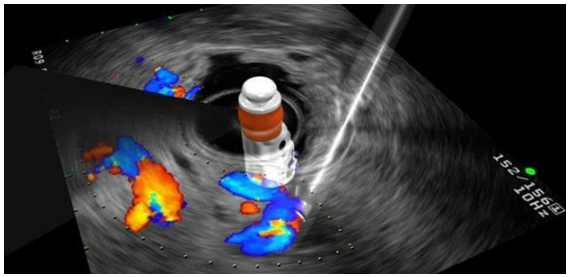
MACMURRAY GASTROENTEROLOGY

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND

COUNTIES MANUKAU DISTRICT HEALTH BOARD
A Community Partnership

Pancreatic Disease
GP Update 2011



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8.11.2011

Macmurray CME

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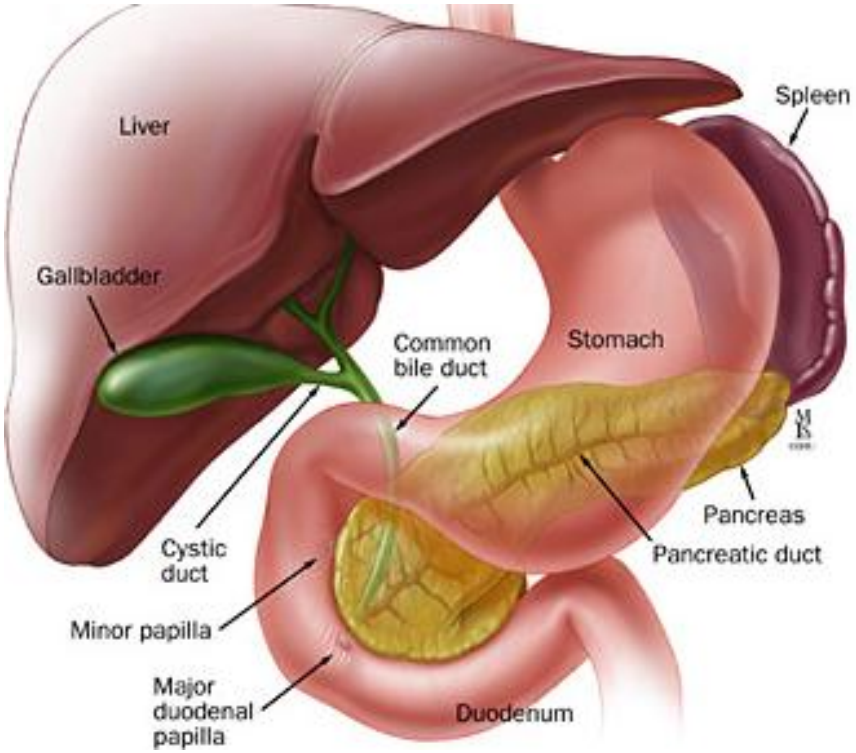
Te Whare Wānanga o Otāgo
NEW ZEALAND

Outline

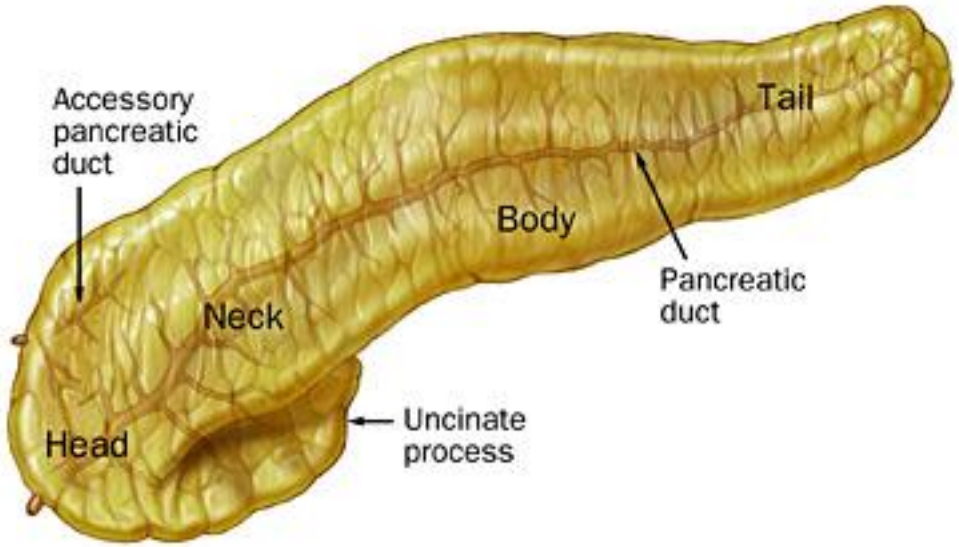
- Basic Anatomy and Physiology of the Pancreas
- Common Clinical presentations of Pancreatic Disease
- Pancreatic Investigations
  - Blood tests, faecal tests, imaging
- Pancreatic Diseases
  - Pancreatitis
    - Acute
    - Chronic
    - Autoimmune
  - Lumps and Bumps
    - Cystic lesions
    - Mass lesions

BASIC ANATOMY AND PHYSIOLOGY OF THE PANCREAS

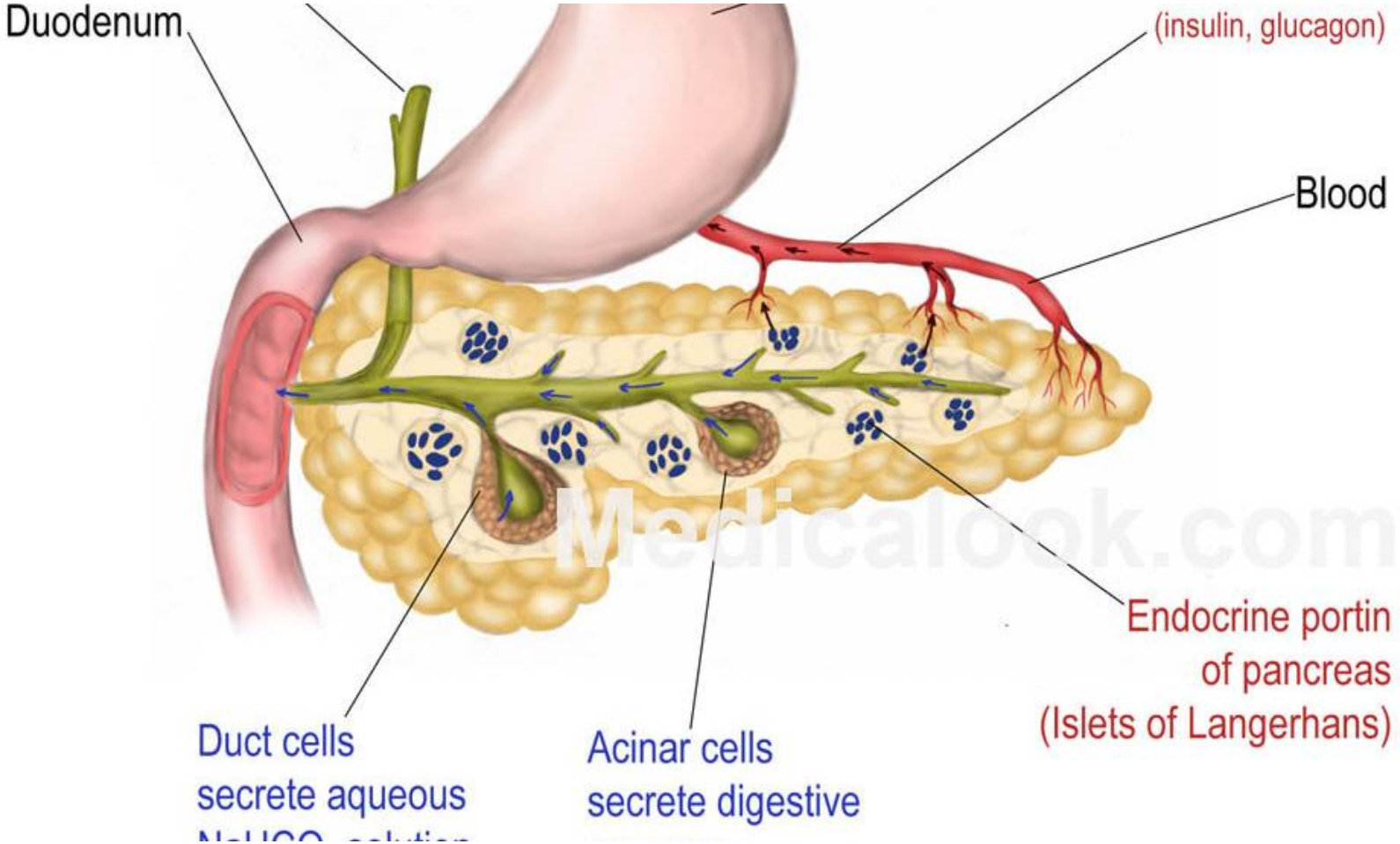
Pancreas : Anatomy



Deep retroperitoneal
12-20cm
Surrounded by stomach and Duodenum
Pancreatic duct calibre
3:2:1 Head:Body: Tail



