Update in Terminologies
An international symposium held in Atlanta, USA provided a clinically based classification system for acute pancreatitis (AP).\(^1\)

AP is defined as an acute inflammatory process of the pancreas that may involve peripancreatic tissues and/or remote organ systems. AP is a multisystem disease when it is severe. The onset is often rapid accompanied by upper abdominal pain, associated with mild tenderness to rebound based on severity. Vomiting, fever, tachycardia, leukocytosis, elevated amylase and lipase in the serum are other findings.

Histologically the findings range from interstitial edema and fat necrosis of the parenchyma to pancreatic and peripancreatic necrosis and hemorrhage.

Severe AP is associated with organ failure and/or local complications such as pancreatic necrosis, abscess or pseudocyst. Mild pancreatitis is associated with minimal organ dysfunction and an uneventful recovery. In severe pancreatitis rarely anek echymosis (Grey Turner’s Sign) or periumbilical echymosis (Cullen’s Sign) may be seen. Systemic manifestations in severe AP is associated with organ failure, which is defined as shock (systolic AP <90mmHg), pulmonary insufficiency (PaO\(_2\) < 60mmHg), renal failure (creatinine >2mg% after rehydration) or gastrointestinal bleeding (>500cc/24 hr).

Systemic complications, such as disseminated intravascular coagulation (platelets < 100,000/mm\(^3\)), fibrinogen <100 mg/dl, fibrin split products >80 Mg/ml or severe metabolic disturbances (Ca< 7.5 mg/dl) may also be seen.

Acute Fluid Collections (AFC) : Occur early in the course of AP, located in or near the pancreas, lacking a wall of granulation or fibrous tissue. In severe AP, AFC occur in 30-50% of cases, over 50% resolving spontaneously. AFC on the other hand are also the early point in the development of acute pseudocysts or pancreatic abscess.

Pancreatic Necrosis (PN): PN is a diffuse in focal area of non-viable pancreatic parenchyma which is typically associated with peripancreatic fat necrosis. Dynamic Contrast Enhanced CT (DCECT) is the gold standard for the diagnosis of PN. Focal or diffuse well marginated zones of non-enhanced pancreatic parenchyma, >3 cm in size or >30% of the area of pancreas are requisite criteria. Contrast
density fails to exceed 50 Hounsfield Units (HU) in areas of necrosis after intravenous administration (normal enhancement 50-150 HU). The biochemical markers of PN include C-reactive protein, PMN elastase and trypsinogen activation peptide (TAP). Not all serum markers are available easily and their clinical usefulness is variable.

PN may be sterile (SPN) or infected (IPN). A differentiation between SPN and IPN is clinically important for the following reasons. (I) The mortality in IPN is substantially higher, (ii) IPN requires surgical treatment without which it may be fatal, (iii) Clinical and laboratory findings are same in IPN and SPN. The definitive diagnostic test is fine needle aspiration (FNA) of the necrotic area under CT guidance and demonstration of bacteria by gram stain and culture of the organism in the aspirated material. FNA is safe, reliable and practical.

Pseudocyst (PC): is a collection of pancreatic juice enclosed by a nonepithelialized wall, which arises as a consequence of acute pancreatitis, pancreatic trauma or chronic pancreatitis. PC formation requires 4 or more weeks following AP. Fluid collections of less than 4 weeks duration lacking a defined wall are termed uid collection. In chronic pancreatitis PC may form without a clearcut episode of AP.

Pancreatic Abscess (PA): Is a circumscribed intraabdominal collection of pus, usually in proximity to the pancreas, containing little or no pancreatic necrosis which arises as a consequence of AP or pancreatic trauma.

There is a clinical difference between PA and IPN. Mortality in IPN is double that of PA and management differs. Indiscriminate use of the term PA leads to confusion with regard to assessment of severity and management.

Terms deleted. The term ‘phlegmon’ is ambiguous and is replaced by SPN and IPN. Hemorrhagic pancreatitis is not a special form of AP.

Mortality in AP

The overall mortality in AP has come down to 2-5% from a previous level of 10% about 20 years ago. Early recognition of severe AP and prompt admission and management in the ICU setting where uid management and respiratory support are better are the reasons for the decrease in mortality. In patients over age 60, multiple organ system dysfunction is more common and mortality is higher. Mortality in AP occurs in many peaks in its natural history. Many patients die even before the diagnosis is made. Only careful autopsy will prove the diagnosis. (Wilson et al, 1990, Lankisch et al 1991).

Two peaks of mortality exist in patients admitted to hospital. Early mortality within a day or two due to the effects of systemic in ammatory response syndrome (SIRS) and multiorgan system dysfunction syndrome (MODS), while a late mortality is caused by the effects of MODS combined with pancreatic sepsis in pancreatic necrosis (Anderssan et al 2003).

Does the etiology in uence the outcome? Uhl et al, noted that once AP is initiated the course is not in uenced by the etiological factor. Lankisch, et al did not find any difference in MODS between alcoholic and biliary AP. The rate of pseudocysts was higher in alcoholic pancreatitis than in other etiologies. Mortality is higher and upto 29% for etiologies other than alcoholism and biliary tract disease in some reports. Post ERCP acute pancreatitis is a severe one and complication rate and mortality are higher.

Amylase or Lipase or Both in the Diagnosis of AP. How Accurate are we in Diagnosing AP?

