ACUTE PANCREATITIS

Guidelines for students and interns.

ГОСТРИЙ ПАНКРЕАТИТ

Методичний посібник для студентів та інтернів.

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ

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ACUTE PANCREATITIS

Абдомінальна хірургія

Тема №3 Гострий панкреатит

ГОСТРИЙ ПАНКРЕАТИТ

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ACUTE PANCREATITIS

HISTORICAL

Acute Pancreatitis is an inflammatory disease of the pancreas. The pancreas was given its name at the end of I to the beginning of the II centuries our era, when ***Rufus*** entered into literature; the term "PANCREAS" (from the Greek – "pan" = all; "creas" = meat).

Andreas Vesalius referred to the pancreas in the fifth book of his opus as a "glandulous organ" and presumed the pancreas to exert a protective effect on the stomach by serving as a cushion upon which it rested. Andreas Vesalius (1514 to 1564) was one of the first anatomists to depict the pancreas.

ANATOMY

The pancreas develops as two buds (ventral and dorsal) from the primitive duodenum. The accessory pancreatic duct (Santorini) is the duct of the dorsal bud. It persists as the main duct of the body and tail of the pancreas and passes anteriorly through the head of the pancreas to enter the second part of the duodenum at the accessory papilla. The ventral bud duct, which forms the main pancreatic duct in the head of the pancreas, fuses with the dorsal duct in the pancreatic head and then runs posteriorly and inferiorly to lie next to, and eventually join with, the bile duct at the ampulla of Vater.

Pancreatic acinar tissue is organised into lobules. The main duct ramifies into interlobular and intralobular ducts, ductules and finally acini. Acinar tissue comprises about 84 per cent of the pancreas, duct cells and blood vessels 4 per cent, and endocrine cells (the islets of Langerhans) about 2 per cent. The rest is connective tissues, and fat. The islets of Langerhans are distributed throughout the pancreas. Islets consist of differing cell types: 75 per cent are B cells (producing insulin), 20 per cent A cells (glucagon), D cells (somatostatin), and a small number of pancreatic polypeptide-secreting cells. Within an islet, the B cells form an inner core surrounded by the other cells. Capillaries draining the islet cells drain into the portal vein, forming a pancreatic portal system.

The pancreas is a retroperitoneal, organ. Composed of head, body, and tail. Superior mesenteric vein and artery lie behind neck of pancreas. The average **weight** of the pancreas is 85 g, and the usual **length** is 12-15 cm. The normal anteroposterior thickness of the head is less than 2.5 cm; the neck, 1.5 cm; the body, 2 cm; and the tail, 2.5 cm. Duct of Wirsung is major duct, 3-4 mm diameter, joins common bile duct at papilla of Vater. Minor duct is Santorini; 5-10% has Santorini as major drainage of pancreas, with vestigial Wirsung. **The head of the pancreas** lies over the aorta and under the stomach and transverse colon. The **common bile duct** courses posteriorly to the head of the pancreas and partially within it.

Arterial supply to head is pancreaticoduodenal arcades from gastroduodenal artery. Splenic, inferior pancreatic arteries supply body. **Venous**

drainage closely parallels arterial supply.

Lymphatic drainage is diffuse. Rich periacinar network that drain into 5 nodal groups: superior nodes; anterior nodes; inferior nodes; posterior PD nodes; splenic nodes.

Innervation of Pancreas:

- Sympathetic fibers from the splanchnic nerves.
- Parasympathetic fibers from the vagus.
- Both give rise to intrapancreatic periacinar plexuses.
- Parasympathetic fibers stimulate both exocrine and endocrine secretion.
- Sympathetic fibers have a predominantly inhibitory effect.

PHYSIOLOGY

The pancreas is made up of two tissues: 1) exocrine tissue and 2) endocrine tissue.

Exocrine tissue. In response to a meal, the pancreas secretes digestive enzymes in an alkaline (pH 8.4), bicarbonate-rich fluid. Acinar cells synthesize and secrete digestive enzymes while the duct cells secrete bicarbonate. The daily secretion is about 1 litre, containing 5-8 g of protein in the form of enzymes.

This secretion is under both neural and hormonal control. Stimulation of para-sympathetic nerves in the vagus results in secretion of bicarbonate and enzymes, whereas stimulation of splanchnic sympathetic nerves inhibits secretion. The rate of secretion and the bicarbonate content of the pancreatic juice are increased by the hormone secretin, which is released from the duodenal mucosa by luminal acid stimulation. Pancreatic enzyme secretion is potently stimulated by pancreozymin, which is released from the duodenal mucosa by luminal fat and peptides. The pancreas is made of four major cell types:

- Alpha (A) cells secrete glucagon.
- Beta (B) cells secrete insulin.
- Delta (D) cells secrete somatostatin.
- F cells secrete pancreatic polypeptide.

Pancreatic secretion can also be stimulated by hormones produced within the pancreas and small bowel, vasoactive intestinal peptide (VIP) and gastrin; and inhibited by the pancreatic hormones somatostatin, pancreatic polypeptide and glucagon.

Pancreatic secretion consists of a cephalic phase, initiated by the thought of food, a gastric phase produced by food in the stomach, and an intestinal phase mediated by secretin and pancreozymin release from the duodenum and jejunum. About 20 digestive enzymes are produced: **proteolytic enzymes -** trypsin; **lipolytic enzymes** - lipase; **starch-splitting enzymes** - amylase and **nucleic acid splitting enzymes** - ribonuclease. Activation by **enterokinaze.**

Endocrine tissue. The endocrine tissue, which consists of the islets of Langerhans, secretes hormones into the bloodstream. The hormones secreted by endocrine tissue in the pancreas are insulin and glucagon (which regulate the level of

glucose in the blood), and somatostatin (which prevents the release of other two hormones).

ETIOLOGY AND PATHOGENESIS

The etiology and pathogenesis of acute pancreatitis have been intensively investigated. The etiology of acute pancreatitis is a complex subject because many different factors have been implicated in the causation of this disease, and sometimes there are no identifiable causes. Two factors, alcoholism and biliary tract stone disease, account for 80 to 90% of the cases. The remaining 10 to 20 % is accounted for either by idiopathic disease or by a variety of miscellaneous causes including trauma, surgery, drugs, heredity, infection and toxins.

Gallstone-induced pancreatitis is caused by duct obstruction by gallstone migration. Obstruction is localized in the bile duct and pancreatic duct, or both. Duct obstruction promotes pancreatitis by increasing duct pressure and subsequent unregulated activation of digestive enzymes. Biliary sludge refers to a viscous bile suspension that contains cholesterol crystals and calcium bilirubinate granules embedded in strands of gallbladder mucus. Sludge is associated with bile stasis, long-lasting fast, distal bile duct obstruction, and total parenteral feeding (Fig. 3.6). Most patients with biliary sludge are asymptomatic. Biliary sludge is commonly seen in patients with recurrent acute pancreatitis of unknown origin, and cholecystectomy might prevent the recurrence of pancreatic disease.

Alcohol abuse is the second most frequent cause of acute pancreatitis, but the correlation between alcohol and pancreatitis is not completely understood. In experimental models, Gorelick showed that ethanol directly sensitizes acinar cells to cholecystokinin stimulation. As the development of pancreatitis might be affected by both genetic and environmental factors, failure to inhibit trypsin activity or to wash active trypsin into pancreatic ducts might promote alcoholic pancreatitis. In fact, the exact mechanism underlying alcoholic acute pancteatitis has not been extensively elucidated.

Pancreas divisum, a common congenital anatomical variant of the pancreatic duct in about 7% of autopsy series, results from the absence of fusion between the dorsal and ventral ductal systems.

The possible consequence of pancreas divisum is a stenosed or inadequately patent minor papilla, preventing normal drainage of pancreatic secretions and leading to increased intraductal pressure. However, whether pancreas divisum is related to pancreatitis is highly controversial. Whether dysfunction of sphincter of Oddi can trigger acute pancreatitis by increasing intrapancreatic duct pressure is also controversial.

Intraduct papillary mucinous tumor might be another cause of acute pancreatitis. Tumor or mucus produced by it obstructs the main pancreatic duct and its side branch, or both. Logically, the consequence is increased pancreatic duct pressure caused by pancreatic hyperstimulation and pancreatic duct obstruction. Thus, these tumors might trigger acute pancreatitis through the same mechanisms underlying acute biliary pancreatitis.

Endoscopic retrograde cholangiopancreatography (ERCP) is a potential cause of acute pancreatitis. Asymptomatic hyperamylasaemia occurs in 35%-70% of patients after the procedure. ERCP has a higher risk of inducing acute pancreatitis when it is performed to treat Oddi sphincter dysfunction than to remove gallstones in the bile duct. Other risk factors for post-ERCP pancreatitis include young age, female sex, number of attempts to cannulate papilla, and poor emptying of pancreatic duct after opacification. Prevention of post-ERCP pancreatitis in high-risk patients might be achieved by placing a temporary pancreatic stent.

Hypercalcaemia is another rare and inconsistent cause of acute pancreatitis. Because the incidence of pancreatitis is low in patients with chronic hypercalcaemia, additional factors are probably needed to induce pancreatitis. Drugs rarely induce acute pancreatitis. Cases of drug-induced pancreatitis have been reported. Many infectious agents are associated with acute pancreatitis, but no microorganism has ever been identified within the pancreas. However, it was reported that acute pancreatitis is associated with viral or bacterial infections, and infestation with parasites.

