Diagnosing Pancreatic Disease: Help from the Laboratory

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University of Utah CME Statement

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- This speaker has nothing to disclose.
Objectives

1. Diagram basic gross and microscopic pancreatic anatomy

2. Given classic patient scenarios, compare and contrast pancreatic cancer and acute pancreatitis

3. When encountering a screening test in the lab, be able to evaluate advantages and disadvantages of the screening tests

4. List commonly used serum biomarkers for evaluating pancreatic disease
FIRST
Let’s do a quick review:

Anatomy
Histology
Physiology
Major duodenal papilla = Ampulla of Vater, Sphincter of Oddi
Normal Pancreatic Histology

- Intercalated Duct
- Islet of Langerhans
- Acinar Cells

http://www.surgpath4u.com
Conduit for acinar cell secretions:
Acinar lumen → intercalated ducts → interlobular ducts → main PD

http://www.hopkins-gi.org
Normal Pancreatic Exocrine Histology
Pancreatic Exocrine Function

- Presence of acid in duodenum cause release of Secretin
- Presence of fats in duodenum cause release of Cholecystokinin
- Vagal Stimulation cause release of pancreatic enzymes
- Secretin causes release of Bicarbonate secretions
- CCK causes secretion of Enzymes

Frank Boumphrey M.D. 2009

http://en.wikibooks.org
### Pancreatic Exocrine Digestive Function

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Enzyme</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates and Starch</td>
<td>Amylase</td>
<td>Saccharides</td>
</tr>
<tr>
<td>Fats</td>
<td>Lipase and Colipase</td>
<td>Triglycerides</td>
</tr>
<tr>
<td>Proteins</td>
<td>Trypsin (trypsinogen)</td>
<td>Peptides</td>
</tr>
<tr>
<td></td>
<td>Chymotrypsin (chymotrypsinogen)</td>
<td>Peptides</td>
</tr>
</tbody>
</table>
Done with the review:
What could possibly go wrong?
Case #1

• 48-year-old female presents to her primary care physician complaining of severe pain in her upper abdomen
  – Pain radiates to back
  – Present for the past 30 minutes
• Medical history: gallstones and obesity
• Family History: Not significant
• Social History: Negative tobacco and alcohol
• Review of Systems: Nausea, low grade fever
Case #1

• Physical Exam:
  – Abdominal tenderness and guarding
  – Decreased bowel sounds

• Labs:
  – Amylase- 6x upper limit normal
  – Lipase- 10x upper limit normal
DIAGNOSIS?

ACUTE PANCREATITIS
Acute Pancreatitis Pathogenesis

Mechanism - Auto Digestion

Co-localization of lysosomal proteases

Trypsinogen is activated to trypsin

Extensive inflammatory response

Intrapancreatic and Extrapancreatic

http://www.hopkins-gi.org
Causes Acute Pancreatitis

Gallstones: Duct obstruction, Reflux of bile
Causes Acute Pancreatitis

Alcohol: Toxic metabolites, sphincter dysmotility

Abnormal sphincter of Oddi motility

Toxic and metabolic effects

Small duct obstruction

http://www.hopkins-gi.org
Causes Acute Pancreatitis

**Medications:**
- Azathioprine
- 6-Mercaptopurine
- Bactrim (TMP-SMX)
- Pentamidine
- Dideoxyinosine (ddI)
- Methyldopa

**Miscellaneous:**
- Triglycerides > 1,000 mg/dL
- Hypercalcemia
- Organophosphates
- Infection (Mumps, Ascaris)
- Cystic Fibrosis
- Trauma
- Scorpion sting
Causes Acute Pancreatitis

Idiopathic: Probable Microlithiasis (small stones)
Acute Pancreatitis

- Pancreatitis ranges from mild (inflammatory process and edema) to severe (necrotic process and secondary extra pancreatic injury)

Normal Histology

[Images of normal histology]
How could we diagnose our patient so quickly?

