Practice Guidelines in Acute Pancreatitis

Peter A. Banks, M.D.
Clinical Gastroenterology Service, Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts

Guidelines for clinical practice are intended to suggest preferable approaches to particular medical problems as established by interpretation and collation of scientifically valid research, derived from extensive review of published literature. When data are not available that will withstand objective scrutiny, a recommendation can be made based on a consensus of experts. Guidelines are intended to apply to the clinical situation for all physicians without regard to specialty. Guidelines are intended to be flexible, not necessarily indicating the only acceptable approach, and should be distinguished from standards of care that are inflexible and rarely violated. Given the wide range of choices in any health care problem, the physician should select the course best suited to the individual patient and the clinical situation presented. These guidelines are developed under the auspices of the American College of Gastroenterology and its practice parameters committee. These guidelines are also approved by the governing boards of the American Gastroenterological Association, American Society for Gastrointestinal Endoscopy, and American Association for the Study of Liver Diseases. Expert opinion is solicited from the outset for the document. Guidelines are reviewed in depth by the committee, with participation from experienced clinicians and others in related fields. The final recommendations are based on the data available at the time of the production of the document and may be updated with pertinent scientific developments at a later time. The following guidelines are intended for adults and not for pediatric patients.

INTRODUCTION

Despite recent advances in diagnosis and treatment, acute pancreatitis continues to be a serious illness with an overall mortality of 5-10%. The purpose of this practice guideline is to review the basis of decisions in the management of patients with acute pancreatitis. There are a number of important issues pertaining to these decisions, including the need for a consensus pertaining to terminology, agreement on the most appropriate criteria for determination of severity of acute pancreatitis, choices of medical versus surgical therapy in the treatment of acute pancreatitis, and treatment options for complications of acute pancreatitis including pancreatic pseudocysts.

CLINICAL CONSIDERATIONS

Definitions

An international symposium in 1992 provided an improved clinically based classification system for acute pancreatitis (1, 2). Acute pancreatitis is best defined as an acute inflammatory process of the pancreas that may also involve peripancreatic tissues and/or remote organ systems. Criteria of severity include the presence of organ failure (including shock, pulmonary insufficiency, and renal failure) and/or the presence of local complications (especially pancreatic necrosis). Early predictors of severity within the initial 48 h of hospitalization, including Ranson's signs and APACHE-11 points, serve as an early warning that an episode is likely to be severe (Table 1).

Pancreatic necrosis is defined as one or more areas of nonviable pancreatic parenchyma, and is usually associated with peripancreatic fat necrosis. Pancreatic necrosis may either be sterile or infected. Infected necrosis is characterized by the presence of bacteria (or fungi) within the necrotic tissue. Approximately 20% of patients with acute pancreatitis have necrotizing pancreatitis, the remainder have interstitial pancreatitis.

An extrapancreatic fluid collection results when pancreatic fluid extravasates out of the pancreas into the anterior pararenal space and at times into other areas as well. Fluid collections may occur in association with either interstitial or necrotizing pancreatitis. Most disappear during the recovery period. Almost all remain sterile.

TABLE I
Severe Acute Pancreatitis

• Early prognostic signs Ranson's signs ≥3 APACHE-11 score ≥8
• Organ failure and/or
• Local complications Necrosis Abscess Pseudocyst

A pancreatic pseudocyst is defined as a collection of pancreatic juice enclosed by a nonepithelialized wall that occurs as a result of acute pancreatitis, pancreatic trauma, or chronic pancreatitis. It usually requires at least 4 wk from the onset of acute pancreatitis to form a well-defined wall composed of granulation or fibrous tissue, and is usually rich in pancreatic enzymes. Most pancreatic pseudocysts are sterile. When infected, a pancreatic pseudocyst is now defined as a pancreatic abscess.

Pancreatic abscess is defined as a circumscribed intraabdominal collection of pus resulting from an episode of acute pancreatitis or pancreatic trauma. It usually occurs in the vicinity of the pancreas and contains little, if any, pancreatic necrosis. A pancreatic abscess usually does not occur until 4-6 wk after the onset of acute pancreatitis. Although the pathophysiology is uncertain, it may represent infection within a previously unrecognized pancreatic pseudocyst or secondary liquefaction and infection of pancreatic necrosis.

During the international symposium in 1992, a variety of terms were deleted. For example, the term hemorrhagic pancreatitis was abandoned because hemorrhage is not usually a major component of acute pancreatitis. The term phlegnion was also deleted because a consensus could not be reached as to the precise meaning of this word.

Pathophysiology

In acute pancreatitis, a variety of toxic materials including pancreatic enzymes, vasoactive materials, and other toxic substances are liberated by the pancreas and extravasate into retroperitoneal spaces, lesser sac, and the peritoneal cavity. These materials cause chemical irritation and contribute to third space losses of protein-rich fluid, hypovolemia, and hypotension. These toxic materials may also reach the systemic circulation by lymphatic and venous pathways and contribute to organ failure including shock, renal failure, and respiratory failure.

Factors that contribute to the intensity of the inflammatory response are largely unknown. In recent years, attention has focused on the possible contribution of leukocytes and their products (such as cytokines, enzymes including elastase, and nitric oxide) in intensifying inflammation of the pancreas and contributing to systemic complications (3). Attention has also focused on the vulnerability of the microcirculation of the pancreas (4, 5).

Clinical diagnosis

Almost all patients with acute pancreatitis experience abdominal pain, which is usually localized to the epiga.,,-trium or generally in the upper abdomen, and radiates to the back in approximately one-half of cases. The onset is frequently acute with pain reaching maximal intensity within 10-30 min, is often unbearable in severity, and persists for many hours without relief. The pain is frequently associated with nausea and vomiting which also persist for many hours. In severe cases, physical examination is noteworthy for severe upper abdominal tenderness and guarding (6).

