A 60-year-old man presented to the emergency department following a syncopal episode. This event was witnessed by his friends at a bowling alley, who noted he slumped in his chair and was unresponsive for 5 minutes. When emergency medical services arrived, he was awake with a systolic blood pressure of 60 mm Hg.

Upon arrival to the emergency department he reported symptoms of mild cramping abdominal pain, an urge to defecate, and bloody diarrhea. Before this episode, he was in his usual state of health and last saw his primary care provider 1 day ago with no medication changes.

His medical history was notable for type 2 diabetes with neuropathy, obesity, chronic kidney disease stage III, hyperlipidemia, tobacco use, and atrial fibrillation. His medications included aspirin, atorvastatin, insulin glargine, metformin, metoprolol succinate, dabigatran, and torsemide.

Physical examination was notable for a blood pressure of 84/43 mm Hg, a pulse of 97 beats/min, and a temperature of 36.8°C. His heart rate was irregular and he had no murmurs, rubs, or gallops. His breath sounds were clear bilaterally. There was a well-healed right extremity below-knee amputation. His abdomen was obese but soft, nontender, and nondistended. Rectal exam showed watery brown stool with maroon streaks intermixed.

Initial laboratory testing revealed the following (reference ranges provided parenthetically): hemoglobin 9.3 g/dL (13.5 - 17.5 g/dL) with a mean corpuscular volume of 103.8 fL; leukocytes 11.9 g/dL (3.5 - 10.5 g/dL); sodium 137 mmol/L (135 - 145 mmol/L); potassium 5.3 mmol/L (3.6 - 5.2 mmol/L), blood urea nitrogen (BUN) 34 mg/dL (8 - 24 mg/dL) and creatinine 2.2 mg/dL (0.8 - 1.3 mg/dL). His hemoglobin had been 12.0 g/dL at his primary care visit 1 day before presentation. His baseline creatinine was 1.5 to 1.7 mg/dL. Electrocardiogram showed atrial fibrillation without rapid ventricular response. Chest radiograph was nonspecific with decreased lung volumes.

Given the history, laboratory findings, and physical exam, multiple potential etiologies were considered including infectious, inflammatory, and cardiac conditions.

1. Which one of the following is the most likely cause of this patient’s abdominal pain and bloody stool?
   a. Diverticular bleed
   b. Colorectal carcinoma
   c. Acute mesenteric ischemia
   d. Colon ischemia (CI)
   e. Inflammatory bowel disease (IBD)

While diverticular bleeding is a common cause of lower gastrointestinal bleeding in this age group, it presents with painless hematochezia; the preceding abdominal pain in this case argues against diverticular bleed. Colorectal cancer is unlikely to present with an acute episode of abdominal pain and bloody diarrhea. Acute mesenteric ischemia (AMI) is caused most commonly by thromboembolism to the superior mesenteric artery and presents with abrupt onset of severe periumbilical abdominal pain with physical examination revealing “abdominal pain out of proportion to physical examination.”1 Diarrhea and hematochezia are uncommon features of AMI. In this case, the most likely diagnosis is CI based upon the preceding syncopal episode followed by abdominal pain and bloody stools. CI is the most common form of ischemic injury to the gastrointestinal tract and can be defined as a...
decrease in blood flow to a level insufficient to maintain colonocyte metabolic function. CI was formerly known as ischemic colitis; however, this entity is now referred to as CI given that many patients do not have an inflammatory or “-itis” phase of their disease. IBD manifests with abdominal pain and bloody stools and is a possibility; however, the preceding hypovolemic shock makes CI more likely.

Given the patient’s hypotension and concern for hypovolemic shock, he was admitted to the medical intensive care unit. Following intravenous fluid resuscitation, his blood pressure improved to 128/59 mm Hg, measured via arterial line. He continued to have intermittent abdominal pain, but denied any other symptoms.

2. Which of this patient’s symptoms represent the most common presenting symptom of CI?
   a. Sudden onset abdominal pain
   b. Urge to defecate
   c. Hematochezia
   d. Vomiting
   e. Syncope

   In patients with CI, the classic and most common presenting triad is sudden onset of mild abdominal pain followed by a need to defecate and hematochezia. Sudden onset of mild, cramping lower abdominal pain is the most common presenting symptom of CI and occurs in greater than 85% of cases. Urge to defecate and rectal bleeding are also very common with the latter occurring in approximately 80% of patients with CI but occur later in the disease course. Other symptoms of CI were less common and include vomiting (30%), dizziness (10%), and syncope (6%). Pathophysiologically, the abdominal pain, urge to defecate, and rectal bleeding can be attributed to colonic mucosal ischemia due to insufficient blood flow to meet metabolic function.

