

ENDOCRINE and EXOCRINE PANCREAS

PA Fundamentals of Surgery



EMBRYOLOGY

- Pancreatic buds (dorsal/ventral) form in 12-15 mm fetus
- Islets appear in 54 mm fetus
- Endocrine/Exocrine cells
 - Neural crest (early theory)
 - Embryonic foregut endoderm (now generally accepted)

Anatomy

- Transverse retroperitoneal organ 18 cm long
- Head, Neck, Body and Tail
- Duct anatomy dependent on fusion of buds to form main duct and GI drainage
- 90% main duct drains into ampulla
- 10% - Pancreas divisum – ducts not fused – main duct thru accessory duct (Santorini)

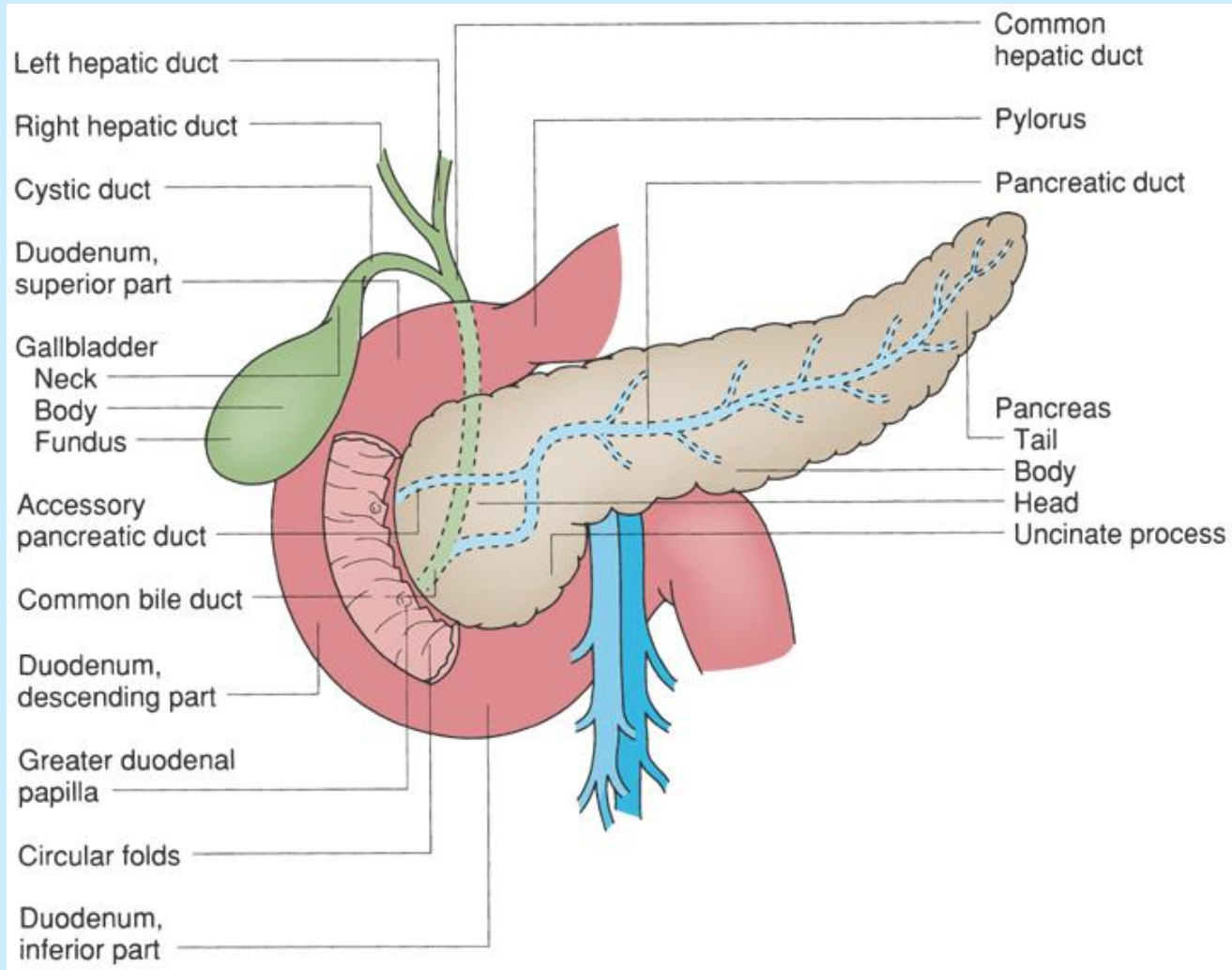


FIGURE 53.1 Relation of the pancreas to the duodenum and extrahepatic biliary system. (After Woodburne RT. *Essentials of human anatomy*. New York: Oxford University Press; 1973.)

