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Gastrointestinal tumors in children and adolescents

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INDEX WORDS
Gastrointestinal tumors;
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Gastrointestinal stromal tumor;
Inflammatory pseudotumor

Tumors of the pediatric gastrointestinal tract are extremely rare. Their infrequent presentation at treatment centers has not allowed for the development of standardized treatment protocols and prospective review. The most prevalent gastrointestinal neoplasms and malignancies are described, including gastrointestinal lymphoma, colorectal carcinoma, carcinoid tumors, gastrointestinal stromal tumors, leiomyomas, juvenile polyps, inflammatory pseudotumors, gastric tumors, and Peutz–Jeghers polyposis syndrome. Current recommendations for the medical and surgical management of these tumors are reviewed and summarized for this vast group of gastrointestinal neoplasms in children.

Primary tumors of the gastrointestinal tract are rare in children. Historical surveys suggest that primary pediatric gastrointestinal malignancies represent less than 5% of all pediatric neoplasms.[1] Estimates of the prevalence of children with malignant tumors are 9 to 12 per hundred thousand.[2] A more recent study places the occurrence of these tumors at 1.2% of all pediatric malignancies.[3] Therefore, tumors of the gastrointestinal tract in children present infrequently at any single medical center or hospital. The true incidence for any specific neoplasm is truly unknown in the pediatric population. It is from the review of small case series and anecdotal reports that we hope to gain an improved understanding of these rare entities and determine the most appropriate intervention and treatment.

Methods

A retrospective review of gastrointestinal tumors of childhood and adolescence was performed at a single, tertiary care, children's hospital (Riley Children's Hospital, Indianapolis, IN). Patients treated from 1972 to 2005 were identified through search of hospital database and office patient files. Only patients whose tumors underwent surgical resection or had a definitive biopsy were included. Some patients included in this review have been described in previous publications.[4,5]

Results

A total of 58 cases of gastrointestinal tumors were identified over this 33-year time frame. The average age of the children was 13.8 years. There were 39 malignant tumors and 19 benign tumors (Figure 1). Lymphomas represented 54% ($n = 30$) of the cases, including 15 patients with Burkitt's lymphoma and 15 patients with non-Burkitt's, Non-Hodgkin's lymphoma (NB-NHL). Six patients had colorectal carcinoma, each in advanced stage (Dukes C or D). One of these children had acquired signet-cell colon adenocarcinoma 4 years following treatment for acute lymphocytic leukemia (ALL). Four patients had inflammatory pseudotumors (IPT) of the gastrointestinal tract, at the gastroesophageal junction, appendix, colon, and rectum.[5] Primary neu-

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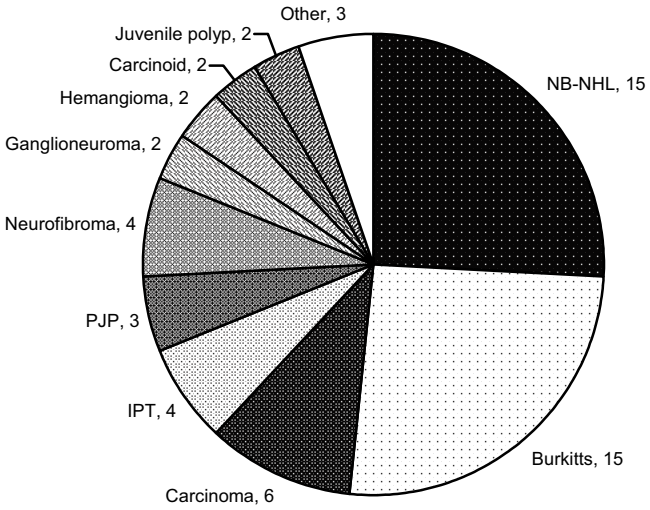

Figure 1 Gastrointestinal tumors of childhood, 1972 to 2005. NB-NHL, non-Burkitts's non-Hodgkin's lymphoma; IPT, inflammatory pseudotumor; PJP, Peutz–Jegher polyp.

rogenic tumors of the gastrointestinal tract were present in 6 patients. Four children had neurofibromas within the bowel wall and mesentery, and 2 children were diagnosed with ganglioneuromas, including 1 with ganglioneuromatosis of the entire colon (Figures 2 and 3). Hamartomas of Peutz-Jegher syndrome were encountered in 3 patients. Carcinoid tumors were identified in 2 children, with 1 patient having diffuse small intestinal, colonic, and retroperitoneal disease. The remaining tumors identified included juvenile colonic polyps (2), leukemic infiltrate of the intestine (1), gastric leiomyosarcoma (1), and hemangiomata (2).

Seven of the patients presented with signs of an intestinal obstruction due to an irreducible intussusception that required operative intervention for either resection or reduction. Subsequent identification of tumor was made by pathologic evaluation of the lead-point, either intraoperatively or on histological analysis of the intussusceptum. Four of the seven cases of intussusception had Burkitt's lymphoma as the pathologic lead-point. The diagnosis of Peutz–Jehger

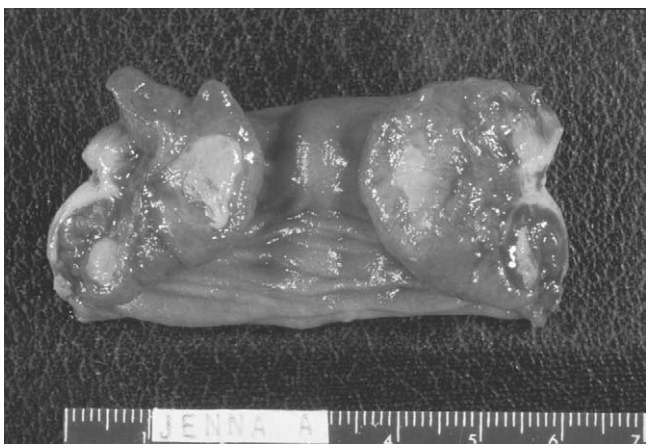

Figure 2 Ganglioneuroma of the small intestine.

