THE MANAGEMENT OF ACUTE PANCREATITIS

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PANCREATITIS

Pancreatitis is an amorphous pathological entity that ranges from minimal oedema to haemorrhagic necrosis; from reversible inflammation to fibrosis with severe reduction in exocrine and endocrine function. The treatment is dictated by the type and severity of the disease process, therefore it is necessary to distinguish clinical types of pancreatitis to make it effective. The classification which has stood the test of time is the Marseilles classification of 1963 and there are four classifications as follows:[1,2]

1	Acute pancreatitis - a single episode of pancreatitis in a previous normal gland
2	Acute relapsing pancreatitis – recurrent attacks that do not lead to permanent functional damage; clinical and biological normalcy in the intervals between attacks
3	Chronic relapsing pancreatitis – progressive functional damage persisting between attacks; frequent pain-free intervals
4	Chronic pancreatitis- inexorable and irreversible destruction of pancreatic function; constant pain

Table 1: Marseilles Classification of Pancreatitis 1963

ACUTE PANCREATITIS AND ACUTE RELAPSING PANCREATITIS

This refers to an acute inflammation in a normal gland, when several such episodes occur it is acute relapsing pancreatitis is said. Acute pancreatitis **i**s a rapidly-onset inflammation of the pancreas. Depending on its severity, it can have severe complications and high mortality despite treatment. While mild cases are often successfully treated with conservative measures, such as abstaining from any oral intake and IV fluid n, severe cases may require admission to the ICU or even surgery in one sitting or often more than one intervention) to deal with complications of the disease process. Acute pancreatitis is common abdominal emergency developed countries, about 80,000 cases occur in the United States each year; some 20 percent of them are severe. Acute pancreatitis occurs more often in men than women. It is rare in the tropics and few cases that are seen, are usually missed because relative frequency of the other causes of acute abdomen. Also, causative factors are very rare in the tropics. Just as the clinical and microscopic manifestation of pancreatitis vary, so do the concept concerning its aetiology[1,2.]

Acute pancreatitis can be divided into mild and severe pancreatitis. Mostly the Atlanta classification (1992) is used. In severe pancreatitis serious amount of necrosis determine the further clinical outcome. About 20% of the acute pancreatitis are severe with a mortality of about 20%. This is an important classification as severe pancreatitis will need intensive care therapy whereas mild pancreatitis can be treated on the general ward. Necrosis will be followed by a systemic inflammation response syndrome (SIRS) and will determine the immediate clinical course. The further clinical course is then determined by bacterial infection. SIRS is the cause of bacterial (Gram negative) translocation from the patients' colon.

CAUSES[1,2]

Alcohol

Alcohol was said to be responsible a third to half of all of all the cases of acute or acute relapsing pancreatitis in United States in any given year. The exact mechanism by which alcohol causes pancreatitis unknown, and efforts to demonstrate direct toxic on pancreas has been unsuccessful. However,-workers have established metabolic effect of alcohol on the pancreas; with prolong alcohol intake; protein is precipitated in pancreatic juice within ductules, leading to obstruction and morphologic changes in ductular system. The most prevalent hypothesis arises from two combined observations:

- Alcohol aids pancreatic secretion by way of acid-induced secreting release.
- Alcohol increases the sphincteric tone at the ampullary region. In view of these, pancreatitis results from increased pancreatic secretory pressure against an unyielding sphincter. However, there is little evidence to support this claim.

Biliary Tract Disease

When taken together, biliary diseases and alcohol are associated with 80 – 90% of cases. Although, the

pancreatitis associated with alcohol tends to occur in under privileged indigenous population, the one due to biliary disease occurs in general population. The mechanism of pancreatitis in biliary disease is also unknown. Pancreatic ductal obstruction by biliary calculi; biliary reflux into pancreatic duct causing acute pancreatitis and '*the common channel theory*" was postulated based on discovery of biliary stones blocking the ampulla of Vater, effectively obstructing both the bile and pancreatic ducts, which shared a final common pathway in a patient who died of acute pancreatitis. Although, the theories provide an attractive explanation for the well recognized association of biliary stone and pancreatitis; the anatomic features supporting only the common channel theory existed in two-third of the patients. Also, bidirectional flow of the bile secretion into pancreatic duct and pancreatic secretion into the bile duct has been observed without causing pancreatitis. Active perfusion of pancreatic duct with normal bile at normal pressure does no harm to the pancreas. Furthermore, pressures in the pancreatic ductal system are consistently higher than in the biliary system. Under these conditions one could reasonably expect bile to perfuse the pancreatic ducts without postulating an additional mechanism. Nevertheless, the hypothesis of that transient obstruction of the pancreatic duct by biliary calculi has received attention because of the frequent association of pancreatitis with passage of stones in the stool. Transampullary migrations of stones appear to be well established as an important cause of acute and acute relapsing pancreatitis.