The differentiaf diagnosis of acute pancreatitis includes mesenteric ischernia or infarction, perforated gastric or ditodenal ulcer, intestinal obstruction, biliary colic, and possibly even inferior wall myocardial infarction and ectopic pregnancy.

The diagnosis of acute pancreatitis can be supported by increases of serum amylase and serum lipase. Values of serum amylase and/or lipase in excess of three times the upper limit of normal are characteristic of acute pancreatitis and do not usually occur in other conditions (7). Smaller increases in serum amylase and lipase may occur in a variety of other conditions including perforated ulcer, mesenteric ischernia, and renal failure. It is usually not necessary to measure both serum amylase and lipase. Serum lipase is preferable if it can be measured as rapidly as serum arnylase because it remains normal in some conditions associated with an elevation of serum amylase including macroamylasemia, parotitis, and some carcinomas. The height of the serum amylase and/or lipase does not correlate with the severity of pancreatitis. Once the diagnosis of acute pancreatitis has been made with confidence on the basis of history, physical examination, laboratory tests including serum amylase and/or lipase, and computed tomography (CT) scan if needed, daily measurement of serum amylase after the diagnosis of acute pancreatitis has little if any value in assessing the clinical progress of the patient or ultimate prognosis. Measurement of amylase in urine including a timed 2-h urine collection and an arnylase-creatinine clearance ratio is not sufficiently accurate to distinguish acute pancreatitis from other intra-abdominal conditions associated with increase in serum amylase (such as a perforated peptic ulcer). Measurement of serum amylase isoenzymes has also been largely abandoned because the fraction of pancreatic isoamylase in serum may be increased in illnesses other than acute pancreatitis.

The distinction between alcoholic pancreatitis and gallstone pancreatitis is facilitated by laboratory tests. In particular, an ALT > 80 units per 100 ml is very specific for biliary pancreatitis. However, the sensitivity is only 50% (8). The amylase/lipase ratio has been proposed as an additional test that may help in this distinction but appears to be inaccurate (9).

TABLE 2
Ranson's Criteria of Severity at Admission

- Age >55 years
- WBC > 16,OOO/MM^3
- Glucose >200 mg/dl
- LDH >350 ITJ/L
- AST >250 U/L

During initial 48 h
Hct decrease of >I 0 vol %
BUN increase of >5 mg/dl
Ca" <8 mg/dl
Pa02 <60 mm Hg
Base deficit >4 niEq/L
Fluid sequestration > 6 L

Criteria of severity

Early prognostic signs. Recommendation: For each patient, a formalized system of scoring should be generated Thc APACHE-II score should be generated on the day of admission to help identify patients with severe pancreatitis. Afier 48 h, the APACHE-11 score andlor Ranson's score should be used for this purpose.

Early prognostic signs should be measured to alert physicians as early as possible which patients have the highest likclihood of developing severe pancreatitis. When patients exhibit indications of severe pancreatitis, they should be transferred to a unit (such as an intensive care unit) that provides closer observation.

Many scoring systems have been developed to serve as early prognostic signs (10). Ranson's 11 prognostic signs provide valuable information (Table 2). The five that are available on admission in general reflect the severity of the actite inflammatory process in the retroperitoneum, and the six that are measured at the end of the first 48 h reflect systemic effects of circulating enzymes on end organs (including respiratory failure, renal failure, and fluid sequestration). In many series, mortality is approximately 10-20% when there are three to five positive signs; > 50% when there are six or more Ranson's signs (11, 12). A major disadvantage of using Ranson's signs to gauge severity is that measurement of these signs is not complete until 48 h after admission.

Clinical reports have indicated that measurement of APACHE-II points on the day of admission has a high sensitivity and specificity in distinguishing mild from severe pancreatitis, and is superior to other grading systems for this purpose (Table 3) (13-15). In general, when APACHE-II points are ≤8 during the first 24-48 h,

TABLE 3
APACHE-II Severity of Disease Classification System

PHYSIOLOGIC VARIABLE	HIGH ABNORMAL RANGE				0	LOW ABNORMAL RANGE			
	+4	+3	+2	+1		+ 1	+2	+3	+4
Temperature-rectal (°C)	≥41°	39°-40.9°		38.5°-38.9°	36°-38.4°	34°-35.9'°	32°-33.9°	30°-31.9°	≤29.9°
Mean arterial pressure (mm Hg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart rate (ventricular response)	≥180	140-179	110-139		70- 109		55-69		≤39
Respiratory rate (nonventilated or ventilated)	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation: A-aD02 or Pa02 (mm Hg)									
a. $F10_2$ ≥0.5 record A-$aD0_2$	≥500	350-499	200-349		<200				
b. $F10_2$ < 0.5 record only $Pa0_2$					$P0_2$ >70	$P0_2$ 61-70		$P0_2$ 55-60	PO_2 <55
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7 15
Serum sodium (mmoUL)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	<110
Serum potassium (mmol/L)	≥7		6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9	<2 5
Serum creatinine (mg/100 ml) (Double point score for acute renal failure)	>3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20
White blood count (total/mm^3) (in 1000s)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		< 1
Glasgow Coma Score (GCS): Score - 15 minus actual GCS									
A Total Acute Physiology Score (APS): Sum of the 12 individual variable points									
Serum HC02 (venous-mmol/L) (Not preferred, use if no ABGs)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15

B AGE POINTS

Assign points to age as follows:

Age (yr)	Points
≤44	0
45-54	2
55-64	3
65-74	5
≥75	6

C Chronic health points.

