Pancreatic Pseudocysts in the 21st Century. Part I: Classification, Pathophysiology, Anatomic Considerations and Treatment

Åke Andrén-Sandberg[1], Christos Dervenis[2]

[1]Department of Gastrointestinal Surgery, Sentralsjukehuset i Rogaland, Bergen University. Stavanger, Norway. [2]First Department of Surgery, Agia Olga Hospital. Athens, Greece

Definitions

A pseudocyst is present as a cystic cavity bound to the pancreas by inflammatory tissue [1]. Typically, the wall of a pancreatic pseudocyst lacks an epithelial lining, and the cyst contains pancreatic juice or amylase-rich fluid [2, 3]. This is the histopathological definition of a pancreatic pseudocyst. In the past, there have been several different clinical definitions of pancreatic pseudocysts - and there are probably more to come in the future. Today, the most used definitions differentiate between peripancreatic fluid collections, pseudocysts and pancreatic abscesses as in the Atlanta classification system for acute pancreatitis [4]:

Acute Fluid Collections occur early in the course of acute pancreatitis, are located in or near the pancreas, and always lack a wall of granulation or fibrous tissue.

Acute Pseudocysts are constituted by pancreatic juice enclosed by a wall of fibrous or granulation tissue, arising as a consequence of acute pancreatitis or pancreatic trauma.

Chronic Pseudocysts are constituted by pancreatic juice enclosed by a wall of fibrous or granulation tissue, arising as a consequence of chronic pancreatitis and lacking an antecedent episode of acute pancreatitis.

Pancreatic Abscess is a circumscribed intra-abdominal collection of pus, usually in proximity with the pancreas, containing little or no pancreatic necrosis, arising as the consequence of acute pancreatitis, trauma or chronic pancreatitis.

The description of the separate entity of acute fluid collections according to the Atlanta classification is important inasmuch as it represents an earlier stage in the development of acute pseudocysts and abscesses as compared to earlier definitions.

The distinction between a pseudocyst and acute fluid collection leads to a better understanding of the natural history of peripancreatic fluid collections and facilitates the progress of the treatment of these two separate entities even though they are a part of a continuous pathological process. The presence of a well-defined wall composed of granulation or fibrous tissue is what distinguishes a pseudocyst from an acute fluid collection.

A pseudocyst is usually rich in pancreatic enzymes and is most often sterile. The formation of a pseudocyst usually requires 4 or more weeks (many clinicians state six) from the onset of acute pancreatitis [5]. In this regard, an acute pseudocyst is a fluid collection arising in association with an episode of acute pancreatitis, lasting more than 4 weeks and surrounded by a defined

wall. Fluid collections lasting less than 4 weeks which lack a defined wall are more properly termed acute fluid collections. In contrast, chronic pseudocysts have a well-defined wall, but arise in patients with chronic pancreatitis and lack an antecedent episode of acute pancreatitis.

The differentiation in the Atlanta classification between an acute and a chronic pseudocyst is important, but it is confusing. It is important to note that, in the classification, the terms "acute" and "chronic" refer to the pancreatitis associated with the pseudocyst and not to the mode of symptomatology of the pseudocyst itself. This means that an acute pseudocyst may have been known for months in one patient, whereas a chronic pseudocyst in another patient may have been documented for only a week or two.

Bacteria may or may not be present in a pseudocyst culture. However, a pseudocyst is defined as a fluid collection without clinical signs of infection. The term "infected pseudocysts" is not a well-chosen term as there is no definition of it. Moreover, from a biological point of view, it is probably impossible to find a clear distinction between these infected fluid collections and an abscess. On the other hand, most positive cultures from pseudocysts without clinical signs of infection are of no clinical significance and probably represent contamination during the culture procedure. When obvious pus is present, the lesion is, of course, more correctly termed a pancreatic abscess [4].

Etiology

The occurrence of a pseudocyst parallels that of pancreatitis and the etiology of pseudocysts resembles the causes of pancreatitis closely. Alcohol-related pancreatitis appears to be the major cause in studies from countries where consumption of strong beverages is relatively high and accounts for 59-78% of all pseudocysts [6]. Not only the differences among the countries, but also the different proportions of acute and chronic pseudocysts in the studies can affect the prevalence of alcohol-related pseudocysts. Alcohol abuse is the presumed cause of pancreatitis in the majority of patients with chronic pancreatic pseudocysts, whereas the acute pseudocyst may complicate the clinical picture of any cause of acute pancreatitis, including ERCP or pancreatic cancer [6].

Pseudocysts may also complicate certain surgical procedures, such as partial gastrectomy, when the pancreas is inadvertently torn near its attachment to the spleen or when an attempt has been made to dig out a peptic ulcer which has penetrated the pancreas.

Pseudocysts in children [7, 8] are known complications of acute pancreatitis and pancreatic trauma. It is not unlikely that a blunt or non-penetrating injury, such as in a steering wheel injury in an automobile accident or a fall from a bike, in which the pancreas sustains a crushing blow, be complicated by a subsequent pseudocyst.

USA

An American study of 69 pseudocysts noted that 78% were related to alcoholic pancreatitis, 7% to complicated gallstone pancreatitis, 6% were of unknown causation ("idiopathic") and 3% each were due to trauma, hyperlipidemia or a recent surgical operation [9]. Another study from America presented similar results with 73% of cases related to alcohol abuse and 6% to biliary disease. Both of these possible causes were present in 14% of patients and 7% had other causes including trauma, penetrating duodenal ulcers and hyperlipidemia [10].

Walt *et al.* reported data collected from Wayne State University Hospital, Detroit. The causative factors in the 357 admissions for pancreatic pseudocysts included alcoholism in 251 cases (70%), biliary tract disease in 28 (8%), blunt trauma in 17 (5%), penetrating trauma in 4 (1%), operative trauma in 1 (0.3%), and idiopathic in 56 (16%) (alcoholism was difficult to exclude in about half of these cases). In only 9 of the 28 patients with demonstrated biliary disease could alcohol be definitely excluded as a

causative factor. One patient in the idiopathic group had hyperlipidemia; most of the others were thought to have been alcoholic, but no definite evidence was recorded [11]. The proportion of acute and chronic pseudocysts was not indicated in these studies.

South Africa

A prospective study of 83 patients from South Africa reported 70% of pseudocysts to be associated with alcohol-induced pancreatitis, 22% were due to blunt abdominal trauma and 8% were idiopathic [12]. Gallstone disease was rare in this population though acute pseudocysts were diagnosed in 54% of cases.

Europe

In a prospective study from France, chronic pseudocysts were associated with alcoholic pancreatitis in 94% of cases. The leading cause of acute pseudocysts was gallstones accounting for 45% of all acute cases. The other causes were trauma (10%), ERCP (7%), alcohol, pancreas divisum, surgery (4% each) and idiopathic (28%) [13].

Alcohol as the principal cause of chronic pancreatitis was demonstrated in 85% of patients with pancreatic pseudocysts in a Finnish study [14].

In recent prospective British study, patients with chronic pancreatic pseudocysts had established chronic pancreatitis as a result of alcoholism in 71% of cases. Other causes encountered were recurrent attacks of acute pancreatitis (5%), cholelithiasis (4%) or unknown causes (20%) [15].

Classification

There is a certain confusion in the literature about the terms "acute" and "chronic" with regard to pseudocysts. According to the Atlanta classification - as described above - an acute pseudocyst is a collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, arising as a consequence of acute pancreatitis or pancreatic trauma, whereas a chronic pseudocyst is a collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, arising as a consequence of chronic pancreatitis and lacking an antecedent episode of acute pancreatitis. This means that the terms acute and chronic regarding pseudocysts are used differently in some respects than the way in which these words are used in other medical conditions.

