Gastrointestinal Bleeding

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Educational Gaps
1. Pediatricians should be familiar with diseases that may present with gastrointestinal bleeding in patients at varying ages.
2. Pediatricians should be aware of newer technologies for the identification and therapy of gastrointestinal bleeding sources.
3. Pediatricians should be familiar with polyps that have and do not have an increased risk of malignant transformation.
4. Pediatricians should be familiar with medications used in the treatment of children with gastrointestinal bleeding.

Objectives
After completing this article, readers should be able to:
1. Formulate a diagnostic and management plan for children with gastrointestinal bleeding.
2. Describe newer techniques and their limitations for the identification of bleeding, including small intestinal capsule endoscopy and small intestinal enteroscopy.
3. Differentiate common and less common causes of gastrointestinal bleeding in children of varying ages.
4. Identify types of polyps that may present in childhood and which of these have malignant potential.

Introduction
An 11-year-old boy is seen in the emergency department after fainting at home. He has a 2-day history of headache and dizziness. Epigastric pain has been present during the past 2 days. His pulse is 150 beats per minute, and his blood pressure is 90/50 mm Hg. An intravenous bolus of normal saline is administered; his hemoglobin level is 8.1 g/dl (81 g/L). He passes a melanotic stool. He is admitted to the pediatric intensive care unit and prescribed intravenous esomeprazole. He receives a transfusion of packed red blood cells, which increases his hemoglobin level to 8.5 g/dl (85 g/L). Esophagogastroduodenoscopy (EGD) reveals nodularity in the antrum of the stomach and a large ulceration with a visible, actively bleeding vessel in the duodenum. The ulcer is coagulated with an argon plasma coagulation (APC) laser. Biopsy specimens taken during the procedure reveal *Helicobacter pylori*, and the patient is treated by continuing esomeprazole therapy and initiating amoxicillin and clarithromycin therapy. No further bleeding occurs, and he is discharged 4 days later.

Gastrointestinal (GI) bleeding is a relatively common and potentially serious problem in pediatrics. It is important for practitioners taking care of children to be familiar with the causes, evaluation, and treatment of GI bleeding. In this article, the etiology of bleeding at different ages and the modalities of evaluation and treatment are discussed. Newer technologies for diagnosis are also addressed.

The spectrum of causes of GI bleeding in children ranges from a small amount of bleeding as seen in an infant with an anal fissure to severe bleeding that may be present in a child...
with varices from underlying chronic liver disease. It is important for the clinician to quickly evaluate the patient with GI bleeding and to differentiate the extent and severity of the bleeding.

GI bleeding in children presents in a number of different ways. Upper GI tract bleeding may present as hematemesis, melena, or hematochezia from rapid transit of blood through the intestinal tract due to acute bleeding. The most common causes of bleeding when investigated by endoscopy in the upper GI tract include gastric and duodenal ulcers, gastritis, esophagitis, varices, prolapse gastropathy, and Mallory-Weiss tears.

Lower GI tract bleeding may present as either melena or hematochezia. The most common causes of lower GI tract bleeding include fissures, allergic colitis, enteric infections, and juvenile polyps. Severe bleeding may be seen with Meckel diverticulum, inflammatory bowel disease, vascular anomalies, and intussusception.

The initial evaluation of a child after presenting with GI bleeding should focus on stabilizing the patient and determining the severity of the bleed. Vital signs should be measured and reviewed. A focused history should be quickly obtained when feasible because it may provide clues to the cause of bleeding. Signs of a significant bleeding episode may include symptoms of hypovolemia, such as tachycardia and hypotension. Orthostatic changes may also be present. Capillary refill may be prolonged. Children with signs and symptoms of significant bleeding and children with active blood loss should be hospitalized in a pediatric intensive care unit if possible. Stabilizing the patient should generally take precedence over evaluation and therapeutic considerations. Large bore venous access should be instituted and fluid resuscitation initiated with Ringer’s lactate or normal saline. Transfusion with packed red blood cells may be indicated, and coagulation factors or platelets may need to be administered in specific cases.

The presence of coffee ground emesis or melena generally implies a slower rate of bleeding when compared with emesis or passage per rectum of bright red blood.

Guaiac of stool or emesis is helpful in defining whether blood is present. Red emesis or stool may reflect ingested red-colored food or other material. Newer guaiac methods using buffered and stabilized hydrogen peroxide are preferred because they have lower false-positive and false-negative detection.

An initial focused physical examination may be helpful in determining the cause of the bleeding. The presence of hepatomegaly and splenomegaly may point to variceal bleeding from liver disease. Scleral icterus, palmer erythema, and spider telangiectasias may be noted with chronic liver disease. Perianal disease may point to the presence of Crohn disease. Careful nasal examination may determine epistaxis as the cause of bleeding. Skin lesions may be seen with Peutz-Jeghers, Cronkhite-Canada (a rare syndrome of multiple intestinal polyps), Osler-Weber-Rendu, and other syndromes, and the presence of multiple skin hemangiomas may be associated with visceral hemangiomas as a cause of GI bleeding.

