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FACULTY OF MEDICINE
DEPARTMENT OF SURGERY DISEASES

ACUTE PANCREATITIS

Methodological matherials for independent study for students

UZHHOROD

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UZHHOROD NATIONAL UNIVERSITY
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Methodical matherials are devoted to issues of etiopathogenesis, symptoms, diagnosis and treatment methods of acute pancreatitis. The authors also tried to highlight, aim questions that also concern various complications of acute pancreatitis. The methodical matherials are intended for senior year students of higher medical educational institutions.

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Background

Pancreatitis is an inflammatory process in which pancreatic enzymes autodigest the gland. The gland sometimes heals without any impairment of function or any morphologic changes; this process is known as **acute pancreatitis**. Pancreatitis can also recur intermittently, contributing to the functional and morphologic loss of the gland; recurrent attacks are referred to as **chronic pancreatitis**.

Both forms of pancreatitis may present with acute clinical findings. Recognizing patients with severe acute pancreatitis as soon as possible is critical for achieving optimal outcomes.

Once a working diagnosis of acute pancreatitis is reached, laboratory tests are obtained to support the clinical impression, to help define the etiology, and to look for complications. Diagnostic imaging is unnecessary in most cases but may be obtained when the diagnosis is in doubt, when severe pancreatitis is present, or when an imaging study might provide specific information needed to answer a clinical question.

Management depends largely on severity. Medical treatment of mild acute pancreatitis is relatively straightforward. Treatment of severe acute pancreatitis involves intensive care; the goals of medical management are to provide aggressive supportive care, to decrease inflammation, to limit infection or superinfection, and to identify and treat complications as appropriate. Surgical intervention (open or minimally invasive) is indicated in selected cases.

Epidemiology

United States statistics. Acute pancreatitis has an approximate incidence of 40-50 cases per year per 100,000 adults. In 2009, approximately 275,000 hospitalizations were attributed to acute pancreatitis. In 2007, approximately 220,000 patients with acute pancreatitis were admitted to non–federally funded hospitals. In 1998, 183,000 patients with acute pancreatitis were admitted. This trend in rising incidence has been recognized over the past several decades.

International statistics. Worldwide, the incidence of acute pancreatitis ranges between 5 and 80 per 100,000 population, with the highest incidence recorded in the United States and Finland. In Luneburg, Germany, the incidence is 17.5 cases per 100,000 people. In Finland, the incidence is 73.4 cases per 100,000 people. Similar incidence rates have been reported in Australia. The incidence of disease outside North America, Europe, and Australia is less well known.

In Europe and other developed nations, such as Hong Kong, more patients tend to have gallstone pancreatitis, whereas in the United States, alcoholic pancreatitis is most common.

Age-related demographics. The median age at onset depends on the etiology. The following are median ages of onset for various etiologies:

- Alcohol-related – 39 years.
- Biliary tract-related – 69 years.
- Trauma-related – 66 years.
- Drug-induced etiology – 42 years.
- ERCP-related – 58 years.
- AIDS-related – 31 years.
- Vasculitis-related – 36 years.

Hospitalization rates increase with age. For people aged 35-75 years, the rate doubles for males and quadruples for females.

Sex-related demographics. Generally, acute pancreatitis affects males more often than females. In males, the etiology is more often related to alcohol; in females, it is more often related to biliary tract disease. Idiopathic pancreatitis has no clear predilection for either sex.

Race-related demographics. The hospitalization rates of patients with acute pancreatitis per 100,000 population are 3 times higher for blacks than whites. These racial differences are more pronounced for males than females. The risk for African Americans aged 35-64 years is 10 times higher than for any other group. African Americans are at a higher risk than whites in that same age group.

The annual incidence of acute pancreatitis in Native Americans is 4 per 100,000 population; in whites, 5.7 per 100,000 population; and in blacks, 20.7 per 100,000 population.

Anatomy

The pancreas is an extended, accessory digestive gland that is found retroperitoneally, crossing the bodies of the L1 and L2 vertebrae on the posterior abdominal wall. The pancreas lies transversely in the upper abdomen between the duodenum on the right and the spleen on the left. It is divided into the head, neck, body, and tail. The head lies on the inferior vena cava and the renal vein and is surrounded by the C loop of the duodenum. The tail of the pancreas extends up to the splenic hilum (fig. 1).

The pancreas produces an *exocrine secretion* (pancreatic juice from the acinar cells) which then enters the duodenum through the main and accessory pancreatic ducts and *endocrine secretions* (glucagon and insulin from the pancreatic islets of Langerhans) that enter the blood.

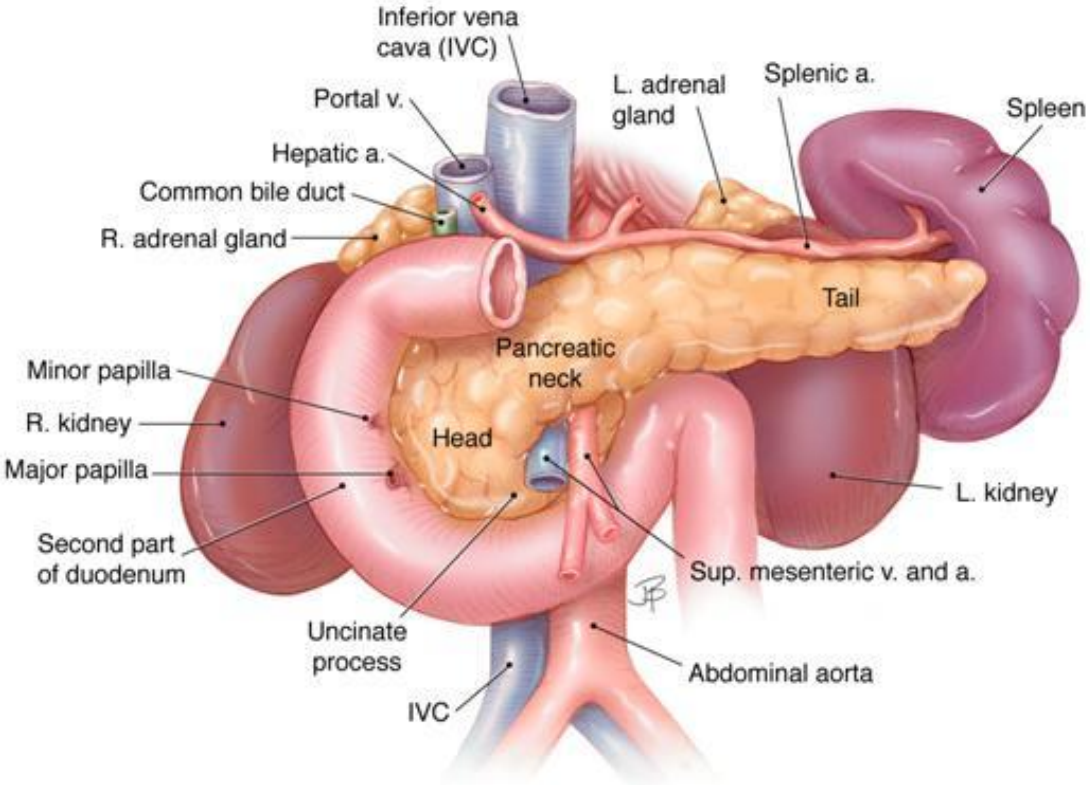

Fig. 1. Pancreatic gland anatomy.

Divisions. The pancreas is divided into 4 parts: head, neck, body, and tail. *The head* of the pancreas is the enlarged part of the gland surrounded by the C-shaped curve of the duodenum. On its way to the descending part of the duodenum, the bile duct lies in a groove on the posterosuperior surface of the head

or is embedded in its substance. *The body* of the pancreas continues from the neck and passes over the aorta and L2 vertebra. The anterior surface of the body of the pancreas is covered with peritoneum. The posterior surface of the body is devoid of peritoneum. It is in contact with the aorta, the superior mesenteric artery (SMA), the left suprarenal gland, the left kidney, and renal vessels.

The neck of the pancreas is short. *The tail* of the pancreas lies anterior to the left kidney, closely related to the splenic hilum and the left colic flexure. The main pancreatic duct carrying the pancreatic secretions joins with the bile duct to form the hepatopancreatic ampulla, which opens into the descending part of the duodenum. The hepatopancreatic sphincter of Oddi around the hepatopancreatic ampulla is a smooth muscle sphincter that controls the flow of bile and pancreatic juice into the ampulla and inhibits reflux of duodenal substances into the ampulla.

Cell types. The majority of the pancreas (approximately 80%) is made up of *exocrine pancreatic tissue*. This is made of pancreatic acini (pyramidal acinar cells with the apex directed towards the lumen). These contain dense zymogen granules in the apical region, whereas the basal region contains the nucleus and endoplasmic reticulum (which aids in synthesizing the digestive enzymes). These enzymes are stored in secretory vesicles called the Golgi complex. The basolateral membrane of the acinar cells contains several receptors for neurotransmitters including secretin, cholecystokinin, and acetylcholine, which regulate exocytosis of the digestive enzymes.

The pancreas also contains the islet of Langerhans, which contain the *endocrine cells*. Unlike the exocrine enzymes, which are secreted by exocytosis, the endocrine enzymes enter the bloodstream via a complex capillary network within the pancreatic blood flow. There are 4 types of endocrine cells (A cells produce glucagon, B cells produce insulin, D cells produce somatostatin, and F cells produce pancreatic polypeptide).

Stellate cells are a direct formation of epithelial structures within the pancreas. In conditions like chronic pancreatitis, these cells promote inflammation and fibrosis.

Ducts. The *main pancreatic duct*, or duct of Wirsung, arises in the tail of the pancreas and terminates at the papilla of Vater in the duodenum. It crosses the vertebral column between T12 and L2. Within the body and tail of the pancreas, the duct lies slightly cephalad to a line drawn midway between the superior and inferior edges. The duct is also more posterior than anterior. In adults, the duct within the head measures 3.1 to 4.8 mm in diameter and gradually tapers to measure 0.9 to 2.4 mm in the tail. With age, the duct diameter can increase. The duct of Santorini (i.e., the minor, or accessory, pancreatic duct) is smaller than the main duct. It extends from the main duct to enter the duodenum at the lesser

papilla. That papilla lies about 2 cm proximal and slightly anterior to the major papilla.

Blood supply and lymphatics. Both the celiac trunk and the superior mesenteric artery provide the *arterial supply* to the pancreas. Variations are common, but for the most part, the body and tail are supplied by branches of the splenic artery, whereas the head and uncinate process receive their supply through arcades originating from the hepatic and gastroduodenal branch of the celiac artery and from the first branch of the superior mesenteric artery. *Venous drainage* is to the splenic, superior mesenteric, and portal veins.

The pancreas is drained by multiple *lymph node groups*. The major drainage of the pancreatic head and uncinate process is to the subpyloric, portal, mesenteric, mesocolic, and aortocaval nodes. The pancreatic body and tail, for the most part, are drained through nodes in the celiac, aortocaval, mesenteric, and mesocolic groups and through nodes in the splenic hilum.

Nerves. The pancreas is innervated by both sympathetic and parasympathetic components of the autonomic nervous system. The principal, and possibly only, pathway for pancreatic pain involves nociceptive fibers arising in the pancreas. They pass through the celiac ganglia to form the greater, lesser, and least splanchnic nerves that pass to cell bodies in the thoracic sympathetic chain. Efferent visceral motor supply to the pancreas is provided by both the sympathetic and parasympathetic systems. The latter involves preganglionic fibers arising from cell bodies in the vagal nuclei that travel through the posterior vagal trunk to the celiac plexus. Postganglionic fibers then innervate pancreatic islets, acini, ducts, and blood vessels. In general, the nerves of the pancreas travel with the blood vessels supplying the organ.

Normal pancreatic function. The is responsible for insulin production (endocrine pancreas) and the manufacture and secretion of digestive enzymes (exocrine pancreas) leading to carbohydrate, fat, and protein metabolism. Approximately 80% of the gross weight of the pancreas supports exocrine function, and the remaining 20% is involved with endocrine function.

Digestive enzymes are produced within the pancreatic acinar cells, packaged into storage vesicles called zymogens, and then released via the pancreatic ductal cells into the pancreatic duct, where they are secreted into the small intestine to begin the metabolic process.

When a meal is ingested, the vagal nerves, vasoactive intestinal polypeptide (VIP), gastrin-releasing peptide (GRP), secretin, cholecystokinin (CCK), and encephalins stimulate the release of these proenzymes into the pancreatic duct.

The proenzymes travel to the brush border of the duodenum, where trypsinogen, the proenzyme for trypsin, is activated via hydrolysis of an N-terminal

hexapeptide fragment by the brush border enzyme enterokinase. Trypsin then facilitates the conversion of the other proenzymes into their active forms.

A feedback mechanism exists to limit pancreatic enzyme activation after appropriate metabolism has occurred. It is hypothesized that elevated levels of trypsin, having become unbound from digesting food, lead to decreased CCK and secretin levels, thus limiting further pancreatic secretion.

