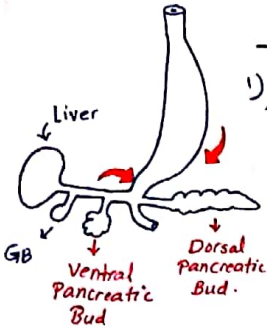
Pancreas

Embryology :



- Caudal foregut develop :

1) Ventral pancreatic bud → develop near the entry of Bile duct into the duodenum & forms the head of pancreas & main Pancreatic duct.

2) Dorsal Pancreatic bud → Give Rise to most of the Pancreas.

* Insulin secretion begin at 10th week.

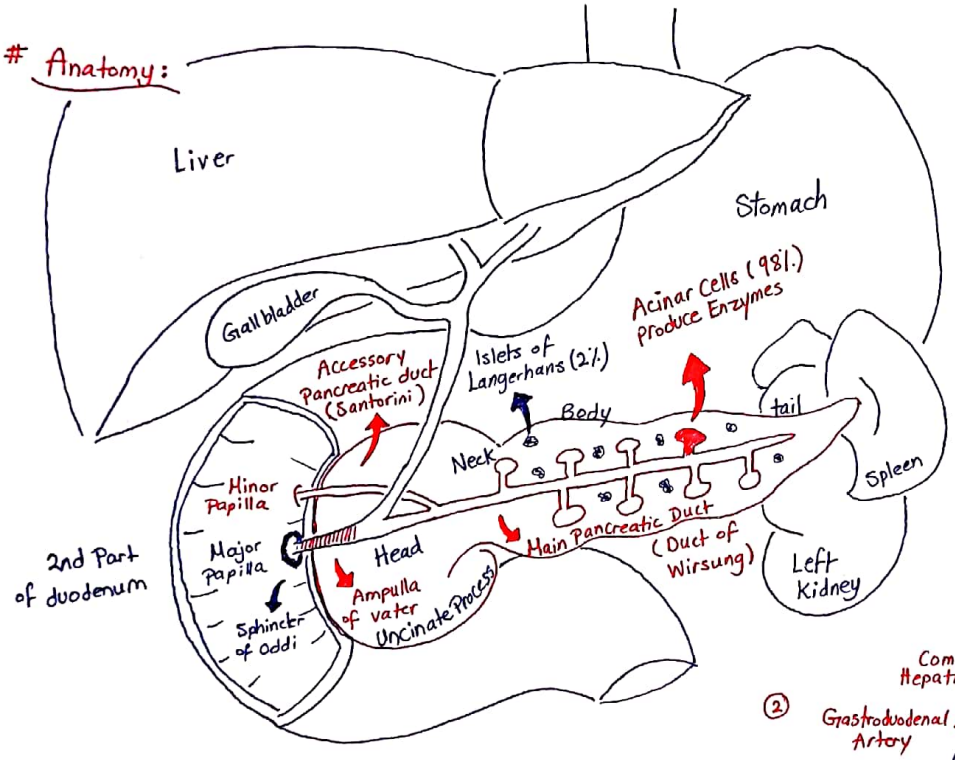
- As the stomach rotates 90° clockwise, Ventral Pancreatic duct rotate posteriorly & fused with dorsal pancreatic duct.

* In 9% of cases the Proximal Part of dorsal duct Persist as Accessory Pancreatic duct & opens into duodenal Papilla

* Annular Pancreas : Pancreas encircling the duodenum (if Obstruction occur → Bypass not resection)

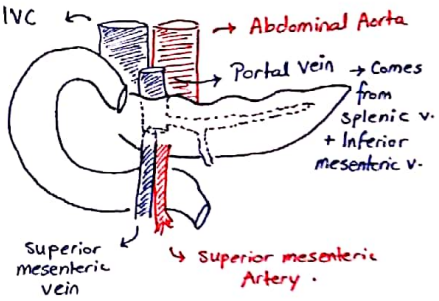
* pancreatic divism : failure of ventral & Dorsal Bud to fuse → Accessory (santorini) duct become the main pancreatic duct but its not enough to drain the pancreas & may lead to chronic pancreatitis.

