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A multimodal approach to manage post op ileus: Effective in reduction of post op expenses

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Abstract
Postoperative ileus is one of the most important and common complications experienced after abdominal surgeries. It is an iatrogenic impairment of propulsive gastrointestinal motility. Postoperative ileus delays hospital discharge, increases costs, and contributes to adverse out comes. Avariety of neural and chemical factors are involved. To shorten the duration of postoperative ileus, we may need to establish standard plans of care that favor earlier feeding, use of nasogastric tubes only on a selective basis, and prokinetic drugs as needed.

Keywords: Postoperative ileus, abdominal surgeries, propulsive gastrointestinal

Introduction
Post-operative ileus can selectively affect the stomach, small lintestine, or large intestine, each with different causes and clinical presentation and each managed differently. Laparoscopic surgery is associated with a shorter dura-tion of postoperative ileus compared with open surgery.
Epidural anesthesia reduces the need for opiate anal-gesia after surgery and thus shortens the duration of post-operative ileus. Drugs are being developed that block the effects of opiates on the gut while preserving their pain-relieving properties.

Discussion
Rather than merely wait for bowel sounds to return after patients undergo surgery, we can try to get the gut working again sooner. An active approach might shorten the dura-tion of postoperative ileus, allow patients to go home from the hospital sooner, and improve their outcomes.
In the pages that follow, were view the patho physiology, diagnosis, and current thera-pies to alter the course of post-operative ileus.

ILEUS Can Affect the Stomach or Small or Large Intestines
Ileus is the absence of intestinal peristalsis without mechanical obstruction; postoperative ileus refers to the time after surgery before coordinated electromotor bowel function resumes. Although ileus classically refers to dysmotility of the small bowel, postoperative ileus can selectively affect the stomach, small intestine, or colon, each with a different mechanism and clinical presentation, and each managed differently (TABLE 1). Gastroparesis refers to abnormal gastric motility leading to impaired gastric emptying. This disabling, potentially chronic condition is associated with certain medical conditions such as diabetes, but can also occur after some surgical procedures, as we will discuss. It has been estimated to affect approximately 4% of the adult population, with a strong female predilection.1 Postoperative gastroparesis is probably most common after pancreaticoduodenectomy, in which it occurs in up to 57% of patients [2]. Consensus guidelines for grading the severity of gastroparesis have been devised to help standardize the reporting of outcomes [2].

Table 1: Features of gastroparesis, small-bowel ileus, and colonic ileus

Gastroparesis	Symptoms	Signs	Diagnosis	Management
	Nausea +++	Distention +	Abdominal x-ray	Nasogastric tube
	Vomiting +++	Succussion splash	Gastric-emptying study	Metoclopramide (Reglan)
	Abdominal pain+			Erythromycin
				Limit narcotics
Small-bowel	Nausea ++	Distention ++	Abdominal x-ray	Nasogastric tube
Ileus	Vomiting ++		Exclude small-bowel	Alvimopan (Entereg
			Obstruction	Limit narcotics
	Abdominal pain +			
Colonic ileus	Nausea +	Distention ++	Abdominal x-ray	Neostigmine
	Vomiting +		Exclude colon	Decompressive
			obstruction	colonos- copy
	Abdominal pain +			Limit narcotics

Acute colonic pseudo-obstruction (colonic ileus) is often seen in elderly hospitalized patients with multiple medical comorbidities. Of note, it often occurs after surgery to parts of the body other than the abdomen, such as after orthopedic procedures. One study documented an incidence of 1.3% after hip replacement surgery and 1.2% after spine

procedures. 3 The small bowel normally resumes activity several hours after surgery, the stomach 24 to 48 hours after surgery, and the colon 3 to 5 days after surgery.4 When postoperative ileus persists longer than this, it can be considered pathologic and is sometimes called paralytic ileus [4, 5].

ILEUS affects outcomes & costs

Although not usually considered life-threatening, postoperative ileus is harmful for the patient and costly for society. For the patient, ileus is uncomfortable, leads to nausea and vomiting, delays return to enteral nutrition, and prolongs the stay in the hospital. For many if not most patients undergoing gastrointestinal surgery, return of bowel function is the factor that delays going home. A prolonged hospital stay increases the risk of hospital-acquired infections, deep vein thrombosis, and other conditions. The economic burden is also considerable.