Summary – causes of acute pancreatitis:

1. Ethanol abuse.
2. Biliary diseases: gallstones; choledocholithiasis; biliary sludge; microlithiasis; mechanical/structural injury: sphincter of Oddi dysfunction; pancreas divisum; trauma; postendoscopic retrograde cholangiopancreatography; pancreatic malignancy.
3. Medications: azathiprine/6-mercaptopurine; dideoxyinosine; pentamidine; sulfonamides; thiazide diuretics; ACEI.
4. Metabolic: hypertriglyceridemia; hypercalcemia.
5. Infectious: viral; bacterial; parasitic.
6. Vascular: vasculitis.
7. Genetic predisposition.
8. Idiopathic.

Under physiologic conditions, the pancreas synthesizes a large amount of protein. A majority of these proteins consist of digestive enzymes. Because the exocrine pancreas produces several enzymes that are potentially injurious to itself, it prevents autodigestion by intracellularly assembling the inactive precursors of these enzymes, called proenzymes or zymogens, which are then transported and secreted outside of the gland. Their activation occurs safely in the duodenum, where the brush-border enzyme enteropeptidase (or enterokinase) activates the trypsinogen, and the resulting trypsin then activates the other zymogens in a cascade reaction. To further protect the pancreas from these potentially harmful digestive enzymes, they are segregated from the cytoplasmic space within acinar cells by being enclosed within membrane-bound organelles, referred to as zymogen granules. Another layer of protection is provided by the synthesis of trypsin inhibitors, which are transported and

stored along with the digestive enzyme zymogens. These are available to inhibit small amounts of prematurely activated trypsinogen within pancreatic acinar cells. It is generally theorized that acute pancreatitis occurs when this process goes awry and the gland is injured by the erroneously activated enzymes that it produces. There are three reasons for this theory: (a) the pancreas is digestible by the activated enzymes of the duodenum; (b) activated digestive enzymes are found within the pancreas during pancreatitis, and (c) the histology of pancreatitis is suggestive of a coagulative necrosis.

When the pancreas becomes damaged or the ducts become blocked, the trypsin inhibitor accumulates and activates the pancreatic secretions that escape into the surrounding tissue, resulting in inflammation, thereby causing acute pancreatitis.

Release of kallikrein and chymotrypsin results in increased capillary membrane permeability, leading to leakage of fluid into the interstitium and development of edema and relative hypovolemia. Elastase is the most harmful in terms of direct cell damage, it causes dissolution of the elastic fibers of blood vessels and cuts, leading to hemorrhage. Phospholipase A_2 in the presence of bile destroys phosholipids of cell membranes causing severe pancreatic and adipose tissue necrosis. Lipase flows into damaged tissue and is absorbed into systemic circulation, resulting in fat necrosis of the pancreas and surrounding tissues.

It has become apparent that there are two phases of acute pancreatitis: an early phase (within the first or second week of onset) and a second phase occurring after the first or second week of onset of the disease. During the first phase, the severity is defined by organ failure that persists for >2 days (persistent organ failure), or by death. Organ failure is secondary to the host's systemic inflammatory response elicited by the tissue injury/cytokine response and not necessarily related to the extent of necrosis. Local or systemic infection is usually not yet present or involved in the systemic response. During the second phase, the severity is defined by persistent organ failure, by complications of the pancreatitis that develop in the pancreatic parenchyma and peripancreatic tissues, or by death.

During the first phase, the pancreatic/peripancreatic conditions evolve dynamically; this process evolves from the initial state of inflammation and variable degrees of pancreatic and peripancreatic ischemia and/or edema either to resolution or to irreversible necrosis and liquefaction, and/or further development of collections containing fluid and/or solid material in and around the pancreas. The extent of the pancreatic and peripancreatic changes is usually but not always directly proportional to the severity of organ failure. Over the first week or so, organ failure related to the systemic inflammatory response either resolves or becomes more severe.

In the second phase, the disease either resolves (edematous pancreatitis without necrosis) or tends to stabilize (but not normalize) or progress and enter into a more protracted course lasting weeks to months related to the necrotizing process—necrotizing pancreatitis. Also, during this second phase, changes in the pancreatic/peripancreatic morphology occur much more slowly. Mortality in the second phase is usually related to persistent organ failure and/or to complications of necrotizing pancreatitis. Severity of the overall disease process in this second phase is defined not only by persistent organ failure, but also by the development of

complications of necrotizing pancreatitis requiring active intervention (operative, endoscopic, laparoscopic, and/or percutaneous), or requiring other supportive measures (such as the need for ventilator support, renal dialysis, or nasojejunal feedings), leading to prolonged hospitalization, or by death.

These two phases have a distinct pathophysiology. Because the need for treatment in the first phase is determined more by the presence or absence of organ failure and less by morphologic findings in and around the pancreas, one should apply "clinical" parameters for its classification of severity and its treatment. In contrast, in the second phase of the disease, the need for treatment is determined by the presence of symptoms and/or complications of necrotizing pancreatitis. The type of treatment is determined mainly by the morphologic abnormalities of the pancreatic/peripancreatic region as seen on the most readily available imaging test (contrast-enhanced computed tomography – CECT) and by the presence/absence of local complications which may manifest systemically, such as infection of necrotic tissues giving rise to bacteremia and sepsis.

CLASSIFICATION AND DEFINITIONS

Mostly the Atlanta classification (1992) is used (H.G. Beger's et al., 1991): divided into **mild** and **severe** acute pancreatitis and the forms of disease:

1. Interstitial edematous pancreatitis.
2. Pancreonecrosis:
   a) non-infected and b) infected.
3. Abscess of pancreas.
4. Pseudocyst of pancreas:
   a) non-infected and b) infected.

In 2012, experts reconsidered the classification of Atlanta and offered the following definitions – **3rd revision based** on worldwide review/suggestions (Table 1.1).

Table 1.1. Acute pancreatitis — comparison of classification schemes

Atlanta Classification (1992)	**New Classification (2012)**
ACUTE PANCREATITIS:	
Interstitial pancreatitis Sterile necrosis Infected necrosis	Interstitial edematous pancreatitis (IEP) Necrotizing pancreatitis: *Pancreatic necrosis with peripancreatic necrosis:* ➢ Sterile and Infected necrosis. *Pancreatic necrosis alone:* ➢ Sterile and Infected necrosis. *Peripancreatic necrosis alone:* ➢ Sterile and Infected necrosis.
(< 4 weeks after onset of pancreatitis) Acute fluid collection.	**(< 4 weeks after onset of pancreatitis)** *Acute peripancreatic fluid collection*

	(APFC): ➢ Sterile and Infected. *Acute post-necrotic collection (APNC)* : *Pancreatic necrosis with peripancreatic necrosis:* ➢ Sterile and Infected. *Pancreatic necrosis alone:* ➢ Sterile and Infected. *Peripancreatic necrosis alone:* ➢ Sterile and Infected
(> 4 weeks after onset of pancreatitis) Pancreatic pseudocyst. Pancreatic abscess.	**(> 4 weeks after onset of pancreatitis)** *Pancreatic pseudocyst:* ➢ Sterile and Infected *Walled-off necrosis (WON)* *Pancreatic necrosis with peripancreatic necrosis:* ➢ Sterile and Infected. *Pancreatic necrosis alone:* ➢ Sterile and Infected. *Peripancreatic necrosis alone:* ➢ Sterile and Infected.

Interstitial edematous pancreatitis (IEP). Contrast-enhanced computed tomography (CECT) in patients with IEP demonstrates diffuse or localized enlargement of the pancreas and normal, homogeneous enhancement of the pancreatic parenchyma.

Similarly, the retroperitoneal and peripancreatic tissues usually appear normal or show mild inflammatory changes in the peripancreatic soft tissues characterized by haziness or mild stranding densities and varying amounts of non-enhancing areas of low attenuation (peripancreatic fluid, see below, pancreatic and peripancreatic collections); the presence of non-enhancing areas of variable density (solid components) in these fluid collections is indicative of peripancreatic necrosis, excludes the diagnosis of IEP, and the process should be termed acute necrotizing pancreatitis with peripancreatic necrosis alone (see below). On occasion, an early contrast enhanced computed tomography (done within the first several days of onset of pancreatitis) exhibits diffuse heterogeneity in pancreatic parenchymal enhancement which cannot be characterized definitively as IEP or patchy necrosis; with these findings, the presence or absence of pancreatic necrosis may have to be classified initially as indeterminate. A contrast enhanced computed tomography done 5-7 days later should allow definitive classification.

Necrosis. Acute necrotizing pancreatitis has three forms: pancreatic parenchymal and associated peripancreatic necrosis (most common), pancreatic parenchymal necrosis alone (rare), and peripancreatic necrosis alone (about 20% of patients). Thus, it is important to determine the absence of necrosis (interstitial

edematous pancreatitis) or the presence of necrosis (necrotizing pancreatitis), the site(s) of necrosis (pancreatic parenchyma and peripancreatic tissue, pancreatic parenchyma alone, or peripancreatic tissue alone), and the absence of infection (sterile necrosis) or the presence of infection (infected necrosis). Necrosis can involve the pancreatic parenchyma and/or the peripancreatic tissues. The presence of necrosis in either the pancreatic parenchyma or the peripancreatic tissues defines the process as necrotizing pancreatitis and differentiates necrotizing pancreatitis from IEP. Necrotizing pancreatitis involves one of three types, either pancreatic parenchymal necrosis with peripancreatic necrosis, pancreatic parenchymal necrosis alone, or peripancreatic necrosis alone (without any discernable pancreatic parenchymal necrosis).

