

# Diagnosis of Chronic Pancreatitis

Christoph Beglinger

Department of Gastroenterology and Hepatology, University Hospital Basel, Basel, Switzerland

## Key Words

Chronic pancreatitis · Pancreas irregularities · Pancreatic insufficiency · Steatorrhea · Imaging procedures · Function tests

## Abstract

The diagnosis of chronic pancreatitis is based on a typical history with recurrent flares of acute inflammation, imaging procedures and some laboratory tests. Using imaging procedures (abdominal ultrasound, computed tomography or magnetic resonance imaging), a diagnosis can only be made when alterations in size (enlargement or atrophy) or shape of the pancreas or changes in intrapancreatic structure (dilation, obstruction of ducts), calcifications, or changes in peripancreatic organs have occurred. Tests of exocrine pancreatic function are not essential for making a diagnosis of chronic pancreatitis.

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## Introduction

Chronic pancreatitis is a chronic inflammatory process leading to irreversible destruction of exocrine and endocrine tissue and fibrosis [1–9]. In chronic pancreati-

tis, acini are gradually destroyed and substituted by fibrotic tissue. The histopathologic changes consist mainly of irregularly distributed fibrosis, reduced number of acini and islets of Langerhans, and variable changes and obstruction of pancreatic ducts of all sizes. The duct system may show strictures, intraductal plugs and calcifications. The irreversible structural changes can be visualized years before any clinical manifestation of chronic pancreatitis is present. The principal clinical events in the course of chronic pancreatitis are episodes of acute pancreatitis, with acute inflammation superimposed on an irreversibly damaged organ [10–15].

## Pain

Pain is the main symptom of chronic pancreatitis [1, 3, 16]. The events that trigger pain in chronic pancreatitis are poorly understood. Pain is described as a constant epigastric pain, often radiating to the back. Sometimes pain is associated with nausea and vomiting. At the beginning of the disease, patients report very little pain, especially in the initial stages of chronic, alcoholic pancreatitis. Over time, pain episodes are more frequent and of longer duration; finally, constant pain can develop. Food intake increases or provokes pain; this can lead to

**Table 1.** Typical symptoms and findings in chronic pancreatitis

Symptom/finding	Prevalence, %
Pain	80–98
Weight loss	5–85
Diabetes mellitus	50–60
Steatorrhea	30–40
Icterus	20–25

weight loss and malnutrition as patients under these circumstances have a tendency to avoid regular meal intake. The principal symptoms and findings are listed in table 1.

### Pancreatic Insufficiency

10–20% of pain-free patients with chronic pancreatitis suffer from exocrine and endocrine pancreatic insufficiency [1, 17–19]. The classical combination of steatorrhea, diabetes mellitus and pancreatic calcifications is found in less than one third of patients at the time of diagnosis. Weight loss is common during the course of the disease. Malabsorption is one of several important causes for it. As mentioned before, many patients limit their food intake because of pain during eating. Patients with severe exocrine pancreatic insufficiency are unable to adequately digest food (maldigestion). Fat hydrolysis is more affected than protein or carbohydrate digestion, because lipase secretion decreases more rapidly than the secretion of proteolytic enzymes. Steatorrhea therefore precedes the development of protein malabsorption. When patients attempt to compensate for malabsorption by over-eating, increased fat intake leads to increased gastrointestinal symptoms such as bloating, abdominal cramps, flatulence [20]. In view of the intact absorptive capacity and enterohepatic circulation of bile salts, malabsorption of vitamins (A, D, E, K), calcium and iron is uncommon in patients with chronic pancreatitis (this is in contrast to patients with untreated celiac disease). About 40% of patients with severe exocrine pancreatic insufficiency have a vitamin B<sub>12</sub> malabsorption, but a clinically relevant deficiency in vitamin B<sub>12</sub> or fat-soluble vitamins is rare [20, 21].

