Pancreatitis in Children and Adolescents

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Several clinical and methodologic difficulties occur when diagnosing acute pancreatitis in the pediatric age group. Due to its uncommonness and heterogeneous symptoms, acute pancreatitis in children is often misdiagnosed, and prospective studies are lacking. Guidelines for classifying, diagnosing, and managing acute pancreatitis are frequently based on standards that are developed and validated in adult patients. Among the broad range of etiologies of pediatric acute pancreatitis in children, gallstones and biliary disease may play a greater role than previously believed. Although it is typically a benign disease in the pediatric population, complications such as pseudocysts may occur. When there are fatalities, they are usually attributed to systemic illness rather than the pancreatitis itself. Improvements in diagnostic and imaging methods and growing awareness cannot account for the recent increases in the observed incidence of pediatric acute pancreatitis.

Introduction

Diagnosing acute pancreatitis in children and adolescents poses unique clinical challenges. Depending on the patient's age and developmental level, assessing heterogeneous symptoms, such as abdominal pain, nausea, and vomiting, can be quite subjective. Nonverbal children may manifest abdominal pain through changes in personality, such as irritability, or by exhibiting decreased activity. In young, but verbal, patients, defining the pain's location and identifying factors that aggravate or relieve the pain may prove difficult. Because of the relative rarity of childhood pancreatitis, many clinicians do not consider the diagnosis when a child presents with abdominal symptoms. Consequently, clinicians often diagnose more common illnesses, such as viral gastroenteritis, in some children who are actually suffering from acute pancreatitis. It is not unusual to encounter children who have had recurrent episodes of pancreatitis but were repeatedly diagnosed with gastroenteritis for their abdominal pain and vomiting before receiving their initial diagnosis of acute pancreatitis.

A fundamental lack of knowledge about childhood and adolescent acute pancreatitis complicates these issues. Although pediatricians have recently demonstrated increased interest in acute pancreatitis, basic information about the disease's nature, methods of diagnosis, and outcomes in the pediatric population have lagged behind adults. To date, there has been no organized effort to define etiologies of acute pancreatitis in children and adolescents. Published reports on childhood pancreatitis are typically retrospective in nature and do not use common etiologic classification schemes. As a result, many participants in these studies have incomplete evaluations for etiology, or the etiology is assumed. For instance, children with evidence of a recent respiratory illness may be diagnosed with viral pancreatitis, despite the lack of direct evidence of viral inflammation in the pancreas and the ubiquitous nature of viral illnesses in children; in brief, associations may be coincidental rather than causal. There are no past or current studies on diagnosing acute pancreatitis in children; most clinicians rely on criteria that have been validated in adults. As mentioned, pediatric patients may not be able to complain of abdominal pain, a universal criterion in the clinical definition of acute pancreatitis. Finally, little information exists about the incidence and outcome of complications and about disease severity for childhood and adolescent acute pancreatitis. It is likely that disease severity, predictors of severity, and common complications differ from those observed in adults. Nonetheless, pediatricians still rely on adult studies to manage patients and to advise families about potential complications and outcomes. As you read on, keep these limitations in mind and remember that what is presented in this review is plagued by inadequate data and colored by the authors' experience.

Prevalence of Acute Pancreatitis

The prevailing opinion among pediatric specialists is that the incidence of acute pancreatitis in children and adolescents has increased over the past 10 to 15 years. Lopez [1] first reported the changing incidence of pediatric acute pancreatitis in a single-institution, retrospective study of

274 young patients who were diagnosed and treated at the University of Texas Southwestern Medical Center in Dallas. At his center, the number of patients diagnosed with pancreatitis steadily increased from 5 to 113 per year over a 6-year period. Subsequent studies from Australia and Mexico have also observed an increasing incidence of acute pancreatitis in children [2••,3]. Our experience has been similar. From 1993 to 2004, the number of patients with acute pancreatitis diagnosed at Children's Hospital of Pittsburgh increased from 30 to 141 patients per year, resulting in an incidence change from 2.4 to 13.2 patients per 100,000 children in our catchment population (Fig. 1). The reason for these increases remains unclear; the combined effects of referral bias, increased awareness, and improved diagnosis do not readily explain the change.