Sometimes, classification of the pseudocysts into acute and chronic types is - unfortunately - based on the time interval (usually 4-6 weeks from the acute attack) in an attempt to help decide on the timing of surgical intervention and, in these cases, it does not take the underlying disease into account. With this use of the term, acute pseudocysts occur in acute pancreatitis but can also develop in chronic pancreatitis after an acute exacerbation. On the other hand, chronic pseudocysts are usually associated with chronic pancreatitis but may develop after an episode of acute pancreatitis as well [12]. The situation is somewhat confusing and some attempts have been made to set it clear by classifying pseudocysts according to the pathological changes underlying acute or chronic pancreatitis.

Sarles' Classification

As early as 1961, Sarles *et al.* [16, 17] proposed a classification of pancreatic pseudocysts depending on whether they were associated with acute or chronic pancreatitis. Pseudocysts associated with acute pancreatitis were called necrotic pseudocysts because they resulted from pancreatic necrosis and extravasation of pancreatic juice. Based on pathological studies, pseudocysts originating from chronic pancreatitis were called retention pseudocysts. Pathological examinations revealed that intrapancreatic fluid collections associated with chronic pancreatitis were frequently true cysts caused by dilation of pancreatic ducts behind calculi, plugs, or strictures. Extrapancreatic pseudocysts complicating chronic pancreatitis were more frequently caused by a rupture of these pseudocysts into the peripancreatic

tissues (retention pseudocysts) rather than by acute necrotic pancreatitis complicating the chronic lesion [13].

Sarles' classification made a clear distinction between acute and chronic pseudocysts based on pathological grounds. They stressed that an important aspect of chronic pseudocyst formation is the underlying pancreatic duct pathology. But they failed to recognize the pseudocysts emerging after an episode of acute-on-chronic pancreatitis even though they reported one such case in their later study [13].

The classification of pseudocysts proposed by D'Egidio and Schein in 1991 [12] took into account all the aspects mentioned above. They identified three distinct types of pseudocysts: Type I, or acute "post-necrotic" pseudocysts, that occur after an episode of acute pancreatitis and are associated with normal duct anatomy, and rarely communicate with the pancreatic duct; Type II, also post-necrotic pseudocysts, which occur after an episode of acute-on-chronic pancreatitis (the pancreatic duct is diseased but not strictured, and there is often a duct-pseudocyst communication) and Type III, defined as "retention" pseudocysts, occur with chronic pancreatitis and are uniformly associated with duct stricture and pseudocyst-duct communication. In this classification, distinction between acute-on-chronic (Type II) and chronic (Type III) can be subtle. It often requires operation to show the presence of necrotic debris, indicating a recent flare-up of acute-on-chronic pancreatitis that may have been missed clinically. Whenever possible, the pancreatic duct should be delineated in patients with chronic pseudocysts, since an independent surgical approach may be required to deal with underlying duct pathology [18].

Classification According to Extent of Necrosis

Whether there is need to further subdivide post-necrotic pseudocysts after acute pancreatitis is matter of discussion. However, with the advance of conservative treatment more and more patients with necrotic pancreatitis survive the acute stage of the disease without surgical intervention. With extensive, i.e. more than 30%, necrosis of the pancreas, the risk of pseudocyst occurrence increases dramatically. Neoptolemos *et al.* [19] divided their patients into two groups: those who had either clinically mild pancreatitis or severe disease but no surgery for local complications and less than 25% necrosis on contrast-enhanced CT, and those who had clinically severe pancreatitis and underwent surgery for local complications and/or had at least 25% necrosis on CT, at surgery or post mortem. The incidence of pancreatic pseudocysts was 10% and 56%, respectively [19].

Moreover, 12 of 18 patients in the group with extensive necrosis of the pancreas underwent diagnostic or therapeutic ERCP 5 days or more after the onset of attack and seven (58%) had disruption of the main pancreatic duct in the head (n=4), body (n=2) or tail (n=1) of the gland. By contrast, in none of the 89 patients with mild pancreatitis or with less extensive pancreatic necrosis was there evidence of main pancreatic duct disruption. In such cases the complete disruption of an otherwise normal pancreatic duct may be observed [20]. Not only pathological differences, but also different treatment results [21, 22, 23, 24] makes distinguishing between these two types of acute pancreatic pseudocysts desirable.

Classification Based on Duct Anatomy

There is also a classification based entirely on pancreatic duct anatomy proposed by Nealon and Walser [20]. This system defines the categories of ductal abnormalities seen in patients with pseudocysts and relates the authors' experiences with different types of treatment.

- Type I: normal duct/no communication with cyst.
- Type II: normal duct with duct-cyst communication.
- Type III: otherwise normal duct with stricture and no duct-cyst communication.

- Type IV: otherwise normal duct with stricture and duct-cyst communication.
- Type V: otherwise normal duct with complete cut-off.
- Type VI: chronic pancreatitis, no duct-cyst communication.
- Type VII: chronic pancreatitis with duct-cyst communication.

So far, this classification, published in 2002, has had limited use.

Incidence

Pseudocysts were once considered to be an unusual complication of pancreatitis. As recently as 1968, Becker *et al.* [25] wrote: "The experience (with pseudocysts) in most large surgical clinics is limited to relatively few patients". Some earlier studies, based on upper gastrointestinal series, reported an extremely low incidence (1.6-4.5%) of pseudocyst formation, regardless of the cause (0.5-1 per 100,000 adults per year) [26, 27, 28, 29, 30, 31, 32].

Incidence of Pseudocysts after Acute Pancreatitis

The estimated incidence of peripancreatic fluid collections after acute pancreatitis is dependent both on how a pseudocyst is defined and on how it should be looked for. Obviously, the incidence has increased with the advent of ultrasonography and CT. However, some authors still favor the terms pancreatic and peripancreatic fluid collections, which now encompass two separate entities such as acute fluid collection and acute pseudocysts [5]. Others have used the term pseudocyst without any explanation [32, 33, 34], which makes it very difficult to evaluate what they have found. Altogether however, there is agreement on the fact that significant fluid collections develop in 30-60% of cases of acute pancreatitis [4].

Theoretical Problems

One problem when calculating the incidence of pseudocysts in relation to acute pancreatitis is that there are many cases of severe acute pancreatitis which are not found until autopsy [35].

Since alcohol is the commonest cause of acute pancreatitis the distinction between acute and chronic pancreatic pseudocysts is frequently blurred clinically. It is frequently difficult to establish in practice whether patients presenting with their first attack of pancreatitis, especially alcoholic pancreatitis, have not had symptoms of the same kind but less severe before. The diagnosis of chronic pancreatitis is only made if there are morphological, specific changes, and testing which can show these changes are seldom performed in uncomplicated cases - whereas in complicated cases, e.g. in cases with pseudocysts, more testing is done. Only routine ERCP in all alcoholic patients could allow the classification of all these patients into the proper groups [12]. In a prospective study by Nealon *et al.*, alcohol was the primary cause of pseudocysts in 93% of cases, but the diagnosis of acute pseudocyst was then made on the basis of clinical data. Notably, nine (38%) of the 24 patients who were originally thought to have pseudocysts as a complication of simple acute pancreatitis were found to have totally unanticipated ERCP evidence of chronic pancreatitis [36].

Incidence Studies

Using ultrasonography, Bradley *et al.* found acute fluid collections within the lesser sac in 52 of 92 patients (57%) with a clinical diagnosis of moderately severe acute pancreatitis. In 14 of these cases lasting less than four weeks, surgical intervention was considered necessary or advisable and an additional 5 patients underwent diagnostic laparotomy for suspicion of other abdominal

disease. However, in 10 cases, the pseudocyst spontaneously regressed within 3 weeks from the time of onset and in 6 other cases, adequate evaluative data were not available. The remaining 17 patients exhibited persistence of the acute pseudocyst beyond the initial three week period of development. Fifteen of these 17 patients later underwent definitive surgery for a confirmed pseudocyst at times ranging from 5 weeks to 6 months after development. According to the Atlanta classification only the latter 15 (16%) are supposed to fulfill the criteria of a pancreatic pseudocysts. Moreover, 65 of 92 patients with moderately severe acute pancreatitis were classified as having relapsing chronic or chronic pancreatitis according to Marseilles classification. Some of these patients may have already presented with the pseudocysts making exact incidence of pseudocysts after acute pancreatitis unclear [5].