Because premature activation of pancreatic enzymes within the pancreas leads to organ injury and pancreatitis, several mechanisms exist to limit this occurrence. Under various conditions, disruption of these protective mechanisms may occur, resulting in intracellular enzyme activation and pancreatic autodigestion leading to acute pancreatitis.

Etiology

Long-standing alcohol consumption and biliary stone disease cause most cases of acute pancreatitis, but numerous other etiologies are known. In 10%-30% of cases, the cause is unknown, though studies have suggested that as many as 70% of cases of idiopathic pancreatitis are secondary to biliary microlithiasis. *Common etiologies* of acute pancreatitis are listed below:

- Gallstones.
- Alcohol use.
- Hypertriglyceridemia.
- Drug-induced pancreatitis.
- Idiopathic.
- Post-procedural, e.g., endoscopic retrograde cholangiopancreatography (ERCP) or abdominal surgery.
- Ampullary stenosis, which is formerly known as sphincter of Oddi dysfunction type I.
- Autoimmune pancreatitis, type I (systemic IgG4 disease-related), and type II.
- Viral infections like *Coxsackie, Cytomegalovirus, Echovirus, Epstein-Barr virus, Hepatitis A/B/C, HIV, Mumps, Rubella, and Varicella*.
- Bacterial infections like *Campylobacter jejuni, Legionella, Leptospirosis, Mycobacterium avium, Mycobacterium tuberculosis, and Mycoplasma.*
- Smoking.
- Trauma.
- Congenital anomalies, e.g., annular pancreas.

- Genetic disorders like hereditary pancreatitis, cystic fibrosis, and alpha 1-antitrypsin deficiency.
- Hypercalcemia.
- Parasitic infections (*Ascaris lumbricoides, Cryptosporidium, Clonorchis Sinensis, Microsporidia*).
- Renal disease (hemodialysis).
- Toxins (scorpion bites, organophosphate poisoning).
- Vasculitis (polyarteritis nodosa, systemic lupus erythematosus).

Biliary tract disease. One of the most common causes of acute pancreatitis in most developed countries (accounting for approximately 40% of cases) is gallstones passing into the bile duct and temporarily lodging at the sphincter of Oddi. The risk of a stone causing pancreatitis is inversely proportional to its size.

It is thought that acinar cell injury occurs secondary to increasing pancreatic duct pressures caused by obstructive biliary stones at the ampulla of Vater, although this has not been definitively proven in humans. Occult microlithiasis is probably responsible for most cases of idiopathic acute pancreatitis.

Alcohol. Alcohol use is a major cause of acute pancreatitis (accounting for at least 35% of cases). At the cellular level, ethanol leads to intracellular accumulation of digestive enzymes and their premature activation and release. At the ductal level, it increases the permeability of ductules, allowing enzymes to reach the parenchyma and cause pancreatic damage. Ethanol increases the protein content of pancreatic juice and decreases bicarbonate levels and trypsin inhibitor concentrations. This leads to the formation of protein plugs that block pancreatic outflow.

Most commonly, the disease develops in patients whose alcohol ingestion is habitual over 5-15 years. Alcoholics are usually admitted with an acute exacerbation of chronic pancreatitis. Occasionally, however, pancreatitis can develop in a patient with a weekend binging habit, and several case reports have described a sole large alcohol load precipitating a first attack. Nevertheless, the alcoholic who imbibes routinely remains the rule rather than the exception for the development of pancreatitis.

Endoscopic retrograde cholangiopancreatography (ERCP). Pancreatitis occurring after endoscopic retrograde cholangiopancreatography is probably the third most common type (accounting for approximately 4% of cases). Whereas retrospective surveys indicate that the risk is only 1%, prospective studies have shown the risk to be at least 5%.

The risk of post-ERCP acute pancreatitis is increased if the endoscopist is inexperienced, if the patient is thought to have sphincter of Oddi dysfunction, or if manometry is performed on the sphincter of Oddi.

Trauma. Abdominal trauma (approximately 1.5%) causes an elevation of amylase and lipase levels in 17% of cases and clinical pancreatitis in 5% of cases. Pancreatic injury occurs more often in penetrating injuries (eg, from knives, bullets) than in blunt abdominal trauma (eg, from steering wheels, horses, bicycles). Blunt injury to the abdomen or back may crush the gland across the spine, leading to a ductal injury.

Drugs. Considering the small number of patients who develop pancreatitis compared to the relatively large number who receive potentially toxic drugs, drug-induced pancreatitis is a relatively rare occurrence (accounting for approximately 2% of cases) that is probably related to an unknown predisposition. Fortunately, drug-induced pancreatitis is usually mild.

Drugs definitely associated with acute pancreatitis include the following: azathioprine, sulfonamides, sulindac, tetracycline, valproic acid, didanosine, methyldopa, estrogens, furosemide, 6-mercaptopurine, pentamidine, 5-aminosalicylic acid compounds, corticosteroids, octreotide.

Drugs probably associated with acute pancreatitis include the following: chlorothiazide and hydrochlorothiazide, methandrostenolone (methandienone), metronidazole, nitrofurantoin, phenformin, piroxicam, procainamide, colaspase, chlorthalidone, combination cancer chemotherapy drugs (especially asparaginase), cimetidine, cisplatin, cytosine arabinoside, diphenoxylate, ethacrynic acid.

In addition, there are many drugs that have been reported to cause acute pancreatitis in isolated or sporadic cases.

Infection. Several infectious diseases may cause pancreatitis, especially in children. These cases of acute pancreatitis tend to be milder than cases of acute biliary or alcohol-induced pancreatitis.

Viral causes include mumps virus, coxsackievirus, cytomegalovirus (CMV), hepatitis virus, Epstein-Barr virus (EBV), echovirus, varicella-zoster virus (VZV), measles virus, and rubella virus. Bacterial causes include *Mycoplasma pneumoniae, Salmonella, Campylobacter,* and *Mycobacterium tuberculosis.* Worldwide, *Ascaris* is a recognized cause of pancreatitis resulting from the migration of worms in and out of the duodenal papillae.

Hereditary pancreatitis. Hereditary pancreatitis is an autosomal dominant gain-of-function disorder related to mutations of the cationic trypsinogen gene (PRSS1), which has an 80% penetrance. Mutations in this gene cause premature activation of trypsinogen to trypsin.

Hypercalcemia. Hypercalcemia from any cause can lead to acute pancreatitis. Causes include hyperparathyroidism, excessive doses of vitamin D, familial hypocalciuric hypercalcemia, and total parenteral nutrition (TPN).

Hypertriglyceridemia. Clinically significant pancreatitis usually does not occur until a person's serum triglyceride level reaches 1000 mg/dL. This type of pancreatitis tends to be more severe than alcohol- or gallstone-induced disease.

Tumors. Obstruction of the pancreatic ductal system by a pancreatic ductal carcinoma, ampullary carcinoma, islet cell tumor, solid pseudotumor of the pancreas, sarcoma, lymphoma, cholangiocarcinoma, or metastatic tumor can cause acute pancreatitis. The chances of pancreatitis occurring when a tumor is present are approximately 14%.

Toxins. Exposure to organophosphate insecticide can cause acute pancreatitis. Scorpion and snake bites may also be causative; in Trinidad, the sting of the scorpion *Tityus trinitatis* is the most common cause of acute pancreatitis.

Surgical procedures. Acute pancreatitis may occur in the postoperative period of various surgical procedures (eg, abdominal or cardiopulmonary bypass surgery, which may damage the gland by causing ischemia). The mechanism is unclear.

Vascular abnormalities. Vascular factors, such as ischemia or vasculitis, can play a role in causing acute pancreatitis. Vasculitis can predispose patients to pancreatic ischemia, especially in those with polyarteritis nodosa and systemic lupus erythematosus.

Autoimmune pancreatitis. Autoimmune pancreatitis, a relatively newly described entity, is an extremely rare cause of acute pancreatitis (prevalence, 0.82 per 100,000 individuals).

The causes of acute pancreatitis can be summarized into the following categories (tab. 1):

Table 1.

Mechanical	Toxic and metabolic	Others
Gallstones	Alcohol	Ischemia
Pancreatic duct obstruction	Hyperlipidemia	Iatrogenic injury
Dysfunction of the sphincter of Oddi	Drugs	Infection
	Scorpion venom	Hereditary
Trauma	Organophosphate poisoning	Autoimmune
Congenital malformations (annular pancreas)	Hypercalcemia	Cystic fibrosis

Pathophysiology

Acute pancreatitis may occur when factors involved in maintaining cellular homeostasis are out of balance. The initiating event may be anything that injures the acinar cell and impairs the secretion of zymogen granules (fig. 2).

At present, it is unclear exactly what pathophysiologic event triggers the onset of acute pancreatitis. It is believed, however, that both extracellular factors (eg, neural and vascular response) and intracellular factors (eg, intracellular digestive enzyme activation, increased calcium signaling, and heat shock protein activation) play a role. In addition, acute pancreatitis can develop when ductal cell injury leads to delayed or absent enzymatic secretion.

Once a cellular injury pattern has been initiated, cellular membrane trafficking becomes chaotic, with the following deleterious effects:

- lysosomal and zymogen granule compartments fuse, enabling activation of trypsinogen to trypsin;
- intracellular trypsin triggers the entire zymogen activation cascade;
- secretory vesicles are extruded across the basolateral membrane into the interstitium, where molecular fragments act as chemoattractants for inflammatory cells.

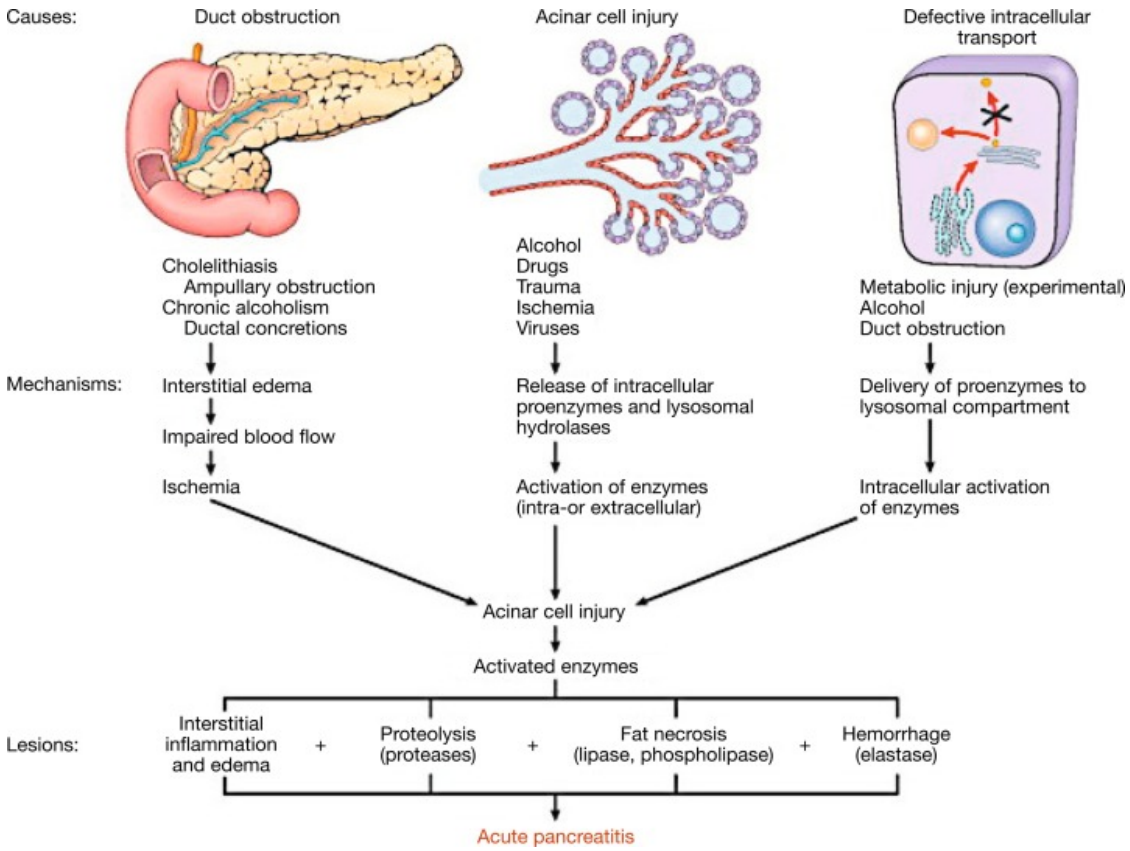

Fig. 2. Pathogenesis of acute pancreatitis.

Activated neutrophils then exacerbate the problem by releasing superoxide (the respiratory burst) or proteolytic enzymes (cathepsins B, D, and G; collagenase; and elastase). Finally, macrophages release cytokines that further mediate local (and, in severe cases, systemic) inflammatory responses. The early mediators defined to date are tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, and IL-8.

These mediators of inflammation cause an increased pancreatic vascular permeability, leading to hemorrhage, edema, and eventually pancreatic necrosis. As the mediators are excreted into the circulation, systemic complications can arise, such as bacteremia due to gut flora translocation, acute respiratory distress syndrome (ARDS), pleural effusions, gastrointestinal (GI) hemorrhage, and renal failure.