A retrospective review of more than 800,000 patients who underwent surgery in the United States in 2002 found a rate of postoperative ileus of 4.25% according to International Classification of Diseases–Ninth Revision (ICD-9) codes [6]. the mean hospital length of stay was 9.3 days in patients with postoperative ileus vs 5.3 days in those without it. The difference in mean total hospital costs was US $6,300 per patient. The costs certainly add up when you consider the number of surgical procedures performed every year.

Neural and Chemical Factors

While observing exteriorized bowel in 1872, Goltz [7] first noted enhanced spontaneous contractions when the spinal cord was severed at the level of the medulla. Not long after, Bayliss and Starling [8] used a device called an "enterograph" to monitor small-bowel activity in vivo in dogs and found that cutting the splanchnic nerves led to vigorous bowel contraction after laparotomy. These early observations formed the foundation of our understanding of postoperative ileus and some of its possible causes. Normal bowel contractility is influenced by a host of neural and chemical factors, the relative contributions of which vary depending on the segment of bowel.

The migrating motor complex is the basal level of activity in the bowel in the fasting state, serving a "housekeeping" function [9]. It has four phases, consisting of escalating electrical and contractile activity punctuated by periods of quiescence. The resumption of this motor complex after surgery is responsible for recovery from postoperative ileus.

Sympathetic-parasympathetic imbalance

The sympathetic nervous system inhibits the small bowel; the parasympathetic nervous system stimulates it. Although vagal (parasympathetic) stimulation appears to have little actual impact on small-bowel activity, if sympathetic activity is blocked, contractility increases, indicating that tonic sympathetic inhibition normally predominates. The balance of these two competing influences determines the amount of acetylcholine released by excitatory nerve fibers in the myenteric plexi of the bowel. These neural pathways can be manipulated clinically. Epidural catheters can block sympathetic output, thus allowing small-bowel function to return faster. Vagus nerve activity appears to be more important in the stomach, where it promotes receptive relaxation of the fundus and contraction of the antrum, facilitating gastric emptying [10]. After vagotomy, emptying of liquids may be normal or accelerated, but emptying of solids is impaired. This can occur after peptic ulcer surgery but is more likely after gastric resection for malignancy or after inadvertent vagal nerve injury during antireflux surgery. The enteric nervous system is a complex, intrinsic network of neurons consisting of two distinct plexi within the bowel wall: the submucosal (Meissner) plexus, and the myenteric (Auerbach) plexus [11]. The enteric nervous system in the small bowel is fundamentally different than the one in the colon in that the former contains gap junctions, allowing for coordinated electrical activity. Lacking these gap junctions, the colon depends more on input from the autonomic nervous system, perhaps explaining the longer recovery from postoperative ileus and the susceptibility to isolated colonic ileus due to a variety stressors and traumatic insults.

Chemical mediators of bowel activity

A host of chemical mediators influence bowel motility. Perhaps the most important non adrenergic inhibitor of gastrointestinal motility is nitric oxide [13]. Animal studies have firmly established nitric oxide as an important factor in postoperative ileus, but its exact role in humans is not clear [14, 15]. Other mediators with possible roles include vasoactive intestinal peptide, substance P, calcitonin gene-related peptide, and endogenous opioids [13]. Lack of duodenal-derived motilin is thought to be one cause of delayed gastric emptying after pancreaticoduodenectomy.

Inflammation

The inflammatory response after surgery has also been an attractive target of study of the factors promoting postoperative ileus. In rat studies, Kalff *et al* [16] found that surgical manipulation of the bowel induced an inflammatory cellular infiltrate in the bowel wall and diminished the response of smooth muscle to cholinergic stimulation. Cyclooxygenase-2, the enzymatic precursor to prostaglandins, has also been shown to be induced in enteric neurons after laparotomy [17].

