Pancreatitis

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Pancreatitis was thought to be an uncommon cause of abdominal pain in children and a disease primarily of adults. Because of better recognition of symptoms in children and the more frequent use of medications that cause pancreatic inflammation, acute pancreatitis currently is being diagnosed more frequently in institutions specializing in pediatric care.[114]

Compared with causes of acute pancreatitis in adults—primarily alcoholism, cholelithiasis, and trauma—causes of childhood pancreatitis are more diverse. Microorganisms account for a significant proportion of cases of pancreatitis in children. In addition, antimicrobial agents have been associated with severe and occasionally fatal episodes of pancreatitis, and bacterial infections may complicate the natural history of acute and chronic pancreatitis. Pediatricians who care for children with pancreatitis must have expertise in the diagnosis and treatment of infectious diseases.

CLINICAL MANIFESTATIONS

More than 80% of children with acute pancreatitis complain of abdominal pain.[94] However, only 30% of pediatric patients have epigastric pain, as usually described by adults.[167] In children, other sites of focal tenderness or diffuse pain include the right upper quadrant of the abdomen, the periumbilical area, the entire abdomen, and, less commonly, the right lower quadrant of the abdomen. The onset of pain usually is rapid and increases to a maximal intensity in a few hours, but occasionally the onset may be slow and gradual. Most often the pain is sharp and excruciating. Only one-third of children complain of pain that radiates to other areas, including the back, lower part of the abdomen, upper abdominal quadrants, and anterior chest wall. In school-aged children, the pain often intensifies after meals.

Two-thirds of children with acute pancreatitis have vomiting.[16] Children younger than 5 years occasionally experience vomiting without abdominal tenderness. Fever is present in only 30% of children with pancreatitis, but temperatures greater than 38.5°C (101.3°F) are observed occasionally. Children may present with only the symptom of cough, and pleural effusions are found on radiography.[92]

On physical examination, children are classically found lying quietly on their sides with their knees flexed. They usually have epigastric tenderness to palpation and decreased or absent bowel sounds. Abdominal distention is found in 30% of children with pancreatitis and occurs more commonly in preschool-aged children.[167] Rebound tenderness, guarding of the epigastrium, jaundice, an abdominal mass, or ascites occasionally is detected. Rarely ecchymoses of the flanks (Grey Turner sign) or the umbilical area (Cullen sign) can be identified but usually only when life-threatening hemorrhagic pancreatitis is present. In severe pancreatitis, children may present with evidence of shock and multiple-organ failure.

Chronic pancreatitis occurs when irreversible damage in the pancreatic architecture causes abnormalities in the function of the pancreas.[85] Children with chronic pancreatitis often have lengthy or recurrent bouts of abdominal pain and vomiting.

LABORATORY DIAGNOSIS

The single most common useful laboratory test for the clinical diagnosis of pancreatitis in children is measurement of the serum amylase concentration, but the level correlates poorly with the severity of the disease. In most studies of childhood pancreatitis, the diagnosis is confirmed when the serum amylase level is greater than three times the normal level for the particular laboratory completing the test. The serum concentration rises quickly within hours after symptoms develop. High serum amylase concentrations can be observed, however, in numerous other illnesses, including acute cholecystitis, intestinal obstruction, perforations of abdominal organs, appendicitis, salpingitis, ruptured ectopic pregnancy, and salivary gland disease. The serum amylase concentration can return to normal in 24 to 72 hours after the onset of symptoms; thus the diagnosis of pancreatitis can be missed. In this situation, the urine amylase concentration can remain elevated for at least 1 week.