The systemic inflammatory response syndrome (SIRS) can also develop, leading to the development of systemic shock. Eventually, the mediators of inflammation can become so overwhelming that hemodynamic instability and death ensue.

In acute pancreatitis, parenchymal edema and peripancreatic fat necrosis occur first; this is known as *acute edematous (interstitial) pancreatitis*. When necrosis involves the parenchyma, accompanied by hemorrhage and dysfunction of the gland, the inflammation evolves into *hemorrhagic or necrotizing pancreatitis* (fig. 3). *Pseudocysts and pancreatic abscesses* (see Complications of acute pancreatitis) can result from necrotizing pancreatitis because enzymes can be walled off by granulation tissue (pseudocyst formation) or via bacterial seeding of the pancreatic or peripancreatic tissue (pancreatic abscess formation).

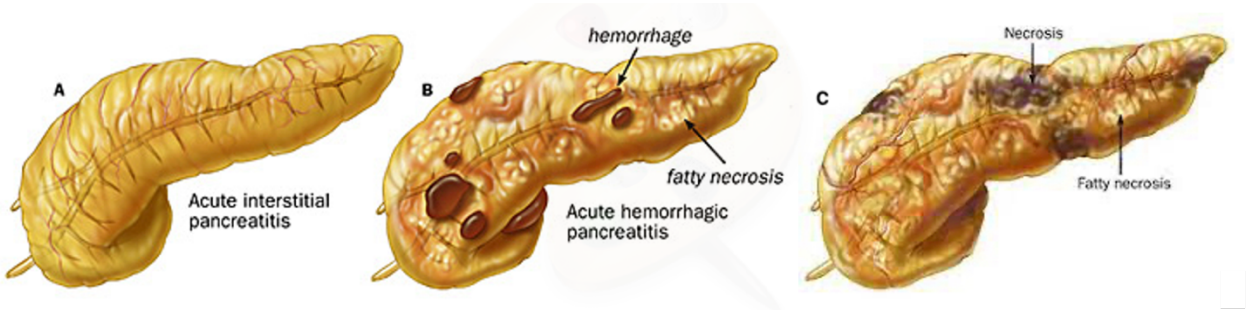

Fig. 3. Morphological forms of acute pancreatitis.

Classification

The **Revised Atlanta classification of acute pancreatitis** from 2012 is an international multidisciplinary classification of the severity of acute pancreatitis, updating the 1992 Atlanta classification:

1. Mild acute pancreatitis:
   - no organ failure;
   - no local of systemic complications.
2. Moderately severe acute pancreatitis:
   - organ failure that resolves within 48 hours (transient organ failure) and/or
   - local or systemic complications without persistent organ failure.
3. Severe acute pancreatitis – persistent organ failure (>48 hours):
   - single organ failure;
   - multiple organ failure.

The worldwide consensus aims for an internationally agreed-upon classification of acute pancreatitis severity, with standardized terminology for pancreatitis and its complications.

Morphological features of acute pancreatitis.

Interstitial edematous pancreatitis – acute inflammation of the pancreatic parenchyma and peripancreatic tissues, but without recognisable tissue necrosis.

Necrotising pancreatitis – inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis.

APFC (acute peripancreatic fluid collection) – peripancreatic fluid associated with interstitial edematous pancreatitis with no associated peripancreatic necrosis. This term applies only to areas of peripancreatic fluid seen within the first 4 weeks after onset of interstitial edematous pancreatitis and without the features of a pseudocyst.

Pancreatic pseudocyst – an encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis. This entity usually occurs more than 4 weeks after onset of interstitial edematous pancreatitis to mature.

ANC (acute necrotic collection) – a collection containing variable amounts of both fluid and necrosis associated with necrotising pancreatitis; the necrosis can involve the pancreatic parenchyma and/or the peripancreatic tissues.

WON (walled-off necrosis) – a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis that has developed a well-defined inflammatory wall. WON usually occurs >4 weeks after onset of necrotising pancreatitis.

Ransons criteria are one of the earliest scoring systems to assess the *severity of acute pancreatitis* and continue to be widely used.

Ranson criteria are used to predict the severity and mortality of acute pancreatitis. Five parameters are assessed on admission, and the other six are assessed at 48 hours post-admission. One point is given for each positive parameter

for a maximum score of 11. The modified criteria have a max score of 10. Five parameters are assessed on admission and the other 5 at the 48-hour mark.

The criteria with 11 parameters are used to assess the severity of alcoholic pancreatitis. The 5 parameters on admission are age older than 55 years, WBC count greater than 16,000 cells/cmm, blood glucose greater than 200 mg/dL (11 mmol/L), serum AST greater than 250 IU/L, and serum LDH greater than 350 IU/L. At 48 hours, the remaining 6 parameters are: serum calcium less than 8.0 mg/dL (less than 2.0 mmol/L), hematocrit fall greater than 10%, PaO2 less than 60 mmHg, blood urine nitrogen (BUN) increased by 5 mg/dL or more (1.8 mmol/L or more) despite intravenous (IV) fluid hydration, base deficit greater than 4 mEq/L, and sequestration of fluids greater than 6 L.

The modified Ranson criteria are used to assess gallstone pancreatitis. The five parameters on admission are age older than 70 years, WBC greater than 18,000 cells/cmm, blood glucose greater than 220 mg/dL (greater than 12.2 mmol/L), serum AST greater than 250 IU/L, and serum LDH greater than 400 IU/L. At 48 hours, the remaining 5 parameters are serum calcium less than 8.0 mg/dL (less than 2.0 mmol/L), hematocrit fall greater than 10%, BUN increased by 2 or more mg/dL (0.7 or more mmol/L) despite IV fluid hydration, base deficit greater than 5 mEq/L, and sequestration of fluids greater than 4 L.

Score interpretation:

- 0 to 2 points: mortality 0% to 3%;
- 3 to 4 points: 15%;
- 5 to 6 points: 40%;
- 7 to 11: nearly 100%.

Clinical symptoms and physical examination

The cardinal symptom of acute pancreatitis is **abdominal pain**, which is characteristically dull, boring, and steady. Usually, the pain is sudden in onset and gradually intensifies in severity until reaching a constant ache. Most often, it is located in the upper abdomen, usually in the epigastric region, but it may be perceived more on the left or right side, depending on which portion of the pancreas is involved. The pain radiates directly through the abdomen to the back in approximately one half of cases. The cause of pain in acute pancreatitis is compression of nerve plexuses, which are located around the pancreas.

Nausea and **vomiting** are often present, along with accompanying anorexia, vomiting sometimes becomes uncontrollable. **Diarrhea** can also occur. Positioning can be important, because the discomfort frequently improves with the patient

sitting up and bending forward. However, this improvement is usually temporary. The duration of pain varies but typically lasts more than a day. It is the intensity and persistence of the pain that usually causes patients to seek medical attention.

Ask the patient about recent operative or other invasive procedures (eg, ERCP) or family history of hypertriglyceridemia. Patients frequently have a history of previous biliary colic and binge alcohol consumption, the major causes of acute pancreatitis.

The following **physical examination findings** may be noted, varying with the severity of the disease.

Fever (76%) and **tachycardia** (65%) are common abnormal vital signs; hypotension may be noted. Temperature is usually subfebrile. In case of suppurative inflammation it may reach 38°C and higher.

Abdominal tenderness, muscular guarding (68%), and **distention** (65%) are observed in most patients; bowel sounds are often diminished or absent because of gastric and transverse colonic **ileus**; guarding tends to be more pronounced in the upper abdomen.

During **percussion** of the abdomen there may be revealed the presence of fluid in the abdomen and tympanic resonance over the intestines. Regional tension in the epigastric area and along the projection of pancreas **(Korte's symptom)** is defined. A minority of patients exhibit **jaundice** (28%).

Some patients experience **dyspnea** (10%), which may be caused by irritation of the diaphragm (resulting from inflammation), pleural effusion, or a more serious condition, such as acute respiratory distress syndrome (ARDS); tachypnea may occur; lung auscultation may reveal basilar rales, especially in the left lung.

In severe cases, **hemodynamic instability** is evident (10%) and hematemesis or melena sometimes develops (5%); in addition, patients with severe acute pancreatitis are often pale, diaphoretic, and listless.

Occasionally, in the extremities, muscular spasm may be noted secondary to hypocalcemia.

A few uncommon physical findings are associated with severe necrotizing pancreatitis:

- The **Cullen sign** is a bluish discoloration around the umbilicus resulting from hemoperitoneum.
- The **Grey-Turner** sign is a reddish-brown discoloration along the flanks resulting from retroperitoneal blood dissecting along tissue planes; more commonly, patients may have a ruddy erythema in the flanks secondary to extravasated pancreatic exudate.

- Erythematous skin nodules may result from focal subcutaneous fat necrosis; these are usually not more than 1 cm in size and are typically located on extensor skin surfaces; in addition, polyarthritis is occasionally seen.
- **Mayo-Robson's sign** – pain while pressing at the top of the angle lateral to the erector spinae muscles and below the left 12th rib.
- Deep palpation of the abdomen in the area of the pancreas reveals the absence of pulsation of the abdominal aorta (**Voskresensky's symptom**).
- **Mondor's symptom** – violet spots on the body (subcutaneous fat necrosis) and face alternating with the sites of the pale skin.
- **Halsted's symptom** – cyanosis of skin of the abdomen. Changes in skin color are the result of the skin vessels dystonia caused by pain, general hypoxia of tissues, elevated level of histamine in blood.

Rarely, abnormalities on funduscopic examination may be seen in severe pancreatitis. Termed Purtscher retinopathy, this ischemic injury to the retina appears to be caused by activation of complement and agglutination of blood cells within the retinal vessels. It may cause temporary or permanent blindness.

Diagnosis

Once a working diagnosis of acute pancreatitis is reached, laboratory tests are obtained to support the clinical impression. In addition to confirming the diagnosis, laboratory tests are helpful in determining the etiology and looking for complications.

Although diagnostic imaging is unnecessary in most cases of pancreatitis, visualization of inflammatory changes within the pancreas provides morphologic confirmation of the diagnosis. Obtain imaging tests when the diagnosis is in doubt, when severe pancreatitis is present, or when a given imaging study might provide specific information needed to answer a clinical question.

Laboratory studies.

Complete blood count and hematocrit. A complete blood count (CBC) demonstrates leukocytosis – white blood cell (WBC) count higher than 12,000/μL. Leukocytosis may represent inflammation or infection.

Hemoconcentration at admission (an admission hematocrit value greater than 47%) has been proposed as a sensitive measure of more severe disease. If blood transfusion is necessary, as in cases of hemorrhagic pancreatitis, obtain type and cross-match.

Amylase and lipase. Serum amylase and lipase levels are typically elevated in persons with acute pancreatitis. However, these elevations may only indicate pancreastasis. Amylase or lipase levels at least 3 times above the reference range are generally considered diagnostic of acute pancreatitis.

Serum amylase determinations are routinely available, but they are not specific for pancreatitis. Preferably, the amylase P level should be measured, which is somewhat more specific to pancreatic pathology. Elevations can occur in patients with small intestinal obstruction, mesenteric ischemia, tubo-ovarian disease, renal insufficiency, or macroamylasemia. Rarely, elevations may reflect parotitis. The serum half-life of amylase is short, and elevations generally return to the reference ranges within a few days.

Lipase has a slightly longer half-life and its abnormalities may support the diagnosis if a delay occurs between the pain episode and the time the patient seeks medical attention. Elevated lipase levels are more specific to the pancreas than elevated amylase levels. Lipase levels remain high for 12 days. In patients with chronic pancreatitis (usually caused by alcohol abuse), lipase levels may be elevated in the presence of a normal serum amylase level.

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 the prognosis.

Evaluation of *urinary amylase (diastase)* level is of great practical importance. Increase of it's activity (over 128 units according to Volgemuth, or more than 21.2 international units per hour (IU/h) is noted in 70% of patients. However, in case of necrosis of the glandular tissue urinary amylase is low.

Liver-associated enzymes. Determine alkaline phosphatase, total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels to search for evidence of gallstone pancreatitis. An ALT level higher than 150 U/L suggests gallstone pancreatitis and a more fulminant disease course.

Serum electrolytes, BUN, creatinine, glucose, cholesterol, and triglycerides. Obtain measurements for blood urea nitrogen (BUN), creatinine, and electrolytes; a great disturbance in the electrolyte balance is usually found, secondary to third spacing of fluids. Measure blood glucose level because it may be elevated from B-cell injury in the pancreas.

Measure calcium, cholesterol, and triglyceride levels to search for an etiology of pancreatitis (eg, hypercalcemia or hyperlipidemia) or complications of pancreatitis (eg, hypocalcemia resulting from saponification of fats in the retroperitoneum).

C-reactive protein (CRP). A 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 (ie, ≥ 10 mg/dL) strongly indicates severe pancreatitis. CRP is an acute-phase reactant that is not specific for pancreatitis.

