CHAPTER 60
Peptic Ulcer Disease in Children

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Introduction

Peptic ulcer disease (PUD) results from a disruption in the mucosal lining of the stomach or duodenum, allowing penetration through the muscularis mucosa. Over the years, the causative role of *Helicobacter pylori* in the etiology of primary PUD has been proven. Despite increasing attention to PUD as a cause of abdominal pain in children, many cases of PUD in children are not recognized until they are complicated by haemorrhage, perforation, or gastric outlet obstruction. This is invariably associated with an increase in morbidity and mortality.

Demographics

PUD is an uncommon disease of childhood, with an estimated frequency of 1 case in 2,500 hospital admissions in the United States. Data for developing countries, especially from Africa, are scarce, but peptic ulceration is being increasingly recognized in children in the developing world. A prevalence rate of 2% has been found among children presenting with abdominal pain. The majority of cases are duodenal ulcers.

The male-to-female ratio for all childhood PUD is 1.5:1. However, no sex difference in the incidence of primary PUD has been noted in infants or young children.

Aetiology

Peptic ulcer diseases in children and adolescents can be classified into two aetiologies, primary and secondary.

Primary PUD is commonly associated with *H. pylori* infection. Primary ulcers are more likely to be chronic, more common in blood group O and may be familial in 30–40% of PUD cases. It may be associated with elevated serum gastrin level, but this finding is inconsistent in children.

Secondary PUD occurs as a result of accompanying stressful medical or surgical conditions. It may follow severe burns (Curling's ulcer), severe head injury (Cushing's ulcer), and ingestion of nonsteroidal anti-inflammatory drugs (NSAIDs). Mucosal ischaemia, in association with increased gastric acid and pepsin production, and with decreased prostaglandins and mucus production, has been implicated in the development of secondary PUD.

In general, PUD results from an interaction between protective forces that prevent a breach in the integrity of the gastric and duodenal mucosa and those that contribute to mucosal inflammation and ulceration (Table 60.1).

Table 60.1: Protective and disruptive mechanisms for PUD.

Protective Mechanisms	Disruptive Mechanisms
1. Secretion of water-insoluble gastric mucus and bicarbonate 2. Protective phospholipids 3. Rapid turnover of gastric mucosal cells 4. Normal mucosal blood flow 5. Inhibited acid secretion	1. Gastric hyperacidity 2. Acid-dependent pepsin 3. Mucosal ischemia 4. *Helicobacter pylori* infection 5. Sepsis 6. Traumatic injuries and burns 7. Drugs (steroids) 8. Alcohol 9. Cigarette smoking 10. Stress

Helicobacter pylori and Peptic Ulcer Disease

H. pylori, a gram-negative microaerophilic spirochete, has been implicated in the development of gastritis and peptic ulcer disease in both adults and children in the presence of acid and pepsin. *H. pylori* infection is mainly acquired during childhood. In India, almost 80% of the population has been infected by the age of 10 years, compared to less than 10% of the population in developed countries. *H. pylori* infection is thought to be transmitted mainly through the faecal-oral route in developing countries. Most infected individuals are asymptomatic; approximately 15% develop peptic ulcer disease and 1% develop gastric cancer. The organism has a unique ability to survive in the harsh acidic environment of the stomach by producing the enzyme urease, which allows it to alkalinize its microenvironment and survive for long periods of time. The organism also produces myriad other virulence factors such as catalase, vacuolating cytotoxin, and lipopolysaccharide. The organism has been classified as a class A carcinogen by the World Health Organization (WHO) because it has been causally associated with gastric carcinoma and lymphoproliferative disorders.

Clinical Presentation

History

A detailed history and physical examination are the mainstays of diagnosis, supplemented by diagnostic investigations where available. The most common symptom in PUD is abdominal pain. A high index of suspicion is necessary in children because abdominal pain is a common complaint; distinguishing the pain of PUD from other causes of abdominal pain is a major challenge. The child's inability to describe the symptoms very well may hinder the diagnosis. Not uncommonly, the diagnosis is not considered at all in children because PUD is thought largely to be a disease of adults.

The pain of PUD in toddlers and preschool age children is usually dull and vague, quite unlike what is described in adults, and may or may not be aggravated by food intake. The older child and adolescent may, however, present in the typical adult fashion with sharp and burning pain localized to the periumbilical or epigastric regions. The pain may exhibit periodicity with frequent exacerbations and remissions over weeks to months. There may be recurrent vomiting, leading to poor weight gain. Vomiting of food ingested over a few days should raise the suspicion of gastric outlet obstruction. A possibility of a family history of peptic ulceration should be sought as well as a history of ingestion of NSAIDs.