Pathophysiology of Acute Pancreatitis

Acute pancreatitis results from injury and inflammation of the pancreas that may extend to peripancreatic tissues and remote organs [4]. The process requires an initiating event that triggers alterations in the acinar cells, most likely activation of intracellular trypsinogen and other digestive enzymes. The resultant acinar cell damage produces pancreatic edema and a local inflammatory response associated with the release of inflammatory mediators. These cytokines and chemokines subsequently mediate a systemic inflammatory response. In large part, the magnitude of the inflammatory response determines the clinical severity of acute pancreatitis. A brisk response may lead to pancreatic necrosis, inflammation in distant organs, and systemic complications.

Etiology

In adults, alcohol consumption and gallstone disease account for most acute pancreatitis cases. In children and adolescents, the associated triggers are broadly divided among several entities (Table 1). Systemic illness, biliary disease, trauma, and side effects of certain medications comprise the suspected etiology in most young patients, regardless of age. Many patients have no discerned etiology and are classified as idiopathic [5•]. However, a wide range of prevalence in etiologies exists among the various published reports. For instance, the rate of acute pancreatitis associated with documented systemic illness ranges from 3.5% to 48% in various studies. The author's (Lowe) experience at two large children's hospitals has shown that 40% or more acute pancreatitis cases in children are associated with a systemic illness. Because many of these patients are in an intensive care init (ICU), the variation from center to center may depend on the presence or size of a hospital's ICU or the inclination of the ICU physicians to test for pancreatitis. A growing awareness of the association of acute pancreatitis with systemic illnesses may explain the apparent increases in recent reports of acute pancreatitis in patients who have multisystem diseases [2••].

The overall variation in etiologies also reflects the retrospective nature of the studies, the bias or experience of the clinicians caring for the patients, and incomplete investigations for etiologies in many patients. Additionally, the growing incidence and recognition of new etiologies among pediatric patients has resulted in the splitting of some categories and some ambiguity in categorization. For instance, a small Korean study of acute pancreatitis in children classified an anomalous pancreatobiliary junction as being a biliary etiology, whereas many would categorize this as an anatomic etiology, and yet other groups might classify it as a biliary etiology with an anatomic subclassification [6,7]. An Australian study documented five recent cases of acute pancreatitis in children following bone marrow transplantation [8]. Four of the five children had adenovirus infections, and whether these cases should be classified as viral in etiology or post-transplant is difficult to say. There are also disparities in recreational behaviors among various cultures that predispose children to developing traumatic acute pancreatitis, influencing observed rates of this etiology. Examples include a study from Taiwan that noted that acute pancreatitis in the 2- to 18-year-old age group was most frequently associated with traumatic injury caused by motorcycle accidents, whereas several cases in a recent study out of Victoria were attributed to underage Australian rules football injuries [9,10].

Contrary to previous belief, biliary disease does play an important etiologic role in acute pancreatitis among children and adolescents, even in infants and toddlers (Table 1). A recent population-based study presented at the national meeting of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition suggests that biliary disease may be even more prevalent than indicated in the studies listed in Table 1 [11]. The authors determined etiologies of acute pancreatitis from a large national database that incorporated data from community hospitals and free-standing children's hospitals. In this study, gallstone disease was reported as the most common cause of acute pancreatitis and was four times more common in females than in males, accounting for one half of acute pancreatitis cases among adolescent females. Many of the adolescent patients were treated in community hospitals and would not have been included in surveys of patients in children's hospitals. Regardless of its limitations, this study reinforces the significant prevalence of gallstone pancreatitis in the pediatric population. Furthermore, the study highlights some of the difficulties in accurately determining etiologies and other clinical parameters specific to acute pancreatitis in single-center studies.

