A. V. ZHURA

ACUTE PANCREATITIS

Minsk BSMU 2015

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
2-я КАФЕДРА ХИРУРГИЧЕСКИХ БОЛЕЗНЕЙ

А. В. Жура

ОСТРЫЙ ПАНКРЕАТИТ
ACUTE PANCREATITIS

Учебно-методическое пособие

Минск БГМУ 2015

УДК 616.37-002-036.11(811.111)-054.6(075.8)
ББК 54.13(81.2 Англ-923)
Ж91

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Отражены основные вопросы этиологии, патогенеза, диагностики, оказания помощи и лечения пациентов с острым панкреатитом. Описаны международная классификация, основные осложнения и методы их коррекции, современные направления терапии.

Предназначено для студентов 4–6-го курсов медицинского факультета иностранных учащихся, обучающихся на английском языке.

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MOTIVATIONAL CHARACTERISTIC OF THE TOPIC

Total in-class hours: 6.

During last 30 years the incidence of acute pancreatitis (AP) has increased in 40 times. Nowadays, it is on a 3rd place among acute surgical diseases, following acute appendicitis and cholecystitis. In acute pancreatitis, total mortality rate is 4–15 %, but when necrosis of the gland develops (necrotizing pancreatitis) it considerably grows up to 24–60 %. According to modern view, AP is responsible for approximately half of the deaths due to acute surgical diseases and 50–73 % of the surviving necrotizing pancreatitis patients get disability or lose ability to work for a long time.

The purpose is to study the basics of acute pancreatitis formation, pathogenesis, diagnosis and treatment.

Objectives are:

1) to learn main etiological causes of acute pancreatitis formation;
2) to learn methods of investigations of acute pancreatitis;
3) to learn common clinical features of acute pancreatitis;
4) to make diagnosis of acute pancreatitis;
5) to know current treatment methods of acute pancreatitis;
6) to prescribe correct medicines for conservative treatment;
7) to assess severity of acute pancreatitis;
8) to clerk patients with alcoholic- and gallstone-associated acute pancreatitis.

Requirements for the initial knowledge level. To learn the topic completely the student must know:

- propaedeutics of internal diseases (methods of clinical evaluation of abdominal organs)
- human anatomy (localization and structure of pancreas)
- topographic anatomy and operative surgery (main surgical approaches to pancreas and retroperitoneal space)
- normal physiology (exocrine and endocrine functions of pancreas)
- pathologic physiology (physiologic changes in acute pancreatitis)
- general surgery (basic principles of surgical infections and sepsis)

Test questions from related disciplines:

1. Normal and topographic anatomy of pancreas.
2. Function of pancreas.
3. Clinical evaluation of pancreas pathology.
4. Physiologic changes in acute pancreatitis.
5. Surgical approaches to pancreas and retroperitoneal space.

Test questions:

1. Anatomy and physiology of pancreas.
2. Definition and incidence of acute pancreatitis.
3. Etiology of acute pancreatitis.
4. Gallstone (biliary) acute pancreatitis.
5. Alcoholic acute pancreatitis.

6. Pathogenesis of acute pancreatitis.
7. Atlanta classification.
8. Clinical features of acute pancreatitis.
9. Diagnosis of acute pancreatitis.
10. Principles of acute pancreatitis treatment.

STUDY MATERIAL

ANATOMY AND PHYSIOLOGY OF PANCREAS

The pancreas is a retroperitoneal organ that lies in an oblique position, sloping upward from the C-loop of the duodenum to the splenic hilum. In an adult, the pancreas weighs 75–100 g and is about 15–20 cm long. The fact that the pancreas is situated so deeply in the abdomen and is sealed in the retroperitoneum explains the poorly localized and sometimes ill-defined nature with which pancreatic pathology presents. Due to its retroperitoneal location, pain associated with pancreatitis is often characterized as penetrating to the back.

REGIONS OF THE PANCREAS

There are four anatomical parts of the pancreas: the head, neck, body, and tail (fig. 1). The head of the pancreas is nestled in the C-loop of the duodenum and is posterior to the transverse mesocolon.

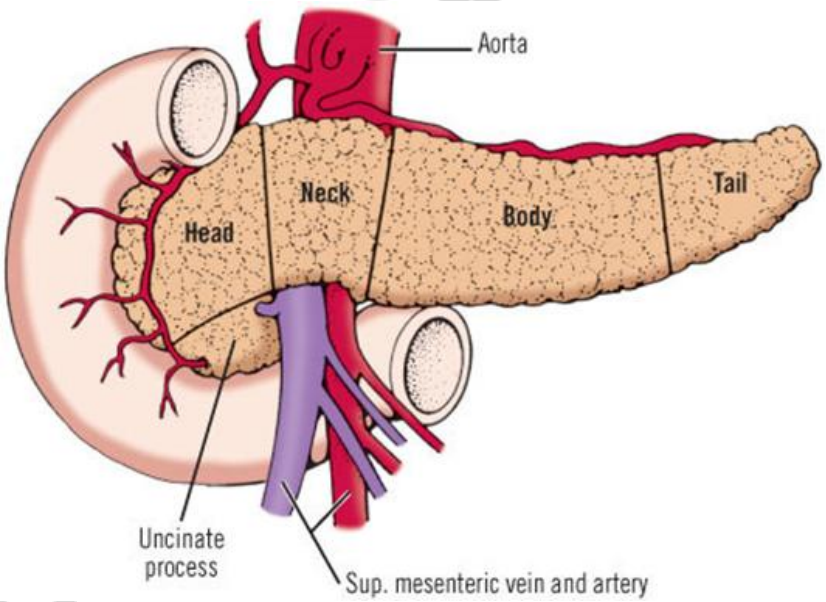


Fig. 1. Anatomical parts of pancreas

Just behind the head of the pancreas lie the vena cava, the right renal artery, and both renal veins. The neck of the pancreas lies directly over the portal vein. At the inferior border of the neck of the pancreas, the superior mesenteric vein joins the splenic vein and then continues toward the porta hepatis as the portal vein. The

inferior mesenteric vein often joins the splenic vein near its junction with the portal vein (fig. 2).

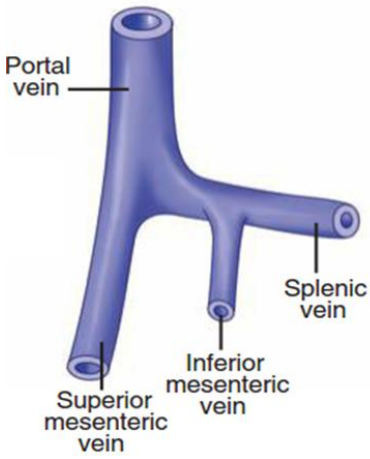


Fig. 2. Portal venous anatomy

PANCREATIC DUCT ANATOMY

The main pancreatic duct (of Wirsung) is usually only 2–3 mm in diameter and runs midway between the superior and inferior borders of the pancreas. The main pancreatic duct joins the common bile duct and empties at the ampulla of Vater or major papilla, which is located on the medial aspect of the second portion of the duodenum. The accessory duct from the pancreatic head (of Santorini) fuses with the main pancreatic duct and empties into the duodenum at the minor papilla, that's present in 60–80 % (fig. 3).

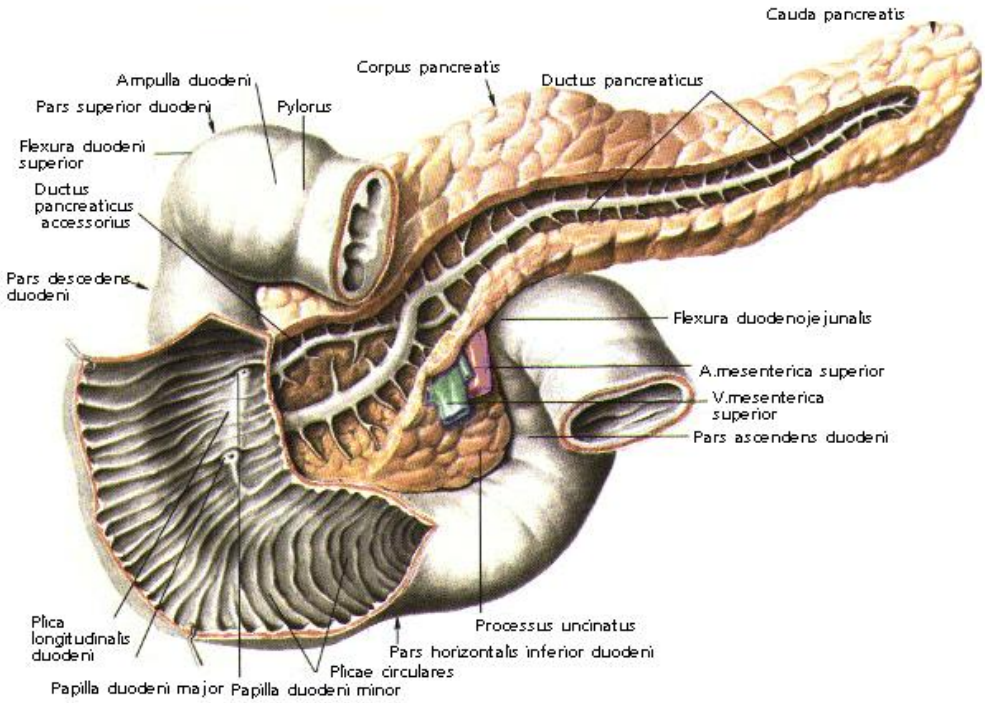


Fig. 3. Pancreatic duct system

In 10 % of patients, Wirsung and Santorini ducts fail to fuse. This results in the majority of the pancreas draining through the duct of Santorini and the lesser papilla, while the inferior portion of the pancreatic head and uncinate process drains through the duct of Wirsung and major papilla. This normal anatomic variant, which occurs in one out of 10 patients, is referred to as *pancreas divisum* (fig. 4).

