Gastrointestinal Bleeds

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PRACTICE GAPS

- Pediatricians should be aware that gastrointestinal bleeds (GIBs) (upper and lower) are not rare events. They are often not catastrophic and can be managed conservatively; however, they can be serious, requiring emergency measures.
- Pediatricians should realize that not all red or dark material in stool or vomitus is blood. Testing is required. There are separate guaiac tests for stool and vomitus.
- Pediatricians should be aware that for the range of causes of upper and lower GIBs, there are endoscopic, imaging, and surgical techniques for identifying the source of bleeding.
- Pediatricians should realize that GIBs are often self-limited. For GIBs that do not stop on their own or stop incompletely, there are medicinal, radiologic, and endoscopic methods of achieving homeostasis. Surgical intervention is a last resort.

OBJECTIVES *After completing this article, readers should be able to:*

1. Know the potential causes and sources of upper and lower gastrointestinal (GI) bleed in the pediatric population in various age groups.
2. Be able to list the causes of red or dark stool that can mimic blood in pediatric patients.
3. Learn the approach to investigation and management of acute and chronic GI bleed in children.
4. Be aware of the role of the latest laboratory, imaging, and endoscopic technologies in the approach to occult GI bleed.

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ABBREVIATIONS

CD	Crohn disease
GI	gastrointestinal
GIB	gastrointestinal bleed
HAEC	Hirschsprung-associated enterocolitis
IBD	inflammatory bowel disease
IC	indeterminant colitis
LGIB	lower gastrointestinal bleed
NEC	necrotizing enterocolitis
RBC	red blood cellUC ulcerative colitis
UGIB	upper gastrointestinal bleed

DIAGNOSIS

Gastrointestinal bleeding (GIB) in a child, whether through the mouth/nose or through the anus, is not a rare event. GIB varies from life-threatening variceal bleeding that requires urgent endoscopy to minor occult bleeding due to milk protein intolerance that is treated with dietary interventions. A systematic approach to the initial response and diagnosis will almost always result in finding the cause of the bleeding and an appropriate treatment. In this article we

review the presentation, causes, investigations, and treatments of upper GIB (UGIB) and lower GIB (LGIB). (Table 1)

Assessment

The first and most important assessment is whether a child is hemodynamically unstable or is at risk for becoming unstable. If stable, investigations and planned interventions can occur without excessive time pressure. If the child is not hemodynamically stable, then the child must be stabilized. Initial measures include ensuring an airway, inserting 2 large-bore intravenous lines, and resuscitating with normal saline or lactated Ringer solution. Transfusions may be indicated, based on the clinical state, but should be approached with caution because the adult literature suggests that restricting transfusions might improve outcomes, (1) and having a lower hemoglobin threshold for transfusion did not affect outcomes. (2) Some centers use saline lavage to assess for UGIB, but this maneuver does not add information. Iced saline should not be used because it can lower the core temperature. In general, laboratory testing includes a complete blood cell count, platelet count, chemistries, liver function tests, blood urea nitrogen and creatinine levels, prothrombin time, and partial thromboplastin time. If the child likely has other comorbidities, then assessment for disseminated intravascular coagulation should also be considered.

If the child is stable or if steps to stabilize the child have been initiated, it is important to determine whether the bleed is truly from the GI tract. Nosebleeds, posttonsillectomy/adenoidectomy, dental bleeds, and hemoptysis can all lead to presentations that mimic a GIB. One should also determine whether the apparent bleed is truly blood. Ingested red crayon, red-colored beverages, beets, and medications containing red coloring can look almost exactly like red blood. Items that can mimic blood in the stool are listed in Table 2.

Testing for Blood

The most commonly used test (stool occult blood test) for GIB is based on a peroxidase reaction of hemoglobin that turns guaiac to a blue color on a test paper. The fecal occult blood test is inaccurate for gastric blood because the gastric acid can interfere with the reaction. The gastric occult blood test corrects for this by including sodium hydroxide in the test paper. Both the fecal and gastric tests can have false-positive results and false-negative results, so immunologic tests that measure heme and porphyrin are available to verify the results of guaiac testing.

The next step in the evaluation of GIB is endoscopy because it offers both the possibility of diagnosis and therapy. In high-risk adults with acute UGIB deemed to be at risk for further bleeding or death, endoscopy performed 6 to 24 hours after GI consultation showed no disadvantage to earlier endoscopy in terms of 30-day mortality. (3) This time frame for endoscopy is likely valid for children because it allows for stabilization and additional studies.

Investigating Obscure Sources of Bleeding

Infrequently, the source of a GIB is not readily apparent. Sources of obscure GIBs are typically in the small intestine, from the ligament of Treitz to the terminal ileum. The esophagus, stomach, and duodenum, as well as the entire

Table 1 . Definitions

Upper GI bleed	Bleeding proximal to the ligament of Treitz, duodenum, stomach, esophagus.
Lower GI bleed	Bleeding originates distal to the ligament of Treitz, small bowel, colon.
Occult GI bleed	Bleeding not visible to parent, patient, or physician, identified by positive fecal occult blood test. Leads to iron deficiency anemia.
Hematemesis	Vomiting blood. Source usually proximal to the ligament of Treitz. Blood is bright red, or if it is old or has been in contact with stomach acid, it can be "coffee ground" material.
Hematochezia	Bright red or dark blood per rectum. Usually colonic in origin but can be from upper GI bleed and still be bright red if the bleed is massive or there is rapid transit.
Melena	Black, tarry, foul-smelling rectal blood. Bleeding site is proximal to the ileocecal valve.
Obscure GI bleed	Documented persistent or recurring GI blood loss, the origin of which is not determined despite GI imaging and both upper and lower endoscopy.
Fictitious bleeding	Material from upper or lower GI tract that appears to be blood but proves not to be. Also, heterologous blood.