Laboratory studies should be performed to help elicit the cause and define the extent of bleeding. A complete blood cell count documents the hemoglobin level and hematocrit to help determine the extent of bleeding and whether platelet numbers are adequate. A low mean corpuscular volume may point to chronic loss of blood and the presence of iron-deficiency anemia. Abnormal coagulation study results may point to underlying liver disease or malabsorption. Measurement of alanine aminotransferase, aspartate aminotransferase, and bilirubin may point to the presence of liver disease. Blood urea nitrogen and creatinine may help determine fluid status and the presence of renal insufficiency. A low serum albumin level suggests hypoproteinemia, which may herald significant liver disease or protein-losing enteropathy, such as inflammatory bowel disease. With any sign of significant bleeding, blood should generally be obtained for type and cross-match.

Many clinicians favor placing a nasogastric tube for lavage in a patient with suspected GI bleeding. Presence of blood from lavage indicates bleeding in the upper GI tract proximal to the ligament of Treitz. Sources in the small bowel, including the duodenum, may or may not lead to blood being present in the stomach, which can be noted when lavage is performed. Lavage should be performed with warmed normal saline to reduce the risk of hyponatremia and hypothermia. In the past, lavage was often performed using cold or iced saline. This is no longer recommended because it may be associated with hypothermia. Clearing of blood from returned lavage fluid indicates that active bleeding may have ceased.

Hematochezia generally indicates a colonic source of bleeding, although hematochezia may be seen with upper GI tract bleeding sites, such as bleeding ulcers when brisk bleeding causes rapid transit of blood through the intestine. Melena is more commonly seen from bleeding proximal to the ligament of Treitz and from more proximal colonic sites due to slow loss of blood.

Abdominal radiography may be performed for evaluation of possible obstruction or bowel perforation. In the past, barium studies were performed to evaluate for ulcer disease and other causes of bleeding, but now endoscopy is preferable because this method is more sensitive and specific and can provide therapeutic intervention. On occasion, ultrasonography may be useful to identify portal
hypertension or an intussusception. A Meckel scan should be considered in children with painless rectal bleeding.

EGD and colonoscopy are helpful in the evaluation of the child with bleeding. Endoscopy is generally the favored method for evaluating the cause of bleeding and may provide a method of therapy as well. In general, these procedures are performed once the patient is stabilized, although this procedure may be necessary to control bleeding in an unstable patient. Administration of an intravenous proton pump inhibitor is helpful before endoscopy for upper GI tract bleeding to aid in control of bleeding and in reducing the chance of additional bleeding. Some practitioners administer a prokinetic agent, such as metoclopramide or erythromycin, before the procedure in an attempt to empty material from the stomach and better visualize the mucosal lining. EGD and colonoscopy are performed with the child asleep under either conscious sedation or anesthesia. Endoscopy allows the direct visualization of the mucosal lining and identification of any visible bleeding lesions. With active bleeding or when therapeutic measures are being considered, general anesthesia with endotracheal intubation is generally preferred to best protect the child’s airway.

Complications of endoscopy have been reported in approximately 2% of cases. The most frequent complications include hypoxia or bleeding during the procedure, although both are relatively uncommon. Perforation of the intestinal tract may occur but is infrequent.

Control of bleeding from gastric or duodenal ulcers may be accomplished with cautery or an APC laser. Figure 1 shows a large duodenal ulcer with a cherry red bleeding spot, indicating a bleeding vessel. Coagulation with cautery by heater probes or electrocautery is accomplished by application of electrical current through a probe to or around the bleeding lesion. Epinephrine may be injected locally via the scope before cautery to decrease the risk of rebleeding. The bleeding lesion may then be compressed and coagulated. Laser coagulation using ACP lasers is an alternative procedure. With this technique, argon gas is passed through a probe introduced through the endoscope. The gas is electrically activated to an ionized state, causing tissue coagulation. Figure 2 shows the ulcer in Figure 1 after use of the APC laser. Endoscopically placed clips are also useful to control bleeding from ulcers that have a visibly bleeding vessel. Preloaded clips are attached to the end of an endoscope and deployed over vessels believed to be at high risk of bleeding. All these techniques have been reported to be effective. Technique preference varies, depending on the endoscopist’s experience and institution resources. On occasion, these techniques can cause bleeding, which may require surgical intervention to correct.

Variceal bleeding may be controlled with sclerotherapy or elastic band ligation. Sclerotherapy is performed by injecting varices with a solution of varying sclerosants, causing clotting of the varix. Complications include the development of esophageal strictures. Endoscopic variceal ligation may also be accomplished by the placement of small elastic bands with an endoscope. An apparatus designed to place small bands to a varix is attached to the end of an endoscope. Suction is applied through the channel of the endoscope, drawing the varix into the apparatus and placing a band around the vessel. In general, banding is preferred by most pediatric gastroenterologists because it has a lower risk of complications.

Identified polyps may generally be removed endoscopically using cautery applied via an endoscopic snare. Electrical current is passed through a snare deployed through an endoscope. The snare is carefully closed as the current is applied. The polyp may then be retrieved and sent to the laboratory for histologic evaluation.