Severe abdominal pain

Elevated serum amylase & lipase levels

Initial diagnosis of acute pancreatitis
USEFUL LAB TEST: Amylase
Amylase

- Amylases are glycoside hydrolases
  - Alpha amylase
    - Ca^{2+} metalloenzyme (unable to function in absence of Ca^{2+})
    - Acts at random locations along a starch chain, yielding:
      - Maltotriose, maltose and limit dextrin from amylose
      - Maltose, glucose and limit dextrin from amyllopectin

[Chemical structures of starch, maltose, glucose, etc.]
Amylase Sources/ Activators

• Salivary
  – S-amylase

• Pancreatic
  – P-amylase

• CALCIUM AND

• Chloride

http://embryology.med.unsw.edu
http://leavingbio.net
www.wikipedia.org
Amylase

- Plasma enzyme found in the urine (small molecule- 54,000- 62,000 MW)
- Magnitude of elevation not correlated to severity
- Magnitude of elevation = greater probability acute pancreatitis
Should serum pancreatic lipase replace serum amylase as a biomarker of acute pancreatitis?

Smith et al 2006
## Causes of Increased Amylase

False positive test if looking for acute pancreatitis

Lack of specificity for total AMY

<table>
<thead>
<tr>
<th>Pancreatic Disease</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Pancreatitis (P-AMY)</td>
<td>Pancreatic Trauma (P-AMY)</td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Intraabdominal Disease</th>
<th></th>
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<tbody>
<tr>
<td>Biliary Tract Disease (P-AMY)</td>
<td>Intestinal Obstruction (P-AMY)</td>
<td>Mesenteric Infarction (P-AMY)</td>
<td>Perforated peptic ulcer (P-AMY)</td>
</tr>
<tr>
<td>Gastritis, Duodenitis (P-AMY)</td>
<td>Ruptured Aortic Aneurysm</td>
<td>Acute Appendicitis</td>
<td>Peritonitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Trauma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genitourinary Disease</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruptured Ectopic Pregnancy (S-AMY)</td>
<td>Salpingitis (S-AMY)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian Malignancy (S-AMY)</td>
<td>Renal Insufficiency (mixed)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Misc | | | |
| Salivary gland lesion, Acute alcoholic abuse, DKA, Macroamylasemia | | | |

Adapted from Teitz Textbook Ch 21 Enzymes
Macroamylasemia

- Complexes: amylase (usually S-type) and IgG or IgA

- Cannot filter through the glomeruli (MW > 200,000); ultrafiltration assay, decreased amylase to CrCl ratio (<1%), or urine amylase level

- No clinical symptoms associated

- 2.5% of hyperamylasemic patients and 1% of healthy subjects
Decreased Amylase

False Negatives:
Serum amylase may be normal (10% of cases)
Depleted acinar cell mass (necrosis)
Acute pancreatitis caused by high triglycerides
*Take note of lipemic samples*

Increase Sensitivity if use P-AMY, may be increased (in 80% of patients) up to 7-days post episode
Amylase Method

- Can measure substrate decrease viscometrically, turbidimetrically, nephelometrically, amyloclastically
- Saccharogenic and kinetic (spectrophotometric) measurements used more commonly now
  - Saccharogenic assays measure glucose production
- Kinetic method correlates with HPLC measurement

\[
\text{(\(\alpha\)-Amylase)} \\
5\text{ET-}G_7\text{PNP} + 5\text{H}_2\text{O} \rightarrow 2\text{ET-}G_5 + 2\text{ET-}G_4 + \text{ET-}G_3 + 2\text{G}_2\text{PNP} + 2\text{G}_3\text{PNP} + \text{G}_4\text{PNP}
\]

\[
\text{(\(\alpha\)-Glucosidase)} \\
\text{G}_2, \text{G}_3, \text{G}_4\text{-PNP} + 14\text{H}_2\text{O} \rightarrow \text{p-nitrophenol} + 14\text{G}
\]

ET = ethylidene  
G = glucose  
PNP = p-nitrophenol

Measure absorbance increase at 405 nm
Measuring P-Amylase Activity

Inhibit S-AMY with monoclonal antibodies

\[(\alpha\text{-Amylase})\]
\[
5\text{ET-}G_7\text{PNP} + 5\ H_2\text{O} \rightarrow 2\ \text{ET-}G_5 + 2\ \text{ET-}G_4 + \text{ET-}G_3 + 2\ G_2\text{PNP} + 2\ G_3\text{PNP} + G_4\text{PNP}
\]

\[(\alpha\text{-Glucosidase})\]
\[
G_2, G_3, G_4\text{-PNP} + 14\ H_2\text{O} \rightarrow \text{p-nitrophenol} + 14\ G
\]
USEFUL LAB TEST:

Lipase
Human Pancreatic Lipase (HPL)