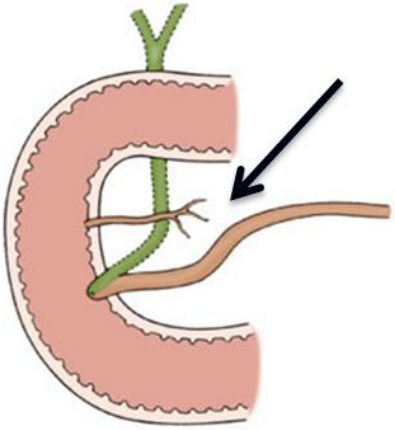


Fig. 4. Pancreas divisum (arrow)

The length of the common channel is variable. In about one third of patients, the bile duct and pancreatic duct remain distinct to the end of the papilla, two ducts merge at the end of the papilla in another one third, and in the remaining one third, a true common channel is present for a distance of several millimeters (fig. 5). The muscle fibers around the ampulla form the sphincter of Oddi, which controls the flow of pancreatic and biliary secretions into the duodenum. Contraction and relaxation of the sphincter are regulated by complex neural and hormonal factors.

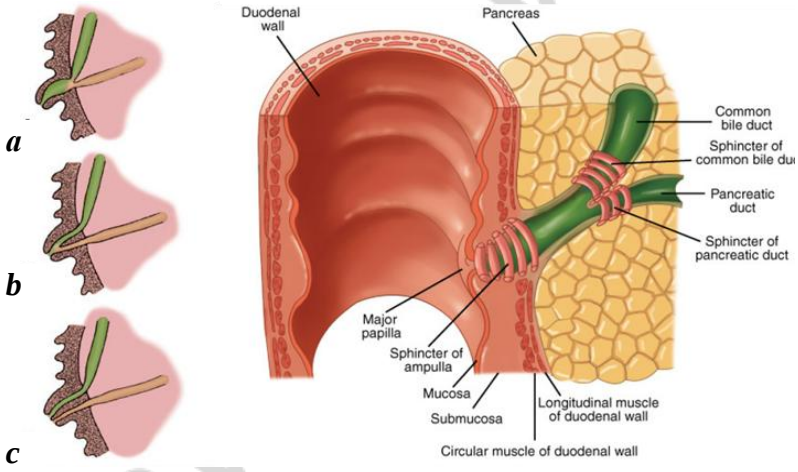


Fig. 5. **Left picture**: types of bile (green) and pancreatic (yellow) ducts junction: *a* — *Y-shape* distinct common channel — the hepatopancreatic ampulla (of Vater); *b* — *V-shape* — the common channel is almost nonexistent; *c* — *U-shape* — common bile and pancreatic ducts have separate openings at the tip of the papilla. **Right picture**: sphincter of Oddi structure

EXOCRINE PANCREAS

The pancreas secretes approximately 500 to 800 mL per day of colorless, odorless, alkaline, isosmotic pancreatic juice. Acinar pancreatic cells secrete amylase, proteases, and lipases, enzymes responsible for the digestion of all three food types: carbohydrates, proteins, and fats. Near the apex of each cell there are numerous enzyme-containing zymogen granules that fuse with the apical cell membrane (fig. 6).

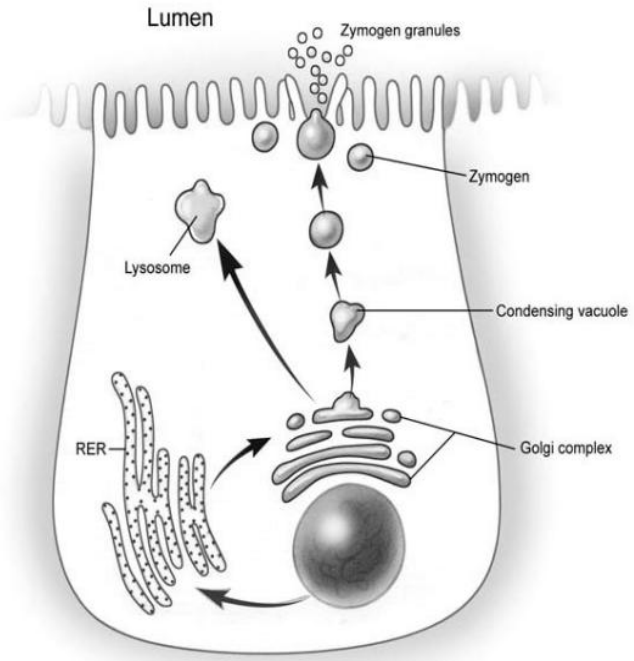


Fig. 6. Pancreatic acinar cell

Pancreatic *amylase* is secreted in its active form and completes the digestive process started by salivary amylase. Amylase hydrolyzes starch and glycogen to glucose, maltose, maltotriose and dextrins. The *proteolytic* enzymes are secreted as proenzymes that require activation. Trypsinogen is converted to its active form trypsin by another enzyme enterokinase, which is produced by the duodenal mucosal cells. Trypsin in turn activates the other proteolytic enzymes (fig. 7). Trypsinogen activation within the pancreas is prevented by the presence of inhibitors that are also secreted by the acinar cells. Pancreatic *lipase* hydrolyzes triglycerides to 2-monoglyceride and fatty acid. Pancreatic lipase is secreted in an active form. Colipase is also secreted by the pancreas and binds to lipase, changing its molecular configuration and increasing its activity. Phospholipase A2 is secreted by the pancreas as a proenzyme that becomes activated by trypsin. Phospholipase A2 hydrolyzes phospholipids and as with all lipases requires bile salts for its action.

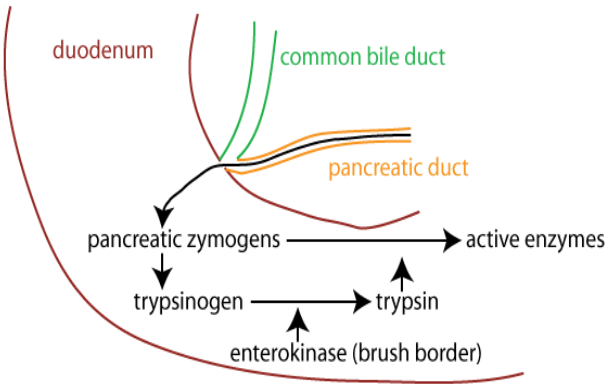


Fig. 7. Normal path of enzyme activation

ENDOCRINE PANCREAS

There are nearly 1 million islets of Langerhans in normal adult pancreas. They vary greatly in size from 40 to 900 mm. Larger islets are located closer to the major arterioles and smaller islets are embedded more deeply in the parenchyma of the pancreas. Most islets contain from 3000 to 4000 cells of five major types: alpha cells that secrete glucagon, β-cells that secrete insulin, delta cells that secrete somatostatin, epsilon cells that secrete ghrelin, and PP cells that secrete PP (tabl. 1).

Table 1

Pancreatic islet peptide products

Hormones	Islet cell	Functions
Insulin	β (beta cell)	Decreased gluconeogenesis, glycogenolysis, fatty acid breakdown, and ketogenesis Increased glycogenesis, protein synthesis, and glucose uptake
Glucagon	α (alpha cell)	Opposite effects of insulin; increased hepatic glycogenolysis and gluconeogenesis
Somatostatin	δ (delta cell)	Inhibits GI secretion Inhibits secretion and action of all GI endocrine peptides Inhibits cell growth
Pancreatic polypeptide	PP (PP cell)	Inhibits pancreatic exocrine secretion and section of insulin Facilitates hepatic effect of insulin
Amylin (IAPP)	β (beta cell)	Counterregulates insulin secretion and function
Pancreastatin	β (beta cell)	Decreases insulin and somatostatin release Increases glucagon release Decreases pancreatic exocrine secretion
Ghrelin	(epsilon cell)	Decreases insulin release and insulin action

ACUTE PANCREATITIS

DEFINITION AND INCIDENCE

Acute pancreatitis is an inflammatory disease of a complex etiology that is associated with intra-pancreatic enzymes activation and can result in the gland and regional tissue necrosis and development of systemic complications. It can be initiated by several factors, including gallstones, alcohol, trauma, and infections, and, in some cases, it is hereditary. Very often, patients with acute pancreatitis develop additional complications such as sepsis, shock, and respiratory and renal failure, resulting in considerable morbidity and mortality. The clinical outcome has improved over recent decades, even in the absence of specific treatment that target outcome determining pathophysiology, probably because of a more consistent approach to diagnosis, monitoring and management.

The *incidence* rate of acute pancreatitis per 100,000 inhabitants per year differs considerably. Remarkably, the incidence is high in all Scandinavian countries, Russia, Ukraine and Belarus. The increased incidence of acute pancreatitis is significantly correlated with alcohol consumption. In Germany the incidence rate of

acute pancreatitis is 19.7 per 100,000 inhabitants per year. This is more than three times higher than the same incidence for chronic pancreatitis. Acute pancreatitis is the most common gastrointestinal discharge diagnosis in the United States (274,119 patients in 2009), an incidence which has increased 30 % since 2000, and is associated with the highest aggregate inpatient costs more than 2 billion dollars per year. Worldwide the incidence of acute pancreatitis ranges from 5 to 80/100,000 population.

ETIOLOGY

Two main groups of factors are responsible for inducing acute pancreatitis:

– elevation of the pressure in the pancreatic duct system – pancreatic hypertension

– direct injury of the pancreas by toxins, drugs, trauma etc.

The etiology of acute pancreatitis is a complex subject because many different factors have been implicated in the causation of this disease, and sometimes there are no identifiable causes. Two factors, biliary tract stone disease and alcoholism, account for 70 to 90 % of the cases. The remaining 10 to 30 % is accounted for either by idiopathic disease or by a variety of miscellaneous causes including trauma, surgery, drugs, heredity, infection and toxins.

Etiology of acute pancreatitis:

1. Alcohol.
2. Biliary tract disease.
3. Hyperlipidemia.
4. Hereditary.
5. Hypercalcemia.
6. Trauma:
   - External;
   - Surgical;
   - Endoscopic retrograde cholangiopancreatography.
7. Ischemia:
   - Hypoperfusion;
   - Atheroembolic;
   - Vasculitis.
8. Pancreatic duct obstruction:
   - Neoplasms;
   - Pancreas divisum;
   - Ampullary and duodenal lesions.
9. Infections.
10. Venom.
11. Drugs.
12. Idiopathic.

Alcoholic Acute Pancreatitis. The disease commonly occurs in patients who have consumed alcohol for at least 2 years, and often much longer, up to 10 years. In a patient with an exposure history to ethanol and the total absence of other possible causative factors, a first attack of pancreatitis is considered alcohol-related acute pancreatitis.