There are instances when EGD and colonoscopy may not be able to determine the source of bleeding. In these circumstances, a number of other modalities may be helpful. Nuclear medicine scans with technetium Tc 99m-labeled red blood cells may point to a source of bleeding and are capable of detecting bleeding at a rate greater than 0.1 ml/min. However, these scans may not always accurately localize the source of bleeding because false-positive and false-negative scan results occur. Blood may pool in areas such as the ascending colon when the actual source is higher in the intestinal tract. Angiography may be more helpful in localizing bleeding sites when the rate of bleeding is as little as 1 to 2 ml/min.
Recently, capsule endoscopy has been used to identify bleeding sites in the small intestine in areas that are inaccessible by upper and lower endoscopy. Endoscopy capsules contain a camera that can take several pictures per second. These pictures are transmitted wirelessly to a recording device attached to the patient. Pictures are viewed at a computer workstation after completion of the study to determine whether bleeding lesions are present. A disadvantage to using capsule endoscopy is that the capsule cannot precisely locate a bleeding lesion and cannot obtain biopsy specimens or perform therapeutic interventions. The capsule is either swallowed or placed endoscopically if the child is unable to swallow it. A complication of capsule endoscopy is retention of the capsule by a narrowed lumen due to intestinal strictures or other causes, a situation that may require surgery to correct. To reduce the chance of a retained capsule often an imaging study of the small intestine to exclude narrowing (such as small intestinal followthrough, MRI with enterography or CT with oral contrast) is obtained. As an alternative a dissolvable patency capsule may be swallowed with an abdominal radiography obtained 24 hours later to show that the capsule has transversed the small intestine. The patency capsule will dissolve if it becomes stuck in the small intestine showing that the capsule study would likely result in capsule retention. The size of the capsule limits the use of this technique in children younger than 2 years.

Identification of occult bleeding in select patients may require small intestinal enteroscopy, a technique using specialized, longer endoscopes that have single or double balloons attached to the distal end of the scope. Enteroscopy may help identify bleeding in the distal small bowel in areas inaccessible by conventional endoscopes and may allow therapeutic intervention, such as control of bleeding and polyp removal. Enteroscopy is more commonly performed in adults yet has been performed in children.

Laparoscopy should be considered when other measures cannot identify a bleeding source. Examples include patients who have a Meckel diverticulum, bowel duplication, or other bleeding conditions not identified on scans.

The following sections discuss the common causes of GI bleeding, depending on age at presentation. Table 1 lists common and less common yet important causes of GI bleeding for different age groups.

**Newborns and Infants**

**Causes of Upper GI Tract Bleeding**

Swallowed maternal blood is a common cause of hematemesis in a newborn. Blood may be ingested during birth and may also occur from blood swallowed during nursing. The Apt test is helpful in defining the source of blood as being maternal. This test uses the fact that fetal hemoglobin resists alkali denaturation, leading to a positive test result in infants who have ingested maternal blood. A positive test result generally eliminates the need for further evaluation of causes of bleeding.

Hematemesis from esophagitis is another relatively common cause of bleeding in this age group. Esophagitis from underlying gastroesophageal reflux may lead to ulcerations and subsequent bleeding. The amount of blood seen from esophagitis is generally relatively small.

Ulcers, particularly in stressed, hospitalized infants, may also present with hematemesis. Gastric stress ulcerations are more common than duodenal ulcers in this age group, as opposed to older children where duodenal causes are more common. The amount of bleeding may be significant.

Gastritis may develop for a number of reasons in infants. It is seen with stress from severe illness, trauma, burns, and increased intracranial pressure. Gastritis may also be seen with viral infections, including cytomegalovirus.

Bleeding from hemorrhagic disease of the newborn may be seen if vitamin K has not been administered. Bleeding due to thrombocytopenia may occur and should be considered in this age group as well. Of note, as the infant ages, coagulopathies may also be seen in children with underlying malabsorption due to cystic fibrosis or liver disease.

Intestinal duplications, although relatively rare, may present with GI bleeding and should be in the differential diagnosis at this age.

**Causes of Lower GI Tract Bleeding**

Cow’s milk protein sensitivity may cause bleeding early in life. Milk protein may be associated with a proctocolitis. Melena or hematochezia may also be signs of this
Blood in the stool is generally the presenting symptom and is seen most commonly in the first 3 months of life. Children who are nursed may also develop sensitivity to cow’s milk protein, a relatively common entity. β-lactoglobulin and casein are the most commonly associated immunogens. Infants with sensitivity to cow’s milk are likely to react to soy protein too. Laboratory studies may reveal anemia and eosinophilia. Treatment is with hypoallergenic formula. Both hydrolyzed and amino acid–based formulas may be used, depending on the severity of the sensitivity. Allergy is the second most common cause of bleeding in this age group, with only anal fissures being more common. Guaiac-positive stools may continue for up to several weeks after elimination of the offending protein.

Volvulus is a serious yet less common cause of GI bleeding. The occurrence of bilious vomiting should always initiate evaluation for a volvulus or other serious cause of intestinal obstruction. Volvulus can also present with hematemesis along with abdominal distention; such a presentation suggests bowel ischemia and is a surgical emergency. Abdominal radiographs may suggest obstruction, an indication for further additional imaging studies or surgical consultation. Volvulus treatment is prompt surgical intervention.

