Hypothesis: A review of the spectrum of illness associated with pneumatosis intestinalis enables us to identify the probable causes of, the best diagnostic approaches to, and the most appropriate treatments for this condition.

Data Sources: A review of all published material in the English language regarding pneumatosis intestinalis was conducted using the PubMed and MEDLINE databases. Any relevant work referenced in those articles and not previously found or published before the limit of the search engine was also retrieved and reviewed.

Study Selection: There were no exclusion criteria for published information relevant to the topic. All of the studies cited in the present review make a point that contributes to the portrayal of this condition. In circumstances in which the same point was made in several different studies, not all were cited herein.

Data Extraction: All published material on pneumatosis intestinalis was considered. Information was extracted for preferentially selected ideas and theories supported in multiple studies.

Data Synthesis: The collected information was organized by theory.

Conclusions: Mucosal integrity, intraluminal pressure, bacterial flora, and intraluminal gas all interact in the formation of pneumatosis intestinalis. Radiography and computed tomography are the best diagnostic tests. Nonoperative management should be pursued in most patients, and underlying illnesses should be treated. When acute complications appear, such as perforation, peritonitis, and necrotic bowel, surgery is indicated.

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Pneumatosis intestinalis (PI), the presence of gas within the wall of the gastrointestinal (GI) tract, is not a diagnosis but a physical or radiographic finding that is the result of an underlying pathologic process. The significance of PI depends on the nature and severity of the underlying condition. Therefore, PI represents a tremendous spectrum of conditions and outcomes, ranging from benign diseases to abdominal sepsis and death.

We review 4 cases from Mayo Clinic to illustrate this complex process and then present a thorough subject review to provide surgeons and gastroenterologists with a comprehensive approach to managing this condition.

CASE REPORTS

CASE 1

A 29-year-old woman with no serious medical or surgical history arrived at the emergency department with emesis and epigastric discomfort. A computed tomographic (CT) scan revealed gastric pneumatosis, portal venous gas in the periphery of the liver, and small bubbles in the right gastroepiploic vein (Figure 1). No pneumoperitoneum, ascites, or bowel wall thickening was seen. The patient was admitted to the hospital for observation. She remained clinically stable. The following day she was discharged, tolerating oral intake and free of symptoms. Seven months later, she has had no recurrence of symptoms.

CASE 2

A 28-year-old man with a 3-year history of ulcerative colitis treated with corticosteroids was admitted to the hospital with an acute exacerbation of his condition. He had diffuse, cramping abdominal pain and frequent blood-tinged liquid stools. Abdominal radiographs on hospital day 3 showed intramural gas in the ascending colon. On hospital day 6, repeated radiographs and CT scans revealed extensive...
pneumatosis coli of the ascending colon and a pneu-
moretroperitoneum extending superiorly into the porta
hepatis at the level of the inferior vena cava and duode-
num (Figure 2). Because the patient was clinically stable,
nonoperative management was continued. During the
next 72 hours, however, his abdominal pain worsened,
and surgery was advised. At celiotomy, pneumatosis was
present in the ascending colon, but no perforation was
identified. Proctocolectomy and ileal J-pouch–to–anal ca-
nal anastomosis plus loop ileostomy were performed. The
patient’s recovery was uneventful, and the ileostomy was
closed 2 months later. Three years later, he remains in
excellent health.

CASE 3

A 70-year-old woman with CREST syndrome (sclero-
derma with subcutaneous calcinosis, Raynaud phenom-
eron, esophageal dysfunction, sclerodactyly, and telan-
giectasia) and chronic intestinal pseudo-obstruction with
bacterial overgrowth arrived at the emergency depart-
ment with mild abdominal pain of several days’ dura-
tion. A CT scan of the abdomen revealed diffuse colonic
pneumatosis with pneumoperitoneum (Figure 3). No
free fluid or inflammatory changes were noted. The pa-
tient was clinically stable without evidence of abdomi-
nal sepsis. She was treated with 3 days of bowel rest and
was discharged without event. Eight months after her
initial presentation, she remains healthy with few GI
symptoms.

CASE 4

A 74-year-old man with corticosteroid-dependent chronic
obstructive pulmonary disease and autoimmune hepa-
titis underwent a 6-vessel coronary artery bypass. His post-
operative course was complicated by a pulmonary air leak
that required pleurodesis, cavitary pneumonia, ulcer-
ated Candida esophagitis, pulmonary embolism, and ex-
acerbation of hepatitis. Worsening sepsis prompted a CT
scan, which revealed extensive colonic pneumatosis, an
air-fluid boundary in the superior mesenteric vein,
copious portal venous gas, and bilateral renal infarcts
(Figure 4). After discussion with his family, support-
ive measures were withdrawn, and the patient died a few
hours later.

