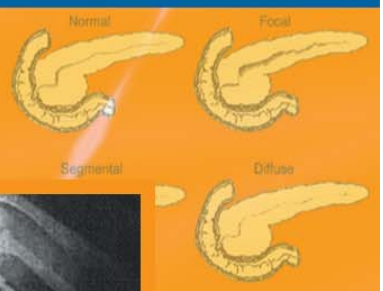
JANUARY 2005 VOL 13 NO 1 ISSN 1681-5552

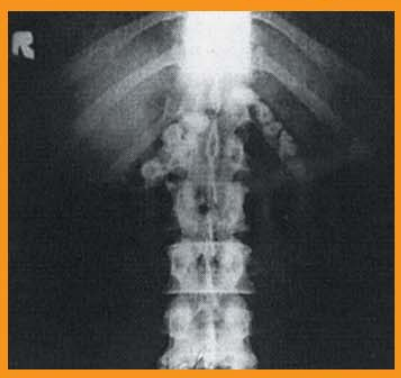
Happy New Year !

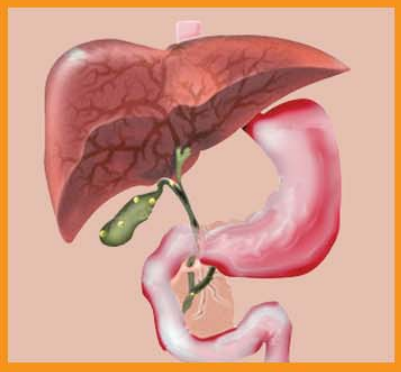
the SQUARE

healthcare bulletin

- Gallstones
- Chronic Pancreatitis
- Critical Care
- Product Profile- Zitrol XR®
- Glimpse of MSD Activities-2004
- Medical Breakthrough







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IN THIS ISSUE:

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From the Desk of Managing Editor

Dear Doctor:

Happy New Year!

Welcome to this edition of **"the SQUARE"** healthcare bulletin!

At first we express out heartiest appreciation for your encouraging response regarding **"the SQUARE"**. We are delighted to know that you enjoy reading this bulletin very much!

In this issue we aim to focus on the management of the "critically ill patient" who require aggressive care in multiple settings, such as emergency department, critical care unit, medical/surgery units, and home care. We have published a special feature on "gallstones" which is a common gastrointestinal problem in day to day practice. We also have a special feature on "chronic pancreatitis", refers to a syndrome of destructive, inflammatory conditions that encompasses the many sequel of long-standing pancreatic injury. Furthermore, we have one of our "product profile", some fascinating news in the "medical breakthrough", and "glimpse of MSD activities in 2004".

We believe you will enjoy this issue as well!

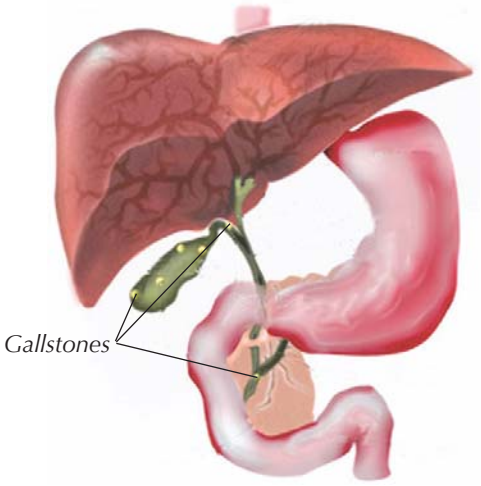
Let me take the opportunity to notify you that our healthcare online **"e-SQUARE"** is back again with a new look! If you are not yet registered, please send us your e-mail address for your registration, free! Besides, if you find any of your doctor friend or colleague who is missing **"e-SQUARE"**, please do not hesitate to send their e-mail address also! We are just a click away!

On behalf of the "**SQUARE** family", we wish you and your family a very joyful, healthy and prosperous year 2005!

Omar Akramur Rab

Gallstones

Gallstones are crystalline bodies formed within the body by accretion or concretion of normal or abnormal bile components. Usually these are collections of cholesterol, bile pigment or a combination of the two, and usually form in the gallbladder; however, they also may form anywhere there is bile--in the intrahepatic, hepatic, common bile, and cystic ducts. Gallstones also may move about within bile.



Hepatobiliary System

Causes of gallstones

There are several types of gallstones and each type has a different cause.

Cholesterol gallstones

Cholesterol gallstones (most common types) are made primarily of cholesterol, comprising 80% of gallstones in individuals from Europe and the Americas. Bile acids and lecithin secreted by the liver dissolve cholesterol so that it can be carried by bile. If the liver secretes too much cholesterol for the amount of bile acids and lecithin it secretes, some of the cholesterol does not dissolve. Similarly, if the liver does not secrete enough bile acids and lecithin, some of the cholesterol also does not dissolve. In either case, the undissolved cholesterol sticks together and forms particles of cholesterol that grow in size and eventually form larger gallstones.

There are two other processes that promote the formation of cholesterol gallstones though neither process is able to cause cholesterol gallstones by itself. The first is abnormally rapid formation and growth of cholesterol particles into gallstones. The second is reduced contraction and emptying of the gallbladder that allows bile to sit in the gallbladder longer so that there is more time for cholesterol particles to form and grow.

Pigment gallstones

Pigment gallstones are the second most common type of gallstone composed of calcium bilirubinate, or calcified bilirubin. Although pigment gallstones comprise only 15% of gallstones in individuals from Europe and the Americas, they are more common than cholesterol gallstones in Southeast Asia. Pigment stones can be black or brown.

Black stones are the more common types and they are more likely to develop in people with hemolytic anemia or cirrhosis. If there is too much bilirubin in bile, the bilirubin combines with other constituents in bile, for example, calcium, to form pigment. Pigment dissolves poorly in bile and, like cholesterol, it sticks together and form particles that grow in size and eventually form black stones.

Brown stones are more common in Asian populations. If there is reduced contraction of the gallbladder or obstruction to the flow of bile through the ducts, infection may ascend from the duodenum into the bile ducts and gallbladder. When there is obstruction and infection, the bacteria alter the bilirubin, which then combines with calcium to form pigment. The pigment combines with fats in bile to form particles that grow into brown stones. It is softer than black pigment gallstones.

Risk factor for gallstones

Risk for cholesterol gallstones

There is no relationship between cholesterol in the blood and cholesterol gallstones. Individuals with elevated blood cholesterol do not have an increased prevalence of cholesterol gallstones. A common misconception is that diet is responsible for the development of cholesterol gallstones, however, it isn't. The risk factors for developing cholesterol gallstones include:

- **Gender:** Gallstones form more commonly in women than men.
- **Age:** Prevalence increases with age.
- **Obesity:** Obesity is a major risk factor for gallstones, especially in women.
- **Estrogen:** Excess estrogen from pregnancy, hormone replacement therapy, or birth control pills appears to increase cholesterol levels in bile and decrease gallbladder movement, both of which can lead to gallstones.

- **Rapid weight loss:** Rapid weight loss causes cholesterol gallstones in up to 50% of individuals. As the body metabolizes fat during rapid weight loss, it causes the liver to secrete extra cholesterol into bile, which can cause gallstones. Many of the gallstones will disappear after the weight is lost, but many do not. Moreover, until they are gone, they may cause problems.
- **Fasting:** Fasting decreases gallbladder movement, causing the bile to become overconcentrated with cholesterol, which can lead to gallstones.
- **Crohn's disease:** In Crohn's disease of the terminal ileum, bile acid recycle blocked and there are not enough bile acids to keep cholesterol solubilized in bile, and gallstones form.
- **Increased blood triglycerides:** People with diabetes generally have high levels of triglycerides and gallstones occur more frequently in individuals with elevated blood triglyceride levels.
- **Cholesterol-lowering drugs:** Persons with low HDL cholesterol levels or high triglyceride levels are at increased risk for stones. Cholesterol-lowering drugs gemfibrozil and clofibrate reduce cholesterol levels in the blood actually increasing the amount of cholesterol secreted into the bile, thus creating a higher risk for gallstones. Other cholesterol-lowering agents do not have this effect.
- **Ethnicity:** Hispanics and Northern Europeans have a higher risk for gallstones than people of Asian and African descent do. People of Asian descent who develop gallstones are most likely to have the brown pigment type. Native North and South Americans, such as Pima Indians in the US and native populations in Chile and Peru, are especially prone to developing gallstones.
- **Other risk factors:** Prolonged intravenous feeding reduces the flow of bile and increases the risk for gallstones. Thiazide diuretics may slightly increase the risk for gallstones.

Risk for pigment gallstones

Black pigment gallstones form whenever there is an increased load of bilirubin that reaches the liver. This occurs whenever there is increased destruction of red blood cells as there is in sickle cell disease and thalassemia. Black pigment gallstones also are more common among patients with cirrhosis of the liver. Brown pigment gallstones form when there is stasis of bile, for example, when there are narrow, obstructed bile ducts.

Risks in children

Gallstone disease is relatively rare in children. When gallstones occur in this age group they are more likely to be pigment stones. Girls do not seem to be at a higher risk than boys. The following conditions may put children at higher risk:

- Spinal injury
- History of abdominal surgery
- Sickle-cell anemia
- Impaired immune system
- Intravenous nutrition

Symptoms of gallstones

The majority of people with gallstones may remain silent. Their gallstones often are found as a result of tests (e.g., ultrasound or X-ray of the abdomen) performed while evaluating medical conditions other than gallstones. Over a period of five years, approximately ten percent of people with silent gallstones will develop symptoms.

