Systemic Causes of Abdominal Pain

J. Matthew Fields, MDa, *, Anthony J. Dean, MDb

A variety of systemic and extra-abdominal diseases can cause symptoms within the abdominal cavity (Box 1). This article discusses the most important and common of these diseases. Systemic and extra-abdominal diseases may include abdominal symptoms caused by several mechanisms listed in Table 1. Mechanisms include direct pathologic effects on intra-abdominal organs (e.g., gallstone formation in sickle cell disease); conversely, systemic illnesses (e.g., congestive heart failure, diabetic ketoacidosis [DKA], or addisonian crisis) may themselves be precipitated by diseases in the abdomen. Some systemic illnesses have a direct (e.g., constipation in hypercalcemia) or indirect (e.g., nausea and vomiting in diabetic or alcoholic ketoacidosis [AKA]) effect on the functioning of the gastrointestinal (GI) tract. Abdominal symptoms may be caused by disease in contiguous organs outside the abdomen (e.g., diaphragmatic irritation from disease of adjacent structures in the lung and mediastinum).1–4 Finally, symptoms may be referred to the abdomen from extra-abdominal organs via neural pathways (e.g., nausea and vomiting in acute coronary syndrome, glaucoma, ureterolithiasis, or testicular torsion).5–8 Many diseases cause abdominal symptoms by a combination of these mechanisms. For example, hypercalcemia can cause abdominal symptoms as a result of intestinal dysfunction, ureterolithiasis, pancreatitis, and/or neuropathy. The range of mechanisms gives rise to a similarly wide variety of clinical findings. For example, the painful crisis of sickle cell disease or a widow spider envenomation may cause a rigid abdomen; conversely, the abdominal symptoms of a life-threatening splenic sequestration crisis may be minimal. Careful attention to the patient’s history and due consideration of apparently unrelated complaints or findings on the physical examination may guide an astute clinician to consider and perform the appropriate evaluation for an underlying systemic disease.
### Box 1
**Extra-abdominal and systemic causes of abdominal pain**

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<th>Thoracic</th>
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<td>Acute coronary syndrome</td>
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<td>Pneumonia</td>
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<td>Pulmonary embolism</td>
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<td>Congestive heart failure</td>
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<td>Pericarditis/myocarditis</td>
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<th>Metabolic/endocrine</th>
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<td>Metabolic acid syndromes (diabetic ketoacidosis, alcoholic ketoacidosis)</td>
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<td>Uremia</td>
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<td>Thyrotoxicosis</td>
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<td>Adrenal insufficiency</td>
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<td>Porphyria</td>
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<td>C1 inhibitor deficiency</td>
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<td>Hypocalcemia/hypercalcemia</td>
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<td>Pheochromocytoma</td>
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<th>Hematologic</th>
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<td>Sickle cell disease</td>
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<td>Ileocecal syndrome</td>
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<td>Acute leukemia</td>
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<td>Lymphoma</td>
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<th>Inflammatory</th>
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<td>Familial Mediterranean fever</td>
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<td>Eosinophilic gastroenteritis</td>
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<td>Polyarteritis nodosa</td>
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<td>Henoch-Schönlein purpura</td>
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<td>Systemic lupus erythematosus</td>
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<td>Food allergy</td>
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<td>Chronic angioedema</td>
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<th>Infectious</th>
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<td>Tuberculosis</td>
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<td>Epididymitis</td>
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<td>Prostatitis</td>
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<td>Lyme disease</td>
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<td>Pneumonia</td>
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<td>Streptococcal pharyngitis</td>
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<td>Pediatric infections</td>
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<th>Toxin/environmental</th>
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<td>Heavy metals</td>
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Abdominal pain is present in nearly half of patients with DKA and its intensity is associated with worsening metabolic acidosis. The mechanism of abdominal pain in DKA is poorly understood, however gastritis, gastric distension and ileus secondary to metabolic derangement have been suggested. While abdominal pain in DKA is most often non-specific in up to 30% of cases pain is actually secondary to the stressor that precipitated the DKA state. Fluid resuscitation and insulin are the mainstays of therapy of DKA, however abdominal pain that persists despite correction of acidosis warrants further investigation. While abdominal manifestations are common in DKA they are not commonly seen in hyperosmolar hyperglycemic syndromes.