Necrotizing enterocolitis (NEC) needs to be considered in the perinatal period as a cause of bleeding. NEC may present as blood in the stool. Abdominal radiographs may reveal bowel wall pneumatosis. NEC commonly occurs in premature infants who have begun enteral feedings, usually after 2 to 3 weeks of life. Treatment is supportive with the use of antibiotics and cessation of enteral feeds. Surgical intervention is often indicated to treat bowel ischemia or infarction due to NEC.

Hirschsprung disease classically presents with failure to have a bowel movement in the first 2 days of life, severe constipation, or symptoms of abdominal obstruction. A few infants, particularly if the diagnosis has been delayed, may present with an enterocolitis. Hirschsprung-associated enterocolitis (HAEC) also occurs after surgical repair of Hirschsprung disease and should be considered in any child with a history of Hirschsprung disease who presents with diarrhea or abdominal distention. Children with HAEC may appear toxic and lethargic and are often febrile. Blood loss may be severe. HAEC should be considered in an infant who appears toxic and has bloody diarrhea. Recommended treatment includes bowel rest, intravenous fluid administration, and antibiotics that include coverage for anaerobic bacteria. Careful rectal irrigation with normal saline is often performed as well. HAEC is a significant problem that in the past was associated with a high mortality rate and should be treated aggressively.

Anal fissures are the most common cause of rectal bleeding. The occurrence of bilious vomiting should always initiate evaluation for a volvulus or other serious cause of intestinal obstruction. Volvulus can also present with hematemesis along with abdominal distention; such a presentation suggests bowel ischemia and is a surgical emergency. Abdominal radiographs may suggest obstruction, an indication for further additional imaging studies or surgical consultation. Volvulus treatment is prompt surgical intervention.

**Table 1. Common Causes of Gastrointestinal Bleeding in Children**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Often With More Severe Bleeding</th>
<th>Often With Milder Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td>Coagulopathies, including vitamin K deficiency, Necrotizing enterocolitis, Hirschsprung enterocolitis, Volvulus, Stress ulcer</td>
<td>Gastritis, Esophagitis, Anal fissure, Protein intolerance, Enteric infection, Nodular lymphoid hyperplasia</td>
</tr>
<tr>
<td>Children</td>
<td>Varices, Ulcer, Intussusception, Volvulus, Meckel diverticulum, Gastritis, Henoch–Schönlein purpura, Mallory-Weiss tear, Hemolytic uremic syndrome, NSAID use</td>
<td>Esophagitis, Enteric infection, Juvenile poly, Nodular lymphoid hyperplasia, Perianal streptococcal cellulitis</td>
</tr>
<tr>
<td>Adolescents</td>
<td>Varices, Ulcer, Gastritis, Ulcerative colitis, Crohn disease, Meckel diverticulum, Henoch–Schönlein Purpura, Mallory-Weiss tar, Meckel diverticulum, NSAID use</td>
<td>Hemorrhoids, Enteric infections, Esophagitis, Anal fissure</td>
</tr>
</tbody>
</table>

NSAID = nonsteroidal anti-inflammatory drug.
is an important part of the physical examination of a child with blood in the stool. Most commonly, anal fissures are associated with the passage of hard stools. Less commonly, fissures that cause bleeding may be seen with diarrhea. Pain with passage of stool is often present. Conservative therapy with stool softeners is almost always effective.

Intussusception is another cause of GI bleeding in children. The classic presence of currant jelly stools is a relatively late manifestation of bowel ischemia. Intussusception usually presents with abdominal pain along with lethargy. Abdominal radiographs may suggest intestinal obstruction, and the diagnosis may be confirmed with ultrasonograms demonstrating a doughnut-appearing sign. Most cases involve intussusception of the ileum into the cecum. Reduction of the intussusception may be accomplished by air or hydrostatic reduction by barium. A pediatric surgeon should be available during reduction attempts in case bowel perforation occurs during the procedure. Surgical intervention is indicated if the intussusception cannot be reduced by air or hydrostatic enema.

Less common causes of bleeding in this age group include intestinal duplications and vascular lesions. Vascular lesions may include arterial-venous malformations, venous malformations, and hemangiomas. Vascular lesions are rare causes of bleeding at any age.

**Children**

**Causes of Upper GI Tract Bleeding**

Many of the causes of bleeding in infants, such as esophagitis, also occur in older children. Pill esophagitis may develop from retention of ingested medications. Esophagitis may be severe after caustic ingestion.

Mallory-Weiss tears from forceful vomiting are more common in this age group and may be diagnosed at endoscopy. Tears can occur in the lower esophagus and the gastroesophageal junction or in the cardia of the stomach just below the gastroesophageal junction. Prolapse gastropathy, in which forceful vomiting or retching propels the proximal stomach into the distal esophagus and produces submucosal bleeding and superficial ulceration, also presents with hematemesis. Blood loss may be significant after forceful emesis. Mallory-Weiss tears may be treated during endoscopy.

Gastritis in children may be caused by stress and viral infections as in infants. Gastritis at this age may also occur after ingestion of nonsteroidal anti-inflammatory drugs. In addition, caustic ingestion, bile reflux, and vasculitis may have manifestations of gastritis.