Ethanol can induce pancreatitis by several ways. The «secretion with blockage» mechanism is possible because ethanol causes *spasm of the sphincter of Oddi*, and, more important, ethanol is a *metabolic toxin* to pancreatic acinar cells, where it can interfere with enzyme synthesis and secretion. The initial effect of ethanol is *a brief secretory increase followed by inhibition*. This can lead to elevation of enzyme proteins that can *precipitate within the pancreatic duct*. Calcium then can precipitate within this protein matrix, causing multiple ductal obstructions, while continued secretion can cause pressure build-up. Ethanol also increases ductal permeability, making it possible for improperly activated enzymes to leak out of the pancreatic duct into the surrounding tissue. Ethanol also transiently *decreases pancreatic blood flow*, possibly causing focal ischemic injury to the gland.

Gallstone (biliary) Pancreatitis. Between 3 and 8 % of patients with symptomatic gallstones develop acute pancreatitis, representing an increase in relative risk of developing pancreatitis for patients with gallstones of up to 35 times that of the general population. It is now widely accepted that gallstone-associated pancreatitis results from the passage of stones through the sphincter of Oddi into the duodenum. There are essentially three hypotheses how gallstones induce acute pancreatitis: common channel, duodenal reflux, and ductal hypertension.

Common Channel Hypothesis. Opie in 1901 suggested theory, in which a blockage by gallstone below the junction of the biliary and pancreatic ducts would cause bile to flow into the pancreas (fig. 8), which could then be damaged by the detergent action of bile salts. That reflux of bile into the pancreatic duct may be the precipitating cause of acute pancreatitis.

Important ***objections*** to this theory include the anatomic reality that the majority of individuals have such a short common channel, that a stone located there would block both the pancreatic and biliary ducts, effectively isolating the two systems. Furthermore, hydrostatic pressure in the biliary tract is lower than in the pancreas, a condition that would favor abnormal flow of pancreatic juice into the bile duct rather than in the opposite direction. These reservations are bolstered by the observation that, in experimental animals, the flow of normal bile through an unobstructed pancreatic duct does not result in acute pancreatitis. However, even in the absence of a significant anatomical common channel, it is possible that passage of a stone may cause a functional common channel in some patients by causing a stenosis of the ampulla of Vater (fig. 9).

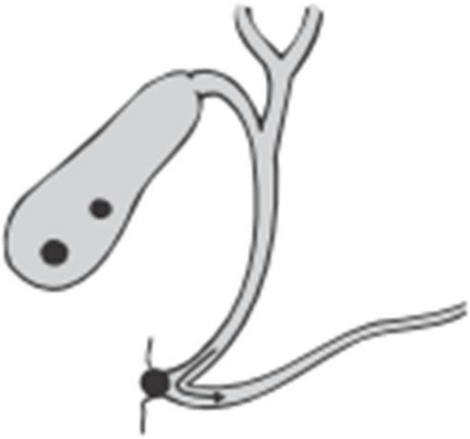


Fig. 8. Reflux of bile into the pancreatic duct (Common channel hypothesis)

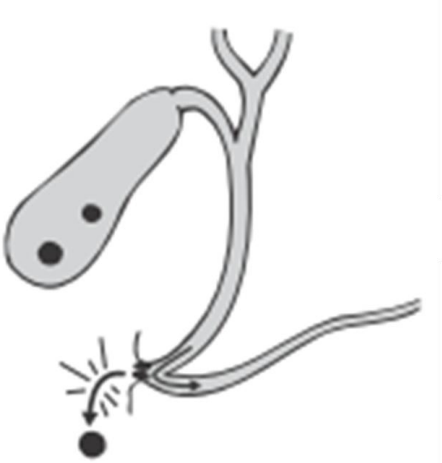


Fig. 9. Stenosis of the ampulla of Vater after the passage of a stone

Duodenal Reflux Hypothesis. A second potential mechanism of pancreatitis induced by the passage of gallstones invokes the reflux of duodenal content containing activated digestive enzymes into the pancreatic ductal system (fig. 10).

Passage of a gallstone may allow reflux of duodenal contents either directly at the time of passing or later by damaging the sphincter mechanism. However, it is questionable whether the transit time through the sphincter of Oddi is long enough to cause sufficient incompetence.

Ductal Hypertension Hypothesis. Obstruction of the main pancreatic duct alone is sufficient to induce pancreatitis (fig. 11). However, the mechanism by which increased ductal pressure leads to pancreatitis is not clear. It has been generally assumed that it acts either by causing rupture of small pancreatic ductules and extravasation of secretions into the interstitium of the gland with subsequent activation of enzymes, or by prevention of discharge of secretions from the acinar cells into the ductal space.

Fig. 10. Duodenal reflux after the passage of a stone

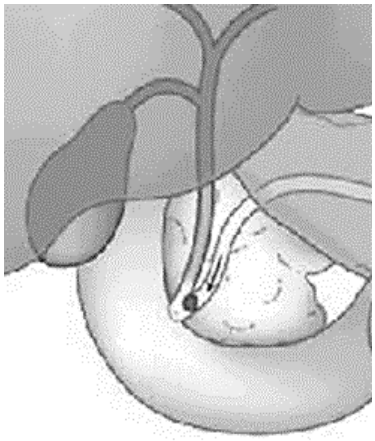


Fig. 11. Obstruction of the main pancreatic duct by a stone

Iatrogenic. Acute pancreatitis can result from a number of treatments, including pancreatic biopsy, exploration of the extrahepatic biliary tree and ampulla of Vater, distal gastrectomy, splenectomy, colectomy, nephrectomy, aortic aneurysmorraphy, and retroperitoneal lymphadenectomy. As the pancreas is susceptible to ischemia it can also occur secondary to splanchnic hypoperfusion with cardio-pulmonary bypass or cardiac transplant. Most commonly, acute pancreatitis occurs as a complication of ERCP in 5 % to 10 % of procedures.

Hereditary Pancreatitis. Hereditary pancreatitis is an autosomal dominant disorder usually related to mutations of the cationic trypsinogen gene (PRSS1). Mutations in this gene cause premature activation of trypsinogen to trypsin and cause abnormalities of ductal secretion, both processes promote acute pancreatitis.

Tumors. A pancreatic or periampullary tumor should be considered in any patient with idiopathic acute pancreatitis. Approximately 1 % to 2 % of patients with acute pancreatitis have a pancreatic tumor, and an episode of acute pancreatitis can be the first clinical manifestation of the tumor.

Hyperlipidemia. Patients with types I and V hyperlipoproteinemia can experience episodes of abdominal pain that often occurs in association with marked hypertriglyceridaemia. Lipase is thought to liberate toxic fatty acids into the pancreatic microcirculation, leading to microcirculatory impairment and ischemia.

Drugs and Miscellaneous Causes. Many *drugs* can produce hyperamylasemia and/or abdominal pain, and drug is considered to be the cause if the pancreatitis-like illness resolves with its discontinuation. Certain drugs are known to be capable of causing acute pancreatitis (thiazide diuretics, furosemide, estrogens, azathioprine, l-asparaginase, 6-mercaptopurine, methyldopa, the sulfonamides, tetracycline, pentamidine, procainamide, nitrofurantoin, dideoxyinosine, valproic acid, and acetylcholinesterase inhibitors). In addition, lipid-based intravenous drugs and solutions, such as propofol, can also cause acute pancreatitis.

Hypercalcemic states arising from hyperparathyroidism can result in both acute and chronic pancreatitis; the mechanism most likely involves hypersecretion and the formation of calcified stones intraductally. Infestations are also implicated by *Ascaris lumbricoides* and the liver fluke *Clonorchis sinensis*, which is endemic to China, Japan, and Southeast Asia. Other implicated factors include *azotemia, vasculitis*, and the *sting of the Trinidadian scorpion* by massive production of pancreatic juice. Poisoning with antiacetylcholinesterase insecticides has a similar effect. Finally, no apparent cause can be ascribed to some episodes of acute pancreatitis, and these constitute the group referred to as idiopathic pancreatitis. Some of these patients are eventually found to have gallstone-related pancreatitis, which calls for caution in labeling any episode «idiopathic».

PATHOPHYSIOLOGY

In 1896, Chiari advanced the understanding of acute pancreatitis by proposing the concept that pancreatitis is essentially premature, *intrapancreatic activation of digestive enzymes*, resulting in auto-digestion of the organ with the key role of *intracellular trypsin activation*. The mechanisms by which injurious stimuli

lead to intra-acinar activation of trypsinogen and autodigestion of the gland have been the focus of research in pancreatitis for decades.

Normally, because the exocrine pancreas produces enzymes that are potentially injurious to it, several protective mechanisms have evolved to prevent autodigestion under normal conditions:

1. Enzymes are synthesized as inactive precursors called proenzymes or *zymogens*, which are then transported and secreted outside the gland. Their activation occurs safely in the duodenum. This separates the site of production of these enzymes from the site of activation and thus the pancreas is insulated against enzymatic attack. Within the acinar cell itself, the potentially harmful digestive enzymes are segregated from the surrounding cytoplasm by being enclosed within membrane-bound organelles referred to as zymogen granules.

2. Another layer of protection is provided by the synthesis of trypsin inhibitors, which are transported and stored along with the digestive enzyme zymogens. In the presence of injurious stimuli, the zymogens responsible for initiating the disease are not secreted outside, but are observed to *co-localize* with cytoplasmic vacuoles that contain lysosomal enzymes such as cathepsin B. Lysosomal hydrolase cathepsin B activates trypsinogen to trypsin within the co-localization vacuoles (fig. 12). How activation of trypsin in the co-localization vacuoles leads to pancreatic damage is not clear yet.