In a study by Imrie *et al.* [37], pseudocysts developed after emergency hospital admission for an episode of acute pancreatitis in 86 patients. Sixty-two of the 86 pseudocysts consequent to acute pancreatitis were derived from the local hospital population area, in which 879 patients with acute pancreatitis were admitted to hospital during the same time period. This resulted in a 7% overall incidence of pseudocysts as a complication of acute pancreatitis.

London *et al.* [38] prospectively investigated 102 patients with acute pancreatitis by abdominal computed tomography scans within 72 hours of admission, at one week and after six weeks. CT detected fourteen (14%) pseudocysts. There is no certain definition of a pseudocyst in this study and acute pancreatitis was diagnosed on the basis of clinical findings including serum amylase elevation. This means that some patients with acute fluid collections or acute-on-chronic pancreatitis have probably been included in the study. These statements are supported by 7 pseudocysts diagnosed on admission and 5 new pseudocysts diagnosed after 1 week. From 12 pseudocysts diagnosed within one week of admission, 7 resolved, 1 was drained and 4 were still apparent on CT scan after six

weeks. These 4 pseudocysts together with 2 new pseudocysts diagnosed after six weeks can be considered true pseudocysts, and not fluid collections. In this case the incidence of pancreatic pseudocysts is calculated to be about 6%, i.e. the figure is in agreement with the data from a more recent prospective cohort study [38] where the Atlanta classification definitions have been used to distinguish between acute fluid collections from acute pseudocysts.

In a series of 926 patients with non-alcoholic acute pancreatitis, fluid collections were observed in 83 (9%). At the end of six weeks, 48 (5%) still had a fluid collection evaluated as a pseudocyst [39].

Kourtesis *et al.* included 128 consecutive patients with acute pancreatitis diagnosed by an elevated serum amylase level of 3 times above normal into their prospective CT study. Forty-eight (37%) developed fluid collections in the pancreatic region. The majority of these resolved spontaneously. In 15 (12%) patients, symptomatic pseudocysts developed. Most of these patients had alcohol-induced pancreatitis [34].

Although precise documentation may be lacking, it has been estimated that 5,000-7,000 new cases of pancreatic pseudocysts are discovered each year in the United States in the clinical setting of acute pancreatitis [40].

Incidence of Pseudocysts in Chronic Pancreatitis

Pseudocysts in chronic pancreatitis have a higher incidence as compared to acute pancreatitis. Incidence figures of 20-40% have been reported in the literature [41, 42, 43]. However, there is a lack of precise data based on the long-term follow-up of patients with chronic pancreatitis - in contrast to acute pseudocysts where the patient with chronic pancreatitis may have had the disease for 10, 20 or more years giving him a high risk of developing a pseudocyst at least once over a long period of sickness. Also, there must be some criteria concerning the size of chronic pseudocysts; is it a pseudocyst if it is only seen at resection or in the microscope or must

it be larger than 0, 0.5, 1 or more centimeters in diameter? There are pathologists who argue that microcysts are an integral part of the histologic picture of chronic pancreatitis, which makes the term pseudocyst merely a matter of definition of size - and maybe severity of the desmoplastic reaction and duration of the disease.

In a Swiss longitudinal study of a mixed medical-surgical series of 245 patients, 163 had painful alcohol-induced pancreatitis [42]. The indication for operation was pancreatic cyst or pseudocyst in 34% of the patients in this group. But it should be mentioned, however, that most of these patients were observed and operated on before ultrasonography, CT, and ERCP were available. With these diagnostic techniques, the incidence of cysts and pseudocysts among patients with chronic pancreatitis could be higher.

Influence of Etiology on the Incidence of Pseudocyst Formation

There are few studies in the literature addressing this issue. Imrie *et al.* [37] found the acute pseudocyst to be more common in those with an alcohol-related cause (12%) than in those with gallstones (4%). However, in their prospective long-term follow-up of patients with severe alcohol-related pancreatitis, Imrie [44] found that acute alcohol-induced pancreatitis does not have a greater predisposition to pseudocyst formation.

In a prospective study from Italy, patients with alcohol-related pancreatitis were excluded. In the study population, biliary pancreatitis was associated with a lower incidence of fluid effusions or pseudocysts as compared to other etiologies [39].

Anatomic Considerations

Knowledge of the anatomy of the pancreas and the pathogenesis of pancreatic fluid collections is essential for choosing the right treatment method. Each patient has unique ductal and parenchymal anatomy, which combine in a unique pathophysiologic mechanism. Once the anatomy and mechanism are understood in each patient, the management principles are directed towards resolution of the anatomical basis of the disease and the right management can be proposed.

In the study by Bourliere and Sarles, most pseudocysts were located in or near the tail of the pancreas [13]. In another study, most extrapancreatic pseudocysts were located in the body and tail region, whereas most intrapancreatic pseudocysts were in the head of the pancreas [45].

Pancreatic pseudocysts are most often retrogastric [46]. Blood-stained ascites and abdominal fat necrosis have been explained by fluid escaping via the foramen of Winslow into the greater sac, and blockage of the foramen may cause the fluid to become "encysted" in the lesser sac [47].

There are also reports of pancreatic pseudocysts in the heterotopic pancreas, usually a silent gastrointestinal malformation, such as a case of pancreatitis and extensive pseudocyst formation in the gastric antrum, which caused gastric outlet obstruction [48].

Pathogenesis of Acute Pseudocysts

Acute pseudocyst formation can be viewed as the maturation of an acute inflammatory process, with collection of pancreatic secretions and the products of inflammatory response with or without rupture of a pancreatic duct. In acute pancreatitis, duct disruption can occur as a consequence of pancreatic necrosis. However, in some cases, peripancreatic collection might also follow leakage of juice from the inflamed surface of the gland, analogous to the pleural effusion which complicates pneumonia.

Although the pancreas does not have a firm capsule, collections of pancreatic juice may remain as focal masses in the region of the duct disruption. If secretions breech the thin layer of connective tissue that surrounds the gland, the anterior pararenal space and the lesser sac are immediately involved [49]. The most common site of accumulation of the

leaking pancreatic juice is the potential space of the lesser omentum (lesser sac) limited anteriorly by the stomach, inferiorly by the transverse mesocolon, laterally by the spleen, and by splenic flexure on the left and the duodenum on the right [6].

At first, these fluid collections are poorly demarcated, generally amorphous in configuration, extending along the peripancreatic and pararenal boundaries, and should best be called acute fluid collections in this phase. Most of these peripancreatic fluid collections that follow an attack of acute pancreatitis will probably resolve themselves unless they become infected or contain large quantities of necrotic tissue [50]. Only if acute fluid collection persists more than 4 to 6 weeks and is well-defined by a wall of fibrous or granulation tissue, can one say that an acute pseudocyst has appeared. Such a pseudocyst usually contains enzymatic fluid and necrotic debris [6].

Evidence on Pancreatic Duct Disruption in the Pathogenesis of Acute Pseudocysts

There are also observations which support the concept that, at its origin, a pseudocyst must have communication with the pancreatic duct. The amylase levels of the aspirated cystic fluid are many times greater than the simultaneous serum levels and percutaneous drainage of pseudocysts results in a prolonged period of drainage indicating a communicating fistula [6]. With time, however, communication may or may not persist because the inflammatory reaction that follows cyst formation may occlude the fistula [2]. This possibly explains the different rates of pseudocyst-duct communication presented in the literature.