GI=gastrointestinal.

Table 2. Causes of Red or Dark Stool That Can Mimic Blood

Causes of red stool
Medications (cefdinir, vehicles with red dye)
Beets
Colored foods and drinks (snacks, drinks, and candies that contain red dye)
Causes of dark stool
Bismuth (Pepto-Bismol, Kaopectate)
Activated charcoal
Blueberries, dark chocolate, cranberries, spinach, grape juice
Iron

colon, must be carefully examined via endoscopy, making it unlikely that a source of bleeding would be missed. The small intestine can be visualized via capsule endoscopy. A capsule the size of a large vitamin pill is swallowed or can be endoscopically placed beyond the stomach. The capsule traverses the entire GI tract and sends images of the intestine to an external device. The capsule is expelled with a bowel movement and not retrieved. The images can be reviewed on a monitor. However, bleeding sites can be missed if there is no active bleeding or if the capsule fails to capture the location. If the site is found, the exact location in the GI tract may be difficult to pinpoint. There is no therapeutic option beyond a surgical approach as the capsule contains no capacity for an intervention. Balloon endoscopy, in which an endoscope is advanced stepwise through the small intestine, is not widely available for use in pediatric patients. If the appropriate expertise and equipment are available, this technique allows for examination of the entire small bowel. It is time-consuming but does have some therapeutic options as well as the ability to guide future surgery. (4)

Two radiologic techniques are used to identify obscure bleeding sources. The tagged red blood cell (RBC) scan uses technetium-99–labeled RBCs to identify sites of small intestine bleeding. The RBC scan can pick up a slow bleed as low as 0.1 mL/min. Angiography has low sensitivity of 40% to 70% and requires active bleeding of at least 0.5 mL/min. If a localized bleeding point is found, embolization can be performed at the time of angiography. (5)

A procedure now rarely used, but described in the past, entails the surgeon manually telescoping an enteroscope through the entire small bowel, either antegrade or retrograde, at the time of exploratory laparotomy.

Hemostasis

Both UGIBs and LGIBs in children are often self-limiting. So, the decision of whether and when to intervene must be made carefully. Medical hemostasis can be obtained by infusion of octreotide or vasopressin. (6) Some of the available modalities for controlling bleeding from the GI tract are listed in Table 3.

Surgery is rarely required, but when it is, the diagnosis is most often made before surgery. (8) The most common reasons for surgery are tumors, duodenal ulcers, vascular pathology for UGIBs, and ectopic gastric mucosa for LGIBs.

Table 3. Methods of Hemostasis

Embolization	Transcatheter arterial embolization performed by an interventional radiologist is useful if the site of bleeding is identified and localized.
Powder spray (7)	Endoscopically applied. Practical for upper and lower GI bleeds, especially when the bleeding is diffuse.
Adhesive	"Glue" such as cyanoacrylate applied endoscopically to bleeding lesion.
Endoscopic band ligation	A small rubber band is placed around a varix to occlude the vessel. Effective for treatment of esophageal or gastric varices. Can be used to stop bleeding or to prevent a nonbleeding varix from bleeding.
Injection sclerotherapy	Sclerosants such as ethanolamine, tetradecyl sulfate, or sodium morrhuate are injected into the varix to sclerose and obstruct the vessel.
Epinephrine injection	Dilute solution injected in and around the bleeding point. Used in conjunction with bipolar, monopolar cautery or with hemoclips.
Bipolar electrocautery	Direct application to the nonvariceal bleeding point. Better results when combined with epinephrine injection.
Monopolar electrocautery	Similar to bipolar but requires a grounding pad.
Argon plasma laser	Noncontact thermal method. Depends on local availability and expertise.
Hemoclips	Clips deployed either "through the scope" or "over the scope." Similar results as electrocautery when combined with epinephrine injection. Bleeding must be localized.

GI=gastrointestinal.

UPPER GIB

UGIB originates proximal to the ligament of Treitz, and areas of bleeding include the esophagus, stomach, and duodenum. UGIB is characterized by vomiting blood that can be bright red if there has been little to no contact with gastric acid or dark brown, coffee ground in appearance if there has been contact with acid. The stools have blood that can be occult or black (melena) and on rare occasions when the bleed is massive, red. Common clinical signs of UGIB include hematemesis (73%), melena (21%), and coffee-ground emesis (6%). (9) Worldwide pediatric mortality ranges from 2% to 15%, (10)(11) and this reflects the diversity of populations, the cause of the bleed, (11) and the competence of the endoscopist. (12) In the United States, an interrogation of the Pediatric Health Information System database found that there were 19,528 UGIBs between January 2007 and September 2015. Overall mortality was 2.07%; mortality in patients with the principal diagnosis of UGIB was 0.37%. (10) In this report, almost 55% were boys, the median age was 9 years, and nearly half had no documented complex chronic conditions, 30% had 1 or 2 chronic conditions, and 20% had 3 or more. The causes of UGIB vary with age (Table 4).