Anatomy :

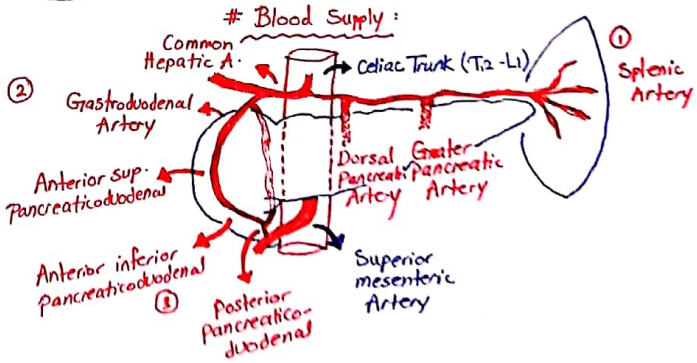


- The Pancreas is (Retroperitoneal organ) (except the tail) & its 12-15 cm long.

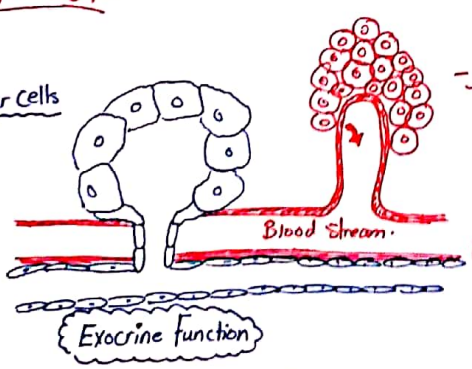
- Lies behind the stomach & lesser sac, & wraps around superior mesenteric A & V.



Blood Supply :



Physiology :



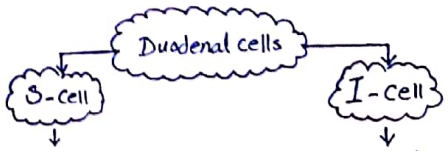
Exocrine function:

- α-amylase → starch digestion
- Lipase → fat digestion (Specific for pancreas)
- Proteases (Trypsin, Chemotrypsin, elastase & carboxypeptidase) → Protein digestion.

* Trypsinogen (zymogen or proenzyme) contained in granules in each acini —(Brush Border Enzymes, Enterokinase & enteropeptidase)→ Trypsin → cleavage of other Trypsinogen & enzymes (+ve feedback)

Endocrine function:

- α-Cells → Glucagon
- β-cells → Insulin
- δ-cells → Polypeptides
- ∇-cells → Somatostatin.



S-cell → Secrete Secretin in response to Acids & fatty acids
1. ↓ Gastric Acid secretion
2. Bile secretion
3. ↑ Pancreatic HCO3 (to Neutralize gastric acid in duodenum)

I-cell → Secretes Cholecystokinin in response to fat, proteins
1. ↓ Gastric Emptying
2. Contraction of GB.
3. Relaxation of sphincter of Oddi
4. Stimulate Pancreatic secretions.

Acute Pancreatitis

* **Definition:** Acute Inflammation of Pancreas due to Insult that lead to Premature Activation of Pancreatic Enzymes & Autodigestion of Pancreas & Peripancreatic tissues. (Assoc. with little or no fibrosis)

- **Incidence:** 3% of all cases
- **Occur at any age** → But mainly young men & older women.

Acute Pancreatitis

Mild	Severe
- 80% of patients	- 20% of patients
- Mortality 1%	- Mortality 50%
- Interstitial edema & minimal organ dysfunction	- Necrosis & severe systemic inflammation & MOF.
- Resolve spontaneously.	- 1/3 of deaths are early due to MOF, Late deaths are due to septic complications.

* **Mechanism:**
- Injury to Acinar cells & impair secretion of zymogen granules.
- Damage to ductal epithelium thus delay enzymatic drainage.

or =

* **Etiology:** (either due to malnutrition or direct toxicity.)

I GET SMASHED

- **I** — Idiopathic
- **G** — Gall-stones (Main cause worldwide (50-70%))
- **E** — Ethanol
- **T** — Trauma (↳ external, ↳ ERCP) / Scorpion Bite.
- **S** — Steroids
- **M** — Mumps, coxacki B.
- **A** — Autoimmune.
- **S** — Scorpion Bite.
- **H** — Hyperlipidemia or Hypercalcemia (or Hyperparathyroid.)
- **E** — ERCP
- **D** — Drugs: Estrogen, corticosteroids, Azathioprine, Valproic Acid, Thiazide

* **Clinical Presentation:**

* **Pain** is the cardinal symptom →
- **Site:** epigastric, or upper quadrant or diffuse.
- **Onset:** Sudden, reach maximal intensity within minutes.
- **Radiation:** To the back.
- **Assoc. with:** N/V, low grade fever, ↓ Bowel sounds.
- **E & R factors:** ↑ with lying down, not relieved by Analgesia
- **Severity:** very severe.