Serum amylase concentrations occasionally are not elevated during the course of pancreatitis in children.[34] Marked hyperlipidemia may interfere with the laboratory measurement of amylase.[17] Serum lipase is useful in these situations; however, high serum concentrations often are not detected until 24 hours after the beginning of the illness. Because lipase is produced only in the pancreas and intestinal cells, measurement of its serum concentration helps distinguish children with high serum amylase concentrations of pancreatic as opposed to salivary origin. Some children with pancreatitis have high amylase levels without an elevation of serum lipase.[86] Laboratory findings in children with severe and/or necrotizing pancreatitis may include leukocytosis with increased immature polymorphonuclear leukocytes, an elevated erythrocyte sedimentation rate, and elevated C-reactive protein level. In children with fulminant hemorrhagic pancreatitis, anemia develops quickly. Other associated findings include hyperglycemia, hypertriglyceridemia, hypoalbuminemia, and hypocalcemia. Scoring systems for children have been devised to predict severe pancreatitis, but these are extrapolated from adult studies or are difficult to use in clinical practice.[43,82] Procalcitonin or D-dimer plasma levels may be useful in predicting severe pancreatitis and later complications.[20,96] Elevated aminotransferase and alkaline phosphatase levels generally are observed only when the episode of pancreatitis is caused by biliary obstruction, such as in gallstone-related disease.

The radiographic features of childhood pancreatitis also are nonspecific. Radiographs of the abdomen may show localized ileus of the jejunum in the midepigastric or left upper quadrant region adjacent to the pancreas (sentinel loop), a distended transverse colon without visualization of the descending colon because of adjacent pancreatic inflammation (colon cutoff sign), duodenal distention with air-fluid levels, or loss of the left psoas shadow. Occasionally chest radiography reveals an elevated left hemidiaphragm or pleural effusion.

The ability to diagnose pancreatitis in children has been improved greatly by ultrasonography. The echodensity of the pancreas is normally equal to or greater than that of the left lobe of the liver. During acute pancreatitis, edema causes the gland to enlarge and become less dense than the liver. These two findings can aid in establishing the diagnosis of pancreatitis, and complications such as abscesses and pseudocysts can be identified. Also, ultrasonography may delineate dilations of the pancreatic ducts due to obstruction or ductal stones. Visualization of the pancreas by ultrasonography may be obscured because of overlying bowel gas. In such cases, computed tomography (CT) is useful in detecting pancreatic size and density.

CT of the pancreas should be performed in complicated cases of pancreatitis after a few days of treatment to determine the severity of disease and extent of pancreatic necrosis.[30,120] It is especially useful when surgery is being considered for drainage of abscesses and pseudocysts.

Endoscopic retrograde cholangiopancreatography (ERCP) is used in children with pancreatitis to treat gallstones, strictures, or *Ascaris* infection.[123] Because of ongoing improvement in image quality, magnetic resonance cholangiopancreatography (MRCP) is being increasingly used as a noninvasive technique for evaluating children with chronic or recurrent pancreatitis, with results similar to those from ERCP.[31,148]

CAUSES

A cause for childhood pancreatitis can be determined in more than 90% of cases if diagnostic evaluation is thorough, especially in children younger than 6 years. The frequency of each specific cause depends on the patient population of the particular medical center. The most common noninfectious causes of pancreatitis in children include trauma, medications, obstructive diseases, vasculitis, autoimmune diseases, and genetic and metabolic diseases.

Physicians with expertise in the management of infectious diseases are becoming more aware of drug-induced pancreatitis because many antimicrobial agents can cause pancreatic inflammation. Pentamidine isethionate has been used in the treatment of *Pneumocystis jejuni* pneumonia, African trypanosomiasis, and leishmaniasis. It may cause hypoglycemia because of toxicity to pancreatic islet cells and is associated with severe and occasionally fatal episodes of pancreatitis.[95,172] In children, aerosolized pentamidine prophylaxis for *P. jejuni* pneumonia also has been associated with severe cases of pancreatitis in patients with acquired immunodeficiency syndrome (AIDS).[61,95] Similarly, pentavalent antimonial agents such as sodium stibogluconate and meglumine antimonite, used for the treatment of visceral leishmaniasis, can induce pancreatic inflammation.[11,133]