Obstruction

Simple obstruction of the major pancreatic ducts, complete or partial, has been postulated by some as a basic cause of disease. However, the incidence of ductal obstruction in fatal pancreatitis does not support this thesis. Furthermore, ligating the pancreatic duct deliberately did not result in the disease. This does not preclude the development of pancreatitis in the presence of the stimulatory effect of the exocrine system.

Vascular factor

Occlusion of arterial blood supply to the pancreas has been shown to result in pancreatitis. The magnitude of the pancreatic injury appears to correlate well with the degree of occlusion of the terminal vascular ridicules. It has been shown in experimental work that the gradation in severity of pancreatitis may be obtained by injecting microspheres of various sizes into the pancreaticoduodenal arteries of animal. The smallest spheres provoked the severest form of acute pancreatitis. When vascular obstruction is combined with the secretion of pancreatic juice under high intraductal pressure, full blown haemorrhagic pancreatitis develop. Both atheromatous material and intracardiac clots, has been reported to embolize to the pancreatic microcirculation resulting in pancreatitis. Despite these and many other studies, the relative importance of hypoperfusion in the development of clinical disease is unknown.

Hyperlipidaemia

There are two classes of patients with lipid disorder that may suffer from pancreatitis. The first group are those with a genetic predisposition to hyperlipidaemia and pancreatitis and they are usually diagnosed in childhood. Characterization of the lipid abnormality reveals that Frederickson Type 1, 4 and 5 are usually involved. The second class of patients are those which hyperlipidaemia associated with alcohol abuse; whether the hyperlipidaemia represents a cause of pancreatitis or a merely an uncommon response to alcohol is not too clear. It has been suggested that pancreatitis in hyperlipid state results from conversion of triglyceride to toxic free fatty acid within the pancreatic parenchyma by pancreatic lipase.

Miscellaneous

Other cause of acute pancreatitis include idiopathic, hypercalcaemia, renal transplantation, autoimmune disease, an autosomal dominant form of hereditary pancreatitis, parasitic infestation, pancreatic divisum, ampullary stenosis, duodenal diverticulum, superior mesenteric artery syndrome, regional enteritis, drugs (chlorthiazides, furosemide, corticosteroids, phenforminm, azathioprine, Azulfidine), ERCP, trauma, vasculitis, shock, viral disease (mumps, echovirus infection, infectious mononucleosis), scorpion sting, pregnancy, and porphyria.

PATHOGENESIS

The numerous causes would suggest that the pancreas can withstand little irritations; autodigestion by the intrapancreatic enzymes may represent the final common path of pancreatic necrosis. Whatever their initiating mechanisms may eventually be proved to be, it is now clear that that the clinical spectrum of pancreatitis is due to elaboration of toxic products of pancreatic inflammation. Activated pancreatic enzymes, prostaglandins and kinins have been demonstrated in the ascitic fluid of these patients. It explains the initial efficacy of removal of toxic fluid during the peritoneal lavage.

Normally, elaboration of system of antiproteases, of which α_2-macroglobulin is an important example, protects the systemic circulation against activity of activated proteolytic enzymes. Free enzymes are bound by this globulin and removed by the recticuloendothelial system from the circulation. Increased levels of elastase, trypsin, and chymotrypsin have been found in patients with pancreatitis as well as depressed levels of α_2-macroglobulin[8,9] and alpha1-antitrypsin. This overwhelming of the defense mechanisms is the possible cause of remote organ effect in pancreatitis.

CLINICAL PRESENTATION

A high index of suspicion is needed in the diagnosis of acute pancreatitis and acute relapsing pancreatitis as its clinical features may be difficult to distinguish from other causes of acute abdomen that require surgical intervention. The symptoms and signs are variable in expression depending on the degree of structural alteration within the gland. In milder forms acute pancreatitis may present with penetrating upper abdominal pain, often radiating to the flanks, shoulder and back. In severe forms such as haemorrhagic pancreatitis, the patient may present with abdominal distension, sweating, nausea, cold clammy extremities, malaise and prostration. In mild forms the clinical findings may include epigastric tenderness and low grade fever, whereas when acute pancreatitis is very severe abdomen distension and rigidity are common, dehydration, fever, signs of shock, tachycardia and jaundice in about 20-25% of patients. Rarely, discolouration of the skin of the flanks (Gray-Turner sign) due to dissection of peripancreatic haemorrhage or about the umbilicus (Cullen's sign) may be visible.