↳ Pain out of Proportion (Patient have severe pain but on exam. the Abdomen is soft lax (Also seen in Mesenteric Ischemia)

On Examination
- **General:** Patient looks ill, Jaundice
- **Vitals:** Tachycardia, Tachypnea hypotension, hypoxemia, low grade fever
- **Abdomen** → distended
  - * Grey Turner sign (flank)
  - Cullen's Sign (Peri-umbilical)
  - Fox sign (Inguinal lig.)

  *May also be seen in ruptured AAA.
- **Chest** → pleural effusion or pneumonitis

* **Investigations:** → To Confirm Diagnosis, → Assess Severity, → Underlying cause.

- **Lab Tests:**

① **Serum Amylase:** or urine Amylase or Amylase/Cr clearance ratio
- Not specific, if levels > 3-4 times the normal → diagnostic.
- Rise within few hours & decline over next 4-8 days (Normal levels doesn't Rule out pancreatitis, it could be late Presentation or because its rapidly cleared by Urine)

⇒ **False +ve seen in**
1. Parotiditis
2. Upper GI perforation
3. Mesenteric Ischemia
4. Ectopic Pregnancy.
5. Renal failure.
6. Intrabdominal Torsion.

Differential Diagnosis
1. Inferior MI, Pneumonia
2. Mesenteric Ischemia or Ruptured AAA
3. Gastritis, PUD, Perforated PU.
4. Biliary colick, cholecystitis

② **Lipase:**
- More sensitive & specific & stay elevated for longer periods.

(Due to fat Saponification)

③ CBC, LFT (ALT > x3 → GS), ABGs (hypoxemia), Calcium (↓)

- **Imaging:**

1. **X-ray**
↳ **Chest x-ray** ⇒ Pleural effusion esp. on left side (Called Sympathetic effusion)
↳ **Abdominal x-ray** 1. Sentinel loop (localized - Most Common - 2. Colon cut off 3. Renal Halo 4. Calcification Jejunal dilation)

2. **Ultrasound**
- Not diagnostic.
- Can show GS, CBD Cholecystitis, swollen pancreas.

3. **CT scan with contrast**
- Not done in mild cases & only if dx is in doubt.
- Can show edema, Necrosis (no enhancement) & complications → Pseudocyst → fluid collection, Pseudo aneurysm.

4. **ERCP** (Therapeutic)
- Only in cases of severe GS pancreatitis causing cholangitis & jaundice & should be done urgently (because Ampulla of vater get edematous & become hard to go beyond it) ②

Acute Pancreatitis Scoring Systems:

① Ranson Criteria:

⇒ Mortality Rate:
- 0-2 → < 5%
- 3-4 → 15%
- 5-6 → 40%
- 7-8 → 100%

- At Admission:
  - Glucose > 10 mmol/L (200)
  - AST > 250
  - LDH > 350
  - Age > 55 yrs
  - WBC > 16,000
- After 48 hours:
  - Calcium < 8 mg/dL
  - HCT drop > 10%
  - O2 < 60
  - Base deficit > 4
  - BUN > 5
  - Sequestration of fluids > 6 L. ← Occur due to third spacing (Edema & Ileus)

* If score > 3 Admit to ICU.

② Glasgow Scale:

- At Admission:
  - Glucose > 200
  - Age > 55
  - WBC > 15000
  - Arterial O2 < 60
  - Serum Urea > 16 mmol/l
- After 48 hours:
  - Calcium < 8 mg/dL
  - Albumin < 32 g/dL
  - LDH > 600 units/L
  - AST / ALT > 600 units/L

③ APACHE 2 system

* Indications of severe attack:
1. Glasgow score > 3
2. CRP > 150 mg/dL
3. Worsening state with sepsis
4. persistant organ failure

Management:

- Mild Pancreatitis:

① NPO
② IV fluids
③ Analgesics
④ Anti-emetics

- CT scan if severe, deteriorating.
- Abx not Indicated.