Alcoholic ketoacidosis also commonly presents with abdominal pain and similarly to DKA gastrointestinal symptoms may be multifactorial in etiology. There is a direct gastritis effect by alcohol and a secondary effect induced by ketoacidosis on gastric functioning leading to nausea, vomiting, and abdominal pain.

**Adrenal Insufficiency**

Adrenal insufficiency occurs when adrenal gland function is reduced by lack of adrenocorticotropic hormone (ACTH), chronic steroid use, or primary adrenal disease and, as a result, glucocorticoid production is unable to meet physiologic demands. Adrenal (addisonian) crisis generally occurs in patients with underlying adrenal insufficiency in the setting of a physiologic stressor or medical noncompliance; however, it may also occur in normal patients in the settings of blunt trauma, sepsis, meningococcemia, emboli, and other critical illnesses. Symptoms can be acute or insidious at onset but may include weakness, fatigue, prostration, confusion, vomiting, diarrhea, fever,
Table 1
Mechanisms of abdominal symptoms in extra-abdominal and systemic diseases (some diseases cause abdominal symptoms by several mechanisms)

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Systemic disease causes pathologic condition in intra-abdominal organs</td>
<td>Heavy metal toxicity, tuberculosis, CHF, spider envenomation, alcoholic ketoacidosis, sickle cell infarction and biliary disease, neutropenia, hypercalcemia (pancreatitis, ileus, gastritis), C1 inhibitor deficiency, SLE (lupus enteritis)</td>
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<tr>
<td>Systemic disease is precipitated by pathologic condition in intra-abdominal organs</td>
<td>Abdominal disease precipitating DKA, addisonian crisis</td>
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<tr>
<td>Systemic disease causes nausea, vomiting, or other gastrointestinal symptoms</td>
<td>Hypercalcemia and hypocalcemia, sickle cell painful crisis, SLE</td>
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<tr>
<td>Extra-abdominal disease causes abdominal symptoms by neural mechanisms or with functional or poorly understood organic basis</td>
<td>DKA, glaucoma, thyrotoxicosis, porphyria, hypercalcemia (neuropathy, hypomotility), hypocalcemia, adrenal crisis, gonadal torsion, pheochromocytoma</td>
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<td>Disease of extra-abdominal organs causes perception of pain in the abdomen because of irritation of contiguous extra-abdominal structures</td>
<td>Lower lobe pneumonia, pulmonary emboli, pleuritis, inferior wall cardiac ischemia, pyelonephritis, spinal and other musculoskeletal diseases, testicular torsion</td>
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<tr>
<td>Abdominal pain due to referred pain from extra-abdominal structures</td>
<td>ACS and other diseases of mediastinal structures, ureterolithiasis, pyelonephritis</td>
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</table>

*Abbreviations: ACS, acute coronary syndrome; CHF, congestive heart failure; DKA, diabetic ketoacidosis; SLE, systemic lupus erethematosus.*

hypotension, tachycardia, shock, and abdominal pain. Any of these symptoms in a patient who has been taking steroids for more than a week should prompt consideration of addisonian crisis. The abdominal pain may be severe, causing suspicion of an intra-abdominal catastrophe. The basis of the abdominal pain is unknown, although there is evidence to suggest that gastric dysmotility and serositis occur. Hypoglycemia (with concomitant mineralocorticoid deficiency), hyponatremia, and hyperkalemia may occur in acute crisis but are more common in chronic deficiency. Recommended treatment is intravenous dexamethasone. Hydrocortisone may also be used but has the drawback of interfering with ACTH stimulation testing.