- Lipases are a subclass of the esterases; hydrolyze triglyceride substrates to monoglycerides and FFA

\[
\text{Triacylglycerol} + 2 \text{H}_2\text{O} \rightleftharpoons 2\text{-monoacylglycerol} + 2\text{fatty acid anions}
\]

- Activated Ternary Complex
  - Lipase
  - Bile Salt Micelle
  - Colipase
Concentrations remain elevated longer than amylase.
Magnitude of elevation not correlated to severity.
Should serum pancreatic lipase replace serum amylase as a biomarker of acute pancreatitis?
Smith et al 2006
Lipase

- Sensitivity and Specificity are 80-100% depending on patient population and diagnostic cutoff
- Increased if use guideline- likely acute pancreatitis if >5x upper limit of reference range
- False positives: Obstruction of duct (carcinoma), reduced glomerular filtration rate, Opiates (cause sphincter of Oddi to contract)
Lipase Activity: Laboratory Measurement

- Enzymatic method
- Cleavage of chromogenic lipase substrate emulsified with bile acid and colipase in alkaline medium
- Rate of color is directly proportional

1,2-O-dilauryl-rac-glycerol-3-glutaric acid-(6-methylresorufin) ester

1,2-O-dilauryl-rac-glycerol + glutaric acid-(6-methylresorufin) ester

Spontaneous decomposition

Red dye measured at 570 nm

Reference ranges = 16 – 63 IU/L
Diagnosis: Acute Pancreatitis

Thank you Dr. Straseski

ER patients- Point of diagnostic threshold: Amylase set at 143 U/L with a sn of 0.690 and a sp of 0.966; Lipase set at 208 U/L where the sn was 0.861 and a sp of 0.936.

Should serum pancreatic lipase replace serum amylase as a biomarker of acute pancreatitis? Smith et al 2006
Review ROC curves, con’t

PERFECT TEST

USELESS TEST

sensitivity

1 - specificity
Review ROC curves, con’t

AUC: Increased Area = Better Test

PERFECT TEST

1.0 or 100% or the Area is filled

sensitivity

1 - specificity

P(TP)

P(FP)

AUC: Increased Area = Better Test
Receiver operator characteristic (ROC) curve

Area Under Curve:
Amylase 0.906
Lipase 0.948

ER patients- Point of diagnostic threshold: Amylase set at 143 U/L with a sn of 0.690 and a sp of 0.966; Lipase set at 208 U/L where the sn was 0.861 and a sp of 0.936.

Should serum pancreatic lipase replace serum amylase as a biomarker of acute pancreatitis? Smith et al 2006
Amylase vs. Lipase Guidelines

“...not necessary to measure both ...lipase may be preferable ...serum lipase is thought to be more sensitive and specific ...in the diagnosis of acute pancreatitis.”  -Banks et al. American GI Society and American College of Gastroenterology (2006)

Although amylase is widely available and provides acceptable accuracy of diagnosis, where lipase is available it is preferred for the diagnosis of acute pancreatitis (recommendation grade A)“ - UK GI Party
Acute Pancreatitis

Other Factors Contributing to the Diagnosis/ Risk:

Imaging
Additional Labs
## Risk Assessment

### Ranson’s Criteria

<table>
<thead>
<tr>
<th>On Admission</th>
<th>Within 48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 55 years</td>
<td>Hematocrit decrease by &gt; 10%</td>
</tr>
<tr>
<td>WBC &gt; 16,000 mm³</td>
<td>Urea Nitrogen increase &gt; 5 mg/dl</td>
</tr>
<tr>
<td>LDH &gt; 350 U/L</td>
<td>Serum calcium &lt; 8 mg/dl</td>
</tr>
<tr>
<td>Glucose &gt; 200 mg/dl</td>
<td>Arterial PO₂ &lt; 60 mm Hg</td>
</tr>
<tr>
<td>AST &gt; 250 U/L</td>
<td>Base deficit &gt; 4 mmol/L</td>
</tr>
<tr>
<td></td>
<td>Estimated fluid sequestration &gt; 6 L</td>
</tr>
</tbody>
</table>