Pancreas : Physiology



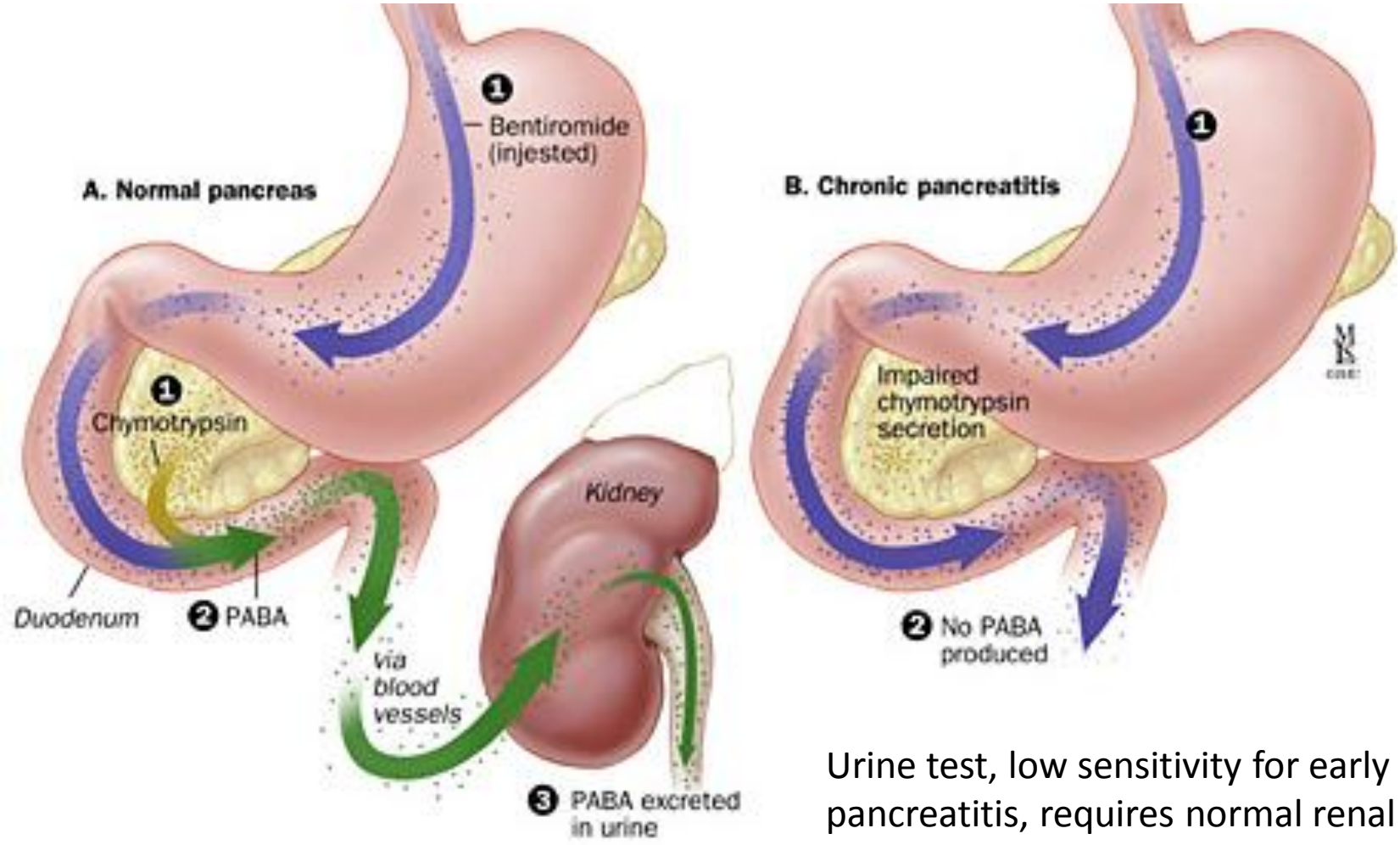
Clinical Presentation of Pancreatic diseases

- Acute Pancreatitis – Acute Abdomen, fever, biliary colic
- Chronic Pancreatitis – recurrent Abdominal pain, chronic diarrhoea, diabetes, weight loss
- Autoimmune pancreatitis
- Cysts – often incidental
- Drug and alcohol history important

Pancreatic Investigations

- Amylase – not specific, more sensitive
- Lipase – more specific, less sensitive
- Liver biochemistry – if raised consider gallstone pathology
- HbA1C
- Genetic testing – eg CFTR
- IgG4 – suspect autoimmune pancreatitis
- Plasma CCK raised in Chronic Pancreatitis
- Secretin test – duodenal aspiration of enzymes (invasive)
- Faecal steatocrit (good screen for steatorrhoea)and pancreatic elastase (not perfect)
- Imaging
  - AXR, USS, CT, MRI, EUS

Bentiromide Test



Urine test, low sensitivity for early pancreatitis, requires normal renal function and proper GI absorption

Table 1. **Pancreatic Function Tests**

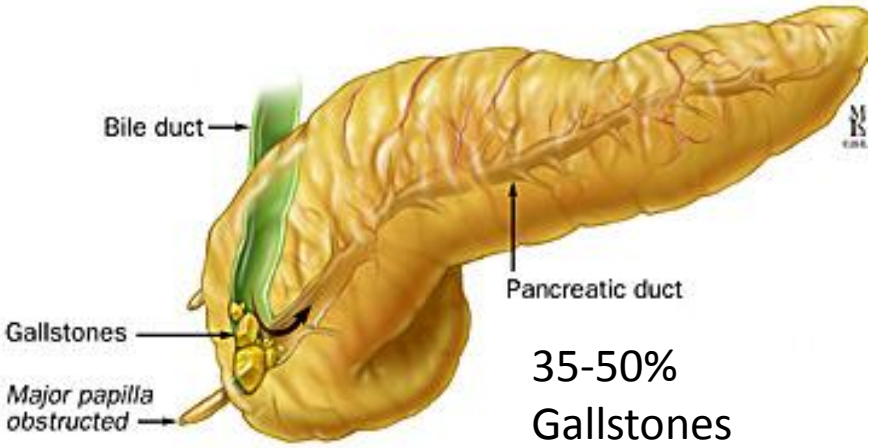
Type	Sensitivity (%)	Specificity (%)
Tubeless		
Fecal elastase	78	94
Pancreolauryl	50–85	82
Bentiromide (discontinued)	85	90
Duodenal intubation test		
Secretin	75–89	80–90

ACUTE PANCREATITIS

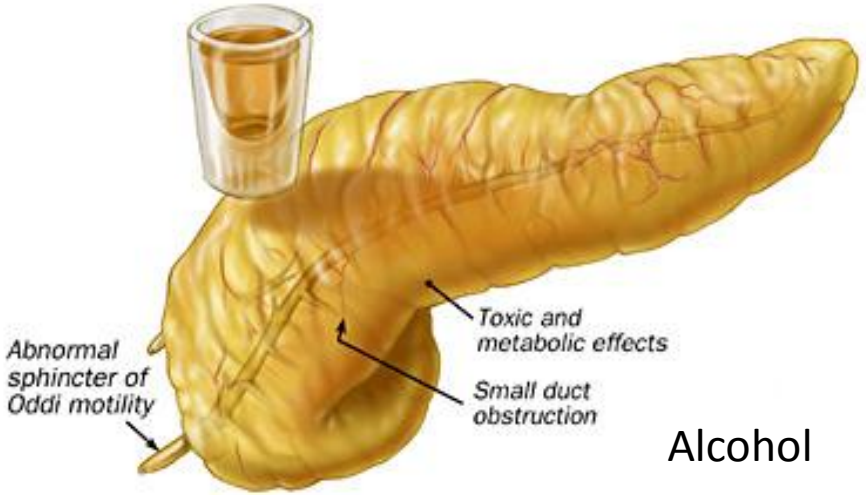
Acute Pancreatitis : IGETSMASHED

- I - idiopathic
- G- gall stones
- E- ethanol
- T- traumas
- S- steroids
- M- mumps and viral disease
- A- auto immune
- S- scorpion bite
- H- hypercalcemia, hyperlipidemia
- E- ERCP
- D- drugs