If the patient has a history of severe organ system insufficiency or is immuno-compromised assign points as follows:

a. For nonoperative or emergency postoperative patients - 5 points or

b. For elective postoperative patients - 2 points.

Definitions. Organ insufficiency or immunocompromised state must have been evident prior to this hospital admission and conforms to the following criteria:

Liver. Biopsy proven cirrhosis and documented portal hypertension, episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma.

Cardiovascular. NY Heart Association Class IV.

Respiratory. Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, e.g., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythernia, severe pulmonary hypertension (>40 mmHg), or respirator dependency.

Renal. Recurring chronic dialysis.

Immunocompromised The patient has received therapy that suppresses resistance to infection (e.g. immuno-suppression, chemotherapy, radiation, longterm or recent high-dose steroids) or has a disease that is sufficiently advanced to suppress resistance to infection (e.g., leukemia, lymphoma, AIDS).

APACHE-II SCORE

Sum of **A + B + C**

A APS points _____

B Age points _____

C Chronic Health points _____

Total APACHE-11 SCORE _____

the patient usually survives. With increasing APACHE-II points during this time interval, morbidity and mortality increase. A particular value of APACHE-II scores is that it can be measured each day, whereas other systems including Ranson's signs require a full 48 h of measurement. At 48 h, Ranson's signs and APACHE-II scores are comparable in distinguishing mild from severe pancreatitis.

The clinician need not rely on a formalized scoring system to recognize a high probability of severe pancreatitis. In particular, the clinician should be aware of evidence of significant third space losses. This evidence may be in the form of hemoconcentration (hematocrit > 50%), oliguria, azotemia, tachycardia, or mild hypotension. When significant third space losses occur, patients should be transferred immediately to a special unit for aggressive fluid resuscitation. Measurements afforded by a Swan-Ganz catheter can provide valuable information that guides the clinician in restoring intravascular volume.

Organ failure. Recommendation: Patients with acute pancreatitis should be monitored closely for the development of organ failure.

The international symposium in 1992 determined that organ failure was the most important indicator of severity of acute pancreatitis (1) (Table 4). Many factors contribute to the development of organ failure including third space losses, toxic materials from the pancreas that reach the systemic circulation, and products of leukocyte secretion (including cytokines, elastase, and phospholipase-A2). GI bleeding may result from a number of causes including gastritis, gastric and duodenal ulcer, Mallory-Weiss syndrome, esophageal varices, and coagulopathy. Patients who demonstrate signs of organ failure must receive more diligent care. This type of care is ordinarily provided in a specialized unit, such as an intensive care unit.

TABLE 4
Organ Failure

- Shock-systolic BP < 90 nim Hg
- Pulmonary insufficiency-$Pa0_2$:5 60 min Hg
- Renal failure, creatinine >2 mg/dL
- GI bleeding, >500 ml/24 h

TABLE 5
Balthazar-Ranson Grading System

A. Normal appearing pancreas

B. Focal or diffuse enlargement of the pancreas

C. Pancreatic gland abnormalities associated with mild peripancreatic inflammatory changes ("stranding")

D. Fluid collection in a single location, usually within the anterior pararenal space

E. Two or more fluid collections near the pancreas (such as within the anterior pararenal space and within the lesser sac) and/or the presence of gas in or adjacent to the pancreas

TABLE 6
CT Severity Index (0-10)

CT Grade	Score	Necrosis	Score
A	0	None	0
B	1	<33%	2
C	2	33%-50%	4
D	3	>50%	6
E	4		
CT Grade (0-4) + Necrosis (0-6) = Total Score			

Local complications. An additional criterion of severity is the presence of local complications, including necrosis, pseudocyst, and abscess. A diagnosis of pancreatic necrosis is best made by dynamic contrast-enhanced computed tomographic scan (9, 16, 17). Pseudocyst and abscess can also be diagnosed by CT scan and at times also by abdominal ultrasound.

Imaging studies

Abdominal ultrasound. Recommendation: Abdominal ultrasound should be part of the evaluation of the initial episode of acute pancreatitis and should be performed within the initial 24-48 h of hospitalization. Its most important use among patients with additional episodes of pancreatitis is to determine whether the cause is gallstones.

Information that may by visualized on ultrasound includes gallstones, dilation of the common bile duct, and ascites. Ultrasound may also document the presence of pancreatic inflammation unless bowel gas obscures the pancreas (18).

Dynamic contrast-enhanced computed tomographic scan. Recommendation: Dynamic contrast-enhanced CT scan should be performed among patients demonstrated to have severe pancreatitis on the basis of a high APACHE-II score andlor evidence of organ failure.

Dynamic contrast-enhanced CT scan is the best available test to distinguish interstitial from necrotizing pancreatitis (16, 17). With this technique, intravenous contrast (usually a 60% iodinated contrast agent) is rapidly administered by pump at a constant rate (approximately 3 mI/s) with a total volume of 100-150 ml. The purpose of administering intravenous contrast is to distinguish interstitial from necrotizing pancreatitis. Interstitial pancreatitis is characterized by an intact microcirculation and uniform enhancement of the gland. Necrotizing pancreatitis is characterized by disruption of the microcirculation such that large areas do not enhance. Whereas small areas of nonenhancement could represent the presence of intraparenchymal fluid, large areas of nonenhancement indicate the presence of a disrupted microcirculation and pancreatic necrosis (16, 17).