Other tests. Evaluate arterial blood gases if a patient is dyspneic. Whether tachypnea is due to acute respiratory distress syndrome (ARDS) or diaphragmatic irritation must be determined. Lactic dehydrogenase (LDH), BUN, and bicarbonate levels should be measured both at admission and at 48 hours in order to help determine the Ranson criteria for survival. Trypsin and its precursor trypsinogen-2 in both the urine and the peritoneal fluid have been evaluated as possible markers for acute pancreatitis (especially post-ERCP pancreatitis) but are not widely used.

Imaging methods.

Abdominal radiography (X-ray). Plain films of the abdomen are part of the initial diagnostic workup of acute abdominal pain. Findings on plain films are nonspecific but are suggestive of acute pancreatitis. The most commonly recognized radiologic signs associated with acute pancreatitis include the following: air in the duodenal C-loop; the sentinel loop sign, which represents a focal dilated proximal jejunal loop in the left upper quadrant; the colon cutoff sign, which represents distention of the colon to the transverse colon with a paucity of gas distal to the splenic flexure.

Ultrasonography (US). US of the abdomen is the most useful initial test in determining the etiology of pancreatitis and is the technique of choice for detecting gallstones. In addition, the ability to identify choledocholithiasis is limited.

More definitive *findings* include a diffusely enlarged hypoechoic gland. Focal enlargement of the pancreatic head and body also may be seen (fig. 4). Extrapancreatic spread of acute pancreatitis may be the only sonographic manifestation of acute pancreatitis in some patients. The pancreas may appear completely normal in mild cases of acute pancreatitis.

Complications of acute pancreatitis may be identified. Peripancreatic free fluid collections are identified as ill-defined anechoic collections. The fluid collections may demonstrate internal echoes/debris or septations if hemorrhage or a superimposed infection has occurred. A primary limitation of US is that often the pancreas cannot be visualized secondary to overlying bowel gas.

Endoscopic ultrasonography (EUS) is an endoscopic procedure that allows a high-frequency ultrasound transducer to be inserted into the gastrointestinal tract to visualize the pancreas and the biliary tract.

Its principal role in the evaluation of acute pancreatitis is the detection of microlithiasis and periampullary lesions not easily revealed by other methods. This modality should not be used to help identify chronic pancreatitis until several months after the episode of acute pancreatitis.

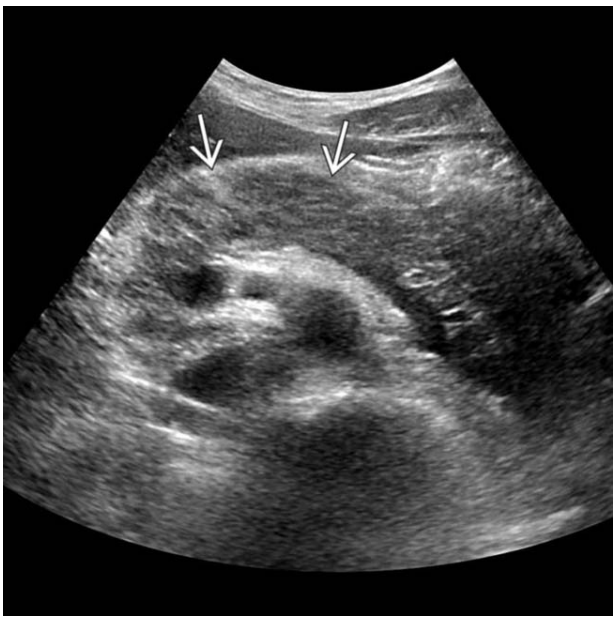

Fig. 4. Ultrasonography. *Acute pancreatitis: transverse ultrasound demonstrates diffuse enlargement of the pancreas (arrows), which appears abnormally hypoechoic, compatible with acute pancreatitis in this patient with a markedly elevated lipase level.*

A secretin-stimulated EUS study may reveal resistance to ductal outflow at the level of the papilla, as evidenced by dilatation of the pancreatic duct to a greater extent and longer duration than in a healthy population. This can be helpful in evaluating patients with recurrent idiopathic pancreatitis.

Computed tomography (CT). Contrast-enhanced CT (CECT) scanning of the abdomen and pelvis is the standard imaging modality for evaluating acute pancreatitis and its complications. Both IV and oral contrast should be administered. Imaging protocols vary, but the most important unifying point is to obtain thin-section images during the peak of pancreatic arterial perfusion. This usually can be acquired by imaging 30-40 seconds after the administration of iodinated contrast at 3-4 mL/s using helical CT.

Typical *CT findings in acute pancreatitis* include focal or diffuse enlargement of the pancreas, heterogeneous enhancement of the gland, irregular or shaggy contour of the pancreatic margins, blurring of peripancreatic fat planes with streaky soft tissue stranding densities, thickening of fascial planes, and the presence of intraperitoneal or retroperitoneal fluid collections (fig. 5). The fluid collections most commonly are found in the peripancreatic and anterior pararenal spaces but can extend from the mediastinum down to the pelvis.

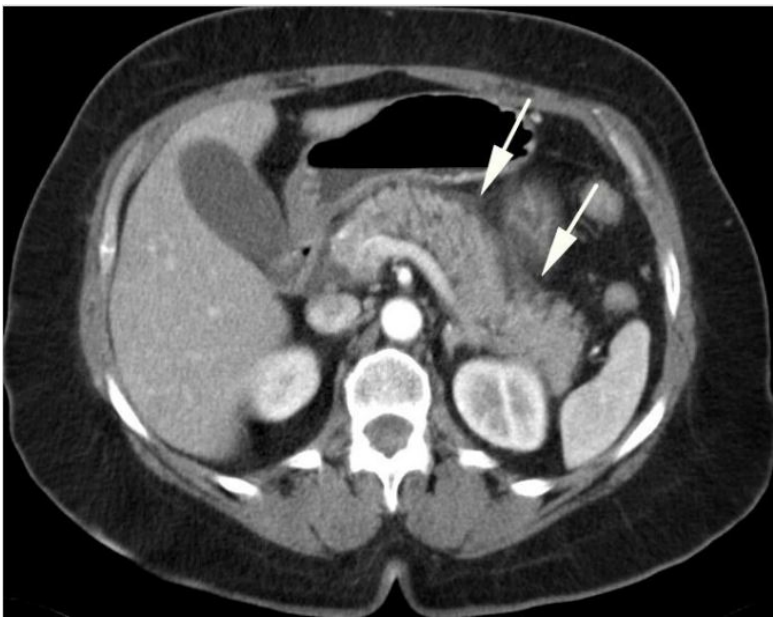

Fig. 5. Computed tomography. *Acute interstitial edematous pancreatitis: normal enhancing pancreas with swelling and little peripancreatic fat stranding (arrows).*

A pseudocyst appears as an oval or round water density collection with a thin or thick wall, which may enhance. A pancreatic abscess can manifest as a thick-walled low-attenuation fluid collection with gas bubbles or a poorly defined fluid collection with mixed densities/attenuation.

Necrotic pancreatic tissue is recognized by its failure to enhance after IV contrast administration. A focal or diffuse well-marginated zone of unenhanced parenchyma (>3 cm in diameter or >30% of pancreatic area) is considered a reliable CT finding for the diagnosis of necrosis.

Hemorrhage appears as high-attenuation fluid collections. Active bleeding is seen as contrast extravasation.

CECT can be used to assess the severity of acute pancreatitis and to estimate the prognosis. Balthazar et al developed a grading system in which patients with acute pancreatitis are classified into 1 of the following 5 grades:

Grade A – normal-appearing pancreas;

Grade B – focal or diffuse enlargement of the pancreas;

Grade C – pancreatic gland abnormalities associated with peripancreatic fat infiltration;

Grade D – a single fluid collection;

Grade E – two or more fluid collections.

In patients with pancreatitis of grade A or B, the disease has been shown to follow a mild, uncomplicated clinical course; most complications occur in patients with pancreatitis of grade D or E.

Magnetic resonance imaging (MRI). Although CT has long been the mainstay for imaging acute pancreatitis and its complications, MRI is an excellent alternative imaging modality, such as in patients with contrast allergy or renal insufficiency.

The morphologic changes of acute pancreatitis are similar on CT and MRI. The pancreas may be enlarged focally (usually the pancreatic head) or diffusely. Acute inflammatory changes appear as strands of low signal intensity in the surrounding peripancreatic fat.

Endoscopic retrograde cholangiopancreatography (ERCP) is an endoscopic procedure used to evaluate the biliary and pancreatic ductal systems. However, ERCP should be used with extreme caution in patients with acute pancreatitis and should never be used as a first-line diagnostic tool in this disease. This procedure should be performed only in the following situations:

- the patient has severe acute pancreatitis that is believed, and is seen on other radiographic studies, to be secondary to choledocholithiasis;
- the patient has biliary pancreatitis and is experiencing worsening jaundice and clinical deterioration despite maximal supportive therapy.

Image-guided aspiration and drainage. CT-guided needle aspiration is used to differentiate infected necrosis from sterile necrosis in patients with severe necrotizing pancreatitis. The needle is placed into an area of low attenuation in or around the pancreas of a patient with fever and tachycardia or other signs of a systemic inflammatory response syndrome, generally following the first week of severe pancreatitis.

The specimen should be delivered to the laboratory within an hour and interpreted promptly. The specimen should always be evaluated for Gram stain, culture, and sensitivity. If the Gram stain shows bacteria or fungi, surgical debridement of the infected necrosis is generally indicated. An exception would be if the patient cannot tolerate surgery; in that case, CT-guided catheter drainage may be more effective.

EUS-guided needle aspiration can often be used to differentiate infected necrosis from sterile necrosis in the same manner as CT-guided needle aspiration.

Laparoscopy. Laparoscopic signs of necrotizing pancreatitis are the presence of plaques of the fat tissue necrosis foci, which may be located along the greater and lesser omentum, gastrocolic ligament, on the peritoneum of the anterior abdominal wall, the round ligament of the liver, and the transverse mesocolon.

Differential diagnosis

Recognizing patients with severe acute pancreatitis as soon as possible is critical for achieving optimal outcomes. The overall differential for abdominal pain constitutes the differential for acute pancreatitis. It can be significantly narrowed down to a specific diagnosis with a good history and physical examination. Differential diagnoses for acute pancreatitis include but are not limited to the following:

- Acute peritonitis.
- Perforated viscus.
- Peptic ulcer disease.
- Cholangitis.
- Cholecystitis.
- Bowel obstruction.
- Bowel/gastric perforation.
- Mesenteric ischemia.
- Acute hepatitis.
- Diabetic ketoacidosis.
- Basilar pneumonia.
- Myocardial infarction.
- Aortic dissection.
- Renal colic.

In many cases of abdominal pain, a lipase level three times the upper limit of normal allows for the diagnosis of pancreatitis as the source of abdominal pain due to its high specificity. An abdominal ultrasound helps to differentiate cholecystitis, whereas high suspicion of mesenteric ischemia warrants a CT angiogram. In high-risk patients, the cardiac source should be concurrently ruled out as it can present atypical epigastric pain. Though the pain of a progressing aortic dissection is more severe and tearing in nature, it should be considered due to its particularly urgent nature.

Treatment

Medical management of mild acute pancreatitis is relatively straightforward. The patient is kept NPO (nil per os – that is, nothing by mouth), and intravenous (IV) fluid hydration is provided. The ideal timing to initiate enteral feeding remains undetermined, administration within 48 hours appears to be safe

and tolerated. Analgesics are administered for pain relief. Antibiotics are generally not indicated.

Patients with severe acute pancreatitis require intensive care. Within hours to days, a number of complications (eg, shock, pulmonary failure, renal failure, gastrointestinal bleeding, or multiorgan system failure) may develop. The goals of medical management are to provide aggressive supportive care, to decrease inflammation, to limit infection or superinfection, and to identify and treat complications as appropriate.

Further inpatient care depends on whether any of the complications of severe pancreatitis develop and how well patients respond to treatment. This ranges from a few days to several months of intensive care.

Components of medical treatment incule the following:

- Fluid resuscitation.
- Nutritional Support.
- Pain management.
- Antibiotic therapy.
- Symptomatic treatment.

Fluid resuscitation. Patients with acute pancreatitis lose a large amount of fluids to third spacing into the retroperitoneum and intra-abdominal areas. Accordingly, they require prompt IV hydration within the first 24 hours.

There is no universal consensus definitively favoring one type of fluid over another type; both crystalloids and colloids are used. Resuscitation should be sufficient to maintain hemodynamic stability. This usually involves administration of several liters of fluid as a bolus, followed by continuous infusion.

The choice of fluid is *Lactated Ringer's solution* given with an initial bolus of 15 to 20 mL/kg and followed by administering at a rate of 3 mL/kg per hour (approximately 250 to 500 mL per hour) in the first 24 hours if there are no other contraindications for fluid. The fluid resuscitation monitoring is done with a combination of labs, BUN, hematocrit, and urine output every 4 to 6 hours in the first 24 hours of resuscitation to adjust the fluid rate.