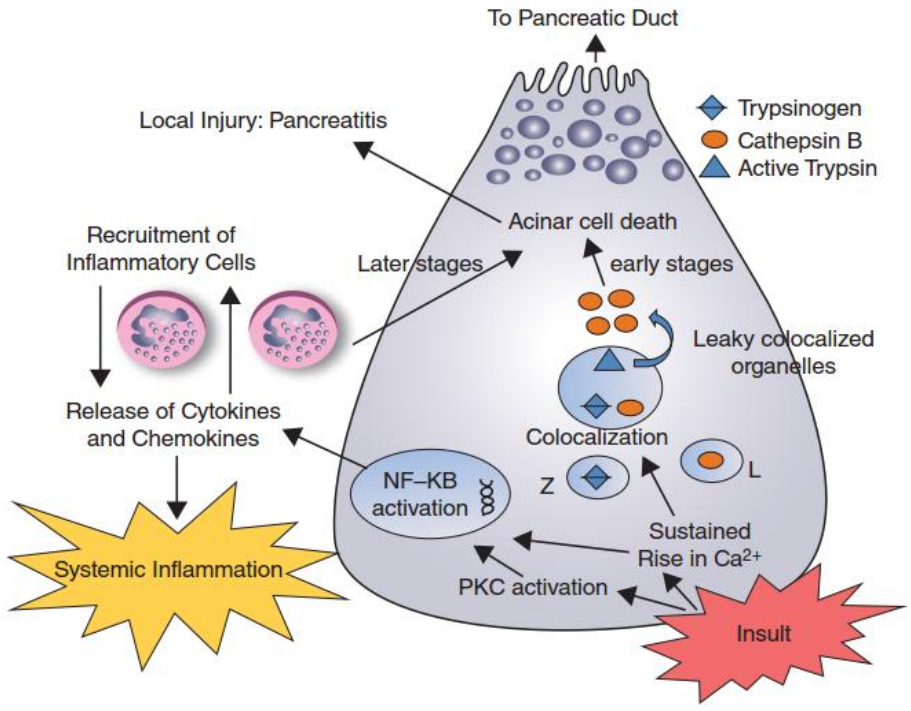


Fig. 12. Schematic representation of the acinar cell events in acute pancreatitis. When acinar cells are pathologically stimulated, their lysosomal (L) and zymogen (Z) contents *colocalize*, consequently *trypsinogen is activated to trypsin* by cathepsin B. Once trypsin has permeabilized the contents of the cytosol, cathepsin B and other contents of these colocalized *organelles are released*. Once in the cytosol, cathepsin B activates *apoptosis* which in turn triggers the release of cytokines that attract inflammatory response cells which mediate local and systemic inflamemation cascades

In majority of cases (85–90 %) intrapancreatic enzymes activation leads to mild pancreatic enlargement and edema only — **interstitial pancreatitis**, that usually resolves during 1–2 weeks. In 10–15 % of cases more severe damage of the pancreas occurs, leading to a pancreatic tissue necrosis — **necrotizing pancreatitis.**

The presence of activated enzymes in the interstitial tissue causes tissue damage and inflammation, resulting in infiltration with activated neutrophils and macrophages and generation of cytokines. The inflammation may spread to peritoneal cavity, lesser sac, peripancreatic tissues and organs, leading to their edema, swelling and necrosis (fig. 13).

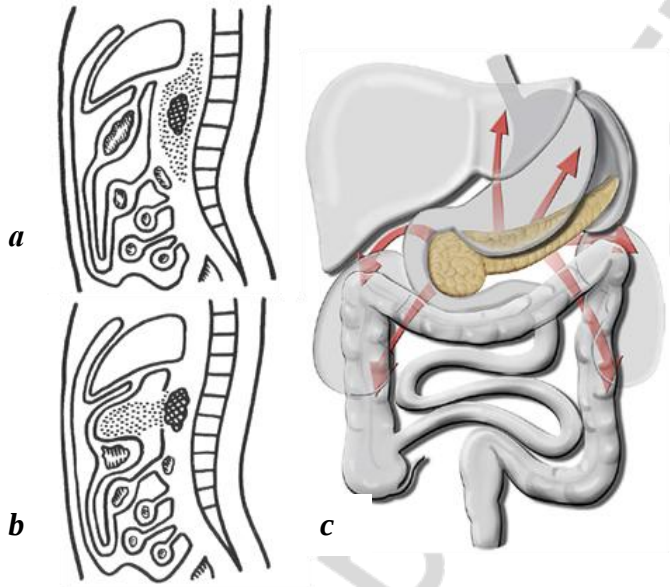


Fig. 13. Pathways of inflammation spreading:
a — peripancreatic; *b* — to lesser sac; *c* — to retroperitoneal spaces

Released inflammatory cytokines include TNF-alpha, interleukin-1 beta (IL-1 beta), IL-6, IL-8, and intercellular adhesion molecule-1 (ICAM-1). These cytokines, active digestive enzymes and necrotic products **get to the systemic blood flow**, causing damage of all over the organism, affecting heart, lungs, liver, intestine, brain etc. and causing various *systemic complications*.

In the late phase (after 2–3 week) of necrotizing pancreatitis in 40–70 % of cases necrosis becomes **infected**. Contamination causes purulent inflammation and greatly increases intoxication that may cause pancreatogenic sepsis and considerably deteriorates the prognosis of the disease.

CLASSIFICATION

The original Atlanta Classification of acute pancreatitis was derived over 20 years ago — in 1992. The last revision was made in 2012 by global, web-based «virtual» consensus conference over the Internet.

According to the classification, acute pancreatitis is divided into:

− **acute interstitial edematous pancreatitis** — 85–90 %. It includes diffuse enlargement of the pancreas due to inflammatory edema, probability of some

fluid collections near the pancreas and some inflammatory changes of peripancreatic fat. Clinical symptoms usually resolve within the first week and mortality rate is low < 3 %.

– **acute necrotizing pancreatitis** — 10–15 %. It is characterized by necrosis of the pancreatic parenchyma and peripancreatic tissues from small local lesion to total pancreatic and peripancreatic necrosis and usually has severe clinical course with local and systemic complications and mortality around 30 %.

When contamination of the necrosis occurs pancreatitis becomes **infected**. It usually happens after second or third week of the disease in about 40–70 % of patients with necrotizing pancreatitis. Infected necrosis is characterized by high morbidity and mortality (nearly 50 %). The presence of infection can be confirmed by CT/Ultrasound (gas bubbles, fig. 14) or by percutaneous, image-guided, fine-needle aspiration (FNA).

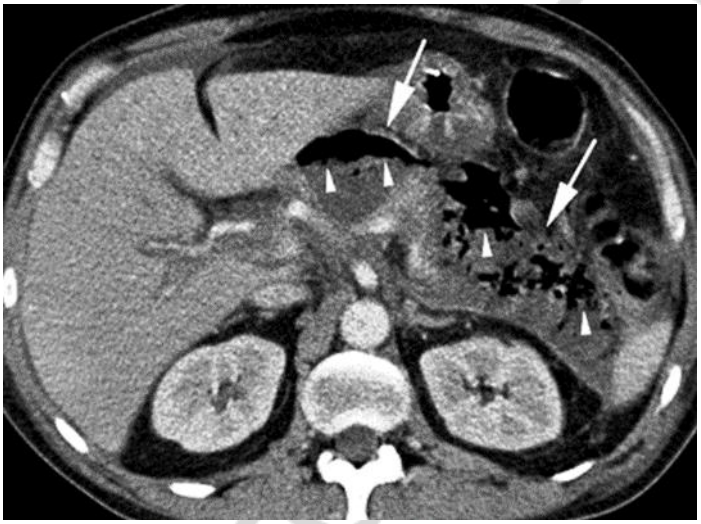


Fig. 14. Presence of gas bubbles in necrotic tissues (arrows)

Complications of acute pancreatitis may be local and systemic.

Local Complications:

– **acute peripancreatic fluid collection** (fig. 15) — is the collection of fluid in peripancreatic tissues that contains pancreatic enzymes, hemolysed blood and necrotic debris and is localized in the retroperitoneal space or in the abdominal cavity (peritonitis, pancreatic ascites). It has *no definable wall* and may develop from the first day of acute interstitial or necrotizing pancreatitis.

– when pancreatic fluid collection persists more than 4 weeks it develops well-defined wall and becomes **pancreatic pseudocyst** (fig. 16).

– **acute necrotic collection** (fig. 17) — is the collection of mostly solid components (necrosis) in the pancreas and peripancreatic tissues. It develops in case of necrotizing pancreatitis (not interstitial!), has no encapsulating wall and may be sterile or infected (pancreatic phlegmon or abscess).

– necrotic collection that persists more than 4 weeks usually becomes encapsulated by a well-defined inflammatory wall — **Walled-off necrosis** (fig. 18). It also may be sterile or infected (pancreatic phlegmon or abscess).

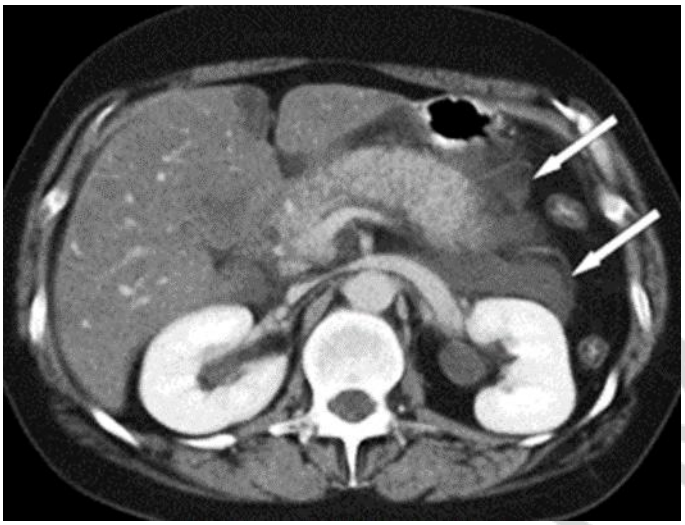


Fig. 15. Collection of fluid in peripancreatic tissues (arrows)