When there is significant renal impairment (such as creatinine ~2 mg% or history of significant allergy to contrast material), CT scan should be performed without the use of intravenous contrast. Although the distinction between interstitial and necrotizing pancreatitis cannot be made unless intravenous (i.v.) contrast is used, a nonenhanced CT scan does provide important information in accordance with the Balthazar-Ranson criteria of severity (16) (Table 5). In 9~,neral, the most severe pancreatitis in terms of organ failure and the presence of pancreatic necrosis occur in gi ade D or E pancreatitis (16). When intravenous contrast is used, a CT severity index developed by Balthazar and Ranson can be used.

This indexawards points on the basis of the CT grade and the amount of necrosis (16, 17) (Table 6). For example, a patient with CT grade E is awarded 4 points; if, in addition, the patient is found to have 33-50% necrosis, an additional 4 points are awarded for a total score of 8. Patients with a total score of 7-10 have a higher morbidity and mortality than those who score less than 7 (16).

Magnetic resonance imaging. Thus far, magnetic resonance imaging (MRI) has not been widely applied in the care of patients with acute pancreatitis. There is preliminary evidence that would indicate that MRI provides the same information as is available on CT scan. The value of MRI in acute pancreatitis remains to be established.

Endoscopic retrograde cholangiopancreatography. Endoscopic retrograde cholangiopancreatography (ERCP) is not required to establish a diagnosis of acute pancreatitis or to provide prognostic information. Its main use is to locate and remove gallstones in the common bile duct among patients with severe pancreatitis attributable to gallstones (19,20).

TREATMENT OPTIONS

Goals

Goals of medical therapy include supportive care, limitation of systemic complications, prevention of pancreatic necrosis, and prevention of pancreatic infection once necrosis takes place (4, 5, 9).

Supportive care. Recommendation: All patients should receive close supportive care including effective pain control, fluid resuscitation, and nutritional support if it is anticipated that oral nutrition will be withheldfor more than 1 wk.

It is important to provide adequate relief of pain. Pain control usually requires injections of narcotic agents or the use of patient-controlled anesthesia (PCA). When pain is severe, adequate relief can be achieved more easily with PCA by increasing the dosage and by permitting more frequent administration under appropriate supervision.

Particular attention must be paid to providing adequate intravenous fluid replacement to prevent hypovolemia caused by third space losses and vomiting (4, 5). A nasogastric tube is not helpful in the treatment of mild acute pancreatitis but plays a role in treating either gastric or intestinal ileus and preventing, aspiration of gastric contents in severe acute pancreatitis (9). Nutritional support in the form of total parenteral. nutrition should be used for patients who have severe pancreatitis and will be without oral nutrition for at least 7-10 days (4, 5, 9). Lipids should be included in total parenteral nutrition unless serum triglycefides are elevated to a level > 500 mg%. There are no precise guidelines pertaining to refeeding. It is reasonable to withhold oral intake as long as there is a need for narcotic agents to relieve pain. Refeeding can be considered when abdominal pain and tenderness have subsided, bowel sounds have returned, and the patient is hungry. Because a diet composed of carbohydrates stimulate pancreatic secretion somewhat less than fat and/or protein, small feedings of carbohydrate-containing foods should be used. There is no evidence that H2 blocking agent or proton pump inhibitor prevents an exacerbation of symptoms (9).

Limitation of systemic complications. Recommendation: Patients with evidence of significant third space losses require aggressive fluid resuscitation. Patients with severe pancreatitis caused by gallstones should undergo urgent endoscopic retrograde cholangiography. If gallstones are found in the common bile duct, sphincterotomy should be performed and gallstones removed.

Systemic complications including respiratory failure, hypotension, and renal failure usually require care in a specialized unit. Vigorous fluid resuscitation and appropriate pulmonary care are the best ways to limit systemic complications. Despite these measures, some patients progress to intractable pulmonary insufficiency, refractory hypotension, and renal failure. There is no available method to prevent these systemic complications. Potentially, therapies designed to eliminate inflammatory mediators such as activated pancreatic enzymes and secretory products of leukocytes may in time prove helpful (3). Thus far, randomized prospective trials designed to eliminate activated pancreatic enzymes either by reducing pancreatic secretion, by directly inhibiting inflammatory mediators such as activated proteases, or by washing out inflammatory mediators by peritoneal lavage have been ineffective (9, 21). There have not as yet been randomized prospective trials designed to neutralize activated white blood cells and their products (including elastase, phospholipase-A2, cytokines, lysosomal hydrolases, reactive oxygen species, and nitric oxide).

In one study from the United Kingdom, endoscopic sphincterotomy within 72 h was shown to reduce morbidity but not mortality in severe gallstone pancreatitis experienced by elderly patients (19). It was not clear whether endoscopic sphincterotomy reduced morbidity by reducing the severity of pancreatitis (such as by preventing pancreatic necrosis) or by relieving biliary sepsis. In a second study from Hong Kong, endoscopic sphincterotomy within 24 h in both mild and severe gallstone pancreatitis also reduced morbidity but not mortality (20). It was ascertained that this improvement was a direct result of eliminating biliary sepsis.

It is difficult to provide a clear recommendation on the basis of the results of these two studies. When biliary sepsis is suspected, the role of endoscopic sphincterotomy is clear. Biliary sepsis should be suspected if there is progressive deterioration of liver enzymes, dilation of the common bile duct on ultrasound, documentation of bacteremia, or possibly the presence of organ failure, which might reflect sepsis. Although organ failure related to biliary sepsis may well improve after endoscopic removal of gallstones from the common bile duct, it is not known whether organ failure associated with severe pancreatitis responds in the same fashion as a result of this therapy. Nonetheless, because it may be impossible for the clinician to know the basis of organ failure, it is recommended that patients with gallstone pancreatitis who demonstrate organ failure undergo endoscopic retrograde cholangiography. If gallstones are discovered either impacted in the sphincter of Oddi or within the common bile duct, they should be removed endoscopically by an experienced therapeutic endoscopist.