Nutritional support. The commonly employed practice is to keep nothing by mouth until abdominal pain, vomiting, nausea, loss of appetite, and ileus improve. Many studies support early feeding in mild pancreatitis and consider it safe as it does not exacerbate symptoms. A soft, low-residue, low-fat diet is recommended for initial feeding. Later it is advanced to regular consistency as soon as it is tolerated. In severe pancreatitis or where per-oral intake is not tolerable, *nasojejunal feeding* is considered superior to parenteral nutrition because it helps minimize bacterial translocation by maintaining the intestinal wall barrier.

Total parenteral nutrition (TPN) may be required when patients cannot meet their caloric needs with enteral nutrition or when adequate jejunal access cannot be maintained; the TPN solution should include fat emulsions in amounts sufficient to prevent essential fatty acid deficiency.

Pain management. Nearly all the patients presenting with acute pancreatitis experience abdominal pain at some point during the disease. The World Health Organization (WHO) analgesic ladder is initially employed in pain management. It includes the use of non-steroidal anti-inflammatory drugs and highly potent opioid analgesics in an escalating manner, along with interventional strategies. Among the analgesics, many choices are available such as *opioids* fentanyl and meperidine, and *non-steroid anti-inflammatory drugs*. Pain management is based on the WHO analgesic ladder, which consists of four steps: step 1 – NSAID, step 2 – low potent opioid ± NSAID ± adjuvant drugs, step 3 – High powerful opioid ± NSAID ± adjuvant drugs, step 4 – interventional treatment ± high potent opioid ± NSAID ± adjuvant drugs.

It was considered in the past that opioids could trigger the spasm of the sphincter of Oddi. Still, a recent Cochrane review of five RCTs with a total of 227 patients shows no difference between opioids and other analgesic options regarding the risk of complications or clinically severe adverse events.

Symptomatic treatment. In cases of severe vomiting prescribe *antiemetic drugs* – metoclopramide, ondansetrone, placement of nasogastric tube. To decrease the acidity in stomach and desrease the risks of ulceration – *proton-pomp inhibitors* (omeprazole) or *H2-blockers* (ranitidine).

Treatment of metabolic complications (eg, hyperglycemia and hypocalcemia) is carried out after the control of electrolytic balance in the blood.

Antibiotic therapy. Antibiotics, usually drugs of the *imipenem class*, should be used in any case of pancreatitis complicated by infected pancreatic necrosis. However, they should not be given routinely for fever, especially early in the disease course, because this symptom is almost universally secondary to the inflammatory response and typically does not reflect an infectious process.

One of controlled clinical trials evaluated the role of imipenem-cilastatin initiated at admission to prevent infected pancreatic necrosis. This drug combination penetrates the pancreatic parenchyma and reduces the risk of intra-abdominal infection. It appeared to offer some benefit in preventing infectious complications. Unfortunately, fungal superinfection tends to develop later in the clinical course, although this risk is probably overemphasized.

A randomized trial failed to show any benefit from giving *ciprofloxacin* and *metronidazole* to prevent infectious complications. Accordingly, this drug

combination is not routinely used for prophylaxis in the setting of acute pancreatitis.

Surgical treatment. Further management is directed at the etiology of pancreatitis. *Indications for surgery* include the following:

- Acute pancreatitis complicated by purulent peritonitis.
- Gallstone pancreatitis (billigenic origin).
- Infected pancreatic necrosis;
- No effect during intensive medical treatment up to 48 hours.
- Increasing obstructive jaundice.
- If you can not exclude acute surgical diseases of the abdominal cavity, requiring emergent surgical treatment.

Gallstone pancreatitis. It is optimal for patients admitted with gallstone pancreatitis to undergo cholecystectomy before discharge, rather than being scheduled for a later date as an outpatient. Patients discharged with gallstone pancreatitis without a cholecystectomy are at high risk for recurrent bouts of pancreatitis.

The most common factors related to surgical delay are the need to stablilize comorbid conditions and preoperatively investigate the common bile duct; other factors are significantly advanced age and an increased incidence of clinical signs indicating the presence of common bile duct stones. Although early laparoscopic cholecystectomy appeares to shorten overall hospitalization, the clinical outcomes are similar between those who underwent early surgery and those who undergo delayed laparoscopic cholecystectomy.

If the imaging and laboratory study findings are consistent with severe acute gallstone pancreatitis that is not responding to supportive therapy or with ascending cholangitis with worsening signs and symptoms of obstruction, early ERCP with sphincterotomy and stone extraction is indicated.

Infected pancreatic necrosis.9 When clinical signs of infection or SIRS are present in the setting of necrotizing pancreatitis, CT-or US-guided needle aspiration is indicated.

Surgery is recommended when large areas of the pancreas are necrotic and percutaneous CT-guided aspiration demonstrates infection on the basis of a positive Gram stain. Antibiotic therapy alone is not sufficient to achieve a cure. Aggressive surgical debridement and drainage are necessary to remove dead tissue and to clear the infection (fig. 6).

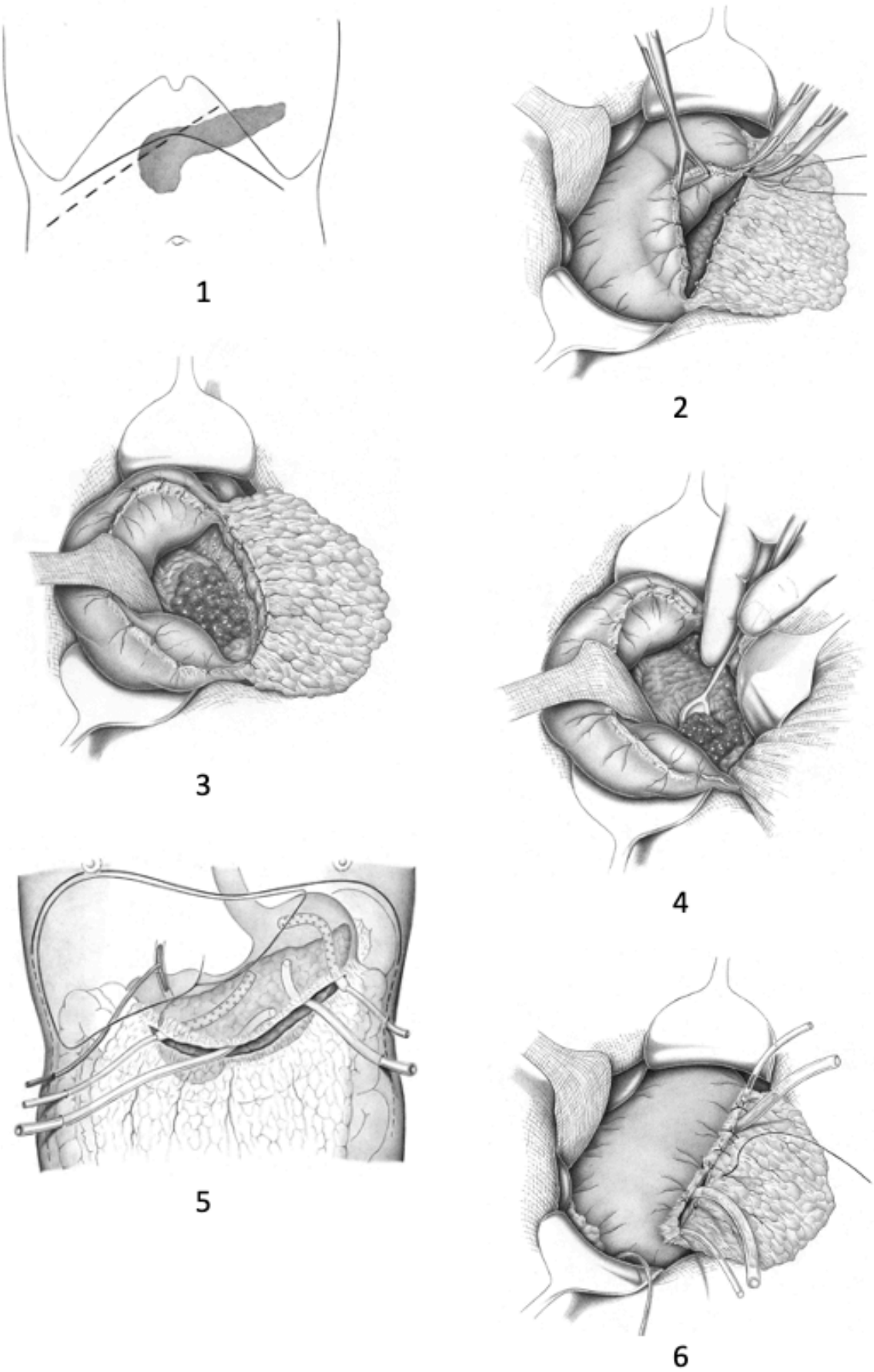

Fig. 6. Necrosectomy.

Necrosectomy of the pancreas.

Skin incision. Access to the pancreas may be gained via a right subcostal incision or even a transverse upper laparotomy. The transverse upper laparotomy is especially recommended for processes in the body and tail of the pancreas because of the better accessibility (fig. 6-1).

Opening the lesser sac. Exposure of the pancreas begins with the opening of the lesser sac. For this purpose, the gastrocolic ligament is divided in a stepwise manner between Overholt clamps along the greater curvature of the stomach. Grasping the greater curvature with Duval clamps will allow the stomach to be displaced in a cranioventral direction, thus exposing the pancreas in the depth of the cavity (fig. 6-2).

Identification of necroses. After completely opening the greater curvature of the stomach, retractors can be inserted behind the stomach to expose the entire anterior surface of the pancreas. Necrotic areas are characterized by blackish or grayish discoloration, in part combined with hemorrhagic areas. A distinction cannot always be made macroscopically between pancreas necrosis and necrosis of the peripancreatic tissue (fig. 6-3).

Necrosectomy. Necrotic material is removed by finger-fracture technique, a Volkmann spoon, or even by superficial excision. Dissection is continued until capillary bleeding of the pancreatic substance signifies the border with viable pancreas tissue. Under no circumstances should well perfused pancreas tissue be removed because this will later cause problems with the subsequent function of the pancreas as well as with regard to rebleeding. Special attention should be paid to the splenic vein and the superior mesenteric vein, which must not be damaged in the course of necrosectomy. This would result in severe and hardly controllable bleeding. (fig. 6-4).

Lavage of the lesser sac. Complete removal of all necrotic material from the lesser sac should then be followed by continuous lavage. For this purpose, the lesser sac is continuously irrigated with up to 20 L of saline in 24 hours via two afferent and two efferent drains. This results in removal of necrotic material, endotoxins, and cytotoxic substances. A T-tube should be inserted into the common bile duct to prevent any biliary component to the pancreatitis and at the same time to drain the biliary tree (fig. 6-5).

Closure of the lesser sac. A closed irrigation system is accomplished by repairing the lesser sac with interrupted sutures. For this purpose, the gastrocolic ligament is reconstructed over the drains in a watertight fashion to seal off the lavage cavity. Irrigation is continued postoperatively until the end of the necrotic inflammatory process is demonstrated by clear, non-sanguineous fluid in the drains (fig. 6-6).

Necrosectomy can be performed through a transperitoneal or a retroperitoneal approach. Most often several operations are necessary to remove all necrotic tissues. The choice of the surgical approach depends on the location of necrosis and collections. Retroperitoneal approach is best indicated when collections develop to the left. Some authors favor planned relaparotomies, others reoperate only if clinical, biological and radiological parameters lead to a suspicion of persisting infected collections and necrosis. Laparoscopic techniques are not yet widely used but allow a limited approach, thus avoiding large wound dehiscence and bowel fistulas.

Risks of surgical treatment include erosion of vessels and adjacent organs (stomach, intestines) with hemorrhage or fistula formation, necessity of cholecystectomy/T-tube or splenectomy, multiple laparotomies/laparostoma.

If at laparotomy the edematous pancreatitis is found out, operation on the pancreas is not carried out.

A study of patients with necrotizing pancreatitis and infected necrotic tissue determined that a step-up approach to treatment (consisting of percutaneous drainage followed, if necessary, by minimally invasive retroperitoneal necrosectomy) yielded better results than standard care with open necrosectomy. Patients who received step-up treatment had a lower rate of major complications (new-onset multiorgan failure, multiple systemic complications, perforation of a visceral organ, enterocutaneous fistula, or bleeding) and death.

Treatment of acute pancreatitis complications – see “Complications of acute pancreatitis”.

Complications of acute pancreatitis

Complications of acute pancreatitis can be divided into *local* and *systemic* (fig. 7, tab. 2).

Peripancreatic fluid collections usually develop in less than 4 weeks after the initial presentation of pancreatitis whereas a pseudocyst and walled-off necrosis more than 4 weeks after the onset of acute pancreatitis.

