

# Postoperative Ileus

by Brian Behmand Neil Stollman

## INTRODUCTION

**P**ostoperative ileus (POI) is a very common problem after many surgical procedures, may lead to significant patient morbidity, and is a common reason for gastroenterological consultation. POI may be generally defined as transient inhibition of normal GI motility in the postoperative setting, typically lasting 3-5 days after surgery. Clinical consequences of POI include worsened postoperative pain, nausea and vomiting, delay in resuming enteral nutrition, and prolonged hospitalization. Other postoperative complications, including deconditioning, malnutrition, and increased risk of nosocomial infections and pulmonary complications, may also be increased. (Table 1) The economic impact of POI is significant, estimated to be \$750 million in the US in 1986 and approaching \$1 billion in 2000 (1).

Despite its pervasiveness, the pathophysiology of POI remains poorly understood, and treatment options are currently limited. Several mechanisms are thought to play a role in POI, including sympathetic neural

reflexes, local and systemic inflammatory mediators, and changes in various neural and hormonal transmitters. Treatment is generally supportive in nature, and clinical trials evaluating different therapies are often limited by small size, retrospective design, and/or endpoints that make comparisons to other trials difficult. This article focuses on our current understanding of the pathophysiology of POI, and will review the clinical presentation, evaluation, and current treatment options in patients with POI.

## PATHOPHYSIOLOGY

Several different mechanisms have been proposed in the pathogenesis of POI. Neural reflexes involving the sympathetic nervous system are thought to inhibit postoperative intestinal motility. Early studies found that intestinal motility could be improved in animals postoperatively by transecting the spinal cord or splanchnic nerves. Subsequent work evaluating the utility of epidural anesthetic agents consistently found decreased duration of postoperative ileus, presumably due to the blockade of neural reflexes at the cord level (2). Local and systemic inflammatory mediators are also thought to play a role in POI (3). Surgical manip-

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Brian Behm M.D. and Neil Stollman M.D., F.A.C.P., F.A.C.G., Division of Gastroenterology, University of California at San Francisco, San Francisco, CA.

**Table 1**  
**Postoperative ileus: potential complications**

- increased postoperative pain
- increased nausea and vomiting
- delay in resuming oral intake
- poor wound healing
- delay in postoperative mobilization
- increased risk of other postoperative complications
  - deconditioning
  - pulmonary complications (pneumonia, pulmonary embolism, atelectasis)
  - other nosocomial infections
- prolonged hospitalization
- decreased patient satisfaction
- increased health care costs

ulation of the bowel produces a local inflammatory response that is associated with smooth muscle dysfunction in small bowel and colonic tissue in animal studies. Nonsteroidal antiinflammatory (NSAID) medications have been found to decrease the duration of POI, thought to be due to their antiinflammatory properties. Various cytokines, including IL-1 and IL-6, are elevated in the postoperative setting and may also play a role in POI. Neural and hormonal factors, including vasoactive intestinal peptide (VIP), substance P, and nitric oxide (NO), also appear to be involved in the pathogenesis POI, but the relative roles of these various mediators remains to be defined.

External factors also influence the duration of POI. The type of surgical procedure can have significant effects on postoperative bowel function. Skin incision has minimal effect on bowel motility, whereas opening the peritoneal cavity completely abolishes coordinated gut motility. Major surgical procedures not involving the abdominal cavity frequently have minimal ileus postoperatively. In addition, intestinal manipulation appears to increase the duration of POI, with the degree of bowel manipulation during surgery being directly proportional to the duration of ileus. Abdominal surgery done laparoscopically may reduce the duration of POI compared to open surgical procedures despite often longer procedure times, presumably due to decreased bowel manipulation with laparoscopy.

Opiates, while frequently necessary for analgesia in the postoperative setting, also delay the return of normal bowel function by binding to peripheral opiate receptors located in the GI tract. Postoperative hypokalemia and infections have also been found to prolong POI (Table 2).

### CLINICAL PRESENTATION

Despite its prevalence, there is no standard nomenclature or grading system for POI. POI may be generally characterized by abdominal distension, lack of bowel sounds, and lack of passage of flatus or stool. Symptoms may include abdominal pain and bloating, nausea, vomiting, and anorexia (Table 3). The pain of POI is typically mild and constant, in contrast to the paroxysmal severe pain associated with mechanical bowel obstruction. POI affects all parts of the gastrointestinal tract to varying degrees. Small intestinal motor function typically returns first, often within several hours of surgery. Gastric motility may return 24–48 hours after surgery. Colonic function is last to return, generally occurring 48–72 hours after surgery. The return of colonic motility is thought to be the frequent rate-limiting step in the resolution of POI.

No single variable has been found to accurately predict the resolution of ileus. Return of bowel sounds may only indicate the return of small bowel motility, and does not appear to be a good marker for resolution of ileus. Passage of flatus also may be an unreliable marker as it may be overlooked or underreported by some patients. The passage of stool is another way to

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**Table 2**  
**Pathophysiology of postoperative ileus:  
proposed mechanisms**

- Spinal and local sympathetic neural reflexes
- Local and systemic inflammatory mediators
- Exacerbating factors:
  - opioid analgesics
  - intraperitoneal surgery
  - degree of bowel manipulation
  - open (vs. laparoscopic) surgical procedures
  - hypokalemia

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**Table 3**  
**Postoperative ileus: signs and symptoms**

Abdominal pain  
Nausea  
Vomiting  
Anorexia  
Abdominal bloating  
Abdominal distension  
Absent bowel sounds  
Lack of passage of flatus or stool  
Tympanic abdomen  
No visible peristalsis

assess the return of bowel function, but does not always correlate well with patients' ability to tolerate a normal diet.

Physical exam should focus on the abdomen. Auscultation of the abdomen will frequently reveal a lack of bowel sounds. There may also be increased abdominal girth, lack of visible peristalsis, and a tympanic abdomen. Abdominal roentgenographs may reveal scattered air-fluid levels or nonspecific patterns of small and large bowel gas. Laboratory tests should include the evaluation of serum electrolytes and evaluation for infection.

## TREATMENT

(Table 4)

### Nonpharmacologic

Nasogastric (NG) intubation has been used for over 50 years as a supportive measure after abdominal surgery. However, recent studies have suggested NG tubes should not be routinely placed after abdominal surgery. In a meta-analysis that evaluated selective versus routine NG intubation, there was no significant difference in the duration of ileus between the two groups, but patients having routine NG tube placement had higher incidences of pulmonary complications including pneumonia, atelectasis, and fever (4). Early postoperative ambulation does not appear to influence the duration of ileus, but does appear to decrease other com-

plications related to prolonged immobilization, and thus should be encouraged. Early enteral feeding also appears safe, and in some studies has led to decreased duration of ileus and earlier hospital discharge.

### Pharmacologic

Numerous studies have evaluated the utility of prokinetic agents in POI with mainly disappointing results. Metoclopramide has failed to improve postoperative bowel motility in several randomized trials. Cisapride showed promise in some prospective trials but has since been withdrawn from the U.S. market due to cardiovascular side effects. Erythromycin has been ineffective in two prospective trials in shortening POI. Domperidone, another prokinetic agent, has not been evaluated in the postoperative setting and is not currently available in the U.S.

Laxatives are another potential agent for the management of POI. One small, nonrandomized study reported a reduction in time to flatus and first bowel movement, as well as decreased length of hospitalization, compared to historical controls (5). However, larger, randomized trials need to be performed before the use of laxatives becomes a routine part of postoperative patient care.

Nonsteroidal antiinflammatory (NSAID) medications may decrease the duration of POI due to their antiinflammatory effects, as well as by decreasing the amount of opiates needed for postoperative pain control. Several animal studies suggest the use of NSAIDs may reduce the duration of POI, but physicians must be wary of potential side effects, including antiplatelet effects, increased risk of gastrointestinal bleeding, and adverse renal effects. Cyclooxygenase (COX)-2 selective inhibitors have been reported to be effective in reducing ileus in a recent small study (6), and may decrease the risk of bleeding associated with the nonselective COX inhibitors.

Epidural anesthetics have been found to be effective in reducing the duration of POI, possibly by inhibiting sympathetic neural reflexes at the cord level and by reducing postoperative narcotic use. The location of the epidural catheter is important, as lumbar epidurals may not effectively block the inhibitory sym-

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**Table 4**  
**Treatment options for postoperative ileus**

*Nonpharmacologic treatment options*

| <i>Treatment</i>        | <i>Potential Mechanism</i>  | <i>Comments</i>  |
|-------------------------|---|--|
| Nasogastric tube        | Gastric/small bowel decompression   | No evidence NG tubes reduce duration of POI. May increase pulmonary post-operative complications |
| Early enteral nutrition | Stimulates GI motility by eliciting reflex response and stimulating release of several hormonal factors | Appears safe, well tolerated. Some, but not all, studies suggest decrease in POI                 |
| Early mobilization      | Possible mechanical stimulation   | No significant change in duration of POI, but may decrease other postop complications            |
| Laparoscopic surgery    | Decreased opiate requirements, decreased pain, less abdominal wall trauma                               | Most studies find decreased duration of POI with laparoscopic compared with open surgery         |

*Pharmacologic treatment options*

| <i>Treatment</i>      | <i>Potential Mechanism</i>  | <i>Comments</i>   |
|-----------------------|---|---|
| Metoclopramide        | Dopamine antagonist, cholinergic agent                                  | Majority of RCTs suggest no benefit   |
| Cisapride             | Dopamine antagonist, cholinergic agonist, serotonin receptor agonist    | Possibly effective; withdrawn from US market due to arrhythmic side effects   |
| Erythromycin          | Motilin agonist   | 2 RCTs suggest no benefit   |
| Laxatives             | Stimulant, prokinetic effects   | No RCTs. One nonrandomized, unblinded study suggests possible benefit   |
| Opiate antagonists    | Block peripheral opiate receptors                                       | One RCT shows ADL8-2698 decreases time to flatus, BM, hospital discharge, but not currently available outside of clinical trials. Other agents have not been evaluated in POI |
| Epidural anesthesia   | Inhibits sympathetic reflex at cord level, opioid-sparing analgesia     | Several RCTs suggest benefit in decreasing POI; most effective when inserted at thoracic level  |
| NSAIDs                | Opiate-sparing analgesia, inhibits COX-mediated prostaglandin synthesis | Probable benefit. COX-2 selective meds need further evaluation  |
| Multimodality therapy | Combination therapy may work via multiple mechanisms                    | Possible benefit in reducing POI. No RCTs have been reported  |

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pathetic reflexes involved in the pathogenesis of POI, whereas thoracic epidurals should.

Opiate antagonists are an intriguing class of agents that have recently been evaluated in the postoperative setting. Opiate antagonists have been found to improve bowel motility in patients with chronic constipation. More recently, the selective peripherally-acting opiate antagonist ADL8-2698 has been found to significantly shorten the duration of POI after major abdominal surgery (7). Other agents, including naloxone and methylnaloxone, have not been evaluated in this setting but may hold promise.

Several authors have advocated the use of multimodality therapy to decrease the duration of POI. This approach combines several different potential therapeutic options, including early mobilization and enteral intake, use of opioid-sparing medications such as NSAIDs and epidural anesthesia, aggressive laxative use, and avoidance of routine NG tube placement (8). While this may represent a logical treatment approach, it requires further study with larger, randomized trials before it is routinely incorporated into postoperative care.

### SUMMARY

Post-operative ileus is a common sequela of abdominal surgery that imparts considerable morbidity and expense to the care of patients, and is a common consultation for the practicing gastroenterologist. Despite its prevalence, the pathophysiology of POI remains incompletely understood, with sympathetic neural reflexes and inflammatory mediators likely playing etiologic roles, with exacerbating factors including degree of bowel manipulation, opioid analgesia and electrolyte abnormalities. While non-pharmacologic treatment options such as NG tubes, enteral alimentation and mobilization have historically been utilized initially, high-quality data supporting their efficacy is

lacking. Likewise, pharmacologic options including laxatives and prokinetic agents also remain without strong data in support of their use. Peripherally acting opioid antagonists and NSAIDs show early promise, but await further trials. ■

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### Other Suggested Reading

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