- Severe Pancreatitis:

① Admit to ICU
② NG Tube (if vomiting)
③ Aggressive IV fluids (monitor UO, Vitals, CVP)
④ Supplemental O2
⑤ TPN
⑥ Prophylactic Abx (IV imipenem or ceforoxime or ciprofluxacin + Metronidazole)
⑦ CT scan
⑧ Urgent ERCP + Sphincrotomy (within 72 hours) if Jaundiced.

⇒ Closely monitor:
① CBC (Hb)
② LFT / clotting Profile
③ KFT
④ Ca, Mg.
⑤ Blood Glucose.

Complications of Acute Pancreatitis

Develop after 1st week. ← Should be R/o if Pt. not improving or signs of sepsis → Local

More common in 1st week → Systemic → due to Inflammatory mediators released into circulation.

① Acute fluid Collection:

- Leakage of fluid around the Pancreas.
- Early → sterile → Pseudocyst
- Late → Infected → Abscess
  ] if not resolved
- Usually resolve spontaneously
- Can cause pressure symptoms → Percutaneous Aspiration under guidance → if infected → Abx

② Pancreatic Necrosis: - Non-enhancing CT scan-

↳ Sterile: Diffuse or focal Areas of non viable parenchyma (Early 2 wks), treated conservatively.

↳ Infected: Due to translocation of GIT bacteria, 50% mortality rate. If high suspicion of sepsis we do CT guided Aspiration → If pus drained we should do percutaneous drainage (debridement)

↳ Patients need ICU Admission & TPN & if not improving may need Necrosectomy

③ Pancreatic Abscess:

- Infected Purulent collection
- Fever, unresolving Pancreatitis
- Need Abx + Percutaneous drain.

④ Hemorrhagic pancreatitis:

- Bleeding into Pancreatic Parenchyma or retroperitoneal structures
- Diffuse Bleeding either from Large Necrotic Area or pseudoaneurysm
- Dx by CT Angio or MRA
- Treated by Embolization

⑤ Portal or Splenic vein Thrombosis:

- Silent, detected on CT
- ↑ platelets count
- Management: - Aspirin for Thrombocytosis
  - Systemic Anticoagulation (if early may cause recanalization)
  - Splenic Thrombosis cause Gastric Varices → splenectomy. on long-term but Acutely may lead to Intestinal edema & Necrosis → Death.

⑥ Pseudoaneurysm.

Systemic

- Neurological ↔ Confusion, Encephalopathy, Visual disturbance.
- Respiratory ↔ ARDS, Pleural effusion ⇒ Could be with Ascites.
- Cardiovascular ↔ shock, Arrhythmias
- Gastrointestinal ↔ Ileus, Pancreatic Ascites → Peritoneal effusion rich in Amylase on paracentesis with disruption of pancreatic duct on ERCP.
- Hematological ↔ DIC, Shock.
- Renal → Renal failure
- Metabolic ↔ Hypocalcemia, Hyperglycemia, Hyperlipidemia

Treatment
1. Nasojejunal feeding
2. paracentesis
3. Octreotide (somatostatin) → ↓ GIT Enzymes

⑦ Pancreatic Pseudocyst :

- Encapsulated collection of Amylase rich fluid in fibrotic wall (called pseudocyst because its not lined with epithelium)
- Often Singe, Requires 4 weeks to form either after Acute, chronic Pancreatitis or Trauma
  ↳ MC cause in US
- 50% resolve spontaneosly → Communicate with pancreatic duct & drains to it.
- Diagnosed by: ① US – fluid filled mass
  ② CT scan
  ③ ERCP – If the cyst communicating with Pancreatic duct, the radiopaque material will fill it.
- Pseudocyst is less likely to resolve spontaneously if:
  ① Thick wall
  ② Large (> 6 cm)
  ③ lasted for long
  ④ Arise in Chronic Pancreatitis
  ⑤ Symptomatic (causing Pressure Symptoms on the stomach → early satiety, full stomach all the time)

- Always should R/o cystic Tumors (Cystadenoma, Cystadenoca.)
  By EUS & Aspiration: - Pseudocyst → High Amylase, Inflammatory cells in cytology
  - Tumor → CEA > 400 ng/l

Complications of Pseudocyst:

① Infection (Abscess, Sepsis) → Percutaneous Drainage + IV Abx.
② Rupture into gut (fistula)
③ Rupture into peritoneum (Peritonitis)
④ Pressure Symptoms (GOO, Jaundice)
⑤ Erosion into a vessel (Hemorrhage into cyst) → Angiogram + Embolization
⑥ Pain.