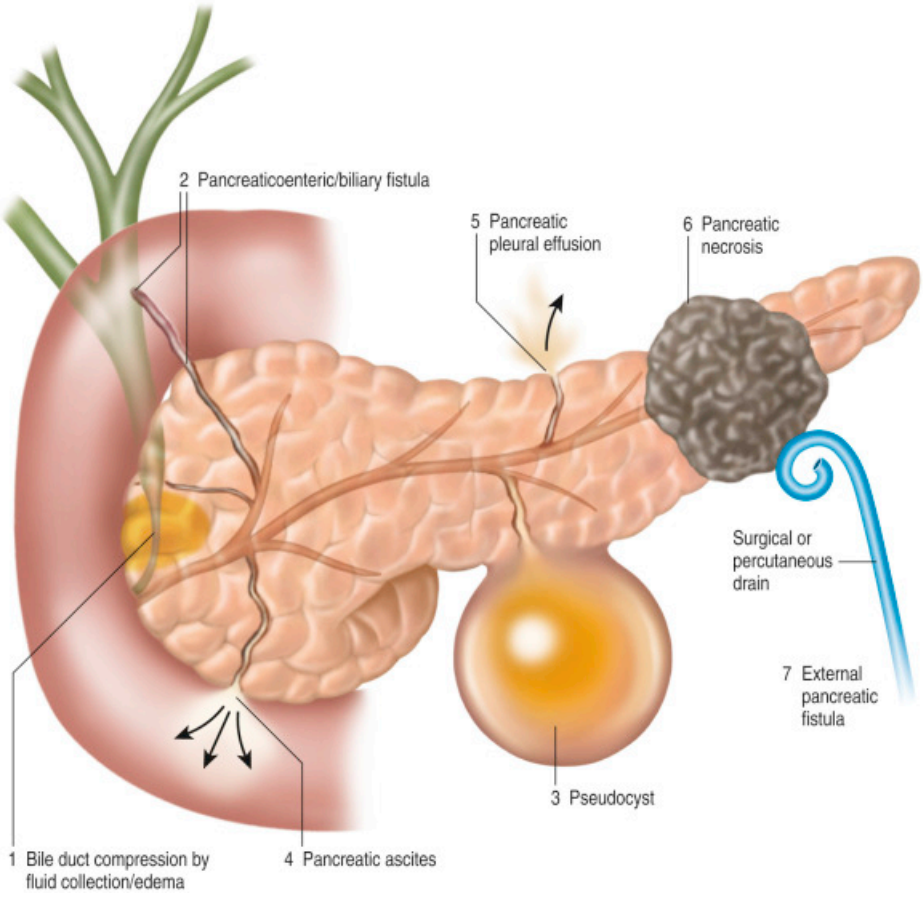

Fig. 7. Complications of acute pancreatitis.

Local complications based on the revised Atlanta criteria (tab. 2) include the following:

- Pancreatic pseudocyst (> 4 weeks).
- Walled-off necrosis (> 4 weeks).
- Peri-pancreatic fluid collection (early phase).
- Acute necrotic collection (< 4 weeks).

Systemic complications include the following:

- Acute respiratory distress syndrome (ARDS).
- Compartment syndrome.
- Acute kidney injury (AKI).
- Pleural effusion.
- Disseminated intravascular coagulation (DIC).
- Pancreatic ascites.

Chronic pancreatitis has several complications including:

- Formation of pseudocysts.
- Diabetes.
- Pseudoaneurysms.

- Splenic vein thrombosis.
- Recurrent acute pancreatitis.
- Risk of progression to pancreatic cancer.

Table 2.

Types of fluid collections (Revised Atlanta Classification)

Type of Collection	Type of Pancreatitis	Description	CECT Criteria
Acute peripancreatic fluid collection (APFC)	Acute interstitial edematous pancreatitis	Areas of peripancreatic fluid seen within the first 4 weeks after onset. No associated necrosis	Homogeneous fluid collection; confined by normal peripancreatic fascial planes; no definable wall encapsulating the collection; no intrapancreatic extension
Pancreatic pseudocyst (PP)	Acute interstitial edematous pancreatitis	Usually occurs more than 4 weeks after onset	Well circumscribed, usually round or oval; homogenous fluid density; no non-liquid component; well defined wall, completely encapsulated
Acute necrotic collection (ANC)	Acute necrotizing pancreatitis	Usually occurs less than 4 weeks after onset	Heterogeneous and non-liquid density of varying degrees in different locations; no definable wall encapsulating the collection; location – intrapancreatic and/or extrapancreatic
Walled-off necrosis (WON)	Acute necrotizing pancreatitis	Usually occurs more than 4 weeks after onset	Heterogeneous with liquid and non-liquid density with varying degrees of loculations; well defined wall, that is, completely encapsulated; location – intrapancreatic and/or extrapancreatic; maturation usually requires 4 weeks after onset of acute necrotising pancreatitis

1. Pancreatic pseudocyst (PP). A pancreatic pseudocyst is an encapsulated collection of homogenous fluid with little or no necrotic tissue located near the pancreas. A *true cyst* is a localized fluid collection that is contained within an epithelial lined capsule. In contrast, a pseudocyst is a fluid collection that is surrounded by a *non-epithelialized* wall made up of fibrous and granulation tissue, hence the name “pseudo” cyst.

Pseudocysts can occur after pancreatitis in any age group. The incidence of pseudocysts is higher in males as it follows the incidence of pancreatitis, which is slightly male predominant. In acute pancreatitis, the incidence of pseudocysts ranges from 5% to 16%. Pseudocysts tend to be more common in the setting of chronic pancreatitis, with incidence rates between 20% to 40%. This can be explained by its long course posing an increased risk of damaging the pancreatic ducts with fibrosis, calculi, or protein plug formation.

Symptoms and physical examination. There are no specific symptoms that are pathognomonic of pseudocysts. However, the presence of vague, chronic abdominal pain in someone with a recent bout of pancreatitis should always raise suspicion as the diagnosis.

Some of the signs and symptoms that are suggestive of pseudocyst are: persistent abdominal pain, anorexia, new abdominal mass after an episode of pancreatitis, jaundice or shock (less commonly).

Findings that are of limited sensitivity: abdominal tenderness, palpable abdominal mass, signs of peritonitis, including guarding and rigidity (in case of a ruptured cyst), fever, scleral icterus, pleural effusion.

Diagnosis. With *serum enzyme* levels of limited diagnostic utility, identification of a pancreatic pseudocyst is usually made with the combination of high clinical suspicion and imaging studies. *Transabdominal ultrasound* has a sensitivity of around 70% to 90%.

The better option for initial imaging is a *contrast-enhanced CT* of the abdomen (fig. 8). It allows for better visualization of surrounding structures, helps identify evidence of biliary stones or calcifications, and helps discern debris from areas of necrosis. All of which aide in distinguishing pseudocysts from areas of walled of necrosis (WON).

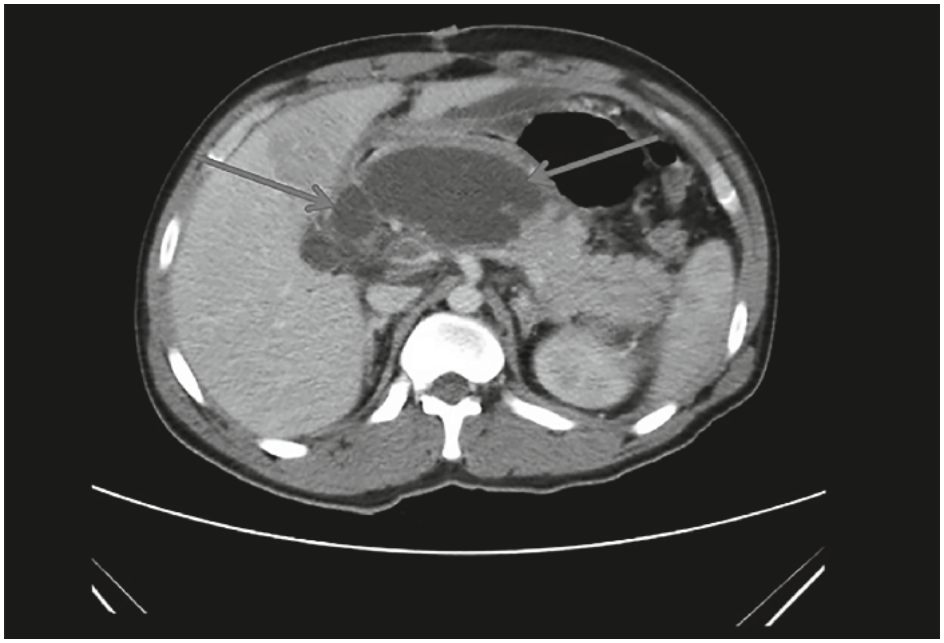

Fig. 8. Computed tomography. *Pseudocyst of the head of pancreas.*

Endoscopic ultrasound (EUS) proves resourceful in this regard as it is a minimally invasive procedure that allows for close up, detailed images of the pancreas. Findings suggestive of a cystic neoplasm include a cyst wall thickness greater than 3 mm, multiple septations, the presence of a solid mass or nodule, and cystic dilation of the main pancreatic duct.

An *MRI-MRCP* is the most accurate tool to study the anatomy of the pancreatic ducts. It is superior to CT scan imaging in characterizing debris within the pseudocyst. However, MRI-MRCP is not routinely used because a CT scan typically offers adequate diagnostic information.

Carcinoembryonic antigen (CEA) and *CA-125* (low in pseudocysts and elevated in tumors).

Treatment. Spontaneous resolution of pseudocysts is common, especially for those that occur after an episode of acute pancreatitis. Since stable, non-enlarging pseudocysts rarely cause any symptoms, the gold standard for the treatment of uncomplicated pseudocysts is conservative management. This includes analgesics and antiemetics as needed and a low-fat diet.

Indications for surgical treatment: PPs which are symptomatic, growing; complications (infected PP, hemorrhage, biliary or bowel obstruction); occurring with chronic pancreatitis and when malignancy cannot be excluded.

The three categories of invasive interventions are percutaneous, endoscopic, and surgical drainage or excision. Ideally, any intervention should be delayed to around six weeks after the inciting pancreatitis episode, in the absence of complicating factors, to allow the pseudocyst wall to thicken and mature.

Percutaneous drainage (PD) is performed with either US or CT guidance. A pigtail catheter is placed into the pseudocyst and is left in place until the fluid output is minimal. It is contraindicated in patients with strictures of the pancreatic duct and those who cannot manage catheter care at home. PD should only be considered in critically ill patients who cannot tolerate surgical or endoscopic procedures or for patients with an immature infected or complicated pseudocyst as PD does not require wall maturation before the intervention.

Endoscopic drainage. The aim of these methods is to create a canal that helps to drain the pancreatic pseudocyst into the gastrointestinal tract, avoiding the need to place an external drain. Construction of the canal can be done either through the transpapillary method using ERCP or directly across the stomach or duodenal wall with transmural drainage (fig. 9).

1.Transpapilliary drainage (TPD). This is an option when there is a communicating tract between the pseudocyst and the main pancreatic duct. In this technique, a catheter is threaded through the pancreatic duct, and a stent is deployed within the communicating tract between the pseudocyst and the lumen of the pancreatic duct under ERCP guidance. An advantage of using the TPD technique is the ability to dilate other pancreatic duct strictures encountered while threading the catheter to access the pseudocyst-pancreatic duct communicating tract. TPD has a success rate, which ranges from 81% to 94%.

2.Transmural drainage (TSM) is performed across the stomach or the duodenal wall using EUS or the conventional endoscope to guide drainage of the pseudocyst. The advantage of using EUS is the ability to identify and access a pseudocyst that is non-bulging, pseudocysts that are adjacent to, but not directly abutting the gastrointestinal wall and pseudocysts that are located more distally along the pancreas. EUS helps identify and avoid overlying blood vessels, and thus, decreasing the risk of bleeding complications. Once the puncture site is established, a needle is inserted into the pseudocyst, and positioning is confirmed using fluoroscopy. After the cyst-gut tract is confirmed, it is dilated pneumatically, and multiple pigtail stents are deployed for drainage.

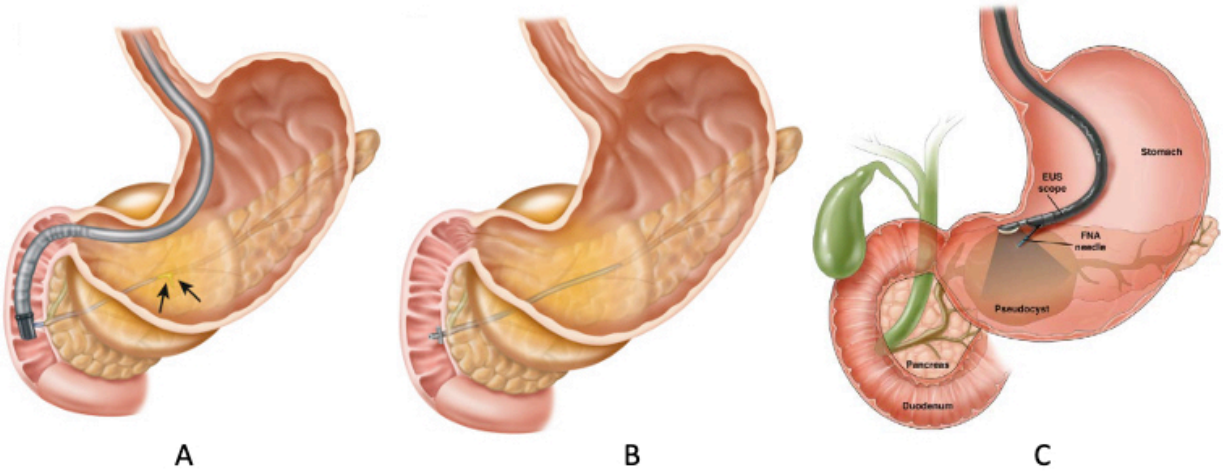

Fig. 9. Endoscopic methods of pseudocyst drainage. *A, B – transpapillary drainage and stent placement; C – transmural drainage.*

Surgical drainage includes the following procedures:

- *cystogastrostomy* (fig. 10) – a connection is created between the back wall of the stomach and the cyst such that the cyst drains into the stomach;
- *cystoduodenostomy* – a connection is created between the duodenum and the cyst to allow drainage of the cyst content into the duodenum;
- *cystojejunostomy* with Roux-en-Y-loop – a connection is created between the cyst and the small intestine so that the cyst is drained directly into the small intestine.

