isoforms led to the development of COX-2–specific inhibitors (e.g., celecoxib, rofecoxib, valdecoxib), drugs that maintain their anti-inflammatory properties while preserving the biosynthesis of protective prostaglandins (Fig 36-5). Unfortunately, adverse cardiovascular effects of COX-2 inhibitors have limited the use of these drugs.

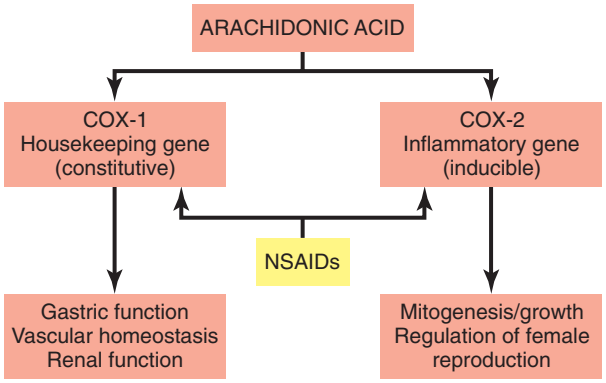

FIGURE 36-4 Biosynthesis of prostaglandins and leukotrienes through the cyclooxygenase and lipoxygenase pathways.

The spectrum of NSAID-related mucosal injury includes a combination of subepithelial hemorrhages, erosions, and ulcerations that is often referred to as *NSAID gastropathy.* Erosions are likely to be small and superficial, whereas ulcers tend to be larger (more than 5 mm in diameter) and deeper. Although no area of the stomach is resistant to NSAID-induced mucosal injury, the most frequently and severely affected site is the antrum. Microscopically, a *reactive* pattern of injury can be found that is characterized by mucin depletion and little or no increase in inflammatory cells. Endoscopic studies have shown a prevalence of gastroduodenal ulcers of 10% to 25% in patients with chronic arthritis treated with NSAIDs, which is 5 to 15 times the expected prevalence in an age-matched healthy population.

In addition, at least 60% of individuals with complicated ulcers (e.g., hemorrhage, perforation) report the use of NSAIDs, including aspirin. NSAID-induced ulceration occurs with all traditional NSAIDs, regardless of enteric coating or delivery as a prodrug formulation. The risk for NSAID-induced ulceration and complications is dose related and increases with age older than 60 years, concurrent corticosteroid use, increasing duration and dose of therapy, anticoagulant therapy, and a history of prior ulcer disease.

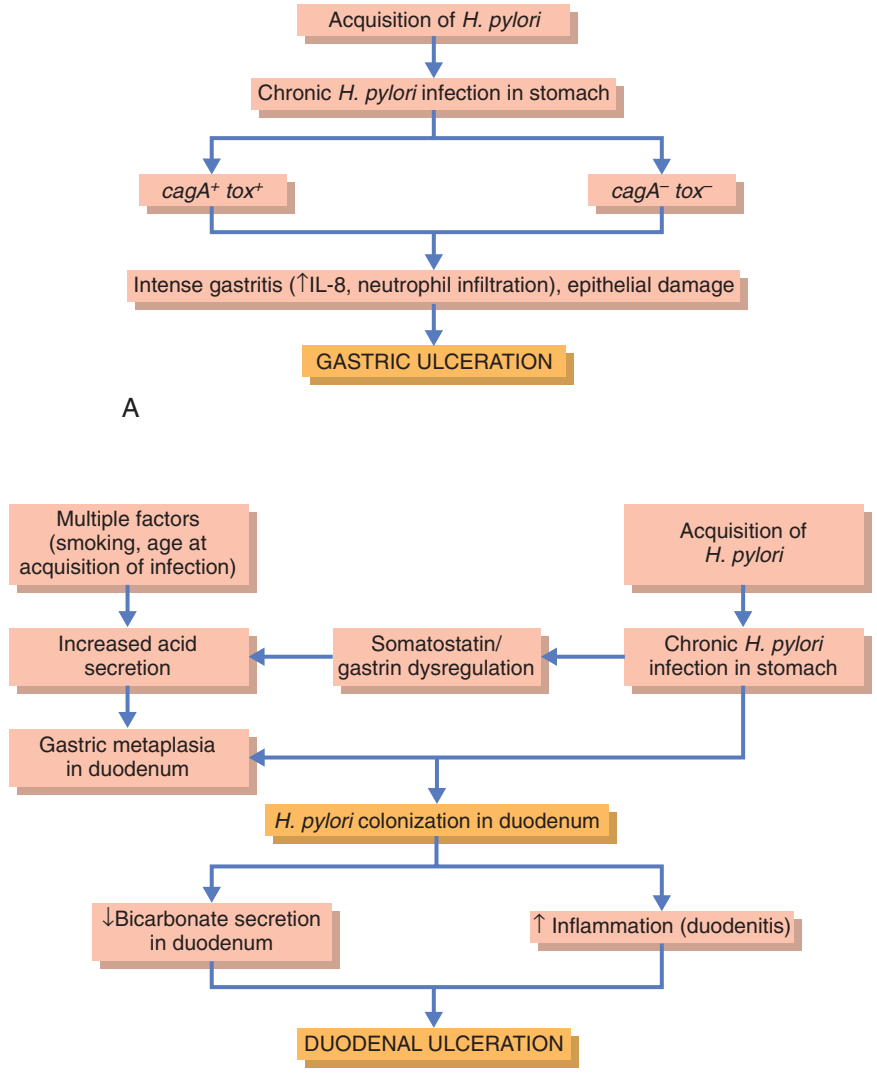

FIGURE 36-5 Depiction of the two cyclooxygenase isoenzymes that catalyze the synthesis of tissue prostaglandins from arachidonic acid.