Pancreatic Necrosis. About 80% of patients with necrotizing pancreatitis have a variable extent of pancreatic parenchymal necrosis on contrast enhanced computed tomography evident by the lack of parenchymal enhancement with intravenous contrast. Most commonly, pancreatic necrosis is associated with a variable extent of peripancreatic necrosis, but on occasion, pancreatic necrosis alone will be seen. The contrast enhanced computed tomography may demonstrate only minimal gland enlargement or diffuse or localized enlargement of the pancreas with one or more areas of non-enhancing pancreatic parenchyma. The extent of pancreatic parenchymal necrosis is quantified in three categories: < 30%, 30-50%, and > 50% of the total pancreatic parenchyma.

The presence of pancreatic parenchymal non-enhancement differentiates pancreatic necrosis from IEP and from peripancreatic necrosis alone. The appearance of a limited area of pancreatic parenchymal necrosis estimated to be < 30% of the gland may, on follow-up imaging, prove to be due to fluid within the pancreas rather than necrosis. Therefore, estimates of pancreatic necrosis of < 30% on the initial contrast enhanced computed tomography are less reliable to establish a diagnosis of pancreatic necrosis. A follow-up contrast enhanced computed tomography 4-6 days later depending on the clinical situation would be required to distinguish IEP from pancreatic necrosis when the estimate for pancreatic necrosis is <30% on the initial contrast enhanced computed tomography; an MRI may be preferred if facilities are available.

Peripancreatic necrosis alone. The presence or absence of necrosis in the peripancreatic tissues is difficult to confirm by contrast enhanced computed tomography early in the course of the disease. contrast enhanced computed tomography suggests the presence of peripancreatic necrosis when there are non-homogeneous non-enhancing areas of variable density containing solid components in one or more areas, especially in the regions of the lesser sac and retroperitoneum. The necrotic area(s) may be exclusively extrapancreatic (peripancreatic necrosis alone) with no recognizable areas of pancreatic parenchymal necrosis on contrast enhanced computed tomography; this entity is recognized in up to 20% of the patients who require operative or interventional management of necrotizing pancreatitis. This distinction proves important clinically, because patients without recognizable pancreatic gland necrosis have a better prognosis and outcome than patients with pancreatic parenchymal necrosis, but more morbidity than interstitial edematous

pancreatitis. The Atlanta Classification had no way to subclassify this unique group of patients. If concern is great enough, MRI or ultrasonography may aid in the recognition of solid components within the peripancreatic "fluid" collection.

Infection. Sterile necrosis and infected necrosis are distinguished according to the absence or presence of infection in the non-enhancing pancreatic and/or peripancreatic area(s). Distinction between sterile and infected necrosis is very important clinically, because the presence of infection confers a different natural history, prognosis, and approach to treatment. Patients with sterile necrosis usually do not require intervention unless they remain persistently unwell with ongoing pain, anorexia, early satiety, vomiting, fever, and/or inability to resume oral intake by 4 or more weeks after onset of acute pancreatitis. Infection can be diagnosed definitively only by percutaneous, image-guided, fine-needle aspiration (FNA) with a positive Gram stain and culture. The presence of infection can be presumed when there is extraluminal gas in the non-enhancing area(s) on contrast enhanced computed tomography, usually a pathognomonic sign, which reflects the presence of a gas-forming organism without or with perforation (a rare event) of an adjacent hollow viscus. FNA has a false-negative rate of about 10%. Therefore, a negative FNA should be repeated after an appropriate interval, such as 5-7 days, if a clinical suspicion of infection persists. It must be recognized that proof of infection preoperatively in the absence of extraluminal gas requires image-guided, fine needle aspiration; not all patients with necrotizing pancreatitis, however, require FNA; indeed, FNA should be reserved for the persistently ill patient in whom infection is suspected based on the clinical findings or imaging-based findings.

Pancreatic and peripancreatic collections. Acute pancreatitis can be associated with pancreatic and peripancreatic collections.

IEP can be associated with acute peripancreatic collections and pancreatic pseudocysts. In contrast, the three forms of necrotizing pancreatitis can be associated with pancreatic and peripancreatic collections, including acute peripancreatic fluid collections, pancreatic pseudocysts, acute post-necrotic collections, and walled-off necrosis.

Acute peripancreatic fluid collection (APFC) (1st 4 weeks after onset of IEP**):** a) sterile and b) infected.

These fluid collections arise within a few days of onset of IEP and may persist for several weeks. They have no solid components and result from parenchymal and/or peripancreatic inflammation. APFCs exist predominantly adjacent to the pancreas, have no definable wall, and are confined by the normal peripancreatic fascial planes, primarily the anterior pararenal fascia. These APFCs should be differentiated from ascites. In contrast, apparent "fluid" collections that replace pancreatic parenchyma should be considered to represent necrosis. APFCs arise presumably from rupture of a small, peripheral, pancreatic ductal side branch, or they result from local edema related to the pancreatic inflammation and have no connection with the ductal system. These APFCs do not necessarily reflect pancreatic parenchymal tissue necrosis or even a minor or major ductal disruption.

Most APFCs remain sterile and are reabsorbed spontaneously within the first several weeks after onset of acute pancreatitis. Intervention at this setting for these collections is usually not necessary and, in fact, may be detrimental, because any mechanical intervention by operation or drain insertion may convert a sterile fluid collection to an infected one.

Pancreatic pseudocyst: a) non-infected and b) infected (suppurative).

Pseudocysts on contrast enhanced computed tomography become defined usually > 3-4 weeks after onset of pancreatitis as a well-circumscribed, usually round or oval, homogeneous peripancreatic fluid collection surrounded by a well-defined wall with little to no associated tissue necrosis within the fluid collection; an MRI or ultrasonography may be required to confirm the absence of necrosis within the fluid collection. Pseudocysts develop from an APFC that persists for > 4 weeks after onset of pancreatitis. Prior to 4 weeks, a definite wall may not have formed, and these collections are categorized as an APFC. On rare occasions, an APFC may develop a clearly evident wall (capsule) prior to 4 weeks after onset of acute pancreatitis and be better termed a pseudocyst. Analysis of the pseudocyst fluid usually shows increased amylase and lipase levels indicative of an ongoing communication with the pancreatic ductal system; however, the ductal disruption that led to extravasation of amylase/lipase-rich fluid and pseudocyst formation may eventually seal off spontaneously, explaining the well-known phenomenon of spontaneous regression of pancreatic pseudocysts. The absence or presence of a recognizable ductal communication or a dilated main pancreatic duct at the time of diagnosis may be important clinically, because these findings may dictate different management algorithms; however, the presence or absence of ductal communication cannot be determined reliably by contrast enhanced computed tomography, and it is not necessary to identify the presence or absence of a communication by ERCP for classification in this new, imaging-based classification. MRI or EUS may allow this communication to be determined; the presence or absence of ductal communication may be important in determining therapy, but is not required in this classification.

Determination of presence or absence of infection in a pancreatic pseudocyst is also potentially important. An infected pancreatic pseudocyst contains purulent liquid without an associated solid component (necrosis). This definition differentiates pseudocyst from infected APNC and infected walled-off necrosis (see below). As with all peripancreatic collections, image-guided FNA with Gram stain and culture for bacteria and fungal organisms or the presence of extraluminal gas are necessary to confirm the pre-interventional diagnosis of infection. A diagnosis of infection may change the management, but a FNA is not required for all peripancreatic fluid collections.

Acute post-necrotic collection (APNC):

Site: a) pancreatic parenchyma and peripancreatic tissues; b) pancreatic parenchyma alone; c) peripancreatic tissues alone.

Infection status: a) sterile; b) infected.

Persistent collections in patients with acute necrotizing pancreatitis are termed

APNCs to distinguish them from APFCs and pseudocysts. An APNC contains both fluid and necrotic contents to varying degrees as well as areas of loculations; therefore, this classification has avoided use of the term "fluid collections" and has used the term "collections" to emphasize this concept and to differentiate these collections from an APFC and a pseudocyst. In APNCs, a continuum exists from the initial solid necrosis to liquefaction necrosis depending on duration since onset of the disease. It should be understood that not all pancreatic and peripancreatic collections can be categorized readily into an APFC or an APNC, especially within the first week after onset of acute pancreatitis. Both APFCs and APNCs may appear as homogeneous, non-enhancing areas of low density; however; after the first week or two, APNCs should become evident on contrast enhanced computed tomography, MRI, transabdominal ultrasonography, or EUS.

As pancreatic parenchymal or peripancreatic necrosis matures, liquefaction develops as the necrotic tissue breaks down, usually beginning 2-6 weeks after the onset of pancreatitis. This entity of an APNC has imaging-based morphologic features on contrast enhanced computed tomography (or MRI, EUS, or transabdominal ultrasonography) of both necrosis and fluid within the same circumscribed area. An APNC is not a pancreatic pseudocyst, because it arises from the necrosis of necrotizing pancreatitis and contains necrotic tissue. It is often, but not invariably, associated with disruption of the main pancreatic ductal segment within the zone of parenchymal necrosis. Thus, an APNC may or may not have a connection with the pancreatic ductal system.

Walled-off necrosis:

Site: a) pancreatic parenchyma and peripancreatic tissue; b) pancreatic parenchyma alone; c) peripancreatic tissues alone.

Infection status: a) sterile; b) infected.