Neonates

UGIB in the first 28 days of life is rare. Most commonly, vomited blood or tarry stools are caused by swallowed maternal blood that occurs at the time of delivery or from the mother's breasts. Maternal blood is distinguished from infant blood by the Apt-Downey test, based on the fact that neonatal and young infancy blood contains fetal hemoglobin that is resistant to denaturation in an alkaline solution compared with adult blood. Fetal hemoglobin remains pink or red, and adult hemoglobin becomes brown. (13) True UGIB in the neonate is rare and generally occurs in sick newborns. It can be caused by gastritis, an ulcer, vitamin K deficiency, a vascular malformation, gastric duplication, congenital coagulation factor deficiency, and trauma caused by nasogastric tube placement. (10)

Infants, Toddlers, and Adolescents

After the neonatal period the etiology of an UGIB also varies with the site from which the bleeding occurs. The causes of bleeding can be considered as occurring in 2 categories: variceal bleeding or nonvariceal bleeding. Variceal bleeding occurs in children who have liver disease that results in abnormal flow around and through the liver because the liver is scarred and stiff. The stiff liver causes increased portal pressure and shunts blood to smaller vessels, which then become engorged. The increased pressure in these vessels can cause their rupture and bleeding. Portal vein thrombosis can produce a similar picture without primary liver disease. (14) The most common site for GI varices is the esophagus, but varices can also occur in the stomach and the duodenum. When a vessel ruptures, the bleeding can be large and catastrophic. Most often, children known to have liver disease undergo endoscopic monitoring with band ligation of enlarged vessels to prevent catastrophic bleeding. For children younger than 1 year it may be difficult or impossible to insert an endoscope with a banding apparatus, and in that instance, injection of a sclerosant is used for esophageal varices.

Children not known to have liver disease can present with variceal bleeding, especially if they have not had

Table 4. Causes of Upper Gastrointestinal Bleeding

AGE GROUP	COMMON	UNCOMMON
Neonate	Swallowed maternal blood Nasogastric tube placement trauma	Gastritis Ulcer Vitamin K deficiency Vascular malformation Gastric duplication Congenital coagulation factor deficiency
Infants		Varices Esophagitis
Toddlers	Caustic ingestion Esophagitis Foreign body ingestion	Varices Infections, candida Stress bleeding Vascular malformations
Adolescents	Medications Nonsteroidal anti-inflammatory drugs Corticosteroids Caustic ingestion Alcohol ingestion Foreign body ingestion Crohn disease *Helicobacter pylori* infection	Varices Tumors Stress bleeding

access to care. These children are often jaundiced and small for age, with signs of acute as well as chronic malnutrition.

Nonvariceal bleeding is generally less catastrophic and can be caused by esophagitis, Mallory-Weiss tears, gastritis, ulcers, arteriovenous malformations, caustic ingestions, and foreign body or substance ingestions.

Esophagitis

Esophageal bleeding occurs with erosive esophagitis. The cause is most often reflux of gastric contents into the esophagus. Esophagitis presents with long-standing pain, vomiting, and regurgitation. The vomiting can be bright red or coffee ground in appearance but rarely occurs as a major emergency. (15)

Caustic ingestions, either accidental in young children or intentional, such as a suicide attempt in teenagers, can cause lifelong disability and suffering. After a caustic ingestion, bleeding can be present immediately or, as a result of a perforation, can occur days later. (16) Ingestion of foreign bodies is common in children, and those associated with bleeding are sharp objects and button batteries that need to be removed endoscopically. Most button battery ingestions occur in children younger than 6 years and are a special case of foreign body ingestion because of the battery's composition and ability to cause an electrical discharge. This results in necrosis, and if the battery is left in the esophagus for any amount of time, it can cause a perforation. In rare instances, that perforation can result in an aorto-esophageal fistula from which bleeding is catastrophic. (17)

Esophageal infections, such as candida, can cause bleeding. Infectious esophagitis has been described due to fungi, viruses, bacteria, and yeast. Esophagitis due to these organisms is almost always in the context of an impaired immune system.

Mallory-Weiss tears are characteristically longitudinal intramural dissections in the distal esophagus and proximal stomach that are associated with a history of forceful retching, the tear likely resulting from increased intra-abdominal pressure. They may be the most common etiology of UGIB and have a low risk of severe hemorrhage. (18)

Gastric Bleeding

Gastritis refers to gastric mucosal injury associated with inflammation and most often is caused by drugs or toxins and rarely by ischemia in children. The most common agents include nonsteroidal anti-inflammatory drugs, corticosteroids, and large amounts of iron, as seen in accidental ingestions. Gastritis can also occur in children who are experiencing metabolic stress, as occurs in ICUs after central nervous system injury, thermal injury, or other life-threatening events. Crohn disease (CD) can cause hemorrhagic gastritis, as can infections such as cytomegalovirus or herpes, although rarely. Gastritis caused by *Helicobacter pylori* can be acute or chronic but is usually not associated with bleeding unless an ulcer is present.

Peptic ulcers can be caused by nonsteroidal anti-inflammatory drugs, binge drinking in adolescents, or *H pylori*. The bleeding can be profound if the ulcer overlays an artery. The most common cause of a peptic ulcer is *H pylori,* and treatment is eradication with antibiotics and acid suppression. (19)

Gastric tumors are rare in children; nevertheless, they can present with massive bleeding, as seen with inflammatory myofibroblastic tumors. (20)

Duodenal Bleeding

The most common source of bleeding in the small bowel is a peptic ulcer caused by *H pylori*. The bleeding from *H pylori* infection can present as iron deficiency anemia with heme-positive stools or as a massive bleed if the ulcer overlies an artery.