**Thyrotoxicosis**

Although abdominal complaints receive scant attention in most texts, they are fairly common in thyrotoxicosis and include nausea, vomiting, loose frequent stools, and weight loss. Perhaps they are overlooked because of the protean and more life-threatening derangements of this disease. In 1 retrospective series, GI symptoms occurred in 36% of cases. Although most patients with abdominal pain and thyrotoxicosis have no demonstrable intra-abdominal pathologic condition, in 1 case series, 16% had an intra-abdominal cause requiring surgery, serving as a reminder that the search for serious medical conditions that have precipitated thyroid storm should not be overlooked.

**Porphyria**

Acute intermittent porphyria is a rare autosomal dominant condition that presents most commonly with abdominal pain. With variations in penetrance and
expressivity, the gene is symptomatic in 1 to 2 persons per 100,000.24 The mutation leads to a deficiency of porphobilinogen deaminase, a hepatic enzyme involved in heme synthesis. δ-Aminolevulinic acid and porphobilinogen accumulate in tissues, leading to a neurovisceral crisis that results in acute abdominal pain. Attacks can be precipitated by stimulation of the cytochrome P450 system with medications (eg, rifampin, barbiturates, and sulfonamides), estrogens or progesterones, smoking, or alcohol. Attacks may also occur when heme oxygenase is induced by physiologic stressors such as fever, fasting, or infection.23,24 Pain is thought to be caused by visceral autonomic neuropathy leading to regions of overactive and underactive bowel. Pain may be persistent or colicky and is usually located in the lower part of the abdomen but may also occur in the back or lower limbs.25 Other symptoms include fever, vomiting, constipation, weakness, muscle cramps, paresthesias, seizures, and neuropsychiatric complaints, including anxiety and depression. Dysautonomias can cause extra-abdominal symptoms with diaphoresis, flushing, tachycardia, and hypertension or hypotension. Seizures are generally because of hyponatremia, which may be secondary to vomiting or to the syndrome of inappropriate antidiuretic hormone hypersecretion. Neuropathy may be rapid and severe, leading to life-threatening respiratory involvement. The abdomen is usually soft, with only mild tenderness. Diagnosis is made by detecting elevated urinary porphobilinogen levels. Short-term management involves pain control, resuscitation, and evaluation for potentially life-threatening complications such as respiratory compromise from phrenic neuropathy or hyponatremia.26

**C1 Inhibitor Deficiency**

C1 inhibitor (C1INH) deficiency may be hereditary or acquired and results in angioedema involving the skin, GI tract, or upper airway. Excess active C1 leads to excessive complement activation and overproduction of bradykinin, resulting in submucosal and subcutaneous vascular permeability.27 Approximately 25% of patients with C1INH deficiency have predominantly abdominal symptoms.28 Submucosal edema in the stomach and small bowel leads to episodes of nausea, vomiting, and cramping abdominal pain. Abdominal examination may reveal marked tenderness, guarding, or rigidity, leading to the consideration of intra-abdominal surgical emergencies. Acute attacks may occur without any apparent cause but are more often precipitated by minor trauma (especially dental procedures), menstruation, stress, or use of angiotensin-converting enzyme inhibitors. The diagnosis may be suggested by a history of chronic abdominal complaints with episodic exacerbation. Abdominal symptoms generally precede cutaneous or upper airway symptoms.29,30 Laryngeal edema, when present, is life threatening. Until recently, management involved airway control and standard supportive care.31 In October 2009, C1 esterase inhibitor replacement protein was approved by the Food and Drug Administration. Early trials have shown significant improvement of symptoms in acute attacks.32

**Hypercalcemia**

Hypercalcemia is most commonly caused by hyperparathyroidism and malignancy.33 Elevated calcium levels affect nerve conduction, cardiac rhythm, function of cardiac and skeletal muscles, renal function, and GI motility. Patients may present with isolated abdominal pain that may be multifactorial in etiology.34 Ileus formation leads to abdominal pain, nausea, and vomiting. Elevated levels of gastrin and lower stomach pH predispose patients to gastritis and peptic ulcer formation. Increased secretion of pancreatic enzymes may lead to acute pancreatitis. In the kidneys, in addition to tubular dysfunction that results in fluid and electrolyte losses, calcium deposition
may lead to kidney stone formation and ureterolithiasis. The diagnosis should be considered in patients with diffuse abdominal pain accompanied by weakness, lethargy, and dehydration.