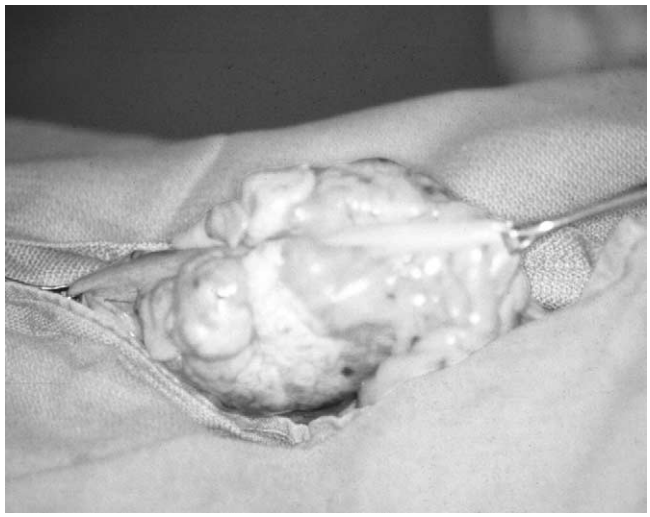

Figure 3 Neurofibroma of the colonic wall.

syndrome was made in two patients through the identification of a hamartoma as the lead-point of an intussusception and the additional polypoid lesions within the gastrointestinal tract. The remaining lesion presenting as intussusception was that of a small intestinal leukemic infiltrate.

Lymphoma

Non-Hodgkin's lymphoma (NHL) remains the most common malignancy of the GI tract in children. This observation, first made in the 1950s, has persisted in various publications on the subject since that time.[3,6-8] Although most commonly encountered in the terminal ileum and ileocecal area, this malignancy can occur in all portions of the gastrointestinal tract from the stomach to the rectum.[3,9,10] An increased incidence of this tumor has been reported in the Columbus Children's Hospital tumor data registry since 1982. Concurrent with this observation, the proportion of Burkitt's lymphoma has increased from 10% of reported gastrointestinal malignancies before 1982, to 50% currently. Burkitt's lymphoma remains the most common tumor of the small intestine and the second-most common pediatric tumor of the colon, after adenocarcinoma. This relative incidence of gastrointestinal tumors in children remains valid internationally. European data registries also show a similar incidence of NHL and anatomic distribution.[11] The male-to-female ratio in children is approximately 7:1.

Clinical presentation of gastrointestinal lymphoma varies from the presence of an occult abdominal mass to more urgent clinical signs of intestinal obstruction with bilious emesis or abdominal pain from possible perforation[3,4] (Figures 4A and B, and 5). As noted, the tumor may act as a lead-point for ileocolic intussusception and a small bowel obstruction[6,12] (Figure 6). Surgical intervention is focused on either complete resection or palliative intervention for the relief of bowel obstruction, in addition to a definitive tumor biopsy. Frozen section analysis of unexpected tumors

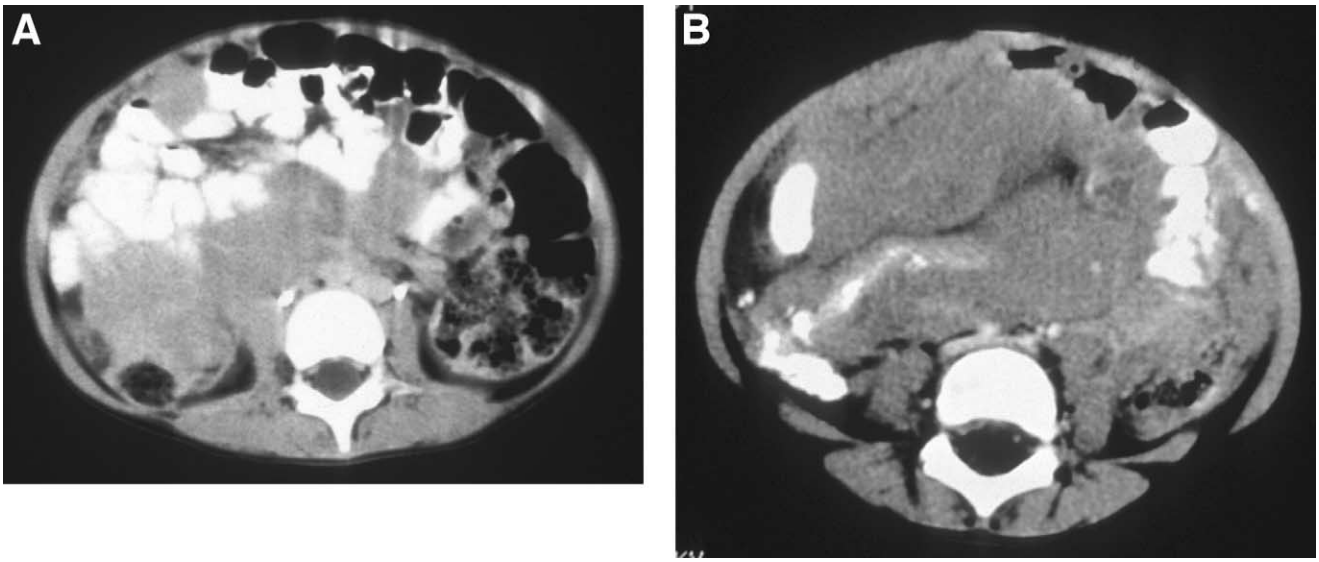

Figure 4 (A) Mesenteric involvement of Burkitt's lymphoma. (B) Ileocecal involvement of Burkitt's lymphoma.

should be obtained intraoperatively to make a correct diagnosis and determine appropriate therapy. The mainstay of treatment for isolated gastrointestinal lymphoma is complete surgical resection when possible, including excision of regional lymph nodes. Nearly 50% of children with gastrointestinal NHL will have tumor infiltrates confined to the gastrointestinal tract with possible regional lymph node involvement. Children that are amenable to localized resection have an 80% survival at 2 years. Those children with more extensive spread of disease have a 33% 2-year survival.[11] Historically, children with metastatic gastrointestinal NHL have been treated with a combination of surgery, adjuvant chemotherapy, and radiotherapy. Review of these reports offers neither a standard of care for these tumors nor a predictable outcome. Current chemotherapeutic agents employed in treatment often include cyclophosphamide, vincristine, doxorubicin, and high-dose methotrexate. Retrospective series have touted an improved survival of NHL of the stomach and cecum; however, more recent studies have not validated this observation.[11,13,14]