*H pylori* is now frequently diagnosed in childhood. *H pylori* may cause bleeding from gastritis and may also be associated with bleeding from gastric or duodenal ulcers.

At endoscopy, the gastric antrum is noted to be diffusely nodular as seen in Figure 3. Published recommendations from the European and North American Societies for Pediatric Gastroenterology, Hepatology, and Nutrition recommend initial diagnosis from EGD biopsies based on positive histologic and urease test results or positive culture results. Eradication of the organism may be based on stool antigen testing or carbon 13–labeled urea breath testing. The stool antigen test is up to 90% sensitive and specific. The urea breath test is performed by orally administering carbon 13–labeled urea. If present, *H pylori* converts urea into carbon dioxide and ammonia. The resulting labeled carbon dioxide is absorbed in the gut, exhaled, and measured. This test is up to 95% sensitive and 95% specific. Neither stool antigen testing nor carbon 13–labeled urea breath testing is recommended if the patient has been taking antibiotics, *H pylori* (H2) antagonists, proton pump inhibitors, or bismuth preparations in the preceding 2 weeks. Serologic assays are available but less useful in children because they are not as accurate as the above tests and are not recommended for diagnosis.

Ulcers have become more commonly diagnosed in children, and both duodenal and gastric ulcers may present with hematemesis, melena, and hematochezia from rapid transit through the intestine. They are often diagnosed at endoscopy. The incidence of ulcers is higher in children with burns, stress due to severe or critical illness, and increased intracranial pressure.

Varices are another source of GI bleeding. Varices can develop from underlying cirrhotic liver or extrahepatic portal vein thrombosis. Portal vein thrombosis can be a complication of umbilical venous catheter placement.
during the newborn period. Portal hypertension causes dilatation of esophageal vessels that can lead to severe bleeding. Chronic liver disease can also lead to coagulopathy due to decreased production of blood clotting factors and to thrombocytopenia seen in hypersplenism due to portal hypertension. Both coagulopathy and thrombocytopenia increase the risk of GI bleeding.

**Causes of Lower GI Tract Bleeding**

Enteric infections are a frequent cause of colitis and bleeding. Pathogens, including *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia coli* O157:H7, and other organisms, can cause diarrhea and colicky abdominal pain. When bloody diarrhea with cramping is present, appropriate stool cultures for these organisms should be obtained. Shigalike toxin may also be obtained to look for non-O157:H7 strains of *E coli* and other organisms. Other bacteria, such as *Aeromonas* and *Plesiomonas*, may cause colitis on occasion.

*Clostridium difficile* colitis is now commonly seen without preceding use of antibiotics and may also present with melena or hematochezia. Polymerase chain reaction testing of the stool for *C difficile* toxin is the preferred method for identifying presence of this organism. However, *C difficile* can be part of normal bowel flora up to 1 year of age and rarely causes symptoms in this age group. Figure 4 shows the appearance of the colonic mucosa in a patient with pseudomembranous colitis due to *C difficile* infection.

Meckel diverticulum commonly presents with painless rectal bleeding, which is often severe. Ulceration of the ileal mucosa is caused by acid secretion from the gastric mucosa-lined epithelium of the Meckel diverticulum. Meckel diverticula are often 2 ft from the ileal cecal valve and 2 in long, are commonly present in children younger than 2 years, and occur in 2% of the population. Meckel diverticulum may also cause volvulus around an associated remnant of the vitelline duct or present as diverticulitis in a manner similar to appendicitis. Diagnosis is frequently based on a Meckel scan using technetium Tc 99m pertechnetate, which is taken up by gastric mucosa. This scan will detect diverticula that contain gastric mucosa (Figure 5). Pretreatment with H2-receptor antagonists or proton pump inhibitors can increase the sensitivity of the Meckel scan. Treatment is by surgical removal.

Intussusception may present in this age group as well, most commonly caused by a lead point of hypertrophied lymphoid tissue due to a recent viral infection. At older than 5 years, the presence of a pathologic lead point, such as a polyp or Burkett lymphoma, can also lead to an intussusception.

Vasculitis may also cause GI bleeding. Henoch-Schönlein purpura can cause significant bleeding and is also associated with an increased risk of intussusception. Most typically, a purpuric rash, first apparent on the lower back and buttocks, precedes GI bleeding. Henoch-Schönlein purpura often develops after a viral infection. Significant abdominal pain, frequently accompanied with bloody stools, can occur in Henoch-Schönlein purpura. Symptoms frequently last for weeks.
Hemolytic uremic syndrome is also associated with GI bleeding caused by colitis from Shiga toxin–producing *E. coli*, most commonly from *E. coli* O157:H7. Systemic complications, including renal failure and seizures, may also be associated with this disease. Bloody diarrhea is followed by the development of hemolytic anemia and thrombocytopenia generally 3 to 10 days later if hemolytic uremic syndrome colitis develops. Children who have been identified as having enterohemorrhagic *E. coli* should be followed up closely for the development of hemolytic uremic syndrome.