However, surgical drainage is now limited to certain situations such as recurrent pseudocysts, pseudocysts of uncertain origin, resection of a malignant cyst, or pseudocysts that are difficult to access endoscopically. For surgical drainage, either the open or laparoscopic method can be opted for as both are effective.

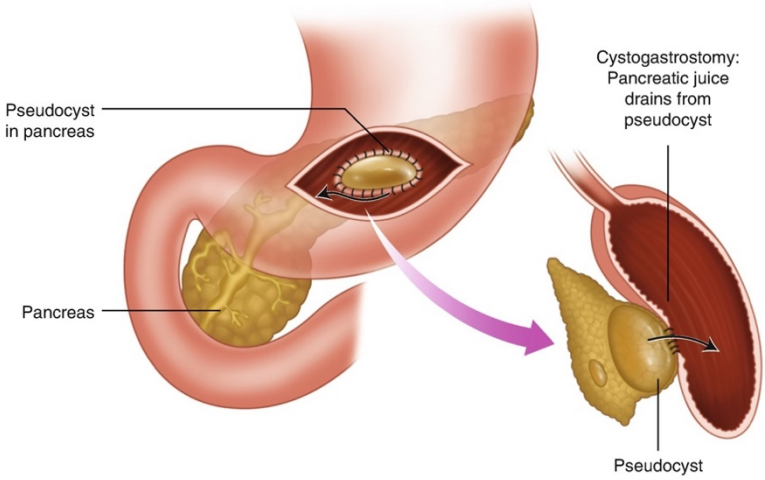

Fig. 10. Cystogastrostomy.

Complications. *Bleeding* is the most feared complication and is caused by the erosion of the pseudocyst into a vessel. Consider the possibility of bleeding in any patient who has a sudden increase in abdominal pain coupled with a drop in hematocrit level or a change in vital signs. Therapy is emergent surgery or angiography with embolization of the bleeding vessel.

Consider the possibility of *infection of the pseudocyst* in patients who develop fever or an elevated WBC count. Treat infection with antibiotics and urgent drainage (see "Pancreatic abscess").

GI obstruction, manifesting as nausea and vomiting, is an indication for drainage.

The pseudocyst can also *rupture*. A controlled rupture into an enteric organ occasionally causes GI bleeding. On rare occasions, a profound rupture into the peritoneal cavity causes acute peritonitis.

2. Pancreatic abscess (PA) is defined as a circumscribed intraabdominal collection of pus that is typically in the vicinity of the pancreas and contains little pancreatic necrosis. Infection is thought to occur via colonic translocation of bacteria (*Escherichia coli, Klebsiella, Pseudomonas* and *Enterococcus*). It usually develops in patients with pancreatic pseudocyst that became infected. Other causes might include penetrating peptic ulcers, gallstones, and excessive alcohol consumption because they increase the risk and the number of pancreatitis episodes. In rare cases, medications, blunt trauma, and the extension of abscesses from nearby structures can occur.

Symptoms and physical examination. History taking plays a major role in the diagnosis of pancreatic abscess – it usually occurs in patients with a history of pancreatitis or in patients prone to develop pancreatitis.

Persistent fevers, worsening abdominal pain, and failure to improve despite appropriate initial management may all be suggestive of superimposed infection of the pancreas. Infection should be suspected in patients who do not improve after 7 to 10 days of hospitalization and supportive care, and in those who rapidly deteriorate. Most common symptoms of PA include abdominal mass and pain, fever, nausea and vomiting, jaundice in cases of biliary obstruction.

Physical examination findings in patients with pancreatic infections generally mimic the symptoms of acute pancreatitis but are usually more severe and often occur after 7 to 10 days of hospitalization. Abdominal pain is located in the mid-epigastric region. An associated mass may or may not be palpable. In severe pancreatitis, patients are often dehydrated on presentation. Hypotension and hypoxia may indicate progression to shock. Fevers can result from underlying infection but also occur in the setting of ongoing pancreatic inflammation.

Diagnosis. A CBC, basic metabolic panel, liver function test, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase and blood cultures should be obtained in patients presenting with pancreatitis and not improving despite conservative management. High levels of CRP and leukocytosis have been associated with the detection of the presence of pancreatic necrosis. A hematocrit of higher than 44% has been established to be a risk factor for pancreatic necrosis and the development of an abscess.

Imaging studies are also required when the patient fails to improve within 72 hours of treatment. Abdominal US, abdominal CT scan with contrast and contrast-enhanced MRI are both options for assessment of pancreatic necrosis and abscesses, although CT is more commonly used. On imaging, the presence of extraluminal gas in the pancreatic and/or peripancreatic tissues is consistent with an underlying infection.

If infection is suspected, needle aspiration is indicated. After aspiration, the liquids are sent to laboratory for culturing and defining the sensitivity to antimicrobial medications.

Treatment. Medical treatment includes antibiotics, aggressive hydration. Broad-spectrum antibiotics should be initiated if cultures are positive, or there are systemic signs of infections. Consider CT- or US-guided fine-needle aspiration if a collection is visualized on imaging and infection is suspected.

For hemodynamically unstable patients, surgical debridement and drainage of the abscess is the treatment of choice. For hemodynamically stable patients, minimal-invasive methods of necrosectomy and drainage can be performed using endoscopy.

The resolution of tachycardia, fevers, hypotension, as well as improvement in the patients' abdominal pain, are all markers of clinical improvement. However,

they are not specific to the pancreatic abscess. For patients with diagnosed pancreatic abscess and bacteremia, serial blood cultures should be obtained to confirm the eventual clearance of the infection.

Complications of PA include multiple abscesses, enlargement of abscess, sepsis, septic shock, multiple organ failure, fistula formation.

3. Pancreatic necrosis. Fluid and necrotic collections can occur as complications of acute pancreatitis. According to the latest classification, these can be divided into acute or delayed, depending on whether such a collection is of less than or more than 4 weeks' duration. Pancreatic necrosis is an acute necrotic collection in which there is a variable amount of fluid and necrosis. By around 4 weeks, a walled-off pancreatic necrosis (WOPN) may form, in which the collection is defined by a fibrotic and inflammatory wall. The term "infected necrosis" refers to bacterial invasion of the necrotic pancreatic tissue.

The mortality rate of pancreatitis may exceed 20% or more in the presence of infected pancreatic necrosis and is largely related to sepsis and multiorgan failure.

The inflammatory processes in acute pancreatitis lead to the collection of fluid in and around the pancreas. The enzyme rich fluid and necrotic collections (in cases of acute pancreatitis) if persistent will eventually develop fibrosis around its periphery leading to pseudocysts and WOPN. These processes often follow severe acute pancreatitis as opposed to mild acute pancreatitis.

Acute necrotic pancreatitis is the most severe end of a spectrum of inflammation associated with pancreatitis. Inflammation in this situation may cause cell death. The resultant devitalized tissue becomes a potential bed for infection. The amount of necrotic tissue is the strongest predictor of mortality in necrotic pancreatitis. After necrotic pancreatitis three potential outcomes exist: resolution, persistent fluid collection (pseudocyst)/necrosis (WOPN), or formation of abscess or infected necrosis.

Symptoms and physical examination. Patients with pancreatic necrosis will have definitive history of pancreatitis (often with a prolonged course), hemodynamic instability, fever, failure of medical therapy, or the presence of peripancreatic fluid collections on CT scan.

Acute infection can set in in the pancreatic bed and lead to infected pancreatic necrosis and sepsis. When this occurs, it usually presents 10-12 days into the course of severe pancreatitis. Pancreatic abscess formation takes weeks to develop, as does WOPN. WOPN can then later become infected.

Patients with WOPN may be asymptomatic (50%) or present with symptoms (50%) such as severe abdominal pain, malaise, relapsing or recurrent pancreatitis, feeding intolerance, and/or weight loss. In severe cases, WOPN can obstruct the

gastrointestinal tract (bowel obstruction), fistulize to adjacent anatomic structures, and compress or erode into blood vessels or the bile duct (obstructive jaundice).

Diagnosis. *Laboratory studies.* No specific hematologic studies define infected necrosis or pancreatic abscess. A persistently elevated WBC count with a left shift and positive blood cultures is suggestive of this diagnosis. The degree of pancreatic enzyme elevation does not directly indicate the degree of necrosis.

Imaging studies. The presence of air in necrotic tissue or in a pseudocyst on imaging studies is specific for infection. The absence of a communication with the gut (often by spontaneous drainage into the gut lumen) is also a sign of infection.

Ultrasonography indicates the presence of stones in the bile ducts, an increasement and changes in the structure of the gland, anechoic foci of necrosis in the pancreas.

CT scan. The current criterion standard for initial evaluation is contrast-enhanced CT scan, which may reveal ischemic pancreatic tissue as evidenced by the lack of uptake of contrast (fig. 11).

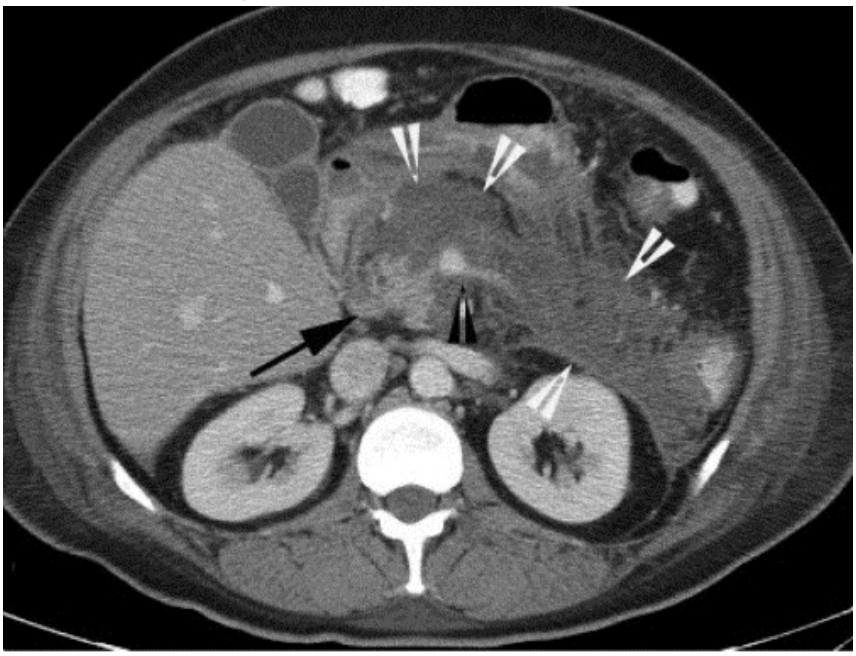

Fig. 11. Contrast-enhanced CT of acute necrotizing pancreatitis. *The black arrowhead notes the junction of the superior mesenteric and splenic veins. The normal pancreas should be seen enhancing anterior to this. Non-enhancing pancreas can be seen in this case (white arrows). Normal enhancing head is seen (black arrow).*

Necrotic pancreatic tissue is recognized by its failure to enhance after IV contrast administration. Balthazar et al point out that the normal unenhanced pancreas has CT attenuation measuring 30-50 Hounsfield units (HU) and that, after IV contrast, the pancreas should display attenuation measuring 100-150 HU. A

focal or diffuse well-marginated zone of unenhanced parenchyma (>3 cm in diameter or >30% of pancreatic area) is considered a reliable CT finding for the diagnosis of necrosis. It should be noted that pancreatic necrosis may be radiologically indistinguishable from a pancreatic abscess.

Splenic vein thrombosis is seen in 40% of patients with WOPN. Venous thrombosis can be identified through a failure of the peripancreatic vein (eg, splenic vein, portal vein) to enhance or as an intraluminal filling defect.

Image-guided aspiration and drainage – see "Diagnosis of acute pancreatitis".

Treatment. *Medical care.* In the acute phase of pancreatitis, the medical care of patients with evidence of pancreatic necrosis is no different from that of those without necrosis. Intravenous hydration aimed at maintaining the patient's intravascular volume and perfusion pressures is the mainstay of treatment of all cases of acute pancreatitis.