HEMATOLOGIC CAUSES OF ABDOMINAL SYMPTOMS

Sickle Cell Disease

Sickle cell disease is an autosomal recessive hemoglobinopathy characterized by production of hemoglobin S, which causes erythrocyte sickling, leading to chronic hemolytic anemia and recurrent vascular occlusion. Vascular occlusion can cause ischemia or infarction in almost any organ. In the abdomen, this may cause pain by a variety of mechanisms including local ischemia, microinfarction, macroinfarction (eg, of the spleen), cholelithiasis, cholecystitis, pancreatitis, splenic sequestration, hepatic crisis, and intrahepatic cholestasis. Even in the absence of a surgical cause, ischemia and microinfarction can result in an examination that strongly suggests an acute surgical abdomen with peritoneal signs and leukocytosis. The clinician is guided by the patient’s description of previous episodes of painful crisis, but in uncertain cases, the increasing availability of bedside ultrasonography and abdominal computed tomography (CT) have made appropriate diagnosis of these patients’ condition easier. Crises can be triggered by many factors including infection, dehydration, cold, stress, menses, alcohol consumption, and hypoxemia; however, most of the time, there is no identifiable cause.

Neutropenia

Abdominal pain in patients with neutropenia may be caused by a spectrum of disorders of the ileocecal region that ranges in severity from mild mucosal inflammation to bacterial and fungal invasion of the bowel, leading to transmural ulceration and/or necrotizing colitis with high mortality rates. The disorder has been variously named neutropenic enterocolitis (NE), typhilitis, and ileocecal syndrome. It is usually seen in patients receiving chemotherapy but occasionally occurs in patients with aplastic anemia, cyclic neutropenia, and AIDS. Presentation is most likely 10 to 14 days after chemotherapy, coincident with the neutrophil nadir. The ileum, cecum, ascending colon, and appendix are the most common sites; however, any portion of the bowel may be affected. Abdominal symptoms in these patients may be masked due to immunosuppression, which inhibits elaboration of the inflammatory mediators that are the primary stimulators of intra-abdominal nociceptors; although focal right lower quadrant pain, abdominal distension, diarrhea, or rebound tenderness may be present. Neutropenia with fever, abdominal pain, and diarrhea should prompt suspicion. *Clostridium difficile* enterocolitis, appendicitis, and diverticulitis are also diagnostic considerations in these patients. CT scan is the preferred diagnostic modality and reveals bowel wall thickening often involving the terminal ileum. *C difficile* colitis is not usually limited to the cecum and rarely involves the ileum in contrast to NE. Ultrasoundography has been shown to be useful in the diagnosis and management of critically ill patients in whom CT cannot be obtained. Ultrasoundography reveals the affected bowel as a mass with a hyperechoic core and thick hypoechoic walls. In the setting of the abovementioned symptoms, a bowel wall thickness of 4 mm is considered diagnostic and increasing thickness correlates with disease severity. Historically, surgery (right hemicolectomy) was the mainstay of treatment. More recent case series support medical management, including therapy with broad spectrum and antifungal antibiotics, and supportive care. Surgery may still be necessary in some patients, and early consultation is often warranted.
INFLAMMATORY CAUSES OF ABDOMINAL SYMPTOMS