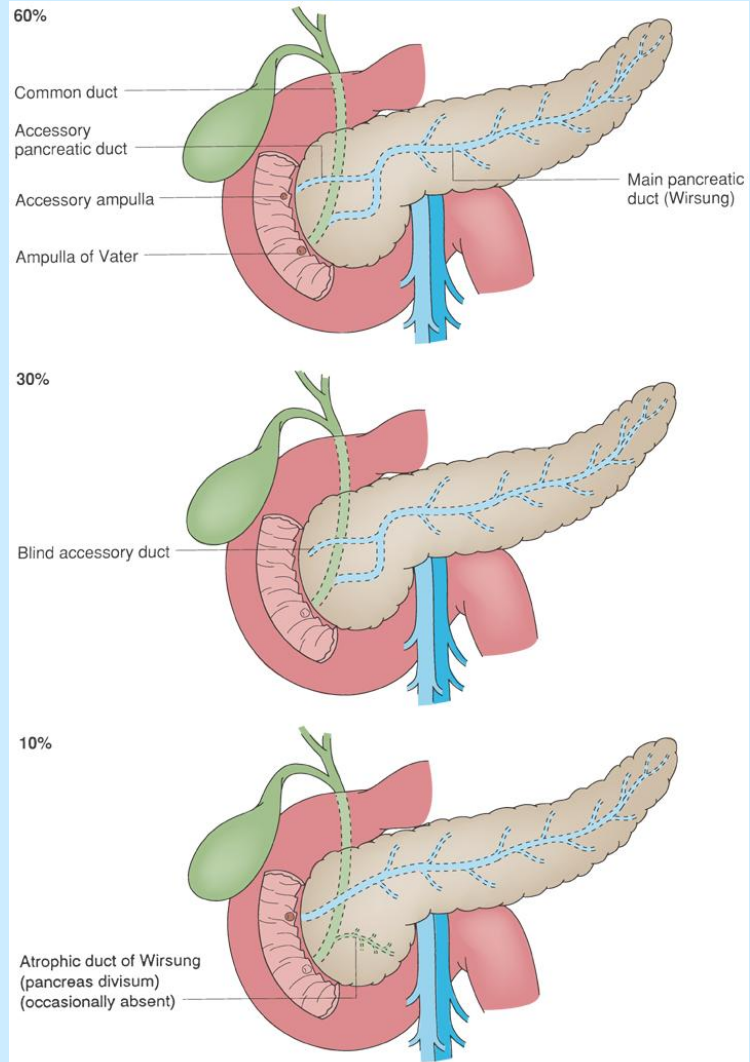


FIGURE 53.3 Anatomic configuration of the intrapancreatic ductal system. A lack of communication between the two ducts, which occurs in 10% of cases, is referred to as pancreas divisum. (After Silen W. Surgical anatomy of the pancreas. *Surg Clin North Am.* 1964;44:1253.)

Exocrine Function

- 1-2 liters alkaline fluid – elevated bicarb otherwise isotonic
- 20 enzymes or precursors
 - Amylase, lipase, trypsinogen, pepsinogen....
- Regulated by hormones
 - CCK
 - Peptides, AA and FFA
 - Secretin
 - Duodenal acid and CCK

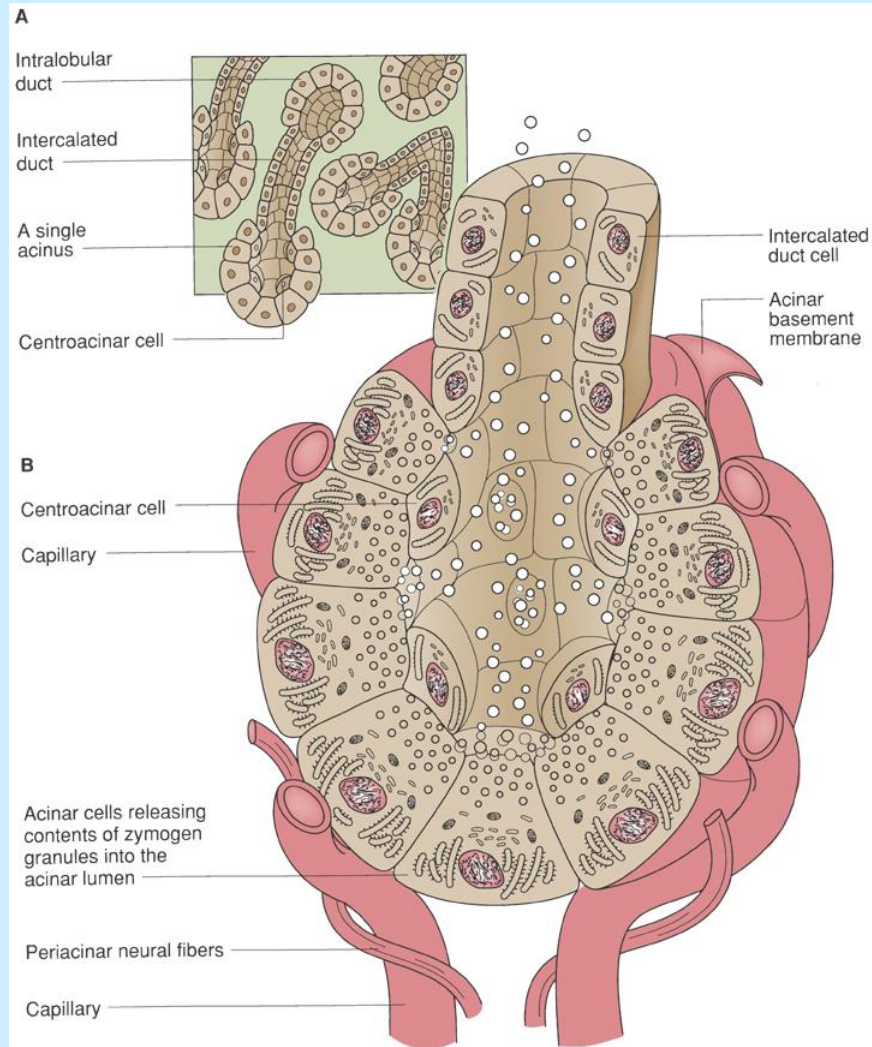


FIGURE 53.13 Histologic anatomy of the acinus. (A) Low-magnification view of a portion of the pancreas. (B) High-magnification view of a single acinus. (After Krstic RV. *Die Gewebes des Menschen und der Säugetiere*. Berlin: Springer-Verlag, 1978, with permission.)

ADULT PANCREAS

- Islet cells approx 2% of pancreatic mass (as opposed to 33% in mature fetus)
- 10^6 islets with 3000 cells/islet
- Four main cell types in islets
 - Alpha (periphery of islet)
 - Beta (center of islet)
 - Delta (periphery)
 - PP (periphery)
- Islets in:
 - Head/uncinate rich in PP cells, poor in Alpha cells
 - Body/tail rich in Alpha cells, poor in PP cells
 - Beta/Delta cells equally distributed

Physiology

INSULIN

- A and B side chains connected by disulfide bridge
- Joined by C-peptide in newly synthesized form (proinsulin)
- C-peptide cleaved in Beta cell, insulin stored in secretory granules
- Secreted insulin to portal system
 - 1/2 cleared by first pass through liver
- Incretins (stimulate insulin secretion):
Glucose, Gastric Inhibitory Peptide, CCK
- Inhibitors: somatostatin, pancreastatin, amylin, leptin
- Function: increase glc trans into cells