Narcotic analgesics

One of the greatest hurdles in preventing postoperative ileus is the use of narcotic analgesics to treat postoperative pain. It is also one of the most important modifiable risk factors. Opiates delay colonic transit in postoperative patients, an effect that can be reversed by the narcotic antagonist naloxone (Narcan) [18]. This inhibitory effect is mediated by peripheral mu-opioid receptors. In a study of patients undergoing colectomy, the more morphine given, and the longer the time to the return of bowel sounds and flatus and the first bowel movement [19]. These observations have led to a search for selective opiate antagonists that allow narcotics to continue relieving pain while counteracting their effect on bowel motility, a topic discussed later in this review. Nonsteroidal anti-inflammatory drugs such as ketorolac (Toradol) are attractive alternatives to opiate analgesics, both for their anti-inflammatory effect and for their opiatesparing properties. However, they can cause bleeding, renal insufficiency, and gastritis, drawbacks that limit their applicability and duration of use.

Diagnosis by Clinical Suspicion and Imaging

The diagnosis of postoperative ileus is driven by a combination of clinical suspicion and imaging tests. Regardless of the segment of bowel involved, it is imperative to exclude an obstructive cause. The diagnosis of ileus is presumed once obstruction has been excluded.

Diagnosing gastroparesis

Postoperative gastroparesis is usually suspected by its symptoms of early satiety, nausea, vomiting, eructation, and gastroesophageal reflux. Abdominal distention is usually not a prominent sign, but a succussion splash may be detected, indicating retention of food and liquid in the stomach. Plain radiographs may reveal a large gastric air bubble in the left upper quadrant but may underestimate the degree of gastric distention. Computed tomography (CT) may show a large, fluid-filled stomach, often containing high-density food debris. The gold standard for diagnosis is gastric emptying scintigraphy after a radiolabelled solid meal. The patient consumes a meal of egg white labelled with technetium 99m sulfur colloid, and scanning is performed at specified intervals to measure the percent retention of the isotope. Retention of more than 10% at 4 hours is considered abnormal [1]. Severity can be graded on the basis of percent retention after 4 hours [20]. This test is rarely indicated in the acute postoperative setting, however, and patients should be treated presumptively to prevent aspiration once mechanical obstruction is excluded.

Diagnosing small-bowel ileus

Small-bowel ileus often presents like gastroparesis, except that it more often causes abdominal distention. Plain radiographs reveal air-fluid levels and dilated loops of bowel. Small-bowel ileus must then be differentiated from small-bowel obstruction by clinical and radiographic features. The presence of crampy abdominal pain, bowel sounds, and some bowel function implies a degree of mechanical obstruction. Plain radiographs showing "step-ladder" air-fluid levels also suggest obstruction. CT is more definitive in diagnosing obstruction by the presence of distended and decompressed bowel loops and may also reveal a source of obstruction (eg, postoperative interloop abscess).

Diagnosing colonic ileus

Colonic ileus is also characterized by abdominal distention, sometimes marked. Although it is the colon that is primarily involved, upstream small-bowel dilatation can also be seen if the ileocecal valve is incompetent. The cecum often shows the greatest degree of dilatation on plain radiographs and is at the greatest risk of perforation. CT, contrast enema studies, and endoscopy help rule out mechanical obstruction due to volvulus or a mass lesion.

Strategies to Prevent and Treat Ileus

Many strategies have been applied to prevent and manage postoperative ileus, ranging from changes in surgical technique, supportive care, and patient-initiated activities, to pharmacologic intervention.

Epidural anesthesia shortens ileus, reduces the need for narcotics

Epidural anesthesia has shown promise not only in improving pain control, but also in shortening the period of postoperative ileus. Most surgical patients either receive an epidural catheter before surgery, which is left in place for postoperative pain control, or are given patient-controlled analgesia with a narcotic. Generally, the surgeon chooses the pain control method. Thoracic epidural analgesia has been shown to hasten the return of bowel function by 1 to 2 days and to reduce the need for opiates compared with systemic opioids alone [21–26]. A likely explanation is that epidural anesthesia interferes with the afferent and efferent sympathetic reflex arcs. The level of the epidural placement is important: a thoracic epidural is needed to effectively block these sympathetic pathways.

