INTRODUCTION:
Acute Pancreatitis (AP) has two types: acute interstitial (edematous pancreatitis) and acute necrotizing pancreatitis. AP is a potentially serious disease with a mortality ranging from 5-10% (1). Over the last several years, significant advances have been made in the management of patients with AP, especially, management in the intensive care (ICU) leading to a decrease in the mortality from 25% to less than 5-10% currently. Even with these medical advances, diagnosis of AP can still be missed and may be detected only at autopsy. Since routine autopsies are seldom performed, it is likely that we miss some of the most serious cases of AP.

The difficult decisions I have focused include: diagnostic dilemma, assessing severity in AP, evaluation and management of pancreatic necrosis. The limited role of ERCP in the management of AP, the controversial role of prophylactic antibiotics as well as of enteral nutrition are discussed. Recently, American College of Gastroenterology and American Gastroenterological Association have published excellent practice guidelines (2, 3) in the management of AP.

DIAGNOSIS:
A. Serum Enzyme Studies:
A small number of patients with AP die prior to hospitalization and only autopsy data will reveal AP (1). This can result from atypical presentation i.e. patients may have painless AP when the clinical suspicion for AP is not there, or present with normal or non-diagnostic levels of amylase misleading the physicians to think that imaging studies are not necessary, or when organ system dysfunction early in the course masks the typical clinical features. Severe AP has been noted to occur in patients with only a modest or no increase in amylase/lipase levels (4, 5).

The diagnosis of AP depends on at least two of the following three. 1) Typical history of upper abdominal pain 2) Elevated serum levels of amylase/lipase and or 3) Characteristic abnormalities on imaging studies (e.g. CT) (2). The above criteria recognizes that any one of the three may be absent in patients with AP.

The limitations of serum amylase estimation include (4): i) Poor specificity since the level in serum is elevated in a host of other abdominal and non-abdominal painful conditions. The specificity is improved when a higher cut-off is used to signify an abnormal value. A significant elevation of amylase (> 3 times normal) in an appropriate clinical setting indicates the diagnosis of AP. However, a high cut-off value will decrease the sensitivity. Normoamylasemia occurs in 19-32% of patients with AP, seen in hypertriglyceridemic pancreatitis, and after a few recurrences in alcoholic pancreatitis. A delayed estimation in the course of AP may also lead to normal levels of serum amylase (4).

Compared to serum amylase level an elevated serum lipase level is generally considered to be more sensitive and specific for the diagnosis of AP. However, non-specific elevation of lipase is increasingly being recognized and has been reported to occur in almost all situations where nonspecific elevation of amylase is seen. It is generally believed that in a typical setting, an elevation of amylase and or lipase > 3 times normal is most likely only due to AP. Doubts are raised with regard to the superior specificity of lipase estimations in the diagnosis of AP (4).

Several studies have established that the height of elevation of serum pancreatic enzymes, amylase/lipase does not correlate with the severity of AP. Routine daily or repeated estimations of enzyme levels after a diagnosis of AP has been established, is not recommended (2). The improvement of AP is to be often decided clinically and only when necessary supported by imaging studies.

B. Imaging Studies In Acute Pancreatitis:
I. Conventional Radiography:
It is a good clinical practice to obtain a roentgenogram of the chest and abdomen, although a diagnosis of AP cannot be ruled out with normal findings. On the contrary, they may give clues to other intra-abdominal conditions that need to be ruled out on any patient with acute abdominal pain. Abnormal bowel gas patterns including focal ileus of the duodenum or jejenum close to the pancreas (sentinel loop) or transverse colon to the splenic flexure (colon cut-off sign) with lit-
tle or no gas seen in the descending colon when present interested the old time clinicians, but carry poor sensitivity in the diagnosis of AP. Chest X-ray findings of AP include pleural effusions (unilateral or bilateral), basal atelectasis, elevation of the left side of the diaphragm reflecting a subdiaphragmatic retroperitoneal inflammation. These findings when present support a diagnosis but by no means are necessary to make a diagnosis of AP. Recent data indicates that presence of pleural effusion denotes severe AP and not just the diagnosis.

2. Abdominal Ultrasound

Ultrasound is a quick, safe, inexpensive, radiation-free investigation that is highly suitable for sequential studies. Easy availability of the ultrasound machine even in doctors’ offices and the relative inability to obtain CT, EUS or MRI even in many tertiary hospitals makes abdominal ultrasound a preferred procedure. The advantage of abdominal ultrasound in pregnant women is emphasized again later.