As in adults, PUD may be complicated by perforation, gastrointestinal tract (GIT) bleeding (hematemesis with melena), and gastric outlet obstruction. These complications may occur even in the absence of pain. Presentation in infants, particularly in neonates, is usually acute and may manifest as acute perforation or haemorrhage, even in the absence of recognizable stress.

The natural history of peptic ulcers in children has been well correlated with age. In early life (2–6 years), there is a tendency towards bleeding and perforation. In the age group of 7–11 years,

the ulcers are usually acute, often perforate, and only rarely bleed or become chronic. In children older than 11 years of age, the behavior of the ulcers approximates that seen in adults.

Physical Examination

A general physical examination in uncomplicated cases is usually not informative. Pallor may suggest blood loss. A combination of chronic epigastric or periumbilical pain and anaemia should raise a suspicion of PUD in a child. Careful inspection, auscultation, and palpation of the abdomen, including rectal examination, are important, although findings may be normal. Haemorrhage accompanies PUD in 15–20% of patients and may be severe enough to require blood replacement. Shock may result from haemorrhage.

Peritonitis resulting from perforation of the GIT occurs in about 5% of children with PUD.

Investigations

Due to the cost and lack of availability of resources, investigating a child with abdominal pain should be focused and targeted. The following investigations may be indicated:

- The haemoglobin level is used to diagnose anaemia and determine its severity. A blood film appearance may show hypochromic, microcytic cells suggestive of iron deficiency anaemia. Sophisticated laboratory tests to diagnose iron deficiency anaemia in chronic cases may not be available in the developing world settings.
- Oesophagogastroduodenoscopy (EGD) is the procedure of choice for detecting PUD in children and adolescents but is often unavailable in most African hospitals. An endoscopy can be performed safely in all paediatric age groups. It allows for direct visualisation of the ulcers; the location and the number can be determined and biopsy can be taken where necessary. In children with severely deformed duodenum or pylorus, there may be some difficulty in visualisation of the duodenum. Urease activity can also be assessed by EGD. Therapeutically, EGD allows for control of bleeding ulcers by using vasoconstricting agents such as epinephrine or by using a heater probe to coagulate the bleeding vessels. Monitoring of response and efficacy of medical treatment can also be done via endoscopy. For peptic ulcer disease in children, a definitive endoscopic and microbiological diagnosis is advisable.
- An upper GI series is an alternative to EGD where such facilities are not available, but it has a high false positive rate of up to 30%. Diagnosis is based on the demonstration of an ulcer crater and deformity of the duodenal cap.
- Serum gastrin estimation may be useful in cases of suspected Zollinger-Ellison syndrome.

Diagnosis of *Helicobacter pylori* Infection

Invasive and noninvasive tests are available for diagnosing *H. pylori* infection. Invasive tests require endoscopy and include rapid urease test (RUT), histopathology, and culture of gastric biopsy. The noninvasive tests, such as urea breath test and stool antigen detection, are used to determine eradication of infection following treatment, whereas serology is used for epidemiological studies but may be unreliable in children.

Medical Care

The initial treatment of PUD in children is medical. The treatment of PUD, as in adults, encompasses eradication of *H. pylori*. This is accomplished by a combination of medications to reduce acid production and/or improve the mucosal defense in combination with antibiotics. The success of histamine-2 receptor blockers and proton pump inhibitors (PPIs), and the eradication of *H. pylori*, has virtually eliminated the need for elective ulcer surgery. Although colonisation by *H. pylori* may be high, there is no evidence that eradication in an asymptomatic patient is warranted. PPIs have been found to be safe in children. Sucralfate, which is an aluminum salt of sulfated sucrose, may also be used. In the presence of acidic pH, sucralfate forms a complex, paste-like substance that adheres to the damaged mucosal area. This forms a protective coating that acts as a barrier between the lining and gastric acid, pepsin, and bile salts.

Recommended Eradication Therapies for *H. pylori* Disease in Children

First-line therapy is the use of one PPI and two antibiotics for 10 to 14 days. This can be either:

- omeprazole + amoxicillin + clarithromycin; or
- omeprazole + amoxicillin + metronidazole; or
- omeprazole + clarithromycin + metronidazole.

Second-line therapy is employed when there is no response to first-line therapy. It consists of either

- omeprazole + bismuth subsalicylate + metronidazole + amoxicillin or tetracycline for 14 days; or
- ranitidine + bismuth citrate + clarithromycin + metronidazole for 14 days.