Sulfonamides, including trimethoprim-sulfamethoxazole, have been implicated occasionally as a cause of acute pancreatitis in adults.[7,161] Symptoms have recurred when patients have been reexposed to the medication. The abdominal pain often is accompanied by a hypersensitivity-type rash. Tetracycline- and doxycycline-induced pancreatitis have been described in children with and without overt liver disease.[152,163] In addition, clarithromycin,[52,130] erythromycin,[146] rifampin,[118] roxithromycin,[121] linezolid,[124] dapsone,[36] nitrofurantoin,[103] isoniazid,[127] tigecycline,[119] and metronidazole[108] have been added to the list of agents that can cause pancreatitis in previously healthy individuals when given in routine doses or when high amounts are consumed. Although uncommonly used in children, quinolone antibiotics, such as gatifloxacin and ciprofloxacin, have been associated with hepatotoxicity and acute pancreatitis.[33,143] An adolescent who was receiving ceftriaxone also developed pancreatitis secondary to obstruction of the biliary tract from gallstones.[91]

Pancreatitis has been a major dose-limiting toxic effect of the human immunodeficiency virus (HIV)-inhibiting nucleoside analogue reverse transcriptase inhibitor (NRTI) class of medications because of mitochondrial toxicity, especially dideoxyinosine andstavudine.[23,47,113] Most episodes of pancreatitis associated with dideoxyinosine occur when the dose is 360 mg/m^2 per day or greater, and usually the pancreatic inflammation resolves when the medication is discontinued. Concomitant administration of pentamidine or another NRTI, such as ribavirin, used in the treatment of hepatitis C infection may increase the risk for developing pancreatitis.[98] In pediatric patients with AIDS, serum amylase concentrations often are elevated in patients without pancreatic symptoms, whereas children with pancreatitis can have normal serum amylase concentrations. The serum lipase concentration is useful in evaluating HIV-infected children for possible pancreatic inflammation.[23,95] Increased liver aminotransferase or lipase concentrations before the administration of an NRTI may be helpful in predicting those children in whom pancreatitis will develop. In all children with symptoms consistent with pancreatitis, NRTIs should be withheld pending the results of a lipase assay, and they should be discontinued if the concentration is elevated. Similarly, they should be discontinued for 1 week after treatment with pentamidine.[46] Because of increased awareness of NRTI toxicity, the incidence rate of pancreatitis in HIV-infected children in the highly active antiretroviral therapy (HAART) era appears to be decreasing.[99]

Interferon-α, which is used in the treatment of chronic hepatitis, has been associated with the development of pancreatitis.[29] The antifungal agents liposomal amphotericin B, micafungin, and itraconazole rarely cause pancreatic toxicity.[117,128,142]

INFECTIOUS CAUSES

Infections caused by various microorganisms have been shown by culture, histologic examination, or antibody titer rise during the course of acute pancreatitis (Box 52.1). A true causal relationship usually is not shown. Although not all of the following infectious agents have been shown to be associated with childhood pancreatitis, they must be considered as possible etiologic agents because adult patients with infectious pancreatitis have been described. Compared with previous decades, infectious agents are being encountered less as a cause of acute pancreatitis, most likely because of mumps vaccination.

BOX 52.1 Microorganisms Associated With Episodes of Acute Pancreatitis

Viruses
- Adenoviruses
- Cytomegalovirus
- Epstein-Barr virus
- Group B coxsackieviruses
- Hepatitis A virus
- Hepatitis B virus
- Hepatitis E virus
- Herpes simplex viruses
- Human immunodeficiency virus
- H1N1 influenza A virus
- Measles virus
- Mumps virus
- Parainfluenza viruses
- Rotavirus
- Rubella virus
- Varicella zoster virus
- West Nile virus

Parasites
- *Ascaris lumbricoides*
- *Clonorchis sinensis*
- *Cryptosporidium parvum*
- *Echinococcus granulosus*
- *Fasciola hepatica*
- *Plasmodium falciparum*
- *Taenia saginata*
- *Toxoplasma gondii*
- *Wuchereria bancrofti*

Mycoplasmas and Bacteria
- *Brucella melitensis*
- *Campylobacter jejuni*
- *Escherichia coli*
- *Legionella* spp.
- *Leptospira* spp.
- *Moraxella catarrhalis*
- *Mycobacterium tuberculosis*
- *Mycoplasma pneumoniae*
- *Salmonella* spp.
- *Streptococcus pyogenes*
- *Yersinia* spp.

