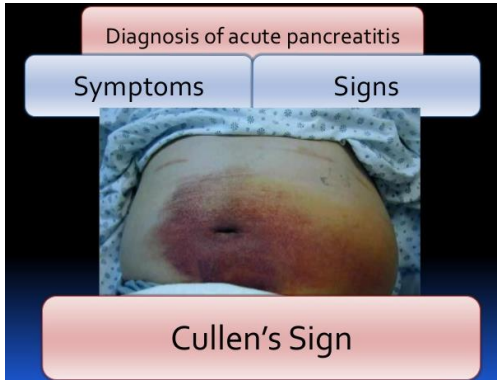
各領域帶狀課程

BestPractice

Guideline



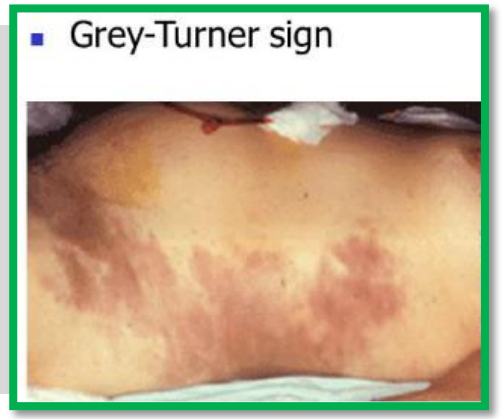

PGY/NP必修課程(2024)

DM/FNP core course

# Acute pancreatitis

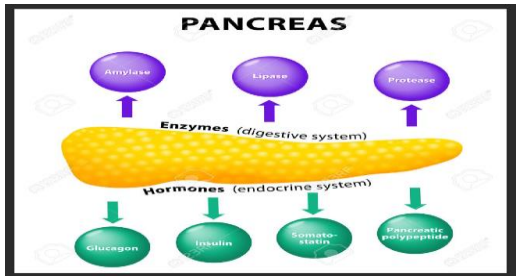
## (2024)

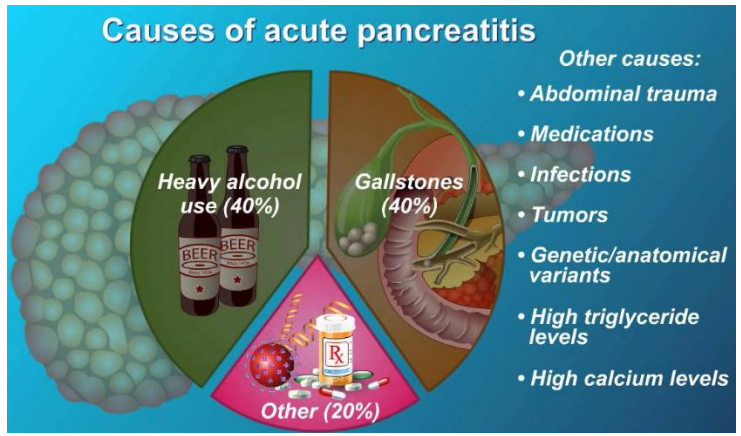
## Causes and discharge plan




王正一

2024.03.01

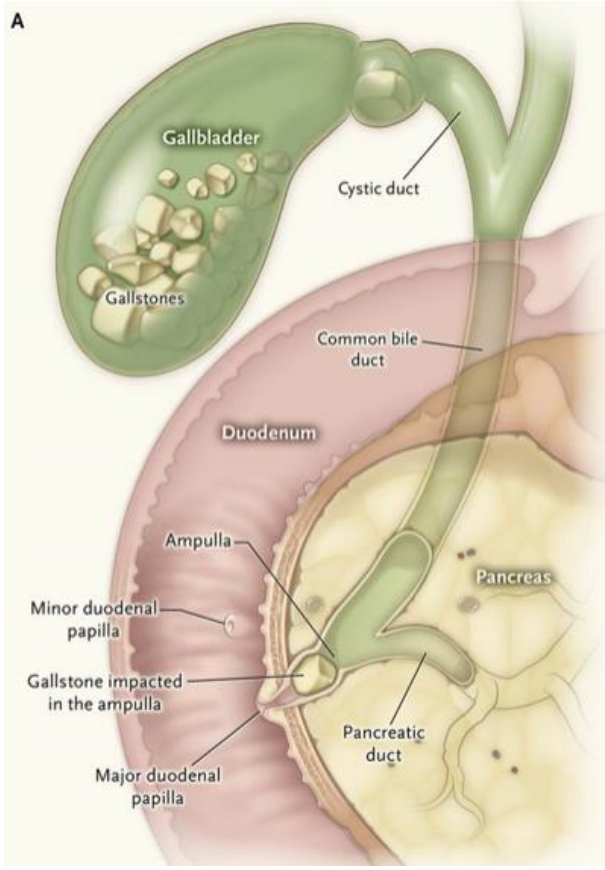


# I. Gall stone → acute pancreatitis

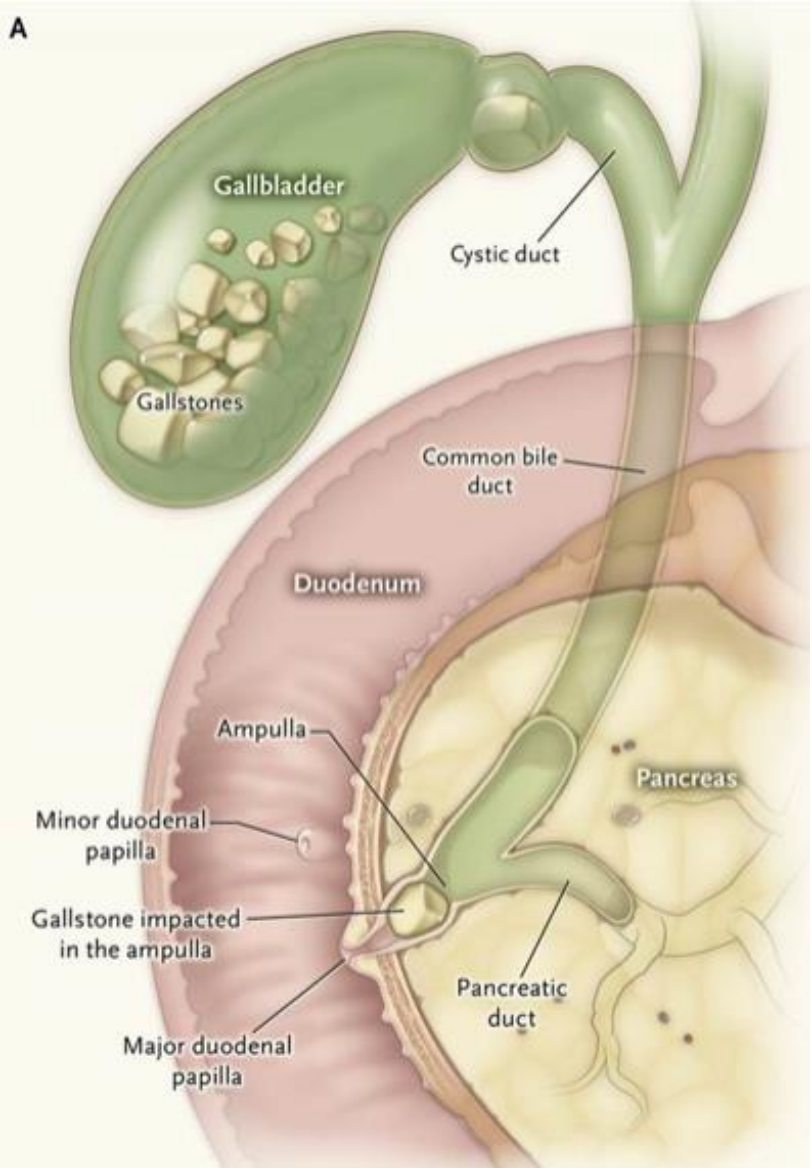
## 1.Case conference on 2017/07/24 (medical center)

- 61 year-old man with several important disorders from his young age.
- Hypertension for 28 years.
- Proteinuria for 30 years.
- Hyperlipidemia for 30 years.
- **Hyperlipidemia**→ Gallstone → obstructive jaundice
- -Acute pancreatitis,
- Hyperlipidemia→ arteriosclerosis→ hypertension→
- Cardiac enlargement→? **CAD**
- Cause of hyperlipidemia in young age: diet or hereditary
- **LMD→ER (serum** bilirubin : 2.4 , CT showed gall stones and
- pancreatitis lipase : 6405, amylase: :4347.)



# I. Gall stone→obstructive jaundice→ acute pancreatitis

- 61 year-old man Hyperlipidemia for 30 years.
- **Hyperlipidemia**→ Gallstone → obstructive jaundice
- -Acute pancreatitis,



# Gall stone colic --------→Acute pancreatitis

- CC: epigastralgia for one week since 2017/07/07
- due to gall stone at first → related to pancreatitis later.
- pain character: colic nature,
- at RUQ of abdomen,
- No tea color urine
- Hyperbuilirubinemia (-)
- **Amylase and lipase** were normal-
- CRP :normal
- GGT and alkaline phosphatase：normal or abnormal

- Migration of stone to the cystic duct→ CBD-→impacted at the most distal part of CBD(near papilla)—
- Pain related to pancreatitis,
- **Mid line pain**, better on bending position,
- **tea color urine**
- **Hyperbuilirubinemia**
- Amylase and lipase became abnormal-→top data at the first 24 hours.--->

  normal after 3 days.
- CRP :normal
- GGT and alkaline phosphatase：abnormal

# Gall stone + cholecystitis → CBD stone,→ obstructive jaundice-→Acute pancreatitis

- Acute and chronic inflammation of gall bladder 1-3 days.
  - wall thickening, gallstone
  - fever and chillness
  - colic pain
  - Leukocytosis---CRP
- Obstructive jaundice 2-3 days.
- Acute pancreatitis, 2 days later

- 2017.07.07
- 2017.07.10-11
- 2017.07.13-14

# II. Alcoholic pancreatitis
# Case conference on 2017/11/06

Upper abdominal pain from noon on 2017/10/27

Pain with nausea and vomiting, without radiation,

**Drinking for 30 years**. (amount ?未敘述) )

No fever nor chill

ER (at 2-4pm ?) on 2017/10/28--- BT : 38.2 degree.

Elevated serum level (lipase),→No follow up

Platelet : 99,000, bilirubin 1.4/3.1, (No GGT, No Alk.P-tase)

CRP: 0.34-→No follow up,

**Ca: 6.7 -**→Why? **No TG.**

**CT showed Peripancreatic fluid, *KUB showed colon cut-off.***

***suggestive of necrotizing pancreatitis.***

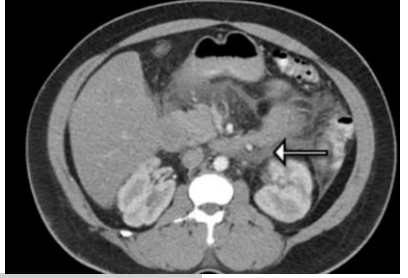
***PE 竟然是 normal.***

**2. Alcohol pancreatitis**;

Alcohol 是 pancreatitis 重要的原因.所以最近一週內有無飲酒非希重要。量也一定要問清楚。**是不是喝了足夠的量(?)**才發生acute abdominal pain-→ pancreatitis.

大部分 **> 100 gm/2 days** 內.
**60-80 gm/day**
一週以上未喝,
一次 **40 gm**也會引發 **pancreatitis.**

# III. Hypertriglyceridemia, Case report by Dr. Khan et al (2015)



- **A 44-year-old female** with a past medical history only of hypertension presented with progressively worsening, generalized, non-radiating abdominal pain of 3 days duration associated with vomiting but not with food intake. As per the patient, her appetite had decreased markedly and there were no episodes of hematemesis or melena. Other significant portions of her history demonstrated that she had undergone **cholecystectomy 5 years prior** and she denied any alcohol use.
- Upon physical examination, the patient was in moderate pain with a blood pressure of 112/74 mm Hg, pulse 81/min, respiration rate 16/min, saturation 99% on room air, and temperature of 99.9 °F. Abdominal examination revealed generalized tenderness in the epigastric region without rebound tenderness or guarding. Laboratory data showed a hemoglobin of 13.9g/dL, hematocrit 35%, WBC 11.1 $\times$ $10^3$/µL, platelets 286 $\times$ $10^6$/µL, glucose 136 mg/dL, BUN 8 mg/dL, creatinine 0.8 mg/dL, calcium 8.8 mg/dL, albumin 3.7 mmol/L, total protein 6.8, sodium 125 mmol/L, potassium 4.4 mmol/L, chloride 88 mmol/L, bicarbonate 2 mmol/L, **lipase 145**, alkaline phosphatase 69 U/L, total bilirubin 0.5 mg/dL, AST 47 U/L, and ALT 41 U/L.
- Further analysis included computed tomography scan of the abdomen correlating with **acute pancreatitis involving the head, uncinate process and pancreatic duodenum** but no pancreatic ductal **dilatation** or obvious calcification.
- The patient was admitted to the hospital with the diagnosis of acute pancreatitis, initially managed with bowel rest and supportive care which did not result in any improvement in her symptoms. Patient's triglyceride level was then reported to be elevated at **3,525 mg/dL** and she was transferred to intensive care unit and insulin drip was initiated. Patient's triglyceride level decreased to **973 mg/dL the next day** and the patient's symptoms resolved

Gastroenterology Res. 2015 Aug; 8(3-4): 234–236.
Published online 2015 Jul 22. doi: 10.14740/gr662e
PMCID: PMC5040532
PMID: 27785302

Hypertriglyceridemia-Induced Pancreatitis: Choice of Treatment

Rafay Khan [a,b] Waqas Jehangir [a] Kalyani Regeti [a] and Abdalla Yousif [a]

# Treatment:

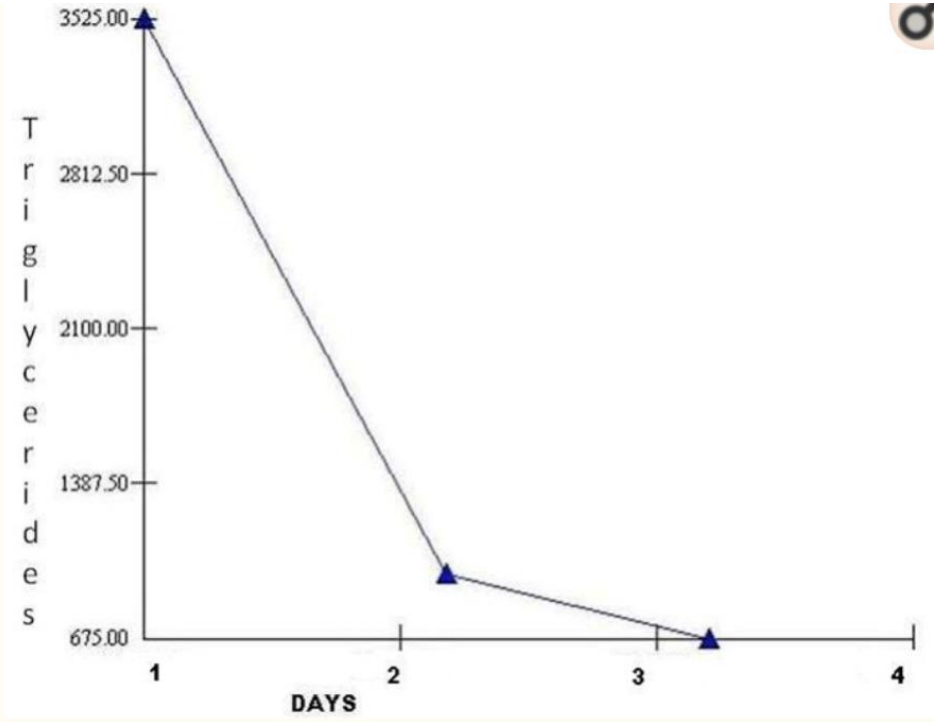



Figure 2

Triglyceride level vs. hospital stay.

- Initial treatment is similar to any case of acute pancreatitis, which involves pancreatic rest by decreased oral intake, intravenous hydration, and pain management. However, after lack of clinical improvement and significantly elevated triglyceride levels, other options need to be considered. Although no standard guidelines are present for its management, **insulin infusion is effective in decreasing triglyceride levels** . The mechanism of action behind this form of treatment suggests that insulin increases lipoprotein lipase (LPL) activity which can degrade chylomicrons and thus reduce serum triglycerides.
- Another form of medical management which remains controversial is the use of **heparin** which can stimulate the release of endothelial LPL into circulation; however, it may only result in transient rise in LPL followed by increased degradation of plasma stores causing LPL deficiency .
- In certain cases, a successful method of treatment relies on apheresis for the lowering of triglyceride levels. This was first reported in 1978 by Betteridge et al and can result in a rapid decrease in triglyceride levels over a short period of time compared to the other treatment options described [9]. Through the use of plasmapheresis compared to insulin use, a triglyceride level reduction of 65-70% has been documented [8].


- 1. Mikhail N, et al. Treatment of severe hypertriglyceridemia in nondiabetic patients with insulin. Am J Emerg Med. 2005;23(3):415–417. doi: 10.1016/j.ajem.2005.02.036
- 2. Betteridge DJ, Bakowski M, Taylor KG, Reckless JP, de Silva SR, Galton DJ. Treatment of severe diabetic hypertriglyceridaemia by plasma exchange. Lancet. 1978;1(8078):1368. doi: 10.1016/S0140-6736(78)92450-9.

# Acute Pancreatitis Secondary to Severe Hypertriglyceridemia

- **Acute Pancreatitis Secondary to Severe Hypertriglyceridemia: Management of Severe Hypertriglyceridemia in Emergency Setting.** Chaudhary A[1], et al (US)
- Gastroenterology Res. 2017 Jun;10(3):190-192.
- Hypertriglyceridemia (HTG) is the third most common cause of acute pancreatitis (AP). The incidence of AP is around 10-20% with levels > 2,000 mg/dL. We present here a case of a 44-year-old male with history of uncontrolled diabetes mellitus and HTG admitted with severe abdominal pain. Labs revealed elevated lipase and amylase. CT of abdomen with contrast showed AP..
- he was started on **IV regular insulin along with dextrose saline**. He had marked improvement in his TG level the next day. He was continued on insulin and dextrose saline with hourly glucose monitoring until TG was < 500 mg/dL. He was discharged on statins and fenofibrate. The goal of management of AP secondary to severe HTG in emergency setting is to lower the TG levels to less than 500 as quickly as possible

# Acute pancreatitis due to hypertriglyceridemia

**3. Acute pancreatitis due to hypertriglyceridemia**
:Triglyceride過高、>1,000 mg/dl也是引發 acute pancreatitis. 的重要原因,約佔 10-15 %

J Investig Med High Impact Case Rep. 2018 Sep 1;6:2324709618798399. doi: 10.1177/2324709618798399. eCollection 2018 Jan-Dec.

**A Rare Case of Acute Pancreatitis Due to Very Severe Hypertriglyceridemia (>10 000 mg/dL) Successfully Resolved With Insulin Therapy Alone: A Case Report and Literature Review.**

Gayam V[1], Mandal AK[1], Gill A[1], Khalid M[1], Sangha R[1], Khalid M[2], Garlapati P[1], Bhattarai B[1].

**Author information**

1 Interfaith Medical Center, New York, NY, USA.

**TG: 10612**
**Improved on insulin therapy.**

Personal experience :
大部分3,000-5,000.
討論會的案例最高 13,000 mg/dl.(MMH)
過去在台大的案例最高是 9,500 mg/dl.

Biomed Res Int. 2018 Jul 26;2018:4721357. doi: 10.1155/2018/4721357. eCollection 2018.

**Management of Hypertriglyceridemia Induced Acute Pancreatitis.**

Garg R[1], Rustagi T[2].

**Author information**

1 Department of Internal Medicine, Cleveland Clinic, Cleveland, OH, USA.

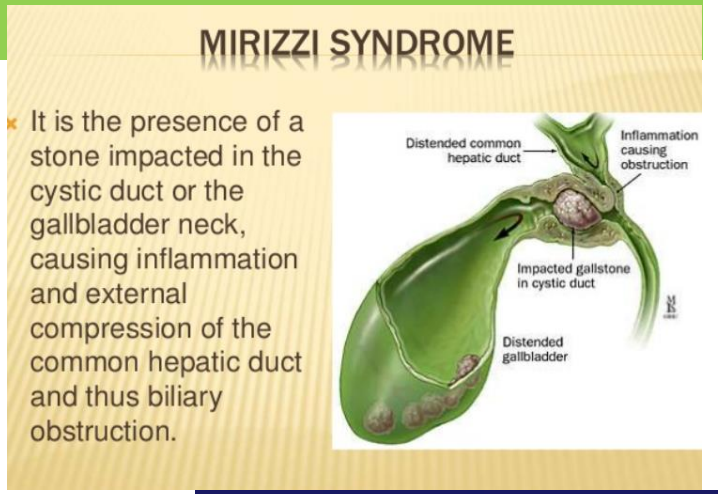
# Plasma TG and severity of AP induced by High TG.

- **Relationship between Plasma Triglyceride Level and Severity of Hypertriglyceridemic Pancreatitis.** Wang SH[1], et al (TSGH):PLoS One. 2016 Oct 11;11(10):e0163984.
- **AIM:** To evaluate the effect of TG level on the severity of hypertriglyceridemic pancreatitis (HTGP).
- 144 patients with HTGP from 1999 to 2013 at Tri-Service General Hospital. Patients with possible etiology of pancreatitis, such as gallstones, those consuming alcohol or drugs, or those with infections were excluded.
- 1. There were 66 patients in the low-TG group and 78 patients in the high-TG group. There was no significant difference in the age, sex ratio, body mass index, and comorbidity between the 2 groups. **The high-TG group had significantly higher levels of glucose (P = 0.022), total cholesterol (P = 0.002), and blood urea nitrogen (P = 0.037), and lower levels of sodium (P = 0.003) and bicarbonate** (P = 0.002) than the low-TG group.
- 2. The incidences of local **complication** (P = 0.002) and severe and moderate form of pancreatitis (P = 0.004) were significantly higher in the high-TG group than in the low-TG group. The mortality rate was higher in the high-TG group than in the low-TG group (P = 0.07).
- **結論Higher TG level in patients with HTGP may be associated with adverse prognosis**

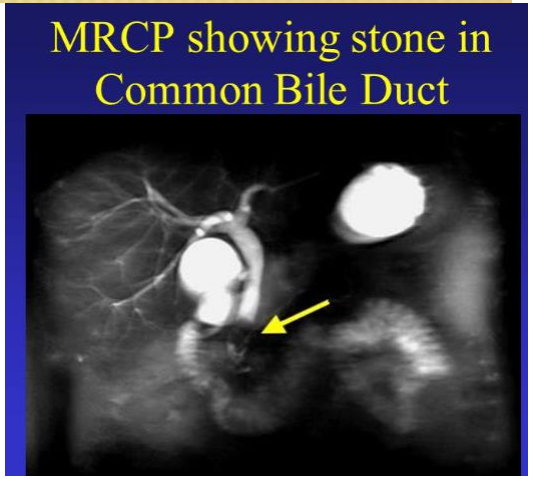
- **Primary Endpoints versus TG Level in Patients with HTGP.**
- **1.**

| | TG: <2648 | TG ≥ 2648 (n = 78) | | |
|---|---|---|---|---|
| **Creatinine (mg/dl)** | 0.98±0.09 | 1.51±0.24 | 2.039 | 0.044* |
| <1.9 | 59(89.39) | 65(83.33) | 0.650 | 0.420 |
| ≥1.9 | 7(10.61) | 13(16.67) | | |
| **2. Shock** | | | — | 0.109 b |
| | 2(3.03) | 8(10.26) | | |
| 3. Respiratory failure | 5(7.58 | 16(20.51) | | o.o51 |
| **4. Local complication on CT scan** | | | | **0.002** |
| **5. Systemic complications :** | | | | **0.0219** |

# Acute pancreatitis due to gall stone之前奏
# Evidence of obstructive jaundice




- Rapid rising of serum bilirubin
- High serum bilirubin :Total bilirubin > 1.2 mg/dl
- Ratio of CB/TB > 55 %
- High biliary enzymes ---
- **gamma GT ---> 3X often ---->5-10x**
- Biliary enzyme ---> 1.5 X-3x. or more.
- Images suggestive of CBD obstruction
- Dilated CBD > 8 mm
- Radiolucent defect at end of CBD—due to stone(s)
- Engorged papilla by duodenoscopy
- Tea color urine (a few days after attack), and clay color stool (often 10 days later)



# IV.第四大原因: medication induced AP ex.: Furosemide, ---

- **Medication as a Cause of Acute Pancreatitis.** Ghatak R[1],et al (University of Medicine and Health Sciences, New York): Am J Case Rep. 2017 Jul 28;18:839-841.
- Drug-induced pancreatitis has recently gained more attention and as a result, physicians are screening more frequently for medications as a cause of acute pancreatitis.
- a 74-year-old man with a significant past medical history for coronary artery disease, sleep apnea, and gastroesophageal reflux disease who presented with epigastric pain radiating to the back. After a careful history was taken, it was found the patient recently started furosemide; therefore, a diagnosis of **furosemide-induced acute pancreatitis** was made

**第四大原因: medication induced Acute pancreatitis.**
約占5-10 %.
必須詳細詢問用藥史,才能判定。

文獻上的報告偏低。
德國報告 1.4 %

@@@

**Table. Drugs and drug classes associated with acute pancreatitis***

| | | |
|---|---|---|
| ACE inhibitors | Estrogens | Pentamidine |
| Acetaminophen | Ethacrynic acids | Pergolide |
| Adrenocorticotrophic hormones | Exenatide | Phenolphthalein |
| Alendronate | Ezetimibe | Pilocarpine |
| All-trans-retinoic acid | Fibrates | Prazosin |
| Alpha-methyldopa | Finasteride | Procainamide |
| Aminosalicylates | Fluoroquinolones | Propofol |
| Amiodarone | 5-Fluorouracil | Propoxyphene |
| Amlodipine | Furosemide | Proton pump inhibitors |
| Ampicillin | Gabapentin | Quinupristin/dalfopristin |
| Antivirals | Gold | Ranitidine |
| Aspirin | HAART agents | Repaglinide |
| Atypical antipsychotics | HMG-CoA reductase inhibitors | Rifampin |
| Azathioprine | Ifosfamide | Rifapentine |
| Bupropion | Indomethacin | Rivastigmine |
| Calcitriol | Interferon/ribavirin | Ropinirole |
| Cannabis | Interleukin-2 | Saw palmetto |
| Capecitabine | Irbesartan | Selective serotonin receptor antagonists |
| Carbamazepine | Isoniazid | Sirolimus |
| Ceftriaxone | Isotretinoin | Sodium stibogluconate |
| Cimetidine | Lamotrigine | Somatropin |
| Cisplatin | L-asparaginase | Sulfamethoxazole |
| Clomiphene | Macrolides | Sulfasalazine |
| Codeine | Mefenamic acid | Sumatriptan |
| Colchicine | 6-Mercaptopurine | Tacrolimus |
| Corticosteroids | Mesalamine | Tamoxifen |
| COX-2 inhibitors | Metformin | Tetracyclines |
| Cyclophosphamide | Methimazole | Thiazide diuretics |
| Cyclosporine | Methyldopa | Thrombolytic agents |
| Cyproheptadine | Metronidazole | TNF-alpha inhibitors |
| Cytosine | Mirtazapine | Topiramate |
| Danazol | Montelukast | Trimethoprim-sulfamethizole |
| Dapsone | Mycophenolate | Valproic acid |
| Diazoxide | Nitrofurantoin | Venlafaxine |
| Diphenoxylate | NSAIDs | Vincristine |
| Dipyridamole | Octreotide | Voriconazole |
| Doxercalciferol | Paclitaxel | Zolmitriptan |
| Doxorubicin | Pegaspargase | |
| Ertapenem | Penicillin | |

*From references 7–11.

