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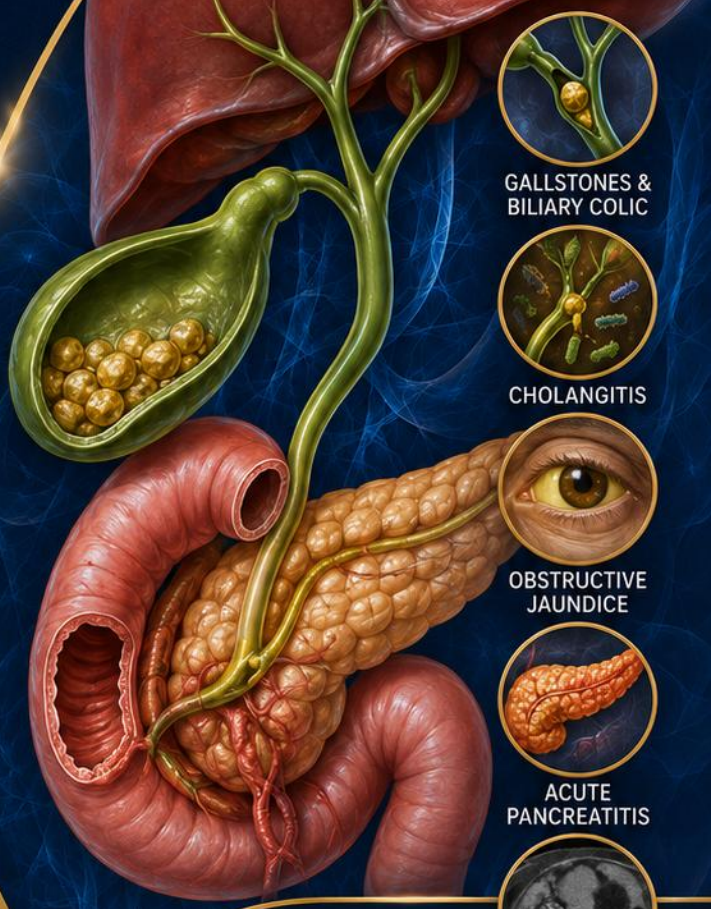

CHAPTER 7

BILIARY & PANCREAS

EXAM-FOCUSED MCQs
Covers All Core Topics

UPDATED & EVIDENCE-BASED
Aligned with Latest Guidelines

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Dedication

In loving memory of my mother,

who recently returned to the mercy of Allah.

Her love, prayers, patience, and sacrifices were among the greatest blessings of my life. Whatever good I achieve carries something of her guidance and support.

May Allah forgive her, have mercy upon her, illuminate her grave, and grant her the highest place in **Jannat al-Firdaws**.

This work is dedicated to her memory.

أسأل الله أن يرحم أمي رحمة واسعه وأن يدخلها الفردوس الأعلى من الجنة، ورجاءً أسألكم لها خالص الدعاء..

Chapter 7 - Biliary & Pancreas

150 Original Consultant-Level Mechanism-Based MCQs