   Overnight, the patient had a single large episode of melena. His hemoglobin in the morning had remained stable at 9.1 g/dL. He began bowel preparation in anticipation of colonoscopy and was started on an intravenous proton pump inhibitor. Furthermore, he was also noted to develop a mild acute kidney injury with a creatinine elevation to 2.8 mg/dL from 2.2 mg/dL on admission.

3. Which one of the following is the most common cause of CI?
   a. Non-occlusive CI
   b. Embolic arterial occlusion
   c. Thrombotic arterial occlusion
   d. Mesenteric vein thrombosis
   e. Trauma

   The most common cause of CI is non-occlusive disease in the colonic microvasculature, generally caused by hypoperfusion, resulting from alterations in systemic circulation (“low flow state”) or from anatomic or functional changes in the mesenteric vasculature. Other less common causes include acute arterial occlusion due to embolus or thrombus, mesenteric venous thrombosis, vasculitis, or medications. Acute thrombus or embolus were also less likely in this case given he was therapeutically anticoagulated with dabigatran, although this would also increase the risk of gastrointestinal bleeding. CI caused by trauma to the colon vasculature is relatively rare.

   While in the intensive care unit, the patient underwent both upper and lower endoscopies. His upper endoscopy revealed severe erosive esophagitis (Los Angeles grade D esophagitis). His colonoscopy showed discontinuous areas of erythematous and ulcerated mucosa in the descending colon and transverse colon at the hepatic flexure. There was clotted blood found in the rectum, sigmoid colon, and descending colon.

4. Which one of the following colon segments is the most likely to be affected in colon ischemia?
   a. Transverse colon
   b. Isolated rectum
   c. Left colon
   d. Distal colon
   e. Isolated right colon

   CI can occur in any portion of the colon, with distributions ranging from isolated left- or right-sided disease to involving the
entirety of the colon. The colon receives its blood supply from several branches of the superior mesenteric artery and inferior mesenteric artery.

Collateral blood flow to the majority of the colon is abundant; however, there are several areas where the collateral vessels meet, known as watershed areas. These watershed regions, including the sigmoid colon and splenic flexure are at higher risk for ischemia given they do not have the same level of collateral supply as other regions of the colon. Areas with abundant collateral blood flow are at lower risk for developing CI and include the transverse colon and rectum, affected in 10% and 1% of cases, respectively. Decreased blood flow to watershed regions explains why CI most commonly affects the left colon, such as in this case, and accounts for 35% of patients with CI. The distal colon and isolated right colon are affected in approximately 25% of patients; although frequent, it is less common than the left-colon cases.

Our patient tolerated the endoscopy well without complications. He remained clinically stable with no further episodes of bleeding or hypotension and was transferred to the general floor for continued management.

5. In addition to supportive care and fluid resuscitation, this patient should be treated with which one of the following?
   a. Antithrombotic therapy
   b. Anticoagulation
   c. Glucocorticoids
   d. Broad-spectrum antibiotics
   e. No additional therapy

As most causes of CI are caused by non-occlusive disease, antithrombotic therapy and anticoagulation are not routinely recommended, although these can potentially be of benefit when the etiology is suspected to be due to mesenteric vein thrombosis or cardiac embolization. The role of glucocorticoids in CI has been evaluated and determined to not be beneficial, other than in cases of CI caused by vasculitis, in which the steroids are used to treat the underlying vasculitis.

There have been several case reports and an animal model showing the harm of steroids in CI. Initial management of CI consists predominantly of early recognition and supportive care. The exception is with moderate-to-severe CI, where the use of broad-spectrum antibiotics is indicated due to the risk of bacterial translocation. In this case, antibiotics are indicated given the severity of his disease. Grading of CI severity is detailed further in the discussion section. Given the indication for antibiotics, no additional therapy is incorrect. Although patients with mild presentations can be managed with supportive care alone, those with moderate or severe disease should be treated with broad-spectrum antibiotics.

Our patient was found to have a pancolonic distribution of ischemia on colonoscopy with additional high-risk factors for poor outcome including male sex, anemia, and elevated BUN, and was thus classified as having severe CI. He was started on empiric antibiotics in the setting of his severe CI and ultimately grew Bacteroides uniformis from blood cultures, which was sensitive to metronidazole. He continued to do well with supportive care and was discharged to complete a course of metronidazole for bacteremia.

