REVIEW ARTICLE

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Acute Pancreatitis

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N Engl J Med 2016;375:1972-81.
DOI: 10.1056/NEJMra1505202

THE INCIDENCE OF ACUTE PANCREATITIS IS INCREASING IN THE UNITED States, and the disorder is now one of the most common reasons for hospitalization with a gastrointestinal condition. In this review, we consider recent changes in the management of acute pancreatitis, as well as common misunderstandings and areas of ongoing controversy.

CAUSES OF ACUTE PANCREATITIS

Table 1 lists the causes of acute pancreatitis. Gallstones are the most common cause.[1,2] Migrating gallstones cause transient obstruction of the pancreatic duct, a mechanism shared by other recognized causes (e.g., endoscopic retrograde cholangiopancreatography [ERCP]), as well as purported causes (i.e., pancreas divisum and sphincter of Oddi dysfunction). A recent trial failed to show that sphincter of Oddi dysfunction contributed to post-cholecystectomy biliary pain,[3] and there are no convincing data from controlled trials that either pancreatic sphincter of Oddi dysfunction or pancreas divisum plays a role in acute pancreatitis.[4-6]

Alcohol is the second most common cause of acute pancreatitis. Prolonged alcohol use (four to five drinks daily over a period of more than 5 years) is required for alcohol-associated pancreatitis[7]; the overall lifetime risk of pancreatitis among heavy drinkers is 2 to 5%. In most cases, chronic pancreatitis has already developed and the acute clinical presentation represents a flare superimposed on chronic pancreatitis. The risk is higher for men than for women, perhaps reflecting differences in alcohol intake or genetic background.[8] The mechanisms by which alcohol causes acute (or chronic) pancreatitis are complex and include both direct toxicity and immunologic mechanisms.[9] The type of alcohol ingested does not affect risk, and binge drinking in the absence of long-term, heavy alcohol use does not appear to precipitate acute pancreatitis.[10]

Drugs appear to cause less than 5% of all cases of acute pancreatitis, although hundreds of drugs have been implicated.[11] The drugs most strongly associated with the disorder are azathioprine, 6-mercaptopurine, didanosine, valproic acid, angiotensin-converting–enzyme inhibitors, and mesalamine. Pancreatitis caused by drugs is usually mild. Recent data do not support a role for glucagon-like peptide 1 mimetics in causing pancreatitis.[12] It is common for patients to be taking one of the many drugs associated with pancreatitis when they are admitted to the hospital with acute pancreatitis,[13] but it is exceedingly difficult to determine whether the drug is responsible.

Mutations and polymorphisms in a number of genes are associated with acute (and chronic) pancreatitis, including mutations in the genes encoding cationic trypsinogen (*PRSS1*), serine protease inhibitor Kazal type 1 (*SPINK1*), cystic fibrosis transmembrane conductance regulator (*CFTR*), chymotrypsin C, calcium-sensing receptor, and claudin-2.[14] These mutations may serve as cofactors, interacting with

Table 1. Causes of Acute Pancreatitis.*

Cause	Approximate Frequency	Diagnostic Clues	Comments
Gallstones	40%	Gallbladder stones or sludge, abnormal liver-enzyme levels	Endoscopic ultrasonography can reveal very small gallbladder or duct stones.
Alcohol	30%	Acute flares superimposed on underlying chronic pancreatitis	Diagnosis rests on history, obtained with CAGE questions.†
Hypertriglyceridemia	2–5%	Fasting triglycerides >1000 mg/dl (11.3 mmol per liter)	
Genetic causes	Not known	Recurrent acute pancreatitis and chronic pancreatitis	
Drugs	<5%	Other evidence of drug allergy (e.g., rash) only in rare cases	The condition is idiosyncratic and usually mild.
Autoimmune cause	<1%	Type 1: obstructive jaundice, elevated serum IgG4 levels, response to glucocorticoids; type 2: possible presentation as acute pancreatitis; occurrence in younger patients; no IgG4 elevation; response to glucocorticoids	Type 1 is a systemic disease affecting the pancreas, salivary glands, and kidneys; in type 2, only the pancreas is affected.
ERCP	5–10% (among patients undergoing ERCP)		The symptoms can be reduced with rectal NSAIDS (diclofenac or indomethacin) or temporary placement of a stent in the pancreatic duct.
Trauma	<1%	Blunt or penetrating trauma, particularly in midbody of pancreas as it crosses spine	
Infection	<1%	Viruses: CMV, mumps, and EBV most common; parasites: ascaris and clonorchis	
Surgical complication	5–10% (among patients undergoing cardiopulmonary bypass)		The condition is probably due to pancreatic ischemia; pancreatitis may be severe.
Obstruction	Rare	Celiac disease and Crohn's disease, pancreas divisum (controversial), and sphincter of Oddi dysfunction (very controversial)	On rare occasions, malignant pancreatic duct or ampullary obstruction is seen.
Associated conditions	Common	Diabetes, obesity, and smoking	

* CMV denotes cytomegalovirus, EBV Epstein–Barr virus, ERCP endoscopic retrograde cholangiopancreatography, and NSAIDs nonsteroidal antiinflammatory drugs.
† CAGE is an acronym for the following questions: Have you ever felt you should cut down on your drinking? Have people annoyed you by criticizing your drinking? Have you ever felt bad or guilty about your drinking? Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye opener)?