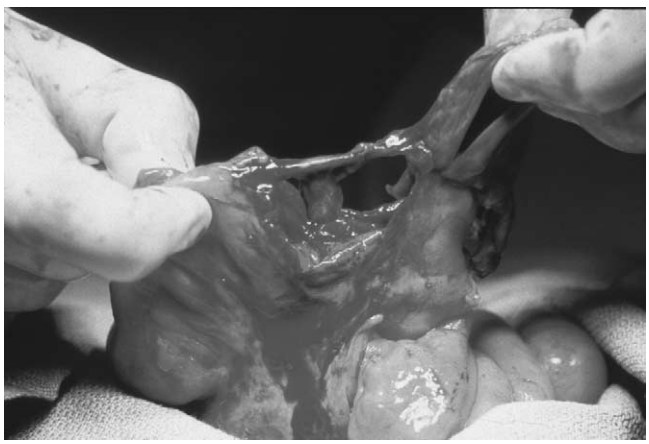

Figure 5 Intestinal perforation from Burkitt's lymphoma.

Isolated gastric lymphoma in children has been recently described in conjunction with infection from *Helicobacter pylori*. Although a causal effect has been identified in adults as to the development of a mucosa-associated lymphoid tissue (MALT) lymphoma from infection with *H. pylori*, no formal causation has been proven in children. Malignant degeneration is often isolated to the stomach wall, but cases of regional and distant metastasis have been reported.[15-17] Treatment of the inciting *H. pylori* infection is often curative for localized, low-grade MALT lymphomas in adults

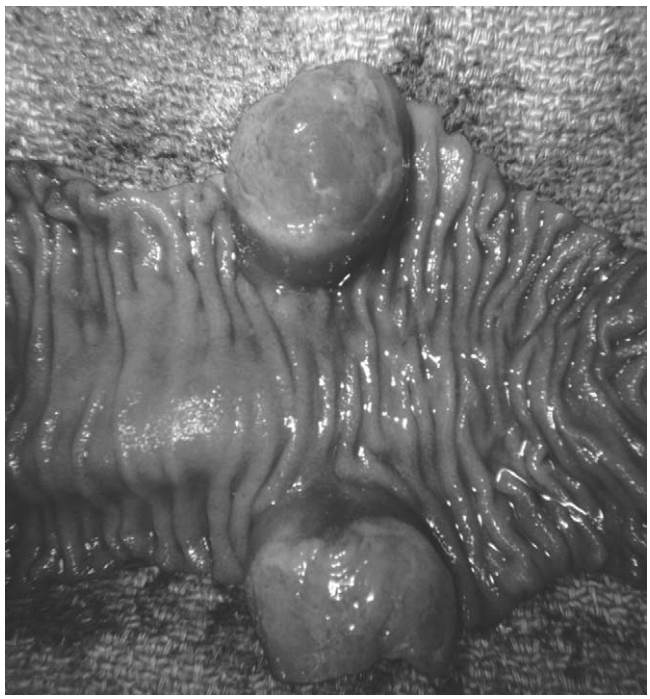

Figure 6 Intestinal lymphoma acting as a lead point for intussusception.