Diagnosis of Acute Pancreatitis

The accepted clinical definition of acute pancreatitis requires the existence of at least two of the following

Table 1. Acute pancreatitis in recent studies of children and adolescents

Study	Location	Patients, *n*	Etiology, %									
			Systemic	Biliary*	Anatomic†	Trauma	Familial	Cystic fibrosis	Metabolic‡	Drugs	Other§	Idiopathic
DeBanto et al. [27]	USA	301	3.5	10.5	1.5	13.5	5.5	3.0	4.0	11.0	13.5	34.0
Lopez [1]	USA	274	48.0	10.0	NA	19.0	"A few"	0.4	0.7	5.0	NA	17.0
Pezzilli et al. [41]	Italy	50	NA	20.0	8.0	10.0	6.0	NA	NA	NA	22.0	34.0
Tiao et al. [10]	Taiwan	61	15.0	NA	11.5	46.0	NA	NA	NA	6.5	NA	19.5
Choi et al. [6]	Korea	56	9.0	27.0	2.0	11.0	NA	NA	NA	30.0	9.0	12.0
Alvarez et al. [42]	Spain	31	6.5	16.0	NA	6.5	NA	NA	NA	10.0	26.0	35.0
Werlin et al. [7]	USA	180	14.0	12.0	7.5	14.0	3.0	0.5	5.5	12.0	23.5	8.0
Sanchez-Ramirez et al. [3]¶	Mexico	55	16.0	20.0	5.5	9.0	18.0	2.0	7.0	13.0	NA	34.5
Nydegger et al. [2••]	Australia	279	22.2	5.4	NA	36.3	NA	NA	5.8	3.2	2.2	25.1
Kandula and Lowe [5•]**	USA	87	51	9.0	NA	8.0	NA	2.0	NA	8.0	2.0	20.0

*Cholelithiasis, biliary sludge, choledochal cyst.
†Pancreas divisum, anomalous junction of the biliary and pancreatic ducts.
‡Diabetic acidosis, hyperlipidemia, organic acidemias, hypercalcemia.
§Associated viral infection, postendoscopic retrograde cholangiopancreatography, otherwise undefined in the reports.
¶Some patients had multiple suspected etiologies.
**Study of patients younger than 3 years of age.