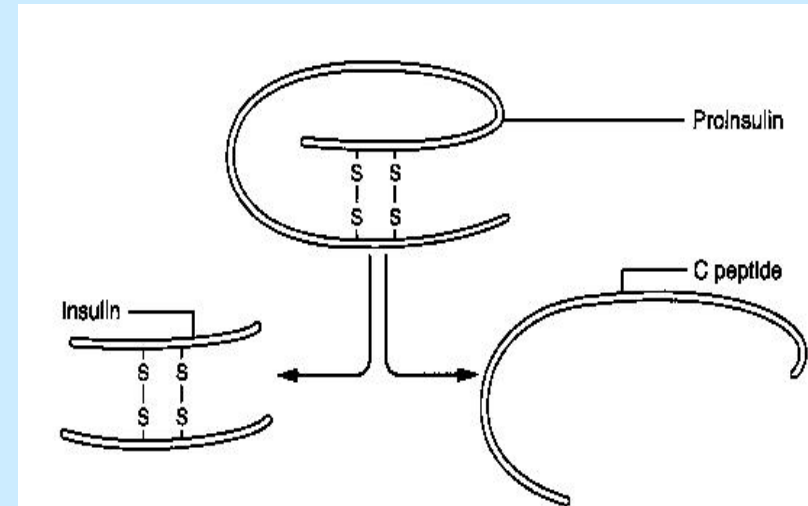


Figure 34-4. Diagram of insulin synthesis. Proinsulin, synthesized by the endoplasmic reticulum, is packaged within secretory granules of the B cell, where it is cleaved to insulin and C peptide. Equimolar amounts of insulin and C peptide are secreted to the bloodstream. (From Andersen DK, Brunicaudi FC: Pancreatic anatomy and physiology. In Greenfield LJ, Mulholland MW, Oldham KT, et al [eds]: *Surgery: Scientific Principles and Practice*, 2nd ed. Philadelphia, Lippincott-Raven, 1997, p. 869.)

PHYSIOLOGY

Glucagon

- 29 amino acid peptide secreted by Alpha cells
- Function: promote hepatic glycogenolysis
- Secretagogues: low blood Glucose, sympathetic stimulation
- Inhibitors: high blood Glucose, Insulin, Somatostatin

PHYSIOLOGY

SOMATOSTATIN

- 14 amino acid peptide secreted by Delta cells
- Universal hormonal “off switch”
- Unknown whether hormone modulation via simple paracrine effect or via transport to other islet cells via islet portovenous system

PHYSIOLOGY

PANCREATIC POLYPEPTIDE

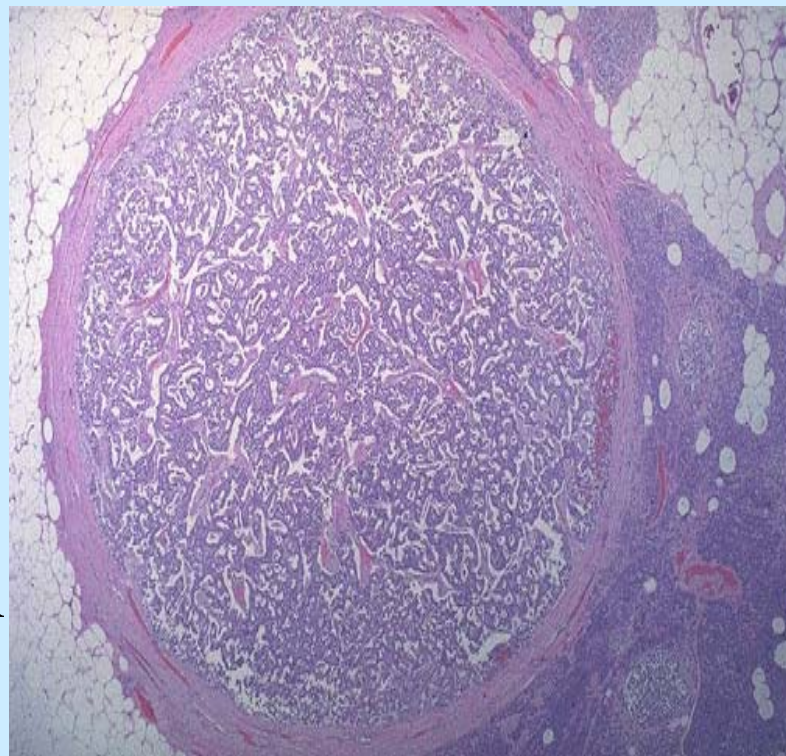
- 36 amino acid peptide secreted by PP cells (formerly known as F cells)
- Effects unknown
- Primarily seen as marker for other pancreatic endocrine tumors

PHYSIOLOGY

- VIP
 - Delta2 cells
 - Stimulates insulin, inhibits gastric secretions
 - Vasodilator/bronchodilator
- Amylin
 - Beta cells
 - Inhibits insulin secretion and uptake
- Pancreastatin
 - Part of chromogranin molecule found in envelope of secretory granules
 - Inhibits insulin secretion

Endocrine Neoplasms

- **Insulinoma**
- Arise from Beta cells
- Equally distributed throughout the pancreas
- 80% solitary and benign
- 15% malignant
- 5% associated with MEN-I, usually multiple



Endocrine Neoplasms (Insulinoma)

- Clinical Presentation - bizarre behaviour, memory lapse, unconsciousness, palpitations, nervousness, sweating, tachycardia
- Related to decreased cerebral glucose and activation of sympathetic nervous system

Endocrine Neoplasms (Insulinoma)

- *Whipple's Triad*
- 1) Hypoglycemic symptoms with fasting
- 2) Blood glucose below 50mg/dl during symptomatic episodes
- 3) Relief with glucose administration

Endocrine Neoplasms (Insulinoma)

- Fasting glucose - Patient fasted with blood samples q6hrs for glucose and insulin levels
- Ratio of insulin to glucose of > 0.3 is diagnostic
- Most are positive within 48hrs; test is carried out to 72hrs maximum
- Provocative testing: tolbutamide, leucine, arginine, calcium; diagnostic only 50% of the time

Endocrine Neoplasms (Insulinoma)

- **Treatment**
- Medical - frequent feedings with slowly absorbed carbohydrate, diazoxide (suppresses release of insulin), streptozocin if unresectable
- Surgical - enucleation, partial or distal pancreatectomy (up to 80%) if tumor is deep seated or cannot be localized, debulking if malignant

Endocrine Neoplasms (Insulinoma)

- **Pre - and intra-operative localization**
- CT scans - usually not seen as 40% < 1cm
- Selective angiography - 50% successful
- Percutaneous Transhepatic Venous Catheterization with sampling (hold diazoxide before testing)
- Intraoperative ultrasound

Endocrine Neoplasms

- **Gastrinoma**

- Most found in pancreas
- 60% non-beta islet cell carcinomas
- 25% solitary adenomas
- 10% microadenomas or hyperplasia
- 25% associated with MEN-I (usually multiple)
- Slow growing