Recognition of PI is increasing as a result of the rapid pro-
liferation of cross-sectional imaging. In most cases of PI,
the surgeon evaluates the patient to determine whether op-
erative intervention is warranted. Because the underlying
conditions resulting in PI encompass medical and surgi-
cal diseases (Table),1-139 the surgeon is empowered by an
understanding of this disorder and its management.

PATHOGENESIS

The pathogenesis of PI has been debated for decades, and
multiple explanations have been offered. The breadth of
pathologic conditions associated with PI formation sug-
gests that its development is a multifaceted phenom-
eron. However, the development can be understood by
resolving 2 considerations: where the gas came from and
how it got there. Figure 5 outlines the relationship of
contributing factors leading to PI.

Three possibilities have been proposed as the source
of the gas within the wall of the GI tract: (1) intralumi-
nal GI gas, (2) bacterial production of gas, and (3) pul-
monary gas.

Figure 1. Portal venous gas (arrows) in the liver of case 1.

Figure 2. Cystic pneumatoses coli with pneunomointestinalis (arrow) in case 2.

Figure 3. Diffuse colonic pneumatosis (arrow) with pneumoperitoneum in
the abdomen of case 3.
Intraluminal GI Gas

A mechanical theory describing the intrusion of intraluminal gas into the gut wall was first advocated in 1952 based on the fact that pyloric stenosis was the most common cause of PI in early studies.9 This theory was supported by studies documenting that the partial pressure of hydrogen and methane in intramural cysts is comparable to intraluminal gas. In these cases, the origin of intramural gas is clear; however, the mechanism by which it enters the gut wall could be the result of intraluminal pressure, mucosal injury, or a combination of both.

Intraluminal Pressure. Pneumatosis intestinalis can occur because of increased intraluminal pressure in the setting of a normal mucosal barrier, as occurs with blunt trauma.1-19 Case 1 is an example of increased intragastric pressure due to vomiting resulting in PI formation despite the absence of underlying GI disease. Many patients with trauma have been subjected to high intraluminal pressures; however, most conditions associated with PI possess at least some degree of mucosal injury as well.

Mucosal Injury. Enhanced gut permeability to gas can be induced by defects in the mucosa, the gut's immune barrier (intramural lymphoid tissue), or both. A review of 17 consecutive patients with PI found mucosal and histologic abnormalities in all cases.12 Attenuation of these barriers may account for PI in circumstances of normal intraluminal pressure, as seen in patients with PI due to congenital immunodeficiency, acquired immunodeficiency syndrome, chronic obstructive pulmonary disease, and necrotizing enterocolitis.
ciency, immunosuppressive therapy, and cytotoxic therapy. When the mucosal or immune barriers of the GI tract are compromised, bacterial intrusion or gas diffusion into the wall becomes more likely. Case 2 illustrates an example of PI predominantly due to a compromise of mucosal and immune barriers from inflammatory bowel disease and immunosuppression.

**Combination of Factors.** Dissection of gas from intraluminal to intramural compartments can result from increased intra-abdominal pressure combined with a defect in the mucosal barrier. Lower intraluminal pressures can lead to PI formation in the presence of more severe mucosal injury and vice versa. Pneumatosis intestinalis due to high intraluminal pressure with less mucosal injury can occur with endoscopy, obstruction, or pseudo-obstruction. This scenario has been documented experimentally by inflating an excised cecum with small mucosal incisions.\(^{62}\) Case 3 exemplifies this combined mechanism. The patient probably had chronically increased intraluminal pressure due to pseudo-obstruction and an abnormal GI mucosal barrier due to a connective tissue disorder.

**Bacterial Gas Production**

Bacterial production of gas has been suggested by several researchers\(^ {71,100,103}\) to be a factor in PI formation. This theory is supported by reports of disappearance of the gas with antimicrobial drug treatment.\(^ 8\)

Two mechanisms enable bacteria to form intramural gas: direct invasion of the wall by bacteria and alteration of the intraluminal gas content by bacteria.