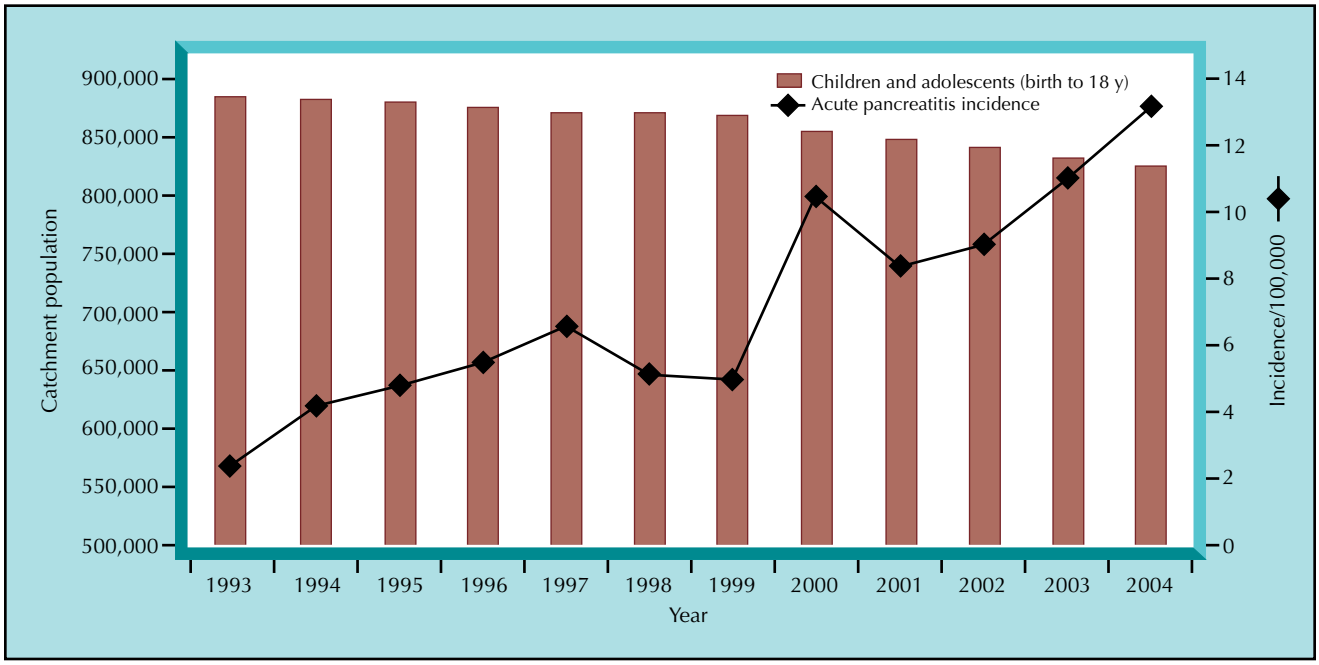

Figure 1. Incidence of acute pancreatitis in children and adolescents at Children's Hospital of Pittsburgh (CHP) from 1993 to 2004. The bars represent the number of children and adolescents (birth to 18 years of age) in the 23-county catchment area of CHP in each of the study years. The line graph represents the number of admissions for acute pancreatitis based on ICD-9 code data per 100,000 children and adolescents. During these years, total admissions to CHP remained stable and the number of lipase and amylase tests increased 2.9- and 2.6-fold, respectively, compared with a fivefold increase in the diagnosis of acute pancreatitis. (Morinville and Lowe, Unpublished data).

features: 1) abdominal pain consistent with acute pancreatitis; 2) serum amylase or lipase activity or both at least three times the upper reference limit; and 3) findings of acute pancreatitis on imaging studies.

Although this definition generally holds true for children and adolescents, there are caveats to relying on these criteria in the pediatric population. Abdominal pain may not be a feature of acute pancreatitis in a sizable number of children. An analysis of the literature from 1965 to 2000 found that abdominal pain was reported in 87% of patients [12]. Two recent studies observed the incidence of abdominal pain to be 94.5% and 67.7% [3,7]. Some of the variation may reflect the age range of patients included in these studies. In a study of acute pancreatitis in patients who were under 3 years of age, only 29% had abdominal pain as a complaint [5•]. If irritability was considered to be a surrogate for pain, the percentage with abdominal pain was still low, at 46%. The most common symptom in this age group was vomiting (50%), a nonspecific and frequent occurrence among young children.

The use of serum lipase and amylase measurements in pediatric patients has not been defined and, unlike in adult patients, it must be acknowledged that the sensitivity and specificity of amylase and lipase levels are unknown for children and adolescents. Pancreatic isoamylase levels are low at birth and may not reach adult levels until 10 to 15 years of age [13–15]. Similarly, lipase levels are low at birth and may not reach adult levels until 1 year of age [16,17]. The clinical significance of the developmental pattern of pancreatic isoamylase and lipase expression is not clear. In one study, almost 40% of patients under 3 years of age with a diagnosis of acute pancreatitis had elevated lipase but normal amylase levels [5•]. The lack of an elevated amylase may be explained in part by the delayed expression of pancreatic isoamylase. Some young patients with acute pancreatitis may go undiagnosed because they do not express enough amylase or lipase for pancreatic inflammation to elevate their levels above a diagnostic threshold. What seems clear from the studies that have been published on children and adolescents is that many patients with acute pancreatitis demonstrate a selective elevation of amylase or lipase at presentation. At this time, it is prudent to perform both assays in patients with suspected acute pancreatitis.

The role and timing of imaging studies in investigating children and adolescents with suspected acute pancreatitis is equivocal. Mounting evidence of pediatric gallstone pancreatitis provides the strongest argument for imaging early in the course of acute pancreatitis. The serum alanine aminotransferase (ALT) level may be a reliable indicator of gallstone pancreatitis in adults, but because its sensitivity and specificity increase with age, ALT may not be as useful in younger pediatric patients [18,19]. Moreover, no studies to date have examined the reliability of clinical criteria that are used to accurately predict gallstone pancreatitis in children and adolescents. Of the various imaging studies, recent reports suggest that endoscopic ultrasound and magnetic resonance cholangiography (MRCP) are superior tests in adult age groups [19–21]. MRCP can reliably diagnose a wide vari-

ety of pancreatobiliary disorders, such as choledochal cysts, gallstones, pancreas divisum, and anomalies of the pancreatobiliary duct junction in children [21,22,23•]. Because MRCP requires general anesthesia for many children, it has limited clinical use in the routine evaluation of pediatric acute pancreatitis. MRCP may be of the greatest benefit in evaluating children and adolescents with recurrent episodes of acute pancreatitis, although this has not been studied systematically.