As the APNC matures, the interface between the necrosis and the adjacent viable tissue becomes established by a thickened wall without an epithelial lining; this process is similar in principle to the development of a pseudocyst. This entity, termed walled-off necrosis (WON), referred to previously in the literature often as organized pancreatic necrosis, necroma, or pancreatic sequestration, represents the late stage of an APNC. WON occurs at the end stages of the necrosis continuum and represents a distinct entity both clinically and therapeutically; this entity was not recognized as such in the Atlanta Conference. A WON may be infected or sterile. The diagnosis of infected APNC can be suspected on contrast enhanced computed tomography by the presence of extraluminal gas, but definitive preoperative diagnosis of infection requires image-guided FNA with Gram stain and culture for bacteria and fungal organisms. Patients with sterile WON may remain ill despite the absence of infection (the so-called "persistently unwell patient"). Rarely, a WON may be mistaken for a pseudocyst on contrast enhanced computed tomography; therefore, MRI, transabdominal ultrasonography, or EUS may be a valuable complimentary test to document the presence of solid debris within the collection. This differentiation is important, because management, especially via a minimally invasive route, is different for WON versus an APFC and a pancreatic pseudocyst and requires removal

of the solid debris.

Just as with APNCs, WON more commonly involves the pancreatic parenchyma with areas of peripancreatic necrosis as well, on rare occasion the pancreatic parenchyma alone, or the peripancreatic tissues alone and not containing any pancreatic parenchymal necrosis.

Determination of the presence of a ductal communication is of potential importance, because it may affect management; however, the presence or absence of a ductal communication will likely not be evident on contrast enhanced computed tomography, and it is not necessary to identify the presence or absence of pancreatic ductal communication in this new imaging-based classification. Therefore, ERCP is not necessary or necessarily indicated in the treatment of APNC. MRI or EUS may allow the presence of ductal communication to be established, but neither test is always warranted.

Clinical classification (1st week):

1. Definition of Acute Pancreatitis. The clinical definition of acute pancreatitis, whether in the presence or absence of underlying chronic pancreatitis, requires two of the following three features: 1) abdominal pain suggestive strongly of acute pancreatitis (acute onset of a persistent, constant epigastric pain often radiating to the back), 2) serum amylase and/or lipase activity at least 3 times greater than the upper limit of normal (although the amylase or lipase activities are usually much greater than three times increased), and 3) characteristic findings of acute pancreatitis on transabdominal ultrasonography or on contrast enhanced computed tomography . Contrast enhanced computed tomography is considered currently to be the best, most universally available imaging modality. Characteristic findings on magnetic resonance imaging (MRI) can replace contrast enhanced computed tomography in centers that have expertise and experience with MRI. If abdominal pain is suggestive strongly of acute pancreatitis, but the serum amylase and/or lipase activity is less than 3 times the upper limit of normal, characteristic findings of acute pancreatitis on contrast enhanced computed tomography, ultrasonography, or MRI are required to confirm the diagnosis of acute pancreatitis. If a diagnosis of acute pancreatitis is established based on abdominal pain and an increased serum amylase or lipase activity, but there are no systemic signs of severe disease (see below), a contrast enhanced computed tomography may not be necessary for patient care.

2. Definition of Onset of Acute Pancreatitis. The onset of acute pancreatitis is defined as the time of onset of abdominal pain (not the time of admission to the hospital). The interval between onset of abdominal pain and admission to the hospital should be noted precisely. This interval refers specifically to admission to the first hospital (not the time that the patient is transferred from the first hospital to a tertiary care hospital).

3. Definition of Severity of Acute Pancreatitis. The definition of severe acute pancreatitis is also based on the two phases of the disease — **the early phase and the late phase.** This classification recognizes two degrees of severity: non-severe acute pancreatitis and severe acute pancreatitis.

The Early Phase. The definition of the severity of acute pancreatitis during

the first 1-2 weeks is based on clinical rather than morphologic parameters. Initially at presentation and during the first 1-2 weeks, patients should be classified temporarily as having severe acute pancreatitis based on persistence of a systemic inflammatory response syndrome (SIRS) for more than 48 hours or based on development of organ failure. SIRS can be defined by presence of 2 or more of the following criteria: pulse > 90 beats/min, rectal temperature < 36ºC or >38ºC, white blood count < 4000 or > 12,000 per mm^3, and respirations > 20/min or PCO_2 < 32mmHg. Ultimately, the definition of severe acute pancreatitis in the first phase of the disease is persistent organ failure for more than 48 hours and/or death. In this early phase of acute pancreatitis, non-severe acute pancreatitis is defined as either the absence of organ failure or the presence of organ failure that does not exceed 48 hours in duration.

Definition of Organ Failure. Three organ systems should be assessed to define organ failure: respiratory, cardiovascular, and renal. Organ failure is best and most easily and universally defined in accordance with the Marshall scoring system (Table 1.2) as a score >2 for at least one of these three organ systems: respiratory (pO_2/FIO_2); renal (serum creatinine in µmol/l or mg/dl); and cardiovascular (systolic blood pressure in mm Hg).

Table 1.2. Marshall scoring system

Organ system	**Score**				
		1	2	3	4
Respiratory (PaO_2/FIO_2)	400	301-400	201-300	101-200	≤ 101
Renal* (serum creatinine, µmol/l)	134	134-169	170-310	311-439	> 439
(serum creatinine, mg/dl)	1.4	1.4-1.8	1.9-3.6	3.6-4.9	> 4.9
Cardiovascular (systolic blood pressure, mmHg)	90	<90 Fluid responsive	<90 Not fluid responsive	< 90, pH<7.3	< 90, pH<7.2

*Considerations should be taken for patients with pre-existent chronic renal failure (baseline serum creatinine ≥ 134 µmol/l or ≧ 1.4 mg/dl.

The Marshall scoring system was chosen for its simplicity, universal applicability across multiple international centers, and its ability to stratify disease severity easily. Although not part of this classification, other scoring systems, such as the modified Marshall score (which includes the Glasgow coma score and platelet count) and the SOFA scoring system for patients managed in a critical care unit, which includes inotropic and respiratory support, can be determined at presentation and daily thereafter, so that a comparison can be made with the Marshall scoring system. Persistent multi-system organ failure is defined as two or more organs failing

over the same 3-day period. Sequential organ failure should be noted in order to determine its overall impact on morbidity and mortality. For patients with hypotension, it is recommended that central venous pressure or pulmonary capillary wedge pressure be monitored to determine which patients are fluid-responsive. Determination of blood gases is recommended when arterial oxygen saturation is < 95% (on room air) and in selected situations when oxygen saturation is > 95% (such as persistent hypotension, persistent tachypnea with respiratory rate >16/minute, or severe peritoneal irritation as manifested by abdominal rigidity).

The Second Phase of the Disease. During the second phase of the disease beginning 1-2 weeks after onset of pancreatitis, severity is defined by persistent organ failure, by the development of complications prolonging hospitalization either requiring active intervention (operative, endoscopic, laparoscopic, or percutaneous) or other supportive measures (such as need for respiratory ventilation, renal dialysis, or nasojejunal feeding), or by death. Severity can be subclassified and stratified for the purpose of clinical studies by a) persistent organ failure, b) need for active intervention to treat pancreatic and peripancreatic collections, c) need for supportive measures, and d) death.

DIAGNOSIS

1. Complains:

- Abdominal pain: sudden, intense, and continuous mid epigastric or in the left upper quadrant.
- May radiate to back.
- Abdominal pain may be lessened in fetal or orthopneic positions.
- Weight loss, nausea and vomiting.
- Jaundice.

2. Objective sings of disease:

Common clinical signs depend on the period of the disease in which the patient is examined by the doctor.

The early phase:

- Tachycardia, decreased blood pressure.
- May be shock.
- Palpable abdominal tenderness.
- Decreased bowel sounds due to paralytic ileus.
- Ascites.
- May be able to palpate pancreas.
- Decreased bowel sounds due to paralytic ileus.
- Left pleural effusion, atelectasis, pneumonia.

The second phase:

With aseptic course:

- Normothermia;
- The fluid isn't infected.

With infected course:

- Severe intoxication;
- Purulent resorptive fever;
- Infected fluid.

3. Pathognomonic signs:

- **Gray-Turner's sign:** discoloration of the skin due to dissection of peripancreatic hemorrhage may be visible in the flanks.
- **Cullen's sign:** bluish discolouration around the umbilicus.
- **Mondor's sign**: violet sports on the body and face.
- **Holsted's sign**: cyanosis of skin of abdominal wall.
- **Grunvald's sign:** petechial skin rash in the navel region.
- **Korte's sign:** regional tension of anterior abdominal wall in epigastria region, along the projection of pancreas.
- **Mayo–Robson's sign**: palpation pain in the left costal-vertebral angle.
- **Gobye's sign:** abdominal distension in upper region.
- **Voskresensky's sign:** absence of pulsation of abdominal aorta in epigastria region (sign of parapancreatical infiltration).

The main tasks of special investigations are:

- Differential diagnosis with other abdominal and extraabdominal diseases.
- Detection of the form (Interstitial pancreatitis or pancreonecrosis).
- Detection of the previous system disorders for immediate correction.

LABORATORY STUDIES

- Amylase and lipase. Serum amylase and lipase levels are typically elevated in persons with acute pancreatitis. Amylase or lipase levels at least 3 times above the reference range are generally considered diagnostic of acute pancreatitis.

The level of serum amylase or lipase does not indicate whether the disease is mild, moderate, or severe, and monitoring levels serially during the course of hospitalization does not offer insight into prognosis.