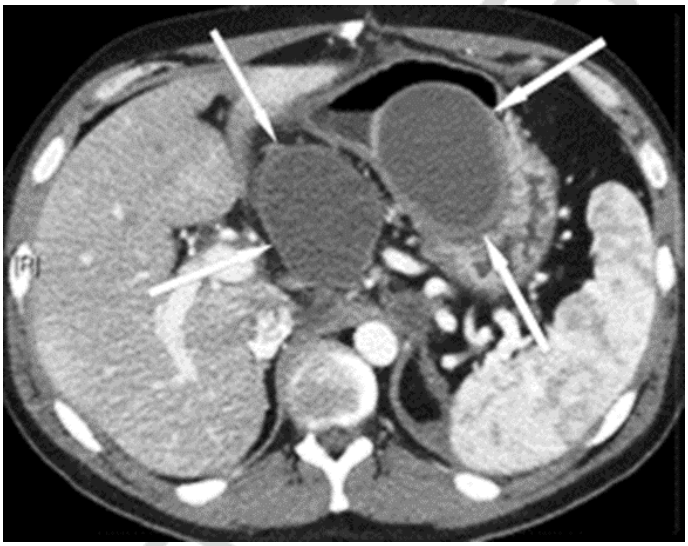


Fig. 16. Pancreatic pseudocysts: fluid collections with no solid component and well defined walls (arrows)

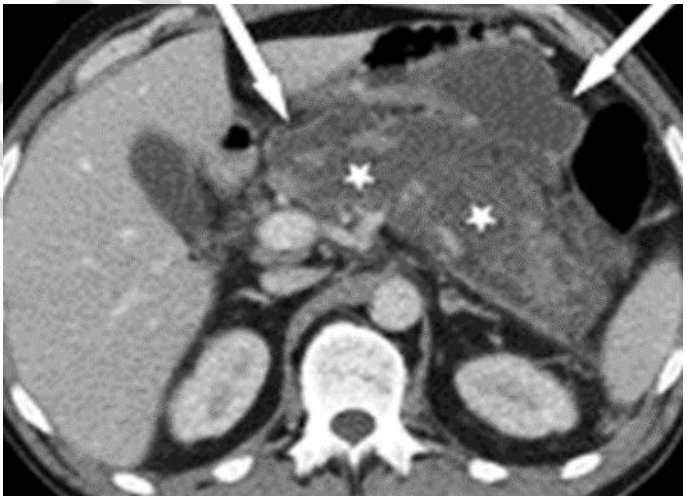


Fig. 17. Collection of necrotic tissues in peripancreatic tissues (arrows)

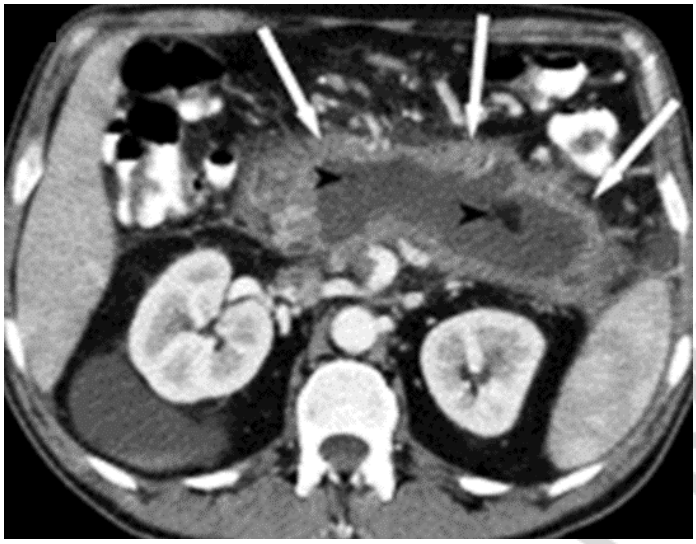


Fig. 18. Necrotic collection with thick encapsulating wall (arrows)

Systemic Complications. An important aspect of acute pancreatitis pathophysiology is the mechanism due to which processes occurring in the pancreas induce systemic inflammation and multiorgan failure. Although intra-acinar processes initiate acute pancreatitis, processes that follow acinar cell injury determine the severity of pancreatitis. Once recruited to the pancreas, various inflammatory cells lead to further acinar cell injury and cause an elevation of various *pro-inflammatory mediators* such as TNF-α; IL-1, IL-2, IL-6, and other chemokines and anti-inflammatory factors. Organ failure can develop at any stage of acute pancreatitis associated with an overwhelming proinflammatory response early or later secondary to the development of infected local complications. This may be associated with the systemic inflammatory response syndrome (SIRS) and multiorgan dysfunction syndrome/failure (MODS/F).

SIRS (systemic inflammatory response syndrome), 2 and > criteria:

- HEART RATE > 90 beats/min
- CORE TEMPERATURE < 36 °C or > 38 °C
- WHITE BLOOD COUNT < 4000 or > 12000/mm^3
- RESPIRATIONS > 20/min or PCO_2 < 32 mm Hg

Organ failure is scored by using the Marshall or Sequential Organ Failure Assessment (SOFA) systems (tabl. 2). Three organ systems are most frequently involved: cardiovascular, respiratory, and renal. Multiple organ failure is defined as two or more organs registering 2 or more points on these scoring systems. Monitoring organ failure over time and in response to treatment is important in clinical care of the disease. A score of 2 or more in any *two* systems indicates the presence of **multiple** organ failure. **Transient** organ failure resolves within 48 h, **persistent** organ failure lasts more than 48 h.

Table 2

Marshall's scoring system, 2 and > scores indicate organ failure

System	0	1	2	3	4
RESPIRATORY (PaO_2/FiO_2)	> 400	301–400	201–300	101–200	≤ 101
RENAL (serum creatinine, μmol/l)	≤ 134	134–169	170–310	311–439	> 439
CARDIOVASCULAR (systolic blood pressure, mmHg)	> 90	< 90 Response to re-suscitation	< 90	< 90 pH < 7.3	< 90 pH < 7.2
Central nervous system Glasgow coma score	15	13–14	10–12	6–9	< 6
Liver Bilirubin (μmol/L)	< 20	20–32	33–101	102–204	> 204
Coagulation Platelets (xl01 per μL)	> 150	≤ 150	≤ 100	≤ 50	≤ 20

Rare Complications. Several other complications are possible.

Gastrointestinal Complications:

1. Upper GI bleeding. Bleeding may complicate the development of erosions or peptic ulcer or represent rupture of the pseudoaneurysm due to pseudocysts into the upper GI tract. It may also indicate bleeding from gastric varices due to splenic vein thrombosis, although this is rare in acute pancreatitis.

2. Bowel necrosis. Bowel necrosis leading to perforation, fistula formation or stricture is a well-known complication. The transverse colon is at the most risk.

3. Bowel obstruction. Bowel obstruction may occur due to compression from pseudocysts, adhesion formation or development of stricture.

Hepatobiliary Complications. A mild picture of hepatocellular dysfunction or obstructive jaundice may occur. Acalculous cholecystitis occurs infrequently, usually at the time oral feeding is started. Although extremely rare, portal vein or hepatic artery thrombosis may occur, causing severe hepatobiliary and systemic dysfunction.

Vascular Complications. Several vascular complications may develop in acute pancreatitis:

1. Massive hemorrhage during acute attack. This uncommon complication represents necrosis and vascular wall digestion by pancreatic enzymes during the early course of severe acute pancreatitis. Bleeding occurres from the gastroduodenal, pancreaticoduodenal, or other pancreatic vessels. Still other vessels that may be involved include hepatic, gastric or even splenic arteries.

2. Pseudoaneurysm formation. This complication can develop either as a result of partial damage to the wall of an artery or secondary to the erosion of a pseudocyst into an adjacent vessel. The latter is more serious because hemorrhage invariably follows. When a pseudocyst erodes into a vessel, it suddenly enlarges, becomes pulsatile, and causes increased pain. This erosion essentially is the formation of a thin-walled pseudoaneurysm, it causes bleeding in one of three ways:

free bleeding into the abdominal cavity (1); erosion into adjacent viscus leading to gastrointestinal hemorrhage (2); or, rarely, bleeding back into the pancreatic duct in the presence of significant communication between the pseudocyst and the main pancreatic duct (3). In the latter case bleeding occurs into the duodenum through the ampulla of Vater, a condition known as hemosuccus pancreaticus.

3. Left-sided portal hypertension and gastric varices. Splenic vein thrombosis sometimes complicates the course of acute pancreatitis. This condition leads to venous hypertension in the area drained by the splenic vein and, therefore, results in splenomegaly and gastric varices. Gastric varices may bleed, leading to upper gastrointestinal hemorrhage.

4. Portal vein thrombosis. An uncommon complication, portal vein thrombosis may contribute to ascites, sometimes in acute pancreatitis.

ASSESSMENT OF SEVERITY AND PROGNOSIS

Accurately predicting acute pancreatitis severity is important in making decisions about whether a patient should be transferred to a tertiary hospital, or admitted to an intensive care unit, and in making decisions about fluid therapy, whether an ERCP is indicated, and other issues. There is a long history of attempts to find prognostic or predictive markers that accurately stratify the risk, with the most widely used being the Ranson's criteria or modified Glasgow criteria (tabl. 3). Both clinical and biochemical parameters are scored over the first 48 hours of admission. When there are 3 or more positive criteria, the disease is considered «predicted severe».

Table 3

Prognostic score systems

RANSON (1974)	IMRIE-GLASGOW (1984)
On admission	
Age > 55	Age > 55
WBC > $16x10^9$/L	WBC > $15x10^9$/L
Blood glucose > 10 mμ/L	Blood glucose > 10 mμ/L
Serum LDH > 350 IU/L	Serum urea > 16 mμ/L
Serum AST > 250 U/L	PaO_2 < 8 kPa (60 mmHg)
During the initial 48 h	
Hematocrit fall > 10 points	Serum calcium < 2 mμ/L
BUN elevation > 5 mg/L	Serum albumin < 32 g/L
Serum calcium < 2 mμ/L	Serum LDH > 600 IU/L
Base deficit > 4 mEq/L	AST/ALT > 600 U/L
PaO_2 < 8 kPa (60 mmHg)	
Fluid sequestration > 6 L	

There are many other approaches to prediction of the severity. In 24 hours after admission an APACHE II score of 8 or more or a serum C-reactive protein level of > 150mg/dl has a similar accuracy in predicting severity as Ranson's criteria. More recently proposed Bedside Index for Severity of Acute Pancreatitis (BISAP) is calculated from blood urea nitrogen (> 25 mg/dl), impaired mental status (GCS < 15), presence of systemic inflammatory response syndrome (SIRS), age > 60 years and pleural effusion.

CLINICAL PRESENTATION

The onset of the disease is usually acute and is related to fatty, spicy, fried meal intake or alcohol consumption.