ACE indicates angiotensin-converting enzyme; COX, cyclooxygenase; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; NSAID, nonsteroidal anti-inflammatory drug; TNF, tumor necrosis factor.

# Drug induced pancreatitis, 1.2-1.4 %

Reports of drug-induced acute pancreatitis (AP) have been published since the 1950s, and each year the list of drugs associated with AP increases. There are many etiological risk factors for AP, including a history of alcohol abuse, gallstones, endoscopic retrograde cholangiopancreatography and manometry, trauma or surgical procedures near the [illegible] tions, hyperlipidemia, infection, and ca[illegible]. Knowledge of the true incidence of drug-induced AP is dependent on clinicians excluding other possible causes and reporting the event. It can be difficult to rule out other causes of AP, especially in patients who have multiple comorbidities, use multiple medications, and have potentially unknown underlying risk factors. A retrospective study conducted in Germany concluded that the incidence of drug-induced AP is 1.4% (3). A national survey performed in Japan in 1999 reported that 1.2% of all cases of AP were drug induced (2). Drug-induced AP is rare but should not be overlooked in a patient who presents with idiopathic AP.

*Proc (Bayl Univ Med Cent)* 2008;21(1):77–81

*Proc (Bayl Univ Med Cent)* 2008;21(1):77–81

常用,引發**pancreatitis**的藥有

Furosemide
Digoxin,
ACE inhibitors.
Estrogens
Metronidazole,
Cyclosporin,
Ranitidine
Macrolides
NSAID,
**Biologicl agents for IBD (TNF-alpha inhinitors)**
INAH ---etc.

Kaurich T :Proc (Bayl Univ Med Cent) 2008;21(1):77–81

# Tamoxifen and acute pancreatitis

## Tamoxifen→Hypertriglyceridemia→Acute pancreatitis

- **Tamoxifen use and acute pancreatitis: A population-based cohort study.** Hsu FG[1et al(CMUH)：PLoS One. 2017 Mar 14;12(3):e0173089
- Taiwan National Health Insurance Research Database. A cohort of 22 005 patients aged ≥20 years with breast cancer from January 1, 2000 to December 31, 2009 was identified and the date of cancer diagnosis was set as the index date.
- the risk of AP was not significant between tamoxifen users and tamoxifen nonusers (adjusted HR = 0.94, 95% CI = 0.74-1.19) in the non-matching cohorts.
- **CONCLUSIONS:**
- **No significant correlation** was observed between tamoxifen use and the risk of AP in patients with breast cancer.

Prz Menopauzalny. 2014 Mar; 13(1): 70–72.
Published online 2014 Mar 10. doi: [10.5114/pm.2014.41089]
PMCID: PMC4520340
PMID: 26327832

Tamoxifen-induced acute pancreatitis – a case report

Rafał Czyżykowski,[1] Joanna Połowinczak-Przybyłek,[1] Anna Janiak,[1] Jerzy Herman,[2] and Piotr Potemski[1]

The influence of hormonal therapy of breast cancer on lipids levels [4]

| Hormonal therapy | TC | LDL | HDL | TG | TC/HDL-C | LDL-C/HDL-C |
|---|---|---|---|---|---|---|
| tamoxifen | ↓ | ↓ | ↑ or ↓ or n.c. | ↑ | n.c. | ↓ |
| anastrozole | ↓ or ↑ or n.c. | ↓ or ↑ or n.c. | ↑ | ↓ | n.c. | n.c. |
| letrozole | ↑ or n.c. | ↑ or n.c. | – | – | ↑ | ↑ |
| exemestane | n.c. or ↓ | n.c. or ↓ | ↑ or ↓ or n.c. | ↓ | n.c. | – |

Tamoxifen-Induced Severe Hypertriglyceridaemia and Acute Pancreatitis. *Hakan Alagozl et al :* Clinical Drug Investigation May 2006, Volume 26, Issue 5, pp 297–302

a patient with tamoxifen-induced acute pancreatitis and hypertriglyceridaemia who was successfully treated with insulin infusion and long-term gemfibrozil.

# Drug induced acute pancreatitis--digoxin

- **Digoxin use may increase the relative risk of acute pancreatitis: A population-based case-control study in Taiwan. Lai SW et al (CMUH):** Int J Cardiol. 2015 Feb 15;181:235-8.
- Utilizing the database of the Taiwan National Health Insurance Program, this case-control study consisted of 6116 subjects aged 20-84years with a first-attack of acute pancreatitis since 2000 to 2011 as the cases and 24,464 randomly selected subjects without acute pancreatitis as the controls.
- The adjusted OR of acute pancreatitis **was 5.29** for subjects with active use of digoxin (95% CI 3.61, 7.73),(Active use of digoxin was defined as subjects who at least received 1 prescription for digoxin within 7days before the date of diagnosing acute pancreatitis when compared with subjects with never use of digoxin.)

Biomedicine (Taipei). 2017 Mar;7(1):4. doi: 10.1051/bmdcn/2017070104. Epub 2017 Mar 3.

NSAIDs

# Etodolac and the risk of acute pancreatitis.

Liao KF[1], Cheng KC[2], Lin CL[3], Lai SW[2].

**Author information**

1 College of Medicine, Tzu Chi University, Hualien 970, Taiwan - Department of Internal Medicine, Taichung Tzu Chi General Hospital, Taichung 427, Taiwan - Graduate Institute of Integrated Medicine, China Medical University, Taichung 404, Taiwan.

NHRI database.
7577 subjects aged 20 years or older with newly diagnosed acute pancreatitis were defined as cases, and 27032 sex-matched and age-matched subjects without acute pancreatitis were defined as controls.

the adjusted odds ratio of acute pancreatitis was **3.78** for subjects with active use of etodolac (95% confidence interval 1.11, 12.9), compared with subjects who never used etodolac

an association between active use of etodolac and acute pancreatitis.

備註:**Etodolac is a nonsteroidal anti-inflammatory drug (NSAID**).

- **UpTo Date**
- There are at least three different inheritance patterns for chronic pancreatitis
- 1. Autosomal dominant hereditary pancreatitis — This is most often associated with mutations in the serine protease 1 gene (*PRSS1*) on chromosome 7q35
- ---
- **Pancreapedia:**
- Celeste A Shelton and David C Whitcomb (U.Pittsburg) July 18, 2016
- broadly to include multiple genes associated with RAP and CP including *PRSS1, PRSS2, SPINK1, CFTR* and *CTRC*. Clinical researchers and geneticists generally define HP as autosomal dominant pancreatitis, and use the term "familial pancreatitis" to describe recessive or complex phenotypes.
- Hereditary pancreatitis typically presents in childhood at a median age of 10-12 years

# V. 第五種pancreatitis, hereditary

- 1. Hereditary pancreatitis is a genetic condition characterized by recurrent episodes of inflammation of the **pancreas** (pancreatitis)
- 2. Signs and symptoms of this condition usually begin in late childhood with an episode of acute pancreatitis. A sudden (acute) attack---
- 3. Recurrent acute pancreatitis leads to chronic pancreatitis, which occurs when the pancreas is persistently inflamed. Chronic pancreatitis usually develops by early adulthood in affected individuals.
- 4. leading to fatty stool (**steatorrhea**), weight loss, and protein and vitamin deficiencies.
- 5. Type I DM
- 6. Increase the risk of developing **pancreatic cancer**. The risk is particularly high in people with hereditary pancreatitis who also smoke, use alcohol, have type 1 diabetes mellitus, or have a family history of cancer.
- 7. Frequency : In Europe, its prevalence is estimated to be **3 to 6 per million** individuals.
- 8. autosomal **dominant** pattern

# Important and most recent references from the PubMed

J Gastrointest Cancer. 2014 Mar;45(1):22-6. doi: 10.1007/s12029-013-9559-6.

**Hereditary pancreatitis: dilemmas in differential diagnosis and therapeutic approach.**

Mastoraki A[1], Tzortzopoulou A, Tsela S, Danias N, Sakorafas G, Smyrniotis V, Arkadopoulos N.

HP usually appears with an acute, a recurrent acute, and a chronic phase, referring to the inflammation of the pancreas and the symptoms' onset and duration. The clinical features of acute pancreatitis begin in childhood and last less than 6 months. HP carries a 50-70-fold increased risk of pancreatic cancer within 7-30 years of disease onset.

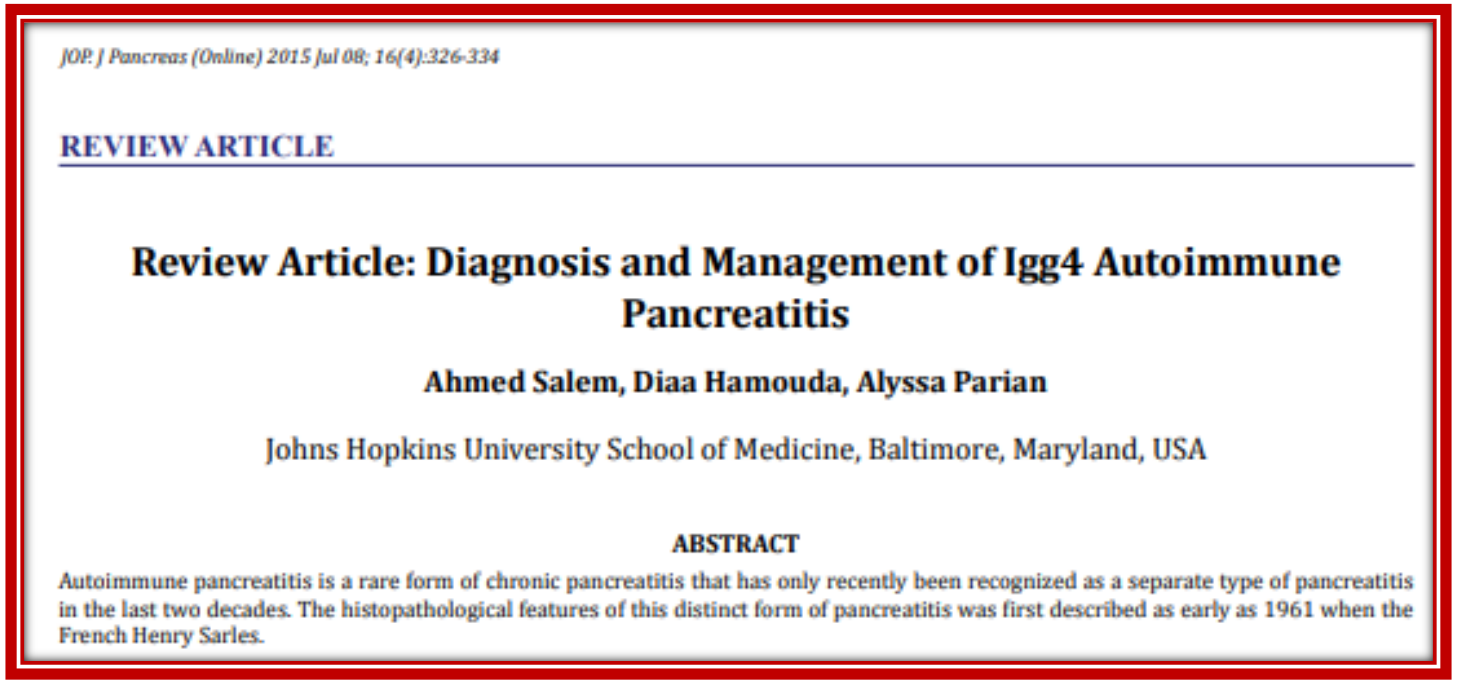
J Gastroenterol. 2018 Jan;53(1):152-160. doi: 10.1007/s00535-017-1388-0. Epub 2017 Aug 31.

@@@

**Nationwide survey of hereditary pancreatitis in Japan.**

Masamune A[1], Kikuta K[2], Hamada S[2], Nakano E[2], Kume K[2], Inui A[3], Shimizu T[4], Takeyama Y[5], Nio M[6], Shimosegawa T[2].

271 cases(153 males and 118 females) in 100 families. 41% had the PRSS1 mutations (p.R122H 33%, p.N29I 8%) and 36% had the SPINK1 mutations . DM :5.5% at 20,28.2 % at 40. **pancreatic cancer diagnosis was 2.8% at 40 years old, 10.8% at 60 years, and 22.8% at 70 years**



JOP. J Pancreas (Online) 2015 Jul 08; 16(4):326-334

REVIEW ARTICLE

**Review Article: Diagnosis and Management of Igg4 Autoimmune Pancreatitis**

**Ahmed Salem, Diaa Hamouda, Alyssa Parian**

Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

**ABSTRACT**

Autoimmune pancreatitis is a rare form of chronic pancreatitis that has only recently been recognized as a separate type of pancreatitis in the last two decades. The histopathological features of this distinct form of pancreatitis was first described as early as 1961 when the French Henry Sarles.

# 第六種Ig G4 autoimmune pancreatitis

The histopathological features of this distinct form of pancreatitis was first described as early as 1961 when the French Henry Sarles [1] described a type of sclerosing pancreatitis associated with hypergammaglobulinemia. Subsequently, most of the early literature about AIP came from Japan where the concept of Autoimmune Pancreatitis (AIP)was first proposed in 1995 by Yoshida et al. [2] after many authors had reported a form of chronic pancreatitis associated with Sjögren's-like syndrome.

**First experience in Taiwan in 1977,** a patient was operated for pancreatitis but frozen showed no malignancy. Postoperative treatment with prednisolone 30 mg/day for 2 weeks showed great reduction of tumor size and also reduction of obstructive jaundice. Later, she was treated with thymosine alpha 1, donated by my sister in US for 6 momths. She remained well for in the leter days. No recurrence of obstructive jaundice and pancreatic mass for 4 years. Unfortunately , she was sacrificed by traffic accident.in 1981. The patient was treated at Prof. Chen CY because of Sjoegren syndrome for a long time.

# 第七 Infection etiology of acute pancreatitis

- **Review of Infectious Etiology of Acute Pancreatitis.** Rawla P[1],et al (US) Gastroenterology Res. 2017 Jun;10(3):153-158.
- about 10% of cases are thought to be caused by infectious microorganisms. These microorganisms include viruses (e.g. mumps, Coxsackie B, and hepatitis), bacteria (e.g. *Mycoplasma pneumoniae* and leptospirosis), and parasites (e.g. Ascaris lumbricoides, Fasciola hepatica, and hydatid disease). Each organism causes acute pancreatitis through diverse mechanisms.
- **Ascaris lumbricoides** is the most common parasite implicated in AP as mentioned by Parenti et al in their extensive review.
- --- Parenti DM, Steinberg W, Kang P. Infectious causes of acute pancreatitis. Pancreas. 1996;13(4):356–371. In a prospective study carried out in India, ascariasis was the leading cause of pancreatitis in 59 of 256 patients (23%) compared to 112 patients (44%) with gallstone pancreatitis
- ----Khuroo MS, Zargar SA, Yattoo GN, Koul P, Khan BA, Dar MY, Alai MS. Ascaris-induced acute pancreatitis. Br J Surg. 1992;79(12):1335–1338.

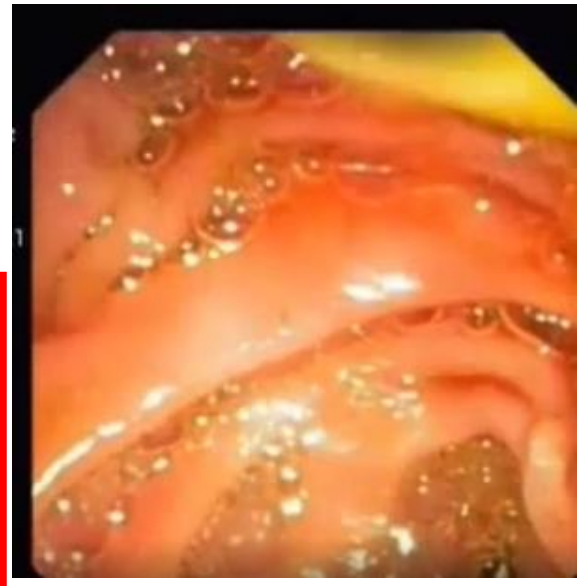
Video Journal and Encyclopedia of GI Endoscopy
Volume 1, Issue 2, October 2013, Pages 571-572

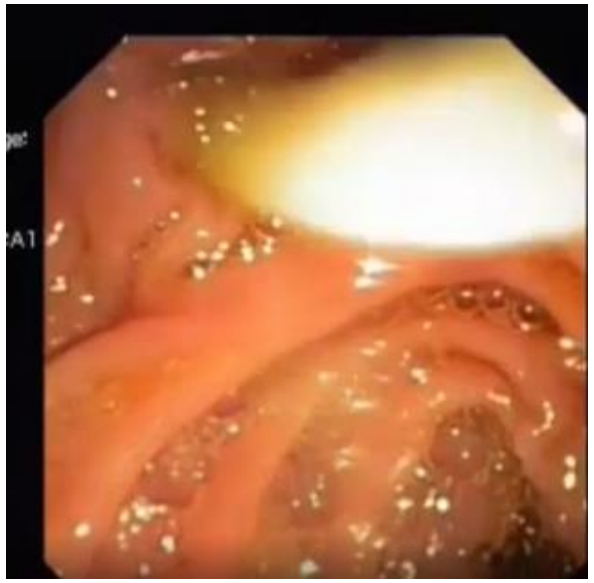
# Pancreatic Ascariasis Causing Acute Pancreatitis

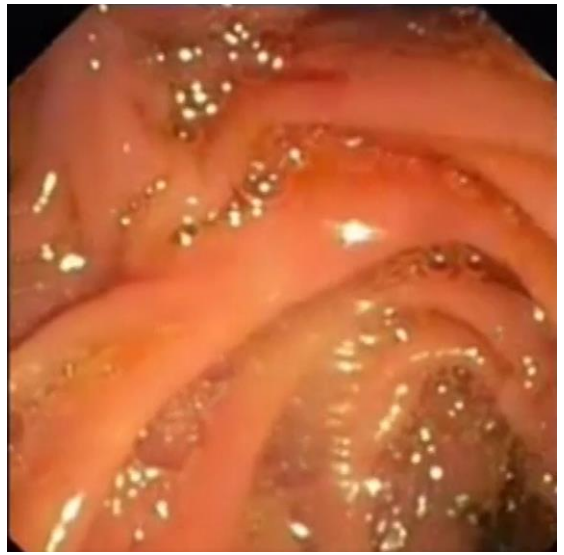
M Sharma, P Rai

Jaswant Rai Speciality Hospital, Meerut, Uttar Pradesh, India

Received 13 July 2012, Revised 13 July 2012, Accepted 10 September 2012, Available online 28 September 2013.







The authors demonstrate a patient with ascariasis-induced acute pancreatits diagnosed by endoscopic ultrasound and managed by endoscopic removal. This article is part of an expert video encyclopedia.

# Rectal NSAID may prevent(reduce) Post-ERCP pancreatitis

第八種
Post-ERCP
pancreatitis

- **Rectal nonsteroidal anti-inflammatory drugs administration is effective for the prevention of post-ERCP pancreatitis: An updated meta-analysis of randomized controlled trials.** Yang C[1] et al ☹四川, China) Pancreatology. 2017 Jul 17.
- Cochrane Library, PubMed, EMBASE, and Web of Science.
- Twelve RCTs, including a total of 3989 patients, were identified and included in the analysis.
- post-ERCP pancreatitis (PEP), **The risk of PEP was lower in the NSAIDs group** than in the placebo group (RR 0.52.)
- The risk of moderate to severe PEP was also lower in the NSAIDs group. (RR 0.44)
- no difference in efficacy between rectal indomethacin and diclofenac,
- :
- 結論: A single rectal dose of NSAIDs is effective in preventing PEP both in high-risk and in unselected patients, regardless of timing of administration (pre- or post-ERCP) and NSAID type (indomethacin or diclofenac).

# Four hours after ERCP, check amylase and lipase

J Korean Med Sci. 2017 Nov; 32(11): 1814–1819.
Published online 2017 Sep 15. doi: 10.3346/jkms.2017.32.11.1814
PMCID: PMC5639062
PMID: 28960034

Prediction of Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis Using 4-Hour Post-Endoscopic Retrograde Cholangiopancreatography Serum Amylase and Lipase Levels

Yeon Kyung Lee,* Min Jae Yang,* Soon Sun Kim, Choong-Kyun Noh, Hyo Jung Cho, Sun Gyo Lim Jae Chul Hwang, Byung Moo Yoo, and Jin Hong Kim

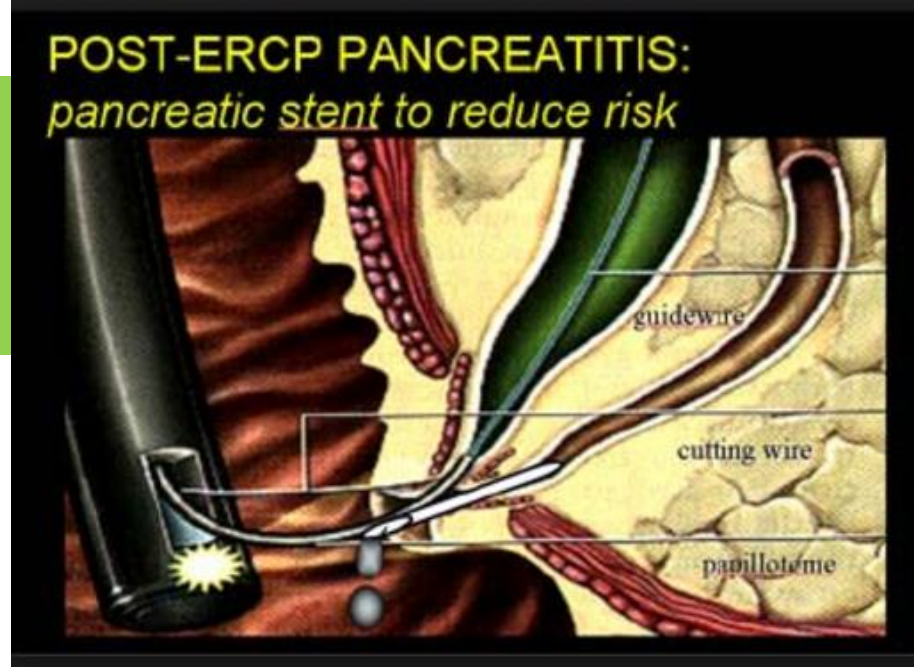
Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

PEP(post ERCP pancreatitis ) occurred in **16 (3.1%) patients** after ERCP (516 cases)

@@@

- The receiver-operator characteristic curve for 4-hour post-ERCP serum amylase and lipase levels showed that the areas under the curve were 0.919 and 0.933, respectively, demonstrating good test performances as predictors for PEP (both *P* values < 0.001).
- The amylase level > **1.5 ×** the upper limit of reference (ULR) was found useful for PEP exclusion with a sensitivity of 93.8%, while 4 × ULR was found useful to guide preventive therapy with the best specificity of 93.2%.
- The lipase level 2 × ULR showed best sensitivity, while 8 × ULR had the best specificity. Logistic regression analysis showed that **4-hour post-ERCP amylase level > 4 × ULR, lipase level > 8 × ULR, precut sphincterotomy, and pancreatic sphincterotomy were significant predictors for PEP.**
- In conclusion, **4-hour post-ERCP amylase and lipase levels are useful early predictors of PEP** that can ensure safe discharge or prompt resuscitation after ERCP.

# III.治療與處置-3
# 16, ERCP之應用




- **16, Acute pancreatitis 如同時有膽道疾病時,應在 24 hours 內執行 ERCP . 如只有 gall stone 而無 biliary obstruction 可不必作 ERCP.**

  **如無膽道炎或無黃疸可以 MRCP, 或 EUS代替,而不必作 ERCP.**

@@@

- **17. ERCP之後應使用 PANCREATIC STENTS或肛門內用NSAID 坐藥以預防發生POST-ERCP PANCREATITIS.**

**第六個常見的原因是 Post-ERCP pancreatitis**

## Prevention of Post-ERCP Pancreatitis (PEP)

*A metanalysis*
*52 studies, 12 RCTs, 6 fulfilled the criteria*

| Author | Year | Patients | Drug | CBD stones | PEP NSAID/controls |
|---|---|---|---|---|---|
| Khoshbaten | 2007 | 100 | Diclofenac | 51% | 2/13 |
| Cheon | 2007 | 207 | Diclofenas | 5.8% | 17/17 |
| Sotoudehmanesh | 2007 | 442 | Indomethacin | 51.2% | 7/15 |
| Montano Loza | 2007 | 150 | Indomethacin | NA | 13/28 |
| Montano Loza | 2006 | 116 | Indomethacin | NA | 12/19 |
| Murray | 2003 | 220 | Diclofenac | 38.5% | 7/17 |

Conclusions, comments: RR 0.46, NSAIDs protective in subgroup of ES and SOD. Mortality 0, severity not mentioned. Introduction into routine care is recommended.

Dai H-F, et al. Hepatobiliary Pancreas Dis Int 2009

# Major topics-1, Taiwan experiences

- Taiwan experiences on acute pancreatitis,
  review of literatures,

# 前言—1，epidemiology

- **Etiology of acute pancreatitis--a multi-center study in Taiwan.**
- Chang MC et al (NTUH) :Hepatogastroenterology. 2003 Sep-Oct;50(53):1655-7
  Patients with acute pancreatitis were collected from 8 major leading hospitals located at northern, southern, middle and eastern Taiwan from July 1, 1998 to June 30, 2000.
- 1,193 patients with acute pancreatitis were identified. There were 852 (71.4%) men and 341 (28.6%) women with **a mean age of 52.5 years, ranging from 9 to 100 years**. Etiology was identified as
- **alcohol in 423 (33.6%),**
- **gallstones in 407 (34.1%),**
- **hypertriglyceridemia in 147 (12.3%),**
- **miscellaneous causes in 109 (9.1%), and**
- **idiopathic causes in 107 (9.0%).**
- Patients with alcohol-related acute pancreatitis were the youngest (mean age: 41.5 years), while those with gallstone pancreatitis were the eldest (mean age: 64.1 years) ($p < 0.001$). The predominant cause of acute pancreatitis in women is gallstones, while alcohol is the leading cause of acute pancreatitis in Taiwanese males. In northern Taiwan, gallstone is the major cause of acute pancreatitis, while alcohol is the predominant etiology in middle, southern, and eastern Taiwan.

# Causes of acute pancreatitis

- **alcohol in 423 (33.6%),-→history**
- **gallstones in 407 (34.1%),→History,US,健檢**
- **hypertriglyceridemia in 147 (12.3%),→Lab.**
- **miscellaneous causes in 109 (9.1%), and**
- **idiopathic causes in 107 (9.0%). –stone?**

→戒酒
→Laparoscopic cholecystectomy
-→Treatment of hyperlipidemia
Diet
?
?