Lymphoid hyperplasia is another cause of lower GI tract bleeding in children; colonoscopy reveals small nodules of lymphoid tissue. Lymphoid hyperplasia may occur after viral infections and also from allergies. Lymphoid hyperplasia is more common in children with IgA deficiency and also those with hypogammaglobulinemia. Bleeding can present as small amounts of red blood in the stool or as melena. Lymphoid hyperplasia is a common finding during colonoscopy in children; however, most lymphoid hyperplasia is not associated with bleeding.

Children may develop polyps that can bleed. Juvenile polyps are the most common form in children, typically seen during the childhood years, most commonly between 1 and 7 years of age. Juvenile polyps are one of the most common causes of bleeding in this age group. Children with juvenile polyps usually have painless rectal bleeding; occasionally a polyp prolapses through the rectum. Less often, juvenile polyps are associated with abdominal pain. Juvenile polyps are usually 1 to 3 cm in diameter and generally attached to the mucosa via a thin stalk. Autoamputation of the stalk can occur with consequent rectal bleeding, which may be severe. Bleeding occurs from erosion of the mucosal lining of the polyp. Figure 6 shows the appearance of a juvenile polyp visualized during colonoscopy. Juvenile polyps are benign hamartomas and do not undergo malignant transformation. Pathologic analysis reveals dilated mucin-filled cysts and an inflammatory infiltrate in the lamina propria. Colonoscopy is indicated to remove the polyp and to evaluate for additional ones. More than three-fourths of juvenile polyps are found in the rectum or distal colon. Most polyps are solitary, but multiple polyps may occur in up to 40% of patients. Recurrent polyps may occur in 5% of children with a juvenile polyp, but routine follow-up colonoscopy is not recommended unless symptoms redevelop. However, if 3 or more polyps are present, the child may have juvenile polyposis and should have colonoscopies performed every few years.

Patients with juvenile polyposis are at increased risk of colon cancer, which may occur in up to 20% of patients with this syndrome. A number of genes have been identified in this syndrome, including *SMAD4*, *BMPR1A*, and *ENG*, which are found in approximately 50% of patients. Hamartomas may also develop in the small intestine in juvenile polyposis. Although there is no consensus regarding frequency of screening, colonoscopy has been recommended every 1 to 2 years beginning in adolescence. Evaluation for small intestinal polyps also needs to be considered using imaging techniques, including magnetic resonance imaging and/or small intestinal capsule endoscopy.

Hamartomas may also occur from *PTEN* mutations. Cowden syndrome, Bannayan-Riley-Ruvalcaba syndrome, and Proteus syndrome are rare genetic syndromes with defects in the tumor suppressor gene *PTEN*. Peutz-Jeghers syndrome is characterized by hamartomatous polyps throughout the GI tract along with pigmentation in the perioral area. Children with this syndrome may present with intestinal obstruction due to polyps in the small intestine.

Patients with a family history of familial adenomatous polyposis may be seen. Familial adenomatous polyposis is a genetic disorder in which hundreds to thousands of adenomatous polyps develop and in which there is a high risk of developing colon cancer over time. Polyps begin to appear in childhood and continue to develop throughout life. Extra intestinal features may include osteomas of the mandible and maxilla, desmoid tumors, and pigmented ocular lesions. Gastric fundic polyps are often present. In addition to colon cancer, patients are at increased risk for ampullary, thyroid, central nervous system,
and gastric cancers. Children are also at risk for development of hepatoblastoma. Genetic testing may be performed if a proband has an identified gene after appropriate discussion with the child and family. Mutations in the APC gene are responsible for familial adenomatous polyposis and may be identified in 70% to 90% of patients. New mutations occur in up to 25% of cases. Screening colonoscopy should be performed yearly beginning at ages 10 to 14 years. Surgical consultation for timing and discussion of colectomy and options should also be obtained.

Lower GI tract bleeding may be seen with C. difficile colitis. Pseudomembranes may develop in association with toxins produced by this organism. Although originally associated with antibiotic use, C. difficile colitis occurs relatively often without the preceding use of antibiotics.

Rectal prolapse may cause blood in the stool. At times, sigmoidoscopy reveals a solitary rectal ulcer due to ischemia from repetitive episodes of prolapse. Rectal prolapse is often accompanied with a history of tenesmus and mucous. Hemorrhoids may accompany fissures but are a less common cause of bleeding in childhood.

Group A β-hemolytic streptococcus can cause a proctitis that can lead to blood in the stool. This condition is often present with moderate to severe erythema of the rectum and perianal area. Treatment with appropriate antibiotics is indicated.

Adolescents and Older Children
Causes of Upper GI Tract Bleeding

The most common causes of bleeding in this age group include esophagitis, gastritis, and ulcers, which have been discussed in the sections above. Variceal bleeding is another, less common, cause.

Esophagitis and gastritis due to nonsteroidal anti-inflammatory drug use may cause GI bleeding. Alcohol may also cause gastritis and should be considered as a cause of hematemesis in adolescents. The concentration of ingested ethanol needs to be 10% or greater for gastritis to develop. Alcohol use is also associated with prolapse gastropathy.

Ulcers and gastritis from H. pylori are more common in this age group. In addition, enteric infections, mentioned in the above section, are a common cause of hematochezia in this age group. Patients usually will present with cramping abdominal pain, tenesmus, and blood and mucus in the stool. Fever may be present with some of the bacterial infections, particularly from Salmonella. On occasion, cytomegalovirus and other viral infections may also cause significant bleeding.