Laparoscopic surgery is less traumatic

Laparoscopy has changed the landscape of surgery over the past few decades. Some of the most common surgical procedures (appendectomy, cholecystectomy) are now done mainly via the laparoscope, as are many procedures that are more complex. Laparoscopic surgery has several advantages over open surgery. With smaller incisions, it is less traumatic to the body. The systemic inflammatory response appears to be less vigorous after laparoscopic surgery than after open surgery, as measured by circulating levels of interleukin [1], interleukin [6], and C-reactive protein [27]. The length of stay after a laparoscopic procedure is shorter than after an open procedure for several reasons, not the least of which is a shorter duration of postoperative ileus. Animal studies show that intestinal recovery is faster after laparoscopic procedures than after open procedures [28–30]. In a study in which their other care was comparable, significantly fewer patients undergoing laparoscopic colectomy had emesis or needed their nasogastric tube to be reinserted than patients who underwent an open operation, and their length of stay was shorter [31]. As technology continues to advance in minimally invasive surgery, it is reasonable to expect these trends to continue.

Nasogastric tubes in selected cases

Patients are often allowed nothing by mouth or only minimal oral intake immediately after abdominal surgery, with or without nasogastric decompression. The role of nasogastric decompression has long been a topic of controversy. In a meta-analysis of 26 trials with 3,964 patients, the groups in which all patients routinely received a nasogastric tube had higher rates of pneumonia, fever, and atelectasis and longer duration to resumption of oral feeding than the groups in which nasogastric tubes were used selectively.32 Most clinicians agree that nasogastric tubes are uncomfortable and do little to prevent postoperative ileus. However, in selected cases they are useful for managing intractable vomiting and for preventing aspiration of gastric contents.

Early enteral feeding

Evidence is mounting that early postoperative enteral

feeding may be advantageous for recovery. In 1,173 patients undergoing both upper and lower gastrointestinal surgery in 13 trials, fewer patients died who were randomized to receive enteral feeding within 24 hours.33 There were also fewer infectious complications and anastomotic problems and a shorter length of stay, but these differences were not statistically significant. Vomiting was more common in the early-feeding groups but did not lead to higher rates of morbidity. Enteral feeding was by the oral, nasoduodenal, or nasojejunal routes, depending on the type of surgery performed. Whether the number of calories given affects the outcome remains to be clarified, but at least for now it seems that feeding patients early in the course of their recovery is not detrimental and may in fact be beneficial.

Gum-chewing

Gum-chewing has been studied over the last decade as a form of sham feeding to stimulate bowel recovery after surgery. The presumed mechanism of action is vagal cholinergic (parasympathetic) stimulation of the gastrointestinal tract, similar to oral intake but with theoretically less risk of vomiting and aspiration. In five such trials in patients undergoing colon resection, gum-chewing shortened the time until first flatus and bowel movement, but made no significant difference in length of stay [34]. At the very least, gum-chewing immediately after surgery is a cheap and harmless strategy for reducing postoperative ileus, and it might make the patient more comfortable.

Drugs that Coax the Gut Back To Work

Drugs that coax the gastrointestinal tract back to work have been tried for many years and have recently gained renewed enthusiasm. Their efficacy varies according to their target organ, with greater success in the stomach and colon than in the small bowel. Cisapride was an effective gas tric prokinetic agent, as shown in several controlled trials. However, it was withdrawn from the market in 2000 because of its propensity to cause cardiac arrhythmias.

Erythromycin

Is a macrolide antibiotic that is also a motilin receptor agonist? In patients who underwent antrectomy and vagotomy, it was shown to accelerate gastric emptying by roughly 40% as measured by solid-phase gastric emptying scintigraphy.35,36 In a randomized controlled trial in 118 patients who underwent pancreaticoduodenectomy, intravenous erythromycin reduced gastroparesis by 37% (measured by solid-phase gastric emptying study) and also reduced the need for nasogastric tube reinsertion.37 A major shortcoming is the development of tachyphylaxis, thought to be mediated by down-regulation of motilin receptors.

Metoclopramide

(Reglan) is an antiemetic and prokinetic that acts as a dopamine D2 receptor antagonist and mixed serotonin 5-HT3 antagonist/5-HT4 agonist. Metoclopramide also stimulates gastric emptying, as shown in controlled trials in patients in intensive care units [38, 39]. The drug should not be used in patients with parkinsonism, in view of its antidopamine properties.