Prevention of pancreatic necrosis. Although many factors may contribute to pancreatic necrosis, impairment of the microcirculation appears to be the most important. Aggressive fluid resuscitation, which appears to be beneficial in limiting renal failure and shock, may also play a role in limiting pancreatic necrosis. However, it is not clear that aggressive fluid resuscitation alone is sufficient to prevent pancreatic necrosis. In the

experimental animal, isovolemic hemodilution has proven to be beneficial in improving the microcirculation of the pancreas and preventing pancreatic necrosis (22). In one unrandomized trial in a small group of patients with severe pancreatitis, this technique was also thought to be beneficial. Although this result appears to be encouraging, randomized prospective trials will be required to evaluate this innovative therapy (23).

Prevention of pancreatic infection. Recommendation: In patients with necrotizing pancreatitis associated with organ failure, it is reasonable to initiate treatment with antibiotics with a good spectrum of activity against aerobic and anaerobic bacteria.

Many randomized controlled studies have failed to sho" a benefit of the use of antibiotics in preventing pancrcatic infection (9). These studies were flawed because the mjority of patients did not have severe pancreatitis (that is, necrotizing pancreatitis) and the antibiotics that were used may not have achieved therapeutic levels within pancreatic tissue (9, 24).

There is increasing evidence that translocation of bacteria from the colon is the most important cause of secondary pancreatic infection in necrotizing pancreatitis. Presumably, the use of an antibiotic that is effective against entoric organisms and also has high penetration of pancreatic tissue would be more successful. Recently, the use of Imipenem in a randomized prospective (but not blinded) trial of patiCnts with necrotizing pancreatitis was associated with a sigrificant decrease in pancreatic infection (from 30 to 12%) (15). However, there was no corresponding improvement in inor tality. Two additional randomized prospective, but not blinded, trials have suggested that prophylactic antibiotics may decrease mortality in necrotizing pancreatitis (26, 27). The lack of a blind protocol may have encouraged clinicians to offer surgical debridement preferentially among control patients but not among patients already receiving antibiotics. Additional surgery on control patients may have resulted in the conversion of sterile necrosis to infected necrosis that may have also increased mortality.

The prevalence of pancreatic infection in recent reports has decreased from 40 to 60% to 20 to 30% (25, 28, 29). Although the use of potent antibiotics may be responsible for this phenomenon, randomized prospective double-blind studies will be required to validate the role of prophylactic antibiotics in reducing pancreatic infection in necrotizing pancreatitis.

PRINCIPLES OF MANAGEMENT IN MILD ACUTE PANCREATITIS

Recommendation: In mild pancreatitis, fluid resuscitation and careful monitoring are the two most important components of treatment.

Mild pancreatitis (as defined by the absence of organ dysfunction) can be managed on a medical or surgical floor with emphasis on appropriate fluid replacement and careful monitoring. Treatment is largely supportive. CT scan is generally not helpful in the management of mild pancreatifis. Most patients with mild pancreatitis have interstitial disease.

PRINCIPLES OF MANAGEMENT IN SEVERE ACUTE PANCREATITIS

Recommendation: Dynamic contrast-enhanced CT scan is recommended at some point beyond the first 3 days in severe acute pancreatitis to distinguish interstitial from necrotizing pancreatitis. It is also recommended when pancreatic infection is suspected clinically.

Severe pancreatitis as evidenced by the development of organ failure requires treatment in a specialized unit by a multidisciplinary team composed of gastroenterology, surgery, and radiology. ERCP is recommended within the first 2-3 days among patients with severe gallstone pancreatitis who are exhibiting organ failure and/or evidence of biliary sepsis. If stones are found in the common bile duct, a sphincterotomy should be performed, and the stones removed (19, 20).

The role of CT scan in the first several days of acute pincreatitis remains controversial. There is general agreement that a CT scan should be performed if a serious surgical condition cannot be excluded clinically, such as a perforated ulcer or mesenteric infarction. Otherwise, the importance of an early CT scan in improving the care of a patient with acute pancreatitis has not as yet been validated by randomized prospective trials. Whereas the distinction between interstitial and necrotizing pancreatitis can usually be made with the use of dynamic contrast-enhanced com puted tomography within the first 3-4 days, this distinction (which certainly has prognostic significance) does not necessarily impact on the quality of care during the first several days, which are devoted to the prevention and treatment of organ dysfunction (4).

Intravenous contrast should not be used when there is significant renal impairment (such as a creatinine ≥2 mg%). When the creatinine is in the 1.5-2 mg% range, intravenous contrast should either not be used or non-ionic contrast should be substituted. Although a CT scan without intravenous contrast cannot define the presence of pancreatic necrosis, it nevertheless provides important information pertaining to severity in accordance with a Balthazar-Ranson A-E grading system (Table 5).

If a CT scan has not been performed during the first 3 days and the patient is demonstrating evidence of severe pancreatitis, a dynamic contrast-enhanced CT scan should be performed at some point within the next several days to distinguish interstitial from necrotizing pancreatitis (14, 15) (Fig. 1). If the CT scan indicates the presence of interstitial pancreatitis, medical therapy in an intensive care unit usually results in survival of the patient. If the patient is determined by CT scan to have necrotizing pancreatitis (and most patients with persisting organ failure have necrotizing pancreatitis), options for therapy depend on whether there is clinical improvement.

Necrotizing pancreatitis with clinical improvement

If there is improvement in organ failure and general systemic toxicity, medical treatment should be continued, including fluid resuscitation and treatment of systemic complications. Total parenteral nutrition may be required.