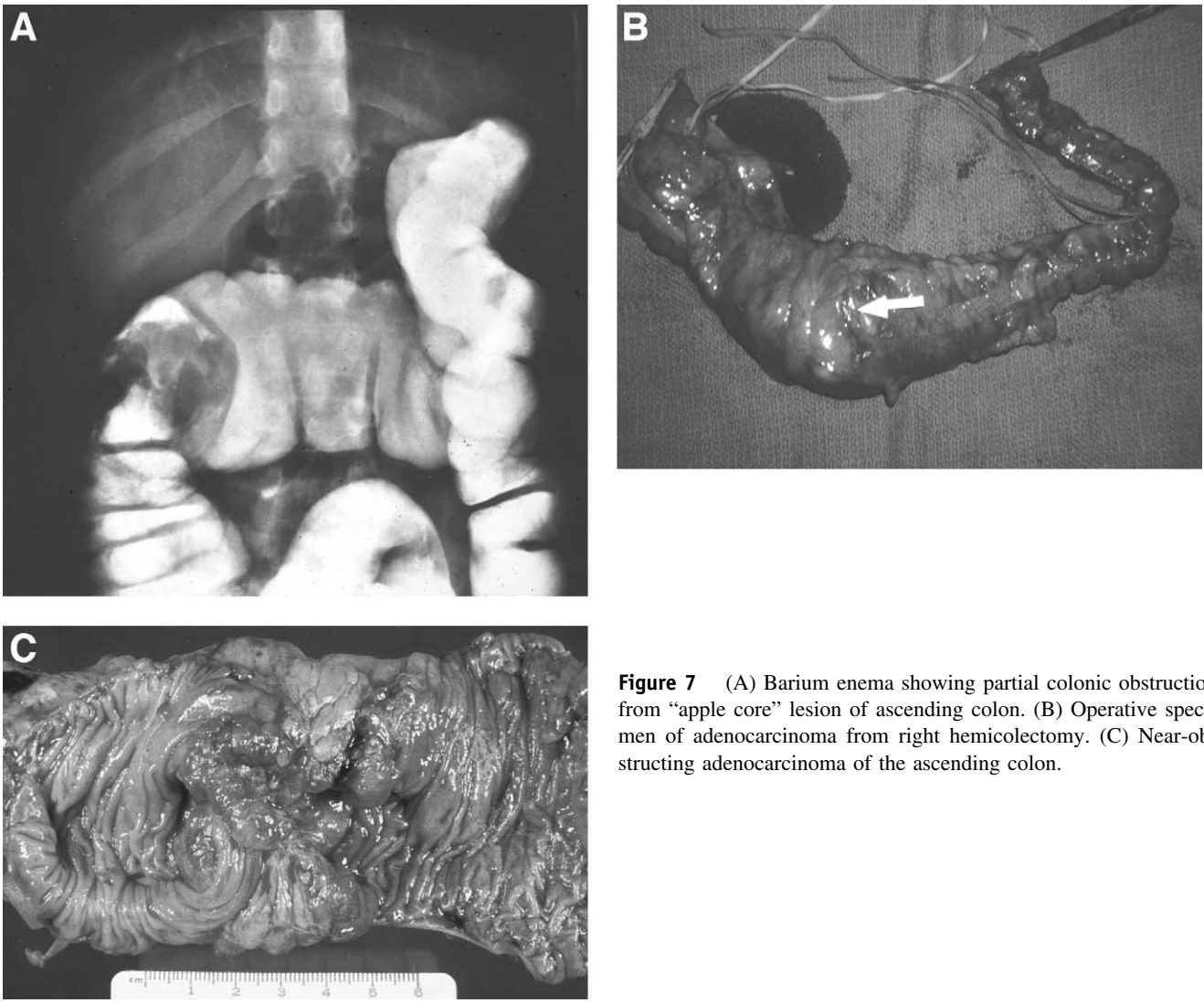

Figure 7 (A) Barium enema showing partial colonic obstruction from "apple core" lesion of ascending colon. (B) Operative specimen of adenocarcinoma from right hemicolectomy. (C) Near-obstructing adenocarcinoma of the ascending colon.

and children. However, more systemic treatment is required for recurrent or metastatic disease.[15-17]

Colorectal carcinoma

After primary liver malignancies, colorectal carcinoma is the second-most common solid malignancy of the gastrointestinal tract with an incidence of 1 to 8 cases per million children.[18-20] Though it constitutes the most common gastrointestinal carcinoma among adults, only 1% of colorectal malignancies are noted in patients less than 30 years of age. Even fewer cases have been documented for those less than 10 years of age.[21] The youngest patient diagnosed with colorectal carcinoma was a 9-month-old child, and it also has been described during fetal development.[22,23] A relative ratio for occurrence between boys and girls is approximately 2:1.

Colorectal cancer during childhood is associated with a poor prognosis. Although notable survival rates occur with this malignancy in adults, colorectal carcinoma in children is usually a fatal condition. The 5-year survival rate for children ranges from 7% to 12%.[24-26] This poor prognosis is related to delay in diagnosis, a greater virulence of these tumors, and the advanced stage of disease at the time of diagnosis.[24,26,27] Up to 50% of carcinomas that present during childhood are mucinous adenocarcinomas. This is in sharp contrast to findings in adults that often are affected with moderately differentiated adenocarcinoma. At the time of diagnosis, greater than 60% of children have evidence of metastasis to local lymph nodes and beyond.[24,27]

The principle presenting symptoms for children with colonic malignancy are abdominal pain and vomiting.[18,20,24] These nondescript complaints are often attributed to more common pediatric illnesses other than colon cancer. The delay in diagnosis of malignancy has been reported from 3 months to 6 years in duration.[26,28] Other symptoms common in adults, including abdominal distension, palpable abdominal masses, or change in bowel habits, are observed less frequently in children[24] (Figure 7A–C). Without a significant index of suspicion for this malignancy in children, delay in diagnosis is inevitable.

Reports vary with regards to the site of greatest involvement for colon carcinoma. A propensity for rectosigmoid disease is present in adult cases. Numerous reports concerning adolescent patients note a high predisposition for tumor occurrence in the sigmoid and transverse colon. This distribution has also been noted internationally in Japanese children with colorectal malignancy.[26]

The majority of cases of colorectal adenocarcinomas in the pediatric age group occur spontaneously.[6] Environmental factors are the most likely cause of this cancer with a Western diet felt to have the greatest influence.[24] Additional predisposing factors for colorectal malignancy have been noted in up to 10% of patients in reported series.[29,30] The presence of familial polyposis and other polyposis syndromes, ulcerative colitis, familial cancer syndromes, and familial occurrence of colorectal cancer notably increases the risk of its future development.[24,26,31] More recent reports have not demonstrated these predisposing health conditions within their patient cohorts.[25,32,33]

Surgical resection remains the mainstay of treatment for colorectal carcinoma in adult and adolescent patients. Complete tumor resection that includes the lymphatic basin of the affected colon and/or rectum has the greatest impact on overall survival. Total proctocolectomy is required for those patients with polypoid disease or ulcerative colitis because of a predilection for carcinoma of the colon. Unfortunately, the vast majority of cases of colon cancer in children have metastasized to lymphatic basins at the time of diagnosis. Adjuvant chemotherapy and radiotherapy are of little value in the treatment of colon cancer with distant disease. However, numerous reports describe the utilization of 5-fluorouracil and leucovorin-based chemotherapy for patients with Dukes stage C tumors. The data remain too sparse to allow for conclusions regarding the success of adjuvant therapy in children. Little to no benefit has been described in its utilization.[24,26,32] Although new data suggest a role for antiangiogenic therapy with the use of bevacizumab (Avastin®, Genentech, San Francisco, CA) in combination with chemotherapy for Dukes stage C lesions in adults, there are no data regarding their use in pediatric-aged colon cancer.[35]

Juvenile polyps

Juvenile polyps are hamartomatous lesions that present in both children and adults with a mean age of presentation of 18 years.[34] These lesions are more frequently found within the colon and rectum, but also may occur in the stomach, duodenum, and distal small intestine. They may present as single polyps in approximately 1% of children or as a rarer, diffuse polyposis of the gastrointestinal tract.[36] Juvenile polyposis has been classified into either juvenile polyposis of infancy, generalized juvenile polyposis, or juvenile polyposis of the colon.[37] Patients with juvenile polyposis of infancy often present with a protein-losing enteropathy, diarrhea, and hemorrhage, with death occurring before the age of 2 years. In the other two varieties, patients often present with anemia from rectal bleeding and prolapse of either the rectum or polyp.