### APACHE III Criteria (Acute Physiology and Chronic Health Eval.)

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Arterial pH</th>
<th>Leukocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BP</td>
<td>Sodium/Potassium</td>
<td>Hematocrit</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>Glucose</td>
<td>Albumin</td>
</tr>
<tr>
<td>Respiratory Rate</td>
<td>Creatinine</td>
<td>Bilirubin</td>
</tr>
<tr>
<td>Oxygenation</td>
<td>BUN</td>
<td>Age</td>
</tr>
</tbody>
</table>
# Mortality in Acute Pancreatitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Median (%)</th>
<th>Range (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>5</td>
<td>2–9</td>
</tr>
<tr>
<td>Interstitial pancreatitis</td>
<td>3</td>
<td>1–7</td>
</tr>
<tr>
<td>Necrotizing pancreatitis</td>
<td>17</td>
<td>8–39</td>
</tr>
<tr>
<td>Infected necrosis</td>
<td>30</td>
<td>14–62</td>
</tr>
<tr>
<td>Sterile necrosis</td>
<td>12</td>
<td>2–44</td>
</tr>
</tbody>
</table>
Treatment

• Aggressive Intravenous Fluids
• Nil per os (“NPO”) = Nothing by mouth
• Parenteral Narcotics
• +/- Antibiotics (necrotizing pancreatitis)
• Transfer to ICU
• Look for Etiology
Pearls of Wisdom

Acute Pancreatitis

- Alcohol and Gallstones account for majority of cases
- Amylase greater than 3x upper limit of ref range
- Lipase greater sensitivity and specificity
- False positives exist for elevated levels of enzymes
Case #2

- 61-year-old male presents to his primary care physician complaining of gradually increasing pain in his upper abdomen
  - Pain radiates to his back
- Medical history is significant for Hypertension
- Family History: Not significant
- Social History: (+) tobacco
- Review of Systems: weight loss; several week history of “painless jaundice” prior to pain starting
Case #2

- Physical Exam (Pertinent Positives):
  - Icteric sclera
  - Palpable left supraclavicular lymph (Virchow’s) node

- Lab
  - Amylase and Lipase 1.5x the upper limit of normal

- Imaging
  - Pancreatic Protocol CT scan
Lymph Node

A: 59.5mm

B: 28.8mm
Biopsy via Endoscopic Ultrasound guided Fine Needle Aspiration
Biopsy via EUS guided FNA
Normal Pancreas

Pancreas is near the duodenum, liver, transverse colon, stomach, spleen, and kidneys

Acinar cells

Ductal cells
Necrosis
“Drunken Honeycomb”
Nuclear Pleomorphism

Nuclear Anisonucleosis

Clumped Chromatin
DIAGNOSIS?

PANCREATIC DUCTAL ADENOCARCINOMA
Pancreatic Ductal Adenocarcinoma (PDAC)

- 43,140 people are diagnosed annually in US
  - incidence 10–12 per 100,000 people

- Mortality rate of 36,800/year in US

- Mortality rate 227,000/year in World

- 4th on the list of cancer related causes of death

- 5 year survival rate is <5%
Wasif N, Ko CY, Farrell J, Wainberg Z, Hines OJ, Reber H, Tomlinson JS. Impact of tumor grade on prognosis in pancreatic cancer: should we include grade in AJCC staging?
WHO 2004 Data (incidence per 100,000)
## Estimated New Cases*

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>217,730</td>
<td>207,090</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>116,750</td>
<td>105,770</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>72,090</td>
<td>70,480</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>52,760</td>
<td>43,470</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>38,870</td>
<td>33,930</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>35,380</td>
<td>30,160</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>35,370</td>
<td>29,260</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>25,420</td>
<td>22,870</td>
</tr>
<tr>
<td>Leukemia</td>
<td>24,690</td>
<td>21,880</td>
</tr>
<tr>
<td>Pancreas</td>
<td>21,370</td>
<td>21,770</td>
</tr>
<tr>
<td>All Sites</td>
<td>789,620</td>
<td>739,940</td>
</tr>
</tbody>
</table>

*Ahmedin Jemal, DVM, PhD et al, Cancer Statistics, 2010*
<table>
<thead>
<tr>
<th>Disease</th>
<th>Males</th>
<th>Females</th>
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</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>86,220</td>
<td>71,080</td>
</tr>
<tr>
<td>Prostate</td>
<td>32,050</td>
<td>39,840</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>26,580</td>
<td>24,790</td>
</tr>
<tr>
<td><strong>Pancreas</strong></td>
<td><strong>18,770</strong></td>
<td><strong>18,030</strong></td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>12,720</td>
<td>13,850</td>
</tr>
<tr>
<td>Leukemia</td>
<td>12,660</td>
<td>9,500</td>
</tr>
<tr>
<td>Esophagus</td>
<td>11,650</td>
<td>9,180</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>10,710</td>
<td>7,950</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>10,410</td>
<td>6,190</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>8,210</td>
<td>5,720</td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
<td><strong>299,200</strong></td>
<td><strong>270,290</strong></td>
</tr>
</tbody>
</table>