- Liver-associated enzymes. Determine alkaline phosphatase, total bilirubin, aspartate aminotransferase and alanine aminotransferase levels to search for evidence of gallstone pancreatitis.
- Calcium, cholesterol and triglycerides. Determine these levels to search for etiology of pancreatitis (hypercalcemia or hyperlipidemia) or complications of pancreatitis (hypocalcemia resulting from saponification of fats in the retroperitoneum). However, be wary of the fact that baseline serum triglyceride levels can be falsely lowered during an episode of acute pancreatitis.
- Serum electrolytes, creatinine, and glucose. Measure these to look for electrolyte imbalances, renal insufficiency, and pancreatic endocrine dysfunction.

- CBC. Haemoconcentration at admission (an admission hematocrit value greater than 47%) has been proposed as a sensitive measure of more severe disease. Leukocytosis may represent inflammation or infection.
- C-reactive protein. A C-reactive protein (CRP) value can be obtained 24–48 hours after presentation to provide some indication of prognosis. Higher levels have been shown to correlate with a propensity toward organ failure. A CRP value in double figures (i.e., >10 mg/dL) strongly indicates severe pancreatitis. CRP is an acute-phase reactant that is not specific for pancreatitis.
- Arterial blood gases. Measure ABGs if a patient is dyspneic. Whether tachypnea is due to acute respiratory distress syndrome or diaphragmatic irritation must be determined.
- Trypsin and its precursor trypsinogen-2 in both the urine and the peritoneal fluid have been evaluated as possible markers for acute pancreatitis but are not widely used.

RADIOGRAPHIC EVALUATION

Abdomen X-ray. X-ray examinations of the chest and abdomen may be useful in establishing the diagnosis of pancreatitis. The identification of a single dilated atonic loop of small bowel ("sentinel loop") or **Gobie's symptom** (gas in atonic transversum colon) provides contributory evidence for the diagnosis.

Ultrasound (US) may show enlarged pancreas with stranding, abscess, fluid collections, necrosis or pseudocyst. US may also demonstrate the presence of gallbladder pathology, such as cholecystitis, cholelithiasis, or a dilated common bile duct. US has a major limitation in that it cannot be performed when excessive bowel gas is present as occurs with an ileus.

Endoscopic Retrograde Cholangiopancreatography and Angiography.

In addition to the diagnosis of IEP versus all three forms of acute necrotizing pancreatitis, the radiologist should address the morphologic findings of: a) Absence or presence of pancreatic parenchymal necrosis (perfusion defects) and, if present, the site(s) and extent (<30%, 30-50%, and >50%); b) characteristics of pancreatic and peripancreatic collections: location—either intrapancreatic or extrapancreatic, homogeneity and density of the collection (i.e. presence of a solid component), presence/absence of a well-demarcated wall, and presence of extraluminal gas, such as bubbles or air-fluid levels; c) other related extrapancreatic findings such as cholecystolithiasis, choledocholithiasis, gallstones, dilation of the biliary tree, venous thrombosis/obstruction of the portal, splenic, and/or mesenteric vein(s) (+/- perisplenic, perigastric varices), arterial (pseudo)aneurysm, pleural effusion(s), ascites, and inflammatory-like involvement of peripancreatic organs-stomach, duodenum, small bowel, colon, spleen, and kidney, and liver; d) other unrelated intraperitoneal or intrathoracic abnormalities.

Together, the radiologist and clinician can thus classify the type of pancreatitis and its complications in the patient and plan appropriate management. A multidisciplinary approach in the care of these patients should lead to better overall outcomes.

Computed Tomography (CT) scan can be very useful in predicting severity

of disease. The contrast enhanced CT, imaging-based morphologic classification is a clinical tool and as such requires close collaboration between radiologist and clinician. The radiologist describes the morphology and the clinician incorporates the radiologic findings into the clinical setting—severity of patient illness, timing since onset of disease, and associated co-morbidities. Dynamic computed tomographic and magnetic resonance imaging have also been used to 'stage' pancreatic inflammatory changes for prognosis. Initial studies focused on pancreatic swelling and extra-pancreatic inflammatory findings. The first CT grading system from New York applied five grades: A, normal; B, pancreatic swelling; C, peripancreatic fat abnormalities; D, single fluid collection; and E, multiple collections or gas. The relationship to general morbidity was poor, even though CT grades correlated well with Ranson scores. Non-ionic contrast agents and more rapid dynamic scanning in the late 1980s led to acceptance of CT for the diagnosis of pancreatic necrosis, but few studies have investigated its prognostic role. The importance of pancreatic necrosis in prognosis was acknowledged by its incorporation within the revised New York grading system. Applied in 88 attacks (25% had necrosis), a high CT severity index was associated with 92% morbidity and 17% mortality, and a low index with 2% morbidity and no mortality. Although both CT and magnetic resonance imaging provide morphological assessments of severity and prognosis, they represent an expensive, and not necessarily more accurate, alternative to existing prognosticators. Significant necrosis may occur without organ-system failure, leading to the aphorism 'treat the man, not the scan', and the converse is also true. A preoccupation with prognosis may detract from the most important function of imaging techniques, which remains primarily diagnostic, and to provide precise localisation, differentiation and management of pancreatic collections.

Magnetic Resonance Cholangiopancreatography (MRCP) newest "fad": decreased nephrotoxicity from gadolinium; better visualization of fluid collections: MRCP allows visualization of bile ducts for stones.

Endoscopic US (even newer but used less): does not allow stone extraction or stent insertion.

Fine Needle Aspiration. Fine needle aspiration (FNA) is useful in the early detection of infected pancreatic necrosis. It is the early detection of this condition that has a major impact on the further management and outcome in acute pancreatitis. Since clinical and laboratory findings can be often similar in patients with either sterile or infected necrosis), this important differentiation is best made by a fine needle aspiration. FNA can be performed either under CT or under ultrasound guidance. Ultrasonographically guided FNA is a fast and reliable technique for the diagnosis of infected pancreatic necrosis. Since complication rates are very low, the procedure can be repeated at short intervals to improve the diagnostic accuracy. This technique has been recommended for all patients with necrotizing pancreatitis in whom a systemic inflammatory response syndrome persists beyond the first week after onset of symptoms or when there is deterioration in the clinical situation. The technique is safe and accurate and a positive result is an indication for surgical intervention without undue delay.

In contrast, it has also been reported that percutaneous aspiration and drainage

can often predispose to secondary infection of an originally sterile necrosis.

COMPLICATIONS

Local Complications Of Acute Pancreatitis

< 4 weeks after onset of pancreatitis:

- Acute peripancreatic fluid collection (sterile and Infected).
- Acute post-necrotic collection (sterile and infected).
- Pancreatic necrosis with peripancreatic necrosis (sterile and infected).
- Pancreatic necrosis alone (sterile and infected).
- Peripancreatic necrosis alone (sterile and infected).
- Pancreatic ascites.

> 4 weeks after onset of pancreatitis:

- Pancreatic pseudocyst (sterile and infected).
- Walled-off necrosis.
- Pancreatic necrosis with peripancreatic necrosis (sterile and infected).
- Pancreatic necrosis alone (sterile and infected).
- Peripancreatic necrosis alone (sterile and infected).

Involvement of adjacent organs, with hemorrhage, thrombosis, bowel infarction, obstructive jaundice, fistula formation, or mechanical obstruction.

Common Complications of Acute Pancreatitis:

- Pulmonary: acute respiratory distress syndrome (ARDS); atelactasis; pleural effusions.
- Cardiovascular: cardiogenic shock.
- Neurologic: pancreatic encephalopathy.
- Metabolic: metabolic acidosis; hypocalcemia; altered glucose metabolism.
- Hematologic: disseminated intravascular coagulopathy (DIC); GI bleeding (peptic ulcer; erosive gastritis; portal vein or splenic vein thrombosis with varices).
- Renal: prerenal failure.

DIFFERENTIAL DIAGNOSIS

- Acute edematous pancreatitis and acute necrotizing pancreatitis.
- Other diseases: acute appendicitis; ileus; perforated gastroduodenal ulcer; biliary disease.

TREATMENT

PRINCIPLES OF TREATMENT OF ACUTE PANCREATITIS:

1. Resuscitations intravascular therapy.
2. Analgesia.
3. Put pancreas to “rest”.
4. Nothing by mouth, nasogastric tube only for ileus or vomiting.

5. Treat complications (pulmonary, shock, renal, metabolic).
6. Remove obstructing gallstone in severe gallstone pancreatitis endoscopically
7. Antibiotics for severe disease (after two weeks).
8. Percutaneous aspiration of pancreas to document infection in patient who fails to respond.

CONSERVATIVE TREATMENT OF STERILE PANCREATIC NECROSIS

Much of the initial therapy of pancreatitis is physiologically based. One of the major principles of medical treatment has been the proposition that pancreatic volume and enzyme secretion must be restricted.

The intravascular volume deficit may exceed 30% due to peripancreatic fluid sequestration and vomiting. Volume restoration must be rapid and efficient to maintain regular monitored urine output of more than 40 ml/hr.

Several approaches to the reduction of pancreatic secretion have been employed. Continuous nasogastric aspiration and H_2-blockers have routinely been used to decrease the hydrogen ion stimulation of secretin. In addition, gastric distention by swallowed air is prevented, and a gastrin-induced pancreatic enzyme response is thereby controlled. While these considerations represent sound application of physiologic principles to therapy, a recent prospective study could find no difference in the outcome of patients with moderately severe alcoholic pancreatitis whether or not nasogastric suction was used. Other methods to reduce acid secretion and other pancreatic stimulation include the use of cimetidine, anticholinergics, and glucagon.