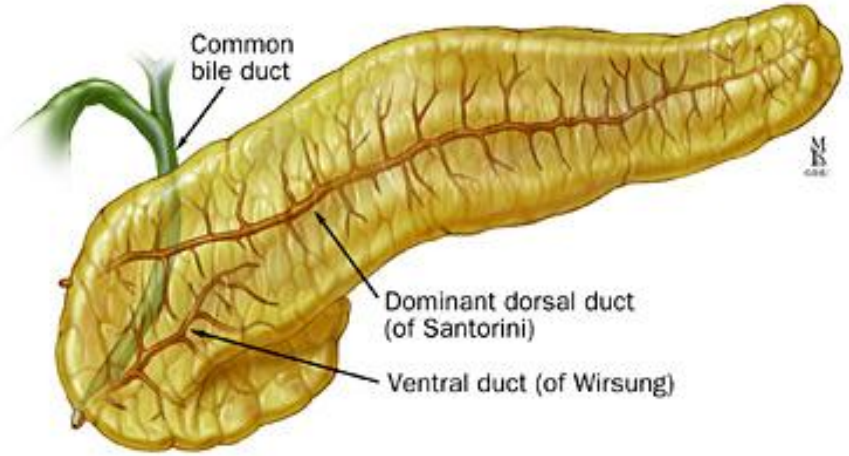
Acute Pancreatitis : Aetiology



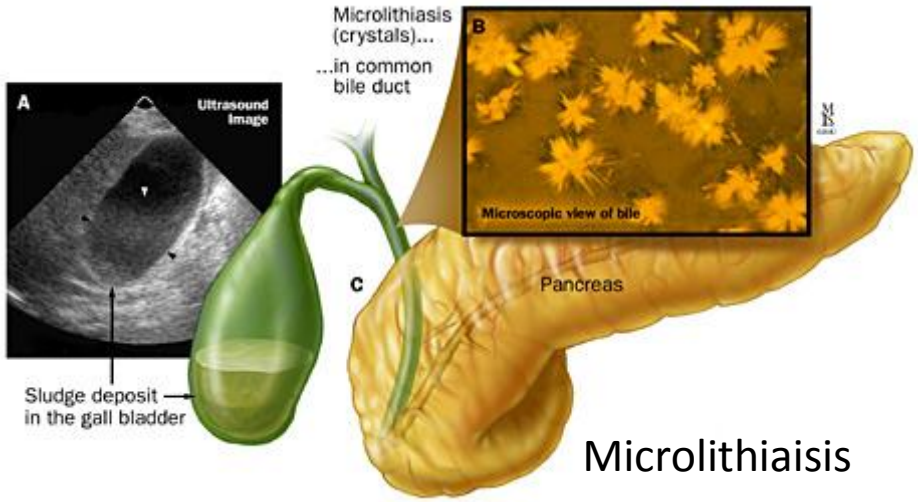
35-50% Gallstones



Alcohol



Divisum



Microlithiaisis

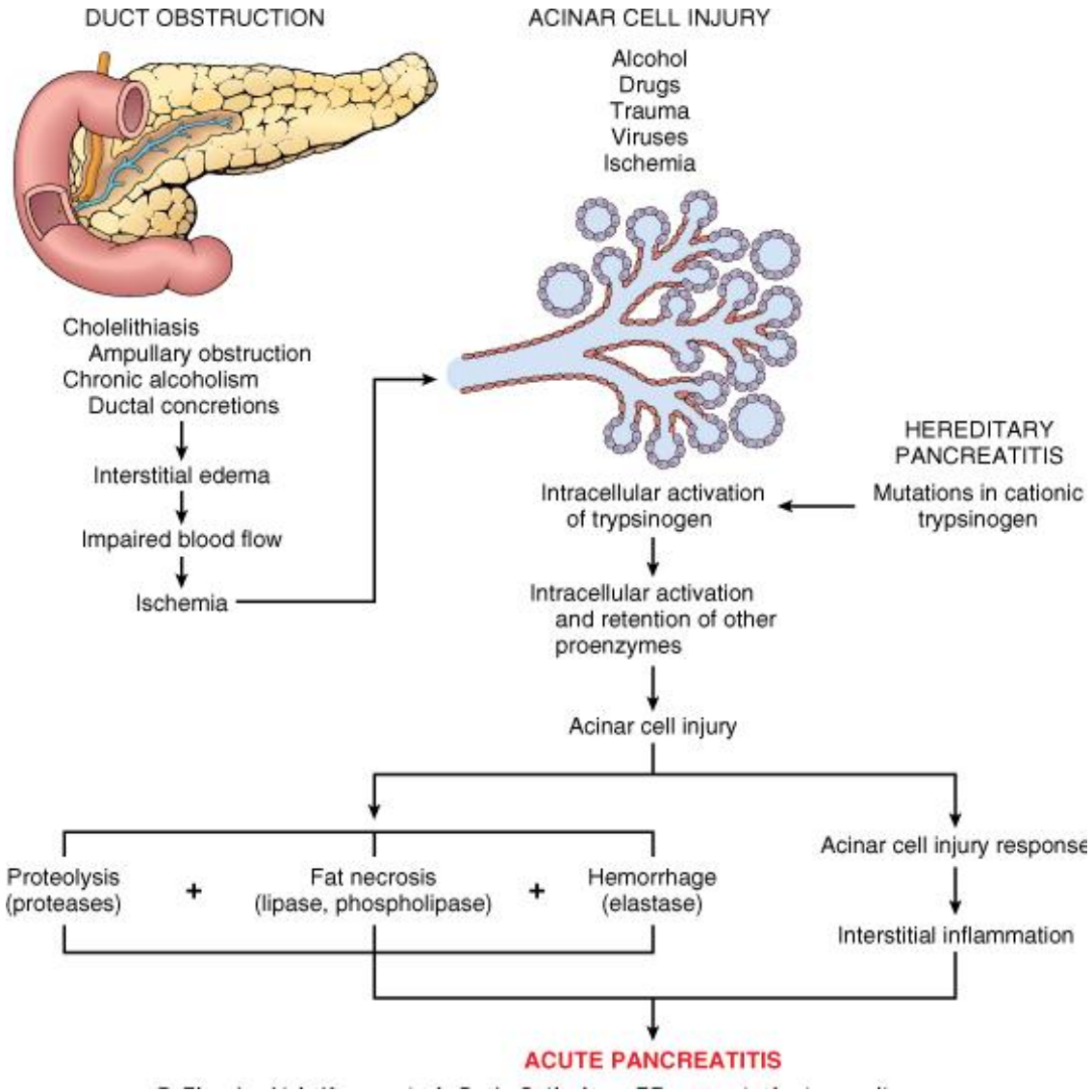
Pancreatitis : Drugs

Clearly linked to pancreatitis	Weaker association	Questionable association
Azathioprine	Sulfasalazine	Acetaminophen
6-Mercaptopurine	Captopril	Cyclosporin
Trimethoprim-sulfamethoxazole	Alfa-interferon	Cytarabine
Pentamidine	Estrogens	Erythromycin
2',3'-Dideoxyinosine (ddI)	Aminosalicylic acid	Roxithromycin
Asparaginase	Corticosteroids	Ketoprofen
Methyl-dopa	Corticotropin	Metolazone
	Acetaminophen	Octreotide
	Sulindac	
	Tetracycline	
	Metronidazole	
	Thiazide diuretics	
	Furosemide	
	Isotretinoin	
	Valproic acid	

Pancreatitis : Less common

- Sphincter of Oddi dysfunction
- Hyperlipidaemia
- Hypercalcaemia
- Trauma
- Scorpian bites
- Ascaris worms in Pancreatic duct

Pathophysiology



Clinical Features

- Major symptom is midepigastric or left upper quadrant pain: described as constant, boring pain that radiates to back, flanks, chest or lower abdomen.
- Nausea/vomiting or abdominal bloating
- PE: low grade fevers, tachycardia, +/- hypotension

Clinical Features

- Respiratory symptoms: atelectasis, pleural effusion, ARDS
- Abdominal exam: epigastric tenderness, peritonitis
- May present in hypovolemic shock and Multi organ Failure
  - Hypotension secondary to 3rd spacing, haemorrhage, increased vascular permeability, vasodilation, cardiac depression, vomiting

Cullen's sign

Grey Turner Sign

Diagnosis

- Amylase: found in pancreas & salivary glands
  - Low levels found in many tissues so this test is nonspecific
  - Amylase may be even normal in acute pancreatitis
  - Poor specificity

Diagnosis

- Lipase: found predominantly in pancreas but also in gastric, intestinal mucosa and liver
  - Cleared by the kidney so renal failure will elevate levels
  - Most appropriate cut-off is 2-3 x normal level
  - More accurate test than amylase, better specificity (90% vs. 75%)

Diagnosis

- Xrays of chest/abdomen: useful for r/o other diagnosis.
  - Calcification of pancreas seen in chronic pancreatitis
  - May see sentinel loop, elevated hemi-diaphragm, pleural effusion
  - U/S may detect gallstones
  - CT best study for grading severity if disease, prognosis.

Diagnosis

- Prognostic markers: Ranson criteria predicts pt. outcome
  - Age >55
  - BS >200
  - WBC >16,000
  - AST >250
  - LDH >700
  - Features portend a worse prognosis, but they have poor predictive value in acute setting and does not improve clinical judgment

Diagnosis

- CT of abdomen:
  - Estimates severity and prognosis
  - Complications include phlegmons, abscesses or pseudocysts.
    - Usually seen 2-3 weeks after acute pancreatitis

Complications of Acute Pancreatitis

- Pulmonary: pleural effusions, atelectasis, hypoxemia, ARDS
- CV: myocardial depression, hemorrhage, hypovolemia
- Metabolic: Hypocalcemia, hyperglycemia, Hyperlipidemia, coagulopathy/DIC
- Others: Colonic perforation, ARF. Arthritis, pseudocyst, abscess

Treatment:

- General principle: rest the pancreas
- Fluid resuscitation
- NG tube only if needed
- Pain control, anti-emetics
- Antibiotics only in severe disease (Controversial)
  - Cover polymicrobial, GNB
  - IV imipenem or quinolone in combination w/Flagyl

Acute Pancreatitis : Summary

- Mild pancreatitis without evidence of systemic disease and low likelihood of biliary disease may be managed as outpaient if tolerating oral fluids and pain control is adequate
- All others need to be admitted
- Suggest refer ALL for acute surgical assessment

CHRONIC PANCREATITIS

Chronic Pancreatitis

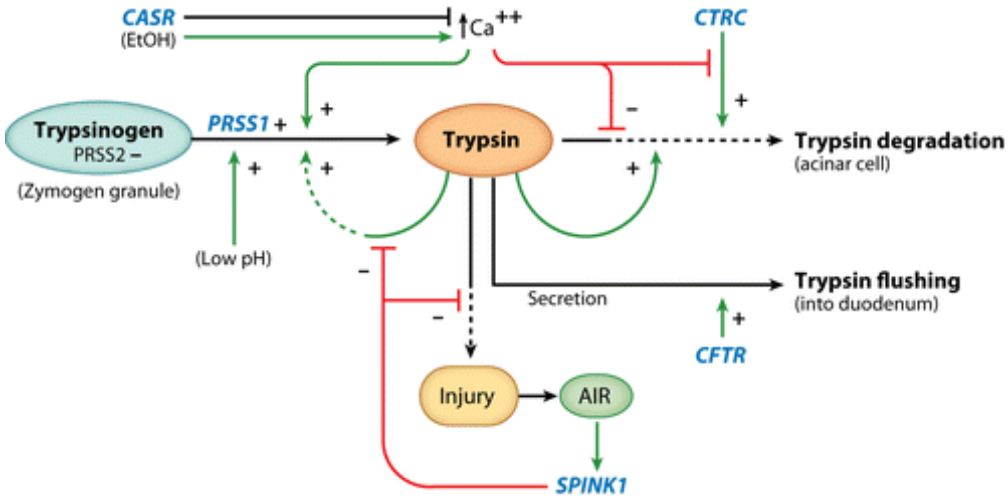
- Uncommon 20/100,000
- Autopsy studies 0.5% - 5%
- True extent of the problem unknown
- Chronic inflammation leading to fibrosis, calcification, pancreatic ductal inflammation and stone formation