In an extensive review of juvenile polyposis by Coburn and coworkers, common presenting signs for polyposis are anemia, gastrointestinal hemorrhage, prolapse, and intussusception.[34] The diagnosis is achieved with endoscopy and concurrent biopsy. Patients with polyposis often have diffuse gastrointestinal involvement with 50 to greater than 200 polyps identified.[36] A family history of polyposis or polypoid disease is present in 50% of these individuals.

Despite the wide-spread belief that solitary juvenile polyps do not have an increased risk of malignancy, case reports in adolescents have noted the presence of cancer.[36,38,39] This risk is amplified in patients with juvenile polyposis syndromes with an 18% to 35% risk of malignancy by an average age of 35 years.[40-42] It is hypothesized that the degenerative process from polyp to adenoma, adenoma to adenoma with dysplasia, and progression to carcinoma may occur in 1 in 1000 polyps.[43]

The treatment of patients presenting with either a single or few polyps is endoscopic polypectomy or local intestinal resection. Those with diffuse juvenile polyposis require both upper and lower endoscopic surveillance and polyp excision. With the theoretic risk of malignancy in each polyp, treatment of significant polyposis will mirror that of familial adenomatous polyposis syndrome with prophylactic proctocolectomy and ileoanal reconstruction by the second or third decade of life. Surveillance must be continued for evaluation of potential involvement of the foregut and small intestine in these individuals.

Carcinoid tumors

Carcinoid tumors in children are quite rare, and the true incidence is unknown. In a recent review of alimentary tract malignancies from pediatric oncology centers, the proportion of occurrence of carcinoid tumors in children was 16%, representing approximately 0.1% of all pediatric cancers.[3,44] Carcinoid tumors have been reported in children as young as 3 years of age, but are more prevalent in older children. An overall female-to-male ratio of 3:1 has been noted.[44]

Carcinoid tumors have been described in all portions of the gastrointestinal tract from the stomach to the rectum. Reports have also documented the presence of carcinoid tumors in gastrointestinal duplication cysts and Meckel's diverticulum.[6,45,46] These tumors are most prevalent in the appendix, followed by involvement of the small intestine. Fewer cases have been reported in the colon and rectum.[47] The diagnosis is often made through the incidental pathologic findings within an appendectomy specimen. However, these tumors may present with clinical signs of hematochezia or anemia from chronic gastrointestinal blood loss, localizing right-lower quadrant abdominal pain, and vomiting associated with small bowel obstruction.[6,44,48] The vast majority of carcinoid tumors are benign. Occasional tumors may be locally invasive, especially if originating from the

colon or small intestine. Few reports have noted their malignant potential in children, with metastasis to the liver, lung, and bone.[48] Additionally, the presence of symptoms of carcinoid syndrome, with cutaneous flushing, explosive diarrhea, asthma-like respiratory distress, and right-sided cardiac failure from serotonin hypersecretion is quite rare and anecdotal.[6,48,49]

No additional treatment is needed for incidental gastrointestinal carcinoid tumors without evidence of metastasis that are completely resected. These tumors are often less than 2.0 cm in diameter and have a low propensity for metastasis. Verification of adequate margins should be performed. For those tumors with evidence of serosal penetration or extension into the local mesentery, a bowel resection with associated mesenteric resection is required, along with abdominal surveillance for metastatic disease. Patients with tumors exceeding 2.0 cm in size should undergo thorough evaluation for possible metastases to the liver, lung, and bone.[44] Serum 5-hydroxyindolacetic acid (5-HIAA) levels may act as a serologic marker of disease, but are not present in all metastatic cases. Abdominal and thoracic computed tomography (CT) or magnetic resonance imaging (MRI) and ^{99m}-Technesium bone scan should be considered in patients with metastatic disease and/or bone pain. Children with metastatic disease often respond poorly to cytotoxic chemotherapy, similar to metastatic disease in adults. Symptomatic relief may be achieved through the administration of octreotide.[44]

Leiomyoma/leiomyosarcomas

Soft tissue sarcomas account for 7% of all childhood malignancies. Sarcomas with intestinal involvement comprise only 2% of this latter group.[50,51] These tumors of smooth-muscle derivation occur anywhere along the gastrointestinal tract. Whereas leiomyomas often involve the stomach and small intestine, leiomyosarcomas are more commonly found in the jejunum in children.[52-55] The age at presentation has varied from the newborn period to adolescence, with over half of the leiomyosarcomas occurring in the newborn period.

Histologic distinction between these benign and malignant entities may be quite difficult. The number of mitoses per high-powered field is considered the most useful criteria for the determination of malignancy. Following parameters established for adult-type tumors, tumors with 10 or more mitoses per 10 high-power fields often prove to be malignant with metastasis. However, nearly 40% of leiomyosarcomas present with less than 5 mitoses per high-powered field. Thus, determination of malignancy must also include pathologic features of tumor size, cellular atypia, tumor necrosis, and myxoid change.[56]

Smooth muscle tumors present with a variety of clinical signs and symptoms. These tumors may present as simple incidental abdominal masses in children. Other findings at presentation include occult or active gastrointestinal hemorrhage with anemia, intestinal obstruction, intestinal perforation, and the tumor as a lead-point for intussusception[57-60] (Figure 8). Symptomatic lesions may also present concurrently in patients with neurofibromatosis and in children with human immunodeficiency virus (HIV-AIDS).[61-63]

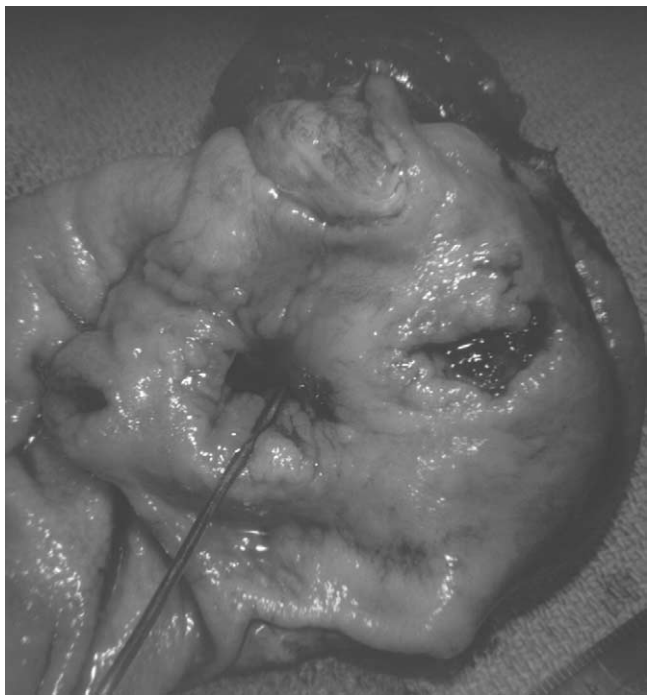

Figure 8 Leiomyosarcoma of the stomach with ulceration causing occult blood loss.