Fungi
- *Aspergillus* spp.
- *Candida* spp.
- *Cryptococcus neoformans*

Viral Infections

Group B coxsackieviruses and mumps virus are the best documented causes of pancreatitis in children. Group B coxsackieviruses usually cause pancreatitis along with other clinical manifestations, including aseptic meningitis, mild diarrhea, rash, and myocarditis.[25,67] They rarely cause death in young infants with myocarditis and pancreatitis.[38] How commonly these enteroviruses cause pancreatic inflammation is unknown. Thirty-one percent of patients with aseptic meningitis during an epidemic of group B coxsackievirus infection had increased serum amylase concentrations.[102] Numerous studies have shown coxsackievirus B–induced damage to pancreatic acinar cells in mouse models of infection, and it is believed that the pancreas is the primary replication site for these viruses.[66,154] Coxsackievirus B strains have caused worsening bouts of pancreatic disease in children with chronic pancreatitis and the primary episode of pancreatitis in children later found to have the hereditary form of disease.[53,139] Group A coxsackieviruses have only rarely been associated with pancreatitis in humans.[5]

Usually mumps pancreatitis occurs in the presence of parotitis; however, abdominal pain and vomiting may occur for days before the development of salivary swelling.[166] Rarely mumps virus can cause pancreatitis without other common clinical manifestations.[100,159] Because more than 80% of children with mumps parotitis have elevated serum amylase concentrations, ultrasonography and serum lipase concentrations should be obtained to aid in establishing the diagnosis.[58] An estimated 15% of children with mumps virus infection have abdominal tenderness and vomiting suggestive of the diagnosis of pancreatitis. In only a single report has the pancreatitis been hemorrhagic and severe.[44] Occasionally chronic or recurring pancreatitis develops after mumps infection.[170]

Researchers previously thought that acute pancreatitis occurred in cases of viral hepatitis only when fulminant liver disease developed.

Increasingly children with mild hepatitis A infection and pancreatitis are being described.[42] In addition, a 16-year-old with acute hepatitis A infection died of severe pancreatitis with multiple-organ failure.[75] Individuals with acute hepatitis and pancreatitis have also been found to have hepatitis E viral infection.[149] Hepatitis B viral antigens have been detected in the pancreatic glandular cells of patients with severe acute hemorrhagic pancreatitis.[137] The role of hepatitis B virus in the pathogenesis of pancreatic inflammation in these patients is unknown; however, a young adult has developed three episodes of acute pancreatitis during acute exacerbations of chronic hepatitis B infection that resolved after lamivudine therapy.[32] It has been suggested that edema of the ampulla of Vater caused by biliary sludge formed during hepatitis viral infection leads to outflow obstruction of pancreatic fluid and the development of pancreatitis.[68]

Human herpesviruses are uncommon causes of childhood pancreatitis in immunocompetent patients. Occasionally pancreatitis develops in children and adolescents with infectious mononucleosis.[76] Acute pancreatitis and occasionally pseudocyst formation also have been reported in previously healthy individuals with varicella infection.[48,80,153] In addition, previously healthy adults have developed pancreatitis during primary cytomegalovirus and herpes simplex virus infections.[74,81,111]

Interstitial pancreatitis occurs relatively commonly in children with congenital rubella syndrome.[97] In addition, severe pancreatitis has been identified in immunocompetent patients with mild and fatal measles virus infection.[50,160] An adolescent has been described with measles encephalitis and pancreatitis that responded to corticosteroids.[145] Influenza A viruses have been shown to be capable of infecting human pancreatic cells, and H1N1 influenza A has caused pancreatitis in a previously healthy adult.[18,26] Rarely other viruses including adenovirus, West Nile virus, rotavirus, and dengue virus have been associated with the development of pancreatitis in previously healthy adults and children.[21,51,78,87,136]