Chronic Pancreatitis : Aetiology

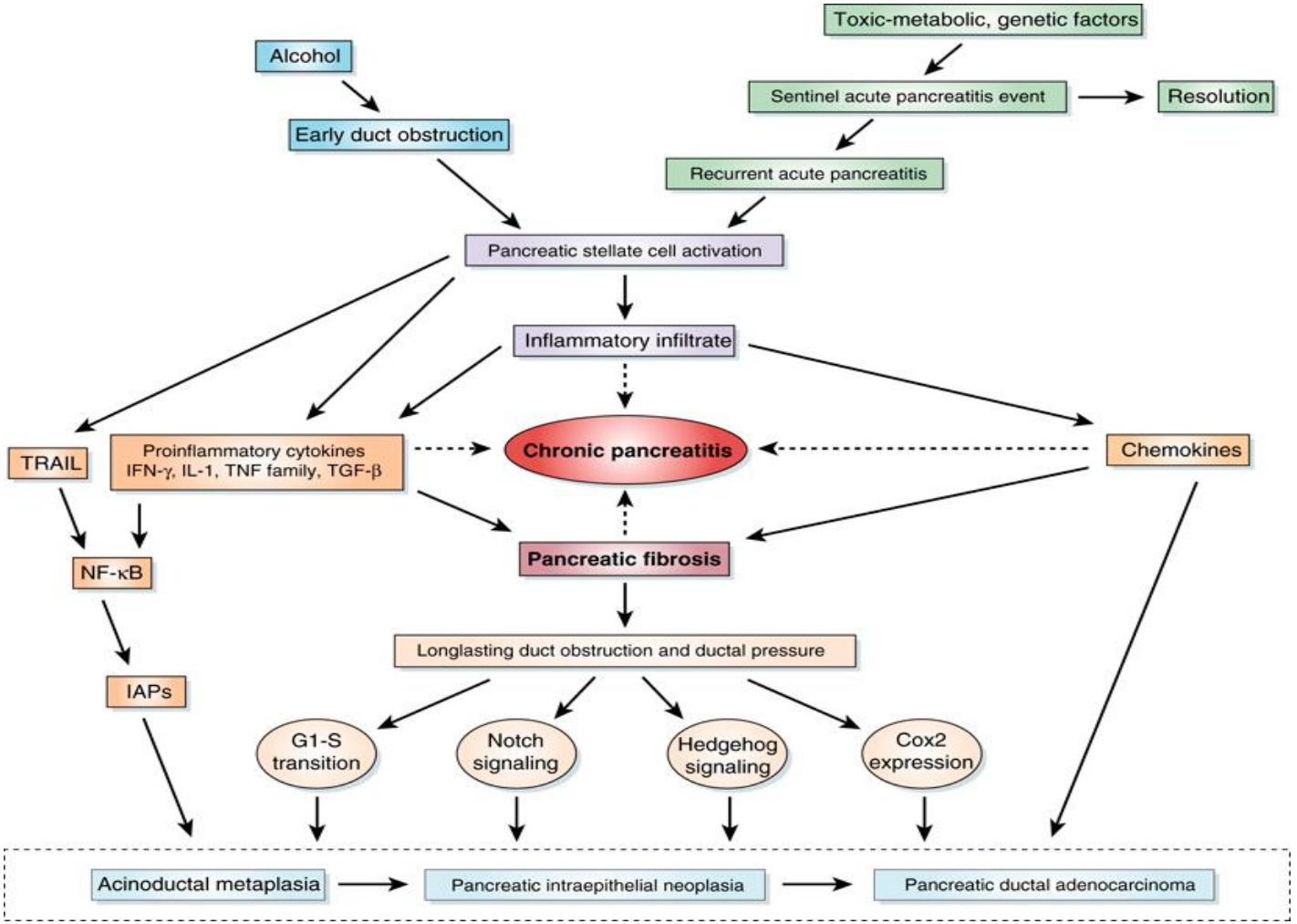
- Alcohol – 70%
- Pancreas Divisum
- Tropical
- Hyperparathyroidism
- Obstructive
- Hereditary Chronic Pancreatitis
- Cystic Fibrosis

Hereditary Chronic Pancreatitis

- Childhood mean age 10-12 yrs old
- Probably diagnosed at Paediatric age group
- Autosomal dominant gene
- Incomplete penetrance
- M:F 1:1
- Majority R122H or N29I in the Cationic Trypsinogen gene (PRSS1)
- Deactivation of trypsinogen -> Autodigestion
- Recurrent attacks of abdominal pain
- Diabetes 20% after 8-10 yrs of disease
- 40% lifetime risk of pancreatic cancer (highest 50-70yrs)
- Referral to genetics service for testing and counselling

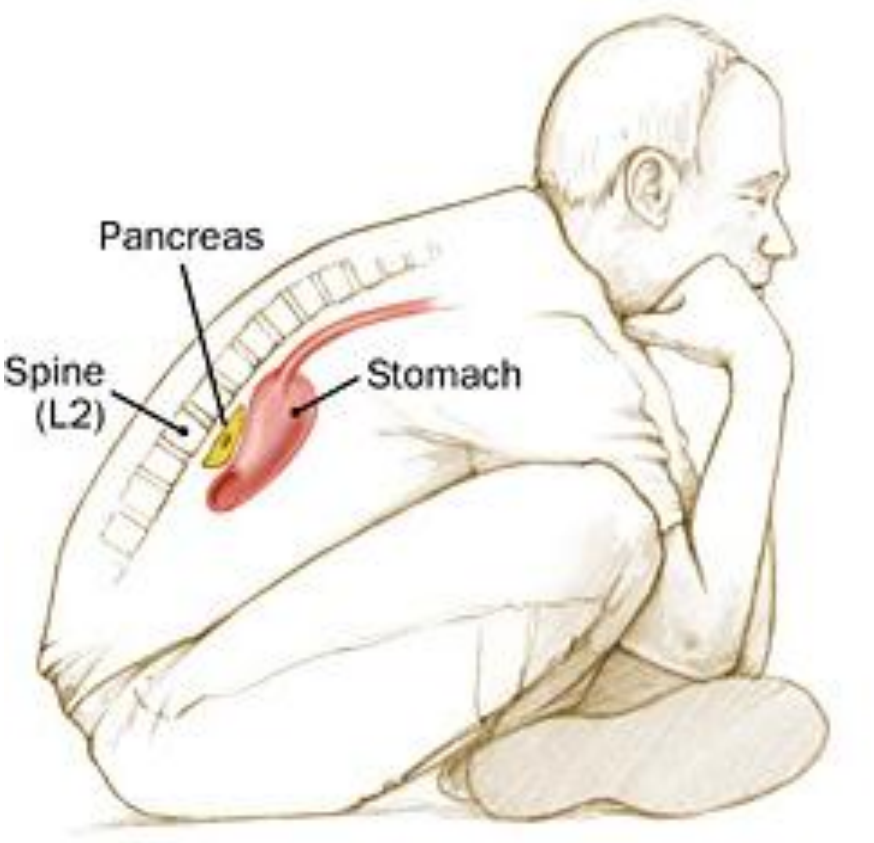


Chronic Pancreatitis :Pathophysiology



Chronic Pancreatitis : Clinical Presentation

- Abdominal pain – deep epigastric
- Associated vomiting
- Dull unremitting pain with epigastric tenderness radiating to the back (HOP at L2)
- Weight loss
- Steatorrhoea and diarrhoea when 90% pancreas lost
- Hyperglycaemia
- Relieved by sitting up and leaning forwards



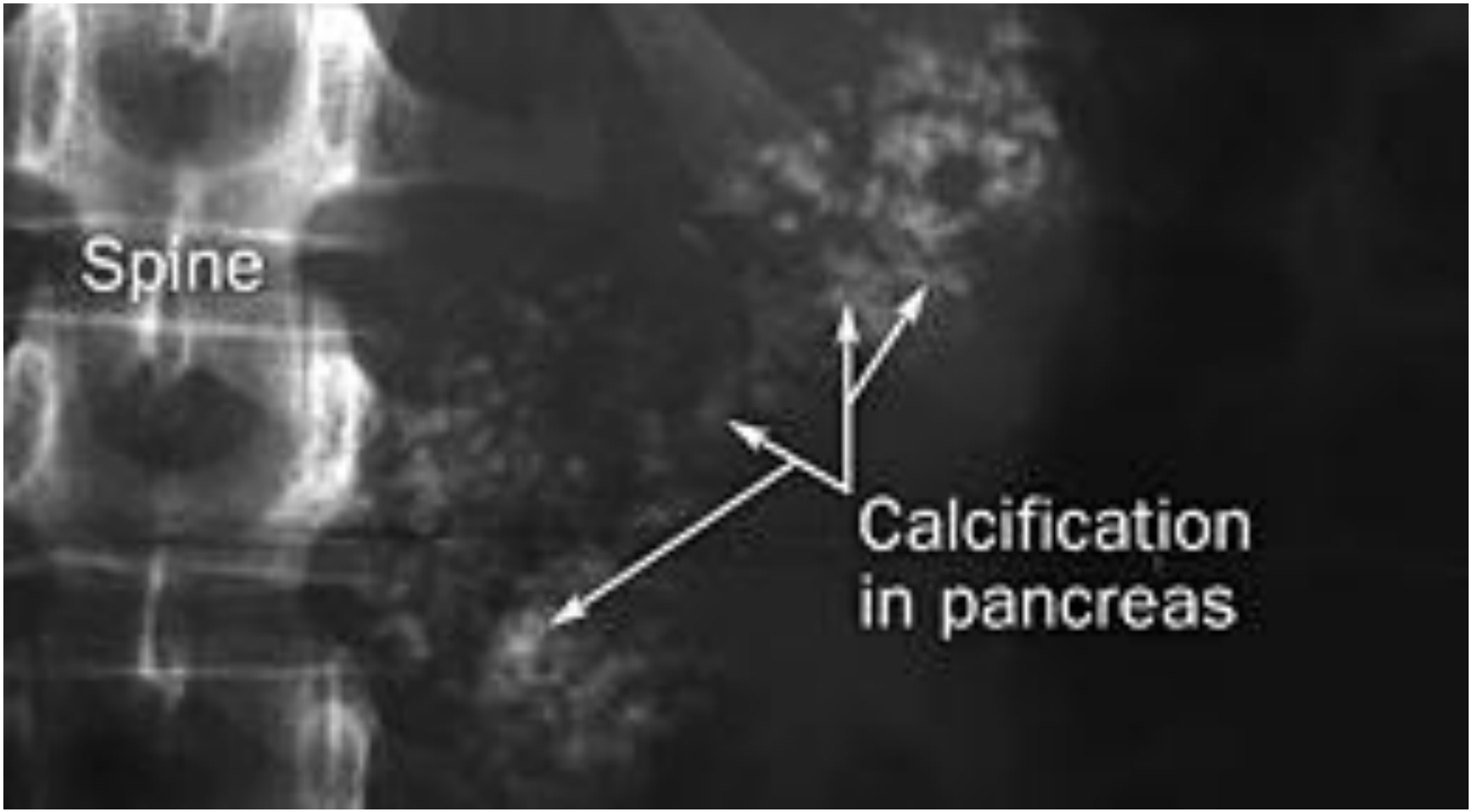
Chronic Pancreatitis

- Amylase and lipase may be normal if pancreas is fibrotic
- CT scan may help identify pseudocyst or abscess
- Treatment : IVF’s anti-emetics, narcotics
- Pancreatic extracts to improve absorption and pain
- If pain is increasing or intractable, image pancreas to look for complications