Gallstones are blamed for many symptoms they do not cause. Among the symptoms gallstones do not cause are dyspepsia, intolerance to fatty foods, belching, and flatulence. Signs and symptoms of gallstones virtually always occur when they obstruct bile ducts.

The most common symptom of gallstones is biliary colic which is the primary or only symptom in 80% of people with gallstones who develop symptoms.

Biliary colic lasts for 15 minutes to 4-5 hours. If the pain lasts more than 4-5 hours, it means that cholecystitis or a complication has developed. The pain usually is severe, but movement does not make the pain worse. In fact, patients experiencing biliary colic often walk about or writhe in bed trying to find a comfortable position. An episode of biliary colic subsides gradually once the gallstone shifts within the duct so that it is no longer obstructing the duct.

Complications of gallstones

- Cholecystitis
- Sepsis
- Cholangitis
- Fistula
- Gangrene
- Ileus
- Jaundice
- Cancer
- Pancreatitis

Diagnosis of gallstones

Ultrasound or other imaging techniques usually detect gallstones readily. Nevertheless, because gallstones are common and most cause no symptoms, simply finding stones does not necessarily explain a patient's pain, which may be caused by numerous other ailments.

Physical exam often reveals tenderness in the upper right area of the abdomen in acute cholecystitis and sometimes in biliary colic. There is usually no tenderness in chronic cholecystitis

Laboratory Tests

The enzyme alkaline phosphatase and bilirubin are usually elevated in acute cholecystitis, and especially choledocholithiasis. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are elevated when common bile duct stones are present. A threefold or more increase in ALT strongly suggests pancreatitis. A high white blood cell count is a common finding in many (but not all) patients with cholecystitis.

Imaging Techniques for Diagnosis of Gallstones

- Ultrasonography
  - Transabdominal ultrasonography
  - Endoscopic ultrasonography
- Magnetic resonance cholangio-pancreatography (MRCP)
- Cholescintigraphy (HIDA scan)
- Endoscopic retrograde cholangio-pancreatography (ERCP)
- Oral cholecystogram (OCG)
- Intravenous cholangiogram (IVC)

Differential diagnosis

- Irritable bowel syndrome (IBS)
- Acute appendicitis
- Inflammatory bowel disease (Crohn's disease or ulcerative colitis)
- Pneumonia
- Peptic ulcer
- Gastroesophageal reflux disease (GERD)
- Hiatus Hernia
- Viral Hepatitis
- Kidney stones
- Urinary tract infections
- Diverticulosis or diverticulitis
- Pregnancy complications
- Heart attack

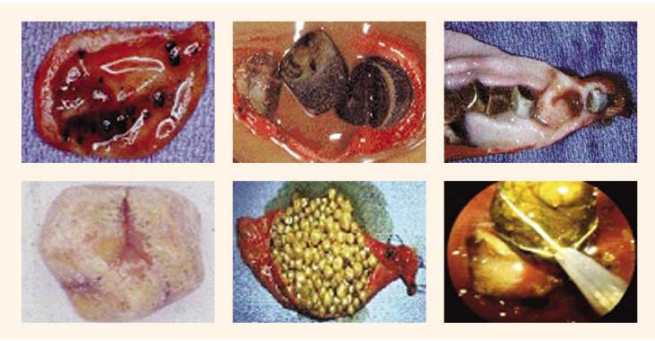


Fig: Pigment Stone, Mixed Stone, Calcium Carbonate Stone, (Upper Left to Right) Mercedes Benz Stone, Cholesterol Stone, Cholesterol Stone (Lower Left to Right)

Potential pitfalls of diagnosing gallstones

Usually, it is not difficult to diagnose gallstones. Problems arise, however, because of the high prevalence of silent gallstones and the occasional gallstone that is difficult to diagnose.

If a patient has symptoms that are typical for gallstones--biliary colic, cholecystitis, or pancreatitis, for example--and has gallstones on ultrasonography, little else usually needs to be done diagnostically to demonstrate that the gallstones are causing the episode unless the patient has complicating medical issues. If episodes are not typical for gallstones, however, any gallstones found may be silent. These silent gallstones may be innocent bystanders, and most importantly, removing the gallbladder surgically will not prevent further episodes, and the real cause of the episodes will not be pursued. In such a situation, there is a need to have further evidence, other than their mere presence, that the gallstones are causing the episode. Such evidence must be obtained during an episode or shortly thereafter.

If ultrasonography can be done during an episode of pain or inflammation caused by gallstones, it may be possible to demonstrate an enlarged gallbladder or bile duct caused by obstruction of the ducts by the gallstone. This is likely to require ultrasonography again after the episode has resolved in order to demonstrate that the gallbladder indeed was enlarged during the episode. It is easier to obtain the necessary ultrasonography if the episode lasts several hours, but it is much more difficult to obtain ultrasonography rapidly enough if the episode lasts only 15 minutes.

Another approach is to test the blood for abnormal liver and pancreatic enzymes. The advantage here is that the enzymes, though not always elevated, can be elevated during and for several hours after an episode of pain or inflammation, so they might be abnormal even after the episode has subsided. It is important to remember, however, that the enzymes are not specific for gallstones, and it is necessary to exclude other liver and pancreatic causes for abnormal enzymes.

Sometimes, episodes of pain or inflammation may be more or less typical of gallstones, but transabdominal ultrasonography may not demonstrate either gallstones or ▶

another cause of the episodes. In this case, it is necessary to decide whether suspicion is high or low for gallstones as a cause of the episodes. If suspicion is low because of less typical symptoms, it may be reasonable only to repeat the ultrasonography, obtain an OCG, and/or test for abnormalities of liver or pancreatic enzymes. If suspicion is high because of more typical symptoms, it is reasonable to go even further with endoscopic ultrasonography, ERCP, and duodenal drainage. Prior to these invasive procedures, some physicians recommend MRCP; however, the exact role of MRCP is not yet clear.

Management of gallstones

Most gallstones are silent. If silent gallstones are discovered in an individual at age 65 (or older), the chance of developing symptoms from the gallstones is only 20% (or less) assuming a life span of 75 years. In this instance, it is reasonable not to treat the individual. Among younger individuals, no treatment also might be appropriate if the individuals have serious, life-threatening diseases, for example, serious heart disease, that are likely to shorten their life span. On the other hand, in healthy young individuals, treatment should be considered even for silent gallstones because the individuals' chances of developing symptoms from the gallstones over a lifetime will be higher. Once symptoms begin, treatment should be recommended since further symptoms are likely.

There are three approaches to gallstone treatment:

- Expectant management
- Non-surgical removal of the stones
- Surgical removal of the gallbladder.

Expectant management

Guidelines from the American College of Physicians state that when a person has no symptoms, the risks of both surgical and non-surgical treatment for gallstones outweigh the benefits. Experts suggest a wait-and-see approach for such patients, which they have termed expectant management. Exceptions to this policy are those at risk for complications from gallstones, including the following:

- People at risk for gallbladder cancer (such as those with calcified gallbladders or large polyps).
- Patients with stones larger than 3 cm. (One study reported that very small gallstones increase the risk for acute pancreatitis. Some experts therefore believe that gallstones smaller than 5 mm warrant immediate surgery.)

There are some minor risks with expectant management for asymptomatic or low-risk individuals. Gallstones almost never spontaneously disappear, except sometimes when they are formed under special circumstances, such as pregnancy or sudden weight loss. At some point, then, the stones may cause pain, complications, or both and require treatment. Some studies suggest that the patient's age at diagnosis may be a factor in the possibility of future surgery. The probabilities are as follows:

- 30% likelihood of future surgery for people diagnosed at 30 years old. (The slight risk of developing gallbladder cancer might encourage young adults who are asymptomatic to have their gallbladders removed.)
- 20% at 50 years old.
- 15% at 70 years old.

Treatment for patients with symptoms

Gallstones are the most common cause for hospital admissions among patients with severe abdominal pain. The approach to patients who come to the hospital with emergency symptoms suggesting gallstones (i.e., steady and severe pain on the right side) may be the following:

- Administration of intravenous fluids and painkillers (Some physicians believe morphine should be avoided for gallbladder disease.)
- Antiemetics.
- Antibiotics for 12 to 24 hours. These may be given to patients with evidence of infection (acute cholecystitis), including fever or an elevated white blood cell count.

Diagnostic tests are also be performed and, depending on results, the approach may be as follows:

Normal Test Results and No Severe Pain or Complications: If the patient has no fever or underlying serious medical problems and shows no signs of severe pain or complications, and if laboratory tests are normal, the patient may be discharged with oral antibiotics and pain relievers.

Tests Show Gallstones and Presence of Pain but No Infection: Patients with pain and tests that indicate gallstones but who do not show signs of infection have the following options:

- They may electively choose to have cholecystectomy at their convenience. The most common procedure is now laparoscopy.

- A minority of such patients may be candidates for a stone-breaking technique called lithotripsy. (The treatment works best on solitary stones that are less than 2 cm in diameter.)
- Drug therapy for gallstones is available for some patients who are unwilling to undergo surgery or who have serious medical problems that increase the risks of surgery. Non-surgical treatment, however, usually cannot be used for patients who have acute gallbladder inflammation or common bile duct stones since delaying or avoiding surgery could be very hazardous in these cases. Recurrence rates are high with non-surgical options. The introduction of laparoscopic cholecystectomy has greatly reduced the use of non-surgical therapies.