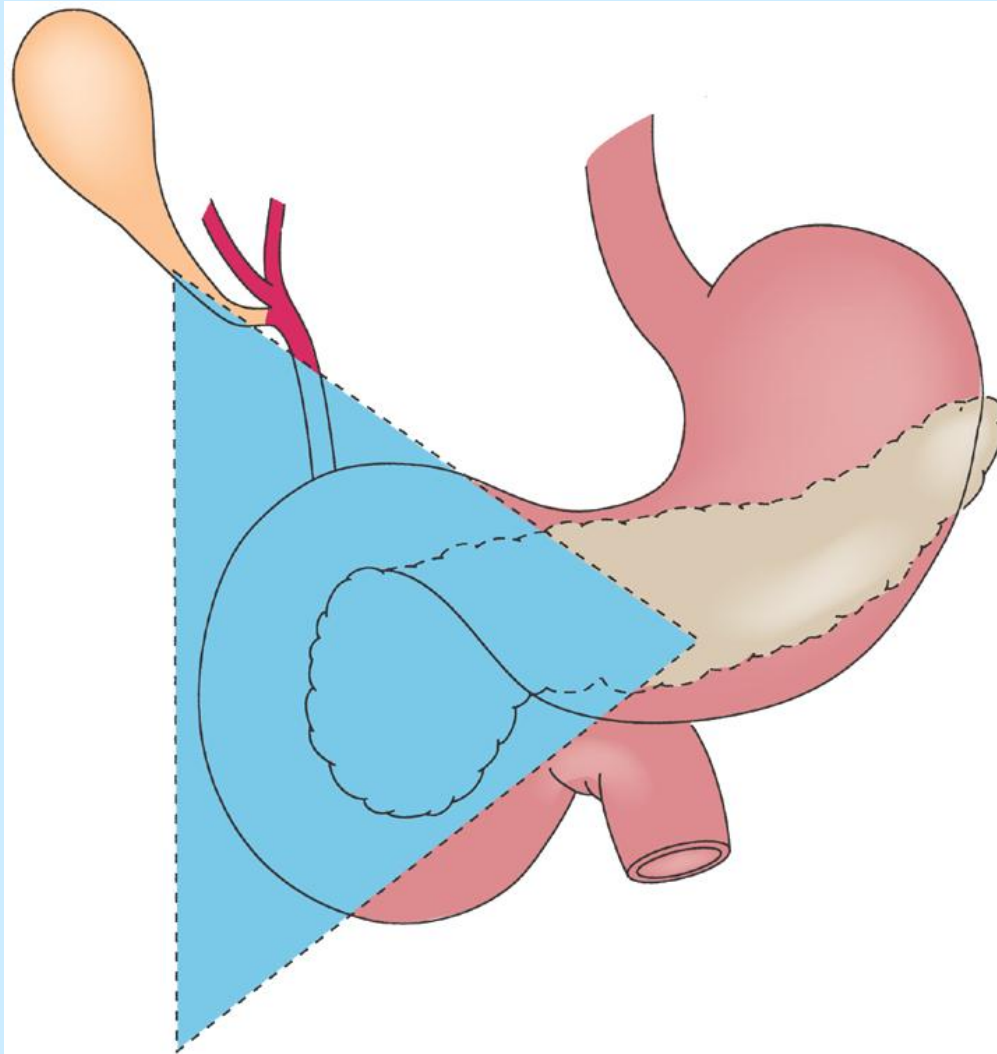


FIGURE 57.8 Most gastrinomas are found within the gastrinoma triangle. (After Stabile BE, Morrow DJ, Passaro E. The gastrinoma triangle: operative implications. *Am J Surg.* 1984;147:26, with permission.)

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Endocrine Neoplasms (Gastrinoma)

- **Clinical Manifestations**

- Zollinger-Ellison syndrome: severe, refractory peptic ulcer disease and diarrhea
- 5% present with diarrhea alone
- Multiple ulcers or unusual locations (3rd and 4th portion of duodenum or proximal jejunum)
- Recurrent ulcers after surgical therapy

Endocrine Neoplasms (Gastrinoma)

- **Diagnosis**

- Fasting hypergastrinemia ($>200\text{pg/mL}$) with gastric acid hypersecretion ($>15\text{meq/h}$ output with intact stomach or >5 after ulcer surgery)
- If gastrin $200\text{-}500\text{pg/mL}$, a secretin provocative test is usually done

Endocrine Neoplasms (Gastrinoma)

- **Secretin test**

- 2 units/kg secretin given with a rise in gastrin of 200pg/mL within 15 mins or doubling of fasting gastrin is diagnostic

- **Other Diagnostic Tests**

- UGI, CT scan, angiography, portal venous sampling

Endocrine Neoplasms (Gastrinoma)

- **Treatment**

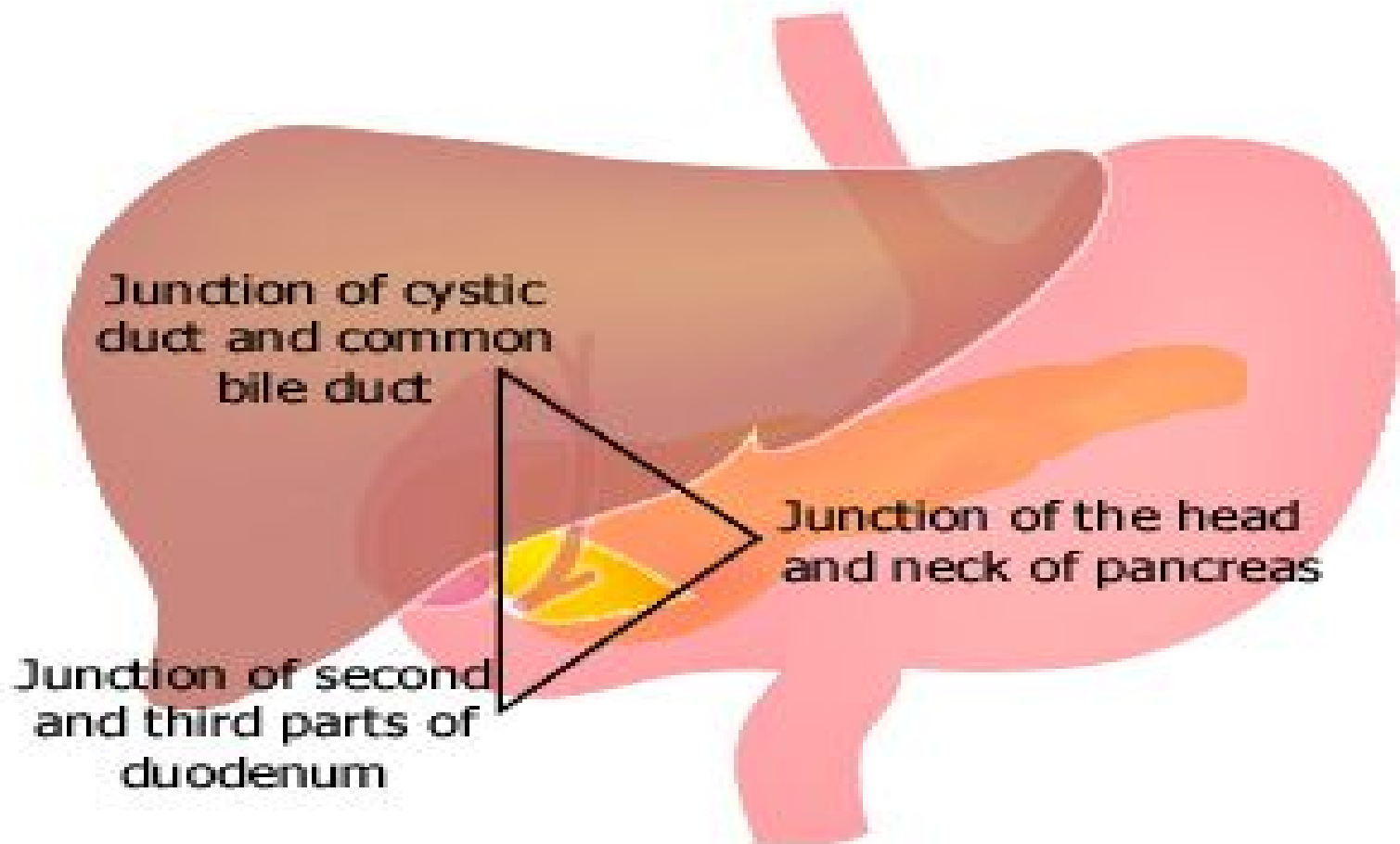
- **Medical**
- Omeprazole is the drug of choice; dose adjusted to keep basal output $< 5\text{meq/hr}$
- If malignancy, streptozocin and 5-FU with or without doxorubicin