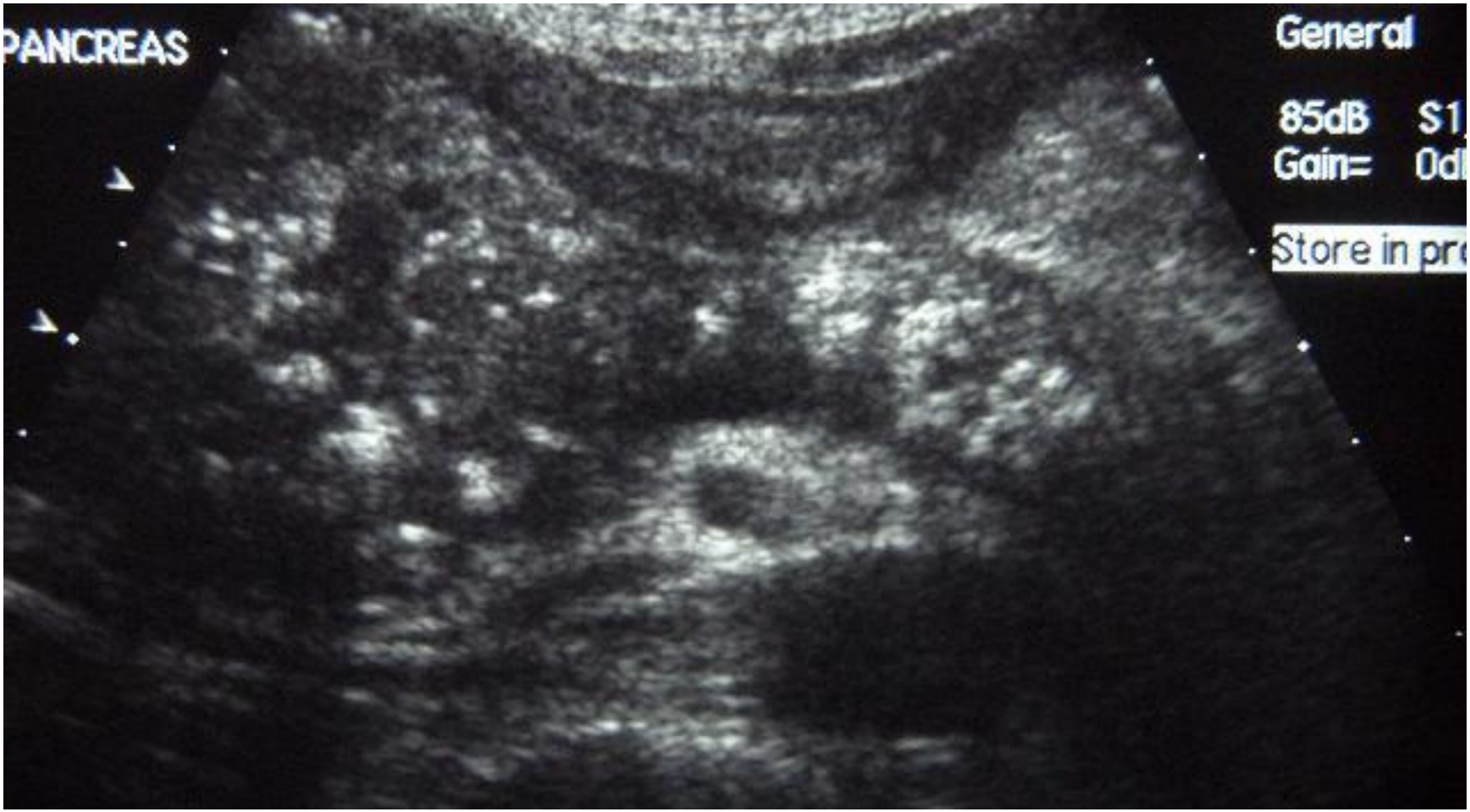
Disposition

- Patients may be discharged home if all the complications have been ruled out
- Hospitalize if intractable pain.