Tests Indicating Acute Cholecystitis: If tests indicate acute gallbladder infection, early gallbladder removal is often warranted. It is usually performed at least 48 hours after admission when inflammation has improved. Some patients can wait longer.

Tests Showing Gallstone-Associated Pancreatitis: Patients who have developed gallstone-associate pancreatitis almost always require surgery, either laparoscopic or open cholecystectomy.

Tests Suggesting Common Duct Stones: If noninvasive diagnostic tests suggest obstruction from common duct stones, the physician performs endoscopic retrograde cholangiopancreatography (ERCP) to confirm the diagnosis and remove stones. This technique is used urgently along with antibiotics if infection is present in the common duct.

Surgical procedure

Only cholecystectomy guarantees that the patient will not suffer a recurrence of gallstones. This is one of the most common surgical procedures performed on women and can even be performed during pregnancy, with low risk to the baby and mother. The primary advantages of surgical removal of the gallbladder over non-surgical treatment are both the elimination of gallstones and also the prevention of gallbladder cancer.

Appropriate Surgical Candidates: Candidates for surgery often have one of the following conditions:

- One very severe gallstone attack
- Several less severe gallstone attacks
- Cholecystitis
- Pancreatitis

Prevention of gallstones

Prevention of cholesterol gallstones is feasible since ursodiol, the bile acid medication that dissolves some cholesterol gallstones, also prevents them from forming. The difficulty is identifying a group of individuals who are at high risk for developing cholesterol gallstones during a relatively short period of time so that the duration of preventive treatment can be limited. One such group is obese individuals losing weight rapidly with very low calorie diets or with surgery. The risk of gallstones in this group is as high as 40%-60%. In fact, ursodiol has been shown in several studies to be very effective at preventing gallstones in these individuals.

Prognosis

Removal of the gallbladder should eliminate all symptoms except in three situations:

- Gallstones were left in the ducts,
- There were problems with the bileducts in addition to gallstones, and
- The gallstones were and are not the cause of the symptoms.

Gene for gallstones!

Genetic factors are important in gallstone. Current scientific studies are directed at uncovering the specific genes that are responsible for gallstones. To date, 8-10 genes have been identified as being associated with cholesterol gallstones, at least in animals that develop cholesterol gallstones. The long-term goal is to be able to identify individuals who are genetically at very high risk for cholesterol gallstones and to offer them preventive treatment. An understanding of the exact mechanism(s) of gallstone formation also may result in new therapies for treatment and prevention.

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Chronic Pancreatitis

Pancreatitis is a global health care problem with varied etiology. Chronic pancreatitis is a condition characterized by irreversible destruction and fibrosis of the exocrine parenchyma, leading to exocrine insufficiency and progressive endocrine failure leading to diabetes. In Western industrialized countries, the dominant etiological factor of chronic pancreatitis is alcohol abuse, accounting for approximately 80% of patients. In contrast with Western countries, in Southern India an alcohol independent form of chronic pancreatitis called tropical pancreatitis is common. Mutations in the cationic trypsinogen gene are present in patients with hereditary chronic pancreatitis. Approximately 30% of patients with idiopathic chronic pancreatitis have mutations in the cystic fibrosis transmembrane conductance regulator gene.

TROPICAL CHRONIC PANCREATITIS (TCP)

Tropical chronic pancreatitis is defined as a juvenile form of chronic calcific non-alcoholic pancreatitis prevalent almost exclusively in the developing countries of the tropical world. The distinctive features of TCP are:

- ❒ Younger age at onset
- ❒ Presence of large intraductal calculi
- ❒ An accelerated course of the disease leading the end points of diabetes and/ or steatorrhea
- ❒ A high susceptibility to pancreatic cancer.

Epidemiology

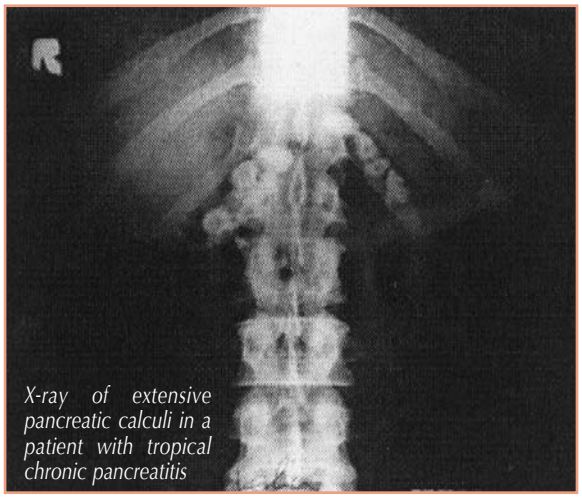
In 1959, Zuidema first reported a series of patients with pancreatic calculi and clinical features of undernutrition occurring in the lower socioeconomic strata of the society. The first case of pancreatic calculi from India was reported by Kini in 1937. Reports from several tropical countries of the world including Nigeria, Uganda, Brazil, Thailand, Bangladesh, and Sri Lanka have subsequently confirmed the existence of TCP.

TCP is endemic in Kerala, one survey done in Kerala reported a prevalence of 125/100000 population. The frequency of TCP is much lower in other parts of India. In Japan the prevalence of chronic pancreatitis was reported to be 45.4/100000 population, which is higher than in western countries where it is reported to be approximately 10-15/100000 population with an annual incidence of 3.5-4/100000 population.

Clinical presentation

- ❒ Abdominal pain
- ❒ Maldigestion leading to steatorrhea
- ❒ Diabetes (fibrocalculous pancreatic diabetes)

Abdominal pain: Abdominal pain is the predominant symptom and usually the presenting complaint in 30%-90% of patients. The pain is typically very severe, upper abdominal in location, radiates to the back, and is relieved by stooping forward or lying in a prone position. The severity of pain trends to decrease and it becomes less frequent as the disease progresses and it usually disappears with onset of exocrine insufficiency and/or diabetes.



X-ray of extensive pancreatic calculi in a patient with tropical chronic pancreatitis

Pancreatic calculi: Pancreatic calculi are detected especially in the later stages in more than 90% of patients with TCP. The calculi are intraductal in location and are seen mostly in the right side of first and second lumbar vertebra in plain abdominal radiography. They may be solitary or multiple, and sometimes the entire pancreas may be studded with calculi. The stones tend to be large, dense, and rounded with well defined edges in contrast to the small, speckled, ill defined stones in alcoholic chronic pancreatitis.

Maldigestion/ steatorrhea: Patients with severe exocrine pancreatic insufficiency complain of passing bulky, frothy, or frankly oily stools. The frequency of steatorrhea is depends on dietary fat intake.

Diabetes: Diabetes is an inevitable consequence of TCP commonly occurring a decade or two after the first episode of abdominal pain. Diabetes in TCP is called fibrocalculous pancreatic diabetes (FCPD). In lean and

undernourished individuals, the diabetes tends to be more severe and polyuria and polydepsia are the major presenting complaints. In the better nourished patients, the symptoms may be insidious and the diagnosis of FCPD is usually made during investigation for abdominal pain. One of the characteristic clinical features of FCPD is that despite requiring insulin for control, patients rarely become ketotic on withdrawal of insulin. Diabetes is usually very severe with a fasting blood glucose from 11.1-22.2 mmol/L and often requires the use of insulin for control.

Etiopathogenesis

The exact etiopathogenic mechanisms still remain elusive. Several hypotheses have been proposed:

- ❒ Malnutrition
- ❒ Cassava and dietary toxins
- ❒ Familial and genetic factors
- ❒ Oxidant stress hypothesis and trace element deficiency states.

Pathology

TCP is a progressive disease, therefore the pathological findings depend on the stage of disease at which the specimen is obtained. The size of the pancreas varies inversely with the duration of the disease and it can be as small as the little finger in advanced stages of the disease. The surface is nodular, the shape of the gland is distorted with loss of normal lobular appearance. The gland may get displaced from its normal position due to uneven shrinkage and fibrous adhesion. The cut section of the pancreas shows the presence of homogenous areas with early to advanced fibrosis and intraductal calculi of varying shapes and sizes with marked dilation of the duct and ductules. Color of the stones vary from chalky white to dirty white.

Microscopic examination reveals a thickened capsule and extensive intralobular and interlobular fibrosis not limited to any zone or area. Interlobular fibrosis is characteristic of early cases and focal, segmental, or diffuse fibrosis of more advanced cases. Marked dilatation with periductular fibrosis is seen in the main duct, collecting ducts, and small ductules with denudation of the ductular epithelium and squamous metaplasia of some areas. The characteristic of cellular infiltration of the pancreas is composed of lymphocytes and plasma cells, distributed mainly around the ducts.

Immunohistochemistry has shown paucity of alpha cells and beta cells. Immunohistochemistry studies show a decrease in the number of islets in some cases and hyperplasia in others.