Endocrine Neoplasms (Gastrinoma)

- **Surgical**
- If it is sporadic, then exploration is warranted.
- If associated with MEN, they are usually multiple and unable to be completely resected.
- Tumors can be enucleated

Endocrine Neoplasms (Gastrinoma)

- **Surgical (continued)**
- 90% found within the Gastrinoma Triangle
- Junction of cystic and common bile duct, junction of 2nd and 3rd portions of the duodenum, junction of the neck and body of the pancreas
- 1/3 are never found
- Total gastrectomy may be indicated if refractory to medical therapy or inability to totally resect the tumor



Endocrine Neoplasms

- **VIPoma (Verner-Morrison Syndrome, WDHA Syndrome, Pancreatic Cholera)**
- 80-90% of cases are associated with an intra-pancreatic tumor
- Extrapancreatic locations include the sympathetic chain and adrenal medulla
- 50% malignant and 75% of those have metastasized by diagnosis

Endocrine Neoplasms (VIPoma)

- Clinical Manifestations

- Watery diarrhea high in potassium which results in hypokalemia (2-3meq/L) and subsequent weakness
- 50% have gastric acid secretions, 50% do not (achlorhydria)
- May have hypocalcemia secondary to PTH-like secretions
- Metabolic acidosis because of HCO_3^- loss in the stool
- 15% with flushing (usually associated with diarrhea)
- Abnormal glucose tolerance due to altered insulin sensitivity

Endocrine Neoplasms (VIPoma)

- **Diagnosis**

- Elevated fasting VIP by radioimmunoassay
- PP and prostaglandin levels may be elevated with a normal VIP
- CT scan, angiography, transhepatic portal and splenic venous sampling

Endocrine Neoplasms (VIPoma)

- **Treatment**

- **Medical**
- Correction of dehydration and electrolyte imbalances
- Somatostatin trial preoperatively
- If metastatic or inoperable, streptozocin with or without 5-FU
- Symptomatic relief noted occasionally with high dose steroids or trifluoperazine

Endocrine Neoplasms (VIPoma)

- **Surgical**
- Tumor resection if located, otherwise explore sympathetic chain and adrenals.
- 80% pancreatectomy if unable to find the tumor
- Tumor debulking if metastatic
- **Prognosis:** if malignant, survival is ~1 yr; benign disease can be cured surgically

Endocrine Neoplasms

- **Glucagonoma**

- Alpha-2 cell derivative
- More common in women
- Age 20-70
- 75% malignant, 25% benign
- Majority have metastasized by diagnosis

Endocrine Neoplasms (Glucagonoma)

- **Clinical Manifestations**

- Migratory necrolytic dermatitis usually on legs and perineum
- Weight loss, stomatitis, anemia, diabetes, hypoaminoacidemia, visual scotoma, increased tendency towards venous thrombosis and PE

Migratory Necrolytic Dermatitis



Endocrine Neoplasms (Glucagonoma)

- Diagnosis

- Elevated plasma glucagon levels
- CT scan and occasionally arteriography

- Treatment

- **Medical** – oral zinc for dermatitis, somatostatin; streptozocin and dacarbazine if malignant
- **Surgical** – excision of tumor or debulking of metastases

Endocrine Neoplasms

- **Somatostatinoma**

- Most located within pancreatic head
- Most malignant
- Most with metastases (primarily to liver) at diagnosis

Endocrine Neoplasms (Somatostatinoma)

- **Clinical Manifestations**

- Weight loss, mild diabetes mellitus, malabsorption and diarrhea, dilatation of the gallbladder with or without cholelithiasis

- **Diagnosis**

- Elevated serum somatostatin levels
- CT scan (mass in the head of the pancreas)

Endocrine Neoplasms (Somatostatinoma)

- **Treatment**

- **Surgery** occasionally indicated if disease is localized
- **Medical** therapy primarily consisting of streptozocin, dacarbazine, doxorubicin independently or in combination

Endocrine Neoplasms

- **Miscellaneous Tumors**

- PPomas, Calcitonin-secreting tumors, Carcinoid (5-hydroxytryptophan secreting) tumors
- Related to pancreatic islet role in Amine Precursor Uptake and Decarboxylation (APUD) system

Exocrine Tumors

- Adenocarcinoma – 30,000 cases/year;
30,000 deaths/year
- Age and Smoking risk factors
- Present as painless jaundice and weight loss
 - Courvoisier's sign
- Usually present late

Diagnosis

- Ultrasound
 - Dilated ducts
- CT
 - Pancreatic mass and nodes
 - Arterial anatomy
- MRCP
 - Ductal anatomy
- ERCP/EUS
 - Same