Familial Mediterranean Fever

Familial Mediterranean fever (FMF) is an autosomal recessive disorder characterized by recurrent episodes of fever and serositis resulting in abdominal, chest, joint, or muscular pain. This condition is primarily diagnosed in people of Sephardic Jewish, Arabic, Turkish, Armenian, Egyptian, and Lebanese descents. Because of the involvement of the extensive peritoneal serosa, abdominal pain in FMF causes peritonitis and findings of an acute abdomen. About 95% of patients report abdominal pain as the main symptom of their attacks, and 50% report abdominal pain as their first symptom of disease.41 Onset is sudden, occurring over 1 to 2 hours, with fever and abdominal pain that may be diffuse or localized. The pain is often worse with movement, and examination reveals distension, rigidity, rebound, and guarding.42 Laboratory abnormalities include a leukocytosis with left shift and elevated sedimentation rate and C-reactive protein levels. Abdominal radiography may show dilated loops of small bowel and air fluid levels. The most common findings on CT of patients with acute FMF are engorged mesenteric vessels and thickened mesenteric folds. A minority of patients may demonstrate mesenteric and/or retroperitoneal lymphadenopathy, ascites, splenomegaly, and dilated small bowel loops.43 Less-severe (incomplete) attacks may occur without fever or peritonitis. Symptoms begin to improve within 12 to 24 hours, and complete resolution generally occurs at 96 hours. Colchicine prophylaxis to prevent attacks is the mainstay of therapy; however, it is not effective in an acute attack. Diclofenac has been shown to be effective in addition to standard pain medication regimens.41 Colchicine has a low therapeutic index, so that in patients on this drug presenting with abdominal pain and diarrhea, the clinician should consider the possibility of colchicine toxicity.

Eosinophilic Gastroenteritis

Eosinophilic gastroenteritis (EG) is a disorder characterized by eosinophilic infiltration of any portion of the GI tract from the esophagus to rectum. The syndrome often presents with abdominal pain. A history of atopy and allergies is present in about 50% of cases. Mucosal EG is the most common subtype and may present with abdominal pain, vomiting, diarrhea, GI bleeding, anemia, or a protein-losing enteropathy.44,45 Rarely, EG presents with signs of peritoneal inflammation.46 Eosinophilia may be present but is not necessary for diagnosis. Management includes allergy testing, changes in diet, steroids, mast cell inhibitors, antihistamines, and leukotriene antagonists.45

Polyarteritis Nodosa

Polyarteritis nodosa (PAN) is a rare form of systemic vasculitis affecting small- and medium-sized arteries. PAN occurs most commonly in patients aged 40 to 60 years, and 30% to 60% of the cases are associated with hepatitis B, hepatitis C, or human immunodeficiency virus infection.47,48 Most patients present with subacute symptoms over weeks to months, most commonly with fever, neuropathy, hypertension, weight loss, malaise, and asymmetric arthritis.49 Approximately half of the patients present with GI symptoms including nausea, vomiting, abdominal pain, and diarrhea. Vasculitis may cause infarction of the GI tract leading to GI bleeding or perforation. Vasculitic cholecystitis, appendicitis, pancreatitis, or even rupture of splenic, hepatic, or renal arteries may occur in severe cases.50

Henoch-Schönlein Purpura

Henoch-Schönlein purpura (HSP) is a small-vessel vasculitis caused by deposition of IgA, affecting skin, joints, kidney, and bowel. It is most common in the pediatric age
group but may occur in adults. Findings in HSP include palpable purpura, arthralgias, glomerulonephritis, hematuria, and GI symptoms of colicky abdominal pain, nausea, and vomiting. In 1 study, 17% of patients presented with abdominal pain as their only symptom. The most frequent GI complication of HSP is intussusception occurring in approximately 3% to 4% of cases. Other more rare GI complications include bowel ischemia and infarction, fistula formation, ileal stricture, gallbladder hydrops, pancreatitis, and pseudomembranous colitis. Treatment is supportive with detection and treatment of potential complications. Retrospective studies suggest that steroids may decrease the duration of symptoms and complications; however, this has not been demonstrated prospectively.