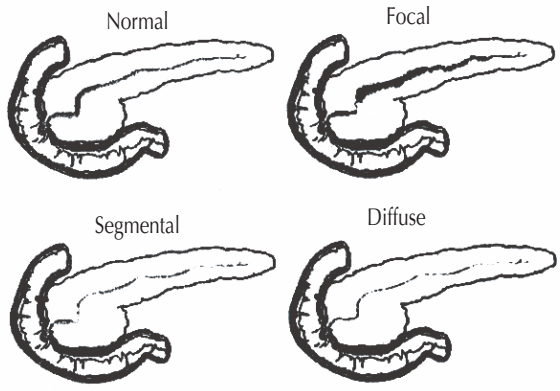
Investigations

- ❒ Plain X-ray of abdomen
- ❒ Ultrasonography
- ❒ Computed tomography
- ❒ Endoscopic retrograde cholangiopancreatography
- ❒ Endoscopic ultrasonography
- ❒ Tests of exocrine pancreatic function
- ❒ Tests of endocrine pancreatic function

Complications

Complications due to chronic pancreatitis:

- ❒ Pancreatic pseudocysts
- ❒ Pancreatic abscess
- ❒ Ascites
- ❒ Obstructive jaundice may also be occasionally seen
- ❒ Pancreatic cancer is the most sinister complication of TCP.



Schematic diagram of the direct pancreatograms in autoimmune chronic pancreatitis, "Focal" means focal type, "segmental" means AIP with segmental irregular narrowing, and "diffuse" means AIP with diffuse irregular narrowing.

Complication related to diabetes:

- ❒ Microvascular diabetic complications in FCPD : the prevalence of microvascular complications is similar to that seen in type 2 diabetes
- ❒ Macrovascular complications are less common in FCPD because the patients are:
  - ◆ Young
  - ◆ Lean
  - ◆ Have lower lipid levels

In the 1960s and 70s, it was reported that TCP patients develop abdominal pain in childhood, diabetes in adolescence, and die of complications of diabetes such as chronic pancreatitis in early adulthood or in the prime of their life. Today TCP patients survive much longer, perhaps due to improved nutrition and better control of diabetes.

Management

Medical management

- ❒ Abdominal pain:
  - ◆ Analgesics
  - ◆ Pancreatic enzyme supplements
  - ◆ Antioxidants
- ❒ Steatorrhea:
  - ◆ Pancreatic enzyme supplements
- ❒ Diabetes:
  - ◆ Oral hypoglycemic agents for early cases
  - ◆ Insulin is needed for majority of patients

Difference between tropical chronic pancreatitis (TCP) and alcoholic chronic pancreatitis (ACP)

	TCP	ACP
Sex ratio M:F %	70:30	Almost all male
Age at onset	2nd & 3rd decade	4th & 5th decade
Socioeconomic status	Usually poor, may occur in others as well	All strata of society equally affected
Course of diabetes	More aggressive & accelerated	Slower rate of progression
Diabetes	Occurs in >90%	About 50% of cases
Pancreatic calculi	Occurs in >90%	About 50% - 60% of cases
Appearance of pancreatic calculi	Large and dense with discrete margin	Usually small & speckled with ill defined margins
Location of calculi	Always in large ducts	Usually in small ducts
Ductal dilation	Usually marked	Usually mild
Fibrosis of gland	Marked	Less severe
Alcoholism	Absent	Heavy alcohol abuse
Prevalence of pancreatic cancer	Very high	Higher than in the general population

Surgical management

Often, the abdominal pain can be intractable and difficult to manage. Surgical intervention is indicated when medical management does not work. Various surgical intervention have been tried with fairly good result.

AUTOIMMUNE CHRONIC PANCREATITIS (AIP)

AIP can be defined as a chronic inflammation of the pancreas due to an autoimmune mechanism. AIP is associated with hypergammaglobinemia, histologic evidence of lymphoplasmacytic infiltration, coexistence of other autoimmune diseases, and a remarkable response to steroid therapy. In the normal pancreas, carbonic anhydrase type II is located in the duct cells and lactoferrin exists in the pancreatic acini. An autoimmune reaction against carbonic anhydrase type II or lactoferrin via Th1-type CD4+ T cells may have a role in the development of AIP.

Clinical presentation:

- ❒ Age: 45 to 75 years, mean age was 59.1 year
- ❒ Male to female ratio: 15:2
- ❒ Major presenting symptom: painless jaundice
- ❒ Other symptoms: non-specific mild abdominal pain, and weight loss

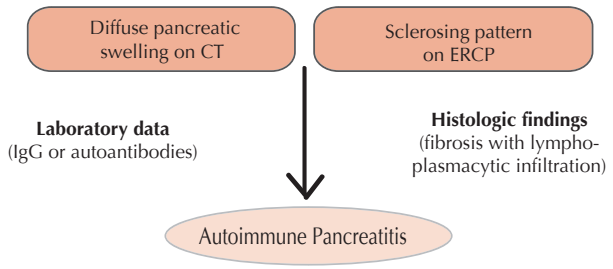
None of the patients had history of alcohol abuse or other predisposing factor of chronic pancreatitis. Diabetes mellitus is often noticed in AIP with reports ranging from 42% to 76%. Patients sometimes visit physicians for symptoms related to other autoimmune diseases, such as Sjogren's syndrome, inflammatory bowel disease and retroperitoneal fibrosis.

Investigation:

- ❒ Pancreatic enzyme level: normal or mild elevation in serum amylase or lipase
- ❒ IgG elevation or hypergammaglobinemia: has been reported in 37-76%
- ❒ Detection of autoantibody: antilactoferrin antibody and anticarbonic anhydrase type II antibody are the most commonly detected autoantibodies in AIP
- ❒ Histologic findings: the characteristics findings on microscopy are medium sized and large interlobular ducts surrounded by the infiltration of inflammatory cells and fibrosis. The inflammatory cells are mainly composed of lymphocytes (mainly CD4+ T cells with some CD8+ T cells and B cells) and plasma cells. Interstitial fibrosis with acinar atrophy is another characteristic feature of AIP
- ❒ CT scan findings: a diffusely enlarged pancreas without peripancreatic fat infiltration, phlegmonous changes, or pseudocysts

❒ ERCP findings: the hallmark finding on direct pancreatogram is diffuse or segmental irregular narrowing of the main pancreatic duct.

Pancreatic Imaging



Approach to the patient suspected with AIP

Diagnostic criteria for autoimmune chronic pancreatitis proposed by the Japan Pancreas Society:

Radiologic imaging

❒ Diffuse or segmental irregular narrowing of the main pancreatic duct and diffuse enlargement of the pancreas

Laboratory data

❒ Elevated levels of serum IgG or presence of autoantibodies

Histopathology

❒ Fibrotic changes with lymphocytoplasmacytic infiltration of the pancreas

Differentiating AIP from pancreatic cancer by radiologic Imaging

	AIP	Pancreatic cancer
Complete cutoff of main pancreatic duct	Uncommon	Common
Ductal stricture	Multiple	Localized (single)
Upstream duct dilatation	Mild	Marked
Duct in the mass	Present	Absent
Diffuse swelling of the pancreas	Almost always	Rare
Double duct sign	Common	Common

Differential diagnosis

❒ Alcoholic chronic pancreatitis

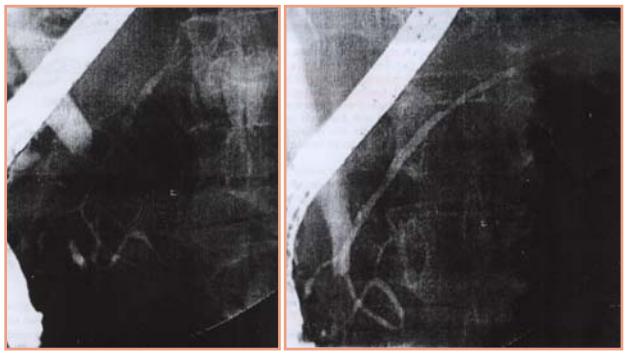
❒ Pancreatic cancer

Treatment

Steroid gives excellent result in the treatment of AIP. Prednisolone is usually initiated at 30-40 mg/day for 1-2 months, and tapered by 5 mg every 2-4 weeks. Some physicians recommend a maintenance dose of 5-10 mg /day of prednisolone to prevent relapses without complete discontinuation of steroid.

ALCOHOLIC CHRONIC PANCREATITIS

In the United States and other industrialized countries, the most common cause of chronic pancreatitis is excessive alcohol consumption. Changes appear to develop slowly



ERCP findings. (Left) Before treatment, diffuse irregular narrowing of the main pancreatic duct is shown. (Right) After steroid therapy, the narrowing sites on preceding ERCP have resolved in the main pancreatic duct

and may develop after excessive alcohol consumption for 10 years or more. Alcoholism is associated with chronic pancreatitis in 60-90% of patients. Studies revealed that the logarithm of the relative risk of chronic pancreatitis increases linearly as a function of the quantity of alcohol and protein consumption. There seemed to be no threshold of toxicity of alcohol. Furthermore, the type of alcoholic beverage, i.e. beer or wine, was of no influence.

Pathogenesis

The pathogenesis of alcohol induced chronic pancreatitis is poorly understood. Researchers try to explain the pathogenesis of the disease by the following four competing hypotheses:

◆ Ethanol induced fatty degeneration of pancreatic acinar cells

◆ Damage to acini by oxygen derived free radicals

◆ Destruction of acini due to ductal hypertension induced by obstruction by protein precipitates

◆ Fibrosis as a consequence of repeated episodes of acute necrotizing pancreatitis.