INVESTIGATIONS.[1,2,3,4]

- **Serum amylase:** Analysis of serum amylase is found to high in acute pancreatitis with 2 to 12 hours of onset of symptoms and return to normal 3 or 4 days. When raised beyond a week, it may indicate the development of a complication of pancreatitis. Although, it may be stated that the higher the serum amylase level, the greater the probability of acute pancreatitis, high serum does predict the diagnosis or severity of acute pancreatitis. Hyperamylasaemia may be found in biliary tract disease, alcoholism in absence of pancreatitis, PUD, intestinal obstruction, mesenteric thrombosis, intra-bleeding, pregnancy, mump and after the use certain drugs such as meperidine. Fractions of Amylase can be isolated according to tissue of origin using various laboratory techniques; in this way pancreas (P-amylase) has been separated from amylase of salivary, lung, ovary, and prostatic origins.
- **Serum lipase:** Serum lipase rises 4 to 8 hours from the onset of symptoms and normalizes within 7 to 14 days. Hyperlipasaemia has also been recorded in patients without pancreatic disease. If the lipase level is about 2.5 to 3 times that of Amylase, it is an indication of pancreatitis due to Alcohol. It is usually not necessary to measure both serum amylase and lipase. Serum lipase may be preferable because it remains normal in some nonpancreatic conditions that increase serum amylase including macroamylasemia, parotitis and some carcinomas. In general, serum lipase is thought to be more sensitive and specific than serum amylase in the diagnosis of acute pancreatitis.
- **Urinary amylase:** Urinary amylase excretion has been found to be a reflection of amylase secreted from the pancreas and release into the blood. Quantification of urinary amylase in addition to serum amylase determination will increase the diagnostic accuracy of acute pancreatitis because urinary level remains elevated for longer periods and lesser rates of excretion are more frequently associated with other diseases.
  - **Amylase-Creatinine Clearance Ratio (ACCR)** is useful in the diagnosis pancreatitis because of the diminished tubular absorption of amylase.

$$A.C.C.R = \frac{\text{Amylase (urine)}}{\text{Creatinine (urine)}} \times \frac{\text{Creatinine (Serum)}}{\text{Amylase (serum)}} \times 100$$

Elevated values greater than 4% is thought to be diagnostic, but false values are also possible in postoperative patients, diabetics renal failure and in severe burns. Its value lies in excluding a diagnosis of pancreatitis if normal values are found.

- **Urinary lipase-** elevated urinary lipase has been associated with acute pancreatitis, however, interpretation of elevated serum lipase is subjected to limitation similar to those applied to amylase determinations.
- **Thoracentesis or paracentesis abdominis** may, also, be necessary in making accurate diagnosis. Examinations of fluid obtained for lipase and amylase activities may be helpful, since these enzymes levels are raised in the fluid from hydrothorax and ascites secondary to pancreatitis. Peritoneal fluid obtained at peritoneal lavage can, also, be analyzed for

amylase and lipase activities, McMahon and his colleagues have constructed criteria for establishing the severity pancreatitis based colour and nature of the peritoneal lavage.[5]

- **Radioimmunoassay of trypsinogen, elastase and other pancreatic proteolytic enzymes** released into the serum during episode of pancreatitis are also useful. Although, the initial results is promising to increase the diagnostic sensitivity and specificity over the serum amylase activity, but further experience is necessary to establish the value.
- **X-Rays**- plain x-rays of the chest posterior-anterior view may show hydrothorax which may be suggestive of acute pancreatitis. X-rays of abdomen of anterior-posterior and lateral views may show biliary and pancreatic calcification suggestive of stones. The identification of a single dilated atonic loop of small bowel (sentinel loop) may provide contributory evidence for the diagnosis. On lateral view anterior displacement of gastric shadow may suggest collections behind the stomach or extensive peripancreatic calcification. When the condition of the patient permits, the contrast study of the stomach may be helpful, C-loop of duodenum may be widened as a result of pancreatic inflammation.
- **Ultrasonographic examination** may detect stones in the biliary ducts or pancreas and may reveal pancreatic oedema or collection behind the stomach in the lesser sac.
- **Computerized Tomography Scan** will also be helpful in doubtful cases or when other simpler investigations was inconclusive. Contrast enhanced CT scan is very reliable in making a diagnosis when there is difficulty and is comparable to non-enhanced Nuclear Magnetic Resonance.

