Margo Shoup, MD Associate Professor of Surgery Loyola University Medical Center

### Introduction

- 38,000 cases a year
- Risk factors
  - Smoking
  - Pancreatitis
    - Real risk, but only 5% of pancreatic cancer patients

### Genetics

- Tumor suppressor gene p53
- Mitogen activating gene k-ras
- COX-2
- VEGF

### Definitions

- Most common malignant pancreatic tumor is pancreatic ductal adenocarcinoma
- Difficult at diagnosis to determine etiology
  - Periampullary tumor
    - Pancreatic –65%
    - Distal bile duct
    - Ampulla
    - Duodenum
    - Islet cell

# Classification of pancreatic tumors

- Cystic tumors
  - Cystadenoma
    - Serous
    - Mucinous
    - Intraductal papillary mucinous
    - Solid and Pseudopapillary

## **Surgical Options**

- Enucleation
- Distal pancreatectomy with or without splenectomy
- Central pancreatectomy
- Ampullectomy
- Pancreaticoduodenectomy

# Classification of pancreatic tumors

- Malignant
  - Adenocarcinoma
    - Mucinous
    - Adenosquamous
    - Anaplastic
    - Duodenal/ampullary/distal bile duct
  - Cystadenocarcinoma
    - Mucinous
    - Intraductal papillary
  - Acinar
- Endocrine

### **Tumor Markers**

#### • CA 19-9

- Most commonly valued marker
- Not specific, high levels seen in benign disease
- Normalization following resection appears to be associated with improved outcome
- Rising level after resection is a marker of relapse
- Levels > 1500 correlate with unresectable tumors
- Not cost effective for screening

## **Clinical suspicion**

- Patients with pancreatic cancer commonly present with advanced disease
  - Head tumors proximity to vascular structures
  - Body and Tail metastatic disease
- Symptoms are nonspecific
  - Vague discomfort, dyspepsia, bloating
  - Jaundice
  - Weight loss, back pain usually a sign of advance disease
  - Significant back pain 9% resectability vs minimal back pain 31% resectability
  - New onset diabetes in patients over 60 should raise suspicion.

# Diagnosis

- History
  - Weight loss
  - Change in urine and stool
  - Gastric outlet symptoms
  - Back pain
- Physical
  - Jaundice
  - Cachectic
  - Palpable mass

### Work up

- CBC
- Liver function tests
- Hepatitis profile
- Hemolytic profile
- Ultrasound
- CT identify mass, evaluate vessel involvement
- ERCP double duct sign for head mass
- EUS If not sure if pancreatitis vs tumor

# **CT** Findings

- Adenocarcinoma
  - Irregular border
  - Not hypervascular
  - Pancreatic ductal dilatation
  - Distal pancreatic atrophy

