Diagnosis of chronic Pancreatitis

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Pancreatitis

- **Pancreas** - an organ that makes **bicarbonate** to neutralize gastric acid, **enzymes** to digest the contents of a meal and **insulin** to signal the body to store ingested nutrients.

- **Acute Pancreatitis** - An acute, potentially life-threatening condition presenting with severe abdominal pain in which the pancreas appears to digest itself. It is usually caused by gallstones, alcohol or is idiopathic.

- **Chronic Pancreatitis** - an irreversible scarring of the pancreas with permanent loss of pancreatic function that typically causes unrelenting abdominal pain.

- **Hereditary Pancreatitis** - a unusual form of acute and chronic pancreatitis that runs in families. The risk of pancreatic cancer is >50 times normal.
The Pancreas

- Gross Anatomy
  - Head
  - Body
  - Tail
1. History
Chronic pancreatitis: medical progress

« Since that early description (1788) of chronic pancreatitis, thousand of reports dealing with this disease have been published, yet chronic pancreatitis remains an enigmatic process of uncertain pathogenesis, unpredictable clinical course, and unclear treatment »

ML Steer, I Waxman, S Freedman
Definition

- A persistent inflammatory disease of the pancreas
  - Irreversible morphologic change
  - Typically causing pain and/or loss of digestive function
Chronic Pancreatitis
Chronic Pancreatitis: the main question:

Progression from acute to chronic pancreatitis in humans?
Chronic Pancreatitis: the natural history

- OH
- First attack
- Cholestasis
- Cirrhosis
- 10 - 18 years
- 10 years
- Pseudocysts
- Diabetes
- Steatorrhea
Calcifications in CP

Alcoholic

- 58%

Nonalcoholic

- 28%

p < 0.01

Time to calcification

- Alcoholic: 7.8 years
- Nonalcoholic: 15.0 years

p < 0.02

Onset of pancreatitis
Exocrine Insufficiency in CP

- Alcoholic: 42%
- Nonalcoholic: 30%

Time to exocrine insufficiency:
- Alcoholic: 8.1 years
- Nonalcoholic: 15.2 years

Onset of pancreatitis

n.s. indicates no statistically significant difference.
Diabetes mellitus in CP

**Alcoholic**
- 39%

**Nonalcoholic**
- 33%

**Time to diabetes mellitus**

- Alcoholic: 7.8 years
- Nonalcoholic: 12.2 years

Onset of pancreatitis: 0 years

Years: 0 5 10 15

n.s.
Normal Digestion and Absorption

- Mechanical mixing
- Enzymes and bile salts
- Mucosal functions
- Blood supply
- Intestinal motility
- Bacterial flora
Fecal fat output vs Lipase

Fecal fat, g/24 h vs % normal lipase output.
Lipase and Trypsin over Time

% normal maximal enzyme output

Years of alcoholism
Gastric and duodenal pH in CP

Postprandial gastric pH

Postprandial duodenal pH

Meal

Threshold for enzyme inactivation

Pancreatic insufficiency

Health

Minutes postprandial
Gastric Emptying in CP

Volume emptied (ml/10 min)

Time, min

Health
Pancreatic insufficiency
Mechanisms of Fat Malabsorption

- *Pancreatic insufficiency*
- Bile salt insufficiency
- Small intestinal bacterial overgrowth
- Reduced absorptive area
- Defects in enterocyte function
- Diseases of the lymph system
Mechanisms of CH Malabsorption

- Disaccharidase defect
- Reduced absorptive area
- Defects in enterocyte function
- Pancreatic insufficiency
Mechanismen der Protein Malabsorption

- Reduced absorptive area
- Defects in enterocyte function
- Pancreatic insufficiency
- Protein-losing enteropathy
Chronic Pancreatitis: Symptoms

- **Clinical Features**
  - Pain
  - Exocrine pancreatic insufficiency
  - Endocrine pancreatic insufficiency
Chronic Pancreatitis: Diagnosis

- Diagnosis: simple
  - History
  - Complaints
  - X-ray, lab studies
Clinical Presentation

- Abdominal pain - primary feature
  (15 – 25% CP may be painless)
- Malabsorption/steatorrhea – usually occurs when enzyme secretion < 10% of normal
- Diabetes
- Jaundice, ascites, or pleural effusions
Diagnosis

- Frequently made by history alone
  - e.g. an alcoholic with recurrent attacks
- Plain abdominal X-ray - calcification in ~30%
  - diagnostic in clinically suspected patients
“Screening” Tests

- **Blood tests**
  - Blood count
  - Electrolytes, Mg, Phos, Ca
  - Albumin, Protein
  - Vitamin B12, Folate, Iron
  - Liver tests
  - Coagulation/INR, Cholesterol
  - Glucose, HbA1c
  - Beta-Carotin (?)

