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Adverse effects of Aspirin on the Gastrointestinal tract & Brain

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Introduction:
Aspirin is an everyday painkiller used to relieve minor pains. Aspirin has also been used as treatment for mild to moderate fever, as an intial emergency treatment of heart attacks and Anxiety strokes. Aspirin, however, can also cause damage to the stomach, Brain, and/or intestinal lining leading to the development of erosions ("small sores") and/or ulcers ("large sores").

Mechanism of Action: Aspirin is a cyclooxygenase-1 (COX-1) inhibitor. It is a modifier of the enzymatic activity of cyclooxygenase-2 (COX-2). Aspirin irreversibly acetylates and inhibit cyclooxygenase. Aspirin helps in preventing platelet aggregation by blocking the formation of thromboxane A2 on platelets. However, by inhibiting this key enzyme in PG synthesis, the aspirin-like drugs also prevented the production of physiologically important PGs which protect the stomach mucosa from damage by hydrochloric acid, maintain kidney function and aggregate platelets when required.(59)
Aspirin therapy is underused by those at high risk for CVD—individuals who could gain cardioprotection from regular use—and overused by those at low risk for CVD, for whom the risk of major bleeding outweighs the potential benefit. Stronger primary care initiatives may be needed to ensure that patients undergo regular screening for aspirin use, particularly middle-aged men at high CVD risk.

Adverse Effects of Aspirin Therapy: Many guidelines recommend long-term use of aspirin for prevention of cardiovascular events among patients with prior cardiovascular disease or multiple risk factors.1, on brain
HOWEVER Long-term low-dose (≤325 mg) aspirin therapy may come with potential for adverse effects. low-dose aspirin therapy is being linked with a significant increase in the risk of GI adverse events as well as cerebral bleeding..10 In a recent survey, 15% of patients receiving low-dose aspirin experienced upper GI symptoms.11 Some of the most common GI complaints reported by aspirin-treated patients are shown in Figure 2.12

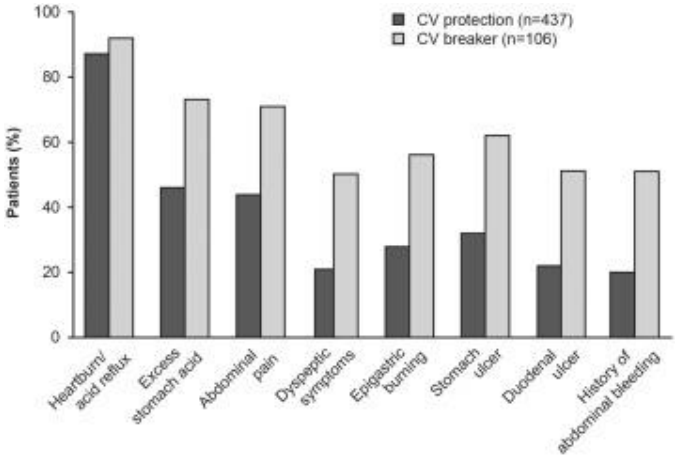

FIG 2. Gastrointestinal complaints experienced by low-dose aspirin-treated patients.12 Patients whose physicians had recommended the use of low-dose aspirin for the secondary prevention of cardiovascular (CV) events completed a questionnaire regarding the gastrointestinal problems they had experienced. Data are shown for the total population of patients requiring CV protection (n = 437 [“CV protection”]), and the subset of patients who had taken deliberate short-term breaks from their aspirin regimen (n = 106 [“CV breaker”]). (Reprinted with permission.)
In another study by Edward S. Huang they found that regular aspirin users (≥2 standard [325 mg] tablets/week) had a significantly higher risk of developing gastrointestinal bleeding compared with non regular users .
Byron cryer et al. concluded in their study that even as low as 10 mg/day dosage of aspirin was significant for gastric injury while submaximally suppressing platelet TXB2 levels by 62% (38% of the baseline value) if administered for long time. Also, when they compared the effect of aspirin on PG levels in the stomach, duodenum and rectum , a proximal to distal gradient of decreasing mucosal PG suppression and decreasing mucosal injury was observed because injury was greatest in the stomach with ulcers found only in stomach, erosions occurred mostly in the stomach but also in the duodenal bulb, little injury occurred in the postbulbar duodenum, and no injury was observed in the rectum. This differential region response was supposed to be due to gastric mucosa being intrinsically more susceptible than the duodenal or rectal mucosa to aspirin-induced injury and PG suppression.
Yeomans et al. in there study on adverse effect of aspirin showed that the incidence rates of ulcer and mucosal erosion in patients due to the long-term usage of low-dose aspirin were as high as 10.7% and 63.1%, respectively [24].
In a large population based study to provide estimates of low-dose aspirin associated upper/lower gastrointestinal bleeding in routine primary care, it was found low-dose aspirin was associated with a 60% increased risk of lower gastrointestinal bleeding but only a minor non-significant increase in UGIB risk.
However, the clinical utility of some of these reviews may be limited because they include studies with aspirin doses outside the ‘low-dose’ range (75–325 mg daily), they do not factor out concurrent medications such as anticoagulants in all included studies, and/or they include very short-term studies which may not allow appropriate assessment of relatively rare GI clinical events.

Conclusions: Low dose aspirin is the most utilized antiplatelet therapy and it is the most effective. However, it has been associated with risk of gastrointestinal toxicity, leading patients to discontinue therapy and increasing their cardiovascular risk& Brain Health. For most people, giving up NSAIDs is the key to

treatment In patients with high risk of gastrointestinal events with aspirin, the use of proton pump inhibitors is presently recommended.
the main mechanism for aspirin toxic effects on the mucosa of the gastrointestinal tract is systemic, through inhibition of cyclooxygenase and the consequent decrease in the synthesis of prostaglandins.
Mucosal prostaglandin synthesis is decreased at higher doses of aspirin.29,30 In addition, experimental animal models have shown that gastric mucosal injury is highly dose-dependent.

6 If there were an orally administered daily aspirin dose that effectively inhibited platelet COX-1 and TXA2 synthesis while having no significant effect on gastrointestinal COX-1 and PG synthesis, such an aspirin dose might be useful in the treatment of vascular disorders while sparing the gastrointestinal tract from injury.