The routine use of prophylactic antibiotics and the routine use of antifungal agents along with prophylactic or therapeutic antibiotics in patients with severe acute pancreatitis are not recommended. In addition, it is not recommended to use antibiotics in patients with sterile necrosis to prevent infected necrosis.

Consider infected necrosis in patients with pancreatic or extrapancreatic necrosis whose condition deteriorates or who fail to improve after 7–10 days of hospitalization. Obtain initial CT-guided fine-needle aspiration (FNA) for Gram stain and culture, or administer empiric antibiotic therapy after obtaining cultures for infectious agents, without CT FNA.

In patients with infected necrosis, administer antibiotics known to penetrate pancreatic necrosis (eg, carbapenems, quinolones, metronidazole), which may delay or avoid intervention, thereby decreasing morbidity and mortality.

Surgical care. In most tertiary care centers, open surgical procedures are being replaced by endoscopic or percutaneous procedures. Surgery is now reserved for cases in which an endoscopic or percutaneous approach is not feasible (ie, infection of the pancreatic bed before a well-formed, walled-off collection is formed; abdominal compartment syndromes).

EUS-guided necrosectomy in specialized centers is the standard treatment for pancreatic necrosis and abscess. Endoscopic access is best performed when the wall is mature, usually 4 weeks or more after the episode of pancreatitis.

Percutaneous drainage followed by percutaneous or sinus tract endoscopy with necrosectomy is an option and a potential minimally invasive alternative for endoscopic drainage. Alternative minimally invasive approaches include retroperitoneal laparoscopic necrosectomy and drainage, in which the entire

necrosectomy is performed via percutaneous access without entry into the abdominal cavity.

An ERCP is needed in most patients with pancreatic necrosis to evaluate and establish continuity of the pancreatic duct if there is ductal discontinuity. Endoscopic sphincterotomy plays a role in patients with gallstone pancreatitis, as well as for those with infected pancreatic necrosis, pancreatic abscess, pseudocysts, and traumatic pancreatitis with a ruptured duct system.

Surgical treatment – surgical debridement and drainage are carried out to remove necrotic tissues and to clear the infection.

Indications for surgical treatment for pancreatic necrosis include the following:

1) Absolute:
- infected pancreatic necrosis;
- pancreatic abscess;
- destructive cholecystitis;
- septic phlegmon of retroperitoneal space;
- purulent peritonitis.

2) Relative:
- sterile necrosis of more than 50% of the pancreatic tissue (according to CT);
- steril necrosis of retroperitoneal tissue;
- choledocholithiasis, obstructive jaundice (ERCP, sphincterotomy, lithoextraction);
- progression of multiple organ failure.

4. Pleural effusion. There are several mechanisms of pleural effusion in pancreatitis. One of the mechanisms is the *transdiaphragmatic lymphatic blockage*. There may be a *disruption of pancreatic duct*, leading to the leakage of pancreatic enzymes and the formation of a pancreaticopleural fistula. The latter is more likely to occur if the duct disruption is posteriorly into the retroperitoneum. Exudation of fluid into the pleural cavity from the subpleural diaphragmatic vessels may also cause pleural effusion.

The incidence of pleural effusion in acute pancreatitis is reported to be about 3–17% in older literature, but recent reports show that the incidence is up to 50% based on detection by CT. Usually, effusions are mild to moderate and are left sided. These left-sided effusions are usually chemically induced or sympathetic in nature, with normal fluid amylase levels. In chronic pancreatitis, pleural effusion is quite rare and is usually due to the formation of pancreaticopleural fistulas. *Chest radiograph* is the primary imaging modality for evaluating pleural effusion in the

setting of pancreatitis. However, typically, the radiographs are taken at the bedside (portable), and due to the inadequate positioning and supine nature, mild to moderate effusions may be missed. *Ultrasonography* is the most sensitive method for detecting even a mild pleural effusion in the intensive care setting and has the advantage of being easily available at the bedside. Septations and internal echoes seen in ultrasonography can indicate infection. *Chest CT* is extremely sensitive in detecting even minimal amounts of fluid in the pleural cavity; however, it is rarely used for this indication. Infected effusions on CT are seen bounded by a thick and enhancing pleural wall on either side ("split pleura sign").

In acute pancreatitis, the pleural effusion usually resolves as the inflammation subsides. If the effusion persists for longer than 2 weeks or if there is right-sided massive pleural effusion, the possibility of a pancreatic pseudocyst or pancreaticopleural fistula should be considered. Overall, only 1% of the pleural effusions in the setting of pancreatitis are secondary to pancreaticopleural fistula.

In case of massive pleural effusion or infected effusions/empyema, *drainage* of the same can be performed through an intercostal drainage tube or a pigtail catheter.

5. Pancreatic ascites results from persistent leakage of pancreatic secretions in the peritoneum from pancreatic duct injury (fig. 12). The severity of this condition varies widely, often depending on the location and degree of ductal injury and infection in the fluid.

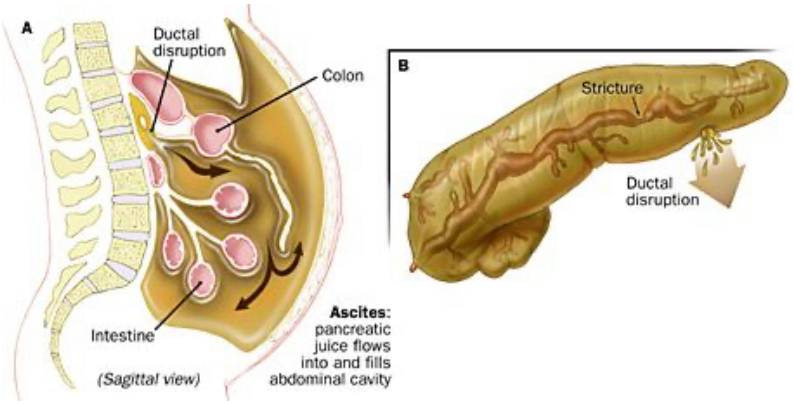

Fig. 12. Pancreatic ascites.

Minor pancreatic duct injuries are common in acute severe pancreatitis resulting in peripancreatic fluid collection and pseudocyst formation. Pancreatic necrosis can cause major pancreatic duct injury. Leakage of pancreatic fluid into the necrosis delays the resorption of walled-off necrosis. A persistent internal fistula into peritoneum causes pancreatic ascites. The presence of a pseudocyst or walled-off necrosis increases the odds of pancreatic ascites. Pancreatic fistula could result from a pancreatic duct injury from blunt abdominal trauma, ductal lithiasis, ampullary stenosis, or an iatrogenic cause. Iatrogenic causes of duct

injuries include pancreatectomy, ERCP, and pancreatic biopsy or fine-needle aspiration. Many cases remain idiopathic, and at times, the site of ductal disruption is unable to be found.

Most often this occurs in the setting of a pseudocyst or walled off necrosis. Pseudocysts, in the setting of chronic pancreatitis, tend to have a less robust fibrinous wall and allow pancreatic secretions to leak from the disrupted duct, into the pseudocyst, and out into the peritoneum. At other times, pancreatic duct disruption without a pseudocyst will form a fistulous tract. Depending on the route of the fistula, fluid collections will manifest differently. Fistulas from an anterior pancreatic duct disruption allow for pancreatic secretions to empty directly into the peritoneum leading to ascites. Posterior pancreatic duct ruptures allow for fistula formation through the aortic or esophageal hiatus or sometimes through the dome of the diaphragm leading to pleural effusions. In either case, the ascites is typically exudative with high amylase activity. Some have attributed this exudative quality to the pancreatic fluid causing an inflammatory process leading to increased vaso-permeability.

Symptoms and physical examination. Patients often will not present with symptoms suggestive of a chronic inflammatory process. Many patients will not have had previous episodes of acute pancreatitis or had previous episodes which occurred months to years before. Symptoms are usually increasing abdominal girth with mild abdominal discomfort. Weight loss may also occur due to loss of appetite despite fluid retention in the abdomen. Patients with concurrent pancreatic effusion will complain of a cough, chest pain, and increased dyspnea on exertion. A physical exam will often reveal a large volume of ascites with little to no abdominal tenderness. In some patients, erythematous lesions may exist on the extremities as a result of metastatic fat necrosis.

Diagnosis. *Diagnostic paracentesis* should be performed, and fluid amylase and protein measurements should be measured along with cell count, culture, Gram stain, and cytology. Pancreatic ascites is characterized by an amylase level over 1000 IU/L and protein level greater than 3 g/dL. The calculated serum-ascites albumin gradient (SAAG) is normally less than 1.1 g/dL. This distinguishes from ascites secondary to portal hypertension where amylase levels of ascitic fluid are not elevated, and fluid albumin levels are normally below 1.5 g/dL with a SAAG greater than 1.1 g/dL.

In patients where pancreatic ascites is suspected based on clinical features and peritoneal fluid assessment discussed above, further diagnostic workup includes ERCP and secretin augmented MRCP to determine the presence and site of the pancreatic duct leak.

Treatment. Management of pancreatic ascites has three approaches: medical, endoscopic, and surgical intervention.

Medical management consists of keeping the patient nothing by mouth and providing nutrition via total parenteral or nasojejunal route. Electrolyte imbalances often associated with active fistulous losses must be carefully managed. Somatostatin or octreotide are used to decrease the exocrine function of the pancreas and allow for healing of the disrupted duct. For patients symptomatic from their ascites, repeated therapeutic paracentesis can be considered. A course of medical treatment for less severe cases is proposed since resolution without intervention can occur in approximately 30% to 50% of patients.

The mainstay of management remains *endoscopic therapy*. A transpapillary stent at the pancreatic duct sphincter decreases intraductal pressure and diverts pancreatic secretion to the small bowel, thereby enhancing healing of the ductal disruption. Ideally, the ductal disruption should be bridged by the stent. In cases with large pancreatic necrosis, stenting through the disruption is challenging. Other endoscopic interventions include the use of injectable endoscopic glues or fibrinogen injections into the fistula to block further leakage of fluid into the peritoneum.

The *surgical approach* is mostly reserved for failure of endoscopic intervention or for cases where there has been complete disruption of the pancreatic duct with no opacity proximal to the duct disruption on cholangiography. Specific surgical interventions depend upon the location of ductal disruption with distal lesions often being amenable to partial pancreatectomy if the remaining pancreatic volume is deemed likely able to carry out sufficient endocrine and exocrine function. More proximal lesions of the main pancreatic duct are often treated via pancreaticojejunostomy.

Multiple choice questions

1. Anatomical parts of the pancreas are:
   A. Fundus, body, neck.
   B. Head, neck, body, tail.
   C. Left lobe, right lobe.
   D. Cardia, body, antrum, pylorus.
   E. Capsule, parenchyma, hilum.

2. The most common cause of acute pancreatitis in most developed countries is:
   A. Gallstones in the bile ducts.
   B. Traumas of pancreatic gland.
   C. Drugs.
   D. Infections.
   E. Tumours.

3. Choose the standard imaging modality for evaluating acute pancreatitis and its complications:
   A. Abdominal ultrasonography.
   B. Abdominal X-ray.
   C. Magnetic resonance imaging.
   D. Contrast-enhanced computed tomography.
   E. Endoscopic retrograde cholangiopancreatography.

4. Components of medical treatment of acute pancreatitis include:
   A. Fluid resuscitation.
   B. Nutritional support.
   C. Pain management.
   D. Antibiotic therapy.
   E. All answers are correct.

5. An encapsulated collection of fluid with a well-defined inflammatory wall usually outside the pancreas with minimal or no necrosis is called:
   A. Pancreatic abscess.
   B. Pancreatic pseudocyst.
   C. Acute necrotic collection.
   D. Acute peripancreatic fluid collection.
   E. Acute necrotizing pancreatitis.

Clinical cases

1. Male patient, 57 y.o., is presented with acute severe pain in the epigastrium, vomiting and nausea. The pain irradiates to the back. Body temperature – 37.4 °C. Rebound tenderness and rigidity are negative. History – chronic alcohol consumption, presense of gallstones in biliary system for the last 10 years. What is the preliminary diagnosis?

A. Acute gastritis.
B. Acute acalculous cholecystitis.
C. Acute pancreatitis.
D. Viral hepatitis.
E. Bowel obstruction.

2. You examine a patient with acute necrotizing pancreatitis. Which method will you use to differentiate infected necrosis from sterile necrosis?

A. MRI of abdomen.
B. Complete blood cell count and liver function tests.
C. Upper GI endoscopy.
D. CT- or US-guided needle aspiration and bacteriology.
E. Laparoscopy.

3. Male patient, 56 y.o. complaints of moderate pain in the epigastrium, nausea. During palpation you find a palpable mass in the epigastrium. Temperature is normal. Bowel movements are normal. In the history he has had severe acute pancreatitis 5 weeks ago. Possible diagnosis?

A. Pancreatic pseudocyst.
B. Perforated peptic ulcer.
C. Acute calculous cholecystitis.
D. Chronic pancreatitis.
E. Acute appendicitis.

MCQ answers						**Clinical cases answers**			
Question	1	2	3	4	5	Case	1	2	3
Answer	B	A	D	E	B	Answer	C	D	A

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