Currently, endoscopic ultrasound has not found widespread use in pediatrics, and its utility in this patient population is unknown. As technology makes the endoscopes for ultrasound smaller, and the trained endoscopists (virtually all adult gastroenterologists) become more comfortable with younger patients (as occurred with endoscopic retrograde cholangiopancreatography [ERCP]), endoscopic ultrasound will undoubtedly gain more widespread use in pediatrics. Diagnostic ERCP has a limited, if any, role in the initial evaluation of acute pancreatitis. Presently, transabdominal ultrasonography represents a reasonable compromise for evaluating children and adolescents suspected of having gallstone pancreatitis. It is widely available, requires neither sedation nor anesthesia, and has been demonstrated to be sensitive at detecting gallstones. The primary drawback to transabdominal ultrasound is the difficulty of adequately imaging the pancreas when bowel gas is present.

Contrast-enhanced CT (CECT) of the abdomen is a second imaging option for pediatric cases and offers the advantage of providing additional information about potential etiologies and the presence or absence of necrosis and other complications. CECT is probably not necessary in most children and adolescents with pancreatitis. In patients in whom the ultrasound study is inadequate, or in patients with a prolonged or difficult course, CECT may assist in defining pancreatic anatomy and peripancreatic complications. When the diagnosis of acute pancreatitis is ambiguous, such as when clinical symptoms coexist with mild enzymatic elevations, CECT is the study of choice. MRI may prove to be superior to CECT for evaluating adults suspected of having acute pancreatitis, but the requirement for general anesthesia in many children will limit its use in pediatrics.

Investigations of Etiology

Given the variety of etiologies reported in children, clinical acumen must dictate which type of testing is required for a patient's initial episode of acute pancreatitis. Systematic consideration of probable, possible, and rare etiologies based on the patient's age, history of present illness, past medical history, family history, and physical examination findings should limit invasive and unnecessary testing. Patients who develop acute pancreatitis in association with a systemic illness may not require additional investigation. Medical history can identify patients who might have drug-induced pancreatitis. Recent history of trauma should prompt imaging studies of the abdomen. Family history of pancreatitis may warrant genetic testing. A transabdominal ultrasound or CECT can identify gallstones or biliary anomalies such as choledochal cysts and should be considered in any patient who presents with abdominal pain and jaundice. Measuring serum calcium and triglyceride levels will identify patients whose pancreatitis is associated with hypercalcemia or hypertriglyceridemia. Although these entities are uncommon in pediatrics, they can be treated, and treatment may prevent future episodes of pancreatitis.

As many as 10% of children have recurrent episodes of acute pancreatitis; these patients require a more thorough etiology investigation [12,24,25]. If they haven't been performed previously, serum calcium and triglyceride levels should be measured, and patients should undergo a thorough evaluation for structural anomalies of the pancreatobiliary tree and upper gastrointestinal tract. MRCP may identify ductal abnormalities in children of all ages and is preferred over ERCP [22,23•,26]. CECT or an upper gastrointestinal series may assist in identifying duplication cysts of the duodenum or stomach. An esophagogastroduodenoscopy can demonstrate duodenal ulcers or tumors of the papilla. Based on their clinical history, some patients warrant testing for inborn errors of metabolism. A careful review of medications should be undertaken. In particular, valproic acid, asparaginase, azathioprine, metronidazole, tetracycline, and acetaminophen are medications commonly prescribed to children or adolescents that have frequently been associated with pediatric acute pancreatitis [7,27]. Genetic testing for *PRSS1* (cationic trypsinogen gene) and *CFTR* (cystic fibrosis transmembrane conductance regulator gene) mutations should be done [28]. The necessity and use of *SPINK1* (serine protease inhibitor Kazal type 1) testing in children are even less clear than they are for adults. Heterozygous *SPINK1* mutations alone do not appear to cause disease [29]. Although homozygous *SPINK1* mutations are strongly associated with chronic pancreatitis, aside from mutations in the signal peptide, they may be part of a polygenic disorder [30]. The role of *SPINK1* mutations in modifying the disease course of patients with *PRSS1* mutations is unsettled; just knowing if a patient has a *SPINK1* mutation may not help in advising the patient and family about the disease [29,31]. Even with comprehensive testing, a sizable percentage of pediatric patients with a recurrence of acute pancreatitis will never have an etiology identified.