Perhaps the most challenging aspect of managing acute pancreatitis is the regulation of intravenous fluid therapy. The amount of fluid required is dictated by the degree of severity of any particular episode. As much as one third of the circulating blood volume may be sequestered in the “third space” as a result of the pancreatic inflammatory process. Careful monitoring of fluid balance by central venous or pulmonary artery pressure along with hourly measurement of urination.

With severe pancreatitis, administration of both crystalloid and colloid solutions may be superior to the use of crystalloids alone. Every effort should be made to ensure that hypoperfusion of the pancreatic microvasculature and subsequent ischemic necrosis; do not occur on the basis of a volume deficit. With early, vigorous, and well-monitored fluid replacement, shock resulting from pancreatitis should decrease in frequency.

About one third of the fatalities due to pancreatitis are associated with respiratory insufficiency. When rapid and shallow respirations are observed, blood gas analysis is indicated, including determination of pO_2, pCO_2, and pH. The finding of abnormal gas exchange should be regarded as an ominous sign indicating the need for respiratory assistance. Ranson and his associates found that 38 per cent of a group of patients with acute pancreatitis exhibited severe arterial oxygen desaturation, as evidenced by an average PaO_2 of 66 mm. Hg. The hypoxemia was improved by the administration of albumin and diuretics. The association between severe pancreatitis and pulmonary insufficiency appears to be more than casual,

although the mechanism involved is not yet known.

The severe pain of acute pancreatitis prevents the patient from resting, and results in ongoing cholinergic discharge, which stimulates gastric and pancreatic secretion. Therefore, pain management is of great importance. Administration of buprenorphine, pentazocine, procaine hydrochloride, and meperidine are all of value in controlling abdominal pain. Morphine is to be avoided, due to its potential to cause sphincter of Oddi spasm. Antibiotic therapy has not proved to be of value in the absence of signs or documented sources of infection.

Cautious resumption of oral feeding consisting of small and slowly increasing meals is permissible after the abdominal pain and tenderness have subsided, serum amylase has returned to normal, and the patient experiences hunger. This usually occurs within a week of the onset of an attack of mild acute pancreatitis. A low-fat, low-protein diet is advocated as the initial form of nutrition following an attack of acute pancreatitis.

As indicated previously, hypokalemia or hypocalcemia or both may occur and precipitate disturbances in cardiac function. Repletion with intravenous potassium salts must be accomplished by electrocardiographic monitoring; potassium salts must be administered cautiously when any degree of oliguria is present. The intravenous injection of calcium salts is reserved for the therapy of incipient tetany, as signaled by the appearance of a positive Chvostek or Trousseau sign, and for the development of previously mentioned electrocardiographic conduction changes.

Pancreatitis is also an autodigestive process, and various protease-inhibiting drugs, including aprotinin, gabexate mesylate, camostate, and phospholipase A_2 inhibitors, as well as fresh frozen plasma, have been tested to prevent proteolysis, but with little success. Theoretically, inhibition of proteolytic activity might affect the course of pancreatitis. The release of trypsin from the affected gland is capable of activating pancreatic kallikrein, another proteolytic enzyme, which splits the vasoactive decapeptide kallidin from a globulin. This peptide is a potent vasodilatory and hypotensive agent. An antitryptic antikallikrein polypeptide (Trasylol) has been extracted from bovine parotid glands. This agent has been shown to inhibit trypsin, chymotrypsin, kallikrein, and plasmin. Despite potent in vitro antiproteolytic activity, in a recent large prospective double-blind study, Trasylol was not found to be any more effective in modifying the course of moderately severe pancreatitis than a placebo, regardless of the dosage given.

Somatostatin is now applied to the treatment of acute pancreatitis, it is used to decrease pancreatic secretion; it also decreases intestinal motility and reduces endocrine/exocrine pancreatic secretion.

Between 15-20% of all acute pancreatitis patients develop severe necrotizing pancreatitis. In this subgroup, stratification according to infection status is crucial. Infection of pancreatic necrosis is currently the most important risk factor contributing to death in severe necrotizing pancreatitis and surgical necrosectomy along with debridement is the most widely accepted modality for management of infected pancreatic necrosis. In contrast, the management of sterile necrosis even when associated with organ failure, is controversial and has evolved considerably in recent years. Although necrosis confirms the presence of severe disease and the extent

of the sterile necrotic tissue is proportional to the rate of organ failure, sterile necrosis is primarily managed conservatively with antibiotics, nutritional support and active intensive care measures.

Although the development of infected pancreatic necrosis confers a significant risk of death, welldesigned trialsand meta-analyses have shown no benefit of prophylactic antibiotics. Prophylaxis with antibiotic therapy is not recommended for any type of acute pancreatitis unlessinfection is suspected or has been confirmed (Fig. 3.8). Nonetheless, many patients continue to receive prophylactic antibiotics despite guidelines to the contrary. Antibiotics are usually administered to patients with severe acute pancreatitis. Antibiotics with high penetration into pancreatic tissue include the fluoroquinolones, imipenem/cilastatin, and metronidazole. The mortality rate of patients with infected pancreatic necrosis treated conservatively is 60 to 100%. The use of antibiotics in patients with necrosis without infection is debated. Overall mortality does not seem to change significantly, but there is a lengthening of time to develop infection with the use of antibiotics. Antibiotic use, however, has been suggested to increase the risk of infection with resistant organisms.

Most systemic complications occur during the first week of illness are treated by standard medical measures. Close patient monitoring is the key to their timely recognition. Circulatory shock arises by a combination of volume depletion and hyperdynamic circulatory state with decreased peripheral vascular resistance. The management includes transfer to an intensive-care unit, volume replacement, and vasopressor substances. The occurrence of shock is frequently followed by pancreatic necrosis. Acute renal failure may be caused by circulatory shock and a selective increase in renal vascular resistance. The treatment is that of acute tubular necrosis arising in any setting. The leading cause of respiratory insufficiency during acute pancreatitis is the adult respiratory distress syndrome, although respiratory depression caused by opiate medications, pleural effusions, intravascular volume overload, and shallow respirations due to abdominal "splinting" may contribute. Sepsis is most commonly caused by infection of the bile ducts, of areas of pancreatic necrosis, or of peripancreatic fluid collections.

Summary – specific pharmacologic therapy of acute pancreatitis:

- Antiproteolytic agent: Aprotinin; Gabexate mesilate (FOY).
- Anti-inflammatory agent: Lexipafant.
- Inhibitor of exocrine secretion: Glucagon; Atropine; Somatostatin; Octreotide.

INDICATIONS FOR SURGERY IN STERILE PANCREATIC NECROSIS

Before considering the indications for intervention, whether endoscopic or surgical, in sterile pancreatic necrosis, it must be pointed out that the mortality rate in medically managed patients with extensive sterile pancreatic necrosis is approximately 10% and surgical intervention has not reduced this mortality rate. Bearing this in mind, the principal indication for surgery should now be infection of an originally sterile pancreatic necrosis documented by fine needle aspiration. Other indications are sterile necrosis with persistent multiple organ failure and situations where sterile necrosis involves more than 50% of the pancreas. The latter two indications however,

need to be individualized to the specific clinical situation. An additional indication for surgery that deserves consideration is symptomatic (severe pain, gastric outlet obstruction etc) sterile pancreatic necrosis where the presence of infection is not the sole determinant of intervention.

Timing of Surgical Intervention

In the last decade, the timing of surgical intervention for all forms of necrotizing pancreatitis has changed remarkably. Currently, it is accepted that surgical intervention should be as late as possible. The primary reason for this is that demarcation between viable and non-viable pancreatic tissue is better defined and this enables a more complete surgical necrosectomy and debridement that is also easier to perform. For all practical purposes, the timing of surgical intervention is around three weeks after the initial attack of acute necrotizing pancreatitis.

Surgical Techniques

The surgical principles and techniques for sterile pancreatic necrosis are essentially the same as those for infected necrosis. The aim for surgical intervention is local and adequate removal of the necrosis. The commonly adopted techniques have been necrosectomy with closed continuous lavage, repeated necrosec-tomies with planned relaparotomies and necrosectomy with "open packing". These surgical strategies have enabled major centers to reduce mortality rates below 15%. Other options such as pancreatic resections are now considered obsolete owing to their high rate of post-operative complications and the problems associated with exocrine and endocrine deficiency. Peritoneal dialysis has also been shown to be ineffective because it has no effect on the inflammatory processes in the retroperitoneum.

Non-surgical Interventions

Though interventional radiology techniques such as percutaneous placement of catheters under CT guidance have been introduced, quite often operative drainage of undrained necrosis is still necessary. The formation of external fistulae is also a problem with percutaneous methods. Endoscopic treatment for pancreatic necrosis has been attempted with some success. There is a belief that endoscopic interventions are less traumatic, reduce the incidence of external fistulae and possibly reduce hospital stay. On the other hand, there is a definite possibility of introducing infection and quite often complete and adequate drainage of necrosis, especially peripheral necrosis, is difficult to achieve. Thus sufficient data in favour of these treatment options is still lacking and surgery appears to be the current gold standard whenever intervention is contemplated in sterile pancreatic necrosis.

Conclusions. The outcome of acute necrotizing pancreatitis depends on the extent of necrosis, organ failure, and the development of infection in a previously sterile necrosis. While documented infection of pancreatic necrosis is a definite indication for surgery, current opinion supports conservative management of sterile necrosis. However, large, controlled, randomized trials are necessary to assess the role of different treatment approaches in the management of sterile pancreatic necrosis. As things stand today, conservative management of sterile necrosis revolves

around judicious use of intravenous antibiotics and nutritional support (enteral or parenteral) along with quality intensive care treatment. Surgical interventions in sterile necrosis, if at all considered necessary, should be carefully individualized to the specific situation.