Chronic calcifying pancreatitis is invariably related to alcoholism. The earliest finding is precipitation of proteinaceous material in the pancreatic ducts that forms protein plugs that subsequently calcify. The ducts and lobules are initially involved in a random manner, and they are surrounded by normal parenchymal tissue. However, as the disease progresses, these normal areas become more diffuse. The pancreatic ductal epithelium undergoes atrophy, hyperplasia, and metaplasia at the site of the protein plugs. Many of the small pancreatic ductules dilate, while others are obliterated by fibrosis.

The main pancreatic duct shows a chain-of-lakes appearance due to alternating stenoses and dilatation. In approximately one half of patients with chronic calcific pancreatitis, the pancreatic parenchyma contains cysts of varying sizes (several millimeters to 5 cm). These cysts are lined by cuboidal epithelium and contain pancreatic enzymes. Peripancreatic fibrosis is usually a late finding that involves the portal and/or splenic veins. Peripancreatic fibrosis causes stenosis or occlusion of retroperitoneal lymph channels. Ascites may complicate chronic calcific pancreatitis as a result of portal hypertension or lymphatic obstruction in 1-2% patients.

Investigations

- Plain radiograph: Plain radiographs show pancreatic calcification in 25-59% of patients
- Ultrasonogram of abdomen: Sonography can help in determining the cause of chronic pancreatitis (eg, alcoholic liver disease, calculus disease) and in assessing the complications of the disease (eg, pseudocysts, ascites, splenic/portal venous obstruction)
- ERCP: Cholangiopancreatography is the most sensitive imaging modality; it is used to show the ductal anatomy directly and when intervention (eg, stricture dilatation, stent placement) is contemplated
- MRI: MRI provides excellent images that may show the changes in the diseased pancreas and also the complications of chronic pancreatitis
- CT scan: CT is useful in differentiating chronic pancreatitis from pancreatic carcinoma.

Management

Image-guided pancreatic biopsy may be performed. Immediate tissue analysis reduces the need for multiple biopsies. Fine-needle biopsy is usually performed because of the risk of acute pancreatitis with the use of larger needles. Patients with acute biliary obstruction in the context of active pancreatitis, with or without pseudocyst in the head of the pancreas, can be treated by using temporary biliary stents. The value of dilatation and stent placement in the pancreatic duct has not yet been established. Currently, patients with recurrent acute episodes of pancreatitis may be treated with dilation of pancreatic duct strictures or the placement of temporary pancreatic duct stents. Further studies are necessary to establish the long-term benefits.

Radiologic findings of autoimmune chronic pancreatitis (AIP) in comparison to alcoholic chronic pancreatitis (ACP)

	AIP	ACP
Direct pancreatogram	Irregular	Irregular dilatation
Phlegmon or pseudocyst	Rare	Common
Calcification or stone	Rare	Common
Pancreatic parenchyma	Enlargement	Atrophy

Surgical approaches are occasionally attempted to control intractable pain. These procedures include celiac ganglionectomies, splanchnicectomies, and various resections of the pancreas. Surgical series report a 70%-90% success rate in alleviating pain. The surgical repair of leaks demonstrated on ERCP may be required.

Medical treatment consists of large-volume paracentesis and total parenteral nutrition. The treatment of pancreatic ascites may be difficult.

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Critical care is the multidisciplinary healthcare specialty that cares for patients with acute, life-threatening illness or injury. Critical care can be provided wherever life is threatened - at the scene of an accident, in an ambulance, in a hospital trauma center or emergency room, or in the operating room. Most critical care today, however, is delivered in highly specialized intensive care units and trauma centers.

Recognizing the critically ill patient

- *Cardiovascular signs*
  - Cardiac arrest
  - Pulse rate < 40 or > 140 bpm
  - Systolic blood pressure (BP) < 100 mmHg
  - Tissue hypoxia
    - Poor peripheral perfusion
    - Metabolic acidosis
    - Hyperlactatemia
  - Poor response to volume resuscitation
  - Oliguria: <0.5 ml/kg/hr
- Respiratory signs
  - Threatened or obstructed airway
  - Stridor, intercostal recession
  - Respiratory arrest
  - Respiratory rate < 8 or > 35/min
  - Respiratory distress: use of accessory muscle; unable to speak in complete sentences
  - $Sp0_2$ < 90% on high-flow 0_2
  - Rising $PaC0_2$ > 8 kPa, or > 2 kPa above normal with acidosis
- Neurological signs
  - Threatened or obstructed airway
  - Absent gag or cough
  - Failure to maintain normal $Pa0_2$ and $PaC0_2$
  - Failure to obey commands; Glasgow Coma Scale (GCS) <10
  - Sudden fall in level of consciousness (GCS fall >2 points)
  - Repeated or prolonged seizures

Major manifestations of critical illness and management

Shock

In shock the organs of the body do not get enough oxygen and blood pressure for them to function normally. The four most common causes are:

- Hypovolemic Shock - severe dehydration or massive blood loss. *Treatment*: intravenous fluids (IV) and/or blood transfusions.
- Cardiogenic Shock- cardiac or heart failure. *Treatment*: medications or devices to improve heart function.
- Septic Shock - severe infection resulting in organ failure. *Treatment*: intravenous fluids (IV) and medications to increase blood pressure and treatment of the infection.
- SIRS or Systemic Inflammatory Response Syndrome - can be caused by any massive trauma to the body such as a car accident, severe infection, or by some medical conditions such as pancreatitis. *Treatment*: intravenous fluids (IV) and medications to increase blood pressure if shock cannot be reversed in a matter of days the body's organs will start to shut down. This may lead to death.

Acute respiratory failure

Acute respiratory failure may be the reason for admission to an ICU or a complication that occurs in the ICU from many different causes. Acute respiratory failure can range from mild to severe. Causes of mild acute respiratory failure include a variety of conditions such as pneumonia or heart failure. These are usually treated with oxygen and respiratory treatments to help strengthen breathing and bring up phlegm.

Moderate respiratory failure may be caused by more severe pneumonia or chronic obstructive pulmonary disease (COPD). Usually these patients need some type of mechanical support to help their breathing. Support may be provided by a tight-fitting mask that delivers oxygen under pressure or through the insertion of an endotracheal tube into trachea. A variety of support can be provided through this tube.

The most severe form of acute respiratory failure is called ARDS (Acute Respiratory Distress Syndrome). In ARDS the lungs can not supply oxygen to the blood, and a ventilator may be needed. ARDS is always caused by something but the list of something is very long. Common examples of cause are: pneumonia, aspiration, trauma, severe infections, and pancreatitis. There is no single therapy for ARDS. The goal is to support the patient until the lungs heal.

Chronic respiratory failure

If patients remain critically ill for a long period, they become very weak. This weakness often prevents them from having the strength to breathe on their own. The ▶

respiratory muscles need to be exercised and slowly built up before the patient will be able to breathe on his or her own again. This may take as long as 2 to 3 months. When the use of a breathing machine is needed for more than a few weeks, tracheostomy may be necessary. This is done to improve patient comfort and help the patient breathe well enough to be removed from the ventilator. A feeding tube may also need to be inserted.

Infections

Infections can also develop while a patient is in the ICU. Infections occur for many reasons. Usually the illness that has brought the patient to the ICU has weakened him or her and lessened the ability to fight off infections. In addition, a patient often needs devices like a breathing tube and intravenous lines. These medical devices are necessary, but foreign to the body and can lead to infections.

The most common infection in a patient on a ventilator is pneumonia. Sometimes the pneumonia can be mild and is treated with antibiotics. Sometimes the pneumonia can be severe and cause sepsis and ARDS.

Another severe infection that can occur is bacteremia. This infection may be caused by the presence of intravenous lines. This is called line sepsis. If this occurs, the intravenous line needs to remove and new line placed in a different location. Most of the time line sepsis can be successfully treated with antibiotics. Line sepsis can also lead to hypertension and ARDS.

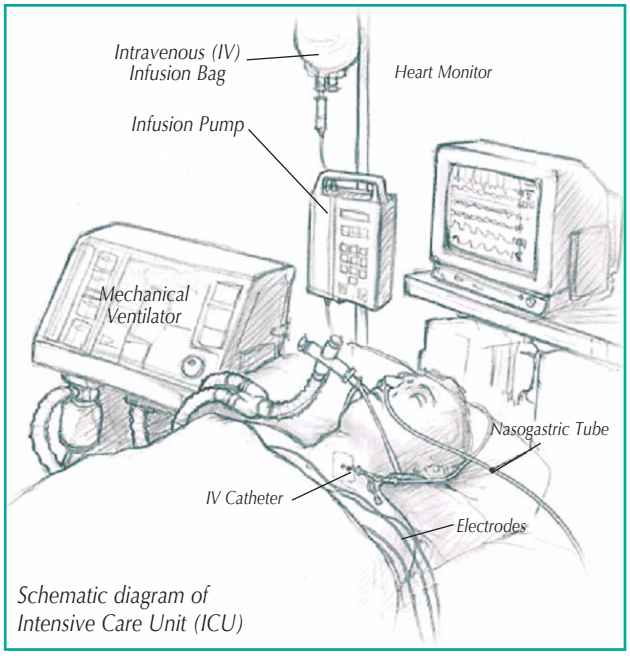
Other infections that can occur include UTI's or urinary tract infections from a Foley catheter. There may be infections in the bowel that may cause diarrhea. Wound infections may occur from a recent surgery in which the surgical incision has not completely healed yet. These infections are usually treated fairly easily with antibiotics.