**Systemic Lupus Erythematosus**

Systemic lupus erythematosus (SLE) is an autoimmune disorder that in 90% of cases affects women. The disorder can cause nonspecific symptoms of nausea, vomiting and diarrhea, pancreatitis and hepatitis, as well as disease in every part of the GI tract from the mouth to anus. Despite the known pathologic effects, there is no agreement about the prevalence of GI disease in SLE because it is often impossible to determine whether GI pathology is a side effect of medications or the result of intercurrent diseases such as renal failure. Reports of the incidence of GI disease in SLE range widely from 1% to 50%. The commonest site of involvement is the oral cavity, where it causes ulcerations, decreased salivation, and a variety of other mucosal lesions. In 1 retrospective review of patients admitted for SLE, 22% presented with abdominal pain, half of who were found to have intestinal vasculitis (referred to as lupus enteritis). In most cases, this condition responds well to supportive care and immunosuppressive therapy, although occasionally, it can progress to infarction. The presence of antiphospholipid antibody increases the risk of thrombosis. In a series of patients with SLE with an acute abdomen, nonvascular causes (mainly cholecystitis, appendicitis, and abscesses) were as frequent as vascular causes. Nearly all patients in this study required surgery either because of a nonvascular source or because of ischemic complications of vasculitis. Medical treatment of lupus flares includes high-dose steroids, increasing the risk of intestinal perforation in the setting of vasculitic ischemia. Abdominal pain in patients with SLE should be approached cautiously with a low threshold to perform abdominal imaging and to obtain surgical consultation.

**Food Allergy**

Symptoms of food-induced allergy most frequently involve the skin, GI tract, and respiratory system. Urticaria, flushing, angioedema, vomiting, abdominal pain, diarrhea, rhinitis, wheezing, and stridor may be present together or in isolation. Symptoms usually occur soon after ingestion so that identification of the offending allergen is apparent whether or not symptoms are primarily gastrointestinal. Many patients have a history of atopy. Treatments include administration of antihistamines, epinephrine, inhaled β-agonists, and systemic corticosteroids. Referral to an allergist is warranted with avoidance of suspected agents until allergy testing has been undertaken.

**INFECTIOUS CAUSES OF ABDOMINAL SYMPTOMS**

**Tuberculosis**

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, persists as an important diagnostic consideration even in well-developed countries. Extrapulmonary TB may involve the peritoneum in up to 4% of cases, and clinical presentation can vary from insidious onset with fever, weight loss, anorexia, night sweats, and malaise to acute focal abdominal pain. Miliary TB less commonly presents with abdominal pain;
however, peritoneal, hepatic, pancreatic, or splenic seeding does occur and may be a focus of pain.\textsuperscript{62,63}

**Pediatric Infections**

Abdominal pain is a frequent manifestation in common pediatric extra-abdominal infections. In a study of more than 1100 children presenting with acute abdominal pain, 59% were diagnosed with extra-abdominal problems including upper respiratory tract infection and/or otitis (18.6%), pharyngitis (16.6%), viral syndrome (16.0%), and acute febrile illness (7.8%). Less than 1% of the group had surgical disease.\textsuperscript{64} In regard to pharyngitis, abdominal pain is seen similarly in both streptococcal and non-streptococcal disease.\textsuperscript{65}

**TOXIN-RELATED OR DRUG-RELATED CAUSES OF ABDOMINAL SYMPTOMS**

Toxins and environmental exposures can lead to abdominal pain by a variety of mechanisms including direct corrosive effects (aspirin, iron, mercury, acids, and alkalis), ileus formation (anticholinergics, narcotics), mechanical obstruction (bezoars), systemic effect (black widow spider bite, opioid withdrawal), bowel ischemia secondary to vasoconstriction (amphetamines, ergotamines, cocaine), or damage to intra-abdominal organs (acetaminophen).