- **Stool tests**
  - Ova and Parasites
  - Stool fat
Stool fat **Quantitative**

- “Gold Standard” for Maldigestion

- 72 hrs collection optimal

- Normal < 7 gr/day

- Low importance in daily clinical life (stool collection, -analysis)
Chronic Pancreatitis: Imaging

- Histology
  - Fibrosis
  - Scattered foci of chronic inflammation
  - Ducts & islets of Langerhans persist
  - Calcifications
Imaging Modalities

- **Abdominal ultrasound**
  Dilated pancreatic duct, calcifications, pseudocysts
  (often incomplete exam due to overlying bowel gas)

- **Abdominal CT**
  Dilated pancreatic duct, atrophy of pancreas, pseudocysts, calcifications
CT in chronic Pancreatitis
Imaging Modalities

- **ERCP**
  - Better test for defining the ductal changes - stricture, ductal irregularities
  - Not for obtaining parenchymal information
  - Provides therapeutics - dilation, stone extraction and stenting of duct

- **MRCP**
  - Imaging alternative for diagnostic purposes; secretin stimulation
Chronic pancreatitis
Imaging Modalities

- **EUS**
  - Duct & parenchyma – ductal dilatation, irregularities, pseudocysts, stones, calcifications, parenchymal scarring evidenced by heterogeneous echogenicity
  - Mass
  - Identify early changes of chronic pancreatitis
  - Overall ~ 85% accurate in chronic pancreatitis diagnosis
EUS: Chronic Pancreatitis
Pancreatic Function Tests

**Indirect tests**

- Stool tests (Elastase)
- Stool fat
- Breath tests etc.

**Direct tests**

Examination of pancreatic secretory responses
Why pancreatic function tests?

Pancreatic function tests should be performed if:

- Diagnosis of CP is suspected and
- Imaging tests normal or inconclusive
Indications for pancreatic function tests

- Characterization of pancreatic function in suspected pancreatic disease
- Differential diagnosis in malabsorption
- Assessment of adequacy of pancreatic enzyme replacement therapy
Invasive tests are the "Goldstandard", but are they necessary?
Requirements for Invasive Pancreatic Function Tests

- Oro-duodenal intubation
- Exogenous hormones (Secretin, Caerulein, CCK)
- Expertise!
- Time! (PFTs are time consuming and expensive)
Should a marker be employed?

- Nonabsorbable marker perfused to the duodenum (e.g., Polyethylene glycol, PEG 4000)

- Precise quantification of pancreatic enzyme output/bicarbonate output
What type of stimulation should be used?

- Hormones (Secretin, CCK/Caerulein)?
- Meals?
Sensitivity and specificity of invasive PFTs

90% sensitivity and 90% specificity for detecting CP with hormonal stimuli

Di Magno, N Engl J Med 1973
Lankisch, Gut 1982
Di Magno, Exocrine Pancreas 1993
Secretin or secretin plus CCK?

- Secretin → Bicarbonate Output
- CCK → Enzyme Output
Problems associated with enzyme measurements

- Use/nonuse of a nonabsorbable marker
- Collection of duodenal samples
- Methods used to analyze enzyme concentrations (standardization has been extremely difficult)
Problems associated with stimuli

- Stimulation of pancreatic function with secretin/CCK = "Goldstandard"

- Stimulation with meals/nutrients less specific

  (they depend on adequate pancreatic stimulation) e.g. Celiac Disease

Regan, Gastroenterology 1980
Lamers, Gastroenterology 1983
Normal Ranges of invasive PFTs-1

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<tr>
<td>Volume (ml)</td>
<td>117 - 392</td>
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<tr>
<td>Bicarbonate Concentration (mEq/l)</td>
<td>88 - 137</td>
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<tr>
<td>Bicarbonate Output (mEq/l)</td>
<td>16 - 33</td>
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Dreiling and Hollander 1950
Normal Ranges in Secretin-Test in Basel

Bicarbonate Concentration
(mmol/L) > 70

Bicarbonate Output
(mmol/hr) > 12
Personal assessment of invasive PFTs

1. Determination of bicarbonate concentration is sufficient

2. Bicarbonate output determination does not add any additional pertinent information

3. Quantification of enzymes is not necessary
Why pancreatic function tests?

Pancreatic function tests should be performed if:

- Diagnosis of CP is suspected and
- Imaging tests normal or inconclusive
Rapid Endoscopic PFT

- Standard endoscopy under sedation
- IV secretin (0.2 microgr/kg)
- Endoscopic fluid collection (0, 15, 30, 45 and 60 min)
- Fluid analysis for bicarbonate conc

Conwell et al 2003; Stevens et al. 2006
Standard vs Endoscopic PFT

Standard vs Endoscopic PFT

Conclusion from Authors

- Simple test, safe
- Can be performed during endoscopy
Rapid Endoscopic PFT - 2

- Standard endoscopy under sedation
- IV secretin (1 CU/kg)
- Endoscopic fluid collection for 10 min
- Fluid analysis for bicarb and enzyme conc

Raimondo M et al 2003; Clin Gastroenterol Hepatol
Patient groups

- Chronic pancreatitis (N=72)
- Patients with normal pancreas (N=117)
Overall accuracy of endoscopic PFT

- 79%

(negative PV 85%, positive PV 73%)
That's all, folks!