Sepsis and Severe Sepsis

Infections are a common cause of ICU admission and are also a frequent complication. The severity of infection, as well as the age and medical conditions affecting the patient, may put them at risk for an uncontrolled inflammation in response to their infection and/or injury. This inflammatory response is called sepsis. Severe sepsis occurs when this inflammation begins to affect the function of the body (renal failure and acute respiratory failure, etc), and the patient becomes very sick. Aggressive antibiotics, fluids, other medications and sometimes surgery may be used to treat sepsis and severe sepsis, while other forms of support (dialysis, ventilation) may be needed to support the body's function. When blood pressure becomes low and specific drugs (vasoconstrictors) to address it are used, this is known as septic shock.

Renal failure

Kidney or renal failure is very common in the ICU and can be the reason the patient came to the ICU. It may also develop at any time while the patient in the ICU. The kidneys are very sensitive to any severe illness and many different illnesses can lead to renal failure.
Two major problems occur with renal failure. First, the



Schematic diagram of Intensive Care Unit (ICU)

body is unable to remove extra water from the body and results in swelling of the arms, legs, and face. The patient will often look puffy. That extra water also builds up in the organs of the body and can cause trouble breathing and problems with the function of other organs.

The second function of the kidneys is to remove toxins from the body. When those toxins start to build up they affect the brain and the patient gets sleepy and can become unresponsive (goes into a coma). These toxins are not damaging the brain and the patient should wake up

again if the toxins can be removed. If the toxins build up enough, the heart may stop and the patient will die from renal failure.

Renal failure can be mild to severe. Mild causes can be treated with intravenous fluids and sometimes medications to help the kidneys work better. Severe renal failure can lead to the need for dialysis. Dialysis does not make the kidneys improve faster. The kidneys must heal by themselves. Dialysis only allows the body to stay alive while the kidneys are improving.

There are 2 major types of dialysis: Intermittent or continuous. Intermittent dialysis is a treatment that uses a machine for 3 to 4 hours a day or every other day. Continuous dialysis is a machine that stays connected to the patient 24 hours a day. The sicker a patient is the more likely they will need continuous dialysis.

Neurological conditions

A variety of neurologic disorders are seen in the ICU. These may include traumatic brain injuries, strokes, infections, or changes that occur when a patient is sleepy, disoriented, frightened or agitated. He or she may become paranoid and scared and require calming medications and restraints to prevent harming him or himself. The patient may not awake at all while they remain critically ill. These changes are related to how sick the patient is, and usually resolves if the overall condition improves. Elderly patients are extremely susceptible to these changes due to the unfamiliar environment and the changes in sleep patterns that occur in the critical care unit.

Bleeding and clotting

Two other common problems deserve mention. The critically ill patient can develop bleeding from the stomach , the stress ulcer. Most critically ill patients are given medication to prevent, but it can occur even if this medication is given. Usually the bleeding stops by itself but often requires blood transfusions. Occasionally surgery or another procedure needs to be considered.

Critically ill patients also are at risk for developing blood clots and are at risk for developing blood clots in their legs and lungs. Most critically ill patients are placed on their legs to prevent this; but, it can occur even with these measures. The blood clot can be minor and only need anticoagulation to treat or it can be life threatening.

Multiple Organ Dysfunction Syndrome (MODS)

Any type of critical illness that brings a patient to the ICU has the potential to affect the other organs in the body. These organs may not have been affected at first, but slowly one organ after another starts to fail. This is called Multiple Organ Dysfunction Syndrome or MODS. There is not specific treatment for MODS, only supportive care. The first and most commonly affected organs are the lungs and the kidneys, followed by the brain and the immune system. Other organ then begin to be involved; the heart, liver, blood, intestines and any other organs of the body can be affected. Once a patient starts to develop MODS, their chances of surviving start to decrease. The more organs that fall the more likely it is that the patient will not survive.

Critical Care Team

The critical care team includes a diverse group of highly trained professionals who provide care in specialized care units and work toward the best outcome possible for seriously ill patients. All members of the team may be asked to teach patients and their families various strategies to improve health, healing, coping, and well being specific to their area of expertise.

Members of the team include: Intensivists (Physicians), Critical care nurses, Pharmacist or Clinical Pharmacologist, Registered Dietician, Social Worker, Respiratory Therapist, Physical Therapist or Occupational Therapist.

Typical examples of critical illness include heart attack, poisoning, pneumonia, surgical complications, premature birth, and stroke. Critical care also includes trauma care, care of the severely injured - whether due to an automobile accident, gunshot or stabbing wounds, a fall, burns, or an industrial accident.

Difference between critical care and emergency medicine

Critical care refers exclusively to the treatment of patients who suffer from threatening conditions. Emergency room physicians and nurses treat patients who suffer from relatively minor emergencies (sprained ankles, broken arms) to those with major problems including heart attack,

Management of critically ill patient

2. Respiratory care
Altered ventilation, poor secretion clearance, impaired muscle function and lung collapse (atelectasis) occur in the supine position. Respiratory care includes assisted coughing, deep breathing and alveolar recruitment techniques (e.g. CPAP), chest percussion, postural drainage, positioning (e.g. sitting up), bronchodilators, tracheal toilette, suctioning and tracheostomy care

3. Cardiovascular care
Prolonged immobility impairs autonomic vasomotor responses to sitting and standing causing profound postural hypotension. Tilt tables may be beneficial prior to mobilization

4. Gastrointestinal (GI)/nutritional care
The supine position predisposes to gastro-oesophageal reflux and aspiration pneumonia. Nursing patients 30° head-up prevents this. Early enteral feeding reduces infection, stress ulceration and GI bleeding. Immobility is associated with gastric stasis and constipation; gastric stimulants and laxatives are essential

5. Neuromuscular
Immobility, prolonged neuromuscular blockade and sedation promote muscle atrophy, joint contractures and foot drop. Physiotherapy and splints may be required

6. Comfort and reassurance
Anxiety, discomfort and pain must be recognized and relieved with reassurance, physical measures, analgesics and sedatives. In particular, endotracheal or nasogastric tubes, bladder or bowel distension, inflamed line sites, painful joints and urinary catheters often cause discomfort and are often overlooked. Fan use is controversial as dust-borne micro-organisms may be disseminated. Visible clocks help patients maintain circadian rhythms

7. Communication with the patient
Use of amnesic drugs makes repeated explanations and reassurance essential. Assist interaction with appropriate communication aids

8. Venous thrombosis prophylaxis
Trauma, sepsis, surgery and immobility predispose to lower limb thrombosis. Mechanical and pharmacological prophylaxis prevent potentially life-threatening pulmonary embolism

9. Infection control
HAND WASHING is vital to prevent transmission of organisms between patients.
DISPOSABLE APRONS are recommended.
STERILE TECHNIQUE (e.g. gloves, masks, gowns, sterile field) is essential for all invasive procedures (e.g. line insertion).
ISOLATION (± negative pressure ventilation) for transmissible infections (e.g. tuberculosis).
THOROUGH CLEANING OF BED SPACES (e.g. routinely and after patient discharge)

10. Skin care, general hygiene and mouthcare
Cutaneous pressure sores are due to local pressure (e.g. bony prominences), friction, malnutrition, edema, ischemia and damage related to moist or soiled skin. Turn patients every 2 h and protect susceptible areas. Special beds relieve pressure and assist turning. Mouthcare and general hygiene are essential

11. Fluid, electrolyte and glucose balance
Regularly assess fluid and electrolyte balance. Insulin resistance and hyperglycemia are common but maintaining normoglycemia improves outcome

12. Bladder care
Urinary catheters cause painful urethral ulcers and must be stabilized. Early removal reduces urinary tract infections

13. Dressing and wound care
Replacement of wound dressings as necessary.
Arterial and central venous catheter dressings should be changed every 48-72 hours

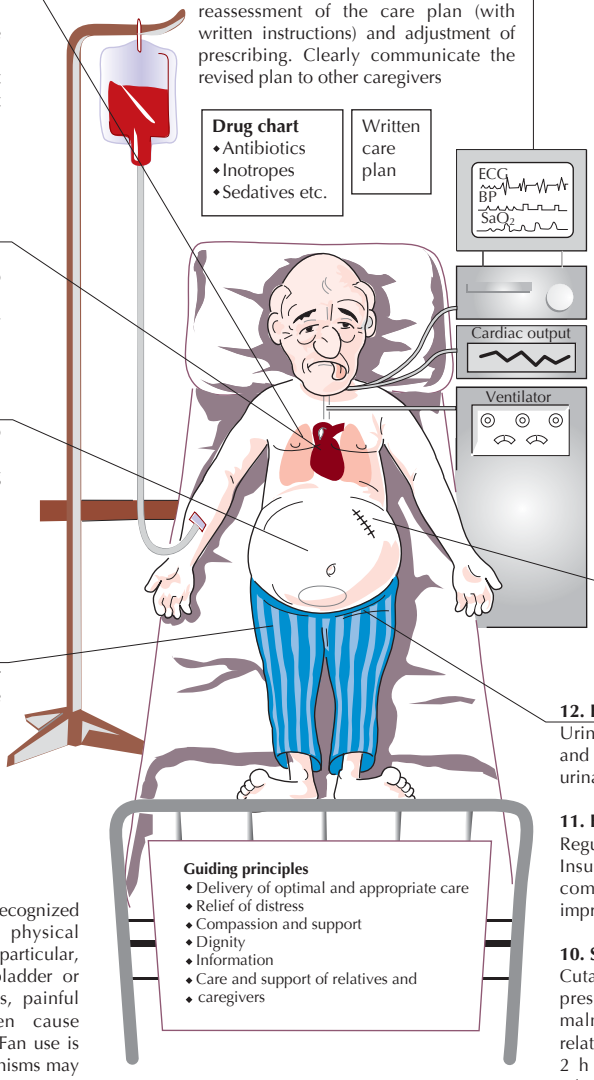
14. Communication with relatives
Family members receive information from many caregivers with different perspectives and knowledge. Critical care teams must aim to be consistent in their assessments and honest about uncertainties. One or two physicians should act as primary contacts. All conversations must be documented.
Compassionate care of relatives is always appreciated, avoids anger and is one of the best indicators of a well-functioning unit

15. Visiting hours
Opinions differ with regard to relatives visiting hours. Some units restrict visits (e.g. 2 periods/day), others have almost unrestricted hours

1. Regular review of monitored trends and response to therapy
Followed by clinical examination, reassessment of the care plan (with written instructions) and adjustment of prescribing. Clearly communicate the revised plan to other caregivers

Drug chart
- Antibiotics
- Inotropes
- Sedatives etc.