* Massive Hg into the cyst is the most common cause of death.

Management:

→ If complicated
→ If symptomatic
→ If we should R/o Tumors.

↳ Drainage Options (should wait 6 weeks until the capsule become mature so it wont rupture)

① Percutaneous – not done –

② Endoscopic → Endoscopic Cystogastrostomy → High recurrance rate

③ Surgical (open or lap.) → Cystogastrostomy / Cystoduodenostomy / Roux-en y cystojejunostomy → Reclosure risk so we put a stent

↳ Biopsy of cyst wall to R/o Ca.

Chronic Pancreatitis

Definition:
Irreversible destruction of pancreatic tissue, result from chronic Inflammation, lead to fibrosis replacing Pancreatic parenchyma & loss of endocrine & exocrine function.

Etiology:
① Most common Is Alcohol Abuse (70%)
② Idiopathic (15%)
③ Hypercalcemia, Hyperlipidemia
④ Autoimmune Pancreatitis (Abs, enlarged Pancreas & narrowed ducts)
⑤ Heriditary (CF)
⑥ Pancreatic duct obstruction (Stricture, after Acute Pancreatitis, occlusion by cancer, pancreatic divisim – pancreas drained by minor duct which is inadequate –, Annular pancreas)
⑦ Small percentage of Biliary pancreatitis (recurrent)

Clinical features:
① Constant Pain (epigastric – head –, left subcostal or Back – Body & tail –)
② Radiate to the back or left Shoulder
③ Dull & gnawing.
④ Severe flare ups
⑤ N/V, weight loss, Steatorrhea (Due to exocrine dysfunction (fat malabsorption)), malnutrition, Diabetes (Due to endocrine dysfunction.)
⑥ Analgesic Abuse.

Prognosis
→ Usually Bad Outcome
→ Risk of Pancreatic Cancer (2%) if disease > 20 yrs.
→ Usually Pain is recurrent

Investigations:
① Amylase (↑ in early stage then depleted)
② GTT
③ Imaging: ① KUB → Calcification of pancreas or pancreatic duct
② CT scan → largest sensitivity
③ ERCP → Ductal Irregularities with dilation & stenosis (chain of Lakes)
④ EUS (Presence of at least 4):
① Stones
② Cysts
③ Lobularity
④ Dilation of pancreatic duct & hyperechoic margins
⑤ visible side branches

Treatment:

↳ Medical
- Treat Alcohol Addiction (↓ Attacks)
- Narcotics for pain
- Insulin (for DM type I)
- pancreatic Enzymes replacement (CREON)
- Diet adjustment: MCT, low fat, high carbohydrates & proteins.

↳ Surgical → if failed medical ttt, severe refractory pain.
↳ Peutsow Procedure → longitudinal (side to side) pancreaticojejunostomy
↳ Frey Procedure → " " + Core resection of head of Pancreas
↳ Duval Procedure → Distal Pancreaticojejunostomy
↳ ERCP with sphincrotomy & stenting. ④

Pancreatic Carcinoma

 # Adenocarcinoma: (90% of malignant exocrine tumors)
- Arise from Pancreatic duct cells.
- M: F ratio 3:2
- Average age > 60 yrs

- **Risk factors:** ① Most imp. is smoking (x3) ④ DM
  ② Chronic Alcoholism ⑤ previous gastrectomy
  ③ Chronic Pancreatitis ⑥ African American.