Necrosis Percentage	Points
No necrosis	0 points
0 to 30% necrosis	2 points
30 to 50% necrosis	4 points
Over 50% necrosis	6 points

Table 3: The CT Severity Score is the sum of the CT Grade and Necrosis Grade Scores. Necrosis score is scored at operation.

- **Magnetic Resonance Imaging**
- **Packed cell volume** should be done serially to be able to show the extent of dehydration.
- **Hypocalcaemia** is a common accompaniment of necrotizing pancreatitis. it may be so low but they never get to develop tetany. Hypocalcaemia may persist for many days even after serum amylase has returned to normal.
- **Serum Protein** may be low in some selected patients, and this calls for infusion of plasma or any form of colloids.
- **Serum Electrolytes and urea** should be monitored; any derangement should be adequately corrected.
- **Blood gases analysis** is indicated; for PO_2, PCO_2 and Ph. The finding of abnormal blood gases should be regarded as an ominous sign indicating the need for respiratory monitoring and possible assistance.
- **ECG** disturbances may be variable prolongation of Q-T segment, suppression of the S-T segment and flattening of the T-waves.

TREATMENT[1,2,4,6].

Pancreatitis is an inflammatory process that is self-limiting but the process of managing it can be tasking and financially sapping. Treatment includes adequate resuscitation to take care electrolytes and fluid deficits from the progression of the disease. In acute pancreatitis,

CT Grade Score**CT Grade**	**Appearance on CT**	**CT Grade Points**
Grade A	Normal CT	0 points
Grade B	Focal or diffuse enlargement of the pancreas	1 point
Grade C	Pancreatic gland abnormalities and peripancreatic inflammation	2 points
Grade D	Fluid collection in a single location	3 points
Grade E	Two or more fluid collections and / or gas bubbles in or adjacent to pancreas	4 points

Table 2: Balthazar Scoring for the Grading of Acute Pancreatitis

depending on the severity of the disease, one-third of the total circulating body fluid may have sequestered in the "third space". Adequate fluid and electrolytes replacement is very important; the replacement should be monitored using continuous urethral catheter drainage of urinary bladder to monitor hourly urinary output with central venous pressure line or pulmonary arterial wedge pressure. Every effort should be made to ensure that hypoperfusion of the pancreatic microvasculature and subsequent ischemic necrosis does not occur on the basis of volume deficit. With early vigorous monitoring of fluid administration, shock resulting from acute pancreatitis should be reduced in frequency.

Continuous nasogastric tube drainage is indicated to reduce the gastric secretory effect on pancreatic secretions and enzymes. Also, gastric distension by swallowed air is prevented, thereby controlling gastrin-induced pancreatic enzyme response.

Enteral feed using endoscopic guided duodenal intubation is preferable to total parenteral nutrition for this group of patients.

MEDICAL TREATMENT

Drugs to reduce gastric secretion and other pancreatic stimulation include cimetidine, anticholinergic, glucagons and 5-fluorouracil. Though, they are of doubtful value in randomized studies of alcoholic pancreatitis[7,8,9,10].

Perhaps the most challenging act is the inhibition of proteolytic activity in acute pancreatitis and this is thought, theoretically, to affect the outcome of the disease. In experimental animals, Antitrypsic antikallikrein polppeptide (Trasylon)[11], extracted from parotid gland of bovine, has been found to inhibit trypsin, chymotrypsin, kallikrein andplasmin.

Strong analgesics are indicated to relief the severe pain in these patients. The most effective drugs are the narcotics, morphine and meperidine which cause the spasm of sphincter of Oddi resulting in intra-biliary pressure. The requirement for these drugs may be side-tracked if splanchinic nerve block or epidural analgesic is successful.

The pulmonary insufficiency is more than casual, though, the mechanism is not known. In case there is respiratory insufficiency providing support for them is necessary.