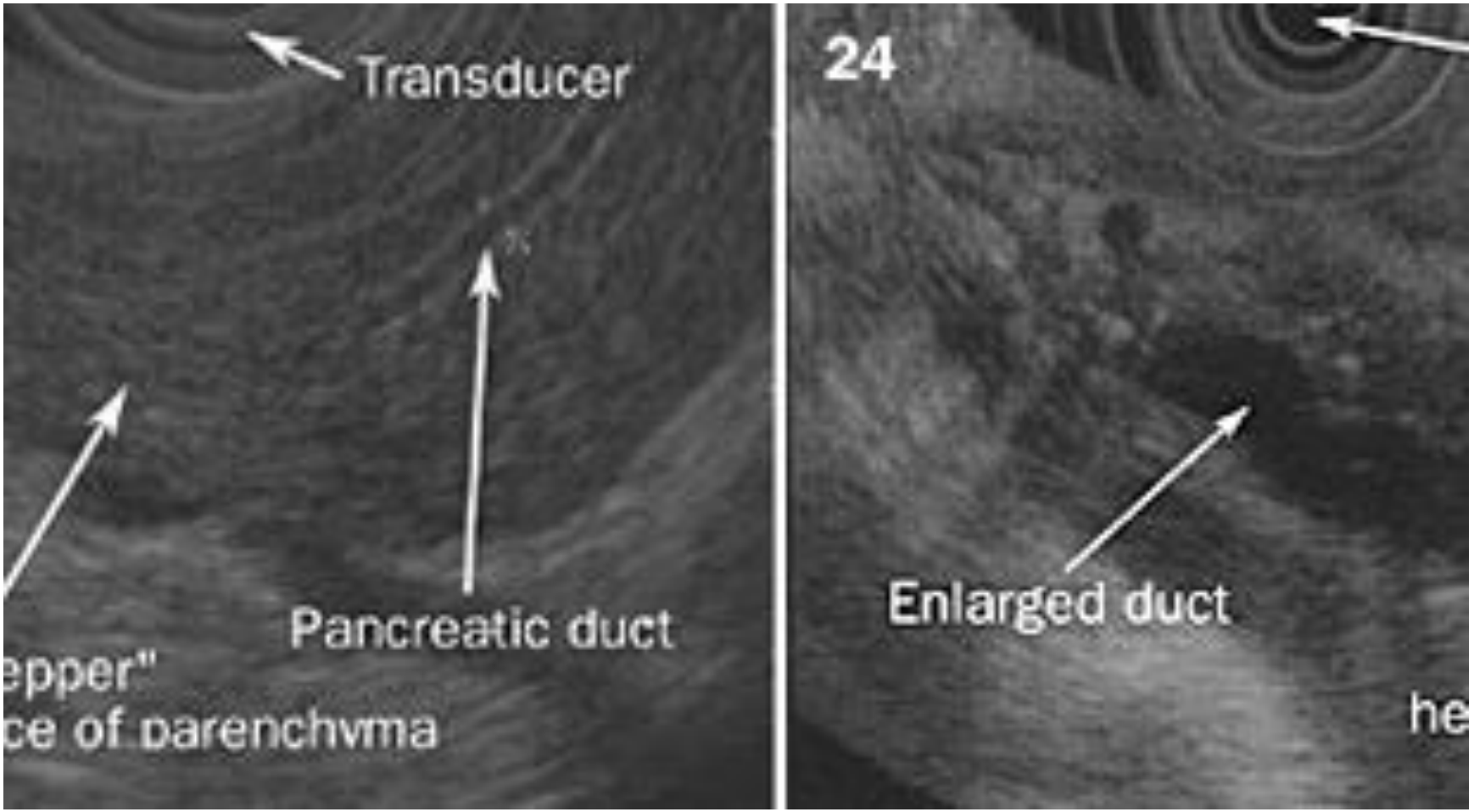
Chronic Pancreatitis : AXR



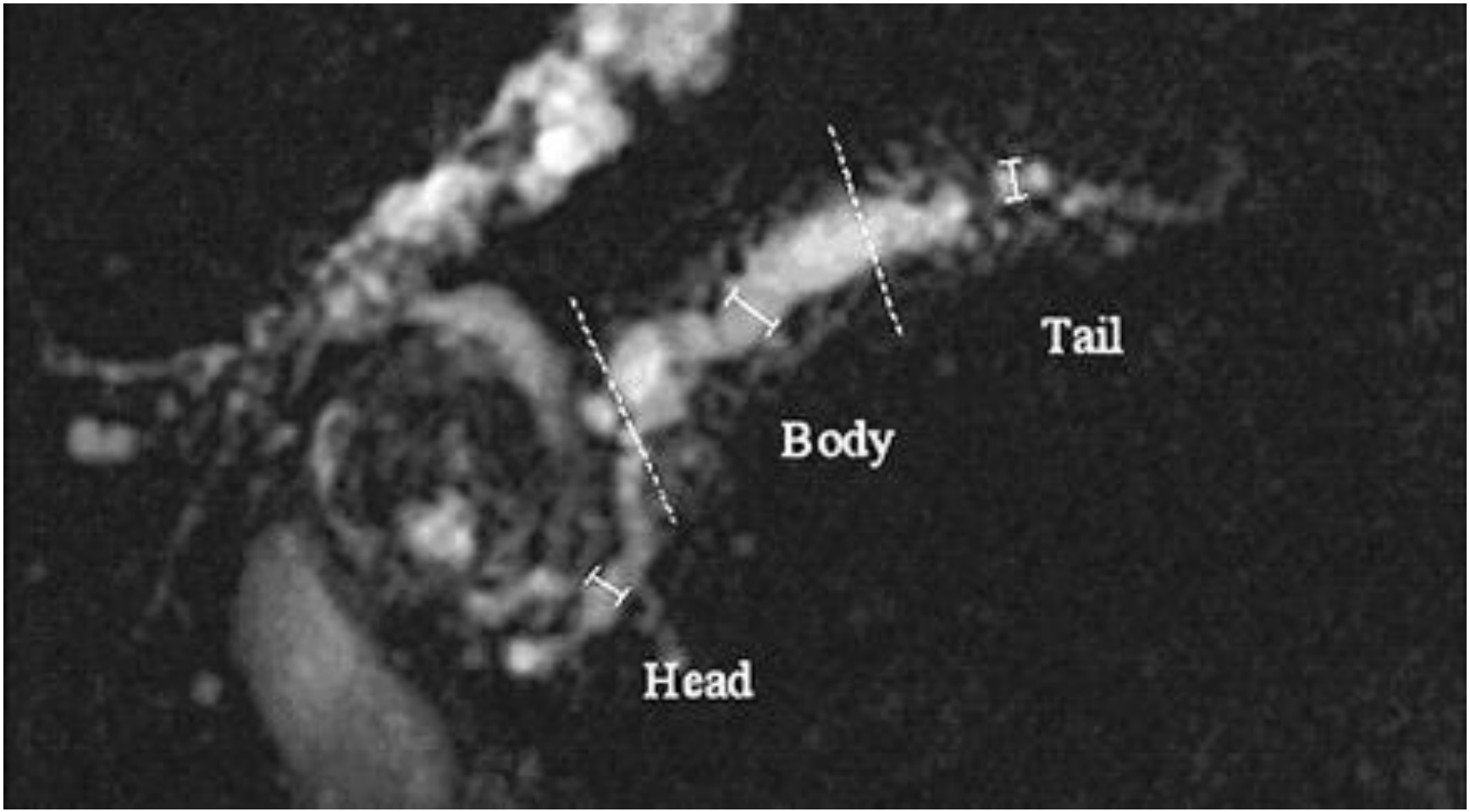
Chronic Pancreatitis : Ultrasound



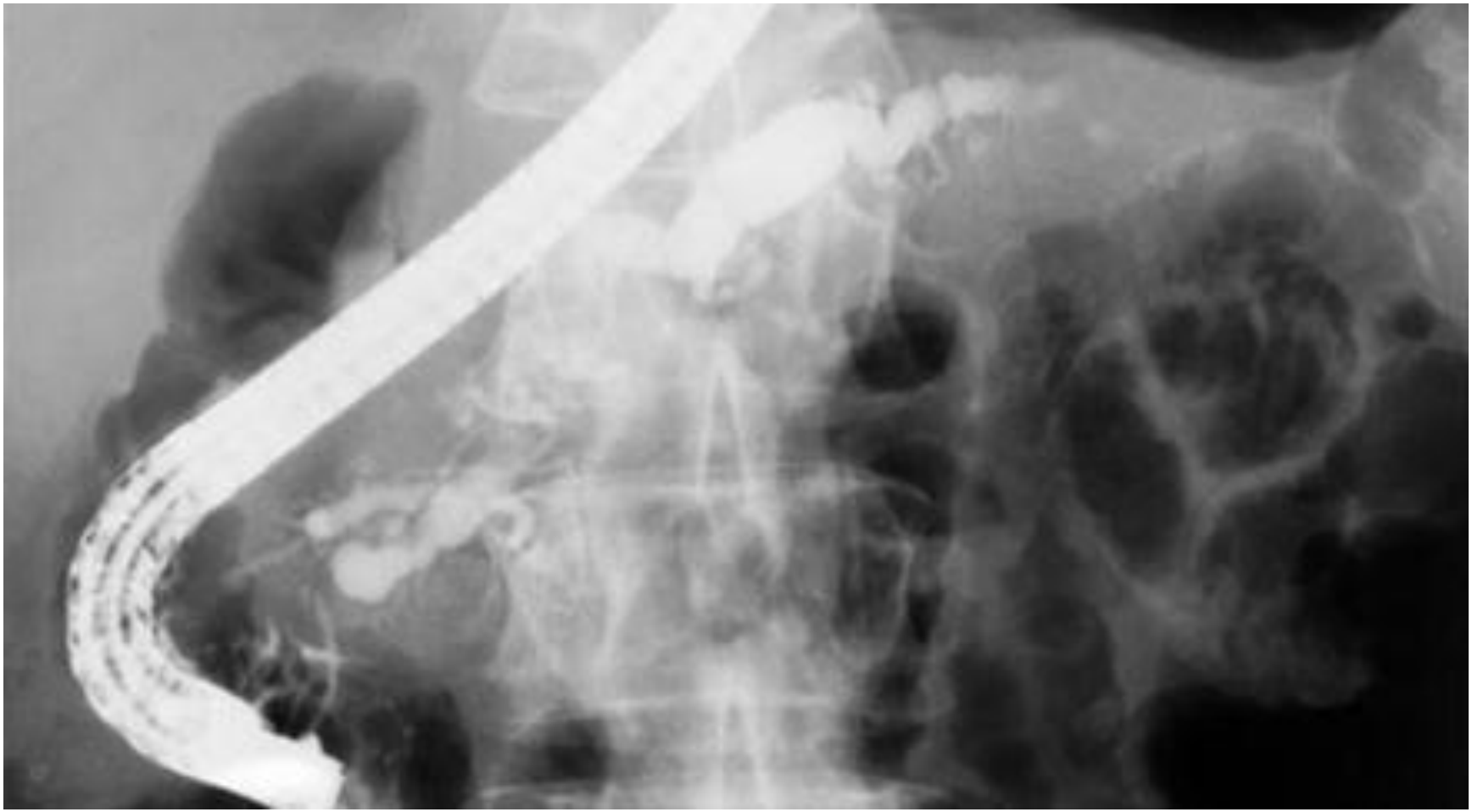
Chronic Pancreatitis : Endoscopic Ultrasound (EUS)



Chronic Pancreatitis : MRCP



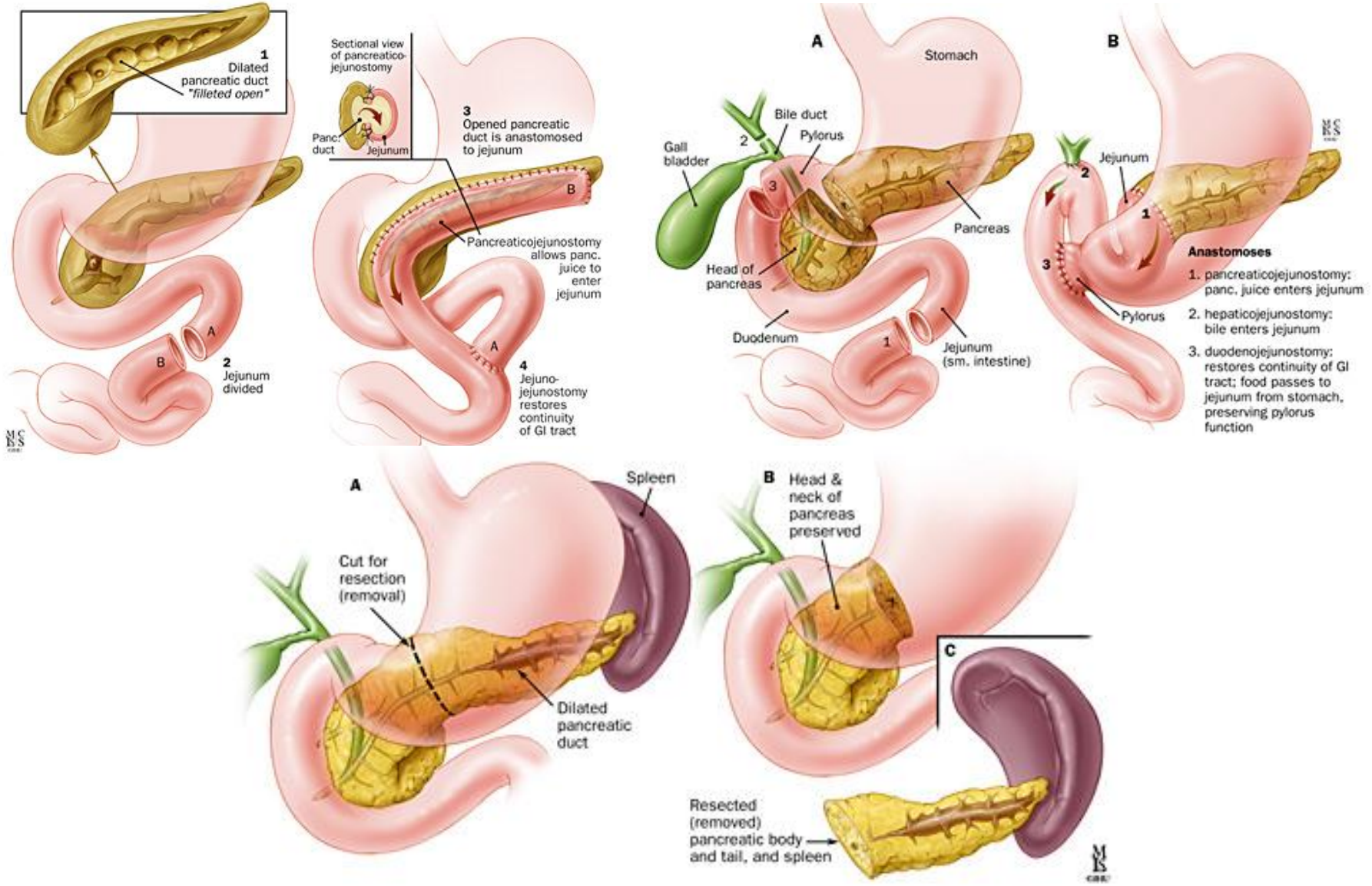
Chronic Pancreatitis : ERCP



Medical Management

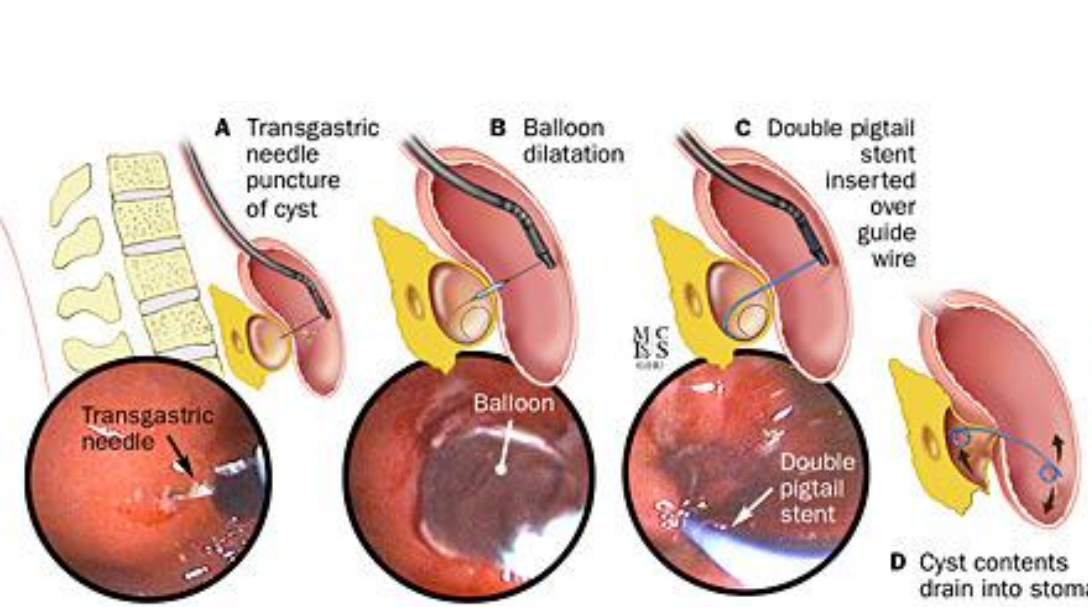
- Stop all alcohol and smoking
- Both associated with progression and more pain
- Non narcotic analgesia – NSAIDs, Panadol, use before meals to prevent post prandial pain
- Step up to Narcotics for severe
- Enzymes – pancreatic supplements (need at least 24000 to 32000 u of lipase)
- Dietician input – high protein, high calorie, median chain trigylcerides (nausea common)