DISCUSSION
As with many other vascular and ischemic diseases, CI predominantly affects the elderly, with a peak incidence in the seventh decade of life. The annual incidence is difficult to assess, given that many cases resolve spontaneously without treatment, but the estimated incidence of CI in a population-based study from Olmsted County, MN, was 23 per 100,000. There are several known risk factors for developing CI, including irritable bowel syndrome, particularly the constipation-predominant form; cardiovascular disease; vascular thromboembolism; vascular surgeries; diabetes; and chronic obstructive pulmonary disease. Beyond the known risk factors...
for CI, several conditions are associated with increased severity, including chronic kidney disease, chronic obstructive pulmonary disease, and a history of mesenteric vascular insufficiency.2

Patient history, laboratory testing, imaging, and colonoscopy are used to differentiate CI from other diseases with similar presentations (IBD and infections). When CI is suspected, the initial test performed is often a computed tomography (CT) scan of the abdomen with intravenous and oral contrast. CT scan is the best modality to detail the distribution and phase of disease and provides insight into severity. When clinical presentation and CT scan leave the diagnosis in doubt, colonoscopy is performed. Colonoscopy is the most useful test to diagnosis CI as it allows direct visualization of the mucosa, provides information on disease distribution and enables biopsy confirmation.11

As the diagnosis of CI is made upon clinical, radiographic, and endoscopic evaluation, the role of laboratory tests in diagnosis is fairly limited. Although clinical practice tests such as lactate are commonly obtained for diagnosis, there have not been any well-designed clinical trials to support this.2 The main role for laboratory evaluation in CI has been to predict the severity of the disease.

The classification of CI severity varies based upon a combination of clinical, laboratory, and endoscopic factors. Moderate is defined as patients with CI who have up to three of the following: male sex, hypotension (defined as <90 mm Hg), tachycardia, abdominal pain without rectal bleeding, BUN greater than 20 mg/dL, hemoglobin less than 12 g/dL, lactate dehydrogenase greater than 350 U/L, serum sodium less than 136 mEq/L, white blood cell count greater than 15,000 cells/mm³ or ulceration of colon mucosa on endoscopy.2 Severe disease is defined as a patient with CI having at least four of the previous criteria or any peritoneal signs, pneumatosis or portal venous gas on imaging, gangrene on colonoscopy or evidence of a pancolonic distribution, or isolated right-sided CI.

The pattern of CI is an important predictor of severity due to the observed impact on clinical outcomes — isolated right CI is associated with worse outcomes including need for surgery, length of hospital stay, and mortality when compared with other patterns of involvement.6 The less favorable outcomes of isolated right CI include that it can be the heralding event of an otherwise clinically silent focal obstruction of the superior mesenteric artery and be associated with or followed by AMI. Therefore, all cases of isolated right CI require dedicated imaging of the mesenteric vasculature with CT angiogram or magnetic resonance angiogram to exclude potentially causative obstructive lesions of the superior mesenteric artery and its branches. In contrast, left-sided CI has a more favorable outcome with less need for surgery and a shorter length of stay.6

CI is a common but under-recognized condition. It is predominantly a disease of the elderly and generally caused by non-occlusive microvascular disease. The classic sequential triad of CI includes sudden onset of mild abdominal pain, followed by a need to defecate, and hematochezia. The initial test of choice is a CT scan of the abdomen and pelvis with intravenous contrast. Although CI can involve any portion of the colon, left-sided involvement is most common. Isolated right CI is associated with unfavorable outcomes because it may represent clinically silent thromboembolism of the superior mesenteric artery and be accompanied or followed by AMI. Therefore, all cases of isolated right CI should have dedicated imaging of the mesenteric vasculature to exclude obstructive process. Management of patients with CI depends upon the severity of illness. Patients with moderate-to-severe CI may benefit from antibiotics given their risk of bacterial translocation across ulcerated colonic mucosa; however, glucocorticoids have not been shown to be beneficial other than in cases of CI caused by vasculitis. Given CI is most commonly non-occlusive, antithrombotic agents and anticoagulation are not routinely used, although they can be considered in uncommon cases of occlusive CI.
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**CORRECT ANSWERS:** 1. d. 2. a. 3. a. 4. c. 5. d