Other drug combinations and durations of treatment are currently being evaluated.

For children in the developing world, cost may be a significant consideration in the treatment options available.

Management of Complications of PUD in Children

Surgical intervention is required in a small percentage of infants and in children with complications of PUD that include perforation, obstruction, intractable pain, and bleeding unresponsive to medical or endoscopic therapy.

Bleeding Peptic Ulcer Disease

Bleeding is the most common complication of PUD in children. Most cases are self-limiting and subside with conservative treatment. However, in an acute bleed, the most important clinical step is resuscitation and the restoration of blood volume. The following steps are critical:

1. Two large-bore intravenous catheters are inserted.

2. A bolus fluid of 20 ml/kg of crystalloid is infused rapidly to combat shock, and is repeated as necessary pending availability of cross-matched blood.

3. An appropriately sized urethral catheter is inserted to monitor urinary output. The urinary output, which may be all that is available in most centres in Africa, gives an estimation of organ perfusion as a response to the fluid resuscitation. An output of 1–2 ml/kg is considered satisfactory but should be used in concert with other clinical parameters. A central venous pressure monitor can be inserted where available. Complete blood counts and chemistry values are also determined.

4. A nasogastric tube (NGT) is placed as a way of performing lavage, preventing aspiration, and monitoring ongoing haemorrhage.

With these initial measures (steps 1–4), most bleeding peptic ulcers will subside.

5. Perform an endoscopy, if available, as soon as the patient is stable, usually within 24 hours of admission. Endoscopy confirms the diagnosis and may be therapeutic. Vasoconstrictive agents, such as epinephrine, 1 in 10,000 dilution, can be injected, and use of a heater probe, electrocoagulation, or photocoagulation can also be employed.

6. Angiography may be necessary in patients with a massive GI bleed in whom endoscopy cannot be performed. Angiography can depict the source of the bleeding, and allow for the direct injection of

vasoconstrictive agents. This is rarely available in resource-poor settings.

Rebleeding is reported to occur in 10–30% of cases and usually occurs within the first week after primary therapeutic endoscopy. Endoscopic treatment can be repeated for rebleeding.

Indications for surgery in bleeding PUD include:

1. failed endoscopic treatment;
2. identified arterial bleeding;
3. identified vessels at the base of the ulcer;
4. rebleeding; and
5. loss of more than 50% of the patient's estimated blood volume in a short period (i.e., 8–24 hours).

Choice of Surgery

Simple plication or oversewing of the bleeding source is usually all that is needed for peptic ulcers. A more definitive procedure, such as vagotomy and pyloroplasty, may be added if the patient is stable and fit. In patients with stress ulcers related to brain injury or burns, the procedure of choice may be vagotomy and antrectomy. Total gastrectomy is rarely performed to treat multiple gastric ulcers in paediatric patients.

Perforated Peptic Ulcer Disease in the Child

When perforation occurs, it is usually on the anterior wall of the first part of the duodenum, resulting in both chemical and bacterial peritonitis. Perforation is accompanied by the sudden onset of abdominal pain, vomiting, and generalised abdominal distention. Shoulder pain may be present due to diaphragmatic irritation. Examination of the acutely ill child reveals evidence of peritonitis with board-like rigidity and diminished bowel activity. In the infant, perforation may occur in the absence of any recognizable stress.

A plain abdominal x-ray may be helpful, as it may reveal pneumoperitoneum.

Late presentations are not uncommon in developing countries because of a lack of suspicion and poor access to health care. Late-presenting patients may be severely toxic and dehydrated, requiring urgent fluid resuscitation and correction of electrolytes and acid-base disorder. An NGT and urinary catheter should be inserted. The child should be started on broad-spectrum antibiotics. Surgery is performed as soon as the child is stabilized.

Operative repair of perforated ulcers may be performed by using a simple closure or oversewing. Where available, this may be accomplished laparoscopically. An omental patch (Graham patch) may be used to cover the area of perforation. This treatment should be followed by medical therapy. In a stable patient with chronic ulcer, a selective vagotomy or a bilateral truncal vagotomy with pyloroplasty may be added.

Gastric Outlet Obstruction

Gastric outlet obstruction occurs following chronic inflammation with fibrosis at the pylorus. This is often accompanied by acute inflammation and mucosal oedema, leading to luminal obstruction. Gastric outlet obstruction is an uncommon complication of PUD in children. It is characterized by recurrent episodic vomiting. The vomitus usually contains food residues eaten over the previous few days. The vomiting is characteristically projectile in nature. Weight loss is not uncommon, and in late presentation the child is severely dehydrated and pale.