Arteriovenous Malformations

The International Society for the Study of Vascular Anomalies defines vascular anomalies as a group of common and rare disorders of blood vessel growth leading to identifiable vascular lesions and their associated deformities. (21) Vascular abnormalities can be complex, widely distributed throughout the body, and associated with specific inherited syndromes, and they may have malignant potential. Some are associated with GIB, and that bleeding can present with visible blood or can be occult and present with anemia. Vascular malformations are found throughout the GI tract and are not a common cause of GIB in children. The most common vascular anomalies in children associated with bleeding include hemangiomas, blue rubber bleb nevus syndrome (cavernous hemangioma), and, rarely, gastric antral ectasia and Dieulafoy lesion (abnormally large artery that penetrates the gut wall). The diagnosis of an arteriovenous malformation is made endoscopically or radiologically. (22)

LOWER GIB

LGIB can vary from occult blood loss to massive, life-threatening hemorrhage. Symptoms likewise vary from being asymptomatic to excruciating pain. Whenever faced with a GIB, the first thing to determine is whether the patient is stable (see the Assessment subsection previously herein) (Table 5).

Melena Neonatorum

The most common reason for melena in a neonate is swallowed maternal blood that occurs during delivery or during breastfeeding. This condition, along with the test used to distinguish the baby's blood from the mother's blood was described by Leonard Apt in 1955. (13) The test, which bears Dr Apt's name, is described previously herein.

Anorectal Conditions

Anorectal fissures are the most common cause of true LGIB in children. They generally occur in children 6 to 24 months of age but can occur at younger and older ages. Anorectal fissures are frequently associated with constipation and the passage of hard stool, but they can also occur with diarrhea or simple failure to relax the anal sphincter during toilet training. Fissures are usually, but not always, painful. The blood is typically bright red and streaked on the outside of the stool. Diagnosis is by history and careful examination. Examination may need to be performed by the parent because examining the anal area of a toddler who has experienced pain with bowel movements may not be possible in an office setting.

Fissures most often respond to stool softening if associated with constipation or to maintaining a dry rectal area if diarrhea is the initiating factor. In fissures resistant to treatment, nifedipine gel with lidocaine has been successfully used. (23) Suppositories and other rectal manipulations should be avoided because they may cause more damage, physical or psychological.

Solitary Rectal Ulcers

Solitary rectal ulcers are uncommon during childhood, presenting as rectal bleeding. They are separate from inflammatory bowel disease (IBD) involving the rectum and from infectious proctitis. Solitary rectal ulcers cause rectal bleeding, tenesmus, and sensation of incomplete evacuation. The etiology is unclear but may be related to rectal prolapse. Despite its name, there can be 1 or more rectal ulcers, mucosal thickening, and polypoid lesions. Treatment has limited success. Constipation should be treated and avoided. Biofeedback has been attempted. Surgery is reserved for the most severe cases. Symptoms often persist despite treatment. (24)

Food Protein–Induced Allergic Proctocolitis (Milk Allergy)

Food protein–induced allergic proctocolitis is a common reason for fecal blood in otherwise well neonates and infants. It usually begins at approximately 2 weeks of age and lasts up to 1 year of age. It is a non–IgE-mediated allergy. Cow milk and soy proteins are the most common antigens. It occurs in both formula-fed and breastfed infants. In breastfed infants the reaction is presumably due to antigens that are transmitted via the breast milk. The quantity of blood is small to moderate and can result in anemia. Because these infants are otherwise well and are thriving, some have suggested not intervening; however, most clinicians recommend treatment by eliminating the antigen from the infant's diet. Diagnosis is through a suggestive history and physical examination and response to eliminating the offending antigen. In equivocal cases a

Table 5. Causes of Lower Gastrointestinal Bleed by Age

AGE GROUP	COMMON	LESS COMMON
Neonates (0–30 d)	Swallowed maternal blood Anorectal fissures FPIAP (milk allergy) Necrotizing enterocolitis Midgut volvulus	Vascular malformation Hirschsprung enterocolitis Intestinal duplication Coagulopathy
Infants (30 d–1 y)	Anorectal lesion Midgut volvulus Intussusception Meckel diverticulum Infectious diarrhea FPIAP (milk allergy)	Vascular malformation Intestinal duplication Thrombocytopenia
Children (1–12 y)	Juvenile polyps Meckel diverticulum Intussusception Infectious diarrhea Anal fissures Nodular lymphoid hyperplasia	IgA vasculitis (HSP) Vasculitis Inflammatory bowel disease Solitary rectal ulcer
Adolescents (12–21 y)	Inflammatory bowel disease Polyps Hemorrhoids	Arterial vascular malformation Adenocarcinoma IgA vasculitis (HSP) Solitary rectal ulcer

FPIAP=food protein–induced allergic proctocolitis, HSP=Henoch-Schönlein purpura, IgA=immunoglobulin A.

rectal biopsy will reveal eosinophilic infiltration; however, this is rarely necessary. Skin allergy testing is not recommended. For the formula-fed baby, treatment consists of changing to a hypoallergenic or amino acid–based formula for the first year of life. Introduction of solid foods progresses normally during the second 6 months of life, ensuring that various food antigens, including the offending ones, are introduced slowly. For the breastfed infant, if the mother chooses to continue breastfeeding, she should eliminate cow milk protein and soy protein from her diet. If these eliminations do not result in resolution of symptoms, further restriction may be necessary. This process of eliminations can be prolonged and onerous because it may take weeks before the infant's stools become free of blood. The condition resolves by 12 to 18 months and usually is not a harbinger of future disease. (25)

Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is predominantly a disease of premature newborns. Only approximately 10% of cases occur in term infants, and of those, most have an underlying predisposing condition such as congenital heart disease or sepsis. NEC is an emergency. There is severe ischemic necrosis and inflammation of intestinal mucosa. Enteric gas-forming organisms cause pneumatosis of the bowel wall and gas in the vascular system. Early detection and aggressive treatment have improved the outlook for infants with NEC. (26) For the purpose of this review, severe NEC can present with an LGIB; however, a comprehensive discussion of NEC is beyond the scope of this review.

Midgut Volvulus

Midgut volvulus occurs when the GI tract twists around the mesenteric root. This results in occlusion of the superior mesenteric artery and subsequent ischemia of the GI tract from the distal duodenum to the midtransverse colon. Midgut volvulus is a surgical emergency. If resection of the entire midgut is necessary, an extremely short bowel will result. Malrotation is the underlying cause in 45% of patients. The remainder are idiopathic, due to adhesions or a Meckel diverticulum. Midgut volvulus is most frequent during infancy but has been reported at all ages. Symptoms of abdominal pain, bilious vomiting, and distention are nonspecific and rapidly progressing. Rectal bleeding is a late sign and indicates vascular compromise. Abdominal radiography usually demonstrates proximal (stomach and duodenum) dilation with a paucity of gas distally. An upper GI series shows the "corkscrew" sign and is 96% sensitive. The corkscrew sign is the appearance of the distal duodenum and proximal jejunum on contrast studies of midgut volvulus. The ribbonlike loops spiral downward on their shortened mesentery. Management is urgent surgical consultation, evacuation of the stomach, fluid resuscitation, and surgery as quickly as possible. (27)

Intussusception

Intussusception occurs when a proximal segment of bowel invaginates into a distal segment. Typically, the distal ileum invaginates into the cecum; however, this location is not always the site for an intussusception to occur. The usual age of occurrence is 6 to 36 months, but cases in younger and older individuals are described. When intussusception occurs outside the usual age range, unusual lead points should be considered, including Meckel diverticulum, enlarged mesenteric lymph nodes, benign and malignant tumors of the mesentery or intestine, polyps, ganglioneuromas or hamartomas associated with Peutz-Jeghers syndrome or neurofibromatosis, mesenteric or duplication cysts, submucosal hematomas that are associated with Henoch-Schönlein purpura or coagulation dyscrasias, or ectopic gastric or pancreatic tissue. In the past, the presentation was the classic triad of severe, intermittent abdominal pain, sausage-shaped abdominal mass, and currant jelly stools. Abdominal ultrasonography is close to 100% accurate, and for this reason early diagnosis is now common and currant jelly stools of the classic triad are seldom encountered. An air enema is almost always successful in reducing an intussusception. Infrequently, if enemas fail, surgery is needed. Recurrences are frequent. (28)

Meckel Diverticulum

Meckel diverticulum is a remnant of the yolk sac that remains attached to the intestine. The "rule of two" is not always accurate but is an easy way to remember the basics: Meckel diverticulum occurs in 2% of the population; there is a 2:1 male-to-female ratio; it occurs within 2 feet of the ileocecal valve; it is 2 inches long; 2% of individuals with a Meckel diverticulum will develop complications; and complication usually occur before 2 years of age. A symptomatic Meckel diverticulum causes painless rectal bleeding when the ectopic gastric mucosa bathes the intestine with acid and causes ulceration. Bleeding can be profuse to occult. Diagnosis is with a technetium-99 scan enhanced with cimetidine, glucagon, or gastrin. The dye collects in gastric mucosa. A Meckel diverticulum that does not have ectopic gastric mucosa will not be visualized by this type of scan. However, a diverticulum without gastric mucosa

is unlikely to bleed. Treatment is surgical. If a Meckel diverticulum is still suspected despite a negative scan, exploratory surgery can be considered. (29)

Infectious Causes of LGIB

The infectious agents that cause LGIB are actually quite limited. They include *Clostridioides difficile*, *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, *Escherichia coli* O157, cytomegalovirus, and parasites.

Usually, diarrhea is the main manifestation caused by infectious agents. The presence of blood in the diarrhea documents that there is severe mucosal inflammation and ulceration. With some exceptions, infectious diarrhea is self-limited and requires only supportive treatment. The exceptions are *C difficile*, *Entamoeba histolytica*, and cytomegalovirus. Infectious enterocolitis in the very young or immunocompromised individual may require antibiotic treatment.