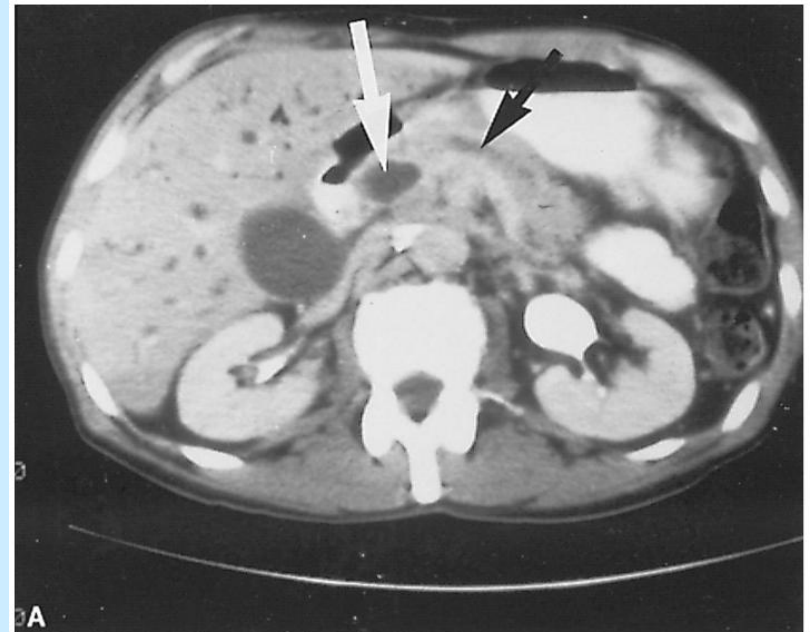
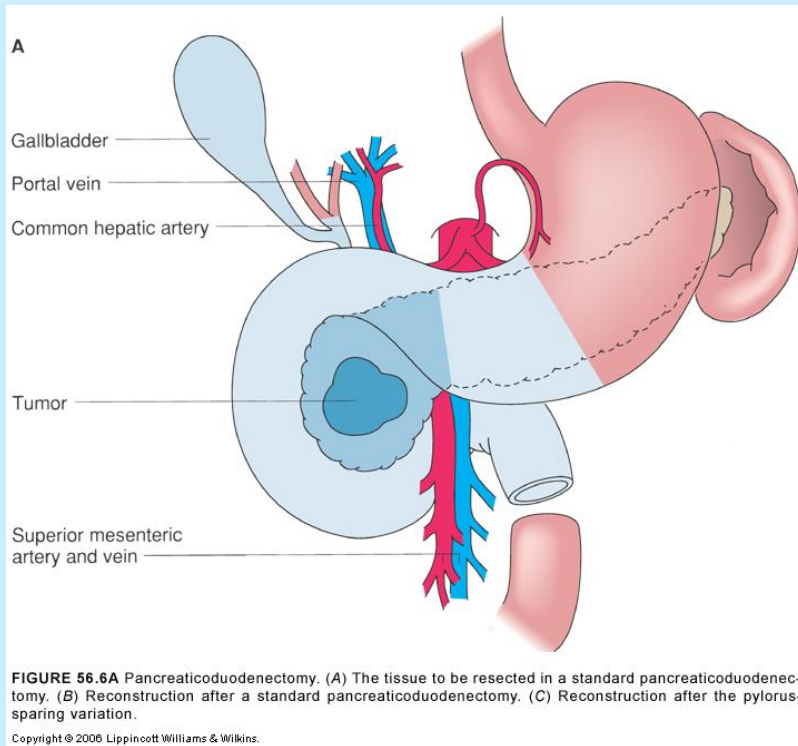


FIGURE 56.3A Computed tomogram of the abdomen of a patient with adenocarcinoma of the pancreas. (A) The obstructed and dilated common bile duct (*light arrow*) and pancreatic duct (*dark arrow*) can be seen. In the adjacent cross section (B), a large mass is present in the head of the pancreas (*arrow*).

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Treatment

- Exploration
- Pancreaticoduodenectomy
- Diversion/Palliation
- Surgery only chance for cure
- Most die from recurrence in less than one year



B

Gastrojejunostomy

Choledochojejunostomy

Pancreaticojejunostomy

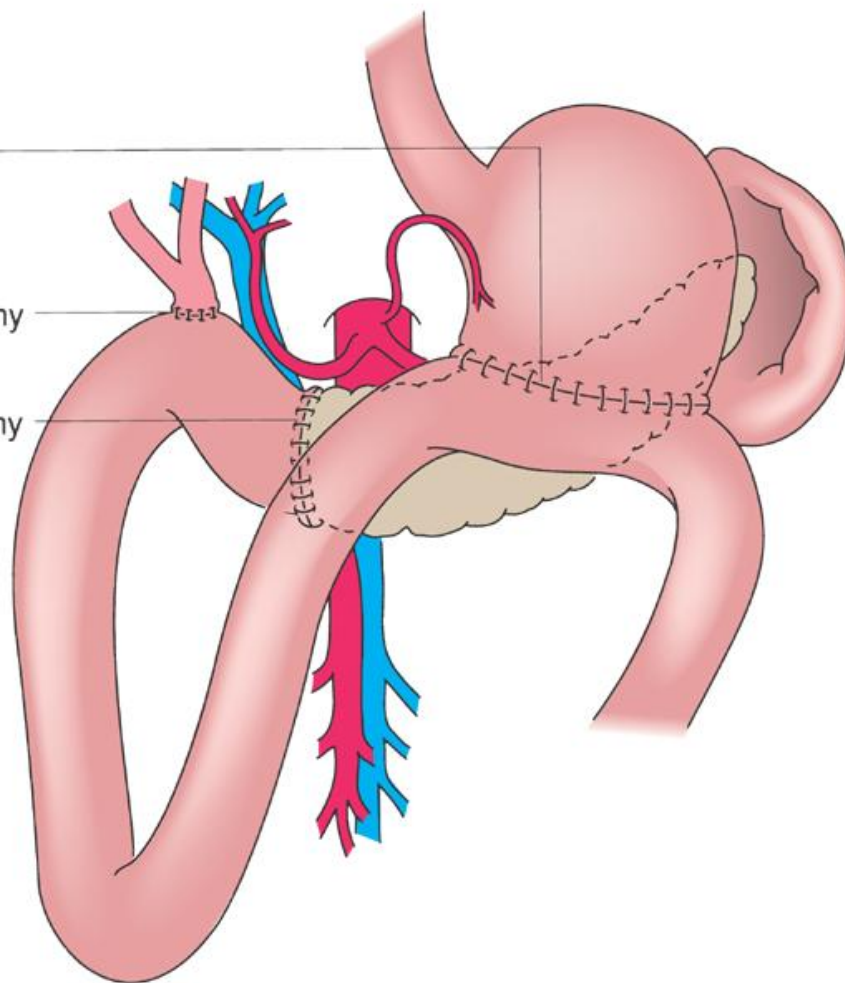


FIGURE 56.6B Pancreaticoduodenectomy. (A) The tissue to be resected in a standard pancreaticoduodenectomy. (B) Reconstruction after a standard pancreaticoduodenectomy. (C) Reconstruction after the pylorus-sparing variation.