Cardiac function derangement should be treated initially with correction of electrolytes and fluid deficit, most important the potassium which should be replaced under ECG monitor and making sure adequate urine is being produced. The intravenous injection of calcium is reserved for therapy of incipient tetany, as demonstrated by Chvostek or Trousseau sign and ECG conduction changes. The cardiac index may reduce and reduced peripheral resistance in patient with severe acute pancreatitis is as a result of myocardial depressant factor in circulation.

Antibiotics are clearly indicated when sepsis supervenes, however their value before sepsis sets in is of doubtful value unless used to prevent or minimize sepsis[12,13,14].

SURGICAL MANAGEMENT[1,2,3,15-19].

The surgical management of acute pancreatitis ranges from mere drainage to management of complications to prevention of recurrence depending on the severity. The various indications for surgery are:

- Treatment of complications
- Uncertain diagnosis
- Associated with biliary lithiasis
- Increasing clinical deterioration
- Prevention of recurrence

Peritoneal lavage was introduced in 1937, became consider for the treatment of acute pancreatitis recently. The procedure used for draining the peritoneal fluid collection which improve the immediately condition of patients with acute pancreatitis. It also, improve the immediate mortality rate but no improvement overall mortality, as progressive sepsis led to the demise of the patients. Presumably, the mechanism by which peritoneal lavage exerts its beneficial effect is the removal toxic products of pancreatic inflammation.

Surgical treatment is indicated in complications such abscess which occurred in 4-10% cases of acute pancreatitis. In a patient with acute pancreatitis with prolong sepsis and small retrogastric are pathognomonic of pancreatic abscess. The mortality is 100% without surgery and the mortality of 30-60% when drainage is employed. The diagnosis can be made on ultrasound, however, serial CT Scan offer the best diagnosis. Laparotomy and drain of abscess is indicated, in some cases the drainage and packing of the abscess cavity and daily change of pack under general anaesthesia may have to be employed.

Other complications of acute pancreatitis are pancreatic pseudocyst and pancreatic ascites are not acute conditions, but represent indications for surgery.

Surgery may be necessary to rule out other conditions that may mimic acute pancreatitis such as perforated PUD, acute cholecystitis, mesenteric infarction and intestinal obstruction. To establish the diagnosis,

exploratory laparotomy may be necessary. Experience has shown that mortality does not worsen on finding of acute pancreatitis, rather if one of the aforementioned is found exploration may be life-saving.

Surgery is required when acute or acute relapsing pancreatitis is associated with cholelithiasis. Although, extensive biliary surgery may be associated with high mortality the drainage of the gall bladder or common bile duct may be life-saving. Definitive biliary surgery may be embarked on later when the pancreatitis resolve.

There is a controversy surrounding surgical techniques of patients with progressive deteriorating clinical conditions. In patients with fatal necrotizing pancreatitis, in order to put such gland in total functional rest Lawson and his associates had advocated "Triple -ostomies" procedure (gastrostomy, cholecystostomy and feeding jejunostomy). The removal of necrotic tissue in near-total or total pancrecatectomy has also been advocated. Other approaches include use of sump drainage and peritoneal lavage. However, the mortality rate of these techniques approaches 30-60%.

Acute or acute relapsing pancreatitis can complicated by acute renal failure, Insulin-dependent diabetes mellitus, disseminated intravascular coagulopathy, multiple organs failure, splenic artery pseudoaneurysms, haemorrhage from erosions into splenic artery and vein, thrombosis of the splenic vein, superior mesenteric vein and portal veins, duodenal obstruction, common bile duct obstruction, pancreatic pseudocyst, chronic relapsing pancreatitis and chronic pancreatitis.

The role of surgery in acute or acute relapsing pancreatitis has not been established with certainty. Because the patients with acute or acute relapsing pancreatitis do fairly well on supportive therapy alone, it is difficult to identify patients with more severe disease that might reasonably be expected to do poorly with conservative therapy.

PROGNOSIS

Acute pancreatitis or acute relapsing pancreatitis diagnosis is a very difficult diagnosis in the tropics and more or less a diagnosis of exclusion. The experience of its management is very limited, as it is a diagnosis is rarely made. The prognosis depends on the severity of the disease and depends less on the mode of management once the standard is followed. Ranson[20] and colleagues in an attempt to determine prognostic factors evaluated 43 factors in a group of 100 consecutive cases of alcoholic pancreatitis. Eleven of these factors were found to be of prognostic significance; these provide bases for the randomization of patients between conservative and surgical treatment. APACHE II Score had been found useful to determine the outcome in acute pancreatitis[20,21].