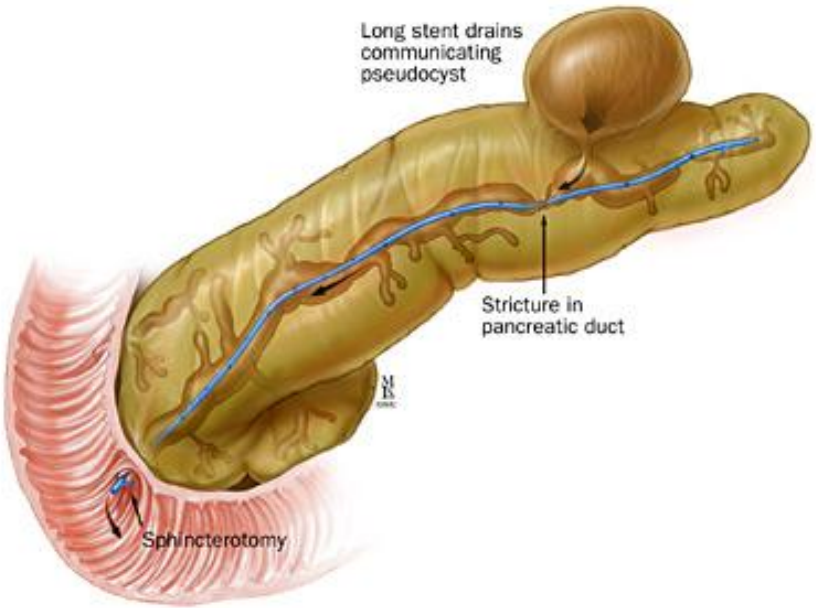
Surgery


1
Dilated pancreatic duct
"filleted open"
2
Jejunum divided
Sectional view of pancreatico-jejunostomy
Panc. duct
Jejunum
3
Opened pancreatic duct is anastomosed to jejunum
Pancreaticojejunostomy allows panc. juice to enter jejunum
4
Jejuno-jejunostomy restores continuity of GI tract
A
Stomach
Bile duct
Gall bladder
Pylorus
Pancreas
Head of pancreas
Duodenum
Jejunum (sm. intestine)
B
Jejunum
Anastomoses
1. pancreaticojejunostomy: panc. juice enters jejunum
2. hepaticojejunostomy: bile enters jejunum
3. duodenojejunostomy: restores continuity of GI tract; food passes to jejunum from stomach, preserving pylorus function
Pylorus
A
Spleen
Cut for resection (removal)
Dilated pancreatic duct
B
Head & neck of pancreas preserved
C
Resected (removed) pancreatic body and tail, and spleen

Endoscopy

- ERCP – Biliary obstruction
- EUS – Pseudocyst drainage, Coeliac axis neurolysis





Chronic Pancreatitis : Summary

- Medical therapy to prevent worsening complications and treat underlying cause
- Surgical and Endoscopic therapy tailored to patients symptoms
- Most patients under the care of Gastroenterologist or Surgeon for MDM approach

AUTOIMMUNE PANCREATITIS

Definition

- Chronic pancreatitis caused by autoimmune inflammatory process
- Lymphocyte infiltration
- Fibrosis of pancreas
- Organ dysfunction

Epidemiology

- Rare
- Increase in number of reported cases past 10 years
- Prevalence and incidence not yet determined—possibly between 5-6% of all cases of chronic pancreatitis
- May have increased prevalence in Japan
- Twice as common in men as in women
- Most patients are > 50 years old

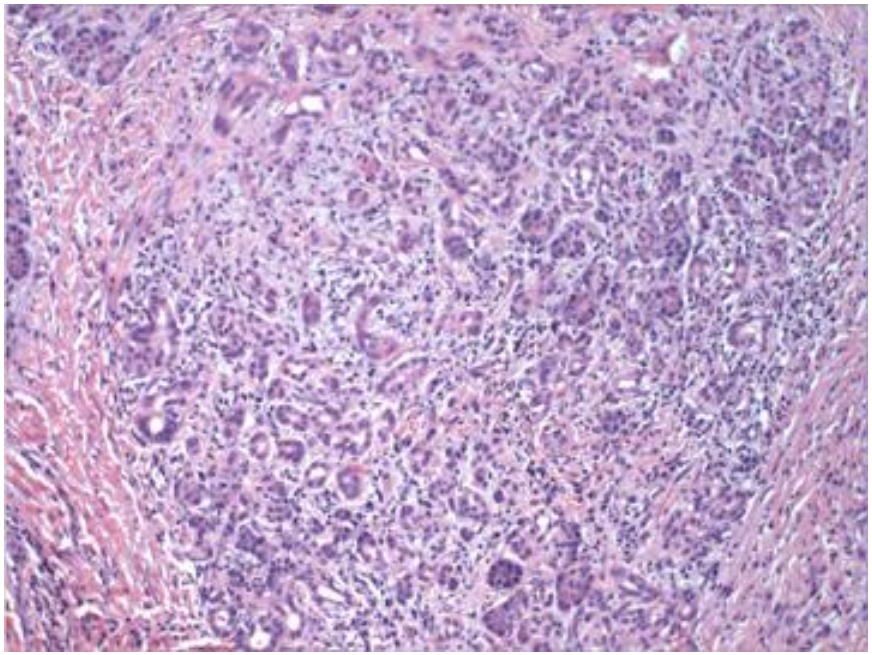
Pathogenesis

- Unknown
- Often associated with other autoimmune diseases (RA, Sjogren's, IBD)
- Has been found to be associated with a specific HLA haplotype in the Japanese population
- hypergammaglobulinemia
- elevated serum IgG4 levels
- Auto antibodies against carbonic anhydrase and lactoferrin

Pathology

- Diffusely indurated and firm pancreas on gross exam
- Focal mass can be found in a subset of patients
- Collar-like periductal infiltrate composed of lymphocytes and plasma cells
- Can also involve gallbladder, bile ducts, kidney, lung, and salivary glands with dense lymphocytic infiltrate

Pathology

- 

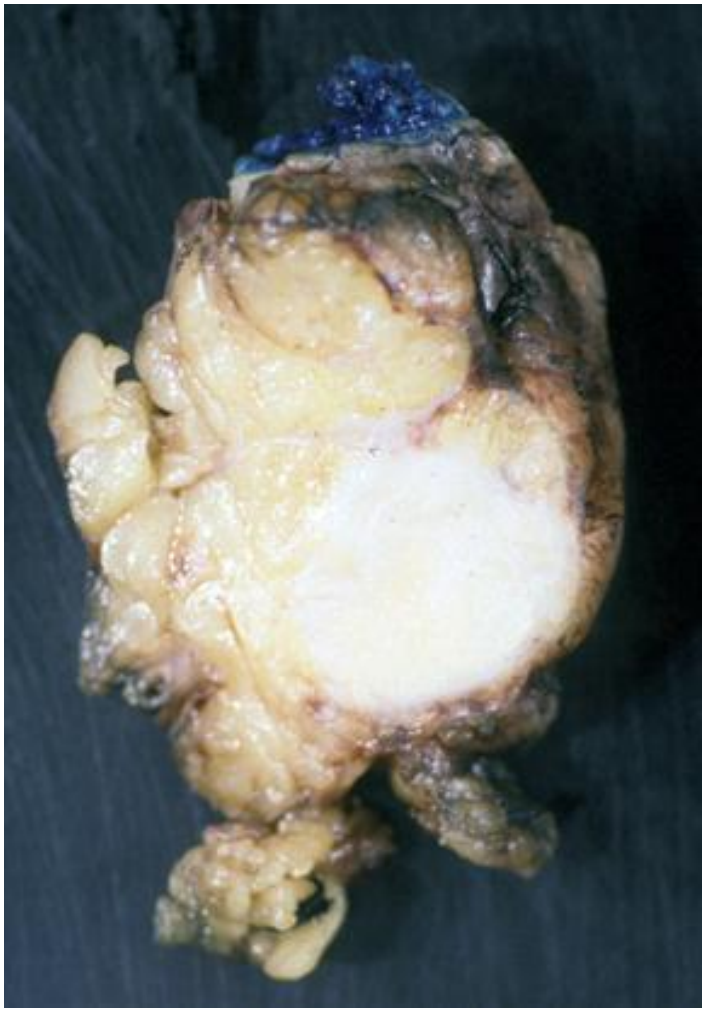
  - Low power view of a pancreas biopsy in a patient with autoimmune pancreatitis. The acinar parenchyma is atrophic and fibrotic and contains a lymphoplasmacytic infiltrate

Clinical Features

- Unusual to present w/ severe abdominal pain
- Usually mild, acute recurrent pancreatitis
- Abdominal pain, weight loss, jaundice, obstructive pattern of LFTs
- Biliary and pancreatic duct strictures
- Pancreatic mass—can be confused with pancreatic carcinoma or lymphoma
- Features of other autoimmune diseases

Gross Specimen

- Surgical specimen in a patient who underwent resection for autoimmune pancreatitis



Imaging

- MRI: sausage-shaped enlargement of pancreas, minimal fat stranding, peripheral rim of hypoattenuation “halo”
- Similar lesions seen on CT
- Can also see focal pancreatic involvement, usually in the head of pancreas (like the mass found in this patient)