Serum electrolytes characteristically show hypochloremic alkalosis with hyponatraemia and hypokalaemia. Blood gas analysis shows a base excess of more than +3. There may be hypoproteinaemia as a result of the malnutrition.

Diagnosis is usually confirmed by upper gastrointestinal series or endoscopic gastroduodenoscopy. A dilated stomach with narrowing of the pylorus and deformity of the duodenal bulb is typically demonstrated.

Treatment consists of aggressive resuscitation with crystalloid, ensuring adequate urinary output. Nasogastric decompression and lavage is necessary while the hypoproteinaemia and anaemia are corrected. In some instances, the nasogastric decompression and treatment with antiulcer drugs will allow oedema to subside enough for gradual introduction of oral feeds. Definitive therapy consists of bilateral truncal vagotomy with pyloroplasty or in the presence of severe fibrosis gastrojejunostomy.

Prognosis and Outcomes

Peptic ulcer is usually a benign disease without a high mortality if diagnosed and treated early. With modern therapy and eradication of *H. pylori*, the cure rate is more than 90%. Mortality rates remain highest in neonates as well as in infants and children with systemic illness or injury who present with acute bleeding or perforation.

Prevention

Prevention involves the avoidance of predisposing factors, such as ingestion of NSAIDs, coffee, smoking, and alcohol in older children and adolescents. Secondary peptic ulceration in severely stressed and traumatized patients can be prevented by prophylactic antacids and H_2-receptor blockers or PPIs. Early recognition and evaluation of abdominal pain will prevent the development of complications of PUD.

Evidence-Based Research

Table 60.2 presents a retrospective study of 45 years of data on surgical treatment of peptic ulcer disease in children.

Table 60.2: Evidence-based research.

Title	A 45-year experience with surgical treatment of peptic ulcer disease in children
Authors	Azarow K, Kim P, Shandling B, Ein S
Institution	Division of General Surgery, The Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada
Reference	J Pediatr Surg 1996; 31(6):750–753
Problem	The role of the proton pump inhibitor on the incidence of surgery for complications of PUD and the outcome of surgical treatment in complicated PUD in children was investigated.
Comparison/ control (quality of evidence)	This is a retrospective study of all patients who required operations for PUD between 1949 and 1994 (n = 43). The patients were classified into three groups: A (n = 38): pre–H_2 receptor blocker era (1949–1975); B (n = 3): pre–proton pump inhibitor era (1976–1988); and C (n = 2): proton pump inhibitor era (1989–1994). The incidence of surgery for complicated PUD in children and the outcome of surgical intervention were compared across the three eras.
Outcome/ effect	The authors concluded that although the incidence of surgery for PUD has declined, the incidence of surgery for obstruction secondary to PUD has not. The obstruction probably is related to scarring from long-standing disease. *H. pylori* may be a risk factor in the development of obstruction. Lesser procedures, such as vagotomy and pyloroplasty for bleeding PUD, simple oversewing of a perforation, and vagotomy plus a drainage procedure for gastric outlet obstruction, may be sufficient with appropriate ulcer medical treatment postoperatively, especially in those who did not have definitive ulcer surgery.
Historical significance/ comments	This study provides indirect evidence that medical treatment has significantly reduced the incidence of complications of PUD, especially bleeding in children. In Africa and developing countries with a low index of suspicion and poor access to health care facilities, this may not be the case. In an environment where late presentation may be the case, the clinical state should determine the surgical approach to those presenting with complicated PUD; extensive surgery may not be indicated and simple surgery as practiced in this study may suffice

Key Summary Points

1. Peptic ulcer disease in children is being recognized increasingly worldwide, including developing countries.
2. A high index of suspicion is necessary to distinguish PUD in children from other causes of abdominal pain.
3. *Helicobacter pylori* is an important aetiological factor in PUD in children.
4. Peptic ulcer may present with such complications as haemorrhage, perforation, and gastric outlet obstruction, even in the absence of pain.
5. Newborns and infants tend to present with acute complications such as haemorrhage or perforation.
6. Oesophagogastroduodenoscopy is the main diagnostic investigation and is safe in the paediatric age group.
7. The mainstay of management of paediatric PUD is medical, consisting of a combination of PPI, sucralfate, or bismuth with two antibiotics.
8. Surgery is indicated only for complications such as uncontrolled haemorrhage, perforation with peritonitis, and gastric outlet obstruction.

Suggested Reading

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