Neoptolemos *et al.* [19] suggested that, in considering the pathogenesis of local necrosis and pancreatic pseudocyst, a distinction should be made between a pseudocyst communicating with the main pancreatic duct during acute pancreatitis and duct disruption with parenchymal staining by contrast as shown by ERCP. In their study, only one of 18 pseudocysts (6%) communicated with the main pancreatic duct and this was quite separate from extravasation into the parenchyma. Similarly, D'Egidio and Schein [12] reported ten patients with acute pseudocysts and pancreatic duct outlined during ERCP and, in only one of their cases of traumatic pancreatitis, was communication to the pseudocyst demonstrated.

However, in other published studies, higher pseudocyst-duct communication rates have been found. In a study by Barthet *et al.* [41, 51], communication between acute pseudocysts and the pancreatic duct system was observed in 20% of the cases. Nealon *et al.* [36] suggested that the incidence of communication in acute pseudocysts could be as high as 60%.

Pathogenesis of Chronic Pseudocysts

The pathogenesis of pseudocyst formation in chronic pancreatitis is less well-known, but at least two mechanisms may be involved. First, the cyst may develop as a consequence of an acute exacerbation of the underlying disease, in which case serial scans should reveal its formation after a more severe attack of pain, perhaps accompanied by transient increases in serum amylase levels. This explanation fits cysts that are diagnosed after an attack of acute-on-chronic pancreatitis and contain necrotic debris. Second, blockage of a major branch of a pancreatic duct by a protein plug, calculus or localized fibrosis could lead to pancreatic cysts or pseudocyst formation [12, 18]. When there is blockage of the major branch of the main pancreatic duct, the ongoing pancreatic secretion proximal to the obstruction leads to a saccular dilatation of the duct, which is filled with pancreatic juice. Such cysts are truly retention cysts. The formed microcysts can eventually coalesce and lose their epithelial lining as they enlarge. Initially, cysts are intrapancreatic fluid collections but can reach the capsule of the pancreas when they grow. If the capsule ruptures, a pancreatic fistula develops. The rupture of the capsule can occur in one, two or even multiple sites, resulting in pancreatic juice entering the retroperitoneal or peritoneal

cavities [52]. Pancreatic juice can migrate from the pancreas, its limits being the adjacent organs or a fibrous layer. Occasionally, an enzyme-rich pancreatic juice collection is noted in either pleural cavity. If the ductal disruption persists, however, then a pancreatic pseudocyst may develop. The pseudocyst is, in fact, a longstanding peripancreatic or intrapancreatic fluid collection which develops a significant wall, as defined by an imaging study [2]. This process would develop insidiously, although the cyst itself can become the source of pain once it reaches sufficient size [18].

The location of pancreatic fluid collections can be explained by the location of the ductal disruption in the pancreatic ductal system. For instance, a ductal disruption dorsally into the space between the pancreas and portal vein can lead to pancreatic fluid accumulation in the right chest by travelling up the pancreatic groove of the portal vein into the hepatoduodenal ligament and then through pleuroperitoneal windows [52]. In some cases, this type of disruption can produce pancreatic fluid collections in the mesentery or left paranephric space. A disruption dorsally from the pancreatic head might lead to pancreatic fluid accumulation in the left chest as it travels in the retroperitoneum underneath the stomach or spleen and through pleuroperitoneal foramina or in the left paranephric space. A ductal disruption ventrally results in fluid accumulation in the lesser sac or in the peritoneum cavity, i.e. pancreatic ascites. Therefore, the location of the fluid collection is a key to the location of the pancreatic duct disruption [52]. There are also cases with extension of the pancreatic juice located far from the pancreatic gland, e.g. to the neck [53].

Regarding chronic pseudocysts, it must be understood that it is extremely difficult - and clinically most often unrewarding - to differentiate between the symptoms caused by chronic pancreatitis and the symptoms caused by the pseudocyst which has its origin in the chronic inflammatory process. However, unique characteristics have also been identified when pseudocysts are associated with a diagnosis of chronic pancreatitis, and special strategies have been employed [36].

Pancreatic Duct Disruption in the Pathogenesis of Chronic Pancreatic Pseudocyst

The term pancreatic ductal disruption is used for a loss of ductal integrity anywhere in the pancreatic ductal system. As demonstrated by ERCP or percutaneous drain study 50% of duct disruptions are located in the head of the pancreas, 30% in the body and 20% in the tail [54].

Traverso and Kozarek [55] credit Longmire [56] who described the head of the pancreas as the pacemaker of chronic pancreatitis suggesting that the head was frequently the cause of complications associated with chronic pancreatitis. In the head of the pancreas, the main pancreatic duct or duct of Wirsung inclines caudally and dorsally, and passes to the left of the intrapancreatic portion of the common bile duct. The accessory duct of Santorini, normally begins near the neck of the gland at its junction with the main duct and anterior to the common bile duct to open at the minor duodenal papilla [57]. In the normal ventral dominant system, the main pancreatic duct changes from its medial and inferior transverse position to course superiorly and anteriorly. As the main pancreatic duct resumes a transverse position in the neck of the gland, it angles to assume a more superficial location in the gland. This angulation is described as the "genu" and may be located in the head or the neck of the pancreas. This knee may represent an anatomically vulnerable region of the pancreas subject to disruption or "blow out", which occurs with complicated pancreatitis [58].

Traverso *et al.* [54] also observed that, in complicated pancreatitis, ductal disruptions are frequent at the bend and occur either dorsally over the portal vein or ventrally into the lesser sac. Persistent pancreatic fistulas result from downstream ductal obstruction which cannot be decompressed (e.g., "genu" strictures) or from the disconnected duct

syndrome, a gland that has been permanently separated from the downstream pancreatic parenchyma (e.g., "genu" obstruction) [54].

According to Nealon and Walser [59], a pseudocyst in chronic pancreatitis always represents a fistula between the main pancreatic duct and the cystic fluid collection, which means that the pertinent focus of evaluation in the management of pseudocysts should be the anatomic abnormality in the main pancreatic duct.

However, duct communication with the cyst is not always identified radiologically in chronic pancreatitis, possibly because the duct or ductules become completely obstructed [18]. Using ERCP and on-table pancreatography, it was noted that only five of 21 chronic pseudocysts communicated with the main pancreatic duct in one study [60]. Others have found a much higher incidence of pseudocyst-main pancreatic duct communication (37-69%) on preoperative ERCP [10, 15, 36, 61, 62, 63, 64].

In the material collected from all patients with pancreatic pseudocysts at the University Hospital in Galveston, Texas from 1985 to 2001, there were 103 patients with pseudocysts and chronic pancreatitis having a main pancreatic duct greater than 7 mm in diameter. Communication between the duct and the pseudocyst was confirmed in 72% of cases with ERCP; in acute pancreatitis the communication between the duct and the pseudocyst is demonstrated in 17-31% of cases [59].

Traumatic Pseudocysts

Pseudocysts may also develop in the aftermath of pancreatic trauma, and are then a direct sign of a rupture or at least a breach in the pancreatic duct. Although adult series of pseudocysts report trauma as the etiological factor in only 3-8% of patients [9, 65, 66], most pancreatic pseudocysts in children are post-traumatic [67, 68]. Traumatic cyst fluid has a high amylase content. Based on this, two possible mechanisms have been suggested. However, it is also possible that a

hematoma following a contusion of the gland turns into a collection of pancreatic juice as the blood is reabsorbed and replaced by seepage from a capsular tear [18].

A direct traumatic disruption of the pancreas as a result of extracorporeal shock wave lithotripsy for left-sided renal calculi has also been reported [69].