Necrotizing pancreatitis without clinical improvement

Recommendation: In the absence of clinical improvement, guided percutaneous aspiration should be performed to distinguish infected necrosisfrom severe sterile necrosis. Infected necrosis requires surgical debridement. Severe sterile necrosis can usually be treated medically. A subset of patients with severe sterile necrosis may require surgical debridement after 4-6 wk.

If there is no clinical improvement during the first 7-14 days, and especially if evidence of organ failure intensifies, the patient either has severe sterile necrosis or infected necrosis of the pancreas. Because an impressive

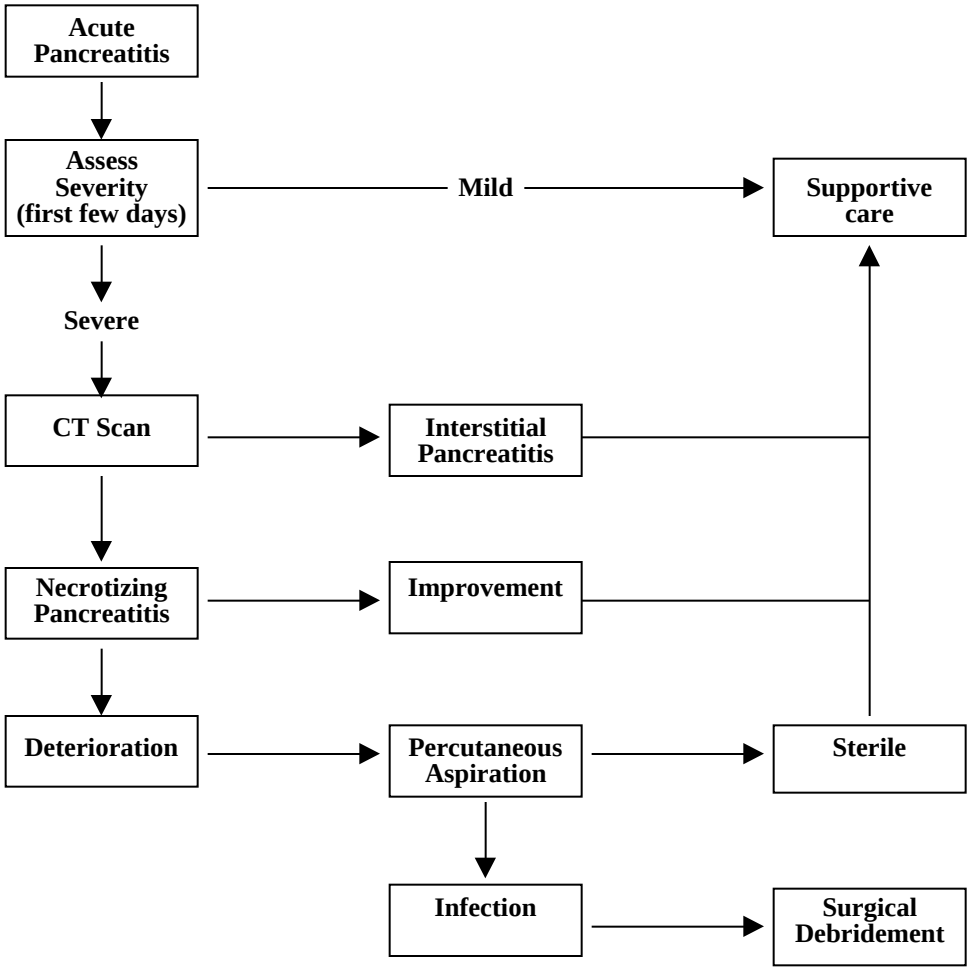

Fig 1. Algoritm for the management of acute pancreatitis

leukocytosis (> 20,000/MM^3) and fever (> 102.5°F) may occur in either situation, it is impossible to distinguish severe sterile necrosis from infected necrosis clinically. The clinician should be aware of the fact that the majority of pancreatic infections take place during the first 2-3 wk of illness (28, 29).

When infected necrosis is suspected on the basis of persistence of systemic toxicity and/or organ failure, it is recommended that a radiologist perform a CT-guided percutaneous aspiration for Gram's stain and culture (28, 29). The technique of guided percutaneous aspiration has proven to be safe and accurate in distinguishing sterile from infected pancreatitis. If infection is documented, surgical debridement should be performed (30, 31). Consideration has been given to two alternative therapies, namely, the use of a potent antibiotic such as Imipenem and/or percutaneous drainage with very large catheters. Presumably, if the infected material has liquefied sufficiently, insertion of multiple catheters may be sufficient therapy and a valid alternative to surgical debridement. At the present time, there are only a few reports of success of catheter drainage (16) and only anecdotal reports of survival in the absence of surgical debridement or multiple percutaneous drains. At the present time, surgical debridement is the treatment of choice in infected necrosis.

If guided percutaneous aspiration does not reveal the presence of bacteria, treatment choices include continuation of medical therapy or debridement of sterile necrosis. There are no randomized prospective trials comparing medical with surgical treatment or comparing early surgical debridement with late surgical debridement among patients with severe sterile necrosis. Patients with sterile necrosis complicated by multiple systemic complications have a high mortality whereas those with fewer systemic complications usually survive with medical treatment alone (13, 32, 33). There is an increasing consensus that patients with sterile necrosis should be managed medically as long as possible in the hope that systemic toxicity will eventually resolve and that surgery will not be necessary (31, 32). If surgery is required after 4-6 wk, presumably most of the acute toxicity has resolved, and debriclement can be performed with greater safety. Indications for late surgery include lingering respiratory insufficiency requiring prolonged intubation thought attributable to persisting intra-abdominal inflammation, refractory pain preventing oral intake of food, and compression of stomach causing intractable nausea and early satiety.