#### Pancreatic adenocarcinoma



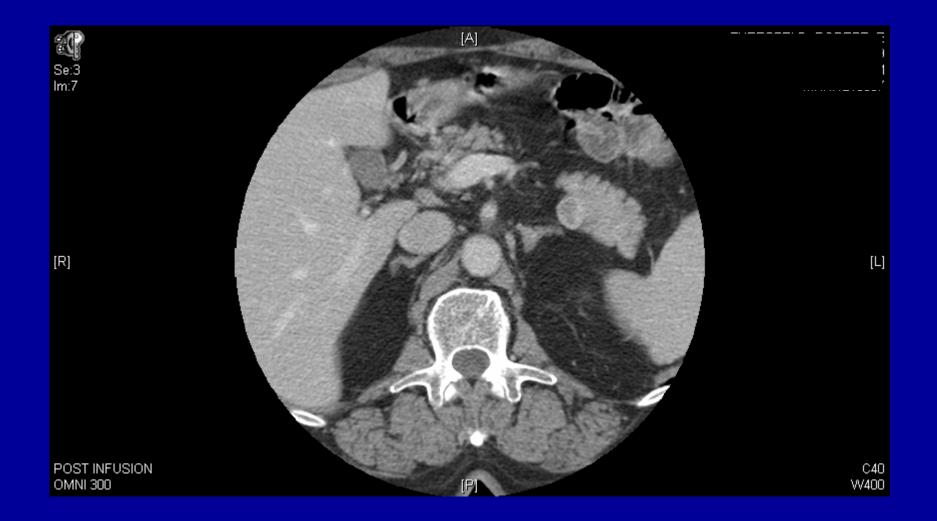
#### Pancreatic adenocarcinoma



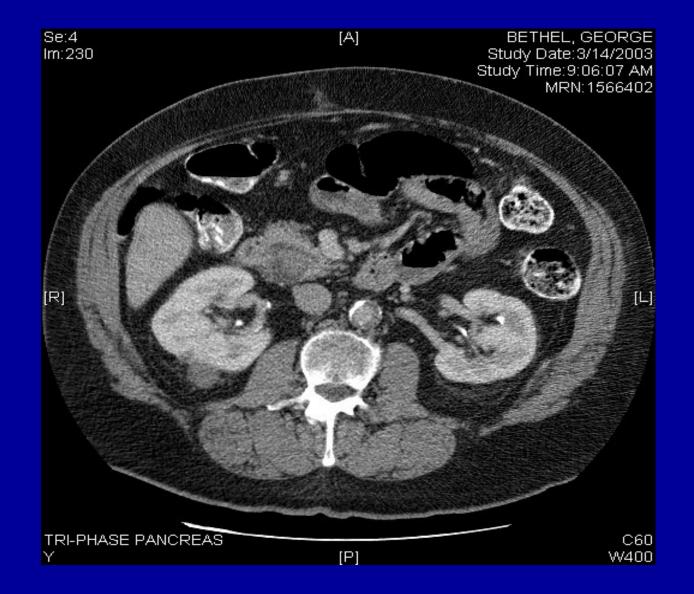
# **CT** Findings

- Neuroendocrine
  - Well circumscribed
  - Hypervascular
  - No atrophy
- Cystic
  - Appear fluid filled
  - Well circumscribed

#### Neuroendocrine Tumor



#### Intraductal papillary mucinous neoplasm



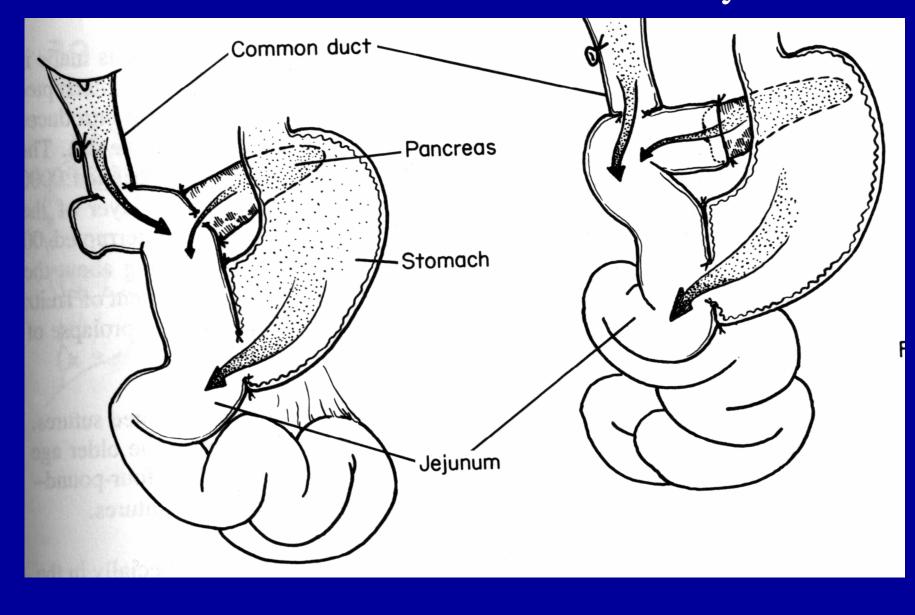
### ERCP

- Not usually necessary
- Often performed if seen by Gastroenterologists
- Necessary if biliary stent is needed
- Double duct sign
  - Strictured common bile duct and pancreatic duct
- Biopsy possible, not always needed

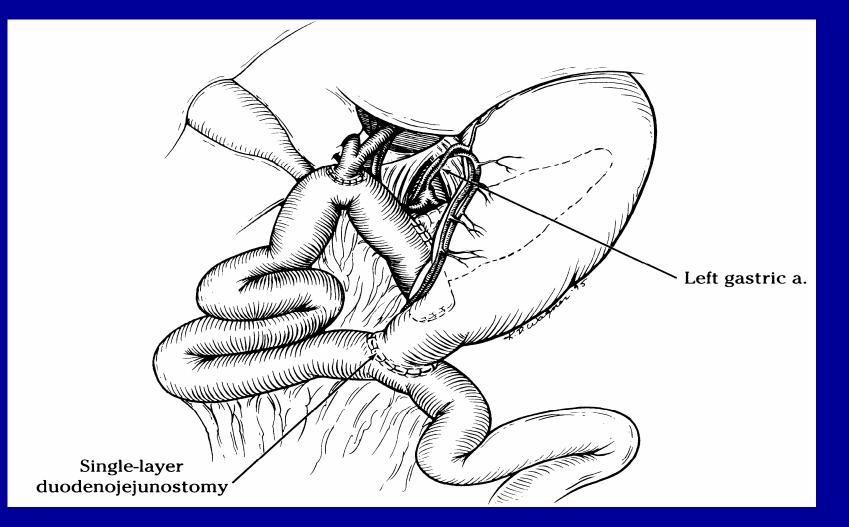
### **Treatment Options**

- Tissue diagnosis NOT NECESSARY
  - Unless surgery is not planned
- Potentially resectable tumors
  - Laparoscopy to rule out metastatic disease
  - Head tumors pancreaticoduodenectomy
    - Pancreatic head, distal common bile duct, duodenum, +/antrum, gallbladder
    - Pancreaticogastrostomy or jejunostomy, hepaticojejunostomy, gastrojejunostomy
  - Body or Tail tumors distal pancreatectomy with splenectomy