Viral pancreatitis also occurs in immunocompromised patients. Cytomegalovirus has been identified in pancreatic specimens obtained during autopsies of patients who had AIDS, transplant recipients, individuals taking corticosteroids for autoimmune diseases, and cancer chemotherapy patients.[70,147] The symptoms of pancreatitis have resolved in a few patients with AIDS treated with ganciclovir or foscarnet.[35] Varicella zoster and herpes simplex viruses have also caused pancreatitis and death in patients with various immunodeficient conditions.[45,138]

Adenovirus has caused hemorrhagic pancreatitis and death in children with bone marrow transplants, whereas an infant with disseminated adenoviral infection and pancreatitis survived with cidofovir therapy.[15,28,107] Researchers have suggested that stool cultures for adenoviruses should be obtained when posttransplant patients develop pancreatitis. A disseminated parainfluenza virus infection in an infant with severe combined immunodeficiency was associated temporally with the development of pancreatitis; however, no attempt was made to culture the virus from postmortem pancreatic tissue.[49]

Whether HIV directly causes pancreatitis is unclear. Laboratory-diagnosed episodes of pancreatitis in adults and children with AIDS do occur, but whether the pancreatic inflammation is caused by HIV or an unrecognized opportunistic pathogen is unknown.[171] HIV-infected children frequently have elevated amylase and lipase levels with no correlation to antiviral therapy.[27] Increasing numbers of adults with primary manifestations of HIV infection have presented with acute pancreatitis, suggesting a role of HIV in the pathogenesis of the disease.[157]

Parasite Infestations and Infections

Ascaris lumbricoides can migrate in the intestines to the ampulla of Vater and subsequently to the pancreatic duct or common bile duct. Obstruction of the biliary or pancreatic duct can cause acute pancreatitis.[2,12] Ascariasis is diagnosed when adult roundworms are identified in the duodenum by radiographs of the upper gastrointestinal tract (Fig. 52.1) or more commonly by ultrasonography or ERCP. Often a history of seeing worms in the feces can be elicited. Other roundworms including hookworms and *Strongyloides stercoralis* can cause obstruction and acute pancreatitis.[89,156] The flukes *Clonorchis sinensis* and *Fasciola hepatica* and the cestode *Taenia saginata* similarly can migrate to the pancreatic and biliary drainage systems and cause pancreatitis.[73,84,140]

FIG. 52.1 An ascaris close to the ampulla of Vater, with the body and tail lying in the second and third parts of the duodenum. The patient was a 9-year-old girl with acute pancreatitis.

Rarely hepatic hydatid cysts caused by *Echinococcus* can obstruct biliary drainage and cause pancreatic inflammation.[71] *Wuchereria bancrofti* occasionally has been found to cause chronic pancreatitis.[69] Parasitic infestations should be considered as a cause of pancreatitis, particularly in immigrant children and patients who have traveled to developing nations.

The protozoan *Cryptosporidium parvum* has been identified in the bile of an AIDS patient with elevated serum amylase levels and right upper quadrant abdominal pain.[54] ERCP demonstrated biliary and pancreatic ductal disease, and no other opportunistic pathogens were isolated. Cryptosporidia also have been observed in the interlobular pancreatic ducts of experimentally infected immunocompromised mice.[158] Whether cryptosporidial infection causes pancreatitis in immunocompetent patients is unknown; however, a previously healthy adolescent developed pancreatitis after having cryptosporidial diarrhea.[62] *Toxoplasma gondii* cysts have been found in the postmortem pancreatic tissue of patients with AIDS.[4,65] Rarely pancreatitis occurs during acute episodes of malaria.[150] Other systemic manifestations of malaria that often are present include high fever, hepatitis, intestinal malabsorption, encephalitis, and pulmonary insufficiency.