PDAC: Implicated Factors

- Smoking (2.5-3.6 x increase risk)
- Family history, a pair of first-degree relatives = familial
- History of chronic pancreatitis, EtOH
- Advancing age
- Male sex
- Diabetes mellitus
- Obesity
- Non-O blood group
- Occupational exposures (eg chlorinated hydrocarbon solvents and nickel)
- African-American ethnicity
- Diet, high fat/high meat and low in vegetables and folate
- Possibly *Helicobacter pylori* infection
- Possibly periodontal disease
Becoming Cancer

Ottenhof NA et al. Molecular characteristics of pancreatic ductal adenocarcinoma
PDAC Pathophysiology

Precursors: PanINs, MCNs, and IPMNs

Vincent A et al, Pancreatic cancer
Molecular Features of PDAC

MORE THAN A DECADE TO PROGRESS... a guess
(creating a window for possible early detection)

Ottenhof NA et al. Molecular characteristics of pancreatic ductal adenocarcinoma
IF WE CAN DETECT DISEASE FOR DIAGNOSIS
IS THERE EFFECTIVE TREATMENT?
LEAD TIME BIAS

- Early-stage pancreatic cancer is usually clinically silent
- Disease becomes apparent after the tumor invades surrounding tissues or metastasizes to distant organs – 80% of the time has already metastasized
IF WE CAN DETECT DISEASE FOR DIAGNOSIS
IS THERE EFFECTIVE TREATMENT?
LEAD TIME BIAS

- Early-stage pancreatic cancer is usually clinically silent
- Disease becomes apparent after the tumor invades surrounding tissues or metastasizes to distant organs
World Health Organization — Principles of Screening (1968)

1. The condition should be an important health problem.
2. There should be a latent stage of the disease.
3. There should be a test or examination for the condition.
4. There should be a treatment for the condition.
5. There should be an agreed policy on whom to treat.
6. Facilities for diagnosis and treatment should be available.
7. The test should be acceptable to the population.
8. The natural history of the disease should be adequately understood.
9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
10. Case-finding should be a continuous process, not just a "once and for all" project.
What Makes a Good Screening Test?

An ideal screening test for early pancreatic cancer would be a highly accurate (high sensitivity and specificity) marker that could be measured fairly non-invasively (blood, urine) in general population.

Unfortunately, none to date have proven sufficiently specific.

Nothing promising yet, lots of research being done. Proteins, aberrantly methylated DNA, autoantibodies, aberrantly glycosylated molecules, microRNAs.
### Screening those with familial risk

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Germline Mutations</th>
<th>Relative Risk PDAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial Atypical Multiple Melanoma and Mole Syndrome</td>
<td>CDKN2A</td>
<td>20-34</td>
</tr>
<tr>
<td>Peutz-Jeghers Syndrome</td>
<td>LKB1</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Hereditary pancreatitis</td>
<td>PRSS1/SPINK1</td>
<td>90</td>
</tr>
<tr>
<td>Familial Breast Cancer</td>
<td>BRCA 2</td>
<td>3-10</td>
</tr>
<tr>
<td>Lynch Syndrome</td>
<td>Mismatch repair</td>
<td>unknown</td>
</tr>
</tbody>
</table>

- **Families with mutated susceptibility genes**
  - Do NOT manifest a high penetrance of PDAC
  - Unexplained, Under reported, Underused
- **Consensus guidelines have not been established for genetic testing of those at risk for inherited PDAC**
Cancer of the Pancreas Screening Study (CAPS)- Imaging and DNA studies

• Multi-center, translational prospective controlled cohort study in **high risk patients**

• Pancreatic cystic lesions were detected more frequently with endoscopic ultrasound (93%) and MRI (81%) than with CT (27%)
  – Best sampled by EUS-FNA

• PanINs are usually not visible by imaging, research is attempting to identify markers in pancreatic fluid that could reliably identify high-grade PanINs
We need better screening tests

• <20% of patients qualify for surgical resection at diagnosis

• Surgical resection—only treatment to improve five-year survival rates
  – < 4% to 25–30%

• Chemo(radiation) therapy administered in (neo)adjuvant setting
We have no good screening tests.