Management

Treating acute pancreatitis has remained unchanged for years; it includes pain control, intravenous fluids, pancreatic rest, and monitoring for complications. Volume expansion early in the course of acute pan-

creatitis maintains cardiovascular stability and may decrease the incidence of pancreatic necrosis. Nutrition should be instituted within a few days, or if a severe course is anticipated. In the past, parenteral nutrition was preferred, but recent data have demonstrated that adults with severe pancreatitis tolerate jejunal feedings with fewer complications than parenteral nutrition [32–34]. Because the difference in complication rates was predominantly related to intravenous catheter-specific problems, enteral nutrition may not be the best choice for patients who already have a catheter in place for medical management. Theoretically, enteral feeding may be advantageous by maintaining or enhancing gut integrity, promoting recovery, and modulating the immune response, and it may be the preferred nutrition route in patients with severe pancreatitis. In a recent meta-analysis of adults with acute pancreatitis, compared with parenteral nutrition, enteral nutrition was associated with a lower infection risk, reduced surgical interventions to control pancreatitis, and reduced length of hospital stay [35]. There are no current studies in children or adolescents concerning feeding methods during severe acute pancreatitis.

A more common question in the care of children who generally have mild acute pancreatitis is when to start oral feedings. No clear evidence-based guidelines exist, and serum levels of amylase and lipase do not provide a reliable measure of severity and are a poor determinant of feeding success. Initiating feeds when vomiting and pain have subsided seems a reasonable guide. A rise in serum lipase and amylase levels without an increase in symptoms after feeding is started is probably not a reason to stop feeds, although pain may be. To date, these issues have not been adequately studied in children and adolescents.

Another issue is what type of diet to start. Tradition holds that patients should begin with a clear liquid diet and advance to more solid foods as tolerated. A recent study in adults with mild acute pancreatitis compared a clear liquid diet to a low-fat solid diet and did not observe any difference in degree of tolerance or other clinical parameters between the two diets [36•]. Of particular interest, starting the patient with a solid diet did not result in shorter hospitalization duration. Nonetheless, the study suggests that it is safe to start patients on a solid diet. The use of the low-fat diet in this study or in the routine treatment of acute pancreatitis patients is not supported by any evidence that it offers any advantage over a regular diet.

In patients with gallstone pancreatitis, management includes removal of any remaining obstructing stone(s). ERCP is as safe and effective in pediatric patients as it is in adults and is currently the preferred method for stone removal, although postprocedure pancreatitis is a significant complication among both populations [37•,38,39]. Other ERCP therapies, including sphincterotomy, stricture dilation, stent placement, snare papillectomy, and cystoduodenostomy, have also been performed safely and successfully in children. The long-term effects of sphincterotomy in childhood have not yet been studied.

Outcome of Acute Pancreatitis

Most children and adolescents with acute pancreatitis have a mild course, and their symptoms resolve without incident. The mean length of hospital stay reported in studies before 1999 was 13.2 ± 2.4 days [12]. Two recent studies report longer average lengths of stay, 24 and 25.7 days [3,7]. Werlin et al. [7] reported a median length of stay of 8 days and suggested that the length of stay reflects the presence of comorbid conditions in many children. This conclusion is supported by a study of infants in which the median duration of hospital stay for the group as a whole was 19.5 days (range: 2–129 days), whereas the median length of stay for patients admitted with uncomplicated acute pancreatitis was only 8.5 days (range: 2–30 days) [5•]. Between 13% and 20% of children with acute pancreatitis will have prolonged courses with persistent symptoms or associated complications [5•,12,27]. The number may actually be lower for patients who have acute pancreatitis that does not occur in the setting of a concomitant illness. Considering that all of the studies include complications in patients with other illnesses, it is likely these conditions, rather than the pancreatitis, account for many of the more significant reported complications, such as renal failure or shock.