Surgical resection is the treatment of choice. Tumors that have elements of spindle-shaped cells and are of indeterminate malignant potential on intraoperative frozen section should undergo wide local excision with lymph node basin resection. Different from their adult counterparts, children with leiomyosarcomas are less likely to be found with metastases. En bloc resections may achieve complete tumor excision and offer the best outcomes.[53]

The use of adjuvant chemotherapy and radiotherapy has been only anecdotal in children. No standardized treatment with the use of these modalities has been offered to children. Few reports note a survival advantage using adjuvant therapy and thus this remains experimental.

The overall survival for benign tumors such as leiomyomas should be excellent provided that complete surgical excision is possible. The long-term outcomes for leiomyosarcomas correlate highly with the histologic virulence of the tumor. However, little long-term follow-up is available to generalize outcomes for this patient population.[52]

Gastrointestinal stromal tumors

Gastrointestinal stromal tumors (GISTs) are a unique variety of mesenchymal tumors that have only recently been described and eventually accepted by the World Health Organization as a distinct neoplasm in 1990.[64] These tumors lack evidence for differentiation from a smooth muscle or

Table 1 Current data and review of literature on sporadic pediatric GISTs*

Series	Case	Age (yrs)	Sex	Location	Outcome
Prakash et al.[66]	1	10	F	Stomach	AWD 24 mos
	2	10	F	Stomach	AWD 148 mos
	3	12	F	Stomach	AWD 80 mos
	4	12	F	Stomach	AWD 36 mos
	5	15	F	Stomach	DOD 138 mos
Kodet et al.[66]	6	15	F	Stomach	AWD 10 mos
Perez-Atayde et al.[66]	7	16	F	Stomach, Duodenum	NED 30 mos
Oguzkurt[66]	8	13	F	Stomach	NED 12 mos
Kerr et al.[68]	9	16	F	Stomach	NED 9 yrs
	10	13	F	Stomach	NED 8 mos
	11	11	F	Stomach	AWD 23 mos
	12	10	F	Stomach	NED 105 mos
Budzynski et al.[66]	13	14	F	Stomach	NED unknown
Haider et al.[66]	14	10	M	Stomach	NED 5 yrs
	15	11	F	Stomach	NED 20 mos
Karnak et al.[67]	16	0.8	F	Colon	NED unknown

*This list does not include pediatric GISTs occurring within Carney's triad. AWD, alive with disease; NED, no evidence of disease; DOD, dead of disease. (Reprinted with permission.[66])

neuron cell origin, but have characteristics of interstitial cells of Cajal.[65] Immunohistochemical and histologic analysis allows for their identification, but historically, these tumors may have been confused with tumors of either smooth muscle or neural origin.

In adults, GISTs are the most common nonlymphoid, mesenchymal tumors of the gastrointestinal tract. They are often benign neoplasms that occur after the third decade of life.[64] The occurrence of this tumor in children is rare with relatively few clinical reports documenting the tumor in the pediatric age group. In a recent study by Prakash and coworkers, approximately 1.4% of all GISTs are encountered in children.[66]

To date, only 16 childhood cases have been reported in the English literature[66,67] (Table 1). These tumors may involve any portion of the gastrointestinal tract. In children, the major site of occurrence is the stomach (88%). Tumors often occur in a multifocal distribution within the pediatric age group. GISTs have predominantly occurred in girls (94%). The presence of metastases at diagnosis has been reported in over 50% of patients less than 18 years of age, although this finding is less common in adults.

GISTs probably arise from interstitial cells of Cajal or their precursor cells. This hypothesis of origin comes from the similarity of ultrastructural features and their shared expression of the KIT receptor tyrosine kinase.[66] In adult cases, GISTs often have mutations in the KIT oncogene that encode for class III receptor tyrosine kinases, although this mutational description has not been proven in pediatric cases. Histologically, GISTs are composed either of spindle-shaped cells, epithelioid cells, or a combination of spindle and epithelioid cells. The majority of pediatric cases have either an epithelioid predominance or a mixed-cellular make-up. Mitotic activity rates are variable within the tumors, and cellular necrosis and hemorrhage are often observed.[64] Immunohistochemistry studies indicate that these tumors stain strongly positive for vimentin—CD-117, a *c-kit* proto-oncogene protein, and CD-34—and stain negatively for smooth muscle actin.[64]

Clinical presentation of GIST includes incidental abdominal mass, occult gastrointestinal bleeding, or signs of intestinal obstruction. Although most are commonly encountered within the wall of the gastrointestinal tract, they may also present within the mesentery of the intestine and the omentum. En bloc resection is the treatment of choice. At operation, assessment of regional lymph node involvement and metastasis to the liver should be accomplished. Postoperative surveillance is important. Tumor recurrence has been noted within the first 24 months, necessitating occasional abdominal re-exploration and resection.[68] Surveillance programs use both follow-up CT and PET scans to evaluate for intraabdominal recurrence. Due to the rarity of this tumor, a standard treatment for pediatric patients has not been devised. Adjuvant therapy often employs adult protocols with the use of imatinib mesylate (Glevac®, Novartis Pharmaceuticals, Basel, Switzerland) as a tyrosine kinase inhibitor.[66] Patients with persistent disease (incomplete resection) or metastases at diagnosis receive treatment. This experimental adjuvant treatment for GISTs remains under clinical trial.