Mycoplasmal and Bacterial Infections

In older children and adults, moderately severe symptoms of pancreatitis have occurred just before or during the course of atypical pneumonia.[6,64] Most patients have had cold agglutinins in their sera, and all have had significant changes in *Mycoplasma pneumoniae* antibody titer. Some controversy has ensued over whether *M. pneumoniae* can cause acute pancreatitis without evidence of pneumonia. Although complement-fixing IgM antibodies against *M. pneumoniae* often increase significantly during the course of acute pancreatitis, researchers have argued that pancreatic cellular antigenic components similar to *Mycoplasma* lipid antigens are exposed during the disease process and that the antibodies elicited cross-react in *Mycoplasma* serologic assays.[83] Rarely *Mycoplasma* has caused severe necrotizing pancreatitis.[101]

Along with *M. pneumoniae* infection, legionellosis must be considered when acute pancreatitis develops along with pneumonia.[94,168] Miliary tuberculosis also can cause symptoms of pancreatitis.[125] Pancreatitis may occasionally be the only manifestation of tuberculosis and is usually diagnosed by fine-needle aspiration of the pancreas.[60,104]

Common pyogenic bacteria usually do not cause acute pancreatitis. Secondary invasion of inflamed pancreatic tissue does occur. Some evidence exists that circulating endotoxin from *Escherichia coli* can cause extrahepatic cholestasis and pancreatitis.[39] Acute pancreatitis also has been seen in children with hemolytic-uremic syndrome.[122,129] Pancreatitis can occur during acute episodes of enteritis. *Salmonella typhimurium, Salmonella typhosa, Campylobacter jejuni, Yersinia enterocolitica,* and *Yersinia pseudotuberculosis* all have been reported to cause clinically evident and laboratory-confirmed cases of pancreatitis.[10,37,93,131] There have been single reports of *Moraxella catarrhalis* and *Streptococcus pyogenes* causing severe pancreatitis in young children.[1,110]

Pancreatitis has been reported in children with leptospirosis.[109,141] *Brucella melitensis* also has been added to the list of uncommon causes of acute pancreatitis.[115] *Helicobacter pylori* has been suggested to influence the clinical course of pancreatitis in humans, but data are still lacking to imply a role in pancreatic pathology.[90]

Fungal Infections

Fungal infections have not been reported to cause acute pancreatitis in immunocompetent patients. *Aspergillus* has caused fatal hemorrhagic pancreatitis, however, in an adult patient with cancer who was undergoing chemotherapy.[56] *Candida* spp. and *Cryptococcus neoformans* have been isolated from the pancreatic tissue of patients with AIDS, but whether they cause clinical symptoms of pancreatitis is unknown.[171]

PATHOGENESIS

When trypsinogen is activated prematurely to trypsin within the pancreatic acinar cells, autodigestion occurs within the pancreas, causing edema. The microcirculation may be compromised, leading to ischemia, hemorrhage, or necrosis. An inflammatory response develops, which may be mild, as occurs in episodes of infectious pancreatitis, or may be more severe with hemorrhagic necrosis. Major mediators of an intense immune response include chemoattractant chemokines and their upregulated receptors; cytokines including tumor necrosis factor, interleukin (IL)-1, IL-6, IL-8, IL-10, and IL-33; and platelet-activating factor.[55,88,116,132,134] Mast cells may also play an active role in the proinflammatory process.[112] If an imbalance of the proinflammatory response occurs within the pancreas, a systemic inflammatory response including shock may occur, leading to high morbidity and mortality. Also sepsis may occur because of extensive necrotic tissue within the pancreas and translocation of microorganisms from the intestines.

TREATMENT

Despite increasing recognition of cases of childhood pancreatitis, no major pharmacologic advances have been made in the treatment of the disease since the mid-1970s. Animal data have shown that medications such as glucagon, aprotinin, 5-fluorouracil, somatostatin, probiotics, and vitamin-based antioxidants may be useful in the treatment of pancreatitis, but human benefit is lacking.[13,40,135] Clinical trials in adults and children using high-dose octreotide or gabexate mesilate have shown no or only modest benefit.[77,164]

The continuing main objectives of treatment are to relieve abdominal pain and treat aggressively systemic manifestations, such as shock, electrolyte abnormalities, and anemia. Meperidine continues to be the medication most commonly used for controlling pain. Meta-analyses in adults and series of pediatric patients have shown that feeding with a low-fat elemental diet decreases the complication rate of patients with acute pancreatitis and now is considered the treatment of choice over total parenteral nutrition.[8,24,144] Intravenous fluids and colloids are used during the acute episode to maintain intravascular volume. During the entire course of acute pancreatitis, the hematologic and biochemical parameters of the child must be monitored closely.