Crohn disease and ulcerative colitis may present with melena or hematochezia. When bleeding is present, it may range from stools that are guaiac positive to massive hemorrhage due to extensive colitis or ulcerations that have eroded blood vessels. Rapid bleeding is more common in ulcerative colitis and Crohn colitis than with small intestinal Crohn disease. However, significant bleeding can occur from affected vessels in the small intestine with Crohn disease. Chronic blood loss is common with both diseases. Abdominal pain is often but not always present. Chronic blood loss may be suggested by the presence of a low mean corpuscular volume. Growth failure is more common in Crohn disease. Endoscopic studies are useful for diagnosis. Figure 7 shows pictures from the small intestine obtained during capsule endoscopy in a patient with chronic blood loss and anemia from Crohn disease. Differentiation between Crohn disease and ulcerative colitis helps to guide therapy, hence the need to obtain biopsy specimens during colonoscopy. Both diseases may have associated gastritis, which may also contribute to bleeding.

There are many other causes of GI bleeding in children. Common causes and some of the less common causes of GI bleeding in children at varying ages are listed in Table 1.

Pharmacologic Therapy

Upper GI tract bleeding related to acid secretion may be controlled by medications that suppress acid production. Intravenous H2-receptor antagonists and proton pump inhibitors may both be used. With acute bleeding of significant extent, proton pump agents given intravenously are generally used because they are more effective. A bolus
dose followed by continuous infusion of esomeprazole or pantoprazole may be considered. After significant bleeding, the chance for subsequent bleeding is greatest in the first 3 days, and use of intravenous proton pump inhibitors is usually continued during this time. After control of the bleeding, the patient may be switched to an oral agent for longer-term administration. Table 2 lists the doses of these agents.

Sucralfate may be useful for esophagitis and peptic disease. This aluminum salt is classified as a protectant and binds to the mucosal lining of eroded areas. Sucralfate forms a complex that protects the erosion from acid and helps the lesion heal. It also increases prostaglandin release, also helping with protection and healing. Sucralfate is available in both liquid and pill form. Doses are listed in Table 2.

Vasoactive medications, including vasopressin and octreotide, may be useful in controlling upper GI tract bleeding. Vasopressin has been used for variceal bleeding because it causes splanchnic vasoconstriction. Potential complications include cardiac toxic effects, such as infarction and arrhythmias, mesenteric ischemia, renal failure,

Table 2. Medications Used for Gastrointestinal Bleeding

<table>
<thead>
<tr>
<th>Agent</th>
<th>Drug Category</th>
<th>Dosagea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intravenous gastric acid inhibition (active bleeding) agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Histamine₂ antagonist</td>
<td>Continuous: 1 mg/kg followed by infusion of 2–4 mg/kg/d Bolus: 3–5 mg/kg/d divided every 8 hours</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>Proton pump inhibitor</td>
<td>Children &lt;40 kg: 0.5–1 mg/kg/d; &gt;40 kg: 20–40 mg/d Continuous dosing: bolus of 80 mg followed by 8 mg/h has been used in adults. This has been adapted in some centers to a bolus of 1 mg/kg followed by an infusion of 0.1 mg/kg/h (maximum to adult dose)/</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td>Proton pump inhibitor</td>
<td>Infants: 0.5 mg/kg/d Children 1–17 years old: &lt;55 kg: 10 mg; &gt;55 kg: 20 mg Continuous dosing: bolus of 80 mg followed by 8 mg/h has been used in adults. This has been adapted in some centers to a bolus of 1 mg/kg followed by an infusion of 0.1 mg/kg/h (maximum to adult dose).</td>
</tr>
<tr>
<td><strong>Intravenous vasoactive agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Octreotide</td>
<td>Somatostatin analog</td>
<td>1–μg/kg bolus (maximum, 50 μg) followed by 1 μg/kg/h may increase every 8 hours to 4 μg/kg (maximum, 250-mg dose every 8 hours) Taper by 50% for 1–2 days when bleeding controlled by 50% every 12 hours</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>Antidiuretic hormone</td>
<td>0.002–0.005 U/kg/min for 12 hours then taper for 1–2 days (maximum, 0.2 U/min)</td>
</tr>
<tr>
<td><strong>Evidence-based standards are not well established for children.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral inhibitors of gastric acid secretion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Histamine₂ antagonists</td>
<td>2–3 mg/kg per dose 2–3 times a day (maximum, 300 mg)</td>
</tr>
<tr>
<td>Famotidine</td>
<td></td>
<td>0.5 mg/kg per dose twice daily (maximum, 40 mg daily)</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>Proton pump inhibitors</td>
<td>1–1.5 mg/kg/d 1–2 times daily (maximum, 40 mg/d)</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td></td>
<td>1–1.5 mg/kg/d 1–2 times daily (maximum, 60 mg/d)</td>
</tr>
<tr>
<td>Esomeprazole</td>
<td></td>
<td>Infants: 3.5–5 kg; 2.5 mg/d; 5–7.5 kg: 5 mg/d Children 1–11 years old: &lt;20 kg: 10 mg/d; &gt;20 kg 20 mg/d Children &gt;12 years old: 20–40 mg/d</td>
</tr>
<tr>
<td><strong>Oral adhesive protectant</strong></td>
<td>Local adhesive paste</td>
<td>40–80 mg/kg/d in 4 divided doses (maximum, 1 g per dose)</td>
</tr>
</tbody>
</table>