**Bacterial Invasion.** Gas-producing bacteria can reach intramural compartments through the same avenue discussed previously for gas intrusion: mucosal or immune compromise. Intramural injection of *Clostridium difficile* has been shown to initiate PI formation in germ-free rats.\(^ {62}\) However, a lack of evidence is present in humans documenting intramural bacteria or bacteria within the pneumocysts.\(^ {103}\)

**Intraluminal Gas Content.** Direct gas diffusion across the mucosa because of a gradient between intraluminal and serum partial pressures is an intriguing theory of causality.\(^ {80,104}\) Patients with PI have been shown to have abnormally high levels of hydrogen in their pneumocysts.\(^ {87,105,106}\) This led to the theory of “counterperfusion supersaturation,” whereby colonic bacteria produce hydrogen tensions that exceed nitrogen tension in blood, leading to a hydrogen diffusion gradient toward the submucosal vessels.\(^ {104}\) This may explain the pattern of pneumatosis near blood vessels, predominantly along the mesenteric border in some cases.\(^ {62}\) This theory has been supported experimentally in rats and in some patients with primary PI due to the ingestion of alkyl halides (chloral hydrate and trichloroethylene).\(^ {80}\) Ingestion of alkyl halides as inciting agents for PI has been supported by case reports and epidemiologic studies.\(^ {78-81}\)

Metabolism of oxygen decreases gas tension in tissues.\(^ {107}\) Oxygen therapy has been used successfully to treat PI.\(^ {12,13,33,43,44,63}\) The benefit of such treatment may be its effect on anaerobic bacteria\(^ {103}\) or simply its dilution of intraluminal and intravascular gas profiles with oxygen to facilitate diffusion of gases out of the pneumocysts. The author of the counterperfusion supersaturation theory postulated that normal oxygen delivery may serve as a safety factor that prevents intramural gas bubble formation. Therefore, poor oxygen delivery provides an explanation for PI development in patients with vascular or pulmonary disease. In addition, low oxygen tensions may compromise mechanical and immune mucosal barriers.

Case 4 represents an interaction of all the aforementioned mechanisms and demonstrates the fulminating extreme in the spectrum of pneumatosis.

**Pulmonary Gas**

Pulmonary gas as the source of PI formation was originally put forward with the theory that alveolar rupture could result in dissection of air along vascular channels in the mediastinum, tracking caudally to the retroperitoneum and then to the mesentery of the bowel.\(^ {62}\) This theory was supported by observations of subserosal GI gas in patients with PI and pulmonary disease. The subserosal deposition of gas in this setting is more likely due to migration of gas along the vessels rather than to a transmural infiltration. However, lack of interstitial emphysema within the lung or in the mesentery in many of these patients has led to skepticism of a pulmonary source by some authors.\(^ {13,63-65,100}\) It has been proposed\(^ {12}\) that the association between pulmonary disease and PI may simply be due to fluctuations in intra-abdominal pressure caused by pulmonary obstruction. Patients with chronic cough have increased intra-abdominal pressure, which, along with attenuation of the luminal barriers due to corticosteroid therapy, could lead to PI. Furthermore, blood oxygen tension in these patients is relatively low, which may facilitate intercompartmental gas transfer.

**DIAGNOSIS**

The clinical manifestations of PI are typically not the consequence of the intramural gas but of the underlying pathologic conditions, as exemplified by our 4 cases. The most common symptoms attributed to PI have been diarrhea, bloody stools, abdominal pain, constipation, weight loss, and tenesmus, in decreasing order.\(^ {105}\) Physical examination is rarely helpful in diagnosis but occasionally reveals abdominal or rectal masses.\(^ {109}\) However, it has been shown that the pattern or extent of PI does not correlate with the severity of the symptoms or the severity of the underlying diseases.\(^ {33,110}\)

**Radiography and Ultrasonography**

On plain radiography, PI is characterized by radiolucency within the wall of the GI tract. Imaging patterns of PI have been described as diffuse, microvesicular, or cystic.\(^ {111}\) The patterns of the radiolucencies are seen as linear, curvilin-
ear, small bubbles, or collections of larger cysts. Abdominal radiographic findings are detected in approximately two thirds of the patients with PI. Barium enema can be helpful in diagnosing PI. Circumscribed attenuations in the contrast column or linear delineations along the margins can be seen. In one series, diagnosis of PI was confirmed in 21 of 22 patients by barium enema. However, several authors have warned that PI can be confused with intestinal polyposis on barium enema.

Multiple studies describe the utility of ultrasonography in the diagnosis of PI and portal venous air. Bright echoes in the bowel wall identify PI by ultrasonography. Computed tomography can distinguish PI from intraluminal air or submucosal fat. Furthermore, it can provide the surgeon with an excellent survey of the abdominal cavity for diagnosis of associated pathologic conditions. In patients with subtle examples of PI that may be difficult to diagnose, “target” air-enema CT has been advocated.