In 2009, the US Food and Drug Administration required that a black box warning be added to metoclopramide because of the risk of tardive dyskinesia with long-term use, and recommended that its use be limited to 3 weeks in the acute setting.40 Prescribers and patients need to decide if this risk is worth the potential benefit on a case-by-case basis. Although erythromycin and metoclopramide are effective in managing gastroparesis, neither has been shown to be effective for small-bowel ileus [41, 42]. However, colonic ileus is highly responsive to drug therapy. Neostigmine (Prostigmin) is a reversible acetylcholinesterase inhibitor that enhances the activity of the neurotransmitter acetylcholine at muscarinic receptors. It is the first-line treatment for colonic ileus [43]. In three randomized, placebo-controlled trials [44–46], the success rates were 85% to 94% after the first dose. Neostigmine is generally given either as an intravenous bolus dose of 2 to 2.5 mg or as an intravenous infusion over 24 hours. It must be given in a monitored setting, as both brady cardia and bronchospasm can occur. Patients should continue to be monitored clinically and with plain abdominal radiography after the drug is given, and they sometimes require a second or third dose. In cases in which neostigmine fails, decompressive colonoscopy can be done as a second-line measure.

Alvimopan (Entereg), a peripherally acting, mu-opioid receptor antagonist, has come on the scene most recently. This agent first showed promise when it precipitated diarrhea in morphine-dependent mice [47]. Early studies in humans focused on its ability to reverse the effect of opiates on gastrointestinal transit without interfering with their analgesic properties [48–50]. Later investigations concentrated on its ability to reduce the duration of postoperative ileus after a variety of major abdominal surgical procedures [51, 52]. A pooled analysis of phase III studies of alvimopan focused on the subset of 1,212 patients who underwent bowel resections; it found a significant reduction in the time to gastrointestinal tract recovery and hospital discharge [53]. A 12-mg dose was more beneficial than a 6-mg dose, especially in females and in older patients (over age 65).

Most recently, a multicenter, double-blind, placebo-controlled trial evaluated alvimopan as part of a standardized postoperative care plan in 654 patients undergoing partial smallbowel and large-bowel resection [54]. The alvimopan group took less time to have their first bowel movements, pass flatus, and tolerate solid food. Patients randomized to alvimopan also had their discharge orders written an average of 1 day sooner than the placebo group. Importantly, opioid use was the same in both groups. Alvimopan is given as a single oral dose of 12 mg 30 to 90 minutes before surgery and twice daily after surgery for up to 7 days, for a total of 15 doses. It is contraindicated in patients receiving therapeutic doses of opiates for more than [7] consecutive days immediately before surgery. Its use is currently limited to hospitals enrolled in the EASE (Entereg Access Support and Education) program. Common adverse effects include constipation, dyspepsia, flatulence, and urinary retention. In a placebo-controlled 12-month study in patients treated with opiates for chronic pain, there were more reports of myocardial infarction in the alvimopan group [55]. This finding has not been replicated in any other study. The need to give the drug preoperatively obviously necessitates identifying patients most at risk of postoperative ileus.

Future Directions

A multimodal approach to managing postoperative ileus seems likely to be the most effective model in the long run. This should involve using minimally invasive surgery when possible, pharmacotherapy, and accelerated standardized postoperative care. Standardized postoperative care has been implemented for a variety of procedures and generally involves minimal (if any) use of nasogastric tubes, early enteral intake and ambulation, and specific discharge criteria such as passage of flatus or stool, adequate pain control, and tolerance of solid food [56–58]. Compared with a "traditional" (nonstandardized) approach, standardized care has led to shorter hospital stays and lower costs with no impact on rates of morbidity or readmission [59, 60]. (However, one clearly cannot underestimate the role of patient expectations in the success of such postoperative care pathways.) There are plenty of incentives for patients, physicians, health care organizations, and third-party payers to support this push. For patients, it means less time in the hospital and a quicker return to eating normally. Surgeons can expect more-satisfied patients and lower rates of hospital-acquired conditions. For hospitals and insurers, it means less use of resources for some patients, making resources available to those who need them more.

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