If the episode of pancreatitis is drug induced, use of the medication should be curtailed immediately. Often the symptoms recur if the medication is restarted. Pancreatitis caused by *M. pneumoniae* or that involve bacteria should be treated with proper antimicrobial agents. Obstructions to pancreatic flow (e.g., gallstones, roundworms, congenital abnormalities) may have to be excised or altered either by surgery or endoscopy.[3,19,72] Overall the mortality rate of acute pancreatitis in children today is 5%, with a mean duration of hospital stay at 13 days.[57]

COMPLICATIONS

During the acute episode of pancreatitis, the systemic inflammatory response syndrome may develop, leading to renal, hematologic, central nervous system, pulmonary, and cardiovascular complications. In 12% of children with pancreatitis, an inflammatory mass develops in the first weeks after the onset of illness; however, these masses more commonly occur after trauma.[165] Continued or increasing abdominal pain, nausea, or vomiting often accompanies the development of a phlegmon, abscess, or pseudocyst. An inflammatory phlegmon usually develops into a thin-walled pseudocyst of the lesser sac but may become secondarily infected and induce the formation of an abscess. Patients in whom an inflammatory mass develops must be monitored closely with frequent physical examinations and serial CT studies. In children with pseudocysts, acute abdominal pain accompanied by hypotension often signifies bleeding into the pseudocyst or rupture of the pseudocyst into the peritoneum. Slowly leaking pseudocysts may cause pancreatic ascites. Pseudocysts should be treated conservatively but have to be resected surgically, drained externally, or drained by endoscopy when complications occur.[9] Approximately 77% of pseudocysts in children resolve spontaneously and require no surgical intervention.[126]

The development of fever and leukocytosis during the course of pancreatitis should suggest an infected pseudocyst, pancreatic abscess, or sepsis. In adults, infectious complications account for 80% of deaths associated with acute pancreatitis.[22] Isolates from pancreatic abscesses and necrotic pancreatic tissue have yielded intestinal flora, including anaerobes, in more than 90% of cases, but *Candida* spp. are being isolated more frequently in many medical centers.[41,79,155] *Candida* skin colonization appears to best predict subsequent pancreatic tissue infection in critically ill patients.[59] Rarely *Streptococcus pneumoniae* can be isolated from infected pancreatic tissues of adults with chronic pancreatitis.[151] Carbapenems, such as imipenem and meropenem, are used commonly to treat adult patients with suppurative complications of pancreatitis because these antibiotics penetrate well into pancreatic tissues and have activity against intestinal flora. Performing percutaneous catheter drainage under CT guidance may reduce the mortality rate associated with treating pancreatic abscesses.[14] Rarely fistulas from pseudocysts or abscesses to other abdominal organs may develop.[63]

The role of prophylactic antibiotics in preventing the suppurative complications of acute pancreatitis remains controversial despite three decades of debate. Most recent meta-analyses on the subject conclude that prophylactic antibiotics do not prevent pancreatic necrotic tissue from being infected and do not prevent death, although a poorly powered 2010 Cochrane review suggests that imipenem may reduce the number of pancreatic infections.[106,162,169] Infections, when they do occur after the administration of prophylactic antimicrobial agents, often are caused by multiresistant bacteria or by fungi.

Osteolytic lesions resembling osteomyelitis may develop weeks to months after an acute episode of pancreatitis.[105] Elevated systemic levels of lipase activity possibly may cause intramedullary fat necrosis in the bone. Usually the lesions are asymptomatic and resolve spontaneously without therapy.

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