Gastric tumors

A variety of tumors of the stomach in children have been described. The volume of published anecdotal and case reports of teratomas, carcinomas, and extra-pancreatic gastrinomas of the stomach implies an increased predisposition of these tumors for the stomach. Herein we summarize the reported literature for these rare tumors.

Teratomas are germ cell tumors that often arise in the ovary, testis, sacrococcygeal region, and mediastinum. The involvement of the stomach is quite rare and accounts for

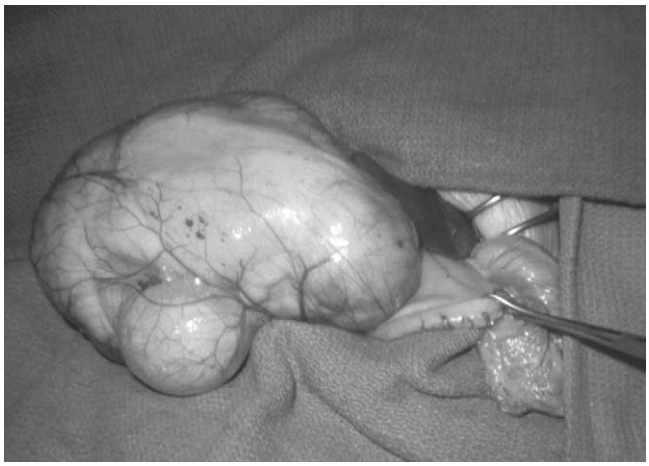

Figure 9 Gastric teratoma of the greater curve.

less than 1% of all teratomas[69,70] (Figure 9). These tumors are often composed of mature tissue elements; immature teratomas are a rare finding. Malignant degeneration has only been described in a few reports.[71] With the latest review, only 102 cases have been identified. The vast majority of cases occur in boys with only 5 reported cases noted in girls.[72] These tumors often present with an abdominal mass, but occasionally as a source of abdominal pain or extrinsic compression leading to outlet obstruction. Hematemesis has also rarely been observed. The treatment of gastric teratoma is complete resection, including a margin of stomach wall and any contiguous structures. To date, there have been no reported cases of recurrence following resection.[73] Adjuvant therapy with cisplatin-based chemotherapy is not recommended for mature or immature tumors, but may be advisable in cases of documented or presumed malignant degeneration. Case reports on the postresection treatment of these tumors as presumed malignancies based on elevation of serum alpha-fetoprotein levels remain anecdotal and nonstandardized. A good prognosis is noted for essentially all nonmalignant cases.[70]

Fewer than 25 cases of gastric adenocarcinoma in children have been documented.[74,75] The youngest presentation was in a child of 2.5 years old, but the median age of presentation among children is approximately 15 years.[76,77] Tumors occur within any portion of the stomach. Based on location, these malignancies may present with symptoms of dysphagia, abdominal pain, distension, anorexia, hematemesis, melena, hematochezia, and/or an abdominal mass.[75,77] Although carcinoma of the stomach may present from de novo degeneration, cases have been reported in association with polyposis syndromes and from the chemotherapy and radiotherapy treatment of lymphoma.[6,75,78] Additional cases of adenocarcinoma have been associated with vitamin B12 deficiency in children and gastritis associated with *H. pylori* infection.[79-81] With the rarity of these cases in children, the surgery and adjuvant treatment for these tumors is taken from adult patient series. Recent reports now support neoadjuvant treatment of gastric adenocarcinomas, despite their determined resectability.[75,82] Postoperative radiation therapy to the postresection field also improves overall survival.[83] Despite such aggressive intervention, the prognosis of children with gastric adenocarcinoma remains poor with median survival after resection of 5 months and only one child surviving more than 30 months after surgery.[77]

Even more rare tumors of the stomach have also been described in children. Tumors with gastroenteropancreatic hormone production, including amine precursor uptake and decarboxylation tumors (APUDomas), extrapancreatic gastrinomas, and vasoactive intestinal polypeptide tumors, have been documented in children.[32,49,84] Malignant mesenchymal tumors of the stomach, including malignant schwannoma, rhabdomyosarcoma, and leiomyosarcomas, have been reported as anecdotal reports of rare tumors. As experience with these tumors is rare, the principles of patient management and treatment parallel adult treatment protocols. The scarcity of these cases does not allow for conclusions as to their relative prognosis and survivability as compared with similar tumors in adults.[85-87]

Inflammatory pseudotumors

Plasma cell granulomas and inflammatory myofibroblastic tumors are synonyms for this solid tumor that is composed of spindle cells, myofibroblasts, plasma cells, and histiocytes.[5,88] Inflammatory pseudotumors most commonly present in the lung but have been reported in nearly every organ system. Its occurrence in the gastrointestinal tract is rare, with the majority involving the stomach[89] (Figure 10). The majority of children afflicted with this tumor are girls, as seen in our own series where all four patients were female.[5]

Abdominal pain is the most common presenting symptom for these patients. They may also present with dysphagia, intestinal obstruction, and iron-deficient anemia. Complete surgical resection is the treatment of choice. Anecdotal

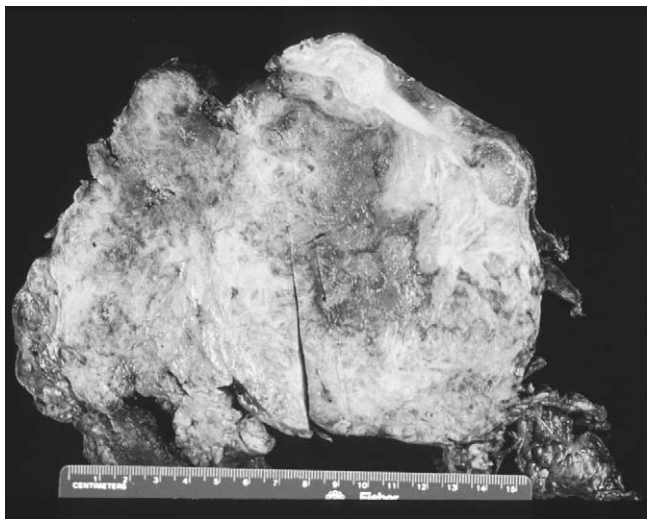

Figure 10 Inflammatory pseudotumor of the gastrointestinal tract.