### Reconstruction Following Standard Pancreaticoduodenectomy



### Reconstruction Following Pylorus Preserving Pancreaticoduodenectomy



### Prognosis after surgery

- 1-3% perioperative mortality rate in the best hands (30-day or same admisstion mortality)
  Previously was 20%
- 5 year survival
  - Pancreas 10-15%
  - Bile Duct 15-20%
  - Duodenum 50%
  - Ampulla 35%
  - Islet cell -40%

### Adjuvant therapy

• Options for chemotherapy and radiotherapy

- Inconclusive evidence that CRT improves survival
- GITSG trial
- 43 patients randomized to CRT vs. no CRT
- CRT had improved survival
- Neoadjuvant therapy
  - Clinical trials

### Predictors of outcome

- Nodal status
- Size (< 2cm)
- Margin status

### Complications

- Pancreatic duct leak/fistula
  - Drain amylase level more than 3x serum
  - 10-20%
- Biliary leak/Gastrojejunostomy leak
  - Less common
- Delayed gastric emptying
- Pancreatitis
- Diabetes
- Dumping syndrome exocrine insufficiency

### Follow-up

- If patients are asymptomatic follow with physical exam and history
- If patients start to become symptomatic, obtain CT
  - Weight loss
  - Anorexia
  - Weakness
- Someone will order a CT sooner
  - Patients peace of mind
- What to do with results if a recurrence is noted?
  - Treatment with chemotherapy in the metastatic setting has not been shown to prolong life.

### Unresectable

- Majority of patients
- Locally advanced, not metastatic May receive chemotherapy with radiation.
  - A small number of patients will respond enough to become resectable.
  - Median Survival 4-5 months if metastatic
  - Median Survival 7-9 months if not metastatic
- Back pain can be palliated with celiac axis blockade alcohol injection

### Unresectable

- Metastatic disease treatment options limited to experimental medications and chemotherapy.
- Patients should have biliary stent placed by ERC (Endoscopic retrograde cholangiogram)
  - If unable to place stent due to technical difficulties, should have operative biliary bypass
  - Choledochojejunostomy, Hepaticojejunostomy, Cholecystojejunostomy
- If considering CRT need biopsy

### **Unresectable Disease**

#### • Biliary stents

- Plastic stent
  - Best if patient considered for surgery
  - 3- month longevity
  - Easily removed
- Metal "Wallstent"
  - Permanent
  - Lasts 6 months to a year
  - Difficult to remove surgically

# **Defining Non-resectability**

- Histologically confirmed hepatic, serosal, peritoneal or omental metastasis
- Celiac or high portal node involvement
- Tumor extension outside of pancreas
- Extensive portal vein involvement by tumor or invasion/encasement of celiac axis, hepatic artery, or superior mesenteric artery.

# Laparoscopically Detected Liver Metastasis



### Locally Advanced Tumors

- Considered candidates for chemoradiation if metastatic disease is not present.
- May be considered for subsequent surgical resection depending on the response to the chemoradiation.
- Patients with pancreatic adenocarcinoma metastatic to the liver or peritoneum are candidates for palliative chemotherapy, but not radiation.

### Locally Advanced Pancreatic Cancer

- Contemporary imaging modalities failed to detect metastatic disease in 37% of patients.
- Patients considered for protocols including radiation for locally advanced pancreatic cancer should be staged laparoscopically prior to initiating therapy.

### End of Life Issues

#### • Pancreatic cancer

- Almost as many people die each year from the disease as are diagnosed each year
- Pain/Back pain
  - Biggest issue
  - Control with celiac block, fentanyl patch
  - Palliative radiation
- Gastric outlet obstruction can be palliated by duodenal stent or gastric bypass (gastrojejunostomy)
- Patients with advanced disease should be referred to a hospice situation early

### End of Life

- Options for treatment vs no treatment
  - Chemotherapy disappointing
    - 5-FU, Gemcitabine, oxaliplatin
  - Quality of Life
- Radiation
  - Time consuming
  - 5 days a week for 6 weeks
  - Benefit not guaranteed

### End of Life

- Questions from patients
  - How much time do I have?
  - Will you still be my doctor?
  - How will I die?
  - What should I do now?

- 52 year old man noted to have icteric sclera and mild jaundice, no pain.
- H&P
- **PE**
- Labs
- Differential Diagnosis

#### • Ultrasound

- Dilated intra- and extra-hepatic bile ducts, no stones. Liver normal
- CT 3 cm mass in head of pancreas. No liver lesions. Dilated CBD and pancreatic duct (Double duct sign)
- Now what?

- 44 year old woman
- CT pancreatic head mass
- Multiple liver lesions
- Now what?

- 65 year old male had a screening CT scan at the mall showing a 2 cm mass in the tail of the pancreas.
- Asymptomatic
- Differential
- Work up
- Treatment

# Recommendations for Pancreatic Cancer

- Laparoscopic
  - Patients with resectable disease
  - No evidence of gastric outlet obstruction
  - Have biliary stent, or can receive biliary stent if needed
  - Patients with locally advanced tumors, no metastasis on imaging, considered for local therapy
- Open Exploration
  - Failed biliary stent
  - Gastric outlet obstruction