

# HOSPITAL PHYSICIAN®

## GASTROENTEROLOGY BOARD REVIEW MANUAL

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The *Hospital Physician Gastroenterology Board Review Manual* is a study guide for fellows and practicing physicians preparing for board examinations in gastroenterology. Each quarterly manual reviews a topic essential to the current practice of gastroenterology.

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## NSAID-Induced Gastrointestinal Damage

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# NSAID-Induced Gastrointestinal Damage

James M. Scheiman, MD

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## INTRODUCTION

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### CASE PRESENTATION

It's 5:30 AM, and you've just left the intensive care unit following successful endoscopic therapy to control a bleeding gastric ulcer in a 55-year-old man. He was generally healthy, but he was taking "one of those new, safer, NSAIDs" for knee osteoarthritis. He also had been taking an enteric-coated aspirin at night, because "all his friends take one, too." He takes no other medications. At the time of the endoscopy, biopsies were obtained for *Helicobacter pylori* status.

### EPIDEMIOLOGY OF NSAID-INDUCED ULCERS

Each year, more than 40 billion aspirin tablets are consumed and more than 110 million prescriptions for nonsteroidal anti-inflammatory drugs (NSAIDs) are filled in the United States. At least one third of the prescriptions are for cyclooxygenase (COX)-2-specific inhibitors (coxibs) at a cost of \$5 billion dollars/yearly.<sup>1</sup> These drugs can have significant adverse gastrointestinal (GI) effects ranging from symptoms such as nausea and dyspepsia (ie, persistent pain or discomfort in the upper abdomen) to serious ulcer complications such as bleeding and perforation. Among chronic NSAID users (defined as daily use for more than 1 year), the risk of developing a symptomatic ulcer, gastrointestinal bleed, or perforation is 1% to 4%.<sup>2</sup>

Although there is a low probability that any individual NSAID user will experience a drug-related complication, the huge number of chronic users translates NSAID toxicity into a major health care problem. It is estimated that more than 100,000 hospitalizations and up to 10,000 to 20,000 deaths each year in the United States can be attributed to NSAID complications.<sup>2</sup>

There is no consensus among clinicians on how best to weigh the potential clinical benefits of various anti-inflammatory agents against the possibility of adverse events associated with their use. Choosing between a generic traditional NSAID and the safer but more costly medications in the COX-2-specific inhibitor class requires a framework for informed decision making.

Considerations include the patient's risk for toxicity, the need for concurrent aspirin therapy, and whether the patient is already taking a gastroprotective agent such as a proton pump inhibitor (PPI). Patient risk factors should drive clinical decision making to target these medications in cost-effective manner.

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## ASSESSING RISK

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NSAID users have an approximately 3-fold elevated risk of an ulcer complication (ie, bleeding, perforation, or a clinical event requiring hospitalization or causing death) compared to nonusers. Although 1% to 4% of chronic NSAID users develop an adverse event, individual risk varies considerably across the population. When chronic NSAID therapy is necessary, it is essential to assess a patient's individual risk for complications. Recognized risk factors (in order of their relative importance) are listed in **Table 1**.

### RECENT OUTCOME STUDIES

Until the recent CLASS<sup>3</sup> and VIGOR<sup>4</sup> outcome studies were completed evaluating the safety of coxibs (celecoxib and rofecoxib, respectively) compared to traditional NSAIDs, the only prospective data regarding the risk of serious complications due to NSAIDs was from the MUCOSA<sup>5</sup> trial, which compared the outcome of rheumatoid arthritis (RA) patients taking non-aspirin NSAIDs plus either misoprostol or placebo. 0.95% of patients on non-aspirin NSAIDs plus placebo developed serious GI complications within 6 months as compared to 0.57% of patients on NSAIDs plus misoprostol. These findings are consistent with the frequently quoted 2% to 4% risk included in the prescribing information for prescription NSAIDs. The CLASS and VIGOR studies confirmed these rates—approximately 2% annually for complicated ulcers, and 4% annually for symptomatic ulcers.<sup>3,4</sup>

### RISK FACTORS

Patients with a history of ulcer complications and those taking concomitant anticoagulant therapy have the highest risk of developing NSAID-associated serious GI complications. Moderate risk factors include advanced age,