**History taking 多少可以指出病因**

# 前言—2，epidemiology:
# Annual incidence in Taiwan ：36.9/100,000(2000-2009

- Epidemiology of First-Attack Acute Pancreatitis in Taiwan From 2000 Through 2009: A Nationwide Population-Based Study
- Shen, Hsiu-Nien et al ( Pancreas: July 2012 - Volume 41 - Issue 5 - p 696–702.)
- **107,349 patients with first-attack AP** from the Taiwan National Health Insurance Research Database between 2000 and 2009. Severe cases were defined according to a modified Atlanta classification. Incidence rates were standardized by direct method. The averaged annual incidence of first-attack AP was estimated **at 36.9 per 100,000** persons and changed only slightly.
- incidence increased in children (<15 years), elderly people (≥65 years), and patients with biliary cause, but decreased in young to middle-aged men (15–64 years). The prevalence of severe cases increased **from 21.0% to 22.3%,** which was mainly caused by an increase of acute organ dysfunction (from 9.7% to 14.1%). Despite that, **hospital mortality decreased from 4.3% to 3.3**% for all cases and from **18.5% to 13.3% for severe ones.**
- The overall incidence of first-attack AP changed slightly in Taiwan, which differs from the increasing trend observed in most Western countries. Although more patients had severe attacks in recent years, hospital mortality declined.**嚴重的有20 %**

# 前言—3，epidemiology

- **Pancreatitis in Children**: Clinical Analysis of 61 Cases in Southern Taiwan Mao-Meng Tiao, et al (高長): *(Chang Gung Med J 2002;25:162-8)*
- Sixty-one patients, ranging in age from 2 to 18 years (mean, 8.8¡ 4.8 years old), with diagnoses of pancreatitis were studied from July 1986 through June 2000.
- **Twenty-eight pancreatitis cases resulted from physical trauma**, 13 cases of which were from traffic accident (53.8% from motorcycle accident). Other pathogenic factors included systemic diseases (N= 9), pancreaticobiliary-tree anomalies (N= 7**), toxin ingestion or drug use (N= 4**), Ascaris infection (N = 1), and idiopathic (N = 12).
- The amylase to creatinine clearance ratio was assayed for 35 cases, of which 28 (80.0%) were elevated (>6%). Ultrasonography revealed inflammatory changes of the pancreas in 40 of 51 patients evaluated, while computed tomogram demonstrated evidence of pancreatic inflammation for all 21 patients evaluated. **One patient died because of acute necrotizing pancreatitis 3 days after L-asparaginase treatment for leukemia.**
- 結論: Physical trauma, especially because of motorcycle accidents, was the leading cause of pediatric pancreatitis in southern Taiwan. The mortality rate was low

# 前言—4，epidemiology.
# Norway : FAAP: 14.6/100,000/year

(First Attack of Acute Pancreatitis)

- **Time trends in incidence, etiology, and case fatality rate of the first attack of acute pancreatitis.** Omdal T et al (U. Bergen, Norway), Scand J Gastroenterol. 2011 Nov;46(11):1389-98
- A total of 874 patients were discharged with a diagnosis of acute pancreatitis from the two hospitals in this region between 1.1.1996 and 31.12.2006. Patient records were reviewed and patients with a verifiable FAAP were identified. Demographic variables, likely etiology, and outcome were registered. FAAP was verified in 567 (65%) of the patients (300 women and 267 men) with a median age of 58 years (range 7-98). **The average yearly incidence rate of FAAP was 14.6/100 000** and the gender-specific incidence rates increased yearly by approx. 6% ($p = 0.006$). There was a decline in diagnoses by s-Amylase from approx. 90% to 62% in 2006 and an increase in diagnoses obtained by CT ($p < 0.001$). **The case fatality rate was low (3.5%), but higher among men (5.8%) than women (2%, $p = 0.037$).** The case fatality rate was lowest among patients with gallstones (0.7%) and higher among patients with alcohol (9%), miscellaneous (10.4%), and non-assessed etiology (6.6%) of FAAP ($p < 0.05$). Male gender, increasing age, and etiology (alcohol, miscellaneous causes, and non-assessed) were associated with increased case fatality rate in an adjusted regression model ($p < 0.001$).
- The incidence rate of FAAP is low and differs from that of official registries. The case fatality rate is low, but related to gender, age, and likely etiology of FAAP.

# 前言—5，epidemiology
# Acute pancreatitis in Southern Taiwan(alcoholic: 66%)

- **Etiology, severity and recurrence of acute pancreatitis in southern Taiwan.** Chen CH et (高雄市聯) J Formos Med Assoc. 2006 Jul;105(7):550-5.
- Eighty acute pancreatitis patients (M/F: 64/16), **including 53 (66.2%) with alcohol abuse,** 16 (20%) with biliary disease, five (6.3%) with hyperlipidemia, and six (7.5%) with other risk factors, etiologies or idiopathic disease, were included. The mean follow-up period was 20 months. Contrast-enhanced computed tomography (CT) was used to assess the severity of acute pancreatitis. Biliary pancreatitis was significantly associated with females while alcoholic pancreatitis occurred predominantly in male. Alcohol abuse was an independent risk factor for recurrent pancreatitis.
- :
- **Alcoholic pancreatitis was the major etiology of acute pancreatitis in southern Taiwan, exhibiting a strong male predominance** and higher risk of severe CT grading. Abnormal serum triglyceride was independently associated with the severity of acute pancreatitis. **Alcoholic pancreatitis had a higher risk of recurrence** than other etiologies.

# 前言—6，epidemiology
# Clopidogrel associated with increased risk of AP

- Actively using clopidogrel correlates with an increased risk of acute pancreatitis in Taiwan. Shih-Wei Lai et al (CMUH) *International Journal of Cardiology Volume 183, 15 March 2015, Pages 263–266.*
- database of the Taiwan National Health Insurance Program from 2000 to 2011. There were 5644 subjects aged 20–84 years with a first-time attack of acute pancreatitis as the case group and 22,576 randomly selected sex-matched and age-matched subjects without acute pancreatitis as the control group.
- actively using clopidogrel to those who never used clopidogrel, the adjusted OR of acute pancreatitis was **8.46** (95%CI 5.25, 13.7). The adjusted OR decreased to 1.16 among subjects not actively using clopidogrel (95%CI 0.95, 1.43).

# 0.24 % of clopidogrel users have pancreatitis

## Clopidogrel and Pancreatitis - from FDA reports

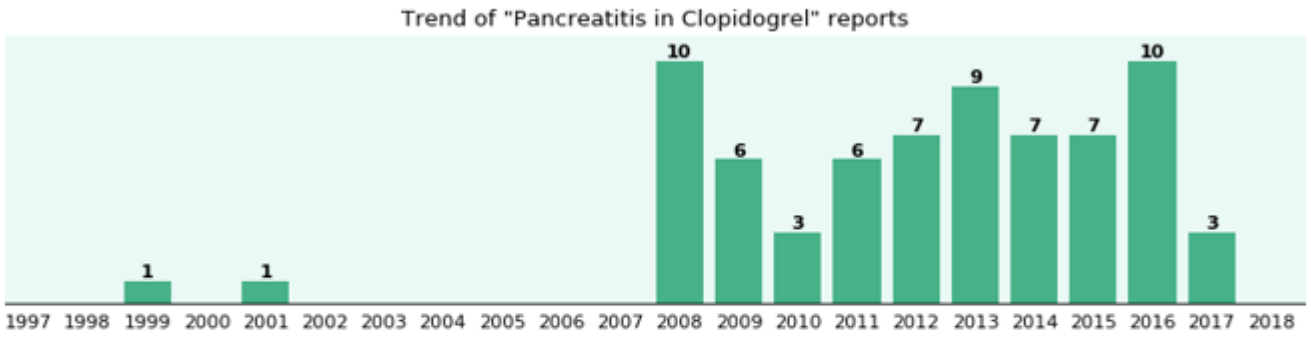
Pancreatitis is found among people who take Clopidogrel, especially for people who are male, 60+ old , have been taking the drug for 6 - 12 months, also take medication Simvastatin, and have Type 2 diabetes. This study is created by eHealthMe based on reports of 28,665 people who have side effects when taking Clopidogrel from FDA, and is updated regularly.

Who is eHealthMe: we are a data analysis company who specializes in health care industry. Our original studies have been referenced on 400+ peer-reviewed medical publications, including The Lancet, Mayo Clinic Proceedings, and EANO. On eHealthMe, you can research drugs and find Care Guides.

On Aug, 16, 2018

28,665 people reported to have side effects when taking Clopidogrel.
Among them, 70 people (0.24%) have Pancreatitis

## Number of reports submitted per year:



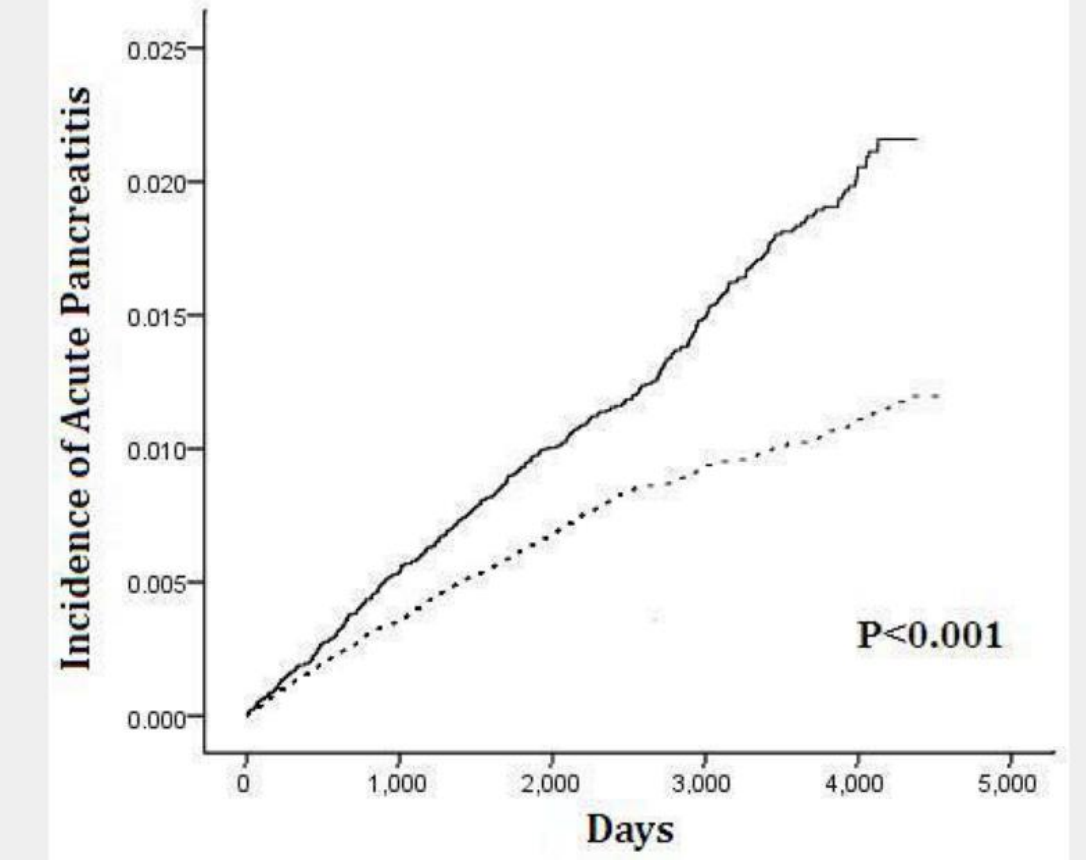

## Time on Clopidogrel when people have Pancreatitis *:

- < 1 month: 0.0 %
- 1 - 6 months: 25 %
- 6 - 12 months: 25 %

eHealthme Aug.16, 2018

# 前言—7，epidemiology
# Acute pancreatitis increased in RA and reduced after corticosteroid.

- Increased Risk of Acute Pancreatitis in Patients with Rheumatoid Arthritis: A Population-Based Cohort Study
- Chi Ching Chang,et al
- Patients newly diagnosed with RA between 2000 and 2011 were referred to as the RA group. The comparator non-RA group was matched with propensity score, using age and sex, in the same time period. We presented the incidence density by 100,000 person-years. From claims data of one million enrollees randomly sampled from the Taiwan NHI database, 29,755 adults with RA were identified and 119,020 non- RA persons were matched as a comparison group.
- The RA cohort had higher incidence density of acute pancreatitis (185.7 versus 119.0 per 100,000 person-years) than the non-RA cohort. The adjusted hazard ratio (HR) was **1.62.** Oral corticosteroid use decreased the risk of acute pancreatitis (adjusted HR **0.83**, 95% CI 0.73–0.94) but without a dose-dependent effect.
- In conclusion, **patients with RA are at an elevated risk of acute pancreatitis**. Use of oral corticosteroids may reduce the risk of acute pancreatitis.




- **Fig 2. Kaplan-Meier curve of cumulative incidence of acute pancreatitis of RA patients and comparison groups.**
- Footnotes: RA group,——; Comparison group,------; *P* < 0.001 by log-rank test.

# 前言—8，epidemiology
# Celecoxib associated with increased risk of AP

- Use of Celecoxib Correlates With Increased Relative Risk of Acute Pancreatitis: A Case–Control Study in Taiwan. Shih-Chang Hung et al :The American Journal of Gastroenterology **110**, 1490-1496 (October 2015)
- **a case–control study using the database of the Taiwan National Health Insurance Program. The participants comprised 5,095 subjects, aged 20–84 years, with a first admission episode of acute pancreatitis from 2000 to 2011 as the cases and 20,380 randomly selected sex-matched and age-matched subjects without acute pancreatitis as the control. The absence of celecoxib prescription was defined as "never used." Current use of celecoxib was defined as subjects who had received at least one prescription for celecoxib within 3 days before diagnosis with acute pancreatitis.**
- **the adjusted OR of acute pancreatitis was 5.62 in subjects with current use of celecoxib (95% CI=3.33–9.46).**
- **The current use of celecoxib is associated with an increased risk of acute pancreatitis.**

# 前言—9，epidemiology
# Finasteride :not associated with AP

- **Finasteride use and acute pancreatitis in Taiwan.** Shih-Wei Lai
- et al (CMUH) : ***The Journal of Clinical Pharmacology Volume 55, Issue 6, pages 657–660,June 2015.***
- This population-based case-control study used the database of the Taiwan National Health Insurance Program. There were 2,530 male subjects aged 40–84 years with a first-attack of acute pancreatitis during the period of 1998–2011 as the case group and 10,119 randomly selected subjects without acute pancreatitis as the control group. Both groups were matched by age and index year of diagnosing acute pancreatitis. Subjects who never had finasteride prescription were defined as “never use.” Subjects who at least received 1 prescription for finasteride before the date of diagnosing acute pancreatitis were defined as “ever use.”
- The crude OR of acute pancreatitis was 1.78 (95%CI 1.33, 2.39) for subjects with ever use of finasteride, when compared with subjects with never use of finasteride. After adjusting for potential confounders, **the adjusted OR of acute pancreatitis decreased to 1.25 (95%CI 0.90, 1.73) for subjects with ever use of finasteride**, but no statistical significance was seen

# 前言—10, epidemiology : AP in hemodialytic patients.

- **Epidemiology and outcome of acute pancreatitis in end-stage renal disease dialysis patients: a 10-year national cohort study.** Chen HJ[1], et al (奇美) Nephrol Dial Transplant. 2017 Jan 14. pii: gfw400.
- National health insurance claims data of 67 078 ESRD patients initiating dialysis between 1999 and 2007 in Taiwan. All patients were followed up from the start of their dialysis to first AP diagnosis, death, end of dialysis or 31 December 2008.
- incidence rates of AP **were 0.6, 1.7, 2.6, 3.4 and 4% at 1, 3, 5, 7 and 9 years**, respectively.
- ESRD patients on HD and PD had an AP incidence of 5.11 and 5.86 per 1000 person-years, respectively
- elderly, being female, having biliary stones or liver disease, and being on PD. Severe AP occurred in 44.9% of the HD patients and in 36% of the PD patients.
- **Overall in-hospital mortality was 8.1%.** The risk factors for mortality after an AP attack were male gender, increased age, AP severity, and the presence of diabetes mellitus or liver disease
- **ESRD patients on PD were at higher risk for AP than those on HD**. HD patients with AP attacks had a greater incidence of UGI bleeding

| Year | incidence |
|---|---|
| 1 | 0.6 % |
| 3 | 1.7 % |
| 5 | 2.6 % |
| 7 | 3.4 % |
| 9. | 4 % |

**PD >>HD.**

# 前言—11, Cholecystectomy Reduces Recurrent Pancreatitis (12.39—23.94/1000)

- **Cholecystectomy Reduces Recurrent Pancreatitis and Improves Survival After Endoscopic Sphincterotomy.** Young SH[1,2] et al (陽明大丿: J Gastrointest Surg. 2017 Feb;21(2):294-301.
- data from National Health Insurance Research Database of Taiwan. Elderly patients (age ≧70 years old) who had gallstone-related acute pancreatitis and underwent successful EST with BD stones clearance were eligible for enrollment.
- a total of 670 elderly patients (male 291, female 379) with a mean age of 79.1 was enrolled for analysis after PS matching. The incidence rate of recurrent acute pancreatitis was **12.39** per 1000 person-years in the cholecystectomy cohort and **23.94** per 1000 person-years in the PS-matched control cohort.
- **The risk of recurrent acute pancreatitis was significantly lower** in the cholecystectomy cohort (HR, 0.56; 95 % confidence interval [CI], 0.34-0.91; P = 0.021). The HR for all-cause mortality among the cholecystectomy cohort was 0.75 (95 % CI, 0.59-0.95; P = 0.016) compared with the control cohort.
- 結論**Cholecystectomy decreased** the subsequent recurrent acute pancreatitis and the all-cause mortality in elderly patients with EST and clearance of BD stones after gallstone-related acute pancreatitis.

Biomed Res Int. 2018 Jul 26;2018:4721357. doi: 10.1155/2018/4721357. eCollection 2018.

**Management of Hypertriglyceridemia Induced Acute Pancreatitis.**

Garg R[1], Rustagi T[2].

Author information

1 Department of Internal Medicine, Cleveland Clinic, Cleveland, OH, USA.

# 前言12.:Insulin therapy to lower TG level.

Hypertriglyceridemia is an uncommon but a well-established etiology of acute pancreatitis leading to significant morbidity and mortality. The risk and severity of acute pancreatitis increase with increasing levels of serum triglycerides. It is crucial to identify hypertriglyceridemia as the cause of pancreatitis and initiate appropriate treatment plan. Initial supportive treatment is similar to management of other causes of acute pancreatitis with additional specific therapies tailored to lower serum triglycerides levels. This includes plasmapheresis, insulin, heparin infusion, and hemofiltration. After the acute episode, diet and lifestyle modifications along with hypolipidemic drugs should be initiated to prevent further episodes. Currently, there is paucity of studies directly comparing different modalities.

Insulin therapy has been used for more than a decade to lower TG level along with heparin. While there are many case reports and series demonstrating TG lowering effect, there are no comparison studies evaluating insulin versus conservative therapy [31–33]. Insulin activates lipoprotein lipase (LPL) activity which in turn accelerates chylomicron degradation thus lowering TGs levels [34]. Insulin will also rest pancreatic tissue and may improve immunoparalysis via upregulating the expression of human leukocyte antigen on monocytes and decreasing cell apoptosis [35]. **Insulin lowers TGs levels by 50-75% over 2-3 days** [34]. Cases of successful management of HTG-AP have been reported even in nondiabetic patients without concomitant serum glucose elevation (75% drop in serum TGs in 24 hours) A. Coskun, N. Erkan, S. Yakan et al., “Treatment of hypertriglyceridemia-induced acute pancreatitis with insulin,” Przegląd Gastroenterologiczny, vol. 10, no. 1, pp. 18–22, 2015. View at Google Scholar · View at Scopus

# 前言13: Methimazole and risk of acute pancreatitis (OR: 0.91)

- **Use of methimazole and risk of acute pancreatitis: A case-control study in Taiwan.** Lai SW[1] et al (CMUH): Indian J Pharmacol. 2016 Mar-Apr;48(2):192-
- National Insurance Data base.
- There were 5764 individuals aged 20-84 years with a first ta baseattack of acute pancreatitis from 1998 to 2011 as the cases and 23,056 randomly selected sex- and age-matched individuals without acute pancreatitis as the controls.
- the OR of acute pancreatitis was 0.91 in individuals with ever use of methimazole, when compared with individuals with never use of methimazole (95% CI, 0.60-1.38).
- **alcohol-related disease, biliary stone, cardiovascular disease, chronic obstructive pulmonary disease, diabetes mellitus, hepatitis B, hepatitis C, and hypertriglyceridemia were factors significantly associated with acute pancreatitis**..
- Conclusions : Our study does **not** detect a substantial association between the use of methimazole and risk of acute pancreatitis on the basis of systematic analysis

- **Acute Pancreatitis Induced by Methimazole in a Patient With Subclinical Hyperthyroidism** Katrina Agito and Andrea Manni

Journal of Investigative Medicine High Impact Case Reports 2015

The sixth case reported in the literature and the first diagnosed in a patient with toxic multinodular goiter. A 51-year-old Caucasian female with a history of benign multinodular goiter and subclinical hyperthyroidism was started on MMI 10 mg orally daily. Three weeks later, she developed sharp epigastric pain, diarrhea, lack of appetite, and fever. Her lipase was elevated 5 times the upper limit of normal, consistent with acute pancreatitis.

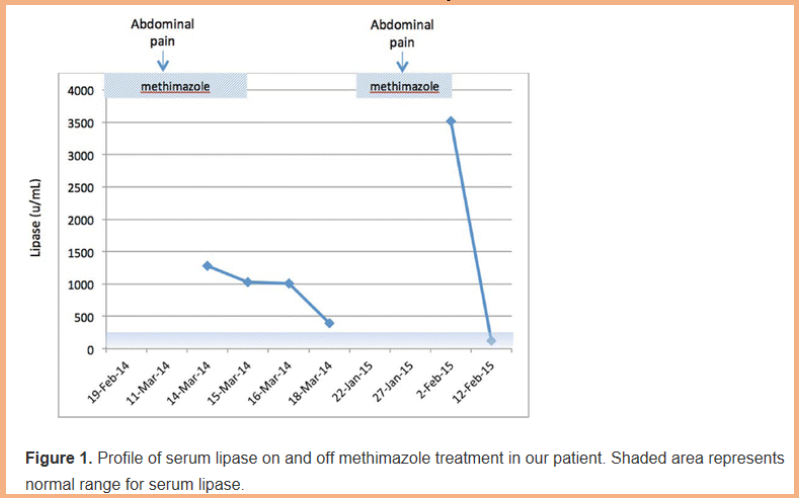



**Figure 1.** Profile of serum lipase on and off methimazole treatment in our patient. Shaded area represents normal range for serum lipase.

# 前言14. Splenectomy and acute pancreatitis

- **Splenectomy Correlates With Increased Risk of Acute Pancreatitis: A Case-Control Study in Taiwan.** Lai SW[1],et al (CMU) : J Epidemiol. 2016 Sep 5;26(9):488-92
- Database of the Taiwan National Health Insurance Program.
- 7666 subjects aged 20-84 years with first-time acute pancreatitis during the period of 1998-2011 as cases and 30 664 randomly selected subjects without acute pancreatitis as controls. Both cases and controls were matched for sex, age, and index year of acute pancreatitis diagnosis. The association of acute pancreatitis with splenectomy was examined using a multivariable unconditional logistic regression model and reported as an odds ratio and its 95% confidence interval (CI).
- The adjusted odds ratio of acute pancreatitis was 2.90 for subjects with splenectomy (95% CI, 1.39-6.05) compared with subjects without splenectomy.
- Conclusions : Splenectomy is associated with acute pancreatitis.

# 前言15, Nabumetone(NSAID) and acute pancreatitis

- **Nabumetone use and risk of acute pancreatitis in a case-control study.** Hung SC[1] et al ( Nantou Hospital): Pancreatology. 2016 May-Jun;16(3):353-7.
- Database from the Taiwan National Health Insurance Program.
- 5384 cases aged 20-84 years who had their first attack of acute pancreatitis during 1998-2011 and 21,536 controls without acute pancreatitis, and matched them according to sex, age and year in which acute pancreatitis was diagnosed.
- one prescription for nabumetone within 7 days before acute pancreatitis diagnosis -→active user.
- The adjusted odds ratio of acute pancreatitis **was 3.69** (95%CI 1.69, 8.05) for subjects with active use of nabumetone compared with those with never use.
- Conclusions : **Active use of nabumetone may increase the risk of acute pancreatitis.**

# 前言16: Sorafenib-induced Acute Pancreatitis: (case report)

- **Sorafenib-induced Acute Pancreatitis: A Case Report and Review of the Literature.** Chou JW[1],et al (CMUH) : Intern Med. 2016;55(6):623-7. (Tokyo)
- Acute pancreatitis is an uncommon complication of sorafenib treatment. Only a few cases of **sorafenib-induced acute pancreatitis** have been reported in the English literature.
- a 56-year-old man with hepatocellular carcinoma treated with sorafenib at 200 mg once daily. After six days of treatment, he suffered epigastric pain. Laboratory tests showed markedly elevated serum amylase and lipase levels. Imaging studies demonstrated negative findings. Sorafenib-induced acute pancreatitis was diagnosed after reviewing his history. The sorafenib treatment was discontinued, and his symptoms were resolved seven days later. To date, this case had the shortest duration and the lowest dosage of sorafenib to have induced acute pancreatitis.
- amylase 1,388 U/L (normal, 28-100 U/L), and lipase 3,685 U/L (normal, 8-58 U/L)

# 前言17: Atorvastatin associated With Acute Pancreatitis (OR : 1.67)

- **Atorvastatin Use Associated With Acute Pancreatitis: A Case-Control Study in Taiwan.** Lai SW[1], et al (CMUH and TC):Medicine (Baltimore). 2016 Feb;95(7):e2545.
- NHI database,
- 5810 cases aged 20 to 84 years with a first-time diagnosis of acute pancreatitis during the period 1998 to 2011and 5733 randomly selected controls without acute pancreatitis. Both cases and controls were matched by sex, age, comorbidities, and index year of diagnosing acute pancreatitis.
- never use of atorvastatin. Current use of atorvastatin was defined as subjects whose last remaining 1 tablet of atorvastatin was noted ≤7 days before the date of diagnosing acute pancreatitis.
- **odds ratio of acute pancreatitis was 1.67** for subjects with current use of atorvastatin (95% confidence interval 1.18, 2.38), when compared with subjects with never use of atorvastatin.
- Clinically, clinicians should consider the possibility of atorvastatin-associated acute pancreatitis when patients present with a diagnosis of acute pancreatitis without a definite etiology but are taking atorvastatin.