Macroscopic Anatomy

Initially, macroscopy referred to the study of the diseased body or organ at autopsy and later on at surgery. Regarding pancreatic pseudocysts, today it is usually based on findings at CT, MR imaging or ultrasonography, but also combined with information from surgery and autopsy.

The Wall

The fact that there are no lines of cleavage between the well-developed pseudocyst and the adjacent viscera is important both for pathogenesis and treatment. If tissue is sent for pathological study, it is often a portion of the wall of the cyst. It is then found to be shaggy, friable, and discolored [70].

On gross inspection of the pseudocyst wall, it is usually not possible to identify the connection with the main pancreatic duct although, by injection study or endoscopic pancreatography, a connection can be demonstrated in many cases [70]. A pseudocyst of the pancreas may, on occasion, have a blue appearance on external inspection, hence the appellation "blue-dome" pseudocyst [71].

The Fluid Content of the Pseudocyst

The pseudocyst is characteristically fluctuant. The contents may vary widely from an almost colorless or turbid fluid to brownish thick fluid containing debris of pancreatic digestion [72]. The fluid can also be blood-tinged or frankly hemorrhagic. Following the removal of the fluid from the cavity, there may be grumsy mud-like material remaining.

Single versus Multiple Pseudocysts

Pseudocysts can be single or multiple. Most cysts (90%) are single [6]. The existence of multiple pseudocysts is usually mentioned only in the largest published series of pancreatic pseudocysts. This might also be of importance from an etiological point of view.

In a series of 114 patients with pseudocysts, Shatney and Lillehei [73] demonstrated that 3% had more than one pseudocyst at the same time. Sankaran and Walt [74] observed multiple pseudocysts in 6% of 112 cases. Frey [65] found the frequency of multiple pseudocysts to be 11% in 131 cases. In a report of Bradley and Austin [75], where extensive use was made of sonography and CT, the diagnosis of multiple pseudocysts was confirmed during surgery in 14 of 137 patients (10%). In another study 12% of 81 patients had multiple pseudocysts at surgery [76]. More recent studies report an 11-18% incidence of multiple pseudocysts with a nearly equal distribution among patients with acute and chronic pseudocysts [13, 15, 77, 78].

Bourliere and Sarles [13] prospectively evaluated 77 patients with chronic pancreatitis and 29 with acute. Multiple pseudocysts were found in 13% of chronic pancreatitis patients and in 17% of those with acute pancreatitis. Similarly, Usatoff *et al.* [15] reported that 18% of their patients operated on for chronic pancreatic pseudocysts had multiple pseudocysts. Aranha *et al.* [77] found multiple pseudocysts in 11% of 93 patients with cystic collections following acute pancreatitis who had serial ultrasound examinations. Multiple pseudocysts were diagnosed in 10-19% of mixed acute and chronic pancreatic pseudocyst series [79, 80, 81].

In a study bt Goulet *et al.* [78], the overall incidence of the multiplicity of pseudocysts in the 91 patients reviewed was 14%. All patients with multiple pseudocysts had a previous history of alcohol abuse. None was noted to have biliary disease. The authors concluded that multiple cysts are seen more often in acute alcoholic pancreatitis [78]. This is in accordance with the experience of Nguyen *et al.* [82]. Multiple pseudocysts were demonstrated in 23% of 90 patients with pancreatic pseudocysts. Multiplicity was found significantly more often in patients with acute alcoholic pancreatitis than in all groups combined (47% vs. 19%) [83]. This might be explained by the fact that alcohol is more likely to cause widespread, diffuse injuries to the pancreatic duct at different sites simultaneously [82, 84] and this may result in the increased incidence of multiple pseudocysts.

Location and Extension of Pseudocysts

There are certain controversial results about pseudocyst location published in the literature. In acute pancreatitis, one report demonstrated that about 50% of all pseudocysts were located in the tail of the gland [85], whereas others found near equal distribution of the pseudocysts in the head and body with only 7% appearing in the tail [86]. The location of chronic pseudocysts is even more variable in studies involving all parts of the pancreas: head [85], body [87] and tail [86] reported as the prevalent sites for pseudocysts. A nearly equal distribution of the pseudocysts between these parts was also noted [14].

However, in the series on pseudocyst location below, it can be seen that, in chronic pancreatitis, there is a preponderance of pseudocysts in the head of the pancreas. This is in agreement with the Traverso "genu blow-out" theory on the pathogenesis of chronic pancreatic pseudocysts. There are few data available on acute pancreatitis but it seems that pseudocysts can occur in all parts of the pancreas with nearly equal frequency.

In one series of acute pseudocysts, 19, i.e. 39%, were located in the lesser sac (or omental bursa), 31% in the anterior pararenal space, 10% within the substance of the liver and 20% in other sites [49].

From the anatomical point of view, pancreatic pseudocysts can also be either intrapancreatic or extrapancreatic. Intrapancreatic pseudocysts are usually small with a reported

incidence of about 80% in chronic pancreatitis and 50% in acute pancreatitis [13, 15, 88]. Patients with multiple cysts can present with a mixture of these two locations [15]. Two-thirds of all intrapancreatic cysts in chronic pancreatitis are located in the head of the pancreas, whereas most of the extrapancreatic pseudocysts originate from the body or tail of the gland [13]. By contrast, there are studies where a relatively even distribution of chronic intrapancreatic pseudocysts was found between the right and the left sides of the gland [15].

The cyst may extend to the adjacent viscera. Extension into the transverse mesocolon may occur because of the anatomic relationship of the transverse colon to the pancreas. The cyst may also extend to the anterior or posterior pararenal space, mediastinum, and retroperitoneum. Posterior pseudocysts, also rare, may extend inferiorly into the pelvic region and groin, and pseudocysts extending to the scrotum have been encountered [6]. The pseudocysts of acute pancreatitis are more prone to extension, but chronic pseudocysts can also reach a considerable size. Sometimes these pseudocysts appear to be contained within the prolongation of the pancreatic capsule and the lesser sac, at least in part, tends to remain patent.

Mediastinal pancreatic pseudocysts are a rare but life-threatening complication of pancreatitis [89, 90, 91, 92, 93]. They may appear as a thoracic mass on X-rays and need to be differentiated from other lesions. Magnetic resonance cholangiopancreatography (MRCP) is a valuable diagnostic tool in such cases [94].

Pseudocyst Size and Content

A pancreatic pseudocyst is commonly round or oval, but some may be multilocular and irregular in shape [71]. The size of pseudocysts varies from 2 to 35 cm [12, 13, 15, 95, 96]. Estimated volumes range between 10 and 6,000 mL [6, 97, 98]. In the material

collected from all 253 patients with pancreatic pseudocysts at the University Hospital in Galveston, Texas from 1985 to 2001 the mean diameter of the pseudocysts in the 103 patients with chronic pancreatitis was 9 ± 1 cm [58].

A case of pancreas divisum associated with a giant retention cyst (cystic dilatation of the dorsal pancreatic duct), presumably formed following the obstruction of the minor papilla has also been described. Computed tomography and ultrasound examinations revealed a giant cystic lesion expanding from the pancreatic head to the tail. Endoscopic retrograde cholangiopancreatography findings showed a looping pancreatic duct which drained only the head and uncinate process of the pancreas to the main papilla. An ultrasound-guided puncture to the cystic lesion revealed that the lesion continued to the main pancreatic duct in the tail of pancreas. The amylase level in liquid aspirated from the cyst was 37,869 IU/L [99].

The cyst contents have been thoroughly studied. The fluid may be clear and watery or xanthochromic or brown because of old blood and necrotic tissue. The amylase, lipase, and trypsin contents are usually markedly elevated, and it is exceptional to find amylase levels lower than serum levels [100]. The amylase level may decrease in some older pseudocysts. It is hypothesized that the cyst may have lost its communication with the duct system coupled with the possibility that the fluid in the cyst exchanges with the plasma. The aforementioned mechanism also explains the spontaneous disappearance of small cysts [6].

