Medication-associated lesions of the GI tract (CME)

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At a Harben Lecture in London in 1908, German scientist Paul Ehrlich described the ideal drug as a "magic bullet" (*Zauberkugel*).[1] Such a drug would be aimed precisely at a disease site and would not affect healthy tissues. Today, over 3.5 billion prescriptions are dispensed each year in the United States to manage a broad number of health disorders.[2] Although many drugs are aimed more accurately than their predecessors, none of them, as of yet, hit their targets exclusively. Several medications are associated with an increasing incidence of drug-induced (iatrogenic) adverse events, a frequent site of which is the GI tract. In fact, 10% of the drug-induced adverse effects are related to the GI tract.[3] The consequences of such can range from asymptomatic histologic changes in the GI mucosa to fatal adverse events. In some instances, the adverse events are worse than the illness for which the drug was prescribed. However, many drug-induced adverse events are preventable. Therefore, it is becoming increasingly important to recognize both the clinical and pathologic manifestations of GI tract drug-induced injury early, so that the offending drug can be discontinued or replaced.

This review uses an organ-based approach to present both clinical information and pathologic findings to increase clinical awareness of the most common drug-induced GI conditions. Although each part of the GI tract has been considered separately, some drugs exert a common local effect (eg, esophagus), whereas others have more specific findings or principally a systemic mode of action. Because the number of drugs that are potentially toxic to the GI tract is almost countless, we focus on the most common and well-documented examples of drug-induced injury, in which endoscopic and/or histologic findings can be recognized.

Abbreviations: COX, cyclooxygenase; MMF, mycophenolate mofetil; NSAID, nonsteroidal anti-inflammatory drug.

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ESOPHAGUS

Pill esophagitis

Pill esophagitis is the most common form of medication-induced esophageal injury and is related to both direct contact and facilitation of mechanisms that eventually lead to disruption of the mucosal lining.[4,5] Damage to the underlying mucosa occurs because of a medication's direct localized toxicity, generally caustic (acidic or alkaline) or hyperosmolar in nature. However, factors such as medication contact time, pill coating, and immediate versus sustained-release formulations likely all play a role. Altered anatomy (eg, stricture), motility disturbances, and ingestion parameters also may be contributing factors. Frequent areas of "hang-up" leading to prolonged mucosal contact include the level of the aortic arch, the level of an enlarged left atrium, and the gastroesophageal junction.[6,7]

The most common presenting symptoms include severe retrosternal pain immediately after ingestion of food and liquid, frequently worse with inspiration, and odynophagia. A typical history usually can be obtained in which a patient took an offending medication immediately before bed, with just a small sip of water, or none at all. Symptoms can be severe but self-limited and generally resolve within a week. "Topical" agents such as sucralfate suspension or viscous lidocaine can provide temporary relief if dosed before meals.[8] At times, narcotic medication may be necessary to alleviate pain. Rarely, parenteral hydration and/or nutrition are needed if pain is so severe that the patient cannot drink. Endoscopy is generally not necessary in the appropriate clinical setting, but if performed, typical findings include either a solitary ulcer or multiple ulcerations with localized exudate (Fig. 1A). Biopsies are generally not helpful, other than to exclude malignancy. Pathologically, the pattern of injury is consistent with a nonspecific esophagitis characterized by mucosal ulceration and