### Glucose Intolerance and Diabetes Mellitus

Patients with chronic pancreatitis often develop glucose intolerance, but overt diabetes mellitus is a late symptom during the course of the disease, typically 20 years after the beginning of the disease. An endocrine insufficiency develops with the progression of the destruction of the organ in about 60% of patients [9]. Most of them develop an insulin-dependent diabetes mellitus, which can be aggravated by a decrease in glucagon secretion. The concomitant maldigestion and the continuing alcohol consumption increase the risk of an islet cell insufficiency with the potential risk of spontaneous hypoglycemia. The treatment of diabetes mellitus in chronic pancreatitis can be difficult, but severe diabetic ketoacidosis is rare.

### Diagnosis

The diagnosis of chronic pancreatitis is in general not difficult: a typical medical history with recurrent attacks of acute pancreatitis, an imaging procedure (ultrasound, computed tomography – CT scan, or endoscopic retrograde cholangiopancreatography – ERCP/magnetic resonance cholangiopancreatography – MRCP) with typical radiologic features of chronic pancreatitis. Additionally, exocrine and endocrine pancreatic function tests can be performed in selected cases. Serum concentrations of pancreatic enzymes (amylase and lipase) are increased during acute attacks, but they are normal in the intervals. In progressive disease state serum concentrations of pancreatic enzymes can be normal even during acute flares [1, 14]. The absolute increase in amylase or lipase concentration does not predict the outcome. An increase in alkaline phosphatase and/or  $\gamma$ -glutamyl-transferase concentrations or in bilirubin in the interval without clinical evidence of an acute flare-up suggests a common bile duct obstruction. The intrapancreatic portion of the common bile duct is obstructed in 5–20% of persons with chronic pancreatitis, but not all of them require a therapeutic intervention [22, 23]. Stenosis of the common bile duct and extrinsic compression of the duct system are possible causes of these findings.

### Imaging Procedures

In about 30% of patients with chronic pancreatitis, a plain abdominal radiograph reveals diffuse or focal pancreatic calcifications. Calcifications are primarily seen in patients with alcoholic or tropical pancreatitis, but they



**Fig. 1.** Plain abdominal X-ray in a patient with chronic pancreatitis; typical calcifications.

are less common in hereditary idiopathic pancreatitis. A typical example of pancreatic calcifications on a plain abdominal radiograph is depicted in figure 1.

**Ultrasonography/CT Scan.** Ultrasonography and CT scan of the abdomen have markedly changed the evaluation of patients with chronic pancreatitis [1, 14, 15]. Thanks to these techniques, focal and diffuse irregularities of the pancreas, dilation of the main pancreatic duct, or calcifications can be observed. CT has been shown to be superior to ultrasonography, for example in detecting pseudocysts. In the presence of overlying gas, ultrasonography is insufficient for visualization of the entire pancreas. The sensitivity and specificity of abdominal ultrasound in detecting pathological changes of the organ is around 60–70 and 80–90%, respectively. CT has a superior sensitivity (>90%) with a similar specificity.

**Endoscopic Ultrasonography.** The indications for endoscopic ultrasonography (EUS) at this stage are: early identification of chronic pancreatitis, differentiation of inflammatory processes from malignant developments, and fine needle aspirations for pathological assessment of suspected lesions [24, 25]. EUS requires high skills and expertise, but can achieve high sensitivity (>90%) with a similar specificity (with an especially high negative pre-



**Fig. 2.** ERCP in a patient with chronic pancreatitis; typical ductal changes; the main pancreatic duct is dilated.

dictive value). As mentioned before, the method is dependent on the skills and expertise of the investigator [26]. EUS-guided fine needle aspiration has become an important diagnostic procedure in the diagnosis of unclear masses of the pancreas [27].