# Simvastatin and acute pancreatitis : odds ratio : 1.3

- **Use of Simvastatin and Risk of Acute Pancreatitis: A Nationwide Case-Control Study in Taiwan . Chih-Ming Lin et al (CMUH): J. Clinical Pharmacology. 2017:57: 918-923**
- **NHRI data base.** 3882 subjects aged 20 to 84 years with their first acute pancreatitis episode occurring between 1998 and 2011 formed the case group, against 3790 randomly selected controls matched for sex, age, comorbidities, and index year of acute pancreatitis diagnosis. Recent use of simvastatin was defined as subjects whose last remaining simvastatin tablet was noted ≤7 days before the date of acute pancreatitis diagnosis.

  adjusted odds ratio of acute pancreatitis was 1.3 for subjects with recent use of simvastatin (95%CI 1.02, 1.73),

# 前言 18； Atrial fibrillation associated with acute pancreatitis

- **Atrial fibrillation associated with acute pancreatitis: a retrospective cohort study in Taiwan.** Lai SW[1], et al (CMUH) : J Hepatobiliary Pancreat Sci. 2016 Apr;23(4):242-7.
- database of the Taiwan National Health Insurance Program from 2000 to 2010.
- There were 8,981 subjects aged 20-84 with newly diagnosed atrial fibrillation as the atrial fibrillation group and 26,643 sex- and age-matched, randomly selected subjects without atrial fibrillation as the non-atrial fibrillation group.
- There were 8,981 subjects aged 20-84 with newly diagnosed atrial fibrillation as the atrial fibrillation group and 26,643 sex- and age-matched, randomly selected subjects without atrial fibrillation as the non-atrial fibrillation group.
- **CONCLUSIONS:**
- **Atrial fibrillation is associated with acute pancreatitis in the Taiwanese population**, even in the absence of alcohol-related disease and biliary stone

# 前言 19:Diabetes Mellitus after First-Attack Acute Pancreatitis ( >3 months, 2.5 x)

- **Risk of Diabetes Mellitus after First-Attack Acute Pancreatitis: A National Population-Based Study.** Shen HN[1,2], et al (奇美) Am J Gastroenterol. 2015 Dec;110(12):1698-706.
- Taiwan National Health Insurance.
- 2,966 first-attack AP patients and 11,864 non-AP general controls individually matched on age and sex, with an AP/non-AP ratio of 1:4.
- In the first partition of time (<3 months), the incidences of diabetes were **60.8 and 8.0** per 1,000 person-years in AP and control groups, respectively;
- In the second partition (≥3 months), **the incidences of diabetes were 22.5 and 6.7 per 1,000 person-years in AP and control groups**, respectively (adjusted HR 2.54)
- the risk of diabetes was greater in men than in women (HR 3.21 vs. 1.58)
- 結論:The risk of diabetes increases by twofold after AP.

# 前言20. Inflammatory bowel disease on the risk of acute pancreatitis

- **Inflammatory bowel disease on the risk of acute pancreatitis: A population-based cohort study.** Chen YT[1], et al (豐原) J Gastroenterol Hepatol. 2016 Apr;31(4):782-7.
- 11,909 patients diagnosed with IBD between 2000 and 2010 from Taiwan National Health Insurance Research Database as the study cohort. A comparison cohort comprised 47,636 age-matched patients without IBD.
- **The overall incidence of acute pancreatitis was 3.56-fold higher** in the study cohort than in the comparison cohort (31.8 vs 8.91 per 10,000 person-years, crude hazard ratio [HR] = 3.56,

- 結論: **IBD is a risk factor for acute pancreatitis.**

# 前言21. ESRD patients on PD were at higher risk for AP

- **Epidemiology and outcome of acute pancreatitis in end-stage renal disease dialysis patients: a 10-year national cohort study;** Chen H, Wang J, Tsay W, Her S, Lin C, Chien C; (台灣)Nephrology Dialysis Transplantation (Jan 2017)
- national health insurance claims data of 67 078 ESRD patients initiating dialysis between 1999 and 2007 in Taiwan. All patients were followed up from the start of their dialysis to first AP diagnosis, death, end of dialysis or 31 December 2008.
- The cumulative incidence rates of AP were 0.6, 1.7, 2.6, 3.4 and 4% at 1, 3, 5, 7 and 9 years, respectively. ESRD patients on HD and PD had an AP incidence of **5.11 and 5.86 per 1000 person-years**, respectively
- Severe AP occurred in 44.9% of the HD patients and in 36% of the PD patients. Patients with AP on HD had a higher incidence of upper gastrointestinal (UGI) bleeding than those on PD (P = 0.002).
- **Overall in-hospital mortality was 8.1%**. The risk factors for mortality after an AP attack were male gender, increased age, AP severity, and the presence of diabetes mellitus or liver disease.

**Incidence :5.11(HD)-5.86 (PD)/1000 patient years**

# Acute pancreatitis and dialysis.

- **RISK OF AND FATALITY FROM ACUTE PANCREATITIS IN LONG-TERM HEMODIALYSIS AND PERITONEAL DIALYSIS PATIENTS.**
- Wang IK[1] et al (CMUH) :Perit Dial Int. 2017 Nov 2. pii: pdi.2016.00313.
- NHRI data base, PD cohort (N = 9,766), a HD cohort (N = 18,841), and a control cohort (N = 114,386) matched by sex, age, and the diagnosis year of the PD cohort.
- 5.68 (95% confidence interval [CI] = 5.05 - 6.39),
- 4.91 (95% CI = 4.32 - 5.59), and
- 7.47 (95% CI = 6.48 - 8.62) in the all dialysis, HD, and PD patients, compared with the controls, respectively.
- Peritoneal dialysis patients under icodextrin(艾考糊精) treatment had a lower incidence of AP than those without the treatment, with an adjusted HR of 0.59
- **CONCLUSIONS:**
- Peritoneal dialysis patients were at a higher risk of developing AP than HD patients. **Icodextrin solution** could reduce the risk of developing AP in PD patients.
- 註:Icodextrin is an iso-osmolar dialysis solution that consists of a mixture of high molecular weight water-soluble polymers of glucose, isolated by the fractionation of hydrolyzed cornstarch

# 23. AMI or acute pancreatitis involving heart

- **Abdominal pain and ECG alteration: a simple diagnosis?**
- Pezzilli R[1],et al (Italy) Adv Med Sci. 2010;55(2):333-6.
- All organs may be involved during an acute attack of pancreatitis: lungs, kidney, heart, liver, brain. The differential is sometime difficult because acute pancreatitis may sometimes mimic an acute coronary syndrome. We report a case of **a 36-year-old** man who was admitted to Emergency Room for persistent epigastric pain. Serial electrocardiograms (ECG) showed signs of **acute myocardial infarction**. However, a coronary angiogram demonstrated no coronary artery disease, and **serum troponin was undetectable**. Later, **serum pancreatic enzyme levels were elevated** and an ultrasonography scan of the abdomen was consistent with pancreatitis. Physicians should keep in mind the possibility of an attack of pancreatitis in a patient with abdominal pain and ECG modifications who is a heavy drinker.

# 24. SSRI and acute pancreatitis (adjusted OR :1.7%)

- **Association of use of selective serotonin reuptake inhibitors with risk of acute pancreatitis: a case-control study in Taiwan.**
- Lin HF[1], et al (CMUH)：Eur J Clin Pharmacol. 2017 Aug 30 · A population base case control study.
- 4631 cases with first attack of acute pancreatitis and 4631 controls without acute pancreatitis were selected using a randomly sampled cohort of one million health insurance enrollees from 2000 to 2013. Both cases and controls were aged 20-84 years and were matched with sex, age, comorbidities, and index year of diagnosis of acute pancreatitis.
- The adjusted OR of the current users of SSRI was **1.7**

# 25. Primary Sjogren's syndrome and acute pancreatitis

- **Primary Sjogren's syndrome and the risk of acute pancreatitis: a nationwide cohort study.** Chang CC et al (CMUH) : BMJ Open. 2017 Aug 11;7(8):e014807.
- 9468 patients with pSS by using the catastrophic illness registry of the National Health Insurance Database in Taiwan. We also selected 37 872 controls that were randomly frequency. followed-up for 4.64 and 4.74 years, respectively.
- A total of 44 cases of acute pancreatitis were identified in the pSS cohort versus 105 cases in the non-pSS cohort. Multivariate Cox regression analysis indicated that the incidence rate of acute pancreatitis was significantly higher in the pSS cohort . **Odds ratio : 1.48**
- Cyclophosphamide use increased the risk of acute pancreatitis (aHR **5.27**, 95% CI 1.16 to 23.86). By contrast, **hydroxychloroquine reduced the risk of acute pancreatitis (aHR 0.23,** 95% CI 0.09 to 0.55).
- The risk of acute pancreatitis was higher in PSS. 但其中有多少 ig G4 pancreatitis ?

# 26. One year after SAP:

- **Morphological and functional consequences and quality of life following severe acute pancreatitis.** Kozi et al (Italy):Ann Ital Chir. 2017 Jun 23;6. pii: S0003469X17026690.
- 99 patients with SAP and 51 with mild acute pancreatitis (MAP).
- **Pancreatic exocrine insufficiency (PEI)** was diagnosed by the concentration of fecal elastase-1.
- Endocrine function was evaluated by measuring hemoglobin A1c, insulin, and C peptide levels.
- Quality of life was investigated using the Health Survey Questionnaire (SF-36)

@@@

1. PEI was observed in **17.2%** of patients after SAP vs. 7.8% of patients after MAP ($p>0.05$).
- 2. changes in pancreatic morphology in 52.5% of patients after SAP and 9.8% of patients after MAP ($p<0.0001$).
- 3.A medium risk of malnutrition was observed in 16.2% of patients after AP vs. 2% of patients after MAP ($p=0.01$).

# III. Diagnosis and treatment; guidelines

- 分成四個部分;
- **1.** 診斷方面: 診斷依據,及病因,及收治
- **2.** 診斷方面:, 嚴重度之評估
- **3.** 治療方面:
- **4.** 出院依據

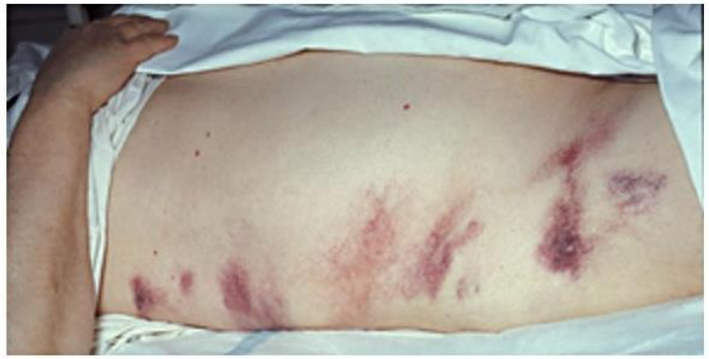
# I. 診斷方面: 診斷依據,及病因,及收治

## 1.診斷依據

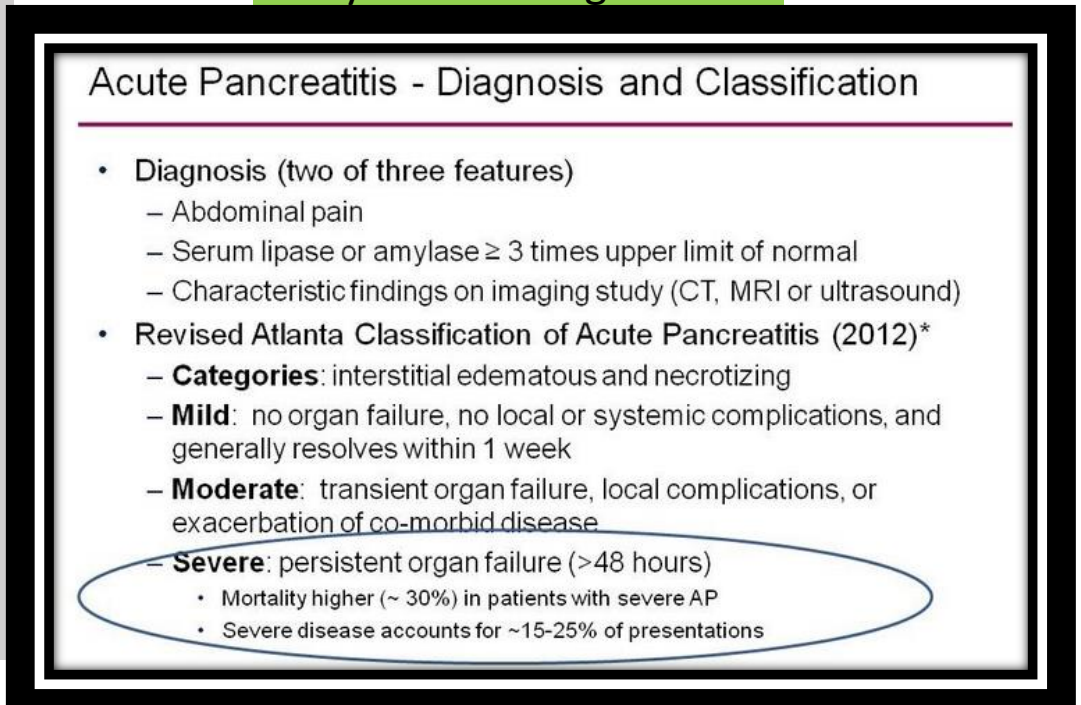
- 1, 診斷急性胰臟炎必需符合以下三
- 個條件之二:
- (1) 典型的上腹痛一向前灣屈較輕,躺平加
- 重、會痛到背後

@@@

- (2) Serum amylase 及 lipase 明顯升高, 即
- 正常值之3倍以上.
- Amylase > 500 .
- Lipase :>200
- (3) Images : US, CT, MR可見胰臟腫大,出水
- 或有壞死或一般X光上出現片段性小腸腫
- 大(sentinel loop).



Grey Turner's sign



# I. 診斷方面: 診斷依據,及病因,及收治
## 2.病因

@@@

- **2.急性胰臟炎之發病原因必需切實尋找, 評估.並確定**
  - **(1)** 病史之詢問包括飲酒史, 平時之喝酒量、有無膽囊結石症, **Hyperlipidemia**,外傷病史, 之前有雖急性胰臟炎之病史,其原因為何.
    發病前 **72 hours** 內之飲食內容,是否高脂肪高熱量,有無飲酒、飲酒量, 特殊用藥,等
    最近兩天內之**invasive procedures**如 **ERCP, duodenoscopy**等、
    家族史:有無家族內叢生之高血脂症及胰臟疾病

- **Etiology of acute pancreatitis**
  - 1. Gall stone
  - 2. Alcohol
  - 3. ERCP induced
  - 4. Hypertriglyceridedmia
  - 5. **Hereditary**
  - 6. Pancreatic divisum
  - 7. Idiopathic
  - 8. others

# I. 診斷方面: 診斷依據,及病因,及收治
## 2.病因

- **(2) Lab tests**
- 看有無肝膽之異常 **(Total and direct bilirubin, GGT, alkaline**
- **phosphatase, AST and ALT等), 有無 Hyperlipidemia**
- **@@@ (TG).1000 mg/dl 以上視為胰臟炎之原因.**

  另發炎指數 **(WBC, ESR, CRP** 及白血球之分類)可藉以判斷發病之時曰及嚴重度、
- **(3) Medical image: US/EUS 看有無膽道結石, CBD擴大>=8 mm).**

  如果**US/EUS** 看不出膽道疾病、即應考慮 **MRCP** 看有無形態學上之異常及**abdominal CT.**看胰臟及膽道上病變、

  如**CT/MRCP** 均看不出原因, 即可列為特發性,

  並在治療後檢查 **ERCP.**排除特殊之發生異常.

# I. 診斷方面: 診斷依據,及病因,及收治
## 3.收治

- 3.所有的 **acute pancreatitis** 病例都應該在
- 專業的醫療機構內治療.

- 專家, 有經驗, 合格的專科醫師及其團隊.
- Lab. Quality
- Medical images
- Radiologists
- Pathologists.
- Drug therapy-pharmacologists
- Nurses—…
- ICUs.
- OR.

# II.診斷方面:, 嚴重度之評估-1

- **4, 每一案例均需仔細詢問病史,確認發作之時間(onset) 以及可能**
- **的原因,以及相關病史.**
- **確認發作之時間(onset)**
- ***typical symptom—abdominal pain 何時發生( time),**
  **參考以下2項:確定發作日時**
- ***** **amylase 不正常之時間 : 6 hours after onset, within 48 hours**
  **After attack.**

  ***** **CRP : 超過 1.0 -→more than 48 hours after onset**

  **Pain lasting > 72 hours ---- severe.**

  **Amylase , abnormal > 72 hours-----severe**

  **CRP >8.0 at any time -----severe**

@@@

# Etiology—very common to very rare:
# 常見的先思考alcohol, gall stone, TG. Drugs---

- **Acute pancreatitis due to malaria: A case report of five patients and review of literature.** Abhilash KP[1] et al (India): J Family Med Prim Care. 2016 Jul-Sep;5(3):691-694.
- five adult patients between 2005 and 2010 who presented with a short duration febrile illness and diagnosed to have malaria with acute pancreatitis. The mean age of the five patients with acute pancreatitis was 40.4 years and four of them were males. None of them were alcohol consumers and did not have any other risk factor for acute pancreatitis. *Plasmodium falciparum* was responsible for all the cases. Pancreatic enzymes were significantly elevated in all the patients with a mean serum lipase level of 1795 U/L (normal value: <190 U/L) and a mean serum amylase level of 584 U/L (normal value: <100 U/L).
- Acute pancreatitis is a very rare complication of malaria, and a high index of suspicion is required in patients presenting with severe malaria and abdominal pain.

# II.診斷方面:, 嚴重度之評估-2

- **5, 每一案例均需確實量測vital signs, 包括 BP, Pulse rate,**
- **Respiratory rate, BT, and consciousness.**
- 以下任何一項均代表 **severe.** 多項表示極為嚴重、
  嚴重例之死亡率為 **5 %** 以上 極嚴重例為 **10 %** 以上,
  輕症在 **1 %** 以下**)**
- **BP:<90 mm Hg----severe**
- **PR:＞104/min.----severe**
- **BT: > 7.5 degrees --- severe**
- **Consciousness : disturbed,** dull and drowsy, ----severe

# II.診斷方面:, 嚴重度之評估-3

- 6.病例應區分為 重症或輕症. 重症病人, 包括已有器官衰竭者,必需住入加護病房. 作
- intensive care.,.


# II.診斷方面:, 嚴重度之評估-4,

## 7, 必需持續監測疾病之發展, 以下幾項化需定期追蹤, 頻率如下:

- **Serum amylase :** 不正期間,一天一次, 正常以後隔天,進食以後連續三天一天一次, 之後可以每三天一次,直至出院.
- **WBC and neutrophilia,** 住院第一週內同 **amylase,** 之後依病情需要檢查,如有發燒, 至少一天一次
- **Lipase :** 同 **amylase,** 兩者同時檢測.
- **CRP** 發病之前三天每天檢查一次,之後與 **amylase/lipase** 之頻率相同.
- **TG :** 來診連續三天檢查 **TG** 各一次, 恢復正常後可不再查、但再發 **recurrent/relapse**時要再查,出院前一天必須檢查一次.

@@@

- **BUN/Cr.** 來診連續三天檢查, 各一次之後每隔三天至少查一次.七天後至少每週檢查一次
- **Ca:** 來診連續三天檢查,如不正常仍隔天檢查一 次
- **Total bilirubin/GGT/alkaline phosphatase,** 來診時必檢查一次,不正常時隔天檢查一次, 恢復正常可每**5~7**天檢查一次.
- **Arterial pH** 如有休克及呼吸喘急者至少每天一次,必要時再檢測,情況好轉時,可不必再檢,
- **Electrolytes (Na, K,Cl.,)**等項,, 來診時必檢查一次, 異常時可隔天檢驗一次.

# II.診斷方面:, 嚴重度之評估-5,

8, 每案例在最初七天,每2天判定嚴重度一次,嗣後每3天判定一次,其判定如下-1

| • 輕症條件 | 重症條件 |
| --- | --- |
| • 1, 症狀在3天內減輕或消失 | --持續五天以上 |
| • 2. Serum amylase 在3天內恢復正常 | --在第四天仍不正常 |
| • 3. WBC < 12,000 | WBC > 15,000 |
| • | Neutrophils > 10,000 |
| • 4. CRP 在發病後 72 hours : < 3, | > 5.0 |
| • CRP 在5天時 < 3 | > 8.0 |
| • CRP 在7天時恢復正常 | > 5.0 |
| • 5. Ca.在3天內均> 8.5 | < 8.0 |
| • Ca 在5天內 > 8.5 | < 7.5 |

# II.診斷方面:, 嚴重度之評估-5,

@@@ 8, 每案例在最初七天,每2天判定嚴重度一次,嗣後每3天判定一次,其判定如下-2

## •輕症條件

- **6. CT 在 3-5 天只有 edematous Change,**
- **未出水, 沒有 necrosis**
- **>5**
- **7. Vital signs: stable.**
- **8. Consciousness : clear**
- **9. Fever (-) or less than 37.5**
- **10. Peritoneal signs (-)----------**
- **11. Bowel sound became active**
- **at the 4th day**
- **12. abdominal tenderness absent at 4th day**

## 重症條件

**CT : necrosis,出水 3-5天, CTSI >4**

CT 在 7天時 : new changes CTSI

**BP< 90 mm Hg, PR > 104/min.**

**Consciousness 變差drowsy/dull**

**> 38 degrees**

**Peritoneal sign (+)**

**Bowel sound still absent**

**at the 4th day**

**Tenderness (+) at the 4th day**

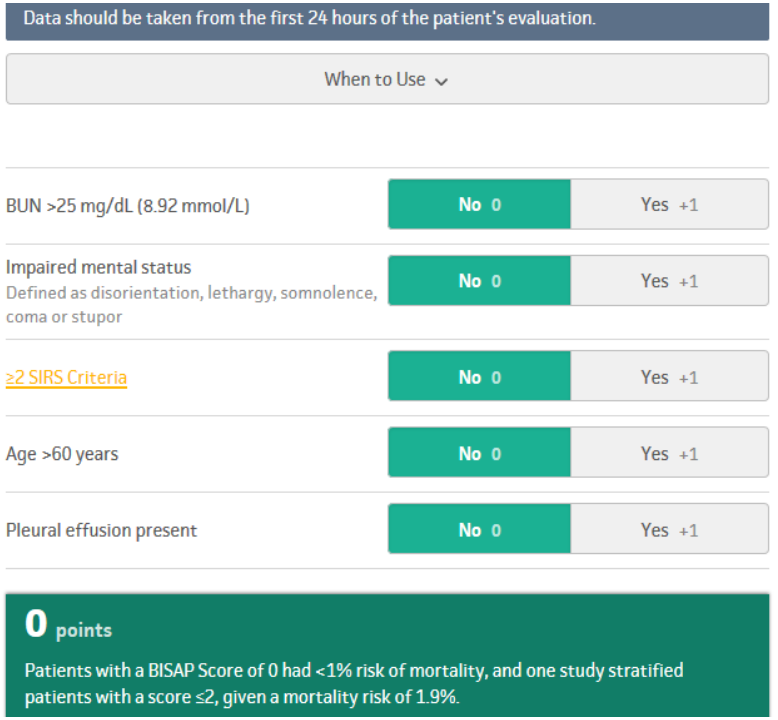
# II.診斷方面:, 嚴重度之評估-5,

## 8, 每案例在最初七天,每2天判定嚴重度一次,嗣後每3天判定一次,其判定如下-3

| • 輕症條件 | 重症條件 |
| --- | --- |
| • 13, BUN/Cr. Normal | abnormal at 48th hour, |
| • | 72 hours and 120 hours. |
| • | |
| • 14.LDH : 1st-5t day 均低於 450, | > 500 |
| • 15.Seum bilirubin | |
| • 在 1-3rd day 均低於 2 mg/dl | > 3.0 mg/dl |
| • 在5th day < 3 mg/dl | > 5 mg/dl.-ray |
| • 16. Chest X-ray normal | pleural effusion (+) |
| • (no change) | 一邊或兩邊 |
| • | |

# BISAP Score for Pancreatitis Mortality
## bedside index of severity in acute pancreatitis

- Predicts mortality risk in pancreatitis with fewer variables than Ranson's
- 1. BUN > 25 mg/dL (8.92 mmol/L)---1
- 2. Impaired mental status----------1
- Defined as disorientation, lethargy, somnolence,
- coma or stupor
- 3. ≥2 SIRS Criteria----------1
  4. Age > 60 years----------1
- 5. Pleural effusion present----------1




- Patients with a BISAP Score of 0 had <1% risk of mortality, and one study stratified patients with a score ≤ 2, given a mortality risk of 1.9%
- BISAP評分≥3的總死亡率敏感性為56%(.PLOS one, 2015)

@@@

# SIRS Criteria (≥ 2 meets SIRS definition): Systemic Inflammatory Response Syndrome (*SIRS*):

- 1. Temp >38°C (100.4°F) or < 36°C (96.8°F)
- 2. Heart rate > 90
- 3. Respiratory rate > 20 or $PaCO_2$ < 32 mm Hg
- 4. WBC > 12,000/$mm^3$, < 4,000/$mm^3$, or > 10% bands

- Sepsis Criteria (SIRS + Source of Infection): Suspected or present source of infection
- Severe Sepsis Criteria (Organ Dysfunction, Hypotension, or Hypoperfusion): Lactic acidosis, SBP <90 or SBP drop ≥ 40 mm Hg of normal
- Septic Shock Criteria: Severe sepsis with hypotension, despite adequate fluid resuscitation
- Multiple Organ Dysfunction Syndrome Criteria: Evidence of ≥ 2 organs failing

# BISAP—prediction of severity and mortality

- **BISAP: A Simple Method for the Early Identification of Mortality Risk in Patients With Acute Pancreatitis**
- Albert B. Lowenfels, MD
- Medscape General Surgery > Viewpoints | March 02, 2009
- **The Early Prediction of Mortality in Acute Pancreatitis: A Large Population-Based Study**
- Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA *Gut.* 2008;57:1698-1703
- Their model includes 5 variables:
- **blood urea nitrogen (BUN),**
- **impaired mental status, systemic inflammatory response,**
- **age older than 60 years, and**
- **presence of pleural effusion.**
- Scores ranged from 0 (absence of all variables) to 5 (presence of all variables) and correlated strongly with survival. The area under the receiver operating characteristic curve (ROC) was 0.82 -- an excellent fit.

- **Comparison of the BISAP scores for predicting the severity of acute pancreatitis in Chinese patients according to the latest Atlanta classification** Zhang J[1] et al (China): J Hepatobiliary Pancreat Sci. 2014 Sep;21(9):689-94
- The AUC for severity predicted by **BISAP** was 0.793 (95% confidence interval [CI] 0.700-0.886), **APACHE II** 0.836 (95% CI 0.744-0.928) and by **Ranson score** was 0.903 (95% CI 0.814-0.992). The AUC for PNec predicted by BISAP was 0.834 (95% CI 0.739-0.929), APACHE II 0.801 (95% CI 0.691-0.910) and by Ranson score was 0.840 (95% CI 0.741-0.939). The AUC for mortality predicted by BISAP was 0.791 (95% CI 0.593-0.989), APACHE II 0.812 (95% CI 0.717-0.906) and by Ranson score was 0.904 (95% CI 0.829-0.979).
- BISAP score may be a valuable source for risk stratification and prognostic prediction in Chinese patients with AP.