C difficile is a complicated bacillus. It is an anaerobic, gram-positive, spore-forming, toxin-producing organism. Neonates and infants (up to 70% of infants) are colonized with *C difficile*, even toxin-producing organisms, and yet remain asymptomatic. Why this asymptomatic carrier state exists and when infants become susceptible is not known. However, the American Academy of Pediatrics Committee on Infectious Diseases discourages testing for and treating *C difficile* in children younger than 1 year. (30) Factors influencing disease-causing infection include 1) changes in the gut microbiota (this is commonly due to previous antibiotic treatment) 2) colonization with *C difficile*, 3) formation of toxins, and 4) injury to intestinal epithelium. In the past, *C difficile* was predominantly associated with previous antibiotic use and hospitalizations. However, community-acquired infection with and without a history of antibiotic use has become common. (31) *C difficile* infections in children aged 1 to 18 years is generally categorized as diarrheal disease, pseudomembranous colitis, or fulminant disease. The diarrheal category is the most common and includes fever, abdominal pain, and blood (only 14% of patients experienced blood). The pseudomembranous variety is seldom diagnosed in children because it requires an endoscopy, which is rarely indicated in pediatric *C difficile* disease. All patients with pseudomembranous colitis experience bloody diarrhea and frequently have significant loss of albumin as well. Fulminant disease includes ileus, toxic megacolon, hypotension, and shock. Diarrhea and blood loss may be absent. Aggressive treatment is required. Initial antibiotic treatment is with fidaxomicin, metronidazole, and/or oral vancomycin. Surgery may be necessary. With all types of *C difficile* infections, recurrences are common and may represent incomplete treatment or reinfection.

E histolytica is the predominant disease-causing amoeba. *E histolytica* causes bloody diarrhea in endemic areas and in recent travelers to those areas. There is little evidence that other types of amoebas contribute significantly to human GI disease. The infective cysts of *E histolytica* are transmitted via water, by contaminated food, and by fecal oral spread. In the GI tract the cysts metamorphose into trophozoites that invade the lining of the colon. In so doing the organisms cause tissue injury and increased secretions, resulting in bloody diarrhea. Amoebas can be detected in stool samples by microscopy, stool antigen testing, and stool polymerase chain reaction. Using a combination of serologic testing and polymerase chain reaction is the preferred testing strategy. Serum antibody testing does not distinguish between active infection and past contact with the parasite. *E histolytica* is susceptible to metronidazole and other antibiotics. (32) After a 10-day course of metronidazole, paromomycin is given to treat luminal parasites and to prevent relapse. In endemic areas, infestations with schistosomes or hookworm can cause rectal bleeding.

Cytomegalovirus can be a cause of bloody diarrhea in immunocompromised hosts. (33) It is frequently found in the context of ulcerative colitis (UC), where its symptoms replicate those of UC, making the etiology of the bloody diarrhea unclear. In elderly, immunologically healthy adults it can cause bloody diarrhea that is usually self-limited.

Polyps

A juvenile (hamartomatous) polyp is the most common reason for painless rectal bleeding in a child. Juvenile polyps are usually single, but as many as 5 may be present. More than 5 polyps suggests a congenital polyposis syndrome. Seventy percent of juvenile polyps are in the rectosigmoid region and sometimes can be seen protruding out of the rectum. Hamartomatous juvenile polyps have no malignant potential; however, when a polyp is suspected, a full colonoscopy should be undertaken because polyps can be found in any of the colonic segments. When found, all polyps (or as many as is clinically feasible) should be removed and retrieved for histologic examination. Histologic examination can exclude the rare instance of polyposis syndromes that carry malignant potential. Juvenile polyps can recur. Repeated colonoscopy with polypectomy is indicated for recurrent symptoms.

Nodular Lymphoid Hyperplasia

The GI tract is rich in lymphoid tissue, especially at the terminal ileum. Hyperplasia of this tissue is common in children and is a frequent normal finding on endoscopy and radiology. It can be associated with selective serum immunoglobulin A deficiency. (34) The lymphoid tissue may respond to viral or other stimuli to become hyperplastic. The hyperplastic tissue can act as a lead point for an intussusception, resulting in painless rectal bleeding. Whether lymphoid hyperplasia can bleed in isolation is controversial. If lymphoid hyperplasia is found via an imaging study in the face of LGIB, colonoscopy to rule out a malignancy or IBD should be performed.

Inflammatory Bowel Disease

IBD consists of 3 entities: UC, CD, and indeterminant colitis (IC). In IBD there is chronic GI inflammation, which can lead to a variable amount of GI blood loss. Although the etiology of IBD remains unknown there are several known components: genetic, immunologic, and microbial. Although IBD always involves the GI tract, extraintestinal manifestations are common. Peak incidence is between 15 and 30 years of age. Recently, very early–onset IBD has been the focus of clinical and research attention. Symptoms that begin before 5 years of age may be associated with immunodeficiency.

UC affects the colon but spares the small intestine. There are no skip areas. Mucosal inflammation starts at the distal colon, usually sparing the rectum, and continues with varying distance to the ileocecal valve. If the cecum is involved, there may be a degree of inflammation in the terminal ileum as well. This is thought to be due to cecal inflammatory agents refluxing into the terminal ileum and is termed *backwash ileitis*. The GI blood loss in UC can be extreme, requiring transfusions. In the worst cases, colectomy may be necessary.

CD includes Crohn enteritis and Crohn colitis. CD involves any portion or portions of the GI tract from the oral cavity to the anus. There is transmural inflammation, so perforation and abscess formation can occur. Stricturing is another consequence of the transmural damage. (35) GI blood loss in CD is usually not as severe compared with UC. However, long-term blood loss can lead to severe anemia.

The features of IC do not clearly permit categorization as UC or CD. Most often IC will eventually be recognized as CD.

IBD should be suspected in a teenager with chronic abdominal pain, diarrhea, blood in stool, unexplained anemia, weight loss or failure to gain weight, retarded growth or retarded pubertal development, and a positive family history. Definitive diagnosis is by way of endoscopy, usually both an upper endoscopy and a colonoscopy.

