Abstract: Gastric acid and bile acids are a particularly noxious combination when they interact with the mucosa of the upper intestinal tract. There is a critical pH range, between 3 and 6, in which bile acids exist in their soluble, un-ionized form, can penetrate cell membranes, and accumulate within mucosal cells. At a lower pH, bile acids are precipitated, and at a higher pH, bile acids exist in their noninjurious ionized form. Experimental, clinical, and immunohistochemical studies show that acid and bile reflux are increased in patients who suffer from GERD, are the key factor in the pathogenesis of Barrett's esophagus, and possibly are related to the development of esophageal adenocarcinoma.