ON ADMISSION	
1	Age greater than 55 years
2	Blood glucose greater than 200mg. per litre
3	White blood cell count greater than 1600 per cu. Mm
4	Lactic dehydrogenase greater than 700 iu
5	Serum glutamic oxalacetic transaminase greater than 250 Sigma-Frankel units
DURING THE INITIAL 48 HOURS	
6	Haematocrit decrease greater than 10% .
7	Serum calcium less than 8mg. per 100ml.
8	Lactase deficit greater than 4mEq. Per litre.
9	Blood urea nitrogen increase greater than 5mg. per 100ml.
10	Estimate fluid sequestration greater than 6litres.
11	Arterial oxygen tension less than 60mm. Hg

Table 4: Ranson et al Prognostic factors in Acute Pancreatitis

REFERENCES

1. Bradley III EL, Zeppa R The pancreas in The Text of Surgery Sabiston Jr DC (eds) 1986 pg 1170-1202.
2. UK Working Party on Acute Pancreatitis ". *Gut* 2005; **54 Suppl 3**: iii1-9
3. Gumaste V, Dave P, Weissman D, Messer J . "Lipase/ amylase ratio. A new index that distinguishes acute episodes of alcoholic from nonalcoholic acute pancreatitis". *Gastroenterology* 1991; **101** (5): 1361-6.
4. Banks P, Freeman M). "Practice guidelines in acute pancreatitis". *Am J Gastroenterol* 2006; **101** (10): 2379-400.
5. McMahon MJ, Playforth MJ, Pickford IR. A comparative study of methods for prediction of severity of attacks of acute pancreatitis. Br J Surg 1980; 67: 22.
6. Petrov MS, van Santvoort HC, Besselink MG, Cirkel GA, Brink MA, Gooszen HG (2007). "Oral Refeeding After Onset of Acute Pancreatitis: A Review of Literature".
7. Meshkinpour H, Molinari MD, Gardner L, Joehler FK. Cimetidine in the acute alcoholic pancreatitis. Gastroenterology 1979; 76: 1201.
8. Saario IA. 5-fluorouracil in the treatment of acute pancreatitis. Am J Surg 1983; 145: 349.
9. MRC Working Party: Death from acute pancreatitis. MRC multicentre trial of glucagon and aprotinin. Lancet 1977; 2: 1977.
10. McMahon MJ, Bowen M, Mayer AD, Cooper EH. Relation of alpha2-macroglobulin and the other antiprotease to clinical features of acute pancreatitis. Am J Surg 1984; 147: 164.
11. Isenmann R, Rünzi M, Kron M, Kahl S, Kraus D, Jung N, Maier L, Malfertheiner P, Goebell H, Beger H . "Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: a placebo-controlled, double-blind trial". *Gastroenterology* 2004 **126** (4): 997-1004.
12. Pederzoli P, Bassi C, Vesentini S, Campedelli A. "A randomized multicenter clinical trial of antibiotic prophylaxis of septic complications in acute necrotizing pancreatitis with imipenem". *Surgery, gynecology & obstetrics* 1993; **176** (5): 480-3.
13. Frey CF Haemorrhic pancreatitis. Am J S 1979; 137: 616.
14. Lawson DS, Daggert WM, Civetta JM, Cory RJ and Barlett MK. Surgical treatment of acute necrotizing pancreatitis. Ann Surg 1970, 170: 605
15. Norton L, Eiseman B. Near total pancreatectomy for haemorrhagic pancreatitis. Am J Surg 1974; 121: 191.
16. Ranson JHC, Spencer FC. The role of peritoneal lavage in severe acute pancreatitis. Ann Surg 1978; 187: 565.
17. Ranson JHC. Timing biliary surgery in acute pancreatitis. Ann Surg 1979; 189: 654.
18. Ranson JHC, Rifkind KM, Roses DF, Fink SD, Eng F, Spencer FC. Prognostic signs and roles operative management in acute pancreatitis. Surg Gynecol Obstet 1974; 139: 69
19. Larvin M, McMahon M "APACHE-II score for assessment and monitoring of acute pancreatitis". *Lancet* 1989. **2** (8656): 201-5.
20. Yeung Y, Lam B, Yip A "[www.hbpdint.com/text.asp?id=837 APACHE system is better than Ranson system in the prediction of severity of acute pancreatitis]". *Hepatobiliary Pancreat Dis Int* 2006 **5** (2): 294-9.