Hemorrhoids

Hemorrhoids are a common cause of anal bleeding in the general population but are exceedingly rare in pediatrics. Finding hemorrhoids in a child should suggest an alternative diagnosis, such as rectal prolapse, an anal skin tag, or an underlying disease such as chronic liver disease with portal hypertension. Hemorrhoids are swollen veins in the anal region. Those proximal to the dentate line are internal hemorrhoids; those below the dentate line are external hemorrhoids. External hemorrhoids are painful because of their cutaneous innervation. In adults, hemorrhoids are associated with obesity, constipation, and prolonged toilet sitting. An occasional older teenager might present with a true hemorrhoid. (36)

Vascular Malformations

Vascular malformations can occur throughout the GI tract and are not a common cause of GIB in children (see vascular malformation described in the section Upper GIB previously herein).

Hirschsprung-Associated Enterocolitis

Hirschsprung-associated enterocolitis (HAEC) is a dangerous complication of Hirschsprung disease. With improved care, mortality from HAEC has decreased from almost one-third of patients to less than 1%. Thirty percent of patients with Hirschsprung disease experience at least 1 episode of HAEC. It is characterized by severe explosive diarrhea, fever, vomiting, and abdominal distention. Rectal bleeding and shock may occur in the most severe cases. It occurs most frequently shortly after definitive pull-through repair of Hirschsprung disease, although it can occur before any surgical intervention (usually in neonates in whom the diagnosis of Hirschsprung disease has been missed), or even years after definitive repair. HAEC is thought to be a microbe-driven entity. Obstruction may lead to bacterial overgrowth and bacterial translocation. Microbial imbalance was present in a murine animal model. (37) Treatment is aggressive fluid resuscitation and broad-spectrum antibiotic coverage.

Intestinal Duplication

A duplication is a tubular structure attached to the intestine that can occur anywhere in the GI tract and can be multiple. The small intestine is the most common site, followed by the colon. Duplications can be asymptomatic or can present with symptoms suggestive of obstruction.

Duplications can contain gastric lining, which can mimic a Meckel diverticulum and present with painless GI blood loss. Duplications that contain gastric lining are detected via a technetium scan (Meckel scan). Treatment is surgical.

Bleeding Disorders

GIB can be a sign of a bleeding disorder. In particular, von Willebrand disease can present with UGIB or LGIB. If on the initial investigation a bleeding disorder is suspected, assistance from a pediatric hematologist should be sought.

Immunoglobulin A Vasculitis

Immunoglobulin A vasculitis (formerly known as Henoch-Schönlein purpura) is the most common cause of childhood vasculitis. Unlike other vasculitides, it is usually self-limited. It presents with 1) purpuric rash usually starting on the lower extremities and moving upward, 2) arthralgias or arthritis, 3) abdominal pain, and 4) renal disease. There is neither thrombocytopenia nor clotting factor abnormality. Intussusception or GI ischemia can result in hematochezia. Treatment is symptomatic. Use of corticosteroids is controversial but seems to relieve severe pain. The long-term outlook is good; however, patients should be followed for possible renal disease and hypertension. (38)

GI Tumors

Malignant tumors of the GI tract are rare in children, but 1 of their presentations is GI blood loss, either overt or obscure. Tumors of the GI tract can be primary or metastatic. The most prevalent are lymphoma, colorectal carcinoma, and carcinoid tumors. Patients with polyposis syndromes or IBD are at increased risk for malignancies.

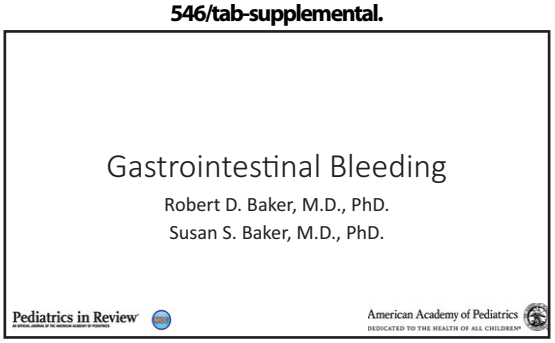
CONCLUSIONS

GIB in a child is not a rare event. Causes are numerous and vary from being of only minor consequence to being catastrophic. A measured plan of response and diagnosis can lead to the appropriate management. For major GIB, the patient should be stabilized before proceeding to diagnostic testing. An extensive history and thorough physical examination should be performed. A physical examination should include guaiac testing of stool and/or gastric contents. Endoscopy, both upper and lower, are the first-line diagnostic interventions. These procedures may offer a treatment as well. The differential diagnoses of UGIB and LGIB are broad but are important for defining management.

Summary

- Based on many observational studies (level B evidence), a gastrointestinal bleed (GIB) in a child is not a rare event, and the severity of GIBs varies widely. (11)
- Based on expert opinion (level D evidence), the first action taken when confronted with a GIB in a child is to ensure hemodynamic stability. (39)
- Based on many case reports and expert opinion (level B evidence), material presumed to contain blood should be tested to ensure that blood is truly present. (Stool occult blood test for stool and gastric occult blood test for vomitus. [40])
- Based on observational studies (level D), endoscopy to identify a source of bleeding can be delayed 6 to 24 hours after presentation to allow stabilization and initial laboratory testing. (12)
- Based on expert opinion and case studies (level D evidence), recent technologic advances, such as video capsule endoscopy and balloon-assisted endoscopy, have joined radiologic techniques, (41) such as tagged red blood cell scanning and arteriography, as ways to identify sources of occult GIB.
- Based on clinical trials and meta-analysis (level B evidence), hemostasis can be accomplished via medication, arteriography, and various endoscopic techniques. (42)(43) Surgery is a last resort.