**Heavy Metals**

Acute exposure to heavy metals such as iron, lead, arsenic, cadmium, and thallium may cause abdominal pain and GI symptoms. Anemia may be a clue to chronic heavy metal exposure but is nonspecific. Although abdominal symptoms may be present in chronic toxicity, other systems are more commonly involved. Iron toxicity occurs mainly because of unintentional ingestion in the pediatric population.\textsuperscript{60–63,66} Toxicity occurs in 5 phases. Phase 1 begins with acute vomiting due to corrosive effects followed by diarrhea that may be bloody. In phase 2, the acute symptoms resolve after 1 to 2 days. This resolution is followed by phase 3 in which GI symptoms recur with lethargy, anion gap metabolic acidosis, leukocytosis, coagulopathy, renal failure, and arrhythmias. In severe cases, disease may progress to cardiovascular collapse and death. Phase 4, consisting of fulminant hepatic failure, is relatively rare, but when it occurs, it is usually fatal. Phase 5 describes the chronic pyloric or small bowel scarring that may lead to future mechanical obstructions.\textsuperscript{67} Emergency management includes supportive care. Deferoxamine should be used in patients with a history or clinical signs of significant exposure.

Lead poisoning is decreasing in incidence because of restrictions on the use of lead in paints and gasoline as well as closer surveillance in work environments.\textsuperscript{68} Still, sources of lead exposure persist and include bullets, fishing weights, and contaminated soil or water. Occupational risk is present in industries such as lead smelting, battery manufacturing, radiator repairing, bridge or ship construction or demolition, soldering, or welding.\textsuperscript{69,70} Acute lead exposure can lead to crampy abdominal pain, nausea, vomiting, constipation, or diarrhea and has been termed lead colic. Other symptoms include headaches, fatigue, anemia, and peripheral neuropathy. In severe cases, there can be end-organ dysfunction, including renal and hepatic failure, convulsions, and coma.

Arsenic may induce varying degrees of systemic toxicity. Exposures occur at home, in occupational settings, particularly those using and manufacturing arsenic-containing pesticides, and in areas containing high levels of arsenic in rock, which contaminates soil or water. Toxicity may also ensue by exposure to semiconductors, smelting, power plants burning coal, industries involved in glass and microcircuit production, fungicides, insecticides, paint, and tanning agents.\textsuperscript{71} Arsenic binds to sulfhydryl groups,
inhibiting glycolysis and disrupting oxidative phosphorylation. Acute poisoning is more common in cases of ingestion or inhalation of arsenic fumes in workers. Initial symptoms include nausea, vomiting, abdominal pain, and diarrhea. Patients often complain of a metallic or garlic taste. Massive hemolysis ensues, and severe cases result in encephalopathy, seizures, coma, cardiac arrhythmias, and death. In chronic poisoning, peripheral nerve and skin manifestations are more common than GI disturbances. Emergency department (ED) management includes decontamination of skin, consideration of charcoal and/or nasogastric suctioning in patients who present within 1 hour of ingestion, administration of fluids, monitoring, and chelation therapy with dimercaprol in symptomatic patients.  

**Caustics**

A common pathway for many toxins is initial vomiting and abdominal pain by corrosive properties. Aspirin impairs the gastric mucosal barrier, leading to abdominal pain, vomiting, and hematemesis. Acids and alkalis are known for causing liquefaction and corrosive necrosis, respectively. This process leads to oropharyngeal and esophageal burns, resulting in drooling, stridor, nausea, vomiting, hematemesis, chest pain, odynophagia, dysphagia, abdominal pain, and esophageal or gastric perforation.

**Lactrodectus mactans (Black Widow Spider) Envenomation**

Spiders of the genus Lactrodectus are found throughout the United States (except Alaska) and are the leading cause of death from arachnid envenomation. The venom acts at the presynapse of the neuromuscular junction, causing release of multiple neurotransmitters and overstimulation of motor end plates. This overstimulation results in pain and cramping of large muscle groups, weakness, hypertension, priapism, and rarely, death. Generalized abdominal or back pain is the most frequent presenting complaint in patients seeking medical attention. The abdomen may be rigid and mimic an acute abdomen. Management includes monitoring, fluid administration, and pain control with opioids. The use of antivenin, which is derived from horse serum, is reserved for severe cases and must be weighed against the risk of potential allergic complications.