PRINCIPLES OF MANAGEMENT OF PANCREATIC PSEUDOCYST

Recommendation: Asymptomatic pseudocysts require no specific treatment. Symptomatic pseudocysts can be decompressed by surgical, radiologic, or endoscopic

methods. In the absence of randomized prospective trials, afirm recommendation cannot be made pertaining to these therapeutic options for symptomatic pseudocyst. Radiologic and endoscopic approaches should be confined to centers with specialists who have a particular expertise in these techniques.

Medical therapy

There is no proven medical strategy for a pancreatic pseudocyst. Twenty-five to fifty percent of pancreatic pseuclocysts after acute pancreatitis resolve spontaneously. There have been no randomized prospective trials that have evaluated alterations in diet, use of total parenteral nutrition, or medications that reduce the flow of pancreatic juice (such as proton pump inhibitors, H2 blocking agents, or octreotide). Hence, there is no proven strategy to facilitate the resolution of a pancreatic pseudocyst.

Until recently, prevailing thinking was that even asymptornatic pseuclocysts; at least 5 cm in size should be decompressed if they have been present for at least 6 wk. The rationale was a perception based on uncontrolled data that there was a high likelihood of a complication such as infection, bleeding, or rupture after this time interval. More recent data based on two retrospective studies would suggest that pseudocysts of any size that remain asymptomatic require no treatment (34, 35) If symptomatic, treatment could be surgical, radiologic, or endoscopic.

Surgical therapy

The time-honored method of decompressing a pancreatic pseudocyst is surgical (3 1). The two most common surgical procedures are cyst- gastrostomy (if the pseudocyst is impacted against the wall of the stomach) or Roux-en-Y cystjejunostomy (if the pseudocyst is not pressing against the stomach). An alternative for a pseudocyst located in the tail of the pancreas is distal pancreatectomy (usually with splenectomy). A pseudocyst that is in the head of the pancreas close to the duodenum can sometimes be decompressed surgically through the inner wall of the duodenum or with a Roux-en-Y loop of jejunum.

The mortality is less than 5%, and recurrence rate no more than 5-10%. Surgical treatment has not been compared with radiologic or endoscopic treatment in a randomized prospective trial.

Radiologic therapy

Radiologic therapy has included percutaneous needle aspiration and catheter drainage. In most instances, percutaneous needle aspiration of a pancreatic pseudocyst is followed by reaccumulation of fluid within several days. Hence, this technique is rarely used.

Percutaneous catheter drainage of a pancreatic pseudocyst is an effective method of decompression. It is important that the radiologist make daily rounds at the bedside to ensure that the care of the catheter is optimal, A radiologist should be available at all times to help in the evaluation of complications such as infection. Infection may occur if particulate necrotic material blocks the catheter.

Catheter drainage may fail if there is obstruction to flow in the main pancreatic duct (36). Accordingly, an ERCP should be obtained before an attempted catheter drainage. If there is obstruction to flow in the pancreatic duct such that the pseudocyst does not fill, pigtail catheter drainage should not be used. If the main pancreatic duct fills completely or if contrast material is seen to enter the pseudocyst, catheter drainage has a higher likelihood of success.

Caution should be exercised if a pseudocyst is associated with considerable underlying necrosis within the pancreas. Under these circumstances, only the fluid component of the pseudocyst can be easily removed through the catheter, and the underlying necrotic tissue may become secondarily infected once the catheter is introduced (37).

Endoscopic therapy

There has been success in the creation of an endoscopic cyst-gastrostomy or cyst-duodenostomy. Drainage can be maintained with the insertion of a double pigtail catheter between the cyst and stomach and/or a naso-cystic catheter. After 3-4 wk, a CT scan should be obtained to confirm closure of the pseudocyst, and the catheter can be then removed.

If an ERCP is obtained and contrast enters the pseudocyst , an alternative method of decompression would be the insertion of a stent via the main pancreatic duct into the cyst itself. Because of the concern that an endoscopically placed stent may induce ductal changes similar to those of pancreatitis, this technique should be used with caution and perhaps should be reserved for a pseudocyst in the head of the pancreas. Similarly, if there is substantial pancreatic necrosis, caution should be exercised with both of these techniques as in the case of the radiologic approach because of the possibility of infecting this necrosis (37).

Because failed radiologic and endoscopic drainage of pancreatic pseudocysts increases the morbidity of the patient and prolongs hospitalization (38), these therapies should be reserved for highly experienced radiologists and endoscopists and performed at centers that are conducting research in the treatment of pancreatic pseudocysts.

Reprint requests and correspondence: Peter A. Banks, M.D., Clinical Gastroenterology Service, Harvard Medical School, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115.

REFERENCES

1. Bradley EL III. A clinically based classification system for acute pancreatitis. Arch Surg 1993;128:586-90
2. Banks PA. A new classification system for acute pancreatitis. Am J Gastroenterol 1994;89:151-2 (editorial).
3. Rinderknecht H. Genetic determinants of mortality in acute necrotizing pancreatitis. Int J Pancreatol 1994;16:11-5.
4. Banks PA. Acute pancreatitis: Medical and surgical management. Am I Gastroenterol 1994;89:S78-85.
5. Banks PA. Acute pancreatitis: Conservative management. Dig Surg 1994; 11:220-5.
6. Banks PA. Acute pancreatitis. In: Haubrich WS, Schaffner F, Berk JE, eds. Bockus Gastroenterology, 5th ed. Philadelphia: WB Saunders, 1994;2888917.
7. Gumaste VV, Roditis N, Mehta D, et al. Serum lipase levels in nonpancreatic abdominal pain versus acute pancreatitis. Am J Gastroenterol 1993;88:20515.