Pain is the cardinal symptom of acute pancreatitis. It is dull, boring and steady with intensity ranging from mild to severe and pain shock. It's usually located in the upper abdomen and in approximately one half of cases radiates to the back or is encircling (fig. 19). Some patients may adopt certain postures to alleviate the pain. Bending forwards, or much more commonly, the patient draws up the knees to ease the abdominal discomfort.

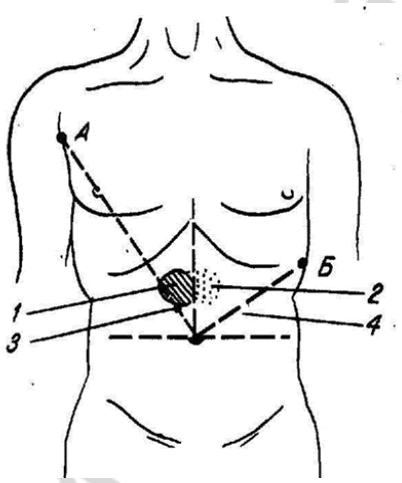


Fig. 19. Location of pain zones in AP

Other common symptoms include nausea (80–90 %), repeated vomiting without relief (40-60 %) and abdominal distension due to the intestinal paresis. The physical findings vary with the severity of the disease but fever, tachycardia, epigastric tenderness and muscle guarding are frequent with some specific signs.

Specific clinical signs of acute pancreatitis:

Körte's sign — painful resistance of anterior abdominal wall in the upper abdomen where the pancreas is located (60–80 %)

Voskresenskiy's sign — impossibility to identify the abdominal aorta pulsation due to pancreatic edema, gastric and colonic paresis (60–80 %)

Mayo-Robson's sign — pain while pressing at the left costovertebral angle (40–50 %)

Kamenchik's sign — pain with pressure under the xiphoid process

In severe cases tachypnoea and dyspnoea may be observed, as well as hypotension. Mild jaundice is frequently present due to abdominal distension caused by paralytic ileus. In severe cases, renal failure or progressive ventilatory difficulty are present and lead to acute respiratory distress syndrome (ARDS). Abdominal tenderness and ileus become more marked. A palpable epigastric mass may be felt several days after the onset of the disease (indicating the development of a pancreatic fluid collections, pseudocyst or marked peripancreatic necrosis). Rarely in severe case of the disease, a bluish discoloration of the skin around the umbilicus (*Cullen's sign*) or in the loins (*Grey Turner's sign*, fig. 20) may be encountered.

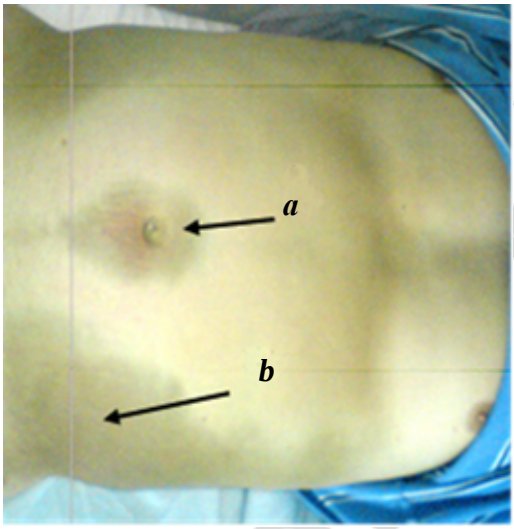


Fig. 20. Skin signs of acute pancreatitis:
a — Cullen's sign; *b* — Turney's sign

There may be other skin signs as manifestation of blood circulation and coagulation disturbances in severe acute pancreatitis:

- *Mondor's sign* (purple spots on the face and body);
- *Lagerlof's sign* (cyanotic color of the face and extremities);
- *Halsted's sign* (cyanotic and mottle abdominal skin);
- *Grünwald sign* (appearance of ecchymosis, large bruises around the umbilicus and on the buttocks).

DIAGNOSTICS

In addition to **characteristic clinical picture**, the diagnosis is confirmed by marked elevation of ***serum amylase*** to a value exceeding **three times normal**. Although hyperamylasaemia can be encountered in other acute disorders, e.g. infarcted small bowel, the levels are much lower. However, amylase levels in the blood decline within a few days of onset and thus may be *normal*. Persistence of hyperamylasaemia indicates the development of local complications such as pseudocyst formation or pancreatic fluid collection. Other biochemical abnormalities that may be present in severe disease include hyperglycaemia and hypocalcaemia.

A ***plain radiograph*** of the abdomen and chest may show intestinal distension in the region of the pancreas (fig. 21, sentinel jejunal loop, colon cut-off, duodenal ileus) or a generalized paralytic ileus. Haziness in the supine plate of the abdomen is caused by retroperitoneal fluid accumulation and may be associated with obliteration of the psoas shadow. The chest x-ray may show basal atelectasis, subdiaphragmatic fluid collection, or pleural effusions.

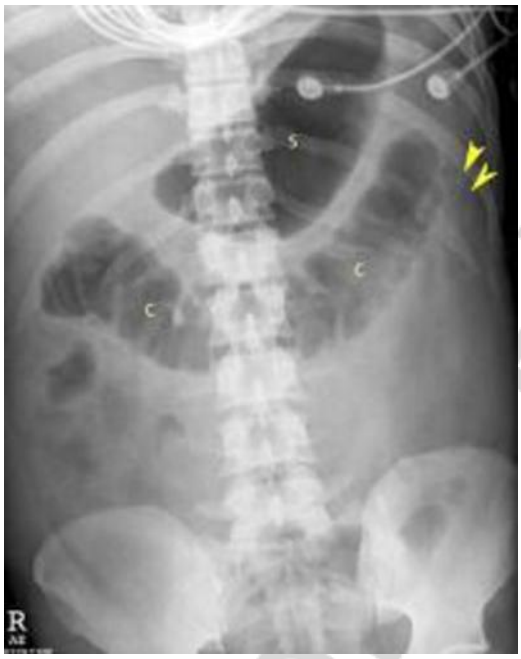


Fig. 21. Gastric and colonic distention (Gobiet's sign)

Ultrasonography may reveal a diffusely enlarged, hypoechoic pancreas and some complications (fig. 22). However, overlying bowel gas (particularly prominent with ileus) limits visualization of the pancreas in a large percentage of cases. Although ultrasonography has poor sensitivity in the diagnosis of acute pancreatitis, it plays an important role in identification of pancreatitis etiology (e. g., the detection of gallstones).

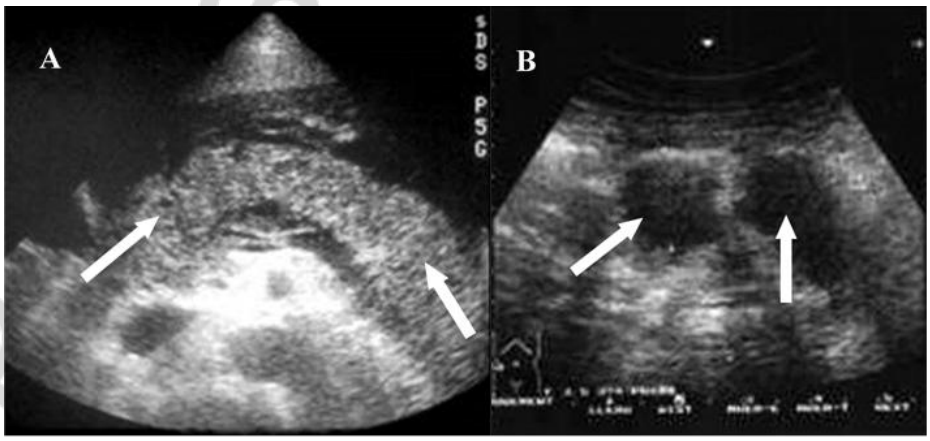


Fig. 22. Ultrasound in acute pancreatitis:

a — enlargement and edema of pancreas (arrows);*b* — acute pancreatic fluid collections (arrows)

Computed tomography (CT) scanning is the most important imaging test in the evaluation of acute pancreatitis. CT findings of mild acute pancreatitis include pancreatic enlargement and edema, effacement of normal lobulated contour of the pancreas, and stranding of peripancreatic fat. In addition, dynamic CT scanning performed after the bolus administration of intravenous contrast can demonstrate regions of pancreas that have poor or no perfusion, as in case of pancreatic necrosis. Detection on CT of necrosis and its size, gland enlargement and complications play an important role in assessment of disease severity (tabl. 4).

Table 4

Balthazar CT severity index (1985)

1	2	3	4	6
gland enlargement	peripancreatic inflammatory changes	single fluid collection	multiple collections or infected collection	
	<30% gland necrosis		30–50 % gland necrosis	> 50 % gland necrosis
Assessment: Score 0–3: mild acute pancreatitis Score 4–6: moderate acute pancreatitis Score 7–10: severe acute pancreatitis				

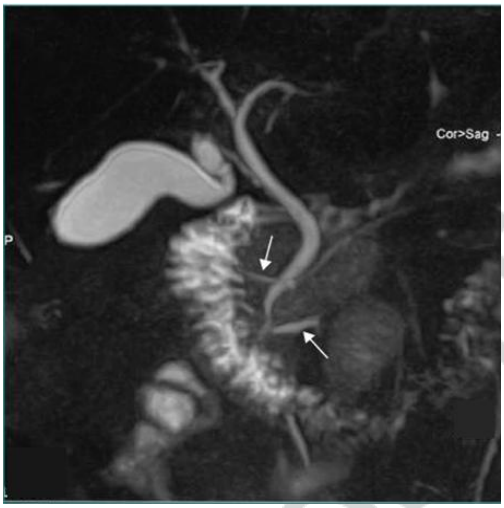


Fig. 23. Magnetic resonance cholangiopancreatography. Common bile and main pancreatic ducts (arrows)

Magnetic resonance imaging (MRI) and ***magnetic resonance cholangiopancreatography*** (MRCP, fig. 23) are being used with increasing frequency in patients with acute pancreatitis. These examinations have the potential to offer better definition of pancreatic and biliary ductal abnormalities than CT scanning, and they are applicable in patients for whom ionizing radiation or iodinated intravenous contrast agents used in CT scanning are contraindicated. Disadvantages of MRI include high cost, limited availability and long duration of examinations.