Bacterial cultures of cyst fluid are usually positive in 20-50% of patients cultured [9, 74, 78, 101, 102]. However, these figures probably overestimate the incidence of positive bacterial growth inasmuch as patient selection is rarely random. Not all specimens of pseudocyst fluid have been cultured; in some series, only cloudy or grossly purulent fluids were checked. It is not clear from the

available information whether all patients with positive cultures had a clinical course suggesting sepsis or abscess [103].

Concluding remarks

For the evaluation of different options in the diagnosis and treatment of pancreatic pseudocysts, it is of utmost importance to note that acute and chronic pseudocysts have different properties. The terms acute and chronic with regard to pseudocysts are used differently than they are in other medical conditions. An acute pseudocyst arises as a consequence of acute pancreatitis or pancreatic trauma, whereas a chronic pseudocyst arises as a consequence of chronic pancreatitis and lacks an antecedent episode of acute pancreatitis.

Knowledge of the etiology and ductal anatomy may be important for the treatment of choice and should be evaluated in each case.

Correspondence
Åke Andrén-Sandberg
Department of Gastrointestinal Surgery
Sentralsjukehuset i Rogaland
4069 Stavanger
Norway
Phone: +30-210.277.5467
Fax: +30-210.277.3969
E-mail: ake.andren-sandberg@chsa.med.gu.se

References

1. Kloppel G. Pseudocysts and other non-neoplastic cysts of the pancreas. Semin Diagn Pathol 2000; 17:7-15. [PMID 10721803]

2. Richter HM. Natural history of pancreatic pseudocysts. In: Howard J, Idezuki Y, Ihse I, Prinz R, eds. Surgical diseases of the Pancreas. Baltimore: Williams and Wilkins, 1998:417-21.

3. Breslin N, Wallace MB. Diagnosis and fine needle aspiration of pancreatic pseudocysts: the role of endoscopic ultrasound. Gastrointest Endosc Clin N Am 2002; 12:781-90. [PMID 12607787]

4. Bradley EL 3rd. A clinically based classification system for acute pancreatitis. Arch Surg 1993; 128:586-90. [PMID 8489394]

5. Bradley EL Jr, Gonzalez AC, Clements JL Jr. Acute pancreatic pseudocysts: incidence and implications. Ann Surg 1976; 184:734-7. [PMID 999349]

6. Pitchumoni CS, Agarwal N. Pancreatic pseudocysts. When and how should drainage be performed? Gastroenterol Clin North Am 1999; 28:615-39. [PMID 10503140]

7. Yeo CJ, Sarr MG. Cystic and pseudocystic diseases of the pancreas. Curr Probl Surg 1994; 31:165-243. [PMID 8168359]

8. Bosman-Vermeeren JM, Veereman-Wauters G, Broos P, Eggermont E. Somatostatin in the treatment of a pancreatic pseudocyst in a child. J Pediatr Gastroenterol Nutr 1996; 23:422-5. [PMID 8956180]

9. O'Malley VP, Cannon JP, Postier RG. Pancreatic pseudocysts: cause, therapy, and results. Am J Surg 1985; 150:680-2. [PMID 3907380]

10. Kolars JC, Allen MO, Ansel H, Silvis SE, Vennes JA. Pancreatic pseudocysts: clinical and endoscopic experience. Am J Gastroenterol 1989; 84:259-64. [PMID 2919583]

11. Walt AJ, Bouwman DL, Weaver DW, Sachs RJ. The impact of technology on the management of pancreatic pseudocyst. Fifth annual Samuel Jason Mixter Lecture. Arch Surg 1990; 125:759-63. [PMID 2189377]

12. D'Egidio A, Schein M. Pancreatic pseudocysts: a proposed classification and its management implications. Br J Surg 1991; 78:981-4. [PMID 1913122]

13. Bourliere M, Sarles H. Pancreatic cysts and pseudocysts associated with acute and chronic pancreatitis. Dig Dis Sci 1989; 34:343-8. [PMID 2646086]

14. Kiviluoto T, Kivisaari L, Kivilaakso E, Lempinen M. Pseudocysts in chronic pancreatitis. Surgical results in 102 consecutive patients. Arch Surg 1989; 124:240-3. [PMID 2916944]

15. Usatoff V, Brancatisano R, Williamson RC. Operative treatment of pseudocysts in patients with

chronic pancreatitis. Br J Surg 2000; 87:1494-9. [PMID 11091235]

16. Sarles H, Muratore R, Sarles JC. Etude anatomique des pancreatites chroniques de l'adulte. Sem Hop 1961; 25:1507-22. [PMID 13746538]

17. Sarles H, Martin M, Camatte R, Sarles JC. Le demembrement des pancreatities: Les pseudokystes des pancreatiles aigues et des pancreatites chroniques. Press Med 1963; 5:237-40. [PMID 13986552]

18. Grace PA, Williamson RC. Modern management of pancreatic pseudocysts. Br J Surg 1993; 80:573-81. [PMID 8518891]

19. Neoptolemos JP, London NJ, Carr-Locke DL. Assessment of main pancreatic duct integrity by endoscopic retrograde pancreatography in patients with acute pancreatitis. Br J Surg 1993; 80:94-9. [PMID 8428306]

20. Nealon WH, Walser E. Main pancreatic ductal anatomy can direct choice of modality for treating pancreatic pseudocysts (surgery versus percutaneous drainage). Ann Surg 2002; 235:751-8. [PMID 12035030]

21. Baron TH, Thaggard WG, Morgan DE, Stanley RJ. Endoscopic therapy of organized pancreatic necrosis. Gastroenteroly 1996; 111:755-64. [PMID 8780582]

22. Lee MJ, Rattner DW, Legemate DA, Saini S, Dawson SL, Hahn PF, et al. Acute complicated pancreatitis: redefining the role of interventional radiology. Radiology 1992; 183:171-4. [PMID 1549667]

23. Hariri M, Slivka A, Carr-Locke DL, Banks PA. Pseudocyst drainage predisposes to infection when pancreatic necrosis is unrecognized. Am J Gastroenterol 1994; 89:1781-4. [PMID 7942666]

24. Spivak H, Galloway JR, Amerson JR, Fink AS, Branum GD, Redvanly RD, et al. Management of pancreatic pseudocysts. J Am Coll Surg 1998; 186:507-11. [PMID 9583690]

25. Becker WF, Pratt HS, Ganji H. Pseudocysts of the pancreas. Surg Gynecol Obstet 1968; 127:744-7. [PMID 5302683]

26. Rosenberg IK, Kahn JA, Walt AJ. Surgical experience with pancreatic pseudocysts. Am J Surg 1969; 117:11-7. [PMID 5782744]

27. Trapnell J. Management of the complications of acute pancreatitis. Ann R Coll Surg Engl 1971; 49:361-72. [PMID 5137573]

28. Elechi EN, Callender CO, Leffall LD Jr, Kurtz LH. The treatment of pancreatic pseudocysts by external drainage. Surg Gynecol Obstet 1979; 148:707-10. [PMID 432782]

29. Bodker A, Kjaergaard J, Schmidt A, Tilma A. Pancreatic pseudocysts. A follow-up study. Ann Surg 1981; 194:80-4. [PMID 7247537]

30. Shetty AN. Pseudocysts of the pancreas: an overview. South Med J 1980; 73:1239-42. [PMID 7414385]

31. Sandy JT, Taylor RH, Christensen RM, Scudamore C, Leckie P. Pancreatic pseudocyst. Changing concepts in management. Am J Surg 1981; 141:574-6. [PMID 7223950]