Types:	Head of Pancreas ↕ Periampullary / Proper head of pancreas (70%)	Body & Tail (30%)
Clinical Manefestation	- Painless obstructive Jaundice (Early presentation from CBD obstruction) - first sign → Darkening of urine. - Clay stool, Pruritis, scleral icterus. - Non severe epigastric Pain, Back Pain (sign of invasion & non-resectable Ca.) - Significant weight loss (>10% of TBW) - Steatorrhea or Diarrhea ↔ Tumor obstruct CBD - Recent onset DM. (5%) ↔ Uncinate tumor obstructing pancreatic duct. - Cholangitis → Not from obstruction but instrumentation (ERCP) - Bleeding → Tumor eroding duodenum. - Migratory Thrombophlebitis → Sign of metastatic Tumor (Trousseau sign) 33% Courvoisier's sign → Painless, distended GB. - Hepatomegally, Ascites.	- Recognized late (not causing Jaundice) - Non-specific symptoms: 1- weight loss 2- fatigue 3- Diabetes 4- Abd. & Back pain 5- Migratory Thrombophlebitis. * Tumors In mid-Body tend to invade Posteriorly (even if small 2-3 cm) & Involves SMA or Celiac Trunk. * Tumors of the tail tend to be resectable (Pancreatectomy)
Lab Investigations	① LFT ⇒ ↑ direct & total Bilirubin, ↑ ALP (x3-5), ↑ AST & ALT (Biliary system work under pressure.) ② CA 19-9 ↑↑ ⇒ Normally < 37 U/ml, if >100 highly suggest ca. if >1000 suggest mets (Good for follow up for recurrance)	① CA 19-9 ⇒ may be elevated.
Imaging Studies * finding atypical mass in head of pancreas the next step is to differentiate Tumor from focal pancreatitis	1- Best Diagnostic Test Is (Pancreas Protocol Helical CT scan) → 3 phases (no Contrast, Arterial phase, Venous phase) 2- High quality MRI (Provide Cholangiogram & Angiogram) # CT shows: 1- lucent mass in head of pancreas 2- dilation of Bile ducts. 3- dilated pancreatic duct in Body & tail & sharp cut off at the head + Atrophy of Body & tail. 4- Double Duct Sign (if with ↑ CA19-9 Diagnostic for ca.) * also if ↑ CA19-9 + Tumor on CT its diagnostic. 3- ERCP (2nd choice if no mass on CT But shows dilated CBD) ↳ Biopsy of Ampullary Tumors ↳ Confirm CBD stricture & its forms ⇒ Double duct sign; focal stricture - malignancy; long stricture limited to intrapancreatic Bile duct - chronic pancreatitis ↳ Brush cytology from pancreatic duct (sensitive in 40-50%) 4- If still in doubt after ERCP do EUS: - Identify small mass not seen on CT & Biopsy it. - Can show LN & Biopsy it (if away from tumor its unresectable) - -ve Biopsy don't exclude malignancy. 5- Ultimate diagnostic test is Pancreaticoduodenectomy.	1- CT scan: lucent mass, extension outside the pancreas, if Ca. Proximal to tail may show distal Pancreatic duct dilation 2- EUS **Surgical staging (Laparoscopic)** - Tumor Is unresectable if: 1. Invade SMA, celiac trunk, PV, SMV, Aorta 2. Enlarged para-aortic LN * Invasion of spleen, stomach, colon, mesocolon left kidney, left adrenal, retroperitoneum is not contraindication for resectability. **Management** - Radical Antegrade Pancreaticosplenectomy ↳ with LN (Regional LN - N1)

Surgical staging of Pancreatic head Tumors :

- Surgical staging starts preop. (CT) & Completed intra op to determine resectability.
- Tumor is unresectable if extend beyond Pancreaticoduodenectomy.
- Staging laparoscopy is effective in finding small hepatic or peritoneal nodules.

Virchow's Node ⇔ Sister mary Joseph nodule.

Reasons for unresectability

1. Vascular Invasion (SMV, Hepatic A. portal vein, SMA) - Relative CI.
2. LN mets outside the Prope of PDectomy.
3. Hepatic Mets, malignant Ascites.
4. Peritoneal mets
5. Extraabdominal mets (lungs frequently)

TNM Stage:

- Stage 0 → Tis (Carcinoma In situ)
- Stage 1 → IA → Tumor limited to pancreas. < 2cm (T_1)
  IB → " " " , > 2 cm (T_2)
- Stage 2 → IIA → Tumor extend outsid Pancreas without SMA or Celiac Invasion. (T_3)
  IIB → " " " " with involvement of " " (T_4)
- Stage 3 → T_4 (Involve celiac or SMA) + LN Involvement + No mets.
- Stage 4 → Any T ± LN + Distal metastasis

If Tumor Unresectable → Palliative Treatment

→ Median survival for locally advanced disease is 6-10 months, for metastatic disease 2-6 months.