THERAPY

Nowadays, the main treatment modality is **maximum conservative treatment** with the use of minimally invasive methods. Early surgical aggressive treatment horrendously increases morbidity and mortality and does not prevent the development of intra-abdominal infection and other complications. Treatment method choice depends on:

- Severity (mild, moderately mild, severe)
- Phase (early, late)
- AP etiology (alcoholic, biliary etc.)
- Morphology (interstitial, necrotizing).

Pain Management. Pain is the cardinal symptom of acute pancreatitis and its relief is a clinical priority. Because of unpredictable absorption analgesia should be administered intravenously, at least at the outset and before oral intake has been established. Those with mild pain can usually be managed with a non-steroidal anti-inflammatory drug while those with more severe pain are best managed with opioid analgesia. Good results may be achieved by continuous epidural anesthesia.

Fluid Resuscitation. Fluid therapy to restore and maintain circulating blood volume is the most important intervention in the early management of acute pancreatitis. It is best to resuscitate with a balanced crystalloid and to restore normal blood volume, blood pressure, and urine output. Patients with severe acute pancreatitis, as well as those for whom initial resuscitation fails, are best managed in a dedicated intensive care unit (ICU). Central venous monitoring may facilitate fluid management. Patients should be closely monitored for development of distant organ failure, particularly respiratory, cardiovascular, and renal failure, so that supportive management of these conditions (positive-pressure ventilation, administration of vasopressor agents, and hemodialysis, respectively) can be administered without delay.

Nutritional Support. Enteral nutrition should be commenced after initial fluid resuscitation and within the first 24 hours of admission. It can be introduced through a nasogastric tube and increased step-wise over 2 to 3 days. The tube can be advanced to the jejunum by endoscopy or fluoroscopy. A delay in commencing enteral nutrition may contribute to the development of intestinal ileus and feeding intolerance. In predicted mild acute pancreatitis the transition from oral fluids to food is usually timed to when the patient's abdominal pain has resolved, but the trend is toward allowing patients to resume intake ad libidum (i.e., patient controlled nutrition). Histamine H2-blockers or proton pump inhibitors should usually be administered.

Antibiotics. Although the use of broad-spectrum antibiotics to treat established infection in acute pancreatitis is a well-established practice, there have been considerable disagreements over the use of prophylactic antibiotics. The overuse of antibiotics has been associated with a documented rise in fungal infections and resistant organisms. Overall, it appears that the most recent and generally better designed studies do not support the use of prophylactic antibiotics to reduce the frequency of pancreatic infectious complications, surgical intervention, and death.

Clinical trials of agents that inhibit activated pancreatic enzymes, inhibit pancreatic secretion, or interrupt the inflammatory cascade have yielded disappointing results. Meta-analyses of clinical trials of proteinase inhibitors (gabexate mesylate, contrical and other), somatostatin, and octreotide suggest these agents

have *limited, if any, efficacy* in improving outcomes in acute pancreatitis. Other adjuncts for which clinical trials have *failed to demonstrate efficacy* in limiting pancreatic injury in patients with acute pancreatitis include glucagon, anticholinergics, fresh frozen plasma, and peritoneal lavage.

Main principles of conservative treatment in acute pancreatitis are shown in tabl. 5.

Table 5

Conservative treatment of acute pancreatitis

TREATMENT OF MILD PANCREATITIS (basic therapy)	**TREATMENT OF SEVERE PANCREATITIS (in addition to the basic therapy)**
Pain control (NSAID)	Treatment in Intensive Care Unit
Antispasmodics	Central venous and urinary catheter
Fluid balance and replacement	Massive fluid and electrolytes replacement
Histamine H2-blockers or proton pump inhibitors	Intravenous wide spectrum antibiotics (imipinem) *
Resting the pancreas (regimen of «nil-per-mouth»)	Early enteral feeding via a transduodenal tube
	Decreasing pancreatic secretion (atropine, somatostatine analogues) *
	Protease-inhibiting drugs (aprotinin, gabexate mesylate, camostate, phospholipase A2 * ****inhibitors)
	Hemo-filtration (plasmapheresis, hemosorption) **
	Continuous arterial infusion of medicines through SMA or celiac trunk *

* the use is under question
** in case of renal failure usually

Fig. 24. Extraction of a stone in common bile duct during ERCP

Therapeutic Endoscopic Retrograde Cholangiopancreatography (ERCP)

The benefits of this invasive modality is the release of the presumed impacted stone, but there is the risks it includes the increase of pancreatitis severity, bleeding, cholangitis, and duodenal perforation. Early ERCP with a stone extraction (fig. 24) has usually benefited in the present of concomitant cholangitis due to the common duct stone (rare situation).

Managing Local Complications. The decisions regarding how and when to intervene are often difficult. This means close monitoring of the patient by serial examination, supplemented by regular measurement of inflammatory markers (e. g., C reactive protein) and a pancreatic protocol CT scan if a local complication is suspected and intervention considered warranted. Indications to surgical *debridement (necrosectomy)* :

– extensive (> 50 %) necrosis with irreversible clinical deterioration despite maximum supportive care for at least 2 weeks from the onset of symptoms;

– presence or suspicion of infected pancreatic necrosis.

Intervention should be delayed in order to allow demarcation of necrosis, and to reduce the risk of bleeding, disseminated infection and collateral damage to adjacent organs. Its appreciation has resulted in a notable trend toward delayed intervention, which is uncommon before *3 to 4 weeks* from the onset of the symptoms. An important emerging approach is the increasing use of *percutaneous catheter drainage* (fig. 25) in patients with suspected infectious complications. Preemptive drainage (under CT or ultrasound guidance) with one or more catheters often produces improvement or stabilization of the patient's overall clinical status. In this way drainage «buys time» and allows the lesion to become more walled off and safer to treat. Primary percutaneous catheter drainage may be the only intervention required in *a third to a half of patients*.

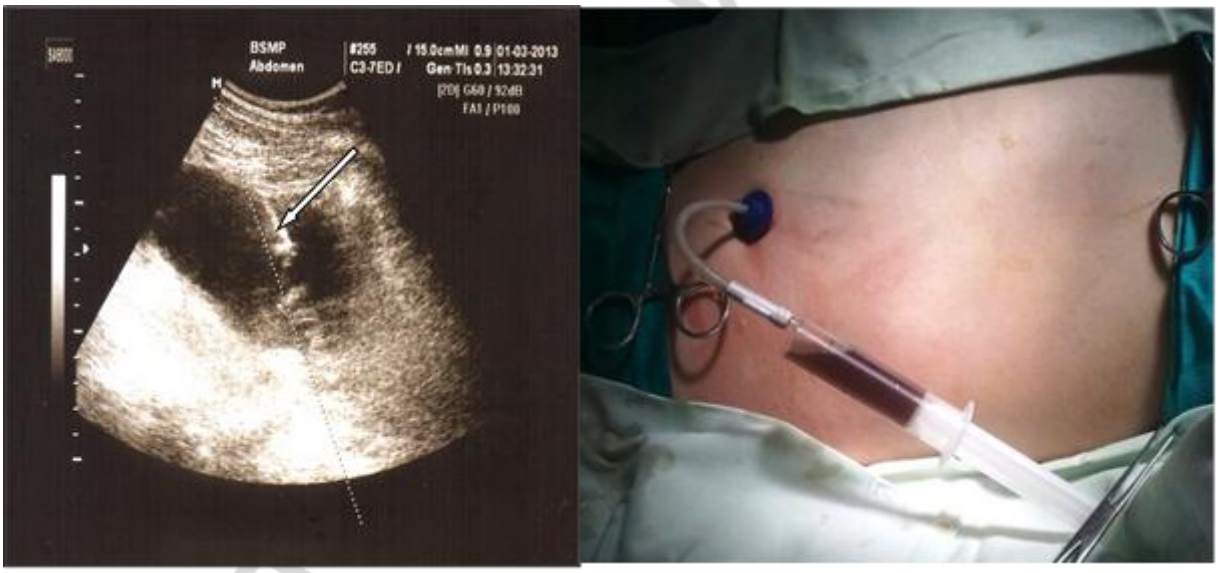
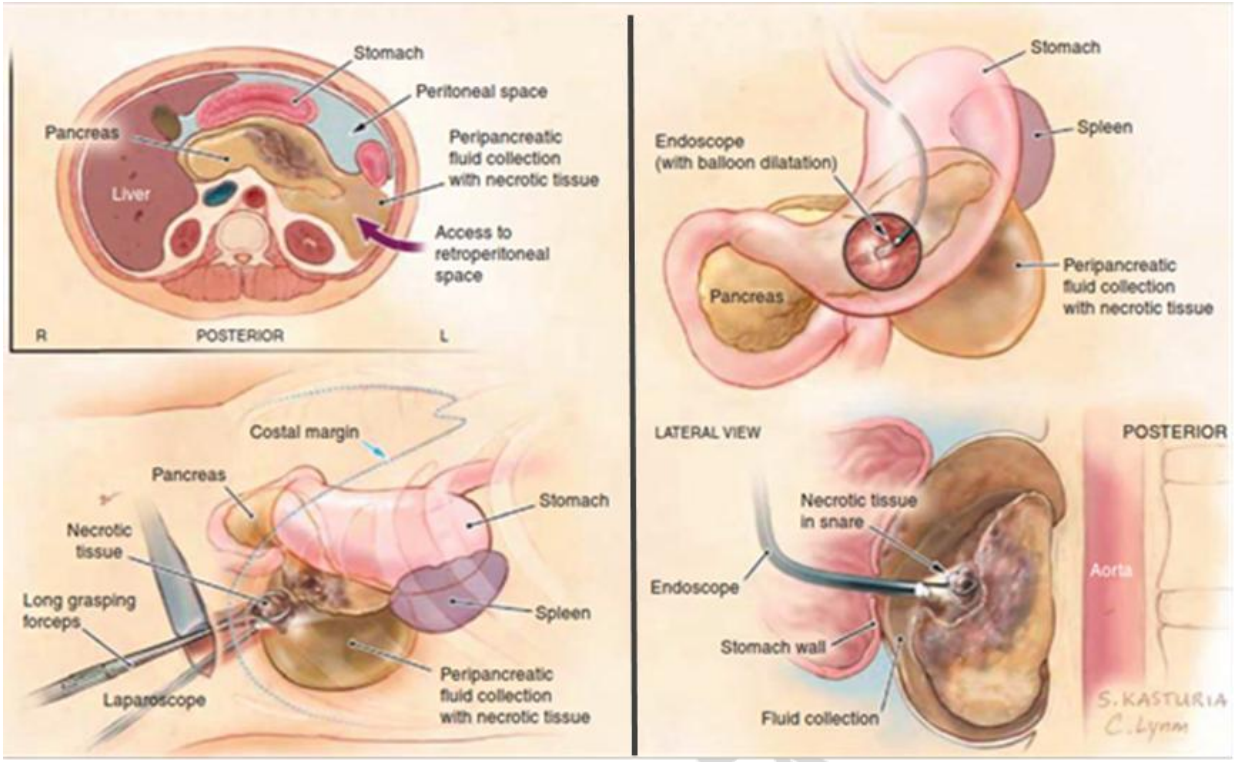