aDoses for these medications are often not well studied, and higher doses are sometimes used in individual cases by pediatric gastroenterologists. Adapted from Boyle J. Gastrointestinal bleeding in infants and children. Pediatr Rev. 2008;29(2):39–52.
and cerebrovascular accidents. Octreotide has a vasodilatory effect on mesenteric vascular smooth muscle and reduces portal blood flow. Experience with this agent is limited in children, but it may be helpful in selected patients. Octreotide is helpful in controlling variceal bleeding. Octreotide may also be helpful in controlling other causes of upper GI tract bleeding, particularly in patients who are not able to undergo endoscopy or in whom endoscopy has been unable to determine or successfully treat the cause of bleeding. Adverse effects include bradycardia and problems with hyperglycemia. Overall, it has fewer complications compared with vasopressin. Octreotide is given first as a bolus dose followed by continuous infusion. The dose is tapered after bleeding has been controlled. Medication doses are listed in Table 2.

Overall, medications in combination with endoscopy are at times effective in controlling GI bleeding. However, sometime such measures are ineffective. Arteriographic embolization has been reported to control GI bleeding due to vascular anomalies. Surgery may be indicated when bleeding cannot be effectively controlled by medications or endoscopy. With portal hypertension, portosystemic shunts may be useful.

Conclusions
Practitioners caring for children should be familiar with the diagnosis and treatment of gastrointestinal bleeding. The initial goals are to establish the extent and severity of the bleeding and, when indicated, to hospitalize and stabilize the patient as quickly as possible. Once stabilized, diagnostic testing with a variety of modalities is indicated to establish the cause of bleeding. Endoscopic studies are often used to help determine the site of bleeding and for therapeutic intervention in specific cases. Newer diagnostic modalities, such as video capsule endoscopy and small intestinal endoscopy, may be useful when bleeding sites are unable to be detected. Pediatricians should be familiar with the common and some of the less common causes of GI bleeding in children and should also be familiar with medications used for these conditions.

Summary
- On the basis of strong research evidence, children with severe upper gastrointestinal tract bleeding should be treated with intravenous proton pump inhibitors.
- On the basis of some research evidence and consensus, children with severe gastrointestinal bleeding should be evaluated by endoscopy.

Suggested Reading
PIR Quiz Requirements

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1. A female patient with chronic abdominal pain and poor growth presents with melena and anemia. After endoscopy and colonoscopy fail to reveal a source of bleeding, a capsule endoscopy is attempted. Which of the following is a current limitation of the capsule endoscopy procedure?
   A. It cannot be used if bleeding is occurring at a rate faster than 0.1 mL/min.
   B. It cannot be used if child is younger than 2 years.
   C. It cannot be used if child is unable to swallow.
   D. It cannot be used if esophagogastroduodenoscopy results are equivocal.
   E. It cannot be used if previous capsule endoscopy has been attempted.

2. A 4-year-old boy presents with a 1-week history of intermittent painless rectal bleeding. The boy has no other symptoms, and the findings of physical examination, including absence of anal fissures and skin or oral lesions, are within normal limits. On colonoscopy, 2 polyps are visualized and removed from the distal colon, which on histologic analysis reveals dilated mucin-filled cysts and inflammatory infiltrates in the lamina propria. A total of 5% of children with these findings will develop which of the following conditions?
   A. Colon cancer.
   B. Dermoid tumors.
   C. Intestinal obstruction.
   D. Recurrent polyps.
   E. Small intestinal hamartomas.

3. A 2-month-old breastfed infant presents with a history of blood in the diaper and occasional vomiting. His growth is within normal limits but lower than expected. He has occasional vomiting, intermittent diarrhea, and occasional hard stools. Behavior and development are otherwise normal. He is slightly anemic and his eosinophil count is slightly elevated. Which of the following is the most likely explanation for these findings?
   A. Anal fissure.
   B. Esophagitis.
   C. Milk protein allergy.
   D. Meckel diverticulum.
   E. Vascular lesion.

4. A 14-year-old girl presents with hypotension, tachycardia, and melanotic stools. Which of the following should be initially performed?
   A. Begin octeotride IV.
   B. Begin vasopressin IV.
   C. Begin esoprazole orally.
   D. Establish IV access and begin fluid resuscitation.
   E. Begin oral Sucralate.

5. A 5-year-old boy presents with blood-streaked stools. On physical examination there is significant erythema surrounding the rectum in the perianal area. He is otherwise well except for pain and itching around the anus and some constipation. Which of the following is the most likely diagnosis?
   A. Anal fissure.
   B. Hemorrhoid.
   C. Perianal streptococcus.
   D. Rectal hamartoma.
   E. Rectal prolapse.
Gastrointestinal Bleeding
Gary A. Neidich and Sarah R. Cole
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