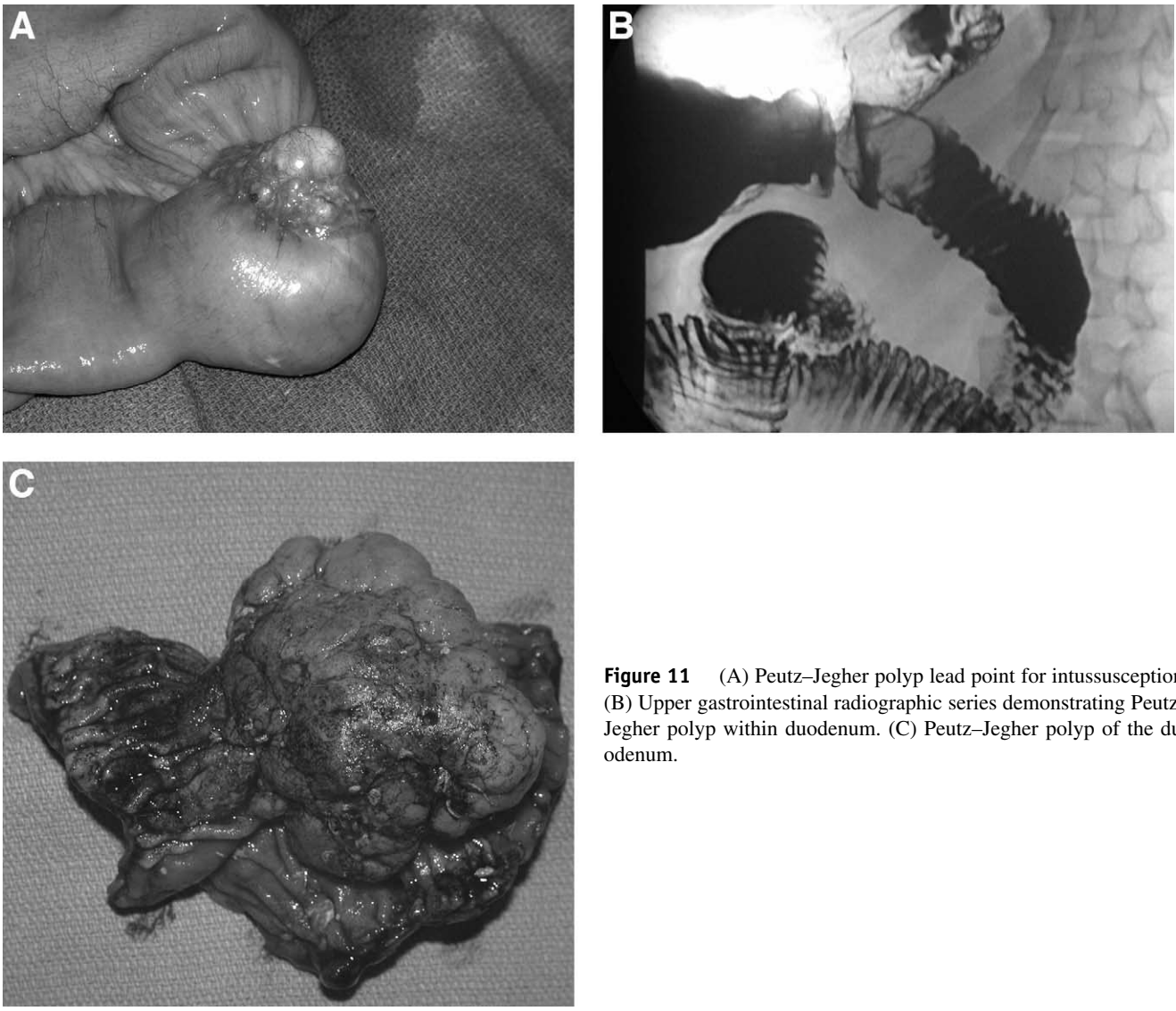

Figure 11 (A) Peutz–Jegher polyp lead point for intussusception. (B) Upper gastrointestinal radiographic series demonstrating Peutz–Jegher polyp within duodenum. (C) Peutz–Jegher polyp of the duodenum.

reports have also trialed the use of nonsteroidal and steroidal antiinflammatory medications for the treatment of large and unresectable masses with variable success.[90] Recurrence rates are reported between 18% and 40%, and are more common in extrapulmonary lesions. A higher rate of malignant transformation with multiple recurrences is also reported, with an overall mortality of 5% to 7%.[91,92]

Peutz–Jeghers syndrome

Peutz–Jeghers syndrome is an autosomal dominant disease characterized by mucocutaneous pigmentation and hamartomatous polyps of the gastrointestinal tract. The most common location of these polyps is in the small intestine, colon, and stomach, respectively. Fifty to sixty percent of patients will develop symptoms of polyposis by 20 years of age that include abdominal pain, recurrent intussusception, and gastrointestinal bleeding.[93] Consensus suggests that Peutz–Jeghers syndrome is a cancer predisposing syndrome that is now identified as a specific genetic mutation of the LKB1 gene encoding a serine/threonine kinase.[94] Although it is still debated whether there is an increased risk of malignancy within the gastrointestinal hamartomas from possible malignant degeneration, there is an increase in the risk of carcinoma of the small intestine and colon, along with the stomach, gonads (particularly the ovary), breast, pancreas, thyroid, and skin.[95,96] Screening protocols are recommended in the surveillance of these organ systems, including upper and lower endoscopy on a biannual basis.[94] Recommendations for the surgical resection of hamartomatous polyps without the presence of malignancy are that of polypectomy or very localized, conservative resection. With the presence of intussusception, as present in our series, the localized resection of the lead-point polyp along with any other synchronous lesions is warranted in this disease process (Figure 11A–C). Intussusception may be the sentinel event leading to the diagnosis of Peutz–Jeghers syndrome in children, as seen in two of our patients. Since the tumors

may recur, extensive bowel resection should be avoided to reduce the risk of subsequent short bowel syndrome.

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