MANAGEMENT OF INFECTED PANCREATIC NECROSIS

Pancreatic necrosis occurs in 10-20% of patients presenting with acute pancreatitis. Attitudes to the surgical approach to this have changed greatly in the last decade, and the role of surgical drainage is gradually evolving. Of those patients that die following an attack of severe acute pancreatitis, over half will succumb to overwhelming early organ dysfunction within the first week. It is generally accepted that attempted pancreatic resection has little role in these patients, and the only randomised trial was discontinued due to unacceptable mortality in the operative group. Rarely, early surgical exploration may be required where the diagnosis is in doubt, or where bowel ischaemia or haemorrhage is suspected. For the majority however, despite the potential for continued deterioration and even death, the only appropriate treatment in the first week is maximal supportive care within an intensive care environment.

The role of surgical intervention in acute pancreatitis therefore lies in the management of local complications that develop during the evolution of the illness. Significant necrosis of either the pancreatic tissue or the surrounding adipose tissue does not in itself require treatment, as occasionally extensive necrosis may resolve without intervention, although the extent of necrosis is related to the risk of developing complications. The most frequent cause of death in patients with acute pancreatitis is multiple organ failure, and recognition of the link between organ dysfunction and the outcome from surgical intervention has revolutionised the approach to the management of these patients in the last few years.

Previously held dogma that development of infection demands urgent radical intervention[9] has been questioned. The overall mortality for radical debridement is between 20 and 30%, however various factors influence this, and mortality rates vary from less than 10% to over 60%[9] in selected series from renowned units. Undoubtedly the results are better following intervention for sterile rather than infected necrosis, minimal rather than extensive necrosis, and drainage/ debridement of a late pancreatic abscess containing necrosis rather than a true infected necrosis requiring debridement within the first 3-4 weeks of the illness. The effect of differing referral patterns and patient co-morbidity must also be taken into account. Series have tended to report results of a single surgical approach applied to a moderately small and diverse cohort of acute pancreatitic patients. The results of these series have therefore often been more influenced by the selection criteria and clinical characteristics of the patients rather than the surgical technique employed. Surgeon preference has often been determined by either good, or bad, past experience, and no consensus has been achieved regarding a current “gold standard”.

Indications for intervention

The widespread use of contrast enhanced computed tomography (CT) has

allowed the early identification of necrosis, which develops within the first 3-4 days of the illness. Retro-peritoneal necrosis secondary to acute pancreatitis is not in itself and indication for surgery, as Bradley and his colleagues have shown that even extensive necrosis can be adequately treated conservatively, at least initially. Secondary infection of pancreatic necrosis is most common in the second and third week following disease onset, however broad-spectrum prophylactic antibiotics may delay this further. There is undoubtedly a relationship between the extent of necrosis and the subsequent development of infection. Once infection has occurred conservative management usually leads to escalating sepsis and death. Bacterial contamination of the necrotic material therefore traditionally mandated urgent and radical debridement for control of sepsis.

Infection is usually heralded by an increase in the SIRS response or a secondary deterioration in organ failure scores. Bacteriological confirmation may be obtained by CT or ultrasound-guided FNA of the pancreatic or peri-pancreatic area. Aspiration and culture of ascitic fluid leads to false negative aspirates and should be discouraged. Identification of gas within the retroperitoneum indicates infection without the need for FNA culture. The confirmation of infection within the necrotic peri-pancreatic tissue should usually still be considered an indication for intervention, however the method chosen will be influenced by the background condition of the patient. Aspiration may be repeated on a number of occasions should the culture be negative. Whilst occasionally sterile necrosis requires intervention, the lower mortality of late surgical drainage suggests that intervention in sterile necrosis should be delayed as long as possible.

Operative techniques

Laparotomy, Retroperitoneal Exploration and Debridement. This is the most widely used approach to the management of infected necrosis. The process of blunt finger debridement of devitalized tissue evolved following recognition that attempts at formal pancreatic resection were associated with unacceptable mortality. The technique has been further developed with particular reference to the management of the postoperative retroperitoneal bed. Skeletization of the coeliac and mesenteric vessels may occur with extensive necrosis. The ease of debridement is dependent on the duration from onset of the acute pancreatitic episode, as the separation of necrotic and vital tissue is incomplete within the first few weeks of the illness. Debridement during this period results in increased oozing and often the need for packing for haemostasis. Some authors have argued that one advantage of antibiotic prophylaxis, is that while their use has often been shown not to influence the ultimate when exploration is less hazardous.

Despite variations regarding the approach to the postoperative management of the retroperitoneum, the initial exploration and surgical technique has changed little in the last 25 years. Most specialists employ a rooftop-subcostal incision, however midline exposure is favoured by some. Following initial laparotomy, the lesser sac is opened either through the gastrocolic omentum or by lifting the omentum from the colon. Both colonic flexures are mobilised to expose the retroperitoneum, and allow

access to the paracolic gutters particularly in patients with extensive 'horseshoe' necrosis. The peritoneum at the base of the lesser sac is usually opened and the necrosis is exposed during this mobilization, but occasionally the peritoneum may remain intact and require incision to gain access to the necrosis behind.

The necrotic material, usually of a soft putty consistency is teased from the underlying viable tissue by a blunt finger dissection technique. This often leaves some adherent devitalized tissue, however overzealous clearance can lead to bleeding from the raw surface that becomes difficult to control. The procedure usually includes a cholecystectomy with an operative cholangiogram. Occasionally the vascular integrity of the colon is questionable and an extended right hemicolectomy with terminal ileostomy may be required. Many authors recommend a feeding jejunostomy although recently we have preferred naso-enteric feeding as this avoids the risks of jejunostomy complications particularly when further surgical exploration may be required. There are several approaches to the management of the residual abscess cavity, the ultimate choice being determined by a combination of personal preference, operative findings and extent of residual necrosis.

With Drainage. Simple drainage, often with multiple retroperitoneal tube drains was the original approach to the postoperative management of the debrided pancreatic and peri-pancreatic bed. Warshaw (1985) has reported respectable mortality figures using this technique, although over 40% of the patients treated had pancreatic abscess rather than true infected necrosis. Whilst mortality was less than with resective procedures, multiple second-look laparotomies were often required for residual sepsis. This led to the development of the packing or lavage techniques described below.

With Open Packing. Bradley and his colleagues (1993, 1997) have been the principal proponents of the open laparostomy technique, which was widely practiced in the 1980s as the treatment of choice. In this, at the conclusion of the debridement, the divided gastrocolic omentum is sutured to the wound edges leaving the wound open. The lesser sac is packed with lubricated cotton gauze, allowing planned re-explorations/wound dressings, every few days until granulation tissue forms. This approach has the advantage that subsequent explorations/dressings can be carried out under sedation in the ITU/HDU without recourse to further anaesthetics. The technique may be modified closing part of the wound leaving the left side open to allow access for gentle manual exploration.

With Closed Lavage. Radical debridement combined with postoperative closed lavage as described by Beger et al. (1988), is now widely used for the management of infected pancreatic necrosis, the aim of the lavage being the continuous removal of devitalised necrotic material and bacteria. Having completed the debridement, the lesser sac is closed over multiple large diameter tube drains (Fig. 3.18). Continuous lavage is then commenced, our own preference being for peritoneal dialysis fluid (isoosmolar) warmed through a blood warmer and delivered at 500 ml/h. The lavage is continued, for around 3 to 4 weeks on average, until the return fluid is clear, and the patient has no residual signs of systemic sepsis. Re-exploration may still be required for residual sepsis, and for blocked or dislodged drains.

Minimally invasive approaches to infected necrosis. CT or ultrasound-guided

aspiration and drainage has revolutionised the management of many surgical conditions and complications. In the presence of pancreatic necrosis, simple aspiration and percutaneous drainage alone rarely result in resolution in that it does not address the solid component within the abscess, and should therefore be discouraged as sole treatment. Percutaneous drainage may however have a role as a temporising measure in the hope of finding a 'window of opportunity' in which to perform more definitive intervention. Freeny and his colleagues (1998), took this approach to its limits by combining aggressive CT guided percutaneous drainage, tract dilatation and continuous post drainage lavage, using a median of four drains per patient. They confirmed that using this technique pancreatic sepsis may resolve, however nearly 75% of the patients will subsequently require surgical intervention for residual sepsis or necrosis. The logistic demands on the radiological department of this approach have restricted its appeal, although other groups have reported series managed by primarily conservative means.

The technique of endoscopic cystgastrostomy for pancreatic sepsis was first described by Baron et al. (1996) and developments in endoscopic ultrasound have greatly facilitated the ease and safety of performing a transmural drainage. Tract dilatation combined with naso-cyst lavage will adequately drain any fluid component however the residual necrotic material results in a significant failure rate in resolution. The same group subsequently reported that extensive necrosis was a contraindication, and highlighted that drainage must be combined with some form of surgical removal of the necrotic material.

Laparoscopy has transformed many surgical procedures and has been shown to reduce the inflammatory stimulus resulting from surgery. Some laparoscopic specialists have presented a small series of patients undergoing a laparoscopic necrosectomy, with encouraging results, however the surgical difficulty limits its universal application. In 2000, Carter et al. (2000) described the technique of percutaneous necrosectomy involving intra-operative dilatation of a percutaneous drain tract, and subsequent necrosectomy using a urological rigid rod lens system, usually from the left flank or right subcostal approach. To avoid contamination by bowel puncture, double contrast CT guided FNA is performed. Autors preferred route is through the left fat plane between the spleen posteriorly and the colon anteriorly, although for right sided collections access can usually be obtained anterior to the duodenum, between colon and liver. The tract is first dilated using a balloon dilator, allowing insertion of a 34FG Amplatz sheath. Initial intermittent copious lavage and suction is performed until the irrigant clears sufficiently to see within the cavity. Devitalised tissue is easily identified and to can be removed by gentle traction in a piecemeal fashion.