All of the local and systemic complications that have been reported in adults with acute pancreatitis have also been reported in children. Peripancreatic fluid collections and pseudocysts are the most frequent complications encountered, occurring in about 13% to 16% of patients [3,7,12]. These complications may be less common in younger patients. In a study of acute pancreatitis among children 3 years of age or younger, only 1 of 79 (1.3%) patients developed a fluid collection [5•]. However, the prevalence of pseudocysts and fluid collections might be higher because not all of the patients in these series underwent imaging studies. Limited data on the outcome of pseudocysts have demonstrated that most resolve without specific therapy. Those that cause persistent symptoms require intervention: surgical, endoscopic, and interventional radiologic approaches have all been used in children [40].

Deaths are reported in all series of acute pancreatitis in children. Death rates range from 2.0% to 11.1% [2••,5•,7,12,27]. In some series, it is difficult to determine whether the patients who died had comorbid conditions. Two series reported that all of the deaths occurred in patients with significant systemic illness and not from complications directly related to acute pancreatitis [5•,7]. Whether acute pancreatitis influenced the outcome in these patients is impossible to ascertain. Although definitive data are lacking, death in children

Table 2. Comparison of acute pancreatitis–related factors in adults and children

Factor	Adults	Children
Etiology	Predominantly gallstones and alcohol consumption; occasionally idiopathic cases	Broad spectrum of etiologies; frequent idiopathic cases
Diagnostic criteria	Abdominal pain present; amylase and lipase levels are sensitive and specific; elevations of amylase and lipase levels	Abdominal pain not always present and may be manifested by irritability; unknown if amylase and lipase levels are sensitive or specific; often selective elevation of amylase or lipase levels
Imaging studies	Contrast-enhanced CT or MRI are preferred diagnostic tests; EUS more widely used; ERCP and MRCP best for diagnosing biliary/gallstone pancreatitis; post-ERCP pancreatitis may occur	Contrast-enhanced CT and transabdominal ultrasound are best diagnostic tests (do not require sedation); EUS not readily available; transabdominal ultrasound is first choice for diagnosing biliary/gallstone pancreatitis; MRCP can be performed at all ages; post-ERCP pancreatitis may occur
Complications	Wide variety; fatalities may be due to pancreatitis episode	Pseudocysts are most common; fatalities generally linked to systemic illnesses

ERCP—endoscopic retrograde cholangiopancreatography; EUS—endoscopic ultrasound; MRCP—magnetic resonance cholangiopancreatography.

and adolescents from complications of acute pancreatitis appears to be uncommon.

Conclusions

For reasons that are not understood, the incidence of acute pancreatitis in children and adolescents has increased in recent years. Acute pancreatitis occurs in all pediatric age groups, including infants. Differences from adults have been described (Table 2). There are many etiologies for acute pancreatitis among children, and a sizable percentage of young patients will never have an etiology established. Gallstone pancreatitis is probably more common than originally thought, particularly in adolescents. As in adults, diagnosing acute pancreatitis requires the presence of a combination of appropriate clinical symptoms, elevated serum amylase or lipase levels, and imaging evidence of pancreatitis. Given the variety of etiologies for acute pancreatitis in children, clinical history should guide the depth of investigation. Imaging may not be necessary for all patients, but the incidence of biliary disease suggests that transabdominal ultrasound or CECT examinations should be considered, particularly when adolescents present with biliary symptoms. In general, the outcome for children and adolescents with acute pancreatitis is superior to that observed in adults. Pseudocysts are the most common complication among pediatric patients. When fatalities occur in the setting of childhood acute pancreatitis, they are most often attributed to systemic illness and not the direct effects of the pancreatitis episode.

Disclosures

Dr. Lowe serves on the advisory board for Solvay Pharmaceuticals. No further potential conflicts of interest relevant to this article were reported.

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