Imaging

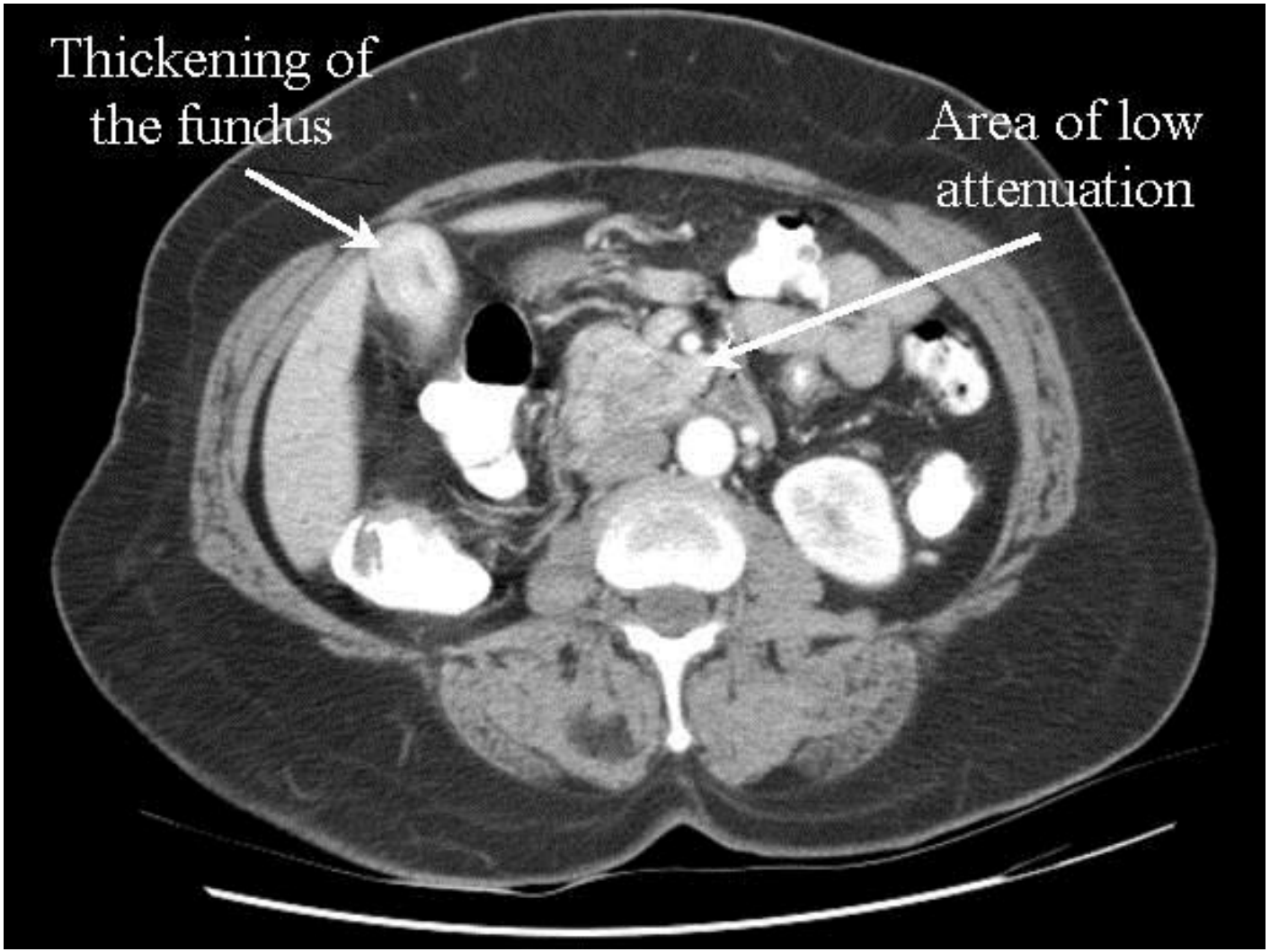
- EUS: diffusely hypoechoic, enlarged pancreas
- ERCP: narrowed main and dorsal pancreatic duct, diffuse, irregular narrowing of duct, focal stricture of duct, irregular narrowing of intrahepatic ducts, lesion in pancreatic head can be seen
- May not be able to distinguish between malignancy and autoimmune pancreatitis based on these results

CT Scan

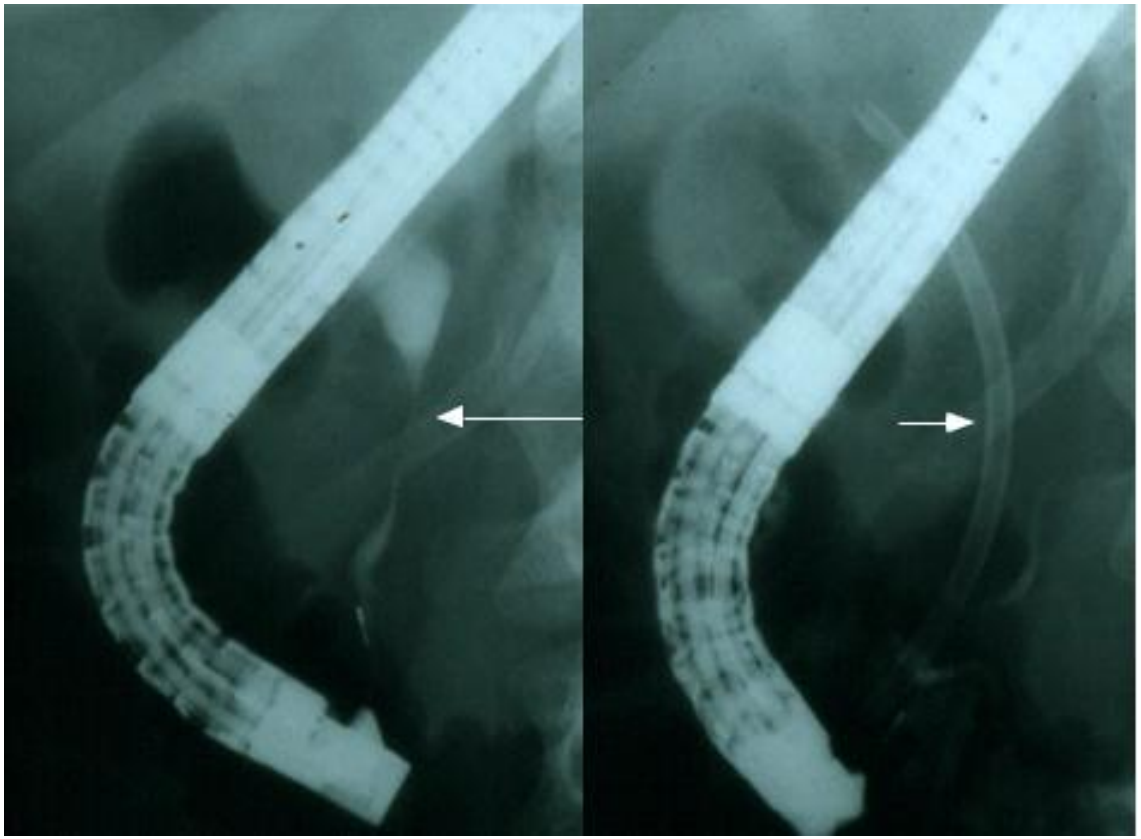
CT scan of a patient with autoimmune pancreatitis. The head of the pancreas is enlarged (long arrow) and the common bile (small arrow) is dilated

Pancreatic Head Mass

CT scan showing low attenuation, ill-defined lesion in the pancreatic head with enhancing mural thickening at the gallbladder fundus



ERCP



Endoscopic retrograde cholangio- pancreatography in a patient with autoimmune pancreatitis. The left panel shows a stricture in the common bile duct due to the surrounding enlarged pancreas. The right panel shows a stent that has been inserted across the narrowed segment

Diagnosis

- Elevated serum IgG4
  - Test characteristics have not been evaluated extensively, especially in western populations
- If discreet mass present, biopsy is crucial to evaluate for malignancy—may need to go to surgical biopsy
- Trial of corticosteroids if typical radiographic, immunologic and pancreatic ductal changes w/o dilation are present

Treatment

- Can respond dramatically to corticosteroids—optimal dose and duration not yet established
- Possible approach: prednisone 40 mg daily for 4-6 weeks, followed by taper of 5 mg/week
- Patients usually followed immunologically and by CT scan while on therapy

Take Home Points

- Autoimmune pancreatitis should be considered in patients with refractory pancreatitis without other identifiable etiology
- Can present with mass that can be confused with pancreatic carcinoma or lymphoma--patients have been taken for Whipple procedure for this!
- Typically responds very well to steroids

PANCREATIC LUMPS AND BUMPS

Solid Lesions

- Adenocarcinoma
  - Ductal Cell
  - Acinar Cell
- Neuroendocrine Tumours
- Lymphoma
- Metastatic Disease
  - Breast
  - Lung
  - Renal Cell
  - Melanoma
- Papillary endothelial tumour
- Focal chronic pancreatitis
- Splenule
- Sarcoidosis
- TB
- Actinomycosis
- Other
  - Lipoma, Fibroma, Teratoma, Lymphangioma, Neuroma, Schwannoma

Cystic Lesions

- Pseudocyst (PC)
- Serous Cystadenoma (SCN)
- Mucinous Cystadenoma (MCN)
- Intraductal Papillary Mucinous Neoplasm (IPMN)
- Cystic Neuroendocrine tumour
- Cystic Adenocarcinoma
- Papillary epithelial tumour
- Lymphangioma
- Lymphoepthelial cysts
- Simple/congenital cysts (rare)

Magnitude

- 20% of 1444 patients undergoing MRI for non-pancreatic disorders were found to have a pancreatic cyst
- 24% of autopsy series harboured pancreatic cyst
- Surgically resected pancreatic cysts at MGH
  - 1997-2002: 212 patients 37% incidental finding
  - 2003-2007: 401 patients 71% incidental finding
- Only 3% of incidentally discovered cysts are pseudocysts

Consquence

- Growing number of cysts and masses incidentally discovered
- Growing potential to diagnose and cure early pancreatic cancer and prevent
- But we can do harm by being overly aggressive for benign and low grade lesions

Role of Gastroenterologist

- Intepret significance of radiographic abnormalities in the correct clinical context
- Develop diagnostic and therapeutic plan
  - No intervention or follow up
  - Periodic radiographic assessment
  - Pursue definitive diagnosis
  - Surgical resection

EUS and EUS-FNA

- Allows characterisation
- Sampling
- Now able to look at histology directly with confocal needle probe
- Adjuctive imaging techniques – eg contrast enhanced EUS

No need for EUS-FNA

- Incidentally discovered lesions <1cm without high risk features
- Cysts developing in the setting of pancreatitis
- Patients who are not surgical candidates
- When a definitive diagnosis won't change management

Take Home Points

- 20-25% patients will have pancreatic cysts on MRI
- If imaging not pathognomonic patient will likely require EUS-FNA unless the result will not alter management
- A dilated pancreatic duct must be evaluated by EUS/ERCP
- Main Duct IPMN and Mucinous lesions highest malignant potential

Pancreatic Disease : Take Home Points

- Pancreatic disease in relatively uncommon
- Pancreatic lumps and bumps more common these days with easy access to radiology
- Acute Pancreatitis easy to diagnose
- Chronic Pancreatitis harder, part of the differential of a young person with abdominal pain and diarrhoea
- Early diagnosis allows early specialist MDM care – remember risk of pancreatic cancer

Macmurray Gastroenterology

- 7 Gastroenterologists
- 1 dedicated Hepatologist
- Dietician
- Health Psychologist
- Comprehensive investigations available on site
- Mandarin and Cantonese speaking Doctor

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DIGESTIVE DISEASES & ENDOSCOPY