# BISAP and BUN –評估 severity 最有用

- **BISAP, RANSON, lactate and others biomarkers in prediction of severe acute pancreatitis in a European cohort.** Valverde-López F[1] et al (Spain) J Gastroenterol Hepatol. 2017 Feb 16.
- 269 patients diagnosed of AP, admitted to Virgen de las Nieves University Hospital between June 2010 and June 2012. Blood urea nitrogen (BUN), C-reactive protein (CRP) and creatinine (Cr) were measured on admission and after 48 hours, lactate and BISAP only on admission and RANSON within the first 48 hours.
- 8(3%) patients died, 17(6.3%) were classified as SAP, and 10(3.7%) were admitted in ICU. **BISAP was the best predictor on admission for SAP**, mortality and ICU admission with an AUC of 0.9(95%CI 0.83-0.97); 0.97(95%CI 0.95-0.99) and 0.89(95%CI 0.79-0.99) respectively.
- @@@ **After 48 hours BUN48h was the best predictor of SAP** (AUC = 0.96 CI:0.92-0.99); BUN48h and BISAP where the best predictors for mortality (AUC = 0.97 CI:0.95-0.99) and Cr48h for ICU admission (AUC = 0.96 CI:0.92-0.99). Lactate showed an AUC of 0.79(CI:0.71-0.88), 0.87(CI:0.78-0.96) and 0.77(CI:0.67-0.87) for SAP, mortality and ICU admission respectively.
- CRP on admission was only a significant predictor of SAP

# II.診斷方面:, 嚴重度之評估-6, 9, CT 之應用規定於後.

- (1) 已確立診斷者,來院3天之後, 即第四~五天才檢查以判定其嚴重度
- (2)第一次之 CT 之後 72 hours, 以上 如仍有明顯症狀及病情並未改善或惡化,而考慮引流或手術等侵襲性處置時,可再執行一次 abdominal CT.
- (3) 診斷不明,但有懷疑為急性胰臟炎可在來院之初即檢查CT.
- (4) 以使用 MDCT 為宜,切片厚度在5 mm 以下/使用非離子化之造影劑 100-150 ml. (每秒輸入 3 ml.)第一次以 triple phase 為原則, 追踪檢查時以 bi phase 為原則、由於 abdominal CT 有高幅射, 醫師應多加考慮、真正之必要性,
- (5) Kidney Function 不佳者先作 pre-contrast CT.

# II.診斷方面:, 嚴重度之評估-7, 10, CT 檢查之後,即判定acute pancreatitis 之 CTSI

- 應用 CTSI 判定acute pancreatitis 之嚴重度
- CTSI < 4 ,mild
- **CTSI >=4 severe,**
- **CTSI >= 8, very severe**

@@@

| Points | complications | mortality |
|---|---|---|
| 0-3 | 8 % | 3 % |
| 4-6 | 35 % | 6 % |
| 7-10 | 92 % | 17 % |

## BALTHAZAR CT severity index(CTSI)-1994

**TABLE** CT Severity Index

| Prognostic Indicator | Points |
|---|---|
| Pancreatic inflammation | |
| Normal pancreas | 0 |
| Focal or diffuse enlargement of the pancreas | 1 |
| Intrinsic pancreatic abnormalities with inflammatory changes in peripancreatic fat | 2 |
| Single, ill-defined fluid collection or phlegmon | 3 |
| Two or more poorly defined collections or presence of gas in or adjacent to the pancreas | 4 |
| Pancreatic necrosis | |
| None | 0 |
| ≤ 30% | 2 |
| > 30–50% | 4 |
| > 50% | 6 |

| CT Severity Index | Inflammation score + Necrosis score |
|---|---|

Mild (0-3) moderate (4-6) severe (7-10)

- **Computed tomography severity index is an early prognostic tool for acute pancreatitis.** Vriens PW et al(荷蘭) J Am Coll Surg. 2005 Oct;201(4):497-502.
- Seventy-nine patients were admitted with acute pancreatitis. The overall complication rate was 57%; mortality was 9%. In patients with a CTSI of 0 to 3, these rates were 42% and 2%, respectively; in those with CTSI of 4 to 6, 81% and 19%, respectively; and in those with CTSI of 7 to 10, 100% and 33%, respectively. Outcomes of subsequent CT scans did not alter the initial prognosis. Early CTSI correlated well with the incidence of complications, sepsis, mortality, and necessity for ICU admission. Early establishment of the CTSI is an excellent prognostic tool for complications and mortality. Patients with a CTSI of 0 to 3 can safely be discharged from the ICU.

| CTSI | Comp. | Mortality |
|---|---|---|
| 0-3 | 42 % | 2% |
| 4-6 | 81 | 19 |
| 7-10 | 100 | 33 |
| All | 57 | 9 |

- Comp.—complication rate

# II.診斷方面:, 嚴重度之評估-7, 11, MR 之應用規定於下

- 1. MR 是non-invasive 也沒有幅
- 射的問題.故對年輕的病人
- (especially 15 歲以下)宜
- 採用 MR 檢查
- 2. 可用於判斷pancreas 有無腫
- 大,邊緣是否完好,有無形成
- pseudocyst. 出血,出水及壞
- 死, Abscess 等合併症.
- 3. 區分輕症及重症有價值.
  Necrosis >30 % 視為重症.

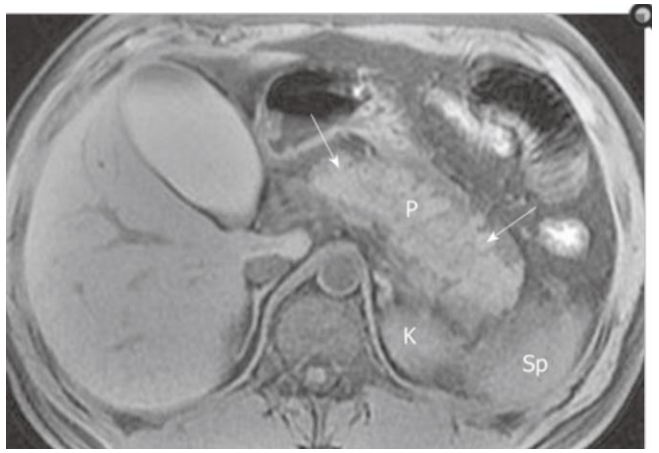
- **4. MR 仍建議使用靜脈造影劑 gadolinium, 先查 FS-T2再作 FS-T1.**
- An MR with T2-weighted images is advised when the differentiation between pseudocysts and collections with necrosis (i.e. acute necrotic collection and walled-off necrosis) is clinically relevant and in young patients because of the radiation burden of CT.

# II.診斷方面:, 嚴重度之評估-8, 12. MRCP之應用規定如下:

- 1.主要看 acute pancreatitis 發炎之範圍
- 2.當有膽道結石之懷疑時, CT 又看不出變化,可利用 MRCP 看膽道
- 結石之變化.即 MRCP可排除 biliary tract stones.
- 3.. Young children或有特別考慮幅射問題時、也應用 MR/MRCP .
- 4. 對 IV contrast medium有過敏者,不必使用 contrast medium, 而使
- 用 T2 照像,可得到 MRCP 之影像.
- 5. 檢查各項合併症,如出血感染及 pseudocysts.fistula.

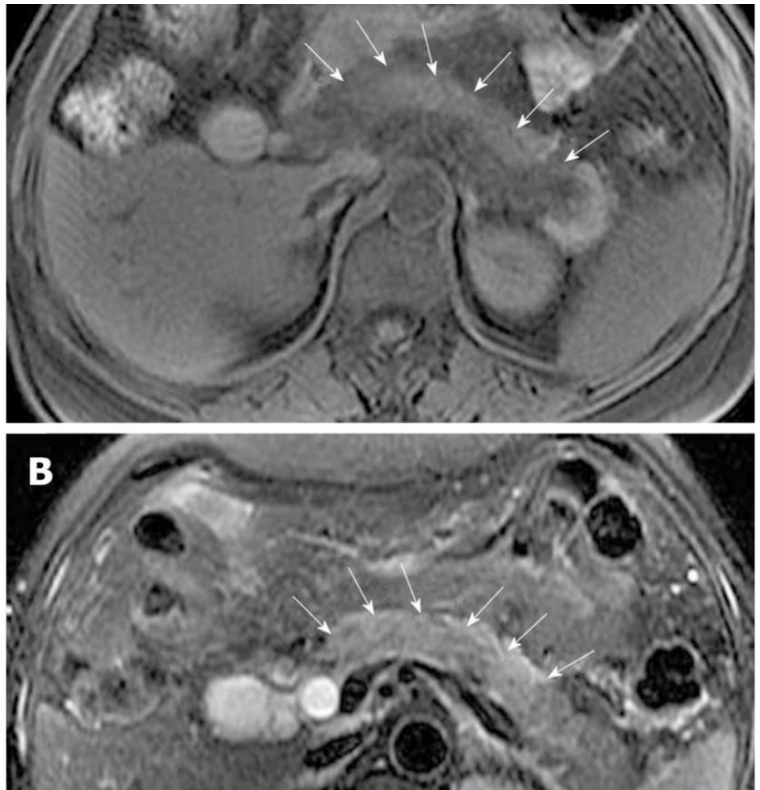
# MR in pancreatitis

- MRI is an excellent noninvasive modality of choice to help stage the severity of inflammatory processes, and detect the presence and extent of pancreatic necrosis. The presence and development of complications of acute pancreatitis such as hemorrhage, fluid collections, pseudocysts, abscesses, pseudoaneurysm, and venous thrombosis are well-demonstrated by MRI.
- **Magnetic resonance imaging for acute pancreatitis.** Bo Xiao and Xiao-Ming Zhang(China):*World J Radiol. 2010 Aug 28; 2(8): 298–308.*

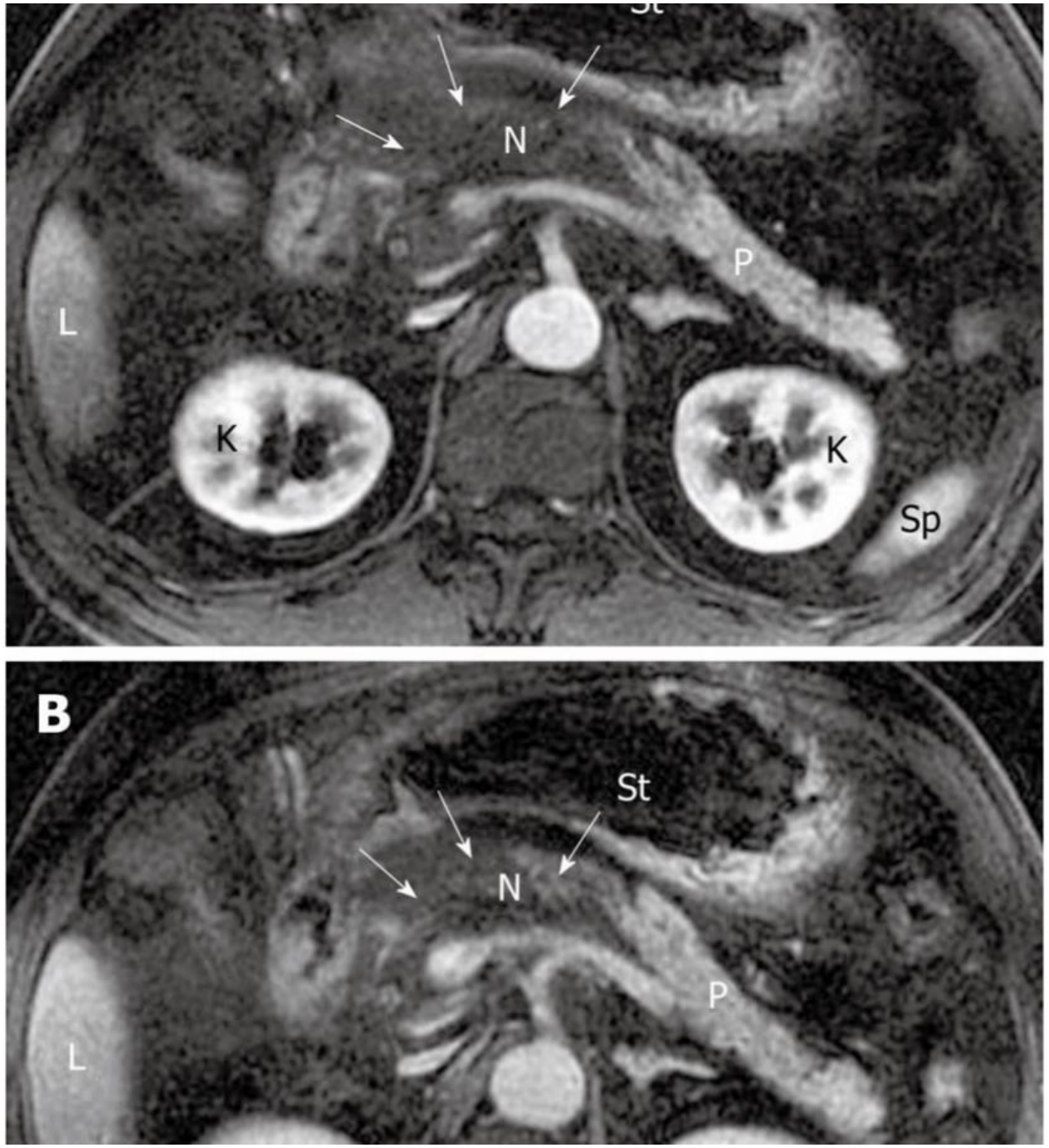



1, edematous swelling
2. Blurred boundaries
3. complications.

Acute pancreatitis in a 37-year-old man. Axial non-enhanced magnetic resonance T1-weighted with fat-suppression image obtained at the time of hospital admission shows an edematous, homogeneously enlarged pancreas (arrows). Pancreatic boundaries are blurred due to peripancreatic fluid exudations. K: Kidney; P: Pancreas; Sp: Spleen



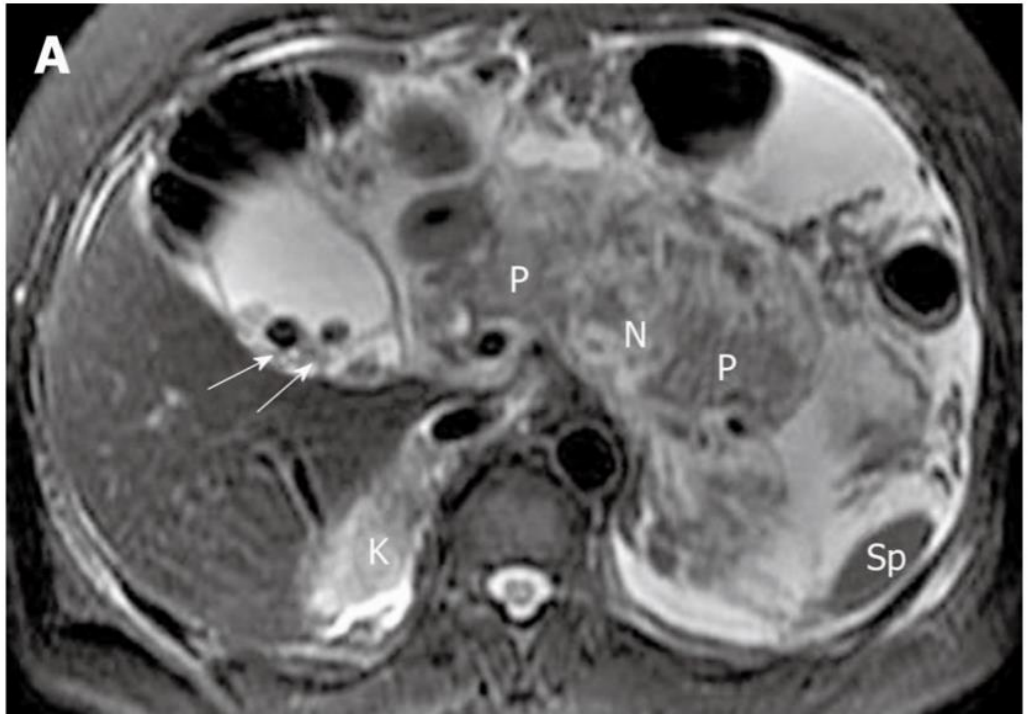

T1 and T2 images **Acute edematous pancreatitis in a 29-year-old man.** Axial non-enhanced magnetic resonance T1-weighted with fat-suppression image (A) and axial T2- weighted with fat-suppression image B) show that the parenchyma of the pancreatic head, body and part of the tail is hypointense (arrows in A) and hyperintense (arrows in B) relative to the liver.

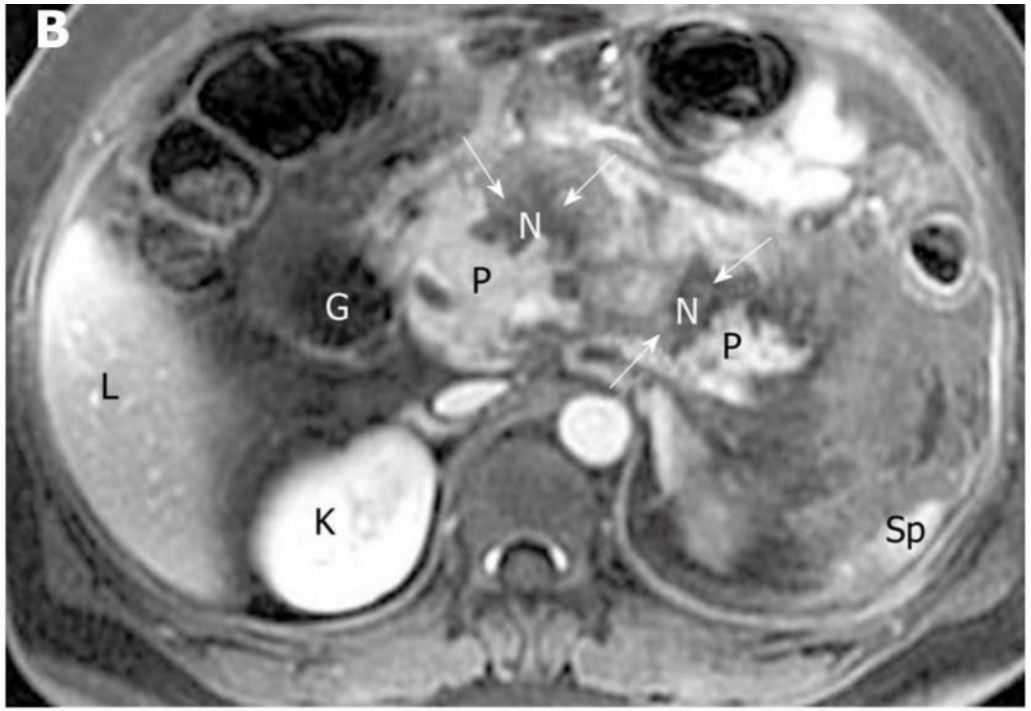


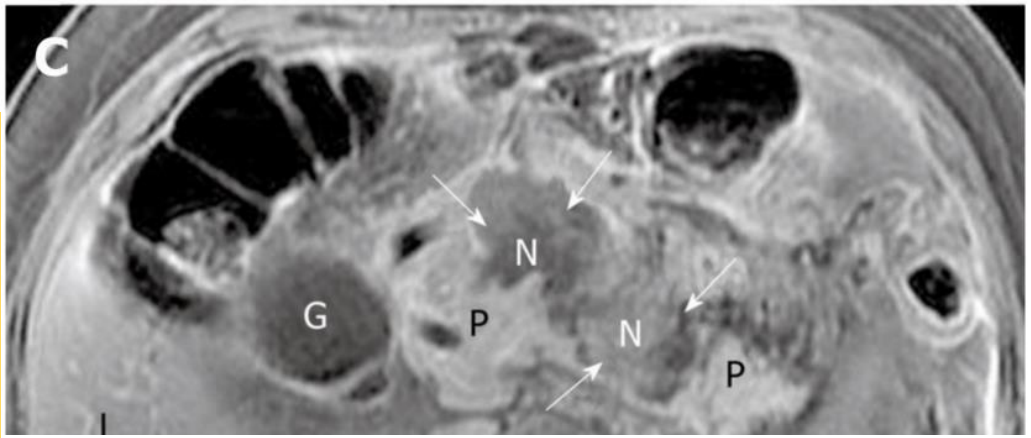

# MR in acute necrotizing pancreatitis 30 -50 %

- **Pancreatic diffuse necrosis in a 65-year-old man after an episode of acute pancreatitis.** A, B: Axial magnetic resonance T1-weighted images obtained in late arterial phase and venous phase reveal large necrotic areas (arrows) (“black pancreas”) in the pancreatic head, neck and part of the body. The extent of necrosis is up to **30-50%** of the pancreatic gland. N: Necrosis; K: Kidney; L: Liver; P: Pancreas; Sp: Spleen; St: Stomach.

- MR in acute necrotizing pancreatitis
- > 50 %




**Gallstones, acute pancreatitis, and gland liquefied necrosis in a 33-year-old woman.** Axial magnetic resonance T2-weighted with fat-suppression image
(A) shows hypointense gallstones (arrows), and axial T1-weighted images obtained in late arterial phase
(B) and venous phase
(C) reveal two zones (arrows) of pancreatic liquefied necrosis in the neck and body of the gland (like “rupture of the pancreas”). The extent of necrosis is > 50% of the pancreatic gland. The head and the tail of the pancreas are still enhancing (P). N: Liquefied gland necrosis; G: Gallbladder; K: Kidney; L: Liver; P: Pancreas; Sp: Spleen.

# AWE (abd. wall edema) in acute pancreatitis (by MR)

- **MR imaging of acute pancreatitis: correlation of abdominal wall edema with severity score.** Yang R et al (南昌) Eur J Radiol. 2012 Nov;81(11):3041-7.
- A total of 160 patients with AP admitted to our institution between December 2009 and March 2011 were included in this study. MRI was performed within 48 h after admission. MRI findings of acute pancreatitis were noted, including AWE on the MRI. The abdominal wall area was divided into quarters, and each area involved was recorded as 1 point to score the severity of **AWE.(abdominal wall edema)**
- he severity of acute pancreatitis was studied using both the MRSI and the APACHE III scoring system. Spearman correlation of AWE with the MRSI and the APACHE III scoring system was analyzed.
- In 160 patients with acute pancreatitis, 53.8% had AWE on MRI. The average AWE score was 1.2±1.4 points.
- **The prevalence of AWE was 30.5%, 64.5% and 100% in mild, moderate and severe AP,** respectively, according to MRSI.
- AWE on MRI in acute pancreatitis is common, which may be a supplementary indicator in determining the severity of AP.

# MRISI (Viremouneix)

- **Prospective evaluation of** nonenhanced MR **imaging in acute pancreatitis.** Loic Viremouneix, et al (法) *JOURNAL OF MAGNETIC RESONANCE IMAGING 26:331–338 (2007*)
- , AP was assessed as grade III by CTSI in four patients (4%), whereas 19 patients were classified grade III by MRISI. The coefficient correlation between CTSI and MRISI was good, with r  0.6 (P 0.001).
- 結論: **NE-MRI seems to be a reliable method of staging AP severity in comparison to CE-CT scan.**

Table 1
CTSI of Imaging Appearances in Acute Pancreatitis

| Imaging appearances | CT severity index |
|---|---|
| Normal | 0 |
| Focal or diffuse enlargement of the pancreas | 1 |
| Pancreatic gland abnormalities associated with peripancreatic inflammation | 2 |
| Fluid collections in a single location | 3 |
| Two or more fluid collections or the presence of gas in or adjacent to the pancreas | 4 |
| Extent of pancreatic necrosis <30% | 2 |
| Extent of pancreatic necrosis 30% to 50% | 4 |
| Extent of pancreatic necrosis >50% | 6 |

*Scale of CTSI: mild acute pancreatitis (grade I): 0-2 points; moderate acute pancreatitis (grade II): 3-6 points; severe acute pancreatitis (grade III): 7-10 points.

Table 3
MRSI Correlated With Morbidity and Mean Length of Hospitalization ($P < 0.001$)

| MRI severity index | Morbidity − (%) | Morbidity + (%) | Mea (day |
|---|---|---|---|
| I (58%) | 47 (91) | 5 (10) | 15 |
| II (21%) | 11 (58) | 8 (42) | 28 |
| III (21%) | 7 (37) | 12 (63) | 44 |
| Total ($N = 90$) | 65 (72) | 25 (28) | 24 |

Table 8
Appearance of Pancreatic Parenchyma on NE MRI and CE CT Scan

| MRI | CT scan | | | |
|---|---|---|---|---|
| | Normal | Edema | Necrosis | Total |
| Normal | 54 | 0 | 1 | 57 |
| Edema | 23 | 0 | 5 | 29 |
| Necrosis | 0 | 0 | 7 | 7 |
| Total | 77 | 0 | 13 | 90 |

# MRCP 之目的

## Acute pancreatitis

- Assess the extension of the inflammatory process
- @@ Rule out a CBD stone
- Detect complications
  - Hemorrhage
  - Pseudocysts, MPD rupture, fistulae
  - Vascular occlusion
  - Infection

## Acute pancreatitis: MRI vs CT

*Lecesne et al Radiology 1999*

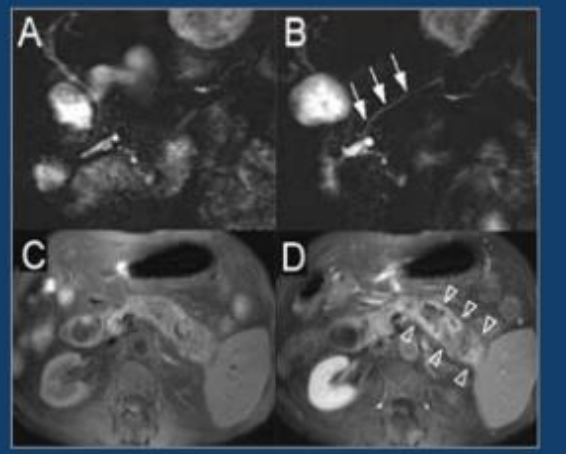
- 30 P

MRCP could be an alternative to CECT for the initial staging of acute pancreatitis

Gd not nephrotoxic

Better evaluation of fluid collections (hemorragic-like)

No specific evaluation of the pancreatic ducts




*from Matos et al. Radiographics 2002*

- **The role of MRCP in acute pancreatitis** Clive Vandervelde *BMJ* 2006;332:1072
- MRCP **is a non-invasive and now widely available technique** utilising T2-weighted MR sequences which can be acquired in a single breath-hold. Intravenous and oral contrast are not required and this investigation provides high quality delineation of the biliary tree and pancreatic duct.
- MRCP is particularly useful in patients with pancreatitis and gallbladder stones **but non-dilated ducts,** in whom exclusion of a bile duct calculus is important. MRCP can be supplemented with conventional MR sequences to assess the pancreas itself and detect fluid collections.

# Dx value of MRCP showing higher sensitivity than CT

- Kingsnorth A, O'Reilly D. Acute Pancreatitis. BMJ 2006 332:1072-1076. (6 May.)
- **UK guidelines for management of acute pancreatitis: is it time to change?** K S Gurusamy et al :Gut:2005, 1344-1345
- a magnetic resonance cholangio(pancreato)gram (MRCP) may be performed, as this has a **higher sensitivity than the CT scan in the diagnosis of choledocholithiasis.**[10]
- **Soto JA**, Alvarez O, Múnera F, *et al.* Diagnosing bile duct stones: comparison of unenhanced helical CT, oral contrast-enhanced CT cholangiography, and MR cholangiography. *AJR Am J Roentgenol*2000;175:1127–34. *The sensitivity of CT cholangiography and MR cholangiography was significantly higher than that of unenhanced helical CT (p<0.01). Differences in specificity were not significant*.