Written care plan



Guiding principles
- Delivery of optimal and appropriate care
- Relief of distress
- Compassion and support
- Dignity
- Information
- Care and support of relatives and
- caregivers

knife or gunshot wounds or drug overdoses. In the Emergency Department, physicians and nurses stabilize patients and transport them to the ICU or other area of the hospital for further treatment. The long-term management of critically ill and injured patients is provided by critical care professionals, often in the ICU.

Commonly used life support measures

Cardiopulmonary resuscitation/Advanced coronary life support (CPR/ACLS)

CPR/ACLS are a group of treatments used when someone's heart and/or breathing stops. It may consist of artificial breathing, and it can include pressing on the chest to mimic the heart's function to restart circulation. Electric shocks (defibrillation) and drugs can also be used to stimulate the heart.

Defibrillation is not always restart the heart

If the heart has lost all of its electrical activity or is so damaged that it no longer has enough muscle to pump blood through the body, defibrillation may not be successful in restarting the heart.

Vasopressors

Vasopressors are a group of powerful drugs that cause blood vessels to get smaller and tighter, therapy raising blood pressure. This therapy is only given in the intensive care unit.

Artificial nutrition and hydration (tube feeding)

Tube feeding is the administration of a chemically balanced mix of nutrients and fluids through a feeding tube. Most commonly, a feeding tube is inserted into the stomach via the nasal passage (nasogastric or "NG" tube) or through the wall of the abdomen [gastronomy tube or percutaneous endoscopic gastrostomy (PEG) tube] by means of a surgical procedure. Another type of feeding tube is inserted surgically through the abdominal wall into the small intestine (jejunostomy tube).

Intravenous feeding

Intravenous (IV) feeding are given to patients who are unable to tolerate tube feedings. Similar to tube feedings, the IV feeding provides the patient with the needed amount of protein, carbohydrate, fat, vitamins and minerals. Nutrition and hydration may be supplied temporarily, until the patient recovers adequate ability to eat and drink, or it can be supplied indefinitely. Although potentially valuable and life saving in many situations, artificial nutrition and hydration do not provide comfort care for dying patients. Available scientific evidence has shown that death without artificial nutrition or hydration may cause less suffering.

Mechanical ventilation (MV)

Mechanical ventilation is used to support or replace the function of the lungs. A machine called a ventilator (or respirator) forces air into the lungs. The ventilator is attached to a tube inserted in the nose or mouth and down into the trachea. MV may be used short term (i.e. treating pneumonia), or it may be needed indefinitely for permanent lung disease or trauma to the brain. Some patients on long term MV live a quality of life that is acceptable to them. For some patients, MV may only prolong the dying process.

Dialysis

Dialysis does the work of the kidneys, which remove waste from the blood and manage fluid levels. This procedure requires a special central venous catheter. Dialysis can be performed in the ICU or in the dialysis unit, depending upon the condition of the patient. Some patients may live on dialysis for years. But, dialysis for the chronically ill/dying patient may only prolong the dying process.

Pacemakers

The heart can be paced temporarily until healing occurs. A surgical procedure to insert a permanent pacer may be required. Patients with non-curable heart disease may choose not to have a pacemaker.

Transport of the critically ill patient

Once identified, critically ill patients have to be transported to the most appropriate area for continuing care. Before intra or interhospital transfer, the patient's condition must be stabilized. Appropriate monitoring should be set up and if there is clinical evidence of progressive respiratory failure or inability to protect the airway, endotracheal intubation and ventilation are indicated. Hypovolemia and hypotension should be corrected and this will often require monitoring of the central venous pressure (CVP). It may be more appropriate to admit the patient to the local ICU for initial stabilization before transfer to another hospital.

Principles of safe transfer

- ❒ Experienced staff
- ❒ Appropriate equipment and vehicle
- ❒ Full assessment and investigation
- ❒ Extensive monitoring
- ❒ Careful stabilization of patient
- ❒ Reassessment
- ❒ Continuing care during transfer
- ❒ Direct handover
- ❒ Documentation and
- ❒ audit.

Scoring system

Scoring system (SS) are used to predict outcome and evaluate care. Two SS have been validated and are widely used in ICUs.

- ❒ APACHE (Acute Physiology And Chronic Health Evaluation) - The identification of the at risk patient or that patient who could benefit from intensive care treatment is largely based on scoring systems which measure severity of illness. The scoring system most frequently used is the APACHE system- usually APACHE II. It should not be used to predict individual outcome. Scoring is based on the primary disease process, physiological reserve, including age and chronic health history (e.g. chronic liver, cardiovascular, respiratory, renal and immune condition), and the severity of illness determined from the worst value in the first 24 h of 12 acute physiological variables, including rectal temperature, mean blood pressure (BP), heart rate, respiratory rate (RR), arterial $P0_2$ and pH, serum sodium, potassium and creatinine, hematocrit, white cell count (WCC) and Glasgow Coma Score (GCS).
- ❒ SAPS (Simplified Acute Physiology Score) is similar to APACHE II with equivalent accuracy.

Intensive care units

Intensive care units (ICUs) are sections in hospitals that contain specialized equipment and highly trained staff to treat patients who have a serious illness or injury. Patients may be admitted to the ICU from an emergency department or other hospital section, after surgery, or after transfer from another health care facility.

Equipment Commonly Used in the ICU

- ❒ Monitors measure body functions such as breathing and heart rate. They often have alarms that sound to alert the ICU staff when such functions are outside of a normal range.
- ❒ Intravenous catheters are inserted in patients' veins to dispense medicine, fluids and nutrition as needed. A nasogastric tube may be inserted through the nose into the stomach. Urinary catheters are used to drain urine from the bladder.
- ❒ Mechanical ventilators (also called respirators) are machines that help patients breathe through a tube that is inserted through the mouth or nose into the trachea and is connected to the ventilator.

Important disorders that may be treated in the ICU

- ❒ Acute respiratory distress syndrome (ARDS) is sudden lung failure that often requires use of a ventilator. It is caused by other illnesses such as infections or serious injuries.
- ❒ Asthma involves obstruction of the airways that causes difficulty breathing, wheezing, chest tightness and coughing.
- ❒ Chronic obstructive pulmonary disease (COPD) makes exhaling difficult. It is usually caused by smoking-related lung disorders such as emphysema and chronic bronchitis.
- ❒ Pneumonia is an infection of the lungs that may interfere with breathing.
- ❒ Respiratory distress syndrome can occur in infants whose lungs are underdeveloped, causing difficulty breathing.
- ❒ Sepsis is a very serious infection in the blood or tissues.
- ❒ Trauma involves injuries, such as from motor vehicle crashes, that often require surgery.

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Product Profile- Zitrol XR ®

Zitrol XR®

(Glipizide Extended Release Tablets)

Composition

Zitrol XR® 2.5: Each extended release tablet contains Glipizide BP 2.5 mg.

Zitrol XR® 5 : Each extended release tablet contains Glipizide BP 5 mg.

Zitrol XR® 10 : Each extended release tablet contains Glipizide BP 10 mg.

Zitrol XR® (Glipizide) is an oral blood-glucose-lowering drug of the sulfonylurea class formulated as a once-a-day controlled release tablet for oral use.

Clinical Pharmacology: *Mechanism of Action*: Glipizide lowers blood glucose by stimulating the release of insulin from the pancreas, an effect dependent upon functioning beta cells. The extrapancreatic effects of Glipizide are increase in insulin sensitivity and decrease in hepatic glucose production.

Pharmacokinetics and Metabolism: The absolute bioavailability of glipizide is 100%. Steady-state effective plasma concentrations are achieved by at least the fifth day of dosing with the preparation in type 2 diabetic patients younger than 65 years. Approximately 1 to 2 days longer are required for patients >65 years. No accumulation of drug is likely in patients during chronic dosing.

Indications and Usage

Zitrol XR Extended Release Tablet is indicated as an adjunct to diet in patients with type 2 diabetes. The preparation can be used as combination therapy with other oral hypoglycemic agents and with insulin.