An initial ultrasonography within 24-48 hours of admission of the patient is necessary to evaluate cholecystolithiasis as well as choledocholithiasis in our attempt to assess a biliary etiology for AP. It also helps to measure common bile duct size (normal up to 7mm) to rule out possibility of a dilated duct and an impacted stone, when an urgent Endoscopic Retrograde Cholangiopancreatogram (ERCP) and stone extraction by sphincterotomy may be needed. Establishing a biliary etiology is important where excellent management options are available.

Limitations of an abdominal ultrasound include that it being operator dependent and the relative inability to visualize the pancreatic morphology accurately in patients with AP. Visualization of the pancreas may be hampered by ileus and obesity.

3. Computed Tomography:

The role of dynamic contrast enhanced computerized tomography (CECT) has been well established a) in the diagnosis of AP, b) staging the severity of the inflammatory process of the pancreas and c) in detecting complications. CT abdomen is most frequently used as a single imaging modality for these purposes. CT scan is performed with an oral contrast to opacify the gastrointestinal tract and an IV contrast that is administered as a bolus during the scanning technique. The several techniques for rapid IV administration of contrast material need not be discussed here. Contrast enhanced CT is needed to diagnose pancreatic morphology, degree of necrosis in guiding a fine needle aspiration to estimate for infection.

Current CT techniques provide high quality images of the pancreas. Helical or Multidetector CT (MDCT) is the newest technique for imaging the pancreas. A rapid bolus injection of 150 cc of 60% nonionic contrast at 3ml/s is followed by abdominal imaging starting at 60 seconds. Normal parenchyma will show an increase in attenuation of 60-80 Hounsefield units above the baseline attenuation of normal non-enhanced parenchyma. The adjacent blood vessels can also be visualized helping one to detect vascular complications, such as pseudoaneurysm.

CT findings in AP involve a spectrum of changes that reflect the severity of the parenchymal and extraparenchymal inflammation. It has to be remembered that not all patients with AP have abnormal CT findings. Although the actual number may be difficult to assess, a normal CT scan is found in atleast 14% - 28% of patients with mild forms of AP. Also to be emphasized is that CT is not required in all patients with suspected AP. An initial CT scan on admission should be considered only in the following situations. i) In patients who have possibility of a disease other than AP on admission where CT helps to exclude other serious intra-abdominal conditions such as mesenteric infarction. On the other hand in order to make a diagnosis of AP an emergent CT scan on admission is less likely to give much data and the best timing appears to be 48-72 hours after the onset of abdominal pain when the morphological changes would have well developed in and around the pancreas, ii) In patients who have severe AP based on clinical judgment or a severity criteria (e.g. shock, hypoxemia, etc) and, iii) in those patients when an intra-abdominal sepsis is suspected. CT scan of abdomen should also be considered in patients who do not improve after 3-4 days of conservative therapy. When a patient is in impending shock it is more important to manage the patient rather than waste time in obtaining CT abdomen.

When the aim of the clinician is to stage the severity of AP, the best time to perform a CECT is not day 1 but day 3 or later. The CT scan changes of necrosis develop 2-3 days after the clinical onset.

4. Endoscopic Ultrasound (EUS):

EUS is not of value in the diagnosis of AP, but may be useful in detecting biliary sludge and common bile duct stones. In this regard, in patients with severe AP where a diagnosis of CBD stones may be needed for subsequent stone extraction, EUS is safer than ERCP which is associated with the risk of another episode of AP and introducing infection. The disadvantages are that EUS is not easily available, expensive, needs sedation and is operator dependant.
Magnetic Resonance Imaging (MRI) / Magnetic Resonance CholangioPancreatography (MRCP):

MRI is not routinely used in the initial evaluation or follow-up of a patient with AP due to cost, difficulty in monitoring critical patients while on the machine and the inability for potential intervention and drainage procedures (e.g., fine needle aspirations or drainage of fluid collections). MRCP does not need contrast, there is no radiation and can be safely performed in the second and third trimester of pregnancy. However, it is expensive and not ideal in the detection of some distal CBD stones. Claustrophobic patients cannot undergo regular MRI or MRCP. When the index of suspicion for CBD stone is low, in order to avoid an unnecessary ERCP one may perform MRCP or EUS.