Cystic Tumors

- Benign
 - Papillary
 - Young women, great prognosis with resection
 - Cystadenoma - resect
 - Mucinous – common, women . men
 - Serous
- Malignant
 - Cystadenocarcinoma – resect – good survival

Pancreatitis

- Acute
 - Single event
 - Majority - gallstones
- Acute relapsing
 - No damage
- Chronic relapsing
 - Damaging, but intervals without
- Chronic
 - Irreversible



Presentation and W/U

- Severe epigastric pain
 - Provoking events
- Upright and moving
- +/- Rebound, distension
 - Cullen's, Grey – Turner's
- Amylase, lipase, WBC
- U/S, CXR, CT abdomen and pelvis

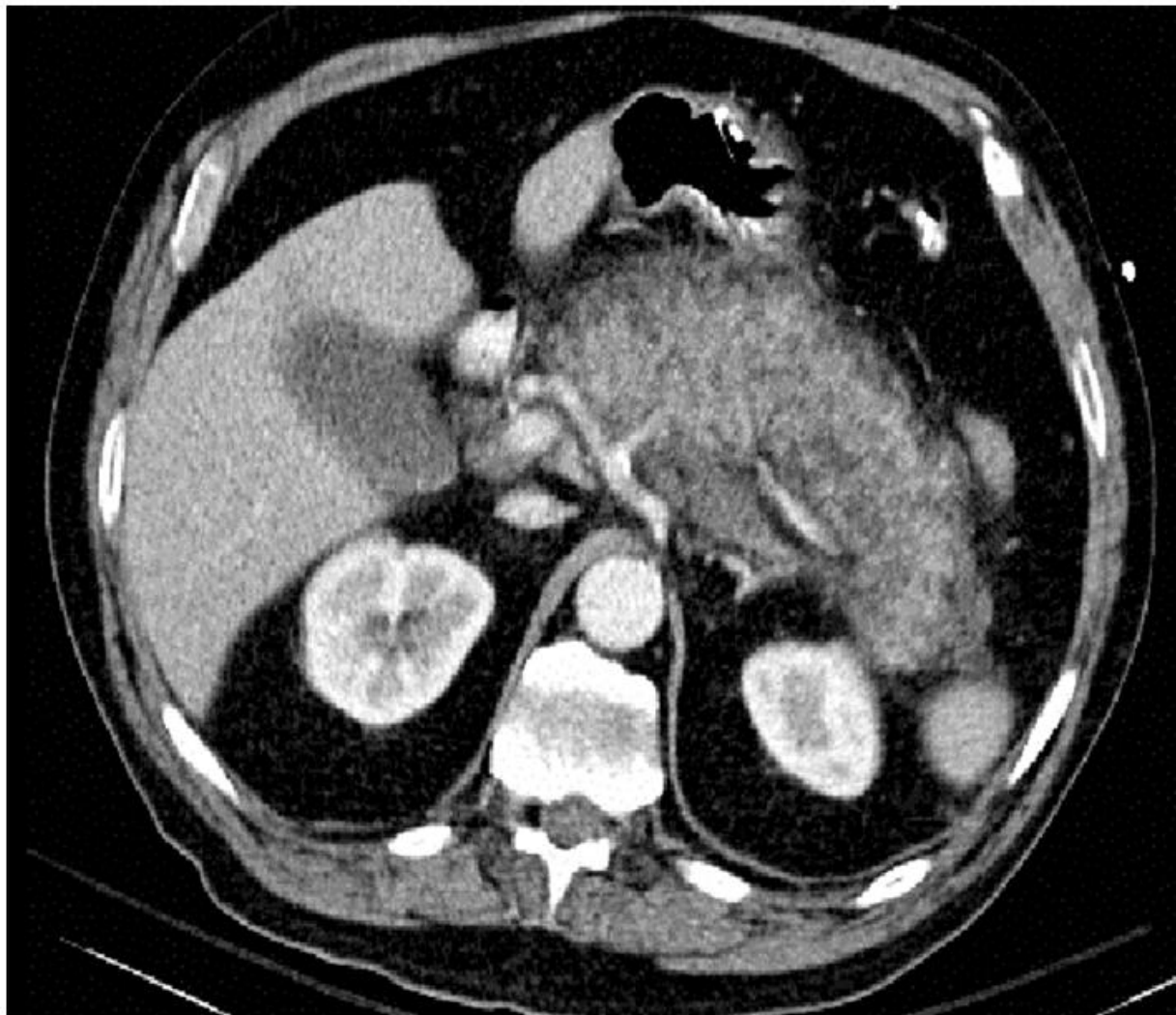


FIGURE 54.3 Computed tomography scan of acute interstitial pancreatitis.

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Ransons's Criteria

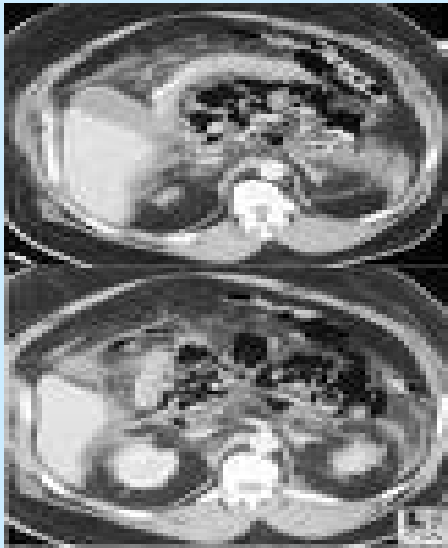
<u>On Admission</u>	<u>Within 48 Hours</u>
Age >55 years	Drop in hematocrit >10%
WBC >16,000/mm ³	Fluid deficit >6 L
Serum glucose >200 mg/dl	Serum calcium <8.0 mg/dl
Serum LDH >350 mg/dl	Hypoxemia (pO ₂ <60 mm Hg)
Serum AST >250 IU/L	Rise in BUN >5 mg/dl
	Albumin <3.2 g/dl