What about tumor markers?
What is a tumor biomarker

- Levels increase with disease
- Lacks sensitivity/specificity for diagnosis
- Used to monitor
  - treatment
  - progression
  - recurrence
- Not acute phase reactants
  - SAA, ICAM-1, CRP, osteoprotegerin
Carcinoembryonic Antigen (CEA)

Glycoprotein involved in cell adhesion
Produced during fetal life; decreases prior to birth

Can Measure in Serum or in Cyst Fluid

http://en.wikipedia.org
Carcinoembryonic Antigen (CEA) CYST

Increased levels indicative of a mucinous cyst (does not distinguish benign from malignant)

ARUP- “body fluid” specimen category-off label

<table>
<thead>
<tr>
<th>TUMOR MARKER</th>
<th>NON MUCINOUS CYST</th>
<th>MUCINOUS CYST</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>Not Elevated</td>
<td>Elevated</td>
</tr>
</tbody>
</table>
# Carcinoembryonic Antigen (CEA)

## SERUM

<table>
<thead>
<tr>
<th>ELEVATED LEVEL = MALIGNANT</th>
<th>ELEVATED LEVEL = BENIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal Carcinoma</td>
<td>Ulcerative Colitis</td>
</tr>
<tr>
<td>Gastric Carcinoma</td>
<td>Crohn’s Disease</td>
</tr>
<tr>
<td>Pancreatic Carcinoma</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Lung Carcinoma</td>
<td>COPD</td>
</tr>
<tr>
<td>Breast Carcinoma</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Medullary Thyroid Carcinoma</td>
<td>Smokers</td>
</tr>
</tbody>
</table>
Carbohydrate or Cancer Antigen (CA 19-9)

• False (+): Increased in colorectal cancer, esophageal cancer, hepatocellular carcinoma, pancreatitis, cirrhosis, and diseases or obstruction of the bile ducts.

• False (-): CA 19-9 is sialylated Lewis (a) antigen (adsorbed RBC antigens)
  – 10% of the Caucasian population lacks the Lewis antigen (deficiency of a fucosyltransferase) = CA19-9 is not expressed
Carbohydrate or Cancer Antigen (CA 19-9)

- Preoperative amounts of carbohydrate antigen 19-9 (CA19-9) of more than 100–200 U/mL predict unresectability

- Biliary drainage lowers nonspecific CA19-9 amounts, allowing for more reliable estimate of disease burden
Treatment - pancreaticoduodenectomy

“WHIPPLE”
## Staging of PDAC

<table>
<thead>
<tr>
<th>Stage</th>
<th>Median Survival (mo)</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>24.1</td>
<td>Limited to pancreas, &lt;2 cm</td>
</tr>
<tr>
<td>IB</td>
<td>20.6</td>
<td>Limited to pancreas, &gt;2 cm</td>
</tr>
<tr>
<td>IIA</td>
<td>15.4</td>
<td>Locally invasive, no involvement celiac or SMA</td>
</tr>
<tr>
<td>IIB</td>
<td>12.7</td>
<td>Locally invasive, Lymph Node metastasis</td>
</tr>
<tr>
<td>III</td>
<td>10.6</td>
<td>Celiac axis or SMA involved (unresectable)</td>
</tr>
<tr>
<td>IV</td>
<td>4.5</td>
<td>Distant Metastasis (unresectable)</td>
</tr>
</tbody>
</table>
Wasif N, Ko CY, Farrell J, Wainberg Z, Hines OJ, Reber H, Tomlinson JS. Impact of tumor grade on prognosis in pancreatic cancer: should we include grade in AJCC staging?
Treatment

• Chemotherapy after resection - gemcitabine

• The addition of erlotinib (small molecule inhibitor of EGFR) or fluoropyrimidine have shown slight improvements of overall survival
  – Erlotinib - modest survival improvement and increased level of toxicity has limited the acceptance
Pearls of Wisdom

- Mortality rate is extremely high; few survivors
- Research on screening for PDAC should focus of **PRE** invasive lesions
- Tumor markers are not synonymous with screening tests
- Much Room for Improvement
  - Screening
  - Biomarkers
  - Treatment
Summary
Commonly used tests for diagnosing or evaluating pancreatic disease

Acute Pancreatitis
- Amylase and Lipase
- Imaging

Pancreatic Cancer
- No good screens (yet)
- EUS, cytopathology for diagnosis
- CEA, CA 19-9 for monitoring
- Imaging
References


References