Fig. 25. Percutaneous catheter drainage under ultrasound guidance

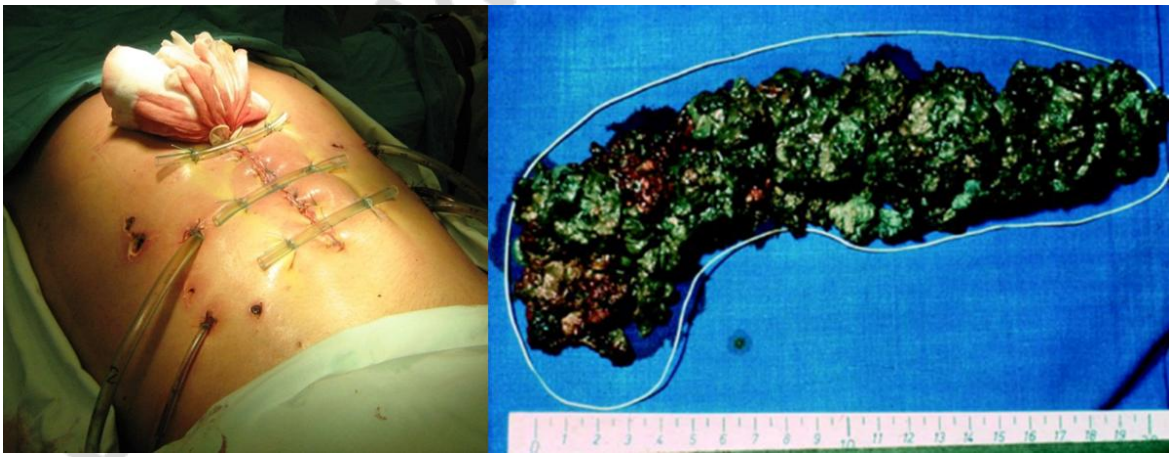
A proportion of patients do however require further treatment when they fail to respond (the so-called «step up approach») and there is a wide array of minimally invasive options to choose (fig. 26).



a ***b***

Fig. 26. Two minimally invasive interventions for local complications of acute pancreatitis: *a* — video-assisted retroperitoneal debridement; *b* — endoscopic transgastric necrosectomy

Open surgical techniques (debridement, fig. 27) ***should only be considered in those who fail to respond to the step-up approach, that is prior percutaneous drainage and minimally invasive intervention.*** The exception is to be found in the rare situation where an *abdominal compartment syndrome* requires open decompression, but it occurs earlier than the optimal time of intervention of local complications.



a ***b***

Fig. 27. Open technique: *a* — debridement through laparotomy; *b* — removed necrotic pancreas

Algorithm for the evaluation and management of acute pancreatitis (fig. 28).

Algorithm for the evaluation and management of acute pancreatitis

1. Diagnosis
   - History of abdominal pain consistent with acute pancreatitis
   - >3x elevation of pancreatic enzymes
   - CT scan if required to confirm diagnosis
2. Initial assessment / management (first 4 hrs)
   - Analgesia
   - Fluid resuscitation
   - Predict severity of pancreatitis
     - Ranson's criteria
     - HAPS score
   - Assess systemic response
     - SIRS score
     - SOFA (organ failure)
3. Reassessment / management (4 to 6 hrs)
   - Assess response to fluid resuscitation
     - mean arterial pressure
     - heart rate
     - urine output
     - hematocrit
   - Determine etiology
     - Ultrasound for gallstones/sludge
     - History of alcohol consumption
     - Laboratory evaluation of other causes
   - MRCP and/or Urgent ERCP if concomitant cholangitis is present
     - not for cholestasis or predicted severe disease per se
   - Transfer to ICU or specialist center as needed
     - Deterioration or failure to respond to initial management
     - Intensive support for persistent organ failure
   - Commence enteral nutrition
     - Once normovolemia restored (usually after 6 hours)
     - Commence via NG tube if no gastric stasis
   - No prophylactic antibiotics or probiotics
4. Conservative management and monitoring (at least daily)
   - Clinical evaluation
     - Assess cardiovascular, respiratory, and renal function
     - Detect peritonitis and abdominal compartment syndrome
   - Daily C-Reactive Protein
   - Classify severity (mild, moderate, severe, critical)
   - Detect intolerance of NG EN
     - Advance tube for NJ feeding if needed
     - Consider supplemental Parenteral Nutrition by day 4
5. Indications for "pancreatic protocol CT scan" (rarely in 1st week)
   - For significant clinical deterioration and elevated CRP
   - For suspicion of local pancreatic complications
   - For suspected bowel ischemia
   - For acute bleeding (CTa) (if stable enough & consider embolization)
   - For abdominal compartment syndrome
6. Invasive intervention
   - For deteriorating patient with suspected infected local complication
   - "Step up approach" with initial drain guided by current CT scan (percutaneous or endoscopic drainage)
   - Delay for 3 to 4 weeks with intensive care support, if possible
   - If failure to respond or secondary deterioration, repeat CT scan, and select appropriate minimally invasive technique based on available expertise and equipment
     - Video-assisted retroperitoneal debridement or percutaneous nephroscopic debridement
     - Endoscopic transluminal debridement
     - Ongoing large bore drainage and irrigation
7. Indication for laparotomy
   - Failed "step-up approach" for further debridement/ drainage
   - Acute abdomen (perforation or ischemia)
   - Severe abdominal compartment syndrome (rarely)

Fig. 28. Algorithm for the evaluation and management of acute pancreatitis

Management of acute pancreatitis remains a formidable challenge due to the variety and severity of many associated complications, and continues to evolve. Although specific treatment for acute pancreatitis remains elusive, progress has been made in pain management, fluid resuscitation, antibiotic prophylaxis, enteral nutrition, therapeutic ERCP and cholecystectomy. Progress has also been made in the intensive care management of systemic complications and in the development of less invasive interventions for treatment of local complications, particularly infected pancreatic necrosis.

TESTS

1. **What are the parts of pancreas?**
   a) Neck; b) Head; c) Body; d) Tail; e) Isthmus.
2. **Name the main pancreatic duct:**
   a) of Wirsung; b) of Oddi; c) Choledocus;
   d) of Vater; e) of Santorini.
3. **What statements about common channel are correct?**
   a) it is connection between common bile duct and main pancreatic duct;
   b) it is usually absent;
   c) it empties the duodenum at the ampulla of Vater;
   d) it empties into the duodenum at the minor papilla;
   e) it allows to mix duodenal content and bile.
4. **Select two main etiological factors of acute pancreatitis**
   a) trauma; b) alcoholic; c) iatrogenic;
   d) hereditary; e) biliary.
5. **What causes SIRS in severe acute pancreatitis?**
   a) released inflammatory cytokines; b) active digestive enzymes;
   c) severe pain; d) necrotic products;
   e) abdominal distension;
6. **Choose systemic complication of acute pancreatitis:**
   a) renal failure; b) acute necrotic collection;
   c) walled-off necrosis; d) respiratory failure;
   e) cardiovascular failure;
7. **Possible ways to assess severity and prognosis of acute pancreatitis**
   a) use RANSON score system;
   b) use APACHE 2 score system;
   c) use IMRIE-GLASGOW score system;
   d) measurement of systolic pressure;
   e) just look at the patient;
   f) use Balthazar CT severity index.
8. **Bluish discoloration of the skin around the umbilicus in acute pancreatitis is:**
   a) cullen's sign; b) grey turner's sign;
   c) mondor’s sign; d) lagerlof’s sign;
   e) halsted’s sign; f) grünwald sign.
9. **Hemorrhagic discoloration of flanks in acute pancreatitis is:**
   a) cullen's sign; b) grey turner's sign;
   c) mondor’s sign; d) lagerlof’s sign;
   e) halsted’s sign; f) grünwald sign.
10. **Absolutely noninvasive method of bile duct assessment is:**
    a) MRI cholangiography; c) ERCP;
    b) EUS; d) Cholecystostomy.

11. What are the main goals of acute pancreatitis treatment nowadays?

a) pain control; b) nutrition support;
c) aggressive antibiotic treatment; d) fluid resuscitation
e) early surgery

12. What is the indication for therapeutic endoscopic retrograde cholangiopancreatography in acute pancreatitis?

a) cholestasis
b) acute calculous cholecystitis
c) cholangitis due to the common duct stone
d) spasm of sphincter of Oddy
e) necrotizing pancreatitis

13. What is the best surgical approach in sterile retroperitoneal acute pancreatic fluid collection?

a) percutaneous catheter drainage; b) laparotomy;
c) laparoscopy; d) minilaparotomy;
e) angiography.

14. What are the indications for surgery in acute pancreatitis?

a) bowel infarction;
b) interstitial pancreatitis;
c) abdominal compartment syndrome;
d) fail to respond to percutaneous catheter drainage;
e) infected necrosis;
f) perforated ulcer.

Answers: 1 – a, b, c, d; **2** – a; **3** – a, c; **4** – b, e; **5** – a, b, d; **6** – a, d, e; **7** – a, b, c, f; **8** – a; **9** – b; **10** – a; **11** – a, b, d; **12** – c; **13** – a; **14** – a, c, d, e, f.

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CONTENTS

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