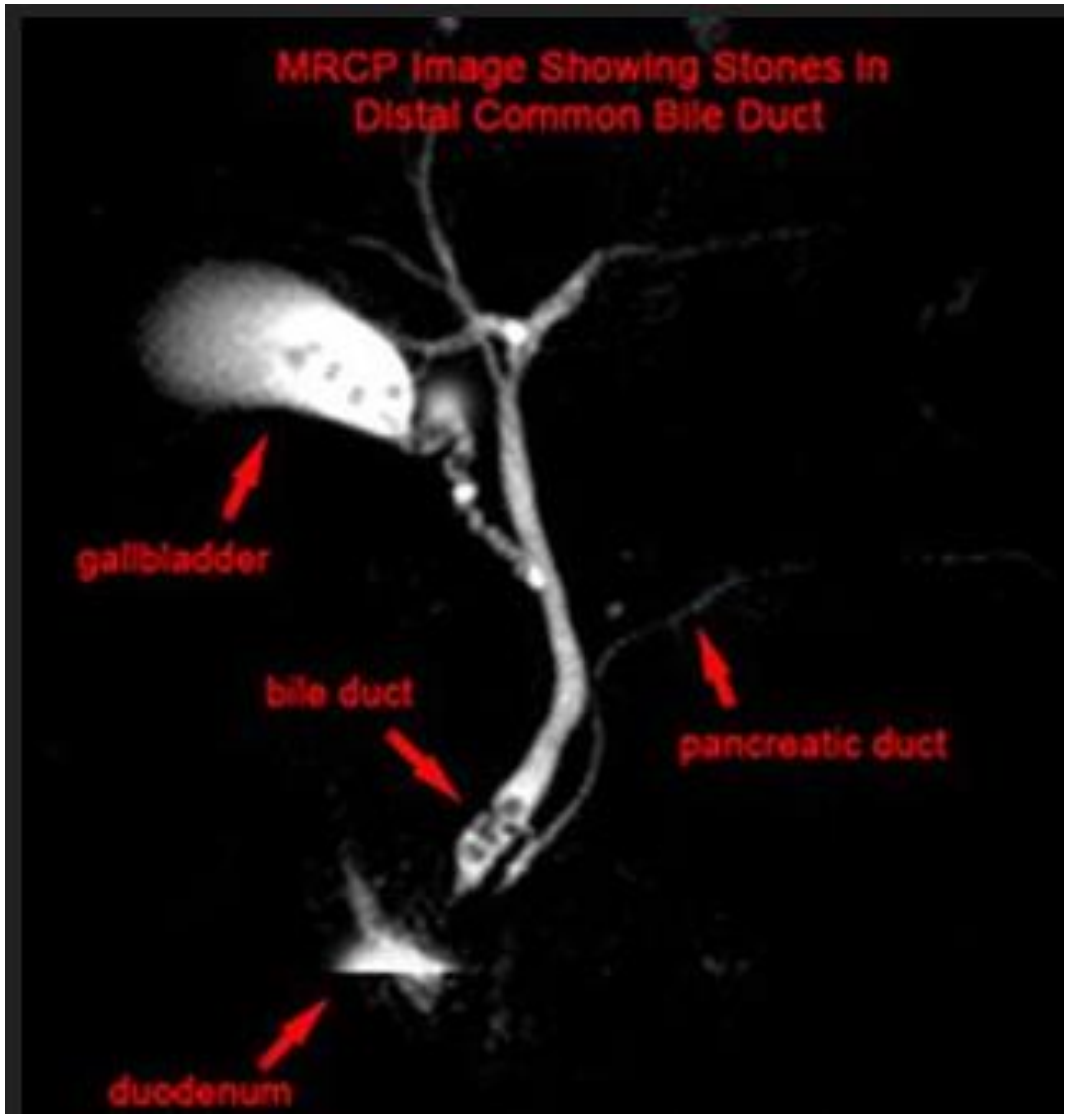
## Choledocholithiasis: evaluation of MR cholangiography for diagnosis.

C Reinhold, P Taourel, P M Bret, G A Cortas, S N Mehta, A N Barkun, L Wang, F Tafazoli

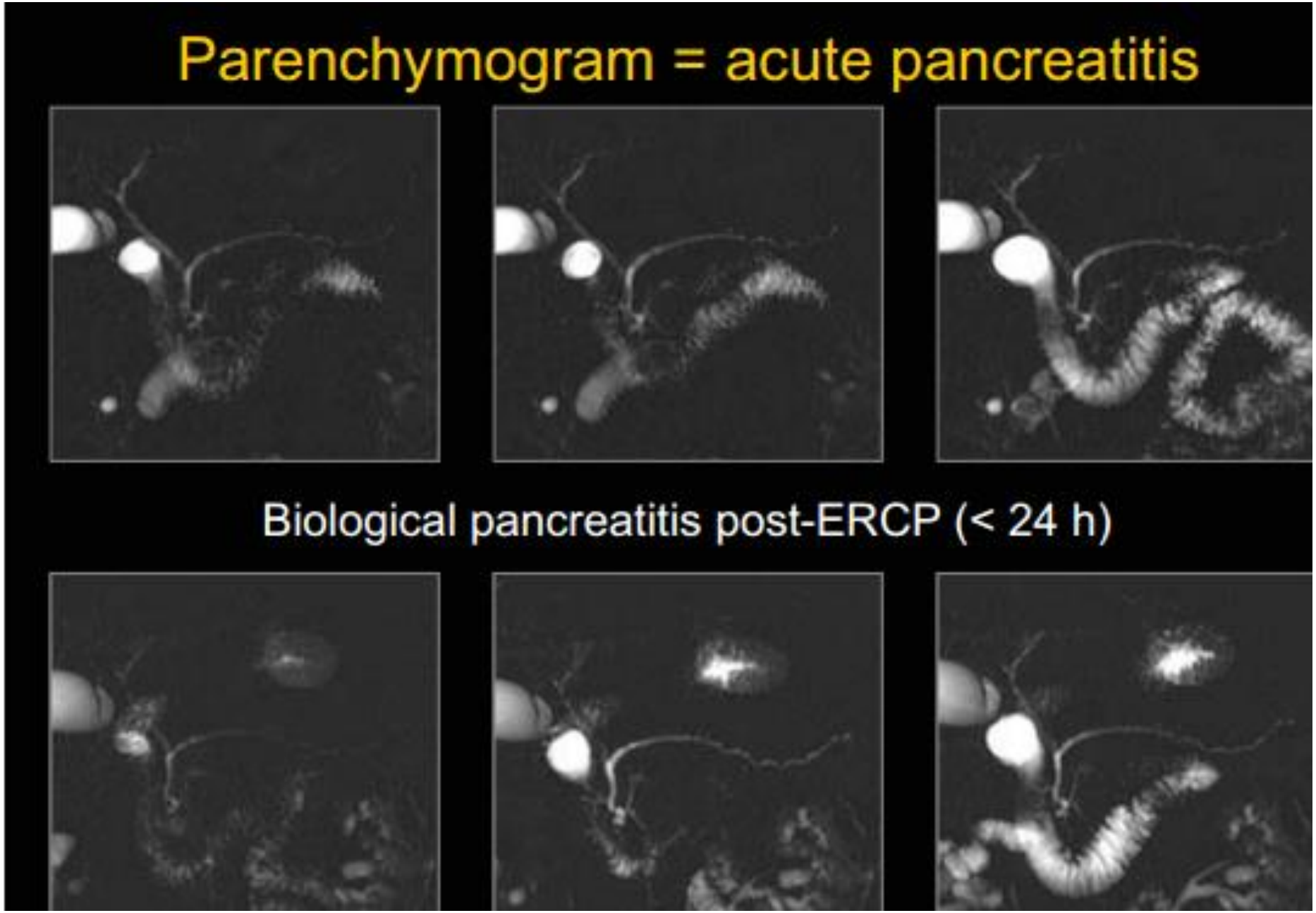
**Published Online:** Nov 1 1998 | https://doi.org/10.1148/radiology.209.2.9807570

Of the 110 patients, 30 (27%) had choledocholithiasis, and 80 (73%) did not. Reviewer 1 used MR cholangiograms to achieve a sensitivity of 90%, specificity of 100%, positive predictive value of 100%, negative predictive value of 96%, and overall accuracy of 97%. Reviewer 2 achieved a sensitivity of 90%, specificity of 93%, positive predictive value of 82%, negative predictive value of 96%, and overall accuracy of 92%. Interobserver agreement for MR cholangiograms was 93% (kappa = 0.82).

CONCLUSION**: MR cholangiography exhibited excellent test performance and resulted in excellent interobserver agreemen**t for the diagnosis of choledocholithiasis.



MRCP


Parenchymogram = acute pancreatitis
Biological pancreatitis post-ERCP (< 24 h)

# Severe acute pancreatitis

## Definition of Severe Acute Pancreatitis (SAP)

- SAP is acute pancreatitis with local and/or systemic complications
- Local complications are:
  - necrotizing pancreatitis
  - Infected necrosis
  - Pancreatic abscess
  - Peripancreatic fluid collection and pseudocystic lesions
- Systemic complications are:
  - Pulmonary and renal failure
  - Shock
  - Cardio-circulatory dysfunctions
  - systemic sepsis
  - coagulation disorder

Bradley EL, III. Arch Surg 1993;128:585-590

AJR Am J Roentgenol. 2018 Aug 30:1-9. doi: 10.2214/AJR.18.19545. [Epub ahead of print]

# Early Prediction of the Severity of Acute Pancreatitis Using Radiologic and Clinical Scoring Systems With Classification Tree Analysis.

Choi HW[1], Park HJ[1], Choi SY[2], Do JH[3], Yoon NY[4], Ko A[1], Lee ES[1].

Author information

1 1 Department of Radiology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, 102 Heukseok-ro, Dongjak-gu, Seoul 06973, Republic of Korea.

CTA: Classification Tree analysis

The Acute Physiology and Chronic Health Evaluation (APACHE)-II score, bedside index for severity in acute pancreatitis (BISAP) score, extrapancreatic inflammation on CT (EPIC) score, and Balthazar grade were included in the **CTA** model.(classification tree analysis)

CTA model showed a trend of a higher AUC (0.853) than the AUC of each single parameter (APACHE-II score, 0.835; BISAP score, 0.842; EPIC score, 0.739; Balthazar grade, 0.700) (all, $p > 0.0125$) while achieving specificity (100%) higher than and accuracy (94.8%) comparable to each single parameter (both, $p < 0.0125$). In the validation cohort, the CTA model achieved diagnostic performance similar to the training cohort with an AUC of 0.833.

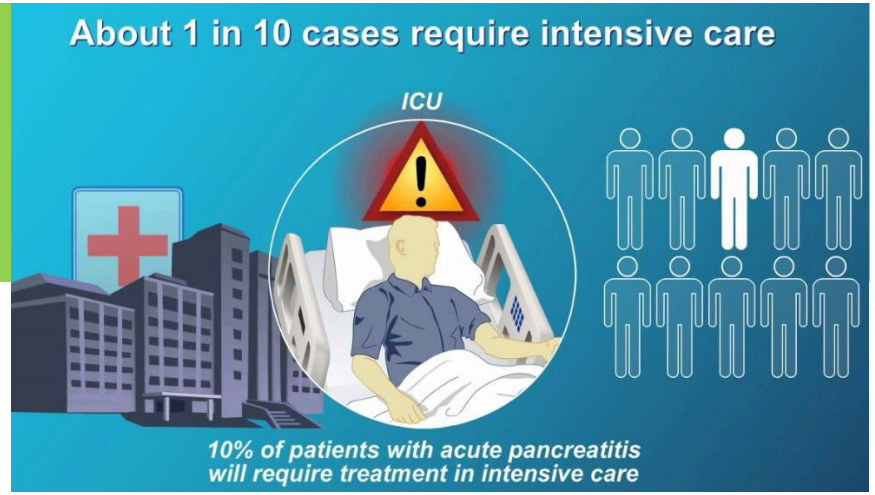
結論:CTA model consisted of clinical (i.e., APACHE-II and BISAP scores) and radiologic (i.e., Balthazar grade and EPIC score) scoring systems and may be useful for the early prediction of the severity of AP and identification of high-risk patients who require close surveillance.

Combination of clinical scores and radiological scores.

# III.治療與處置-1
# 13. 來院第一天立即給予 IV fluid therapy.

- **13. 立即給予 IV infusion. 每一小時 250 -500 ml 的 isotonic solution. 24 hours. (流量訂為 5-10ml/Kg BW/hour) Lactated Ringer's solution是最佳選擇.第一天的 fluid therapy 非常重要、如心血管或腎臟疾病時劑量要調節.**
- **14.在前兩天,每6小時評估一次Fluid replacement的需要性、並檢驗 BUN and Cr.**
- **請每天檢查, vital signs, CBC , BUN and Cr.**

# III.治療與處置-2
# 15.shock 病人之處置



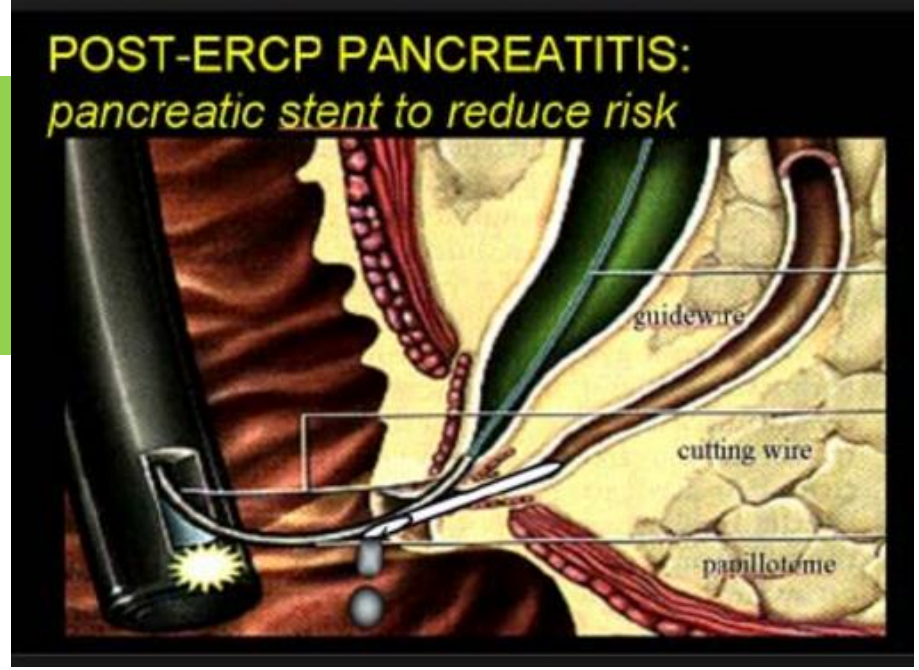

@@@ **15, Shock 病人必需給予 fluid** resuscitation達到

- **heart rate < 108/min.**
- **BP 到達 90 mm Hg.**
- **Urine volume > 30 ml/hour.之目標.**

Admitted to ICU

- Rainer Isenmann et al Shock and acute pancreatitis *Best Practice & Research Clinical Gastroenterology Volume 17, Issue 3, June 2003, Pages 345–355*
- **Haemorrhagic shock complicating acute pancreatitis**. Duszyńska W et al (Poland) Anestezjol Intens Ter. 2011 Jan-Mar;43(1):36-9. *in cases of severe haemorrhage, surgical packing and administration of recombinant factor VIIa concentrate are key components of successful treatment.*

# III.治療與處置-3
# 16, ERCP之應用




- **16, Acute pancreatitis 如同時有膽道疾病時,應在 24 hours 內執行 ERCP . 如只有 gall stone 而無 biliary obstruction 可不必作 ERCP.**

  **如無膽道炎或無黃疸可以 MRCP, 或 EUS代替,而不必作 ERCP.**

@@@

- **17. ERCP之後應使用 PANCREATIC STENTS或肛門內用NSAID 坐藥以預防發生POST-ERCP PANCREATITIS.**

**第六個常見的原因是 Post-ERCP pancreatitis**

## Prevention of Post-ERCP Pancreatitis (PEP)

*A metanalysis*
*52 studies, 12 RCTs, 6 fulfilled the criteria*

| Author | Year | Patients | Drug | CBD stones | PEP NSAID/controls |
|---|---|---|---|---|---|
| Khoshbaten | 2007 | 100 | Diclofenac | 51% | 2/13 |
| Cheon | 2007 | 207 | Diclofenas | 5.8% | 17/17 |
| Sotoudehmanesh | 2007 | 442 | Indomethacin | 51.2% | 7/15 |
| Montano Loza | 2007 | 150 | Indomethacin | NA | 13/28 |
| Montano Loza | 2006 | 116 | Indomethacin | NA | 12/19 |
| Murray | 2003 | 220 | Diclofenac | 38.5% | 7/17 |

Conclusions, comments: RR 0.46, NSAIDs protective in subgroup of ES and SOD. Mortality 0, severity not mentioned. Introduction into routine care is recommended.

Dai H-F, et al. Hepatobiliary Pancreas Dis Int 2009

# Risk Factors for Complications after ERCP

*A multivariate analysis, single, tertiary reference center, 1994-2006,*
*Antibiotic prophylaxis 53.6%, preventive pancreatic stent 9.2%,*
*Biliary manometry 11.5%, pancreatic manometry 13.1%,*
*Biliary sphincterotomy 30.0%, pancreatic sphincterotomy 13.7%*

| | |
|---|---|
| ERCP | 11,497 |
| Complications | 462 (4.0%) |
| Severe complications | 42 (0.36%) |
| Fatality | 7 (0.06%) |
| | |
| Pancreatitis | 298 (2.6%) |
| Severe | 17 (0.14%) |
| RR pancreatogram, major papilla | 1.7 |
| RR pancreatogram, minor papilla | 1.54 |
| RR SOD with pancreatic stent | 1.45 |
| RR SOD without pancreatic stent | 1.84 |

Comments: high rate (50%) of atb prophylaxis, manometry, pancreatic sphincterotomy, profile of endoscopists not given

# ESGE guidelines, 2014-1



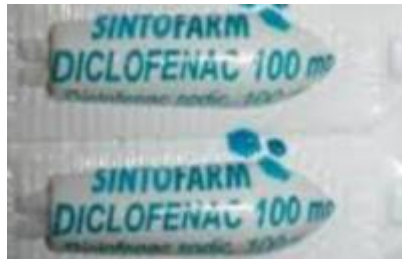
Clip slide

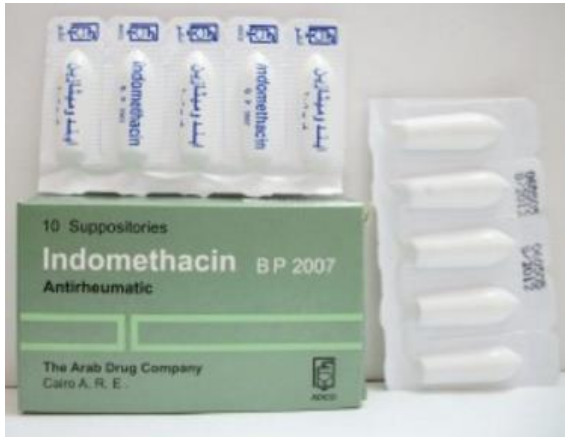
## Main recommendations:

1. ESGE recommends routine rectal administration of 100mg of diclofenac or indomethacin immediately before or after ERCP in all patients without contraindication.

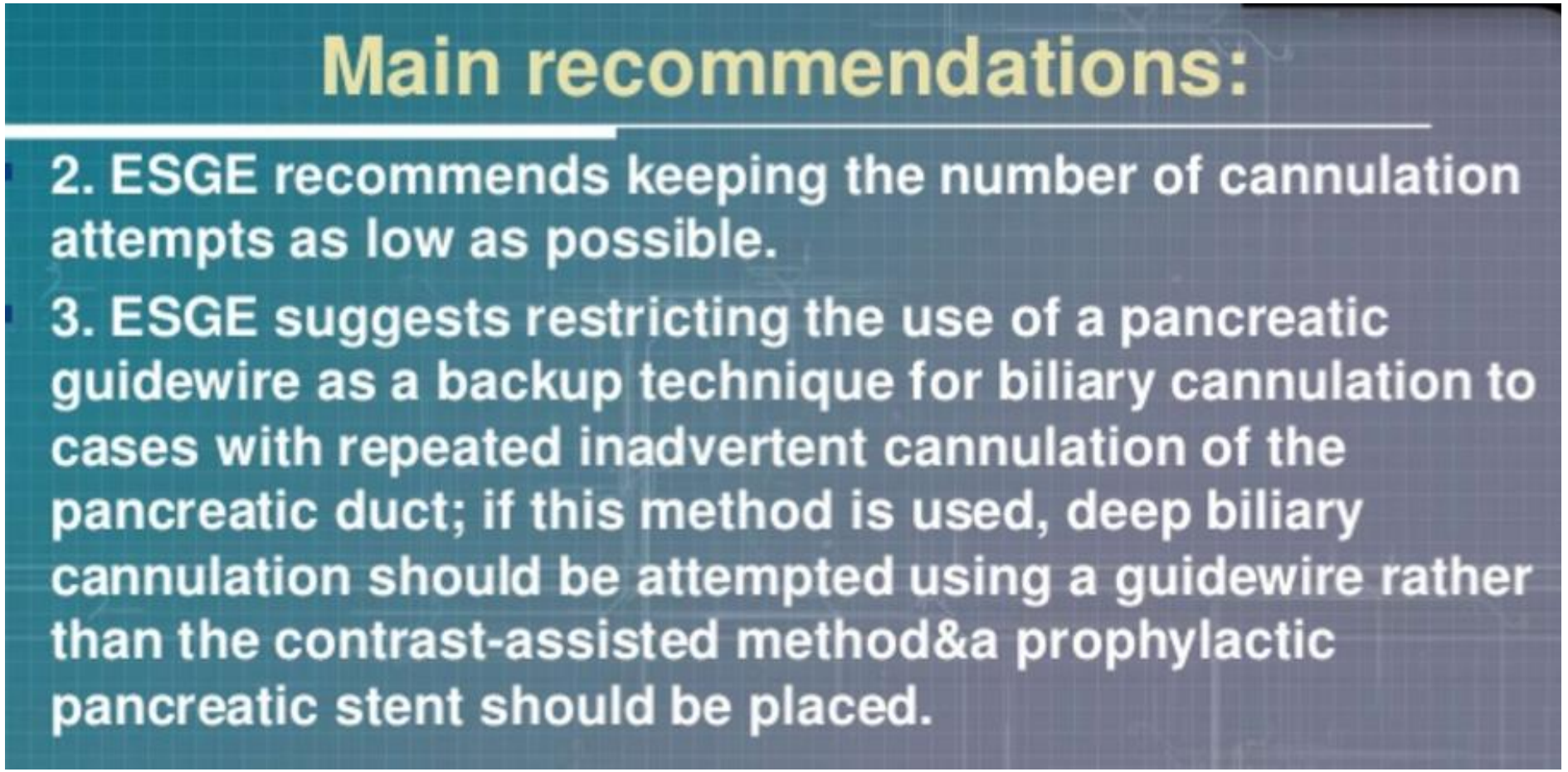
In addition to this, in the case of high risk for (PEP), the placement of a 5-Fr prophylactic pancreatic stent should be strongly considered.

Sublingually administered glyceryl trinitrate or 250 µg somatostatin given in bolus injection might be considered as an option in high risk cases if (NSAIDs) are contraindicated&if prophylactic pancreatic stenting is not possible or successful.

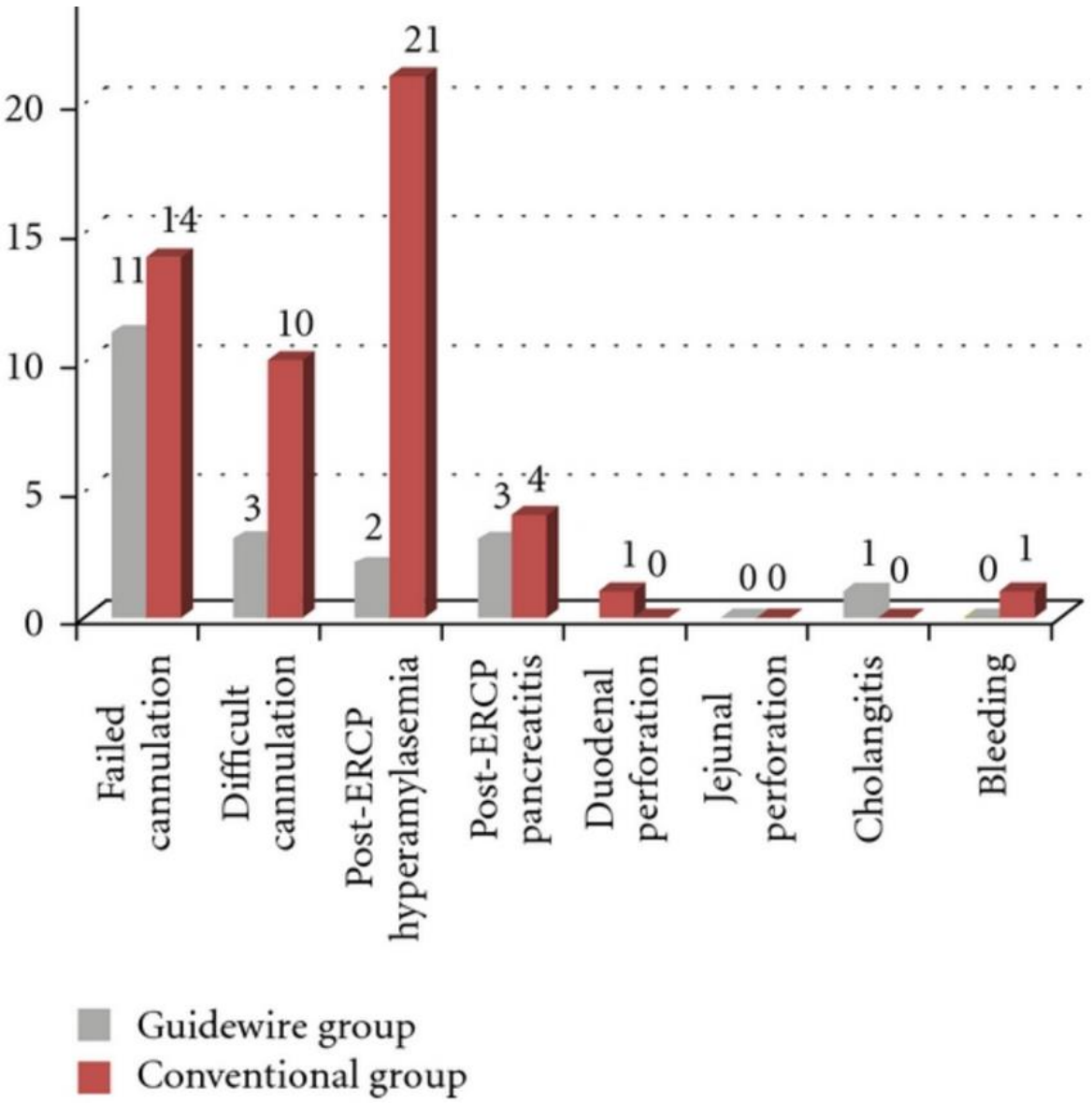
# ESGE guidelines-2



# III.治療與處置-3
# Guideline 18, ERCP cannulation 次數越少越好,

@@@ ERCP 的 cannulation 越少越少,原則上不超過3次、

- A difficult cannulation alone has been shown to carry an inherent risk for a post-ERCP complication[18-20]. Freeman et al. prospectively studied 1963 consecutive patients at 11 centres in the United States[19]. The risk of pancreatitis after a difficult cannulation compared with a standard cannulation increased from 4.3% to 11.3%. In a single-centre study involving 1223 patients, the risk of pancreatitis after a difficult cannulation was 14.9%, compared with a rate of 3.3% for a standard cannulation[20]. Possible reasons for the increased risk of pancreatitis may be excessive manipulation, resulting in mechanical trauma and oedema of the pancreatic sphincter,
- multi-centre study[23], a cannulation time exceeding 10 min, one or more pancreatic duct wire passes, and needle-knife precutting were risk factors for ERCP-related complication
- **Management of difficult bile duct cannulation in ERCP,** Marianne Udd, et al : World J Gastrointest Endosc. 2010 Mar 16; 2(3): 97–103. In a Chinese
- 19. Freeman ML, DiSario JA, Nelson DB, Fennerty MB, Lee JG, Bjorkman DJ, Overby CS, Aas J, Ryan ME, Bochna GS, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study.Gastrointest Endosc. 2001;54:425–434.
- 20. Vandervoort J, Soetikno RM, Tham TC, Wong RC, Ferrari AP, Jr , Montes H, Roston AD, Slivka A, Lichtenstein DR, et al. Risk factors for complications after performance of ERCP. Gastrointest Endosc.2002;56:652–656.