It was known for years that amylase elevation was non specific and would occur in intestinal obstruction, perforated vicsus, acute cholecystitis, ruptured ectopic pregnancy and a number of other intraabdominal conditions. However, higher the amylase level, i.e., more than 5 times the upper limit of normal better is the positive predictive value. A cutoff figure of 3 times the upper limit of normal
increases the specificity without decreasing the sensitivity. Normoamylasemic AP can occur when the etiology is hypertriglyceridemia, or when the patient is seen for the first time 3 or more days after the onset of AP. In alcoholic AP lipase elevations may be more than amylase elevations. Benign hyperamylasemia can occur because of macroamylasemia or as a familial disorder. Amylase elevation occurs in all acidotic conditions.

Lipase elevation is not more specific than amylase levels. Lipase levels are elevated in Crohn’s disease, ulcerative colitis, in diabetic ketoacidosis and in a number of intraabdominal conditions. Recently an entity of familial hyperlipasemia has been described. (Yadav, et al 2002).

Despite the limitation amylase and lipase estimations remain the best diagnostic modalities in the absence of better tests. (Banks 1997).

How to Assess the Severity of AP as Early as Possible?

Early prognostic signs to alert the physician with regard to the need for ICU care for the patient are important. However, the well known Ranson’s Criteria has 11 factors and the modified Ranson’s Criteria which is seldom used is different for different patients based on etiology. Ranson’s Criteria stated that on admission age >55, WBC > 16,000/mm³, Glucose >200 mg/dl, LDH >350 U/L and AST > 250 U/L and during the initial 48 hours, HCT decrease of >10 vol %, BUN increase > 5mg, Ca <8 mg/dl, PaO₂ <60 mmHg, base deficit of >4 mEq/L and uid sequestration >6L indicated bad prognosis. Three or more of the above indicated moderate to severe AP. APACHE II system although better is less often used. Glasgow Criteria is similar to Ranson’s, but emphasized the importance of rapid fall in albumin as a bad prognostic sign.

Among the laboratory parameters levels of elevation of amylase or lipase are unreliable markers for predicting severity. Levels of immunoreactive trypsinogen reflect the leakage of inactivated proenzymes from injured pancreatic acinar cells into the circulation. The quantitative immuno urometric measurement of trypsinogen-2 urine and serum is a highly accurate marker for AP (Hedstrom et al 1996). Phospholipase A₂, PMN elastase, cytokines IL1, IL6, and IL8 are other markers.

Simple clinical and laboratory markers are helpful to practicing clinicians. Obesity is a poor prognostic marker. Patients with a body mass index of >30 kg/m² had a mortality of 35% combined with a considerable morbidity. Recent studies have looked at the prognostic significance of truncal or metabolic obesity as a poor prognostic marker. (Mery et al 2002).

Respiratory and cardiovascular complications occur more frequently in obese patients. Adipose tissue is not only a fat depot, but an endocrine organ capable of secreting active molecules such as TNF alpha and leptin. TNF alpha, a well known proin ammatory cytokine and one of the major mediators in the in ammatory response in AP, is able to induce secretion of other cytokines important in the pathophysiology of pancreatitis, such as IL1, IL6, and IL8. TNF alpha production and its receptors and TNF-R2 are increased in obese people. The role of cytokines in the pathogenesis of multisystem organ failure is become progressively more evident and may be related to obesity and fat distribution.

The most commonly used serum parameter for the staging AP is C-reactive protein. Increased levels of CRP are a direct effect of hepatocyte stimulation by cytokine release. There is a strong correlation between edematous and necrotizing disease with a sensitivity and specificity above 80% and an overall accuracy rate in the detection of pancreatic necrosis of 86%. Current consensus is that the cut off level is 150 mg/l within the first 48 hours of symptoms (Dervenis et al 1999).

Feeding in AP

Enteral nutrition is to be preferred to TPN in a patient with AP who requires prolonged treatment as a result of pancreatic necrosis or other complications. In order to avoid stimulation of the
pancreas it is customary to avoid all oral feedings. IV nutrition and total parenteral nutrition were considered substitutes for oral feeding. TPN is associated with metabolic and septic complications and it is expensive. Parenteral therapy does not prevent enteral mucosal atrophy. It even promoted translocation of bacteria.

Enteral nutrition via a jejunal feeding tube is reported to have a beneficial effect in reducing septic complications. Enteral nutrition by placing the tube into the jejunum and not duodenum helps to avoid stimulation of the pancreas to a great extent. Early reports indicate that in severe AP there is a rapid resolution of the toxicity and stress response to AP. The role of septic complications are markedly reduced. A complete enteral supplement containing MCT and hydrolized peptides only minimally increased plasma cholecystokinin levels and it may be an added advantage to feed MCT through intrajejunal feeding. (Abou-Assi 2002, Shee et al 2003).

Antibiotic Prophylaxis: Pancreatic infection is a major complication and cause of death in AP. Antibiotic prophylaxis is evaluated in a number of studies. Among the newer antibiotics, Imipenem and Quinolones are considered ideal agents. A multicenter study with Imipenem showed a significant reduction of the incidence of pancreatic infection when given prophylactically to patients with pancreatic necrosis. (Pederzoli 1992).

Is Pancreatitis a Genetic Disease?
Although AP has many etiological factors, a genetic predisposition to hereditary, idiopathic, tropical and even alcoholic pancreatitis has come to our attention. Whitcomb (2000) has pioneered many studies in this aspect. The major genetic mutations are in cationic trypsinogen gene (PRSS1) the serine protease inhibitor (SPINK 1) and cystic fibrosis transmembrane conductance regulator gene (CFTR).

References