Contraindications

- Known hypersensitivity to glipizide.
- Type 1 diabetes, diabetic ketoacidosis, with or without coma.

Warnings: The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin.

Precautions: *Renal and Hepatic Disease*: The pharmacokinetics of glipizide may be affected.

GI Disease: Markedly reduced GI retention times may influence the pharmacokinetic profile of the drug.

Hypoglycemia: All sulfonylurea drugs are capable of producing severe hypoglycemia.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by NSAIDs, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta-adrenergic blocking agents. Certain drugs tend to produce hyperglycemia i.e. thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid.

Pregnancy: Pregnancy category C.

Nursing Mothers: It is not known whether glipizide is excreted in human milk or not.

Pediatric Use: Safety and effectiveness in children have not been established.

Geriatric Use: There were no overall differences in effectiveness or safety between younger and older patients.

Adverse Reactions: The most potential adverse reaction is hypoglycemia (1% to 3.4%). Other side effects reported were asthenia, headache, dizziness, nervousness, tremor, diarrhea, flatulence.

Overdosage: There is no well-documented experience with Glipizide Extended Release Tablets overdosage in humans.

Dosage and Administration: The usual starting dose is 5 mg per day, given with breakfast. Dosage adjustment should be based on glycemic control. If no improvement is seen after three months of therapy with a higher dose, the previous dose should be resumed. Most patients will be controlled with 5 mg to 10 mg taken once daily. The maximum recommended daily dose is 20 mg. Patients receiving immediate release or intermediate release glipizide may be switched safely to the extended release preparation once-a-day at the nearest equivalent total daily dose.

Combination Use: Zitrol XR should be initiated at the lowest recommended dose for combination therapy. Patients with stable type 2 diabetes receiving insulin may be transferred safely to treatment with the extended release tablets.

Storage Condition: The tablets should be protected from moisture and humidity and stored at room temperature (below 30° C).

How Supplied

Zitrol XR® 2.5: Box containing thirty (3 X 10's) 2.5 mg Glipizide Extended Release Tablets in blister strips.

Zitrol XR® 5: Box containing fifty (5 X 10's) 5mg Glipizide Extended Release Tablets in blister strips.

Zitrol XR® 10: Box containing thirty (3 X 10's) 10 mg Glipizide Extended Release Tablets in blister strips.

Correct answers of the 'Test Yourself - 17'

1. a,d **2.** b **3.** b,d **4.** b,c **5.** d **6.** a,c

The following are the 10 winners of the "Test Yourself -17"; they have been selected through lottery.

Congratulations from "the SQUARE" Editorial Board

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General Hospital, Narayanganj

Soon our officials will be visiting you with a token of our appreciation

Test Yourself — 18

Q. 1. All the points mentioned below are correct for "critical care" except:
a. Shock, acute respiratory failure, sepsis are among the major manifestations of critical illness.
b. Tissue hypoxia, cardiac arrest, stridor, are some of the signs to recognize critical ill patients.
c. SAPS and ACACHE are the scoring systems used widely in ICU.
d. ARDS, COPD, pneumonia, sepsis, are among the important conditions treated in ICU.

Q. 2. The following features are true for "chronic pancreatitis" except:
a. Abdominal pain, maldigestion, diabetes are the clinical presentations of TCP.
b. TCP cases are not found in Bangladesh.
c. Pancreatic cancer is the most sinister complication of TCP.
d. TCP patient does not survive much longer.

Q. 3. All the followings are true for "gallstones" except:
a. Persons with low HDL and low TG have increased risks for gallstones.
b. Jaundice, cholecystitis, pancreatitis are some of the complications of gallstones.
c. Ultrasonography, ERCP, OCG are the only imaging techniques for gallstone diagnosis.
d. Expectant management, non-surgical treatment and surgical removal are the approaches to gallstone treatment.

Q. 4. All the following points are true for "Zitrol XR® (Glipizide Extended Release)" except:
a. It is a drug of sulfonylurea class formulated as a once-a-day controlled release tablet.
b. Zitrol XR® must not be given in combination with other oral hypoglycemic agents and insulin.
c. The usual starting dose of Zitrol XR® is 5mg/day given with breakfast.
d. Zitrol XR® should be initiated at the highest recommended dose for combination therapy.

Q. 5. All the following are correct for "gallstones" except:
a. Eight to twelve genes have been identified as being associated with cholesterol gallstones.
b. Gallstones occur in children are most likely to be pigment stone.
c. Gallstones cause dyspepsia, intolerance to fatty foods, belching and flatulence.
d. Black pigment gallstones are more common among the patients with cirrhosis of liver.

Q.6. All the following points are true for "chronic pancreatitis" except:
a. Pancreatic pseudocysts, pancreatic abscess, ascitis are among the complications.
b. Course of diabetes is more aggressive and accelerated in ACP.
c. Fibrosis of the gland is less severe in ACP.
d. Diabetes Mellitus is not noticed in AIP.

Glimpse of MSD Activities-2004

Scientific seminar on "Polycystic Ovary Syndrome (PCOS)" at Gyne & Obstetrics department of BSMMU, Dhaka

Scientific seminar & annual general meeting of OGSB, Chittagong

Scientific seminar on "Interventional Management of CHD" at Jhenaidah Sadar Hospital

Clinical meeting on "Diabetes Mellitus: Practical Aspects" at Medicine department of Rangpur Medical college Hospital

Internee reception program of Bangladesh Medical College Hospital, Dhaka

Implantable Computer Chip!

Researchers developed an implantable computer chip that can pass a patient's medical details to doctors, speeding care. The computer chip, known as "VeriChips", radio frequency microchips the size of a grain of rice, have already been fused to identify wayward pets and livestock. And nearly 200 people working in Mexico have been implanted with chips to access secure areas containing sensitive documents.


"VeriChips"

It's the first time the USFDA has approved the use of the device, though in Mexico, more than 1,000 scannable chips have been implanted in the patients. The chip's serial number pulls up the patients' blood type and other medical information.

With the pinch of a syringe, the microchip is inserted under the skin in a procedure that takes less than 20 minutes and leaves no stitches. Silently and invisibly, the dormant chip stores a code that releases patient-specific information when a scanner passes over the chip. At the doctor's office those codes stamped onto chips, once scanned, would reveal such information as a patient's allergies and prior treatments.

Source: Dow Jones Newswires

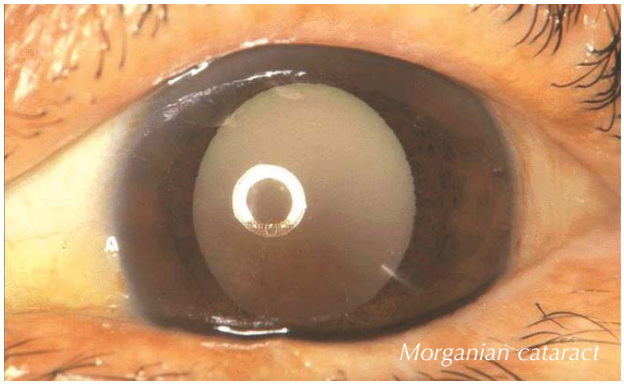
New Device for Stroke Prevention!

Patients suffering from atrial fibrillation may soon benefit from a novel device designed to prevent stroke. About 15 percent of strokes are caused by a condition called atrial fibrillation. During atrial fibrillation, the two upper chambers of the heart quiver rapidly, inhibiting the heart from pumping out all the blood. This can lead to the formation of blood clots in the atria. If these blood clots travel through into the left ventricle and out through the aorta, they may end up in the brain, where they can cause a stroke. The new device, which was implanted successfully in more 200 patients, is designed to block blood clots where they form in the heart, before they can migrate out. According to the study authors, about 90 percent of blood clots in the patients with atrial fibrillation form in the left atrial appendage. The device, which is delivered by a catheter, is designed to completely block the opening of the left atrial appendage, which serves no physiological function. Currently, the standard approach to prevent strokes during atrial fibrillation is anticoagulant therapy, which seeks to prevent the blood from clotting. However, anticoagulants have a range of side effects, including bleeding, swelling and rash. The new device may become a valuable alternative for patients with chronic, non-rheumatic atrial fibrillation in whom standard anticoagulation therapy is contraindicated or poorly tolerated, the researcher said. The new device, called the percutaneous left atrial appendage transcatheter occlusion (PLAATO) system, was developed at the Cardiovascular Center in Frankfurt, Germany. The feasibility study was conducted in 14 centers in Europe and the United States.

Source: HeartCenterOnline

Glue-like Polymer for Cataract Surgery!

A team of researchers has developed a novel, adhesive hydrogel that can be painted over incisions from cataract surgery and offers the potential for faster, improved repair, they say. The hydrogel may help avoid complications associated with sutures - the most common repair method for those types of incisions - or unsutured incisions that are left to heal on their own, another repair method of cataract surgery.


Morganian cataract

The transparent hydrogel is made of special polymer materials which act like the liquid bandages sold in stores for topical wounds. Researcher says, in addition to cataracts that using a hydrogel adhesive instead of sutures shows promise for repairing eye wounds associated with LASIK surgery, ulcers, corneal and retinal injuries, and others. The researchers believe the hydrogel could be available to physicians in three to four years.

Hydrogels have been used for several years in applications ranging from drug delivery to healing injured blood vessels, but using them to repair eye wounds is novel, researcher says.

Source: ScienceDaily

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