Treatment



- Supportive
 - Analgesia and Fluids
- Causative
 - Biliary and abstinence
- Monitored
 - Complications and chronicity

Complications



- Critical Care issues
 - MSOF
- Pancreatic Necrosis
 - Serial CT
- Pancreatic abscess
 - Surgical Drainage
- Pseudocysts
 - > 6 weeks of symptoms

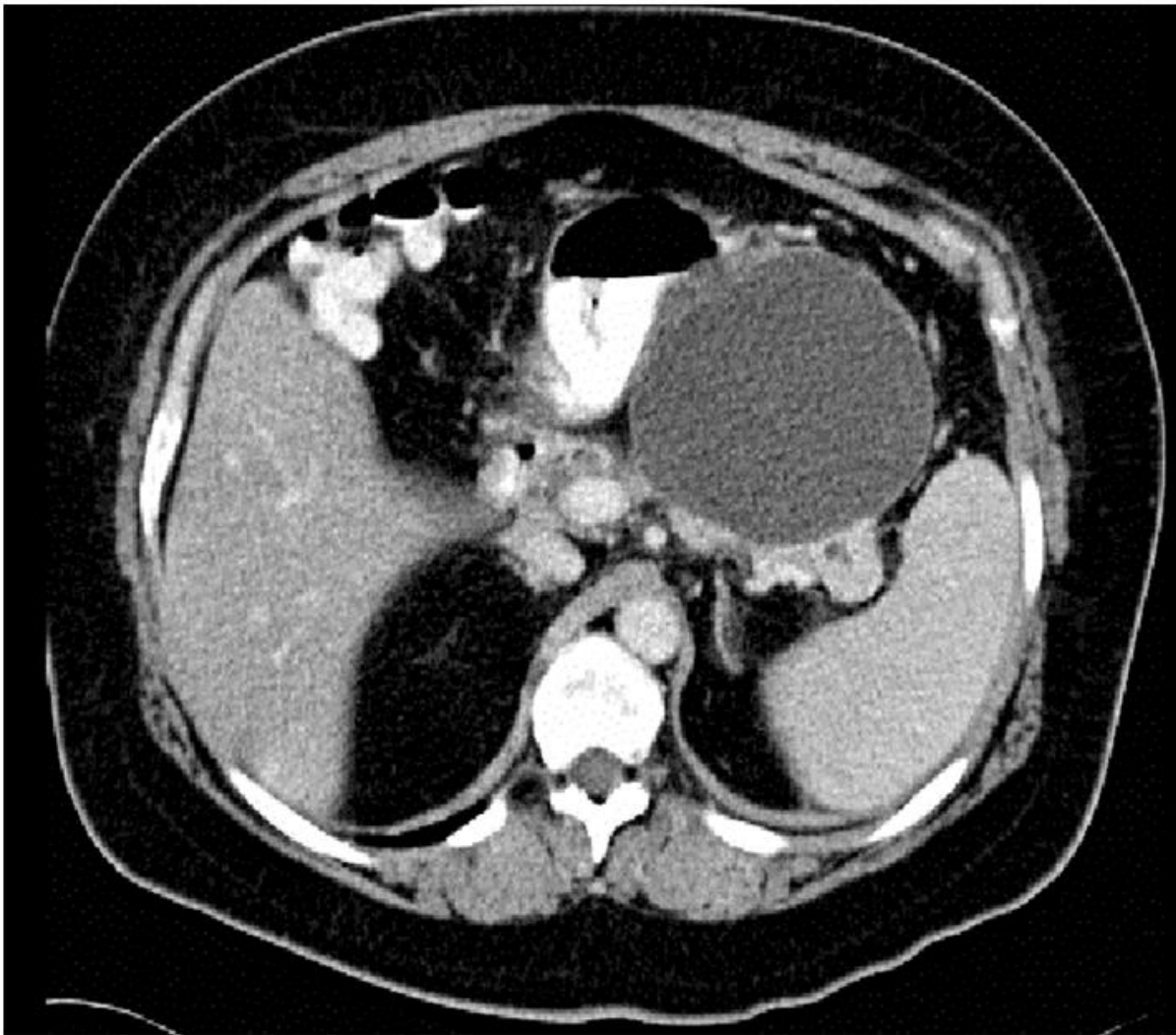


FIGURE 54.5 Computed tomography scan of pancreatic pseudocyst.

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Pseudocyst treatment

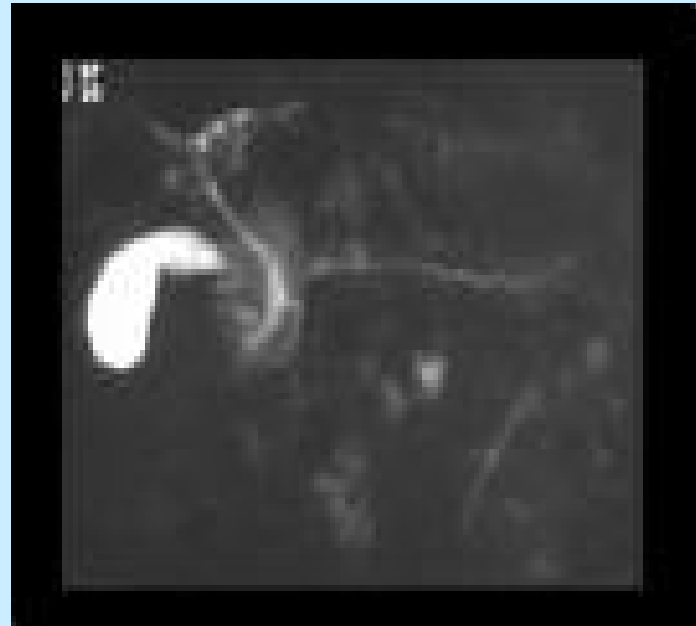
- Observation
- Internal Drainage
 - ERCP/sphincterotomy
 - Cyst - ostomy
- External Drainage
- Complications of cysts
 - Infection and hemorrhage

Chronic Pancreatitis

- Usually alcohol abuse
- Chronic pain, endo- and exocrine gland dysfunction
- Treatment medical
- Surgery only for failure of medical management or obstruction

Evaluation

- ERCP/MRCP
- Outline ductal anatomy
- Stenosis
 - Ampullary
 - Single site
 - Chain of lakes



Treatment

- Drainage
 - Puestow – lateral pancreaticojejunostomy
- Adjunctive
 - Injection of celiac plexus
 - Splanchnesectomy
- Resection
 - Partial/Total
 - Outcomes Dismal – pain still there + diabetes worse