① pain → Analgesia
② Gastric Outlet Obstruction → Gastrostomy
③ Jaundice or Biliary Sepsis → ERCP (stent) or PTC Biliary Bypass.
④ Replacement of Panc. enzymes & treat diabetes.

Management:

- Pre op preperation:
  1- Parentral vit. K to prevent Bleeding
  2- Good hydration
  3- Bile duct decompression if prolonged Jaundice or delayed operation.
- Operation: Whipple Procedure
  - Cholecystectomy & Choledocho-Jejunostomy
  - Anterectomy & Gastrojejunostomy
  - Pancreaticoduodenectomy & pancreaticojejunostomy
  - Truncal vagotomy.

↳ survival Rate (5yrs) 15%.

Benign Exocrine Tumors with malignant Potential (Mucinous Tumors) ⇒ Mucin secreting cancers

	Mucinous Cystic Neoplasms	Intraductal Papillary Mucinous Tumors
Epidemology	- Middle Aged women - Mostly in Body & tail of Pancreas - Unilocular or septated, 1-15 cm.	- Predominently in males, 60's. - Start as metaplasia of cells lining pancreatic duct (low cuboidal serous → mucin producing) → Dysplasia → malignancy. (20% have malignancy at time of dx) - Focal (60% at the head of Pancreas) or diffuse
Presentation	- Left sided Abd. pain. - Rarely Jaundice & Pancreatitis	- present as pancreatitis (pain) due to mucous obstructing pancreatic duct.
Diagnosis	- CEA level in cyst fluid > 5ng/ml (Not ↑ Amylase as in pseudocyst) - Malignancy suggested by solid intracystic or extramural components.	- CT scan, MRI, MRCP, ERCP.
Management	- Surgical staging. - Resection by distal Pancreaticosplenectomy if: ① Symptomatic. ② Asymptomatic & > 2cm.	- Resect the Involved Part of the Gland.

Neuroendocrine Tumors

- < 5% of surgically treated pancreatic Ca.
- Could be ↳ functional → produce hormones
  Non functional → slowly growing, give mass effect (Pain is the most common symp.), can mets to liver & LNs.
  ↳ Due to slow growth they have favorable dx (50-60% 5yr survival rate)

① Gastrinoma

- Gastrin secreted from G-cells in the duodenum & Antrum of stomach.
  → Stimulated by: ① Gastrin releasing peptide ② Stomach distention ③ Amino Acids.
  → Effect: ① ↑ stomach HCL ② ↑ Gastric motility.
- Tumor secrete Gastrin → Zollinger-Elison Syndrome → Peptic Ulcers. → suspect if duodenal or jujenal ulcers seen.
  ↳ Should resect tumor (distal pancreatectomy or pancreaticoduodenectomy)

② Insulinoma (Most common Islet cell Tumor)

- 10% are malignant & mets to Liver or LNs.

- Whipple Triad of Insulinoma: 1) fasting hypoglycemia (< 50mg/dL)
  2) Symptoms of hypoglycemia
  3) Relief of symptoms with Glucose administration.

③ Glucagonoma

① Diabetes

② Dermatitis (Necrotizing Migratory Erythema)

④ VIPoma (Vasoactive-Intestinal Polypeptide tumor)

↔ WDHA syndrome / Verner Morrisson Syndrome.

- VIP secreted from GB & small Intestine
  → Stimulated by: ① Distention ② Vagal stimulation
  → Effect: ① ↑ Intestinal water secretion & Electrolytes ② Relaxation of Intestinal sphincters.
- VIPoma lead to: ① watery Diarrhea ② Hypokalemia ③ Achlorhydria (↓ gastric Acid secretion)

⑤ Somatostatinoma

- D-cells release it (Pancreas & GI mucosa)
  → Stimulated by Acids
  → Effects: ① ↓ Gastric Acid & pepsinogen. ② ↓ Pancreatic & intestinal fluid secretion ③ ↓ GB Contraction ④ ↓ Insulin & Glucagon release.

- Somatostatinoma:
  ① Gallstones.
  ② Diabetes
  ③ Steatorrhea