Experience has suggested that overzeal-ous attempts at cavity clearance are unnecessary and can lead to bleeding. An 8FG umbilical catheter sutured to a 28FG tube drain is then passed to the far end of the cavity to allow continuous post-operative lavage (500 ml/h Dianil 7). Planned second look procedures are then performed every 7-10 days, until the cavity is clean.

Conclusion. Infected necrosis remains a major surgical challenge and the diversity of reported treatment strategies testifies to the lack of a universally agreed

gold standard. Much of this controversy relates to the variability of clinical presentation, particularly of organ dysfunction, and the lack of uniformity in patient selection for procedures. Half of the patients who die as a result of severe acute pancreatitis do so within the first few days of the illness, and may never reach a specialised unit, whilst others may not be considered fit for intervention. Background morbidity of patients within a series is difficult to determine and undoubtedly has a major influence on outcome. The potential effect of patient selection can be seen where overall mortality following surgery for infected necrosis has been reported[37] as being less than the mortality for all-comers, with or without necrosis, recruited to trials in patients with predicted severe pancreatitis.

It is evident that no single treatment or technique is the answer. As these patients are relatively uncommon, most surgeons have adopted a favoured, but consistent, approach to infected necrosis. Within specialized units, it has become increasingly obvious that not all patients respond equally to a given surgical stimulus. As a generalisation, patients with infected necrosis but without significant organ dysfunction will do well regardless of the approach chosen, and in these an aggressive open debridement may be the most appropriate choice as it may hasten recovery.

A patient with multiple organ dysfunction and sepsis however, may be more appropriately managed by a carefully timed percutaneous drain followed by a delayed minimally invasive or even open necrosectomy.

The mortality associated with open surgical exploration in a patient with multi-organ dysfunction and sepsis is unacceptable. Undoubtedly the severity of systemic sepsis and organ dysfunction can be down-staged by percutaneous or endoscopic drainage, however the improvement tends to be temporary unless drainage is maintained together with some means of addressing the solid component of these abscesses. Tract dilatation and minimally invasive necrosectomy achieves drainage, addresses the solid component, whilst minimizing the surgical insult to the patient, and may be the optimum approach in a carefully selected high-risk group of patients. It is only through improved timing of intervention and understanding of the disease process, combining various different techniques tailored to the specific requirements of an individual patient, that the mortality in the high-risk group may fall.

GALLSTONE-INDUCED PANCREATITIS

All patients with pancreatitis should be evaluated for the presence of gallstones. Gallstones initiate the process of pancreatitis by increasing pancreatic ductal pressure and initiation of inflammatory cascade. It has been postulated that early removal of the impacted stone would attenuate the inflammatory response.

Gallstones are present in 60% of non-alcoholic patients with pancreatitis and if allowed to persist, 36-63% will develop recurrent bouts of pancreatitis. Cholecystectomy reduces this risk to 2-8%.

Timing of cholecystectomy. 75% of patients with acute abdominal pain, gallstones, and elevated amylase have no gross evidence of significant pancreatitis. Cholecystectomy is safe in this group. In patients with gross evidence of

pancreatitis, 80% have mild disease and cholecystectomy is safe but does not alter the course of the pancreatitis.

In patients with severe pancreatitis there is an 82.6% morbidity and 47.8% mortality from cholecystectomy if performed within the initial 48 hours. If deferred until the signs of pancreatitis have subsided, morbidity and mortality fall to 17.8% and 11.8% respectively.

In patients with severe pancreatitis and an obstructed biliary tree secondary to choledocholithiasis, ERCP and sphincterotomy significantly reduce morbidity related to biliary complications but do not alter the course of the pancreatic inflammation. Patients with a predicted severe attack of gallstone-associated acute pancreatitis need early endoscopic retrograde cholangiopancreatography.

Severe acute gallstone pancreatitis with obstructive jaundice should undergo urgent ERCP + endoscopic sphincterotomy (is more controvertial when obstructive jaundice is absent). A meta-analysis of four trials suggested a significant reduction in mortality and morbidity in subjects receiving early ERCP (< 24 of admission or < 72 hrs of symptom onset). For gallstone pancreatitis with obstructive jaundice, urgent ERCP should be performed within 72 hrs of onset of symptoms. If ERCP cannot be accomplished (not technically feasible or available) alternative methods of biliary drainage must be considered. When obstructive jaundice is absent, but with SAP due to suspected or confirmed gallstones, ERCP should be strongly considered within 72 hrs of onset of symptoms.

Fluid Collections. Fluid collections occur within or around the pancreas in up to 50% of patients with severe pancreatitis. The majority resolves spontaneously; collections that persist for more than 6 weeks develop a wall of granulation tissue and are then called pseudocysts. Collections that continue to expand or become infected require percutaneous drainage. Pancreatic abscesses contain liquid pus and may be considered to represent infected fluid collections.

A pancreatic abscess occurs 2 to 6 weeks after the initial attack, in contrast to infected necrosis, which occurs in the first few hours or days. The mechanism of delayed infection is not clear, but the treatment consists of external drainage, whether established by surgical methods.

Summary – minimally invasive techniques:

- Laparoscopic retroperitoneal debridement.
- Percutaneous drainage.
- Endoscopic transgastric debridement and drainage.
- Some selected, relatively stable patients might be spared an operative necrosectomy.
- Offer advantages by minimizing the morbidity of laparotomy or temporizing until the retroperitoneal process has sufficiently demarcated.
- But the clinical scenario must be considered firstly.
- Recommend pancreatic debridement or drainage in patients with infected pancreatic necrosis and/or abscess confirmed by radiological evidence of gas or results of FNA.
- The gold standard for achieving this goal is open operative debridement.

- Laparoscopic and/or percutaneous interventions might be effective in selected patients.

Pancreatic Pseudocyst. Pancreatic pseudocysts (PPs) comprise more than 80 % of the cystic lesions of the pancreas and cause complications in 7-25% of patients with pancreatitis or pancreatic trauma. The first step in the management of PPs is to exclude a cystic tumor. A history of pancreatitis, no solid components or mural calcification on CT scan and high amylase content at aspiration favor a diagnosis of PP. Endoscopic ultrasound (EUS)-guided FNAC is a valuable diagnostic aid. Intervention is indicated for PPs which are symptomatic, in a phase of growth, complicated (infected, hemorrhage, biliary or bowel obstruction) or in those occurring together with chronic pancreatitis and when malignancy cannot be unequivocally excluded. The current options include percutaneous catheter drainage, endoscopy and surgery. The choice depends on the mode of presentation, the cystic morphology and available technical expertise. Percutaneous catheter drainage is recommended as a temporizing measure in poor surgical candidates with immature, complicated or infected PPs. The limitations include secondary infection and pancreatic fistula in 10-20% of patients which increase complications following eventual definitive surgery. Endoscopic therapy for PPs including cystic-enteric drainage (and transpapillary drainage), is an option for PPs which bulge into the enteric lumen which have a wall thickness of less than 1cm and the absence of major vascular structures on EUS in the proposed tract or those which communicate with the pancreatic duct above a stricture. Surgical internal drainage remains the gold standard and is the procedure of choice for cysts which are symptomatic or complicated or those having a mature wall. Being more versatile, a cystojejunostomy is preferred for giant pseudocysts (>15cm) which are predominantly inframesocolic or are in an unusual location. In PPs with coexisting chronic pancreatitis and a dilated pancreatic duct, duct drainage procedures (such as longitudinal pancreaticojejunostomy) should be preferred to a cyst drainage procedure.

Percutaneous drainage:

➢ Continuous drainage until output < 50 ml/day + amylase activity ↓ (failure rate 16%; recurrence rates 7%).

➢ Complications (conversion into an infected pseudocyst (10%); catheter-site cellulitis; damage to adjacent organs; pancreatico-cutaneous fistula; GI hemorrhage).

Endoscopic drainage:

➢ Transenteric drainage: cystogastrostomy; cystoduodenostomy.

➢ Transpapillary drainage: 40-70% of pseudocysts communicate with pancreatic duct; ERCP with sphincterotomy, balloon dilatation of pancreatic duct strictures, and stent placement beyond strictures.

Surgical options:

➢ Excision: tail of gland & between proximal strictures – distal pancreatectomy & splenectomy; head of gland with strictures of pancreatic or bile ducts – pancreaticoduodenectomy.

➢ External drainage.

➢ Internal drainage: cystogastrostomy; cystojejunostomy (permanent resolution confirmed in 91%–97% of patients); cystoduodenostomy (can be complicated by

duodenal fistula and bleeding at anastomotic site).

Laparoscopic management:

- The interface between the cyst and the enteric lumen must be ≥ 5cm for adequate drainage.
- Approaches: pancreatitis to biliary etiology → extraluminal approach with concurrent laparoscopic cholecystectomy; non-biliary origin → intraluminal (combined laparoscopic/endoscopic) approach.

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Навчальне видання

Змістовний модуль 1. Хірургічна гастроентерологія
Тема №3 Гострий панкреатит

Гострий панкреатит.

Методичний посібник для студентів та інтернів.

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