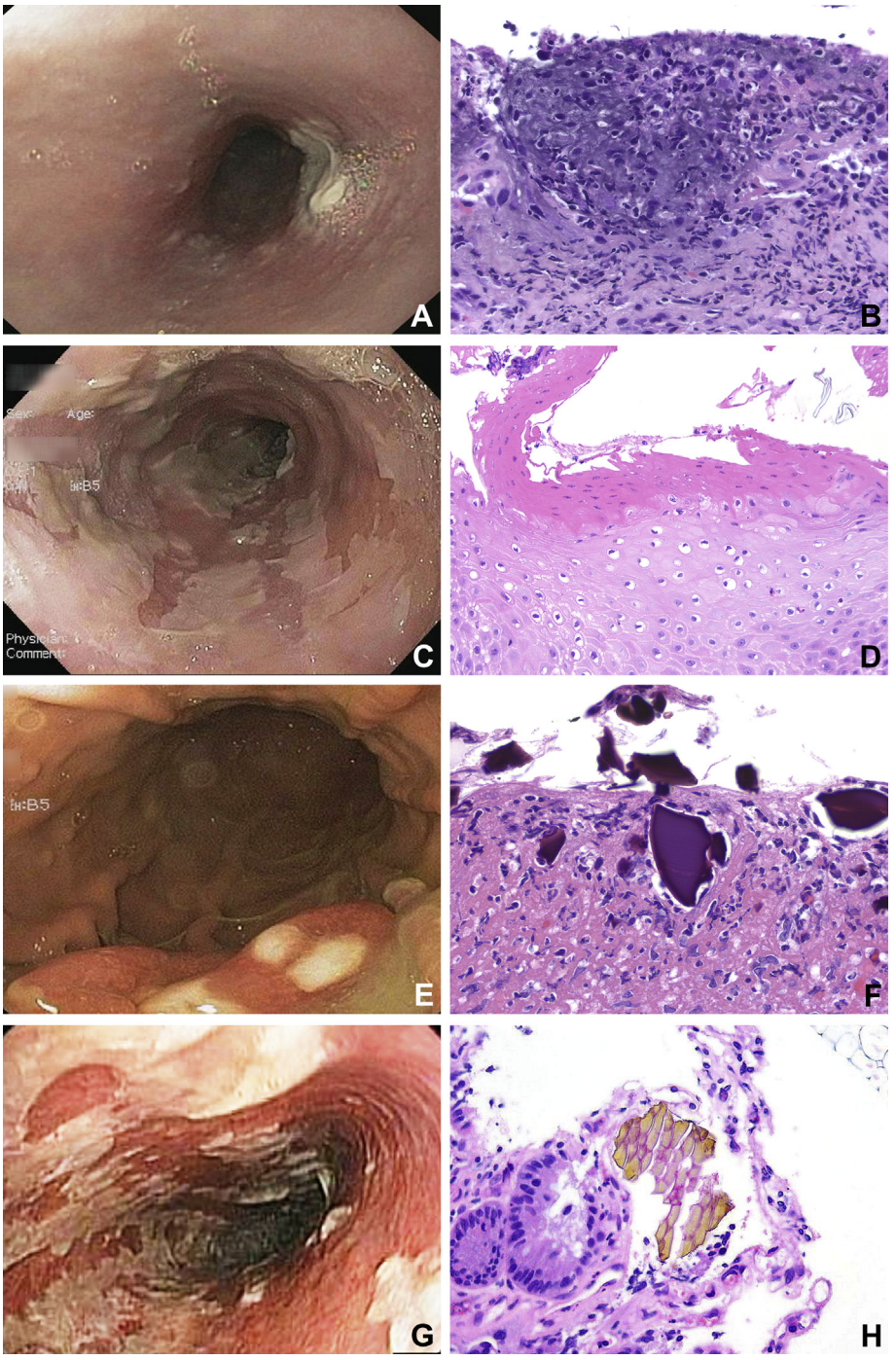

Figure 1. Endoscopic and corresponding microscopic examples of esophageal and gastric drug-induced injury. **A**, The most common form of esophageal medication-induced injury is pill esophagitis. Although the endoscopic findings are nonspecific and characterized by mucosal ulceration with associated fibroinflammatory exudate, certain medications can demonstrate distinct microscopic findings. **B**, In the case of iron pill esophagitis, the iron pill imparts a dusky greyish discoloration within a background of granulation tissue (H&E, orig. mag. ×20). **C**, Sloughing esophagitis features prominent white plaques or membranes within the middle-to-distal esophagus. **D,** The typical histologic findings are a tone-toned appearance, with a superficial eosinophilic zone composed of pyknotic nuclei and an underlying normal-appearing basal zone (H&E, orig. mag. ×20). **E**, Sodium polystyrene sulfonate–induced injury to the gastric mucosa is characterized by erosion and/or ulceration (*right lower corner*) and **F**, rhomboid, basophilic crystals with a mosaic pattern (H&E, orig. mag. ×40). Another exchange resin that can mimic the effects of sodium polystyrene sulfonate is sevelamer carbonate. **G**, Sevelamer carbonate–induced esophageal injury is characterized by mucosal erythema, ulceration, and white exudates (figure kindly provided by Dr William Santangelo). **H,** Similar to those of sodium polystyrene sulfonate, sevelamer carbonate crystals are nonpolarizable with a broad, curved "fish scale" pattern, but of variable color (H&E, orig. mag. ×40).