8. Termer S, Dubner H, Steinberg W. Predicting gallstone pancreatitis with laboratory parameters: A meta-analysis. Am J Gastroenterol 1994;89:1863-6.
9. Steinberg W, Termer S. Acute pancreatitis. N Engl J Med 1994;330:1198-210.
10. Banks PA. Predictors of severity in acute pancreatitis. Pancreas 1991;S7-12.
11. Demmy TL, Burch JM, Feliciano DV, et al. Comparison of multipleparameter prognostic systems in acute pancreatitis. Am J Surg 1988; 156:492-6.
11 Agarwal N, Pitchumoni CS. Assessment of severity in acute pancreatitis. Am J Gastroenterol 1991;86:1385-91.
12. Karimgani 1, Porter KA, Langevin RE, et al. Prognostic factors in sterile pancreatic necrosis. Gastroenterology 1992;103:1636-40.
13. Wilson C, Heath DI, Intrie CW. Prediction of outcome in acute pancreatitis: A comparative study of APACHE-11, clinical assessment and multiple factor scoring systems. Br J Surg 1990;77:1260-4.
14. Dominguez-Munoz JE, Carballo F, Garcia MJ, et al. Evaluation of the clinical usefulness of APACHE U and SAPS systems in the initial prognostic classification of acute pancreatitis: A multicenter study. Pancreas 1993;8:682-6.
15. Balthazar EJ, Freeny PC, van Sonnenberg E. Imaging and intervention in acute pancreatitis. Radiology 1994;193:297-306.
16. Freeny PC. Incremental dynamic bolus computed tomography of acute pancreatitis. Int J Pancreatol 1993;13:147-58.
17. Freise J. Evaluation of sonography in the diagnosis of acute pancreatitis. In: Beger HG, Buchler M, eds. Acute pancreatitis. Berlin: Springer- Verlag, 1987, 118-31.
18. Neoptolemos JP, Carr-Locke DL, London NJ, et al. Controlled trial of urgent endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. Lancet 1988;2:979-83.
19. Fan S-T, Lei ECS, Mok FPT, et al. Early treatment of acute biliary pancreatitis by endoscopic papillotomy. N EngI J Med 1993;328:22832.
20. Buchler M, Malfertheiner P, Uhl W, et al. Gabexate mesylate in human acute pancreatitis. Gastroenterology 1993;104:1165-70.
21. Hotz HG, Schmidt J, Ryschich EW, et al. Isovolemic hemodilution with dextran prevents contrast medium induced impairment of pancreatic microcirculation in necrotizing pancreatitis of the rat. Am I Surg 1995;169:161-6.
22. Klar E, Foitzik T, Buhr H, et al. Isovolemic hemodilution with Dextran 60 as treatment of pancreatic ischernia in acute pancreatitis. Ann Surg 1993;217:369-74.
23. BUchler M, Malfertheiner P, Friess H, et al. Human pancreatic tissue concentration of bactericidal antibiotics. Gastroenterology 1992;103: 1902-8.
24. Pederzoli P, Bassi C, Vesentini S, Campedelli A. A randomized multicenter clinical trial of antibiotic prophylaxis of septic complications in acute necrotizing pancreatitis with Irnipenem. Surg Gynecol Obstet 1993;176:480-3.
25. Sainic, V, Kemppainen E, Puolakkainen P, et al. Early antibiotic treatment in acute necrotising pancreatitis. Lancet 1995;346:663-7.
26. Luiten EJT, Hop WCJ, Lange IF, et al. Controlled clinical trial of selective decontamination for the treatment of severe acute pancreatitis. Ann Surg 1995;222:57-65.
27. Gerzof SG, Banks PA, Robbins AK et al. Early diagnosis of pancreafic infection by computed tomography-guided aspiration. Gastroenterol. ogy 1987;93:1315-20.
28. Banks PA, Gerzof SG, Langevin RE, et al. CT-Guided needle aspiration of pancreatic infection. accuracy and prognostic implications. Int J Pancreatol 1995;18:265-70.
29. Banks PA, Gerzof SG, Chong FK, et al. Bacteriologic status of necrotic tissue in necrotizing pancreatitis. Pancreas 1990;56:330-3.
30. McFadden W, Reber HA. Indications for surgery in severe acute pancreatitis. Int J Pancreatol 1994;15:83-90.
31. Bradley EL III, Allen K. A prospective longitudinal study of obser. vation versus surgical intervention in the management of necrotizing pancreatitis. Am J Surg 1991;161:19-24.
32. Rattner DW, Legermate DA, Lee MJ, et al. Early surgical debridernent of pancreatic necrosis is beneficial irrespective of infection. Am J Surg 1992;162:137-43.
33. Vita GJ, Sarr MG. Selected madagement of pancreatic pseudocysts: Operative versus expectant management. Surgery 1992; 111: 123-30.
34. Yeo CJ, Bastidas JA, Lynch-Nyhan A, et al. The natural history of pancreatic pseudocysts documented by computed tomography. Surg Gynecol Obstet 1990; 170:411-7.
35. Aheame PM, Baillie JM, Cotton PB, et al. An endoscopic retrograde cholangiopancreatography (ERCP)-based algorithm for the management of pancreatic pseudocysts. Am I Surg 1992;163:111-6.
36. Hariri M, Slivka A, Carr-Locke DL, et al. Pseudocyst predisposes to infection when pancreatic necrosis is unrecognized. Am I Gastroenterol 1994;89:1781-4.
37. Rao R, Fedorak 1, Prinz RA. Effect of failed computed tomographyguided and endoscopic drainage on pancreatic pseudocyst management. Surgery 1993;114:843-9.