C. Prognostic Stratifications

A clinician needs a simple and reliable method for assessing the severity of an episode of AP in a given patient. As discussed previously, height of amylase or lipase elevation does not predict severity and cannot be used to monitor disease progression. (1, 6) Complications of AP are tabulated.

i. Scoring systems using multiple criteria:

Among the several scoring systems developed using multiple criteria, the two most commonly used are Ranson’s and APACHE –II. In addition to the need for waiting for 48 hours prior to get a complete prognostic information from the scoring systems (except APACHE-II), the practicing clinician finds these criteria cumbersome and difficult to remember. However Ranson’s criteria have stood the test of time.

Presence of ≥ 3 Ranson’s signs at 48 hours indicates severe AP with a sensitivity of 70% and specificity of 67%. Many clinicians do not recognize that there are two criteria proposed by Ranson, one for biliary and other for alcoholic AP. So the etiology of AP should be known to use either one of the criteria. The APACHE-II criteria use the values of 12 physiological measurements, age and previous health status to provide a general measure of severity of disease. An APACHE –II score of > 8 indicates severe AP. The advantages of APACHE-II criteria include objective determination of AP within hours of admission and the ability to be recalculated daily so as to follow the course of the disease and the response to therapy. A very recent interesting observation is HAPS. “HAPS” is an acronym for “the harmless acute pancreatitis score” of Lankisch. No rebound tenderness and or guarding, normal hematocrit level, and a normal serum creatinine level soon after admission enables identification of patients whose disease will run a mild course. The authors claim that the high level of accuracy of the test (98%) will allow physicians to identify patients who do not need ICU care (7).

ii. Single prognostic markers:

Several simple bedside and routine tests have recently been associated with severe AP including obesity, presence of pleural effusion and hemoconcentration. Increasing BMI has been noted to be an independent predictor for severe AP and has been associated with higher incidence of systemic complications. Pleural effusion is a marker of severe AP. Admission hemoconcentration as well as lack of it has been proposed to be useful. Lack of hemoconcentraon on admission has a good value in excluding serum AP.

C-reactive protein (CRP):

Elevated CRP as a marker of severity of AP has been demonstrated in several studies and it is widely used in Europe. It is an acute phase reactant elevated in several inflammatory conditions and serves as a nonspecific marker for inflammation. In AP, CRP levels peak on the 3rd or 4th day. Values of > 150 mg/l when estimated after 48 hours of onset symptoms are accepted as proven predictor of severity and considered to be a gold standard among laboratory tests for predicting severity. Elevation of creatinine > 2 mg on day two after rehydration is noted to be a sensitive marker for severe AP. A new mortality based prognostic scoring system (BISAP criteria) for use in AP has been derived and validated. The factors of poor prognosis included BUN of > 25 mg/dl, impaired mental status; systemic inflammatory response syndrome (SIRS) age > 60 years, or the presence of pleural effusion (8).

Management Options: (2, 3)

Most patients require conservative empiric therapy with bowel rest, IV fluid administration and pain medications. Under the following circumstances other management options are to be considered. The role of ERCP with papillotomy in acute biliary pancreatitis relies on relief of the obstruction by surgical or endoscopic means in order to ameliorate the disease process.

Many experts feel that early ERCP +/- papillotomy in acute biliary pancreatitis is indicated in a selected group of patients who have evidence of severe acute pancreatitis, biliary obstruction or biliary sepsis.

i. Pancreatic Necrosis:

Twenty to thirty percent of cases of AP have associated pancreatic necrosis. The International Symposium on AP defines pancreatic necrosis as “the presence of one or more focal areas of nonviable pancreatic parenchyma”. The presence of necrosis is the hallmark of a severe form of AP since it is associated to higher morbidity and mortality, especially when the tissue becomes infected.

Necrotizing AP may lead to systemic and local complications including organ failure (renal, respiratory, shock), coagulopathy, hyperglycemia, hypoglycemia, gastrointestinal bleeding, infected necrosis and adjacent bowel necrosis. In contrast to interstitial AP where the mortality is < 2%,
patients with necrotizing AP is associated with a mortality of 10-30% depending on the presence or absence of infection. In sterile pancreatic necrosis, the mortality rate is 10% which increases to 30% in the presence of infection. Patients with sterile necrosis associated with organ dysfunction have a higher mortality. Infected necrosis occurs in 30-70% cases of pancreatic necrosis and accounts for >80% deaths from AP.