**Endoscopic Retrograde Cholangiopancreatography.** ERCP is no longer essential in the diagnosis of chronic pancreatitis, but still has its place in the management and therapy of patients with pancreatic disease [6, 28, 29]. The average normal diameters of the pancreatic duct are <4, <3 and <2 mm in the head, the body and the tail of the pancreas, respectively. According to the Cambridge Classification, ductal changes are described as possible (Cambridge I), mild to moderate (Cambridge II) or severe (Cambridge III) [1, 6, 30]. The correlation of these duct changes with CT is best in severe cases. In advanced chronic pancreatitis, the main pancreatic duct is dilated [31]. A typical example is given in figure 2. ERCP permits the identification of potentially surgically correctable lesions (strictures, cysts). Complications of ERCP include triggering acute pancreatitis and cholangitis, especially in patients with preexisting obstructive jaundice [29, 32].

**Magnetic Resonance Cholangiopancreatography.** MRCP has been developed into an excellent imaging procedure which is able to document small structural changes in the visceral organs of the abdomen including the liver, bile ducts and pancreas. Several randomized comparative investigations have shown that MRCP imaging is equal to ERCP for diagnosing ductal changes in the biliary tract and the pancreas [33, 34]. MRCP is, however,

a noninvasive procedure without a risk for acute pancreatitis compared to diagnostic ERCP. MRCP has therefore become the imaging procedure of choice for diagnostic workup of duct abnormalities of the pancreas. The procedure can be improved by intravenous secretin, which acts as a natural contrast agent [35, 36].

#### *Functional Assessment of Exocrine Pancreatic Secretion*

Exocrine pancreatic insufficiency is best quantified by stool fat analysis or by direct assessment of exocrine pancreatic secretion by duodenal intubation and quantification of pancreatic bicarbonate and/or enzyme responses in response to hormonal stimulation. The procedures are cumbersome; more important pathological results can only be obtained in advanced stages of exocrine pancreatic insufficiency. At this stage of disease, the tests are only necessary in selected cases.

*Fat Malabsorption.* Steatorrhea can be visualized by microscopy using Sudan stain test or by quantitative stool fat analysis (sensitivity and specificity is only acceptable at advanced stages of exocrine pancreatic insufficiency, when the gland is destroyed by >80%). Quantitative stool fat analysis is the gold standard for diagnosing malabsorption. The procedure entails a 72-hour stool collection with a standardized 100 g fat diet per day. The normal fat excretion is <7 g fat/24 h; patients with severe exocrine pancreatic insufficiency can have >30 g fat/24 h.

*Intubation Tests with Direct Assessment of Exocrine Pancreatic Secretion.* Direct stimulation of exocrine pancreatic secretion is the best method for assessment of pancreatic function. The exocrine pancreas is stimulated with secretin alone or in combination with cholecystikinin [37]. The secretin-stimulated function test is probably

the most sensitive procedure for the assessment of the exocrine pancreatic function. Nevertheless, more than 60% of the function has to be destroyed in order to produce a pathological test result. The test procedure is time-consuming and unpleasant for the patient; furthermore, the procedure has been difficult to standardize. The secretin-stimulated function test has lost its clinical importance and is only done at selected centers, mainly for research purposes. A simplified test procedure has recently been published: the duodenal juice before and after secretin stimulation is collected during a routine upper endoscopy [38, 39]. The accuracy of the endoscopic pancreatic function tests is similar to duodenal intubation. There were minimal differences in bicarbonate at each of the timed collections and at peak with an excellent correlation in peak  $\text{HCO}_3^-$  and a high level of diagnostic agreement between the tests. The method simplifies the test procedure, but its value remains limited.

*Indirect Assessment of Exocrine Pancreatic Function.* An alternative approach to the complicated intubation test for the assessment of exocrine pancreatic function is the measurement of stool elastase (sensitivity about 80%). The disadvantage of all indirect tests is that they have sufficient sensitivity only in the presence of moderate to severe pancreatic insufficiency. However, in many places, the assessment of stool elastase has established itself as the easiest test procedure [40].

#### **Disclosure Statement**

The author declares that no financial or other conflict of interest exists in relation to the content of the article.

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