32. Wade JW. Twenty-five year experience with pancreatic pseudocysts. Are we making progress? Am J Surg 1985; 149:705-8. [PMID 3925799]

33. London NJ, Neoptolemos JP, Lavelle J, Bailey I, James D. Serial computed tomography scanning in acute pancreatitis: a prospective study. Gut 1989; 30:397-403. [PMID 2651228]

34. Kourtesis G, Wilson SE, Williams RA. The clinical significance of fluid collections in acute pancreatitis. Am Surg 1990; 56:796-9. [PMID 2268109]

35. Andersson R, Andren-Sandberg A. Fatal acute pancreatitis. Characteristics of patients never reaching hospital. Pancreatology 2003; 3:64-6. [PMID 12649566]

36. Nealon WH, Townsend CM Jr, Thompson JC. Preoperative endoscopic retrograde cholangiopancreatography (ERCP) in patients with pancreatic pseudocyst associated with resolving acute and chronic pancreatitis. Ann Surg 1989; 209:532-40. [PMID 2705818]

37. Imrie CW, Buist LJ, Shearer MG. Importance of cause in the outcome of pancreatic pseudocysts. Am J Surg 1988; 156 (3 Pt 1):159-62. [PMID 2458684]

38. London NJ, Neoptolemos JP, Lavelle J, Bailey I, James D. Serial computed tomography scanning in acute pancreatitis: a prospective study. Gut 1989; 30:397-403. [PMID 2651228]

39. Maringhini A, Uomo G, Patti R, Rabitti P, Termini A, Cavallera A, et al. Pseudocysts in acute nonalcoholic pancreatitis: incidence and natural history. Dig Dis Sci 1999; 44:1669-73. [PMID 10492151]

40. Bumpers HL, Bradley EL. Treatment of pancreatic pseudocysts. In: Howard J, Idezuki Y, Ihse I, Prinz R, eds. Surgical diseases of the Pancreas. Baltimore: Williams and Wilkins, 1998:423-32.

41. Barthet M, Bugallo M, Moreira LS, Bastid C, Sastre B, Sahel J. Management of cysts and pseudocysts complicating chronic pancreatitis. A retrospective study of 143 patients. Gastroenterol Clin Biol 1993; 17:270-6. [PMID 8339886]

42. Ammann RW, Akovbiantz A, Largiader F, Schueler G. Course and outcome of chronic pancreatitis. Longitudinal study of a mixed medical-surgical series of 245 patients. Gastroenterology 1984; 86 (5 Pt 1):820-8. [PMID 6706066]

43. Elliott DW. Pancreatic pseudocysts. Surg Clin North Am 1975; 55:339-62. [PMID 1093266]

44. Imrie CW. Epidemiology clinical presentation and behavior of acute pseudocysts. In: Bradley EL, ed. Acute Pancreatitis Diagnosis and Therapy. New York: Raven Press, 1994:175-9.

45. Kloppel G, Maillet B. Pseudocysts in chronic pancreatitis: a morphological analysis of 57 resection specimens and 9 autopsy pancreata. Pancreas 1991; 6:266-74. [PMID 1862065]

46. Maule WF, Reber HA. Diagnosis and management of pancreatic pseudocysts, pancreatic ascites, and pancreatic fistulas. In: The exocrine pancreas: biology, pathobiology, and diseases. Go VLW, Gardner JD, Brooks FP, Lebenthal E, DiMagno EP, Scheele GA, eds. New York: Raven Press, 1986:601-10.

47. Simpson A, Srivastava VK. Pseudocyst of the pancreas. Br J Surg 1973; 60:45-9. [PMID 4685919]

48. Eisenberger CF, Kropp A, Langwieler TE, Gocht A, Izbicki JR, Knoefel WT. Heterotopic pancreatitis: gastric outlet obstruction due to an intramural pseudocyst and hamartoma. Z Gastroenterol 2002; 40:259-62. [PMID 11961736]

49. Siegelman SS, Copeland BE, Saba GP, Cameron JL, Sanders RC, Zerhouni EA. CT of fluid collections associated with pancreatitis. AJR Am J Roentgenol 1980; 134:1121-32. [PMID 6770619]

50. Ranson JH, Balthazar E, Caccavale R, Cooper M. Computed tomography and the prediction of pancreatic abscess in acute pancreatitis. Ann Surg 1985; 201:656-65. [PMID 3994437]

51. Barthet M, Bugallo M, Moreira LS, Bastid C, Sastre B, Sahel J. Treatment of pseudocysts in acute pancreatitis. Retrospective study of 45 patients. Gastroenterol Clin Biol 1992; 16:853-9 (in French). [PMID 1483554]

52. Traverso LW, Kozarek RA. Interventional management of peripancreatic fluid collections. Surg Clin North Am 1999; 79:745-57. [PMID 10470324]

53. Karantanas AH, Sandris V, Tsikrika A, Karakousis K, Karaiskou E. Extension of pancreatic pseudocysts into the neck: CT and MR imaging findings. AJR Am J Roentgenol 2003; 180:843-5. [PMID 12591707]

54. Traverso LW, Newman RM, Kozarek RA. The management of pancreatic ductal disruptions leading to pancreatic fistula, pancreatic ascites, or pleural effusion. In: Cameron JL, ed: Current Surgical Therapy, ed. 6. Philadelphia: Mosby-Year Book, 1998:510-4.

55. Traverso LW, Kozarek RA. Pancreatoduodenectomy for chronic pancreatitis: anatomic selection criteria and subsequent long-term outcome analysis. Ann Surg 1997; 226:429-35. [PMID 9351711]

56. Longmire WP, Rochlin DB. Malignant neoplasms of the pancreas and the small intestine. Proc Natl Cancer Conf 1960; 4: 435-51.

57. Kuroda A, Nagai H. Surgical anatomy of the pancreas. In: Howard J, Idezuki Y, Ihse I, Prinz R, eds. Surgical diseases of the Pancreas. Baltimore: Williams and Wilkins, 1998:13.

58. Adams DB, Srinivasan A. Failure of percutaneous catheter drainage of pancreatic pseudocysts. Am Surg 2000; 66:256-61. [PMID 10759195]

59. Nealon WH, Walser E. Duct drainage alone is sufficient in the operative management of pancreatic pseudocyst in patients with chronic pancreatitis. Ann Surg 2003; 237:614-22. [PMID 12724627]

60. Desa LA, Williamson RC. On-table pancreatography: importance in planning operative strategy. Br J Surg 1990; 77:1145-50. [PMID 2224464]

61. Binmoeller KF, Seifert H, Walter A, Soehendra N. Transpapillary and transmural drainage of pancreatic pseudocysts. Gastrointest Endosc 1995; 42:219-24. [PMID 7498686]

62. Sahel J, Bastid C, Pellat B, Schurgers P, Sarles H. Endoscopic cystoduodenostomy of cysts of chronic calcifying pancreatitis: a report of 20 cases. Pancreas 1987; 2 :447-53. [PMID 3628239]

63. O'Connor M, Kolars J, Ansel H, Silvis S, Vennes J. Preoperative endoscopic retrograde cholangiopancreatography in the surgical management of pancreatic pseudocysts. Am J Surg 1986; 151: 18-24. [PMID 3946746]

64. Laxson LC, Fromkes JJ, Cooperman M. Endoscopic retrograde cholangiopancreatography in the management of pancreatic pseudocysts. Am J Surg 1985; 150: 683-6. [PMID 3907381]

65. Frey CF. Pancreatic pseudocyst – operative strategy. Ann Surg 1978; 188: 652-62. [PMID 309751]

66. Shan YS, Sy ED, Tsai HM, Liou CS, Lin PW. Nonsurgical management of main pancreatic duct transection associated with pseudocyst after blunt abdominal injury. Pancreas 2002; 25: 210-3. [PMID 12142748]

67. Northrup WF 3rd, Simmons RL. Pancreatic trauma:a review. Surgery 1972; 71:27-43. [PMID 4550235]

68. Vane DW, Grosfeld JL, West KW, Rescorla FJ. Pancreatic disorders in infancy and childhood: experience with 92 cases. J Pediatr Surg 1989; 24:771-6. [PMID 2769544]

69. Florio G, Cicia S, Del Papa M, Carni D. Pancreatic pseudocyst caused by extracorporeal shock wave lithotripsy for right renal pelvic calculi. Chir Ital 2003; 55:279-82. [PMID 12744107]

70. Lack EE. Pancreatitis. In: Lack EE. Pathology of the pancreas, gallbladder, extrahepatic biliary tract, and ampullary region. Oxford: Oxford University Press, 2003:81-117.

