A broad spectrum of parameters have been suggested for the diagnosis and severity stratification of acute pancreatitis and can be classified into activated pancreas- and leukocyte-derived proteases, cytokines, chemokines, and acute-phase reactants. An ideal biochemical parameter for acute pancreatitis should be disease-specific, reliably predict the development of necrosis and/or organ failure during the early stage, and accurately indicate pancreatic infections within the later course of the disease. Currently, there is no single biochemical variable that meets all of these demands; however, there are several useful markers for diagnostic and prognostic purposes.

The diagnosis of acute pancreatitis still relies on the measurement of systemic amylase or lipase concentrations, which remain the “gold standard” despite the recent discovery of several more pancreas-specific enzymes. For an early severity stratification of acute pancreatitis into mild and severe forms within 48 h of symptom onset trypsinogen activation peptide (TAP), carboxypeptidase B activation peptide (CAPAP), polymorphonuclear (PMN)-elastase, serum amyloid A protein (SAA), interleukin (IL)-6, and IL-8 have proven to be good candidates. Because fully automated assays have become available IL-6, IL-8, SAA, and PMN-elastase are interesting parameters in this respect.

Severity stratification beyond 48 h after the onset of symptoms as well as monitoring the course of acute pancreatitis is still the major domain of the acute-phase proteins. C-reactive protein (CRP) is the parameter of choice for the differentiation of mild from severe acute pancreatitis as well as for monitoring purposes due to its fast and widespread availability at low cost. Whereas the development of pancreatic infections or prognosis in terms of nonsurvival can not be reliably predicted by any of the acute-phase proteins or cytokines, procalcitonin (PCT) has emerged as the most promising variable in this setting, followed by IL-8, which is a good candidate to monitor evolving septic multiorgan failure. PCT and IL-8 determinations are available as fully automated tests, thus problems with the assay practicability are no longer a point of issue.

**Background**

During the past decade, major advances in our understanding of the natural history of acute pancreatitis with identification of relevant prognostic factors [1–3] have driven its management toward conservative intensive care, with a marked reduction of aggressive surgical approaches. Hence, it has been well recognized that immediate and goal-directed treatment considerably influences the course and outcome of this disease [4]. Therefore, early and reliable diagnosis of the disease itself and subsequent complications requiring specific intervention are central issues for clinicians. Since their introduction in the 1980s, contrast-enhanced computed tomography (CE-CT) and guided fine-needle-aspiration (FNA) have become indispensable for diagnosing local complications such as pancreatic necrosis and infection, and still represent cornerstones for morphology-based severity stratification and management alike. However, despite being highly accurate, neither CE-CT nor FNA are universally available, they carry the risk of potential complications, and they constitute considerable cost factors.

The era of laboratory markers in acute pancreatitis found its beginnings after the introduction of serum amylase measurements by Elman et al. in 1929, which for the first time enabled a noninvasive diagnosis of acute pancreatitis [5]. This laboratory test profoundly improved the knowledge about the natural course of the disease since it became evident that a mild course with uneventful recovery was the rule rather than the exception, yet severity stratification or assessment of specific complications was not possible. In his hallmark paper published almost four decades later Trapnell et al. provided the first evidence that acute pancreatitis is reflected by abnormalities of many serum/plasma variables [6]. During the subsequent
years, much effort has been made in the search for biochemical parameters that allow an early stratification of patients at risk to develop complications such as necrosis, septic complications, or organ failure. Although a still increasing array of potentially useful parameters is currently available, their large-scale clinical use is often limited by time-consuming and expensive assay procedures. In this chapter, the most important biochemical markers for the diagnosis and severity stratification of acute pancreatitis are discussed.

Biochemical Diagnosis of Acute Pancreatitis

The diagnosis of acute pancreatitis relies on the determination of increased pancreatic enzymes in patients with acute abdominal pain along with specific changes in imaging procedures. However, some patients with acute pancreatitis do not present with the typical clinical picture of sudden-onset upper abdominal pain and the disease is not considered in the differential diagnosis [7, 8]. Clinically suspected acute pancreatitis is usually first diagnosed by the determination of increased pancreatic enzymes in the systemic circulation, whereas urinary enzymes have shown no advantage in this respect [9–13]. A host of serum enzymes such as serum amylase and lipase, amylase isoenzymes, trypsinogen-2, pancreatic elastase-1 (P-elastase-1), phospholipase A2 (PLA2), or procarboxypeptidase B are available to diagnose acute pancreatitis. However, elevated amylase and lipase levels continue to be the “gold standard” among these serum markers.

Amylase and Lipase

The sensitivity of serum amylase and lipase in the diagnosis of acute pancreatitis is difficult to evaluate since the definition of the disease relies on the presence of increased serum enzymes [14]. Although this definition suggests a sensitivity of 100% irrespective of the enzyme measured, imaging or autopsy-based findings have shown that pancreatic enzymes may be below the diagnostic cutoff in a variable proportion of patients [7, 8, 15–17]. There are three major factors that interfere with the diagnostic sensitivity of these tests:

1. The time interval since symptom onset and first blood analysis: Within the first 24 h of symptom onset nearly all enzymes are elevated and no differences in sensitivity are observed. Amylase is the first enzyme to return back to normal concentrations, and as such, after the first in-hospital day it is the least sensitive among the enzymatic tests for pancreatitis. Amylase is cleared faster than lipase or trypsin, lipase and trypsin faster than pancreatic elastase, PLA2, or procarboxypeptidase B [18–21]. Rapid normalization usually indicates early resolution of the disease, or less frequently, extensive destruction of the pancreatic parenchyma with cessation of enzyme production [16, 20].

2. Alcoholic etiology: Patients with alcoholic acute pancreatitis frequently present with normal or only slightly elevated pancreatic enzyme concentrations, and serum amylase levels are reported to be normal in one-third of these patients [17]. In addition, normoamylasemia closely correlated with the number of previous attacks (0.7 versus 0.4, p<0.01) [16], suggesting considerable loss of viable parenchyma that is no longer able to produce sufficient amounts of enzymes [16, 20]. Since the pancreas contains about 4.5 times more lipase than amylase [22] lipase is less affected in this setting. Thus, elevated lipase levels are found in more than two-thirds of patients with normal amylase [16, 19].

3. Hypertriglyceridemia: Hyperlipidemia specifically interferes with the amylase assay, which leads to normal results in both serum and urine in up to 50% of hypertriglyceridemic patients with clinical symptoms and computed-tomography-proven pancreatic inflammation indicating acute pancreatitis [23]. A circulatory inhibitor rather than the triglyceride itself has been found to cause this problem [24]. Additional enzymes such as lipase should be determined in all situations with normal amylase levels and clinically suspected acute pancreatitis.

The greatest limitation of both serum amylase and lipase is their lack of specificity, albeit lipase performs somewhat better than amylase [25]. In addition to acute pancreatitis there are several conditions that increase serum amylase levels including diseases and derangements of the biliary tract, liver, intestine, genitourinary tract, lungs, breast, prostate, central nervous system, and the salivary glands [12]. Abnormal serum amylase levels also occur in the presence of metabolic disturbances such as renal failure, liver dysfunction, diabetic ketoacidosis, shock, eating disorders, abdominal and nonabdominal trauma, as well as with the use of various drugs [12, 26]. Persistent hyperamylasemia may be a normal variant [27] and has been described as a benign abnormality in many members of certain families [28]. Extrapancreatic in-