10 mM in acid solution), decyl sulfate (10 or 20 mM in neutral solution), and urea (1, 2, and 4 M in neutral solution) all break the dog's gastric mucosal barrier and permit back-diffusion of acid into the mucosa. [The SC/® indicates that this paper has been cited in over 335 publications since 1968.]

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"This is my second paper to achieve the notoriety of becoming a *Citation Classic*. The first was on aspirin damage to the gastric mucosa,¹ and when I wrote it I knew that anything making sense about aspirin in the stomach was sure to stir up the animals. This second paper contained a beast-goad in the form of bile salts I did not recognize at the time.

"The gastric mucosal barrier is the property of the stomach that allows it to contain the acid it secretes. If the barrier is broken, as by aspirin in acid solution, acid diffuses back into the mucosa, causing all sorts of damage extending to fatal exsanguinating hemorrhage.² For many years after I had shown that aspirin in acid solution breaks the barrier, I tried to discover the nature of the barrier by some simpleminded experiments in which I attempted to reinforce it or to destroy it. I never published the reinforcing

experiments, for they accomplished nothing. To partition the barrier I used urea just as I used acetylcysteine later.³ Lipids of the cell membrane must be part of the barrier, and I dispersed the lipids with some decyl sulfate given me by the DuPont Company years before. Both broke the barrier.

"Eventually it dawned on me that bile had been acting at oil-water interfaces long before DuPont synthesized decyl sulfate. I got bile from dogs in the student laboratory, and I demonstrated that it broke the barrier and permitted back-diffusion of acid. At the time, I was totally ignorant of the clinical supposition that regurgitated bile is a cause of gastric ulceration, and I did the experiments solely in pursuit of information about the structure of the barrier. I knew I should repeat the experiments with a pure conjugated bile salt. In those days, bile salts were just becoming fashionable, and the conjugated ones were not in supply-house catalogs. I asked Alan Hofmann for advice, and he told me about a magician-chemist who was conjugating bile acids in King Mark's court in Cornwall. I got 100 grams of sodium taurocholate from Tintagel. After I had established that a pure bile salt behaves like bile in breaking the barrier, I knew there were many more experiments to be done. I should run up and down the pH and concentration scales and so on. However, I thought: 'I have done enough. Let some clinician do the rest.'

"It seems that I had done enough. Clinicians immediately took up the problem of the significance of bile regurgitation in breaking the barrier, permitting acid back-diffusion and causing gastric hemorrhage. Until they had papers of their own to cite, they liberally cited mine."

1. Davenport H W. Gastric mucosal injury by fatty and acetylsalicylic acids.

Gastroenterology 46:245-53, 1964.

[Citation Classic. *Current Contents/Clinical Practice* 9(7):16. 16 February 1981.]

2. The gastric mucosal barrier; past, present, and future. *Proc. Mayo Clin.* 50:507-14, 1975.

3. Protein-losing gastropathy produced by sulfhydryl reagents. *Gastroenterology* 60:870-9, 1971.