# Post ERCP pancreatitis. stents

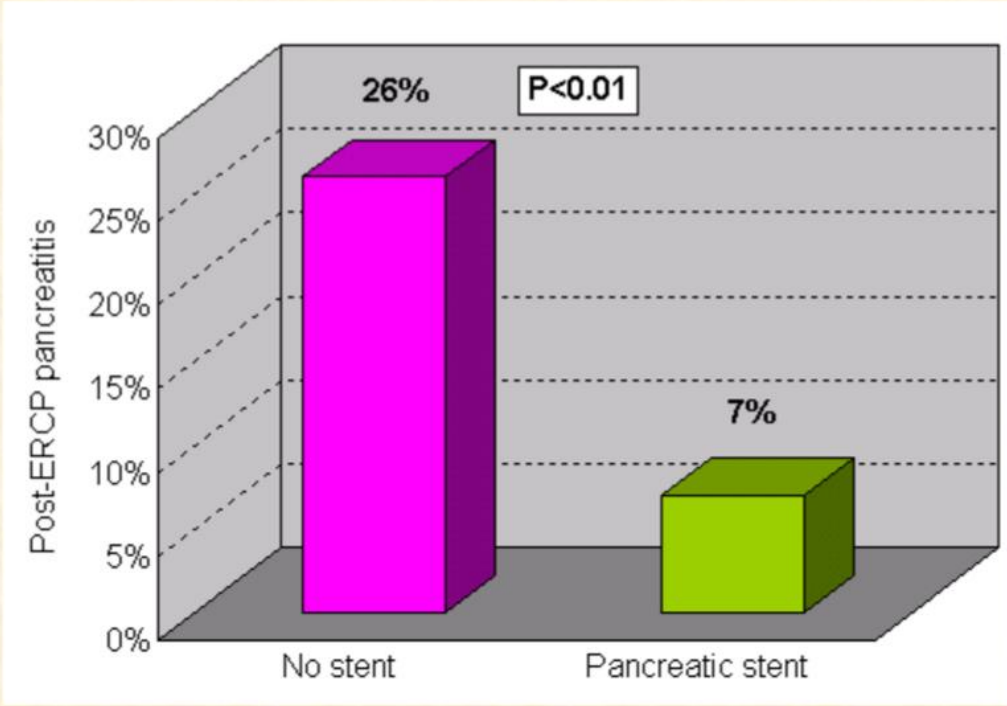



**Figure 3.** Post-ERCP pancreatitis: results of randomized controlled trial of pancreatic stenting to reduce risk of biliary sphincterotomy in patients with sphincter of Oddi dysfunction [53]. Eighty patients with pancreatic sphincter hypertension undergoing endoscopic biliary sphincterotomy randomized to short-term pancreatic stent versus no stent after sphincterotomy.

**Post-ERCP Pancreatitis: Patient and Technique-Related Risk Factors Martin L Freeman:** *JOP. J Pancreas (Online) 2002; 3(6):169-176.*

# III.治療與處置-4,
@@@ 19-21.抗生素之使用:除非証實有感染,不例行使用抗生素

- **19.** 如果有胰臟外之感染,如 **CHOLANGITIS,** 菌血菌,靜脈導管感染, 泌尿系感梁等、應使用抗生素、〔非針對胰臟炎〕.即使是嚴重之 **PNCREATITIS ,** 有明顯的 **NECROSIS,**也不例行使用抗生素.
- **20.**如果壞死組織有感染, 必須使用抗生素,可利用 **CT-**導引下抽吸物作細菌檢查或直接使用抗生素、.通常使用 **carbapenems, quinolones, and metronidazole,** 對壞死部分的感染方才有效,
- 21.一般而言,不必使用 抗真菌類之抗消炎藥 **(ANTIFUNGAL AGENTS)**

# Doripenem

- 醫療院所內金黃色葡萄球菌 (Staphylococcus aureus)對methicillin的抗藥性已經高達60%，腸球菌 (Enterococcus)與綠膿桿菌 (Pseudomonas aeruginosa)對vancomcyin與fluoroquinolone類藥物的抗藥性也達30%。另一個令人擔憂的抗藥性問題是會產生ESBL (extended-spectrum β-lactamase)的腸內菌屬，面對越來越嚴重的抗藥性問題，除了積極的感染管制措施外，很顯然的，我們需要新的抗生素。雖然有這樣的需求，但根據美國食品藥物管理局 (FDA)的資料，1998年到2002年之間，僅有七個新的抗生素上市，2003年到2007年之間僅有4個，2008年到2010年之間只剩下2個。**Doripenem是carbapenem類抗生素的新成員.**

- **Doripenem被核准用於治療複雜性腹腔內感染 (complicated intra-abdominal infections；cIAIs)**或治療複雜性泌尿道感染 (complicated urinary tract infection；cUTIs)，包括腎盂腎炎。其他核准外適應症包括院內肺炎 (hospital-acquired pneumonia；HAP)、呼吸器相關肺炎 (ventilator-associated pneumonia；VAP)，以及治療導管相關菌血症。
- Doripenem使用於腎功能正常病人的建議劑量為500 mg每八小時注射一次

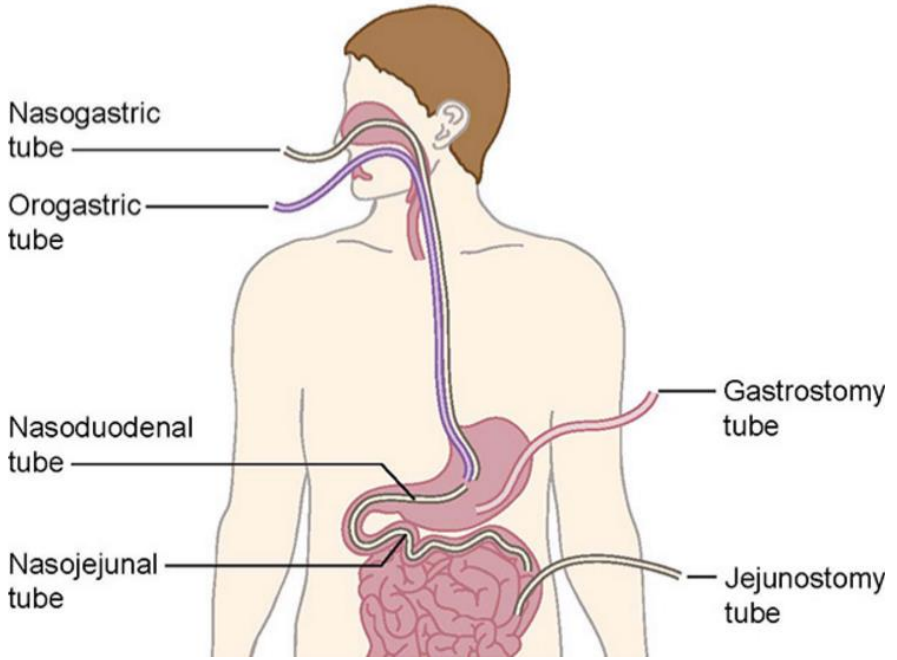

# III.治療與處置-5
# 22-24.飲食注意事項

- **22.** 收治後至少 **48 -72 HOURS** 內不可飲食**.**
- **(**輕症,只水腫**, EDEMATOUS PANCREATITIS,** 無明顯之消化道症狀,停止飲食 **48 HOURS,** 重症者,有壞死性胰臟炎**, NECROTIZING PANCREATITIS,** 及有明顯之消化道症狀,停止飲食 **72 HOURS**以上**)**
- **23**輕症病人開始飲食以溫熱白開水為宜每**2**小時 **200ML. , 6**小時後可改以溫熱之葡萄糖水,每**2**小時 **200ML. ,**進食 **12 HOURS** 後 即詢問有無胃部不適**,** 檢驗 **AMYLASE, LIPASE, CRP** 等項、確定無再發後再增加飲食內容**,** 給予米湯、稀飯及無脂肪之飲食,並在進食 **48 hours** 後方可達一日熱量 **600 k Cal.**
- **24.**進食量增加**(> 600 K Cal.)24 hours** 之後**,** 再一欠檢驗有無胰臟炎再發之現象。確定無再發後再徐徐增加醣類及蛋白質量,、至每日熱量達 1200 k Cal. 進食**5**天,才可以略增脂肪之含量 每日 **5-10 gm .** 以內**,** 兩週後脂肪可增至 **20 gm.** 仍維持低脂肪之飲食至少**2**個月**,** 肪肪之攝取量必需低於 **30 gm./day.**

# III.治療與處置-6
# 25, TPN 是禁食時間之營養方式,之後再改管餵

- **25.** 重症病人不能飲食者,宜執行 **TPN. TPN**三天之後也可考慮 少量之**enteral nutrition.** 食物中仍以醣類為主、部分為蛋白,不要脂肪, **TPN** 七天之後才可以完全換為 **enteral nutrition. Fat** 含量仍以 **20 gm /day** 為限,

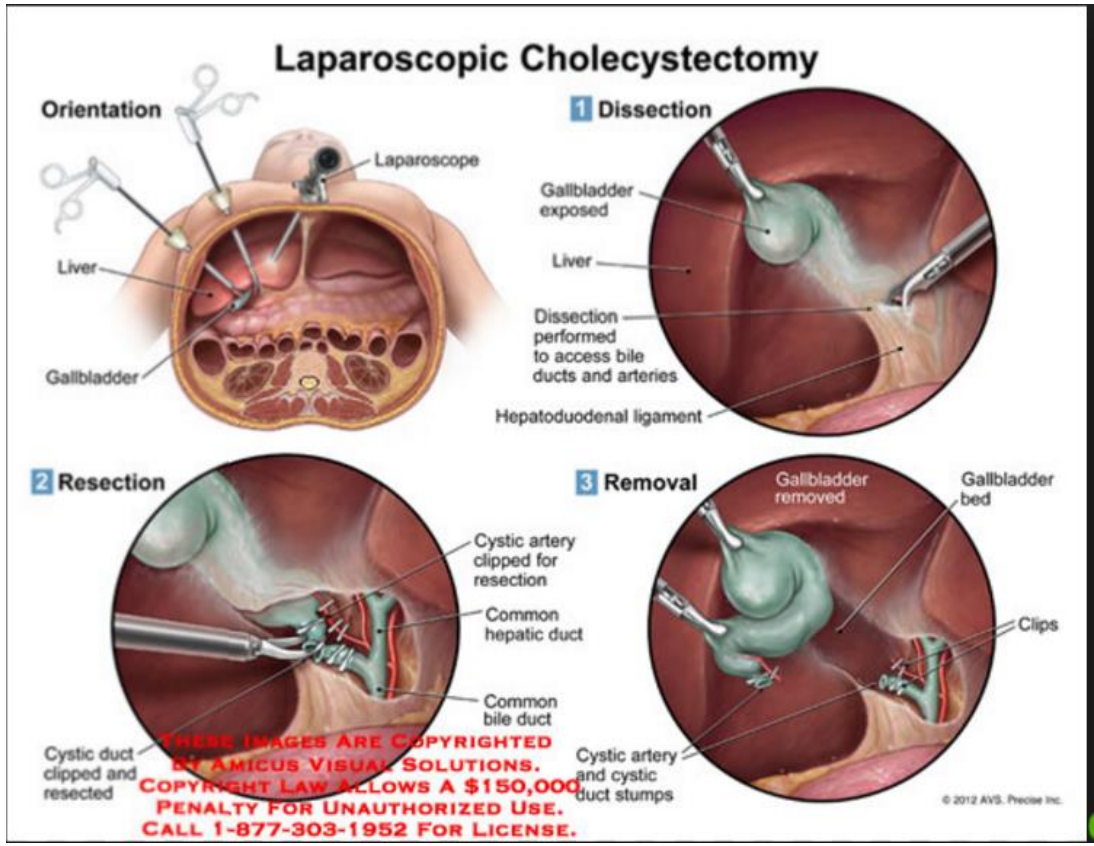
- **Enteral nutrition:** A way to provide food through a tube placed in the nose, the stomach, or the small intestine. 又稱 tube feeding.



# III.治療與處置-7
# 26-27, 有膽結石症之處理

@@@

- 26. **Acute pancreatitis 的病人如果膽囊內有 gallstones應在出院前施行 laparoscopic cholecystectomy.**
- **已作乳頭切開之病人也必需施行**
- **laparoscopic cholecystectomy.**
- 如有 **peripancreatic fluid**
- **collections應延後手術至少等水吸**
- 收之後,大約是發病之六週之後.

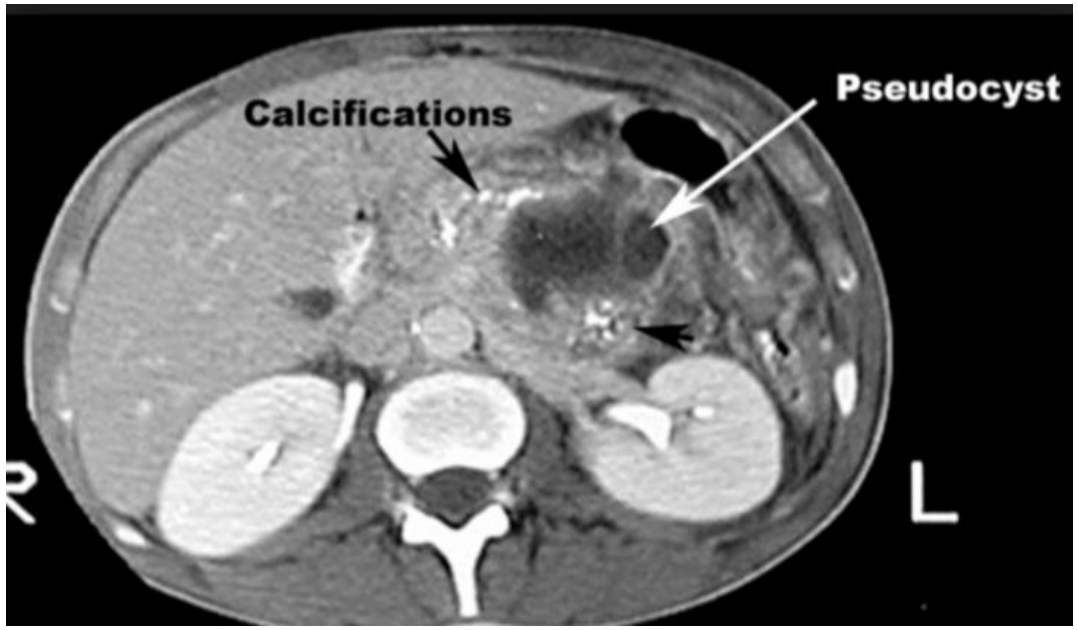


# III.治療與處置-8
# 27.膽道感染時, 延後施行手術

- **27. 如果 acute pancreatitis 併發 biliary tract infection 或有 chronic cholecystitis 在發炎消退,及病情穩定之後施行 laparoscopic cholecystectomy,**

# III.治療與處置-9
# 28. 無症狀(not infected)之 pseudocyst 可不處理, 不必手術、長期追踪

- 28, **Acute pancreatitis**之後發現有
- **pseudocyst**形成, 但無症狀,可
- 以不予手術, 長期追踪即可.




- Pancreatic pseudocysts are best defined as **localized fluid collections** that are rich in amylase and other pancreatic enzymes, that have a **nonepithelialized wall consisting of fibrous and granulation tissue,** and that usually appear several weeks after the onset of pancreatitis. They are to be distinguished from acute fluid collections, organized necrosis, and abscesses.

# Incidence of pseudocyst : 5-7 %

- **Pancreatic pseudocyst:** Samir Habashi, Peter V Draganov, World J Gastroenterol 2009 January 7; 15(1): 38-47.
- The management varies based on local expertise, but in general, endoscopic drainage is becoming the preferred approach because it is less invasive than surgery, avoids the need for external drain, and has a high long-term success rate. A tailored therapeutic approach taking into consideration patient preferences and involving multidisciplinary team of therapeutic endoscopist, interventional radiologist and pancreatic surgeon should be considered in all cases.

**1988: 5 %**

**2009 : 7 %**

- In a study by Imrie, pseudocysts developed after emergency hospital admission for an episode of acute pancreatitis in 86 patients[11]. Sixty-two of the 86 pseudocysts consequent to acute pancreatitis were derived from the local hospital population area, in which 879 patients with acute pancreatitis were admitted to hospital during the same time period. This resulted in **a 7%** overall incidence of pseudocysts as a complication of acute pancreatitis[11].
- ***Imrie CW**, Buist LJ, Shearer MG. Importance of cause in the outcome of pancreatic pseudocysts. Am J Surg 1988; **156**:159-162*
- In a series of 926 patients with non-alcoholic acute pancreatitis, fluid collections were observed in 83 (9%). At the end of 6 wk, 48 (**5**%) still had a fluid collection consistent with a pseudocyst
- ***Maringhini A**, et al Pseudocysts in acute nonalcoholic pancreatitis: incidence and natural history. Dig Dis Sci 1999;**44**: 1669-1673*

# Natural history of pancreatic pseudocysts.

- **Pseudocysts in acute nonalcoholic pancreatitis: incidence and natural history.** Maringhini A et al : Dig Dis Sci. 1999 Aug;44(8):1669-73.
- pancreatic fluid collections from 83 patients (8.9%): 48 of whom developed pseudocysts (5.1%). Both were less frequent after biliary pancreatitis (P < 0.0001). **In the first 60 days** of follow-up, patients with fluid collections or pseudocysts showed more complications than spontaneous disappearance; two of them died. **After the 60th day**, spontaneous disappearance was more frequent, and

  **at one yea**r the cumulative incidence of complications and spontaneous

  disappearance was 36% and 56%, respectively.

  A total of 33 patients with fluid collection needed interventional treatment (surgery or

  percutaneous or endoscopic drainage).

  **Pseudocysts that were small (<5 cm) or developed in the tail had a higher incidence of**

  **spontaneous disappearance: 22/24 (91.7%) and 11/12 (91.7%),** respectively.

In conclusion, fluid collections and pseudocysts after non-alcoholic pancreatitis have a low incidence of complications and mortality with a high rate of spontaneous disappearance. We suggest treating them only after complications.

# Pancreatic pseudocyst.

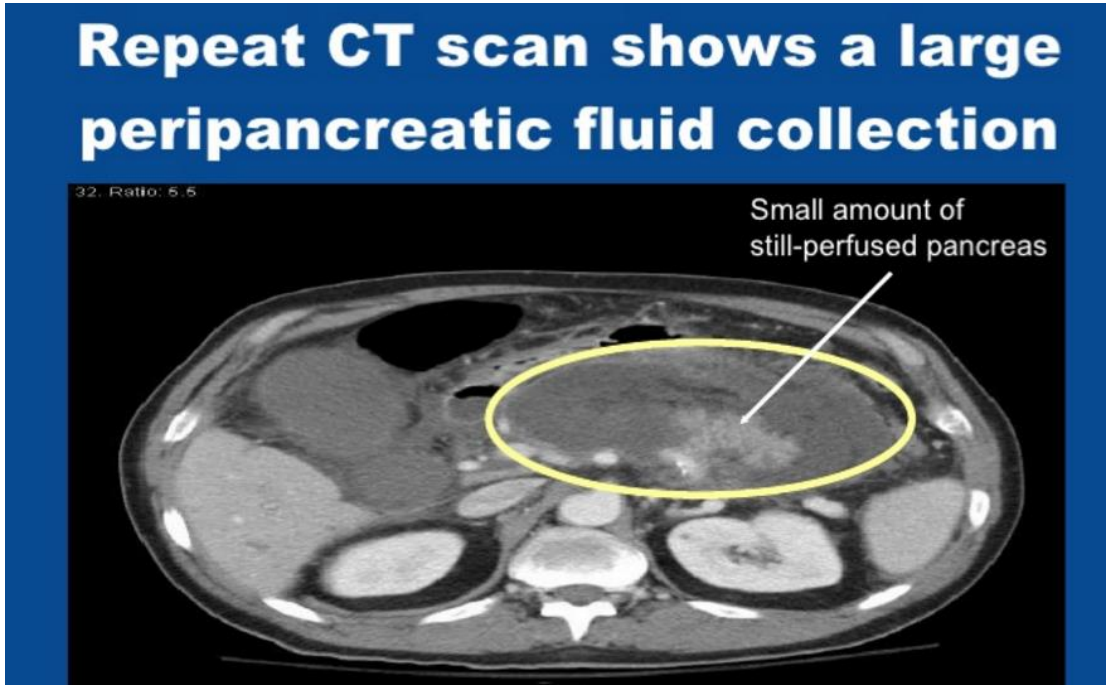
- **Endoscopic and Endosonographic Management of Pancreatic Pseudocyst: a Long-Term Follow-Up . M. Dohmoto, K.Akiyama,Y.Iioka. Rev. gastroenterol. Perú v.23 n.4 Lima oct./dic. 2003.**
- Between 1987 and 2002, 47 patients had been treated for panceatic pseudocysts by transmural or transductal drainage EUS-guided drainage of a pancreatic pseudocyst or pancreatc abscess was carried out in 5 cases.
- In 42 patients pancreatic pseudocysts disappeared completely. Six patients suffered a relapse 7 to 38 months after removal of the drainage. No more recurrences were observed in 22 patients within followed up 5-11 years.
- Advantages of the endoscopic drainage are minimal invasiveness, short period of hospitalization and low costs. These aspects make the endoscopic therapy the first choice of treatment of pancreatic pseudocysts.
- **Percutaneous drainage has a high relapse tendency of 30 to 57 % and pancreaticocutaneous fistulas occur in 40 %.**

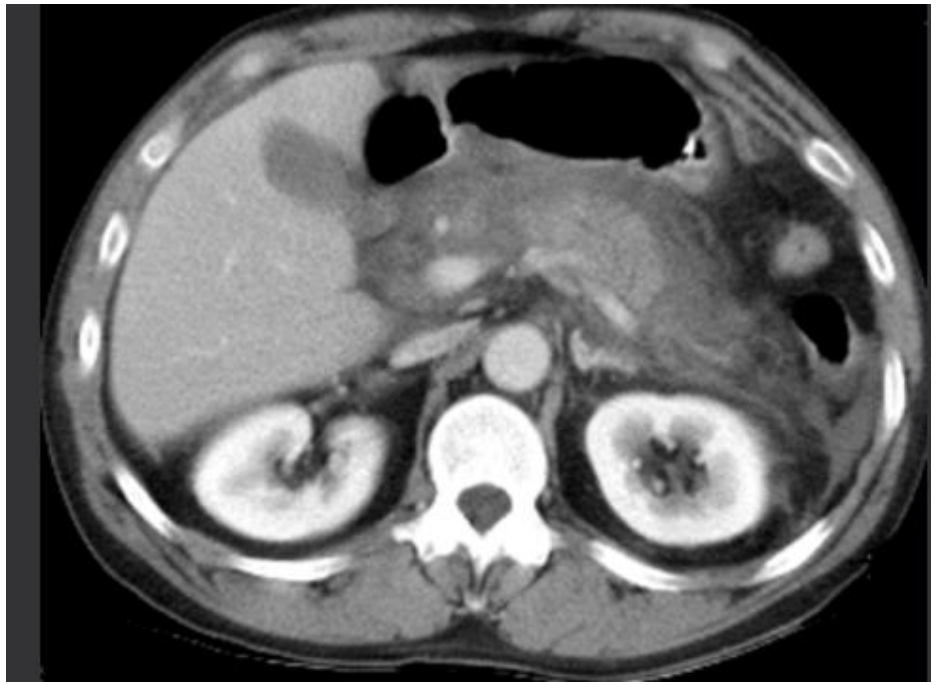
# Drainage options:

- Drainage options are as follows:
- Percutaneous catheter drainage – The procedure of choice for infected pseudocysts; although recurrence and failure rates are high, it may be a good temporizing measure
- Endoscopic drainage, either transpapillary (via ERCP) or transmural – The complication rate appears to decrease and efficacy to increase with experience
- **Surgical drainage** – The criterion standard; internal drainage is the procedure of choice, but laparoscopic drainage has yielded good results in some cases

# III.治療與處置-10
# 29. peripancreatic fluid 不要經皮抽取

- **29.** 即使 **CT** 証明有 **peripancreatic fluid** 也不要經皮抽取,
  只需以臨床常用之評估方法**(Fever, CRP and WBC** 等發炎指數**)** 追踪. 確定**Fever, CRP and WBC** 等發炎指數高, 壞死有感染之跡象. 方給以治療.



# III.治療與處置-11
# 30. 發病4週之後方才考慮胰之引流

- 30, **Acute pancreatitis, necrotizing ,** 有 感染事實, 但胰臟炎已穩定者要在發病**4**週之後，組織充分液化並在壞死組織形成纖維化的週壁後才執行引流. **(**引流可用內視鏡或手術之方式**)**

  引流物必每日或每次敘述量,外觀, **cell counts.** 並送細菌培養及抹片 檢查

# III.治療與處置-12
# 31, 必需照會外科之情況

如果 **acute pancreatitis**有以下各種情形即需照會外科：

**1.gall stone pancreatitis** 要作 **cholecystectomy.**

- 2. 四週之後, 仍有甚多之 peripancreatic fluid, 併發
- fever(38 degree C) leukocytosis, high CRP等、即有
- infection之現象.→drainage/necrosectomy
- 3. 出血 shock, 無法控制.
- 4. Perforation of hollow viscus, 因
- 胰臟酵素導致組織壞死.
- 5. 必須作引流之狀況
- 6. **病情惡化並合併器官衰竭**
- 7. Abscess : surgical debridement and drainage
- 8. 其他

- **Indications for surgery in severe acute pancreatitis.**
- McFadden DW[1], Reber HA. (US) *Int J Pancreatol. 1994 Apr;15(2):83-90.*
- 1. For differential diagnosis, when the surgeon is concerned that the symptoms are the result of a disease other than pancreatitis for which operation is mandatory;
- 2. In persistent and severe biliary pancreatitis, when an obstructing gallstone that cannot be managed endoscopically is lodged at the ampulla of Vater;
- 3. In the presence of infected pancreatic necrosis; and
- 4. To drain a pancreatic abscess, if percutaneous drainage does not produce the desired result. Other indications that are less well defined and somewhat controversial are:
- 1. The presence of sterile pancreatic necrosis involving 50% or more of the pancreas;
- 2. When the pancreatitis persists in spite of maximal medical therapy; and
- 3. When the patient's condition deteriorates, often with the failure of one or more organ systems.