Clinically, it is difficult to differentiate sterile from infected pancreatic necrosis. In both situations, there can be fever; leucocytosis, severe abdominal pain and organ dysfunction. A patient with pancreatic necrosis whose clinical condition deteriorates or fails to improve despite aggressive supportive care should undergo a CT guided fine needle aspiration of the pancreatic or peripancreatic fluid or tissue. This technique is safe, accurate and has a sensitivity and specificity of 96 and 99% respectively.

The role of delayed necrosectomy once the multiorgan failure has improved is unclear. In patients who persist to have systemic symptoms 4-6 weeks after the onset of AP, with fever, weight loss, intractable abdominal pain, inability to eat, failure to thrive, delayed necrosectomy may be beneficial. Postponing necrosectomy until 30 days after initial hospitalization is associated with decreased mortality.

Over the last few years, Baron and colleagues have pioneered endoscopic debridement of organized pancreatic necrosis (8). The details of endoscopic therapy of acute fluid collections and organized necrosis are beyond the scope of this review and interested readers are referred to several excellent reviews on this topic. Endoscopic debridement of pancreatic necrosis is certainly not a routine approach, is experimental and should only be performed by expert endoscopists with considerable experience in this area.

**Antibiotic prophylaxis:**

Bacterial translocation has been shown to be increased in AP and is believed to be due to disruption of the gut mucosal barrier. This, in addition to hematogenous seeding is believed to be an important mechanism for infection of the inflamed pancreatic and peripancreatic tissue. The latter notion has lead to the use of prophylactic antibiotics and selective decontamination of the gut.

The initial studies investigating the role of prophylactic antibiotics in AP are not encouraging. Currently, there is no consensus regarding routine administration of antibiotics or decontamination of the gut for prophylaxis of pancreatic sepsis. (9)

**Nutritional Support:** (9, 10)

The issue of feeding patients with AP has been a subject of intense debate for years. It is now well accepted that the outcome in patients with mild AP is not changed by nutritional supplementation (enteral or parenteral) and no specific form of nutritional support is needed. After an initial treatment by intravenous fluids and bowel rest for 3-5 days, oral feedings can be restarted when pain has subsided, bowel sounds have returned and the patient is hungry. One need not wait for the serum pancreatic enzyme levels to return to normal prior to starting feedings. Initially a diet high in carbohydrates, moderate in proteins and fat can be instituted and gradually advanced according to patient’s tolerance.

The aims of nutritional support in a patient with severe AP are to: i) avoid stimulation of the pancreas (“pancreas rest”), ii) avoid complications arising from the route of delivery, and iii) achieve a positive nitrogen balance and cost consideration. (10)

Several physiologic studies have shown that jejunal feeding by elemental diets does not stimulate pancreatic stimulation. Controlled trials performed over the last few years comparing Total enteral nutrition (TEN) with total parenteral nutrition (TPN) have not shown exacerbation of the disease from TPN in fact, TEN has been found to be more beneficial in regards to decreasing the number of infectious complications compared to TPN and much cheaper. (10, 11)

In severe AP, attempt for enteral feeding via a nasojejunal tube placed either endoscopically or radiologically should be considered as soon as possible after admission. The use of TPN should be considered when the goal for caloric needs is not achieved by nasojejunal feeding or when patients cannot tolerate nasojejunal feeding due to abdominal pain.

**Complications of Acute Pancreatitis**

I. **Pancreatic**
   a. Fluid collections (sterile vs. infected)
   b. Necrotizing (Sterile vs. Infected)
   c. Pseudocyst- infection/ rupture/hemorrhage
   d. Abscess

II. **Local -nonpancreatic**
   1. Involvement of contiguous organs (intraperitoneal hemorrhage, GI bleeding, thrombosis of splenic vein, bowel infarction)
   2. Pancreatic ascites
   3. Obstructive jaundice

II. **Systemic**
   1. Pulmonary
      a. Early arterial hypoxia
      b. Atelectasis, pneumonia, pleural effusion, mediastinal abscess
      c. ARDS
   2. Cardiac: shock, pericardial effusion, KEG changes, arrhythmias
   3. Hematologic: DIC
   4. Gastrointestinal: GI Bleeding(portal-splenic vein thrombosis, colonic infarction)
   5. Renal: azotemia, oliguria
   6. Metabolic: hypocalcemia, hyperglycemia, hypertriglyceridemia, acidosis, elevation of free fatty acids
   7. CNS: psychosis, encephalopathy, Purtscher’s retinopathy
   8. Peripheral: fat necrosis (skin and bones), arthritis
REFERENCES