To view teaching slides that accompany this article, visit https://pedsinreview.aappublications.org/content/42/10/546/tab-supplemental.



References for this article can be found at http://pedsinreview.aappublications.org/content/42/No. 10/546.

PIR QUIZ

1. You are seeing a healthy 6-year-old in your office because the mother called to say her child's stool is red. On physical examination he appears healthy and comfortable. Vital signs are stable, with a normal heart rate. The abdomen is soft, nontender, and without organomegaly. Stool that the mother brought is light red or pink throughout, but the guaiac test result is negative. After additional questioning, and before initiating additional testing or subspecialty referral, you recommend that the child discontinue consuming which of the following foods?

   A. Apple juice.
   B. Carrots.
   C. Cereals containing food dye.
   D. Licorice.
   E. Kale.

2. You are seeing a 2-week-old infant who was brought to the emergency department (ED) by his parents after vomiting "a large amount of blood." The infant was a full-term product of an uncomplicated pregnancy, labor, and delivery. The child received vitamin K shortly after birth. Mother and child were discharged after 2 days with the child breastfeeding. On physical examination, the infant appears well, with a heart rate in the normal range. The oropharynx is clear, but a second episode of bloody emesis occurred when the hypopharynx was examined. His hemoglobin level is 15.1 g/dL (151 g/L), and his hematocrit level is 45%. Which of the following tests will most likely identify the cause of hematemesis in this patient?

   A. Apt-Downey test.
   B. Guaiac test.
   C. Nasopharyngeal endoscopy.
   D. pH probe.
   E. Upper endoscopy.

3. An 8-year-old girl is brought to the ED with a history of melena and pallor. The child was previously healthy until the day of presentation, when the mother noted that the child appeared tired and pale during breakfast. An hour later, the child passed a thick black stool and had two episodes of hematemesis, which prompted the ED visit. The history is negative for vomiting or fever. Her medical history shows that she was a full-term product of an uncomplicated pregnancy, labor, and delivery. The mother and child went home on day 2. She has been well throughout her life and never required hospitalization or an ED visit. She is up-to-date on her immunizations. She takes no medications. On physical examination in the ED she is pale and tachycardic. She is awake, but tired. The abdomen is soft and nontender in the lower quadrants. A liver is not palpated, and there is no ascites. The spleen is palpable 6 cm below the lateral aspect of the left costal margin. There are no abnormalities of the skin and no evidence of digital clubbing. Her laboratory studies were as follows: hemoglobin, 5.6 g/dL (56 g/L); white blood cell count, 3,200/μL (3.2×10^9/L), with a normal differential count; platelet count, 93×10^3/μL (93×10^9/L); blood urea nitrogen, 8 mg/dL (2.86 mmol/L); and creatinine, $<$0.1 mg/dL ($<$76.25 μmol/L). Serum aminotransferase and bilirubin levels are within normal ranges. Which of the following is the most likely diagnosis in this patient?

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A. Arteriovenous malformation.
B. Hemorrhoids.
C. Meckel diverticulum.
D. Peptic ulcer disease.
E. Portal vein thrombosis.

4. You are seeing an 18-month-old boy in the ED with a history of passing a bloody stool earlier in the day. He was a full-term product of an uncomplicated pregnancy, labor, and delivery. He had no medical problems and was otherwise healthy before this episode of passing a bloody stool. Recent history is negative for vomiting, fever, irritability, or rash. His bowel movements have been regular, formed, and without visible blood before this episode. On physical examination he is comfortable and cooperative. He is mildly tachycardic. Capillary refill is less than 2 seconds. The abdomen is flat and soft, without tenderness or guarding. Neurologic examination findings are normal. The stool sample that the mother brought is black and the guaiac test result is positive. His hemoglobin level is 10.8 g/dL (108 g/L). Which of the following studies is most likely to establish the diagnosis in this patient?

   A. Abdominal angiography.
   B. Hepatobiliary iminodiacetic acid scan.
   C. Meckel scan enhanced with cimetidine.
   D. pH probe.
   E. Tagged red blood cell scan.

5. You are seeing a 13-year-old boy in the office with a history of passing a bloody stool. He has been healthy all his life. His history is negative for fever, nausea, vomiting, or rash. He takes no regular medications. Bowel movements are typically soft, formed, and occur once per day in the evening. This morning, however, he passed what seemed to be pure blood that frightened both he and his mother when they looked in the toilet. On physical examination, he is comfortable, alert and in no distress. Vital signs are stable, with a normal heart rate. Height and weight are both at the 60th percentile. The abdomen is flat, soft, and without tenderness or guarding. There is no hepatosplenomegaly. The perianal area was without erythema, fissure, skin tag, or external hemorrhoid. Skin is without rash or other abnormalities. His hemoglobin level is 14.8 g/dL (148 g/L). Which of the following is the most likely cause for this bleeding episode in this patient?

   A. *Clostridium difficile*.
   B. Internal hemorrhoid.
   C. Juvenile polyp.
   D. Meckel diverticulum.
   E. Ulcerative colitis.