71. Rogers JB, Pearce AE, Howard JM. "Blue-dome" pseudocyst of the pancreas. Am J Surg 1970; 120:813-4. [PMID 5488340]

72. van Heerden JA, ReMine WH. Pseudocysts of the pancreas. Review of 71 cases. Arch Surg 1975; 110:500-5. [PMID 1130994]

73. Shatney CH, Lillehei RC. Surgical treatment of pancreatic pseudocysts. Analysis of 119 cases. Ann Surg 1979; 189:386-94. [PMID 443893]

74. Sankaran S, Walt AJ. The natural and unnatural history of pancreatic pseudocysts. Br J Surg 1975; 62:37-44. [PMID 1111673]

75. Bradley EL 3rd, Austin H. Multiple pancreatic pseudocysts: the principle of internal cystocystostomy in surgical management. Surgery 1982; 92:111-6. [PMID 7089862]

76. Aranha GV, Prinz RA, Freeark RJ, Kruss DM, Greenlee HB. Evaluation of therapeutic options for pancreatic pseudocysts. Arch Surg 1982; 117:717-21. [PMID 7073495]

77. Aranha GV, Prinz RA, Esguerra AC, Greenlee HB. The nature and course of cystic pancreatic lesions diagnosed by ultrasound. Arch Surg 1983; 118:486-8. [PMID 6830440]

78. Goulet RJ, Goodman J, Schaffer R, Dallemand S, Andersen DK. Multiple pancreatic pseudocyst disease. Ann Surg 1984; 199:6-13. [PMID 6691732]

79. Henriksen FW, Hancke S. Percutaneous cystogastrostomy for chronic pancreatic pseudocyst. Br J Surg 1994; 81:1525-8. [PMID 7820494]

80. Ng B, Murray B, Hingston G, Windsor JA. An audit of pancreatic pseudocyst management and the role of endoscopic pancreatography. Aust N Z J Surg 1998; 68:847-51. [PMID 9885866]

81. Fedorak IJ, Rao R, Prinz RA. The clinical challenge of multiple pancreatic pseudocysts. Am J Surg 1994; 168:22-8. [PMID 7517648]

82. Nguyen BL, Thompson JS, Edney JA, Bragg LE, Rikkers LF. Influence of the etiology of pancreatitis on the natural history of pancreatic pseudocysts. Am J Surg 1991; 162:527-31. [PMID 1670219]

83. Steer ML. Classification and pathogenesis of pancreatitis. Surg Clin North Am 1989; 69:467-80. [PMID 2658159]

84. Harvey MH, Cates MC, Reber HA. Possible mechanisms of acute pancreatitis induced by ethanol. Am J Surg 1988; 155:49-56. [PMID 3341538]

85. Bradley EL 3rd. Cystoduodenostomy. New perspectives. Ann Surg 1984; 200:698-701. [PMID 6508397]

86. Sanfey H, Aguilar M, Jones RS. Pseudocysts of the pancreas: a review of 97 cases. Am Surg 1994; 60:661-8. [PMID 8060036]

87. Adams DB, Anderson MC. Percutaneous catheter drainage compared with internal drainage in the management of pancreatic pseudocyst. Ann Surg 1992; 6:571-8. [PMID 1632678]

88. Gouyon B, Levy P, Ruszniewski P, Zins M, Hammel P, Vilgrain V, Sauvanet A, Belghiti J, Bernades P. Predictive factors in the outcome of pseudocysts complicating alcoholic chronic pancreatitis. Gut 1997; 41:821-5. [PMID 9462217]

89. Christensen NM, Demling R, Mathewson C. Unusual manifestation of pancreatic pseudocysts and their surgical management. Am J Surg 1975; 130:199-205. [PMID 1080364]

90. Galligan JJ, Williams HJ. Pancreatic pseudocysts in childhood. Unusual case with mediastinal extension. Am J Dis Child 1966; 112:479-82. [PMID 5917985]

91. Edell SL, Good LI. Mediastinal pancreatic pseudocyst. An ultrasonic diagnosis. Am J Gastroenterol 1979; 71:78-82. [PMID 433893]

92. Crombleholme TM, deLorimier AA, Adzick NS, Longaker MT, Harrison MR, Cox KL, Heyman MB. Mediastinal pancreatic pseudocysts in children. J Pediatr Surg 1990; 25:843-5. [PMID 1698218]

93. Colarian JH, Sekkarie M, Rao R. Pancreatic pseudocyst mimicking idiopathic achalasia. Am J Gastroenterol 1998; 93:103-5. [PMID 9448185]

94. Geier A, Lammert F, Gartung C, Nguyen HN, Wildberger JE, Matern S. Magnetic resonance imaging and magnetic resonance cholangiopancreaticography for diagnosis and pre-interventional evaluation of a fluid thoracic mass. Eur J Gastroenterol Hepatol 2003; 15:429-31. [PMID 12655266]

95. Grosso M, Gandini G, Cassinis MC, Regge D, Righi D, Rossi P. Percutaneous treatment (including pseudocystogastrostomy) of 74 pancreatic pseudocysts. Radiology 1989; 173:493-7. [PMID 2798881]

96. Froeschle G, Meyer-Pannwitt U, Brueckner M, Henne-Bruns D. A comparison between surgical, endoscopic and percutaneous management of pancreatic pseudocysts – long term results. Acta Chir Belg 1993; 93:102-6. [PMID 8372580]

97. Barkin JS, Smith FR, Pereiras R, Isikoff M, Levi J, Livingstone A, Hill M, Rogers AI. Therapeutic

percutaneous aspiration of pancreatic pseudocysts. Dig Dis Sci 1981; 26:585-6. [PMID 7249891]

98. Andersson R, Janzon M, Sundberg I, Bengmark S. Management of pancreatic pseudocysts. Br J Surg 1989; 76:550-2. [PMID 2667688]

99. Morise Z, Yamafuji K, Tsuji T, Asami A, Takeshima K, Hayashi N, et al. A giant retention cyst of the pancreas (cystic dilatation of dorsal pancreatic duct) associated with pancreas divisum. J Gastroenterol 2002; 37:1079-82. [PMID 12522543]

100. Sand JA, Hyoty MK, Mattila J, Dagorn JC, Nordback IH. Clinical assessment compared with cyst fluid analysis in the differential diagnosis of cystic lesions in the pancreas. Surgery 1996; 119:275-80. [PMID 8619182]

101. Warshaw AL, Rattner DW. Timing of surgical drainage for pancreatic pseudocyst. Clinical and chemical criteria. Ann Surg 1985; 202:720-4. [PMID 4073984]

102. Mullins RJ, Malangoni MA, Bergamini TM, Casey JM, Richardson JD. Controversies in the management of pancreatic pseudocysts. Am J Surg 1988; 155:165-72. [PMID 3341530]

103. Kane MG, Guenter JK. Pancreatic pseudocyst. Adv Intern Med 1984; 29:271-300. [PMID 6369928]