# Surgery of Acute pancreatitis

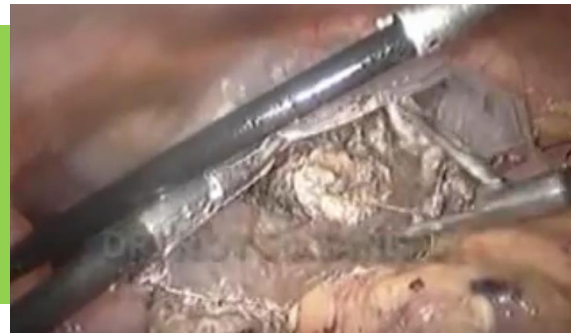
- **Management of acute pancreatitis: from surgery to interventional intensive care. J. Werner yet al (Germany), Gut, 2005:54:426-436**
- Recent technical improvements in interventional therapy and minimally invasive surgery, even infected pancreatic necrosis has successfully been treated in selected patients. However, technical feasibility does not obviate sound clinical judgement. We must be cautious in the application of new technologies in the absence of well designed clinical trials. Thus minimally invasive surgery and interventional therapy for infected necrosis should be limited to clinical trials and specific **indications in patients who are critically ill** and otherwise unfit for conventional surgery.

**Table 1**

Indications for surgical treatment of acute necrotising pancreatitis

| |
|---|
| (1) Infected pancreatic necrosis |
| (2) Sterile pancreatic necrosis: |
| (a) persistent necrotising pancreatitis |
| (b) “fulminant acute pancreatitis” |
| (3) Complications of acute pancreatitis: |
| For example, bowel perforation, bleeding |

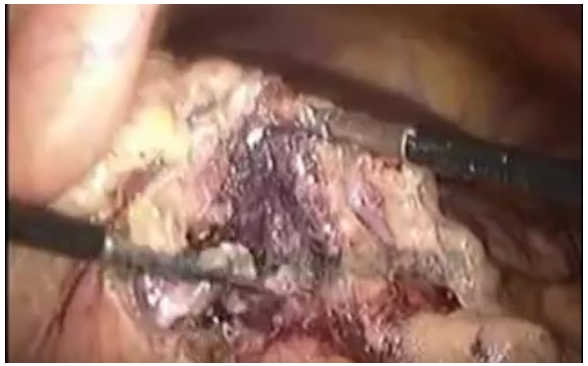
# III.治療與處置-12
# 32.手術以侵襲性小之模式為原則

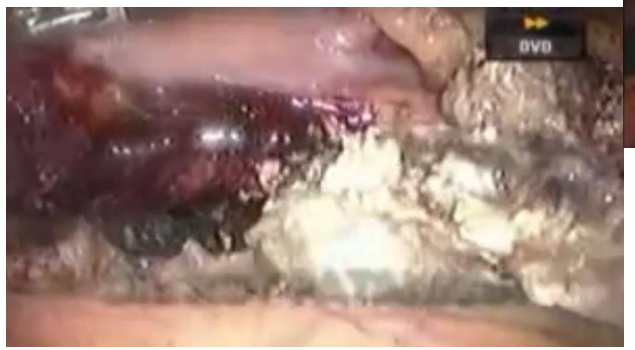


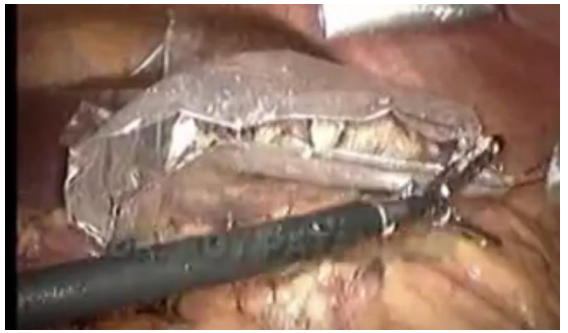
- **Acute pancreatitis, necrotizing ,** 有 感染事實, 但胰臟炎仍未達穩定,即仍有症狀時, 應考慮以最小的侵襲手術模式作 **necrosectomy, (minimal invasive necrosectomy)**

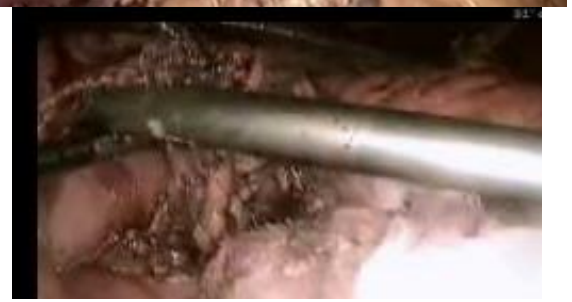
  不採行 **open necrosectomy**

- necrosectomy
  壞死組織切除術







# III.治療與處置-14
# 33-34.Disconnected duct syndrome要手術

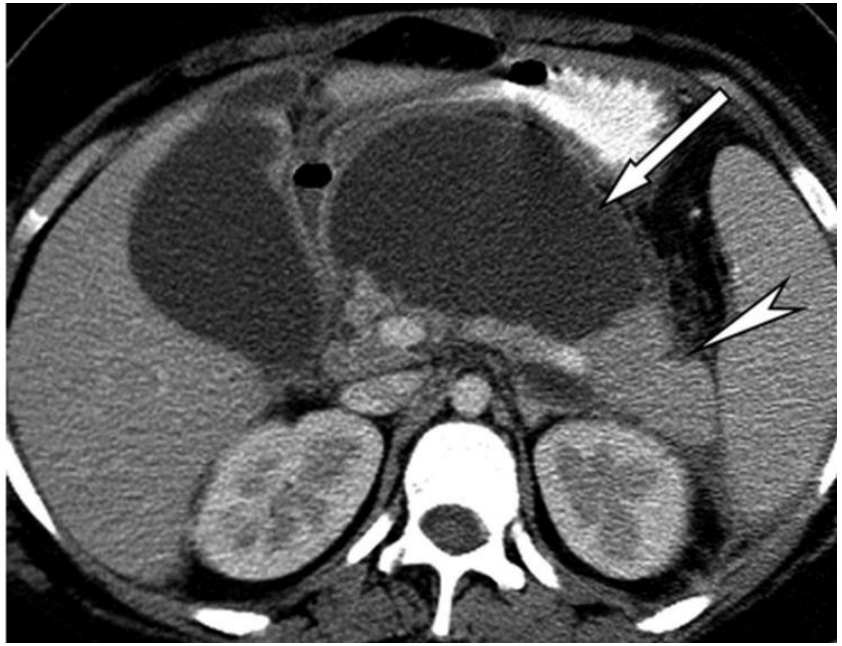
- **33,** 只有在發生胃.腸阻塞明顯之症狀, 在發病之後四~八週方作手術,排除阻塞.
- **34.** 胰臟管之外分泌系統中
- 斷 **(disconnected duct**
- **syndrome)**持續有症狀,
- 只要 無明顯之感染可
- 在**8**週之後 方作手術介
- 入處理、

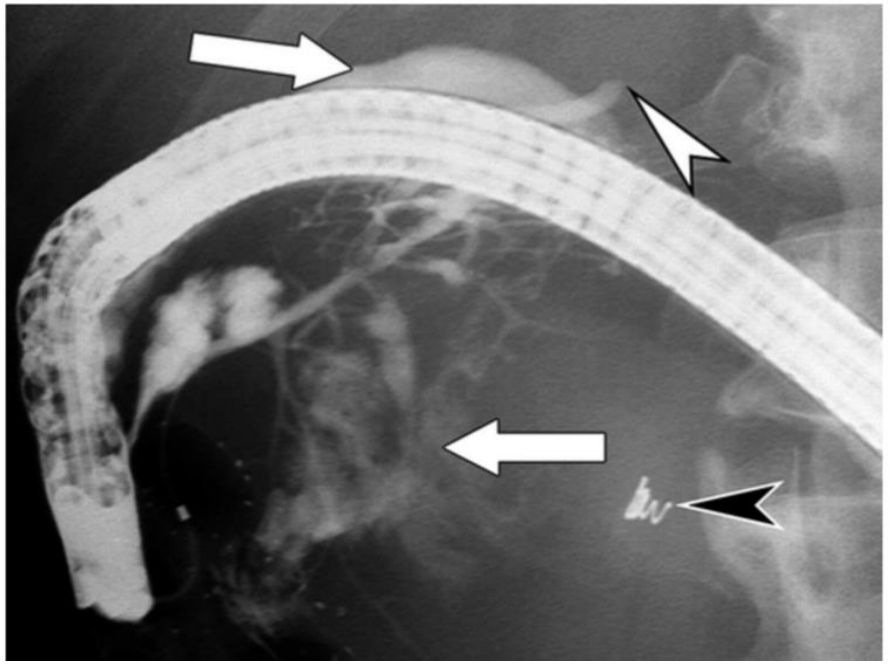
- **Disconnected pancreatic duct syndrome: imaging findings and therapeutic implications in 26 surgically corrected patients.**
- Tann M et al (US) J Comput Assist Tomogr. 2003 Jul-Aug;27(4):577-82.
- 26 consecutive patients
- ERCP showed ductal obstruction at the level of the intrapancreatic fluid collection in all patients with extravasation of contrast in 14 (54%). All patients were treated by operation: **15 (58%) by internal drainage into a Roux-en-Y limb of jejunum and 11 (42%) by distal pancreatic resectio**n. No prior CT interpretation correctly identified DPDS. **The average delay between symptom onset and definitive diagnosis was 9.3 months** (range, 3-36 months).

# Disconnection of the Pancreatic Duct常被忽略

- **Disconnection of the Pancreatic Duct: An Important But Overlooked Complication of Severe Acute Pancreatitis. Kumaresan Sandrasegaran et al (US) Rdaiograohics :**
- **September-October 2007** Volume 27, Issue 5

- Acute disconnection of the pancreatic duct in a 62-year-old man with prior episodes of alcoholic pancreatitis.
- **(a)** Axial CT image shows a 7-cm-diameter fluid collection occupying the pancreatic head and neck (arrow). The collection is confined within the capsule of the gland with no enhancing tissue in the neck. The duct in the viable pancreatic body is dilated (arrowhead).
- **(b)** Image from endoscopic retrograde cholangiopancreatography (ERCP) shows extravasation of injected contrast material (arrows). The main pancreatic duct is abruptly cut off (white arrowhead). Note the embolization coils (black arrowhead) in a pseudoaneurysm of the inferior pancreaticoduodenal artery. Disconnected pancreatic duct was diagnosed, and the patient underwent median segment pancreaticojejunostomy.





# IV.出院依據-1
# 35.Acute pancreatitis
# 依據以下原則出院

**35. 輕症病人五天以後符合以下Ia各點可以出院, 重症病人住院至少 10 天,也必需符合以下Ia 及Ib各點方可出院**

- **Ia :**

  **(1) 症狀完全消失,並已進食 48 hours , 且無任何不適, amylase/lipase, WBC 均正常.**
- **(2) 連續三次之 CRP 均持續下降出**
- **院前已降至 1.6 以下 (2x normal**
- **upper limit.)**
- **(3) 已跟病人說明致病原因, 並指導**
- **避免再發之方法.包括戒酒指導,**
- **hyperlipidemia之治療及飲食指導.**
- **及有膽結石症者及早施行 laparoscopic**
- **cholecystectomy.**

@@@

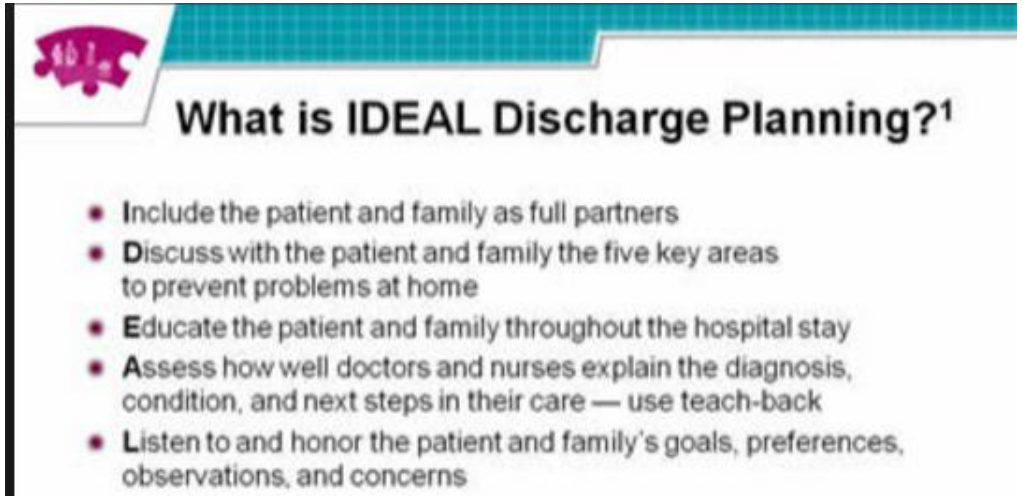
- **Ib. 重症病人、或有合併症/器官衰竭事實者**
- **(1)器官衰竭/各種合併症均已控制,治療,手術**
- **改善之後至少一星期, Fever, 退燒一週, shock 治**
- **好 vital signs 穩定一週,Consciousness 恢復,**
- **peritoneal signs, (-), 尿流正常**
- **(2) BUN, Cr.在正常上限之一倍半以內(BUN < 30,**
- **CR. <1.8)**
- **(3) Amylase < 100, Lipase < 50,**
- **(4) CRP< 2.0 WBC: and neutrophilia 正常**
- **(5) Electrolytes 正常**
- **(6) Lipid profile : 正常**
- **(7) DM 病人控制妥當**
- **(8) Serum bilirubin :direct bilirubin : 0.6 mg/dl 以**
- **下 total bilirubin在 2.0 mg/dl 以下,**

# Risk factors related to progression from MAP→WORSENING(normal :3.9-6.1 m Mol/dl)

- **Risk Factors for Worsening of Acute Pancreatitis in Patients Admitted with Mild Acute Pancreatitis.** Jin Z[1,2] et al (南方醫大, China) : Med Sci Monit. 2017 Feb 26;23:1026-1032.
- from March 2013 to May 2016 were included and prospectively evaluated
- 1. A total of 602 patients admitted with MAP were recruited into this study (256 men and 346 women). Seventy-four patients (12.3%) developed MSAP or SAP.
- 2. 5 significant differences between patients who developed MSAP or SAP and those who did not: **VFA (>100 $cm^2$) (p=0.003), BMI (≥25 $kg/m^2$) (p=0.001), Ranson score(p=0.004), APACHE-II (≥5) (p=0.001), and blood glucose level on admission (>11.1 mmol/L) (p=0.040).** Further multivariate logistic regression analyses revealed that **BMI (≥25 $kg/m^2$) (p=0.005), APACHE-II (≥5) (p=0.001), and blood glucose level on admission (>11.1 mmol/L) (p=0.004) were independent risk factors for developing MSAP or SAP in patients** admitted with MAP.
- 3. a mortality rate of 5.4%.
- CONCLUSIONS Significant risk factors for developing MSAP or SAP in patients admitted with MAP included BMI (≥25 $kg/m^2$), APACHE-II (≥5), and blood glucose level on admission (>11.1 mmol/L). These factors should be used in the prediction of more severe pancreatitis in patients admitted with MAP.(**11.1x18=200 mg/dl**)

# IV.出院依據-2,
# 36.安排在一週內回診

- 36.安排在一週內回診,請預約門診 並在 **3-5** 天內檢查 **CBC, amylase, lipase, CRP, LFT(GOT, GPT, GGT, serum bilirubin, total and conjugate, )TG, and Ca.** 以備評估再發狀況.


# IV.出院依據-3
# 37-38.出院之後

- **37.** 在出院後繼續服用胰臟酵
- 素至少三個月、之後依胰臟
- 功能及臨床需要決定是否繼
- 續.
- **38.** 定期門診,至少每 **1-2** 個月
- 一次、包括至少一年有一
- 次營養師之門診, 並提醒病
- 人避免再發,如有衛教班(戒
- 酒)至少每半年參加一次.



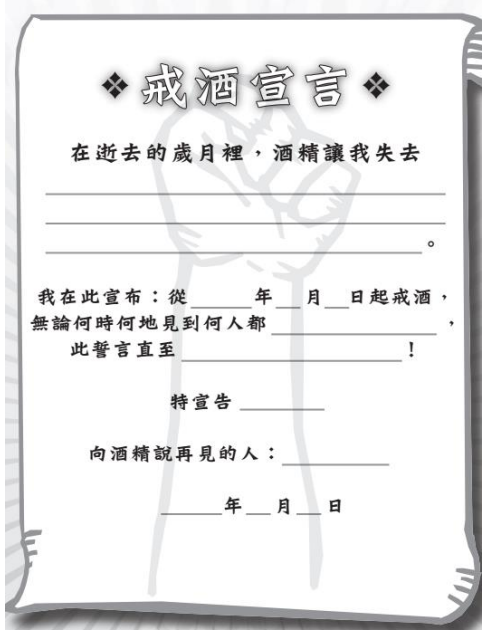
- Best to take pancreatic enzymes at the start of a meal.
- Pancreatic enzymes can reduce the **absorption of folic acid**.
- Taking pancreatic enzymes with acidic foods or fruit juices can deter their efficacy.
- **Wait a couple hours after taking digestive enzymes before taking an antacid,** since acid neutralizers may interfere with the activity of certain enzyme supplements.

# IV.出院依據-4
# 39.請病人不再飲酒

- 39.請病人不再飲酒,方可避免酒精性胰臟炎復發.醫院應成立戒酒小組,協助病人戒酒.
- 

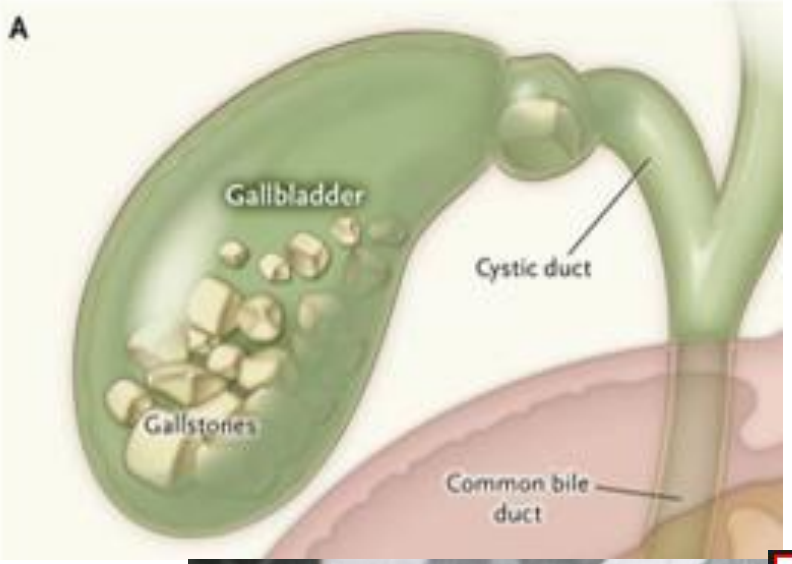

- Since alcohol is one of the main causes of the condition **it is absolutely essential to eliminate alcohol from your diet, i**n case you suspect you are suffering from pancreatitis. There are some people who believe that drinking a small amount of red wine can actually be beneficial to pancreatitis patients. However, there is no clinical evidence to back such claims up. In fact, most doctors advise patients to refrain from drinking after acute pancreatitis too. For best results, avoid drinking alcohol completely for a couple of months after suffering from acute pancreatitis, even if the condition was not caused by alcohol consumption.

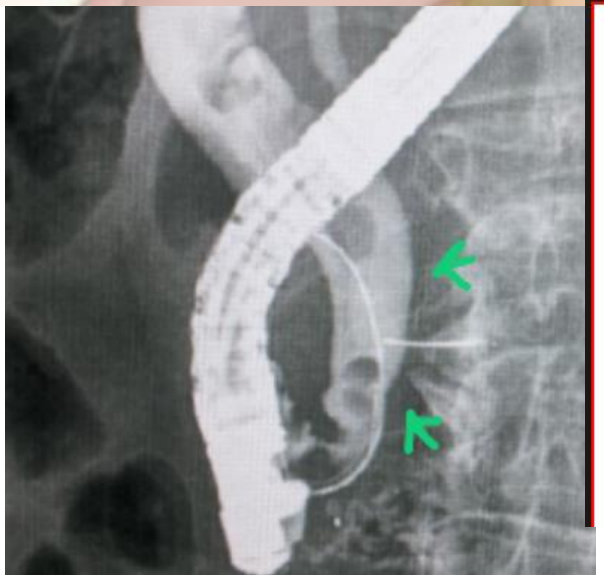
# 1. 戒酒要有恆心,別找理由喝酒

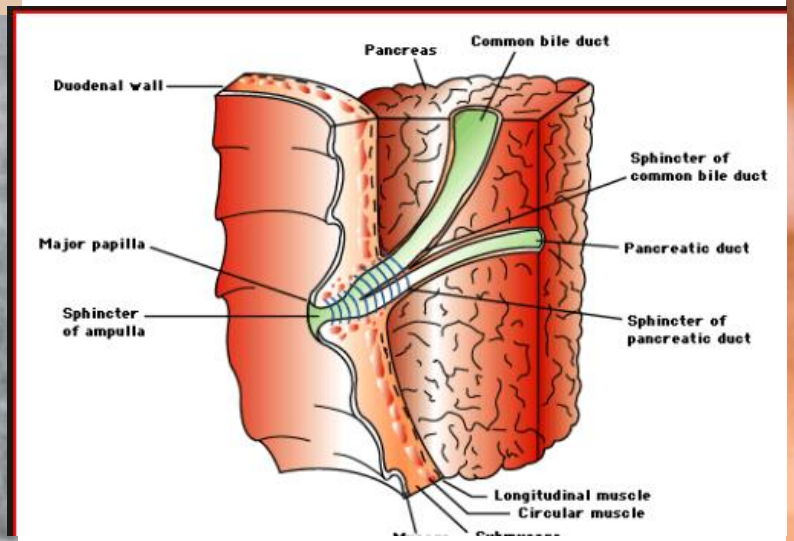


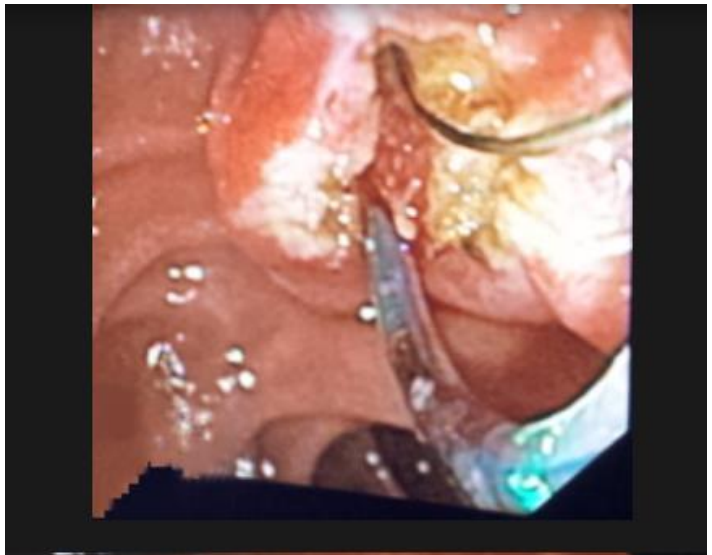


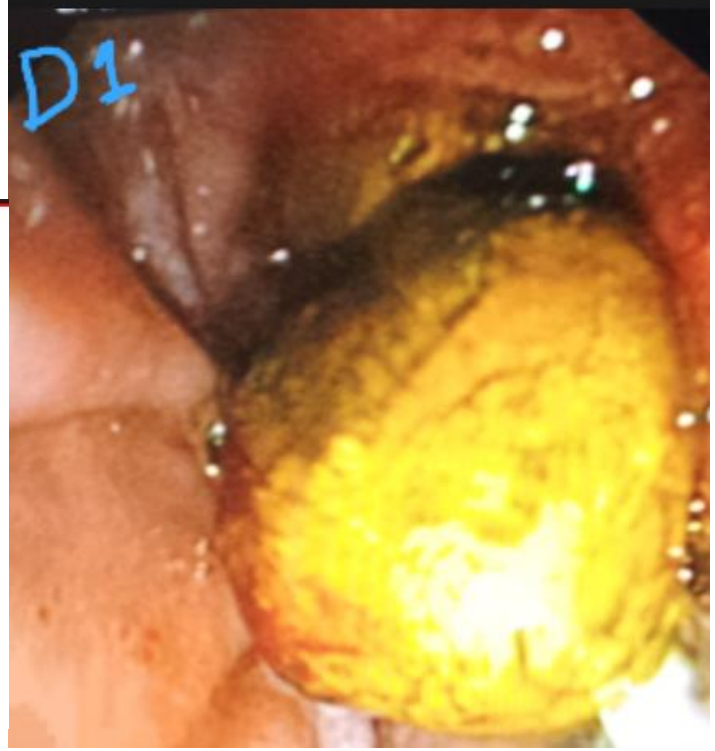
# 2. ERCP + papillotomy for stones impacted at the papilla







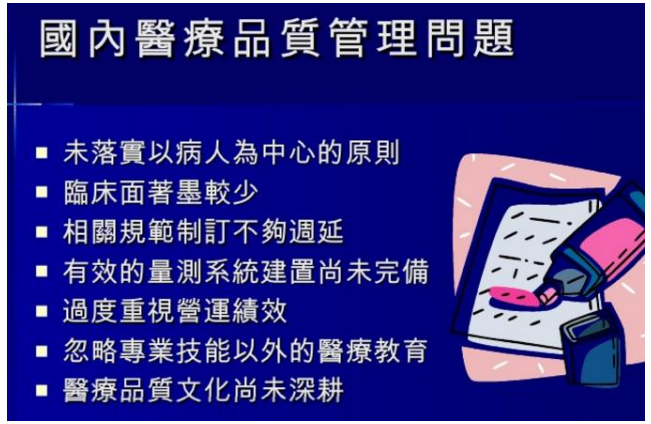
# 2: Laparoscopic cholecystectomy

- Better--- during hospitalization  for acute pancreatitis,
- Or : within 2 weeks after discharge.

# 3. Treatment of hyperlipidemia

- Using Special sheet— Post-discharge reminders
- 提醒照顧者及家人作好home care.

# 結語(2024.02.01. TCHL)




- Acute pancreatitis 是 常見疾病,急性腹痛重要原因.
- 其診斷並不困難,.**原因需要認真搜查及確定**。
- 及時治療死之率低.
- 遵守臨床規範,即可提高醫療品質.
- 仔細參閱臨床規範、注意細節,病人可以照顧得更好、
- Acute pancreatitis 務必查出原因、並作治療,可免再發。原則上有gall stones應及早切除。

# 重點提示

- 1. 診斷依據  abdominal pain better on bending, serum amylase>500
- /lipase >200
- 2.Etiology, usually by history taking (alcohol, gall stone and lab
- findings(LFT, GGT. TG)
- 3.Severity:symptoms >3 days, necrotizing ,(Ca low, abdominal CT,
- Pleural effusion, BUN and CR, vital signs.)
- 4. Disease activity parameters (CRP, amylase, lipase, bowel sound,
- epigastralgia, peritoneal signs)
- **Discharge decision** : symptoms remission, CRP : down to 2.
- No pain on oral intake for 3 days. Amylase and lipase : normal,
- WBC: normal , Bilirubin < 2.0,  GGT < 100.