**Opiates**

A known side effect of opiates is the slowing of GI motility and formation of ileus, leading to abdominal pain in many patients. Conversely, in patients who use opioids for long-term, cessation of intake leads to opioid withdrawal, which often presents with nausea, vomiting, abdominal pain, and diarrhea. Symptoms may begin within 6 to 12 hours after the last dose of a short-acting opioid and 24 to 48 hours after cessation of methadone. Physical examination reveals a patient who is often agitated, in acute discomfort, with myalgias, mydriasis, yawning, hyperactive bowel sounds, and piloerection. Vomiting and diarrhea may be severe enough to cause dehydration, tachycardia, and hypotension. Methadone or other narcotics as well as clonidine or benzodiazepines may be used to control symptoms.

**FUNCTIONAL CAUSES OF ABDOMINAL SYMPTOMS**

**Cyclic Vomiting Syndrome**

Cyclic vomiting syndrome is characterized by recurrent discrete episodes of vomiting. It occurs in both children and adults. Attacks are severe, generally requiring intravenous hydration and causing patients to miss work or school. Episodes may be stereotypical with identified triggers and are often self-limited. Patients with frequent episodes (>1/month) may require prophylactic therapy including propranolol, cyproheptadine, amitriptyline, phenobarbital, or valproic acid. When attacks occur, parental
medications including, ondansetron and ketorolac, are recommended. A change from the patient’s wonted symptoms should prompt the clinician to consider other causes.

**Abdominal Migraine**

Abdominal migraine is similar to cyclic vomiting syndrome, except that the primary complaint is abdominal pain. This term was coined in 1956 by Farquhar, who presumed that these episodes of abdominal pain represented a migraine variant as the source of symptoms. Although this presumption has not been proven, there is an association between migraines, abdominal migraines, and cyclic vomiting syndrome.

**Irritable Bowel Syndrome**

Although primarily a GI disease, irritable bowel syndrome merits mention because of its association with psychological disorders, poor socioeconomic status during childhood, and GI tract infections. Its pathogenesis seems to involve GI motor and sensory dysfunction. Patients often report that specific foods aggravate symptoms. There may be a genetic predisposition in some patients. Most patients have had many similar episodes in the past. ED management is directed at ruling out other intra-abdominal diseases. Treatment is supportive.

**NEUROGENIC CAUSES OF ABDOMINAL SYMPTOMS**

**Herpes Zoster**

Herpes zoster may involve an abdominal dermatome causing severe pain. Pain often precedes the rash; however, a close physical examination may reveal erythema, small papules, or early vesicles. Pain is often hyperesthetic to light palpation. Rarely, visceral varicella zoster infection occurs, usually in immunocompromised patients in who rash may or may not be present. This entity represents disseminated infection and is life threatening. In immunocompetent patients with localized zoster, oral antiviral therapy with acyclovir or famciclovir has been shown to reduce duration of symptoms and incidence of postherpetic neuralgia if started early (<3 days from onset) in the disease process. In disseminated disease, parenteral antiviral therapy and admission are required.

**Abdominal Epilepsy**

Abdominal epilepsy is an exceedingly rare condition in which seizures manifest as GI symptoms, including vomiting and abdominal pain. The criteria for diagnosis include recurrent paroxysmal GI complaints and findings on electroencephalography suggesting a seizure. Central nervous system involvement with changes in mental status and convulsions may occur but is not always present, and abdominal pain episodes generally improve with anticonvulsant therapy.

**SUMMARY**

Abdominal pain is a symptom of many extra-abdominal diseases not infrequently seen in patients in the ED. The prudent clinician will consider extra-abdominal causes when patients presenting with abdominal complaints do not have a clear-cut intra-abdominal cause or in patients with repeat visits despite a supposed diagnosis. Familiarity with mechanisms of nociception and systemic diseases that cause abdominal symptoms will facilitate the consideration of alternative causes. In such situations, a careful history including a thorough review of systems combined with careful physical examination will often prompt laboratory tests and/or imaging that leads to an accurate diagnosis.
REFERENCES