Computed Tomography

Computed tomography is the best imaging modality for establishing the diagnosis of PI, as denoted by findings such as intramural gas parallel to the bowel wall. It has greater sensitivity in diagnosing PI than plain films or ultrasonography. Computed tomography can distinguish PI from intraluminal air or submucosal fat. Furthermore, it can provide the surgeon with an excellent survey of the abdominal cavity for diagnosis of associated pathologic conditions. In patients with subtle examples of PI that may be difficult to diagnose, “target” air-enema CT has been advocated.

Endoscopy

Macroscopic elevations of the mucosa make PI difficult to distinguish from other lesions evaluated by endoscopy. Puncture and complete deflation have been advocated to confirm the diagnosis. However, a high degree of suspicion should be present before undertaking any intervention. Attempts to remove a “polyp” that in fact was a pneumocyst have caused perforation of the bowel.

Histologic Examination

Some authors suggest that the gas cysts present in PI form inside lymphatic channels. Other researchers, however, propose that the gas collects in pockets independent of intramural structures such as lymphatics. Multinucleated giant cells, macrophages, and pericystic inflammatory changes are the most common histologic findings.

TREATMENT

The focus of treatment is almost entirely on the associated illness inciting PI. In PI associated with conditions in which surgical treatment has no role and no other definitive treatment exists, excellent results have been reported with use of inspired oxygen as a treatment. Original studies suggested maintaining arterial oxygen partial pressure higher than 300 mm Hg by using 70% to 75% oxygen at a flow of 8 L/min given by face mask, head tent, hyperbaric means, or mechanical ventilation. However, administration of lower concentrations has also been effective. Pneumatosis intestinalis recurring after oxygen therapy has been treated successfully by reinitiating oxygen therapy.

We wonder whether giving oxygen into the lumen of the GI tract via a nasointestinal tube might be a better way of administering oxygen to treat PI. Intraluminal oxygen should encourage diffusion of oxygen from the lumen into the pneumocysts while favoring diffusion of non-oxygen gases from the pneumocysts into the lumen. The intracystic oxygen might then be taken up by hemoglobin in nearby blood vessels, thus decreasing or resolving the pneumocysts. However, we found no studies in the literature evaluating this approach.

The difficult task of determining the need for operative intervention is compounded by the presence of pneumoperitoneum or portal venous gas. These findings have traditionally been associated with perforation or ischemic bowel, often leading surgeons to operate, even on stable patients, with the hope of diverting a pending crisis. However, as 3 of our cases illustrate, the presence of pneumoperitoneum, portal venous gas, or both does not necessarily represent an abdominal crisis requiring operative intervention. Similarly, the literature contains multiple studies of PI with pneumoperitoneum in which celiotomy was unnecessary.

Rupture of intramural blebs is the hypothesized source of benign pneumoperitoneum in patients with PI, causing free air without true transmural perforation. In support of this theory, lack of communication between the pneumocysts and the lumen of the GI tract has been documented.

Gas in the hepatic portal venous system is recognized radiographically as tubular lucency usually within 2 cm of the liver capsule. This finding is more frequently associated with pending clinical collapse because it often occurs with ischemic bowel. Prospective evaluation of patients with PI found 37% mortality in those with portal venous gas. In a more recently published series of patients with PI and portal venous gas on CT, clinical outcome depended on the severity of the underlying disease and the clinical variables as opposed to radiographic findings. Therefore, surgeons should recognize the higher likelihood of a poor outcome when portal venous gas is detected, simultaneously recognizing the possibility of a benign disease from which the patient can recover with nonoperative management.

CONCLUSIONS

Pneumatosis intestinalis is a secondary finding caused by an underlying disease. Mucosal integrity, intraluminal pressure, bacterial flora, and intraluminal gas have an interactive role in the formation of the pneumocysts. Pneumatosis intestinalis is currently best diagnosed by plain abdominal radiography or ultrasonography and specifically delineated by CT scan. The challenge facing surgeons asked to evaluate patients with PI is to identify those who require surgery. Considering the wide range of possible causes and outcomes of this entity, the surgeon most often should pursue nonoperative management initially while searching for an irrefutable indication to operate.
Surgery should be performed in patients who are not responding to nonoperative management, especially those with signs of perforation, peritonitis, or abdominal sepsis.

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Corresponding author and reprints: Keith A. Kelly, MD, Department of Surgery, Mayo Clinic, 13400 E Shea Blvd, Scottsdale, AZ 85239 (e-mail: kelly.keith@mayo.edu).

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Axiom: On cutting through the abdominal wall, the encountering of a layer of loose areolar tissue is a signal that a change in the direction of muscle fibers is imminent. When you incise the abdominal wall, the direction of muscle fibers, the presence of areolar tissue, and the presence of nerves and of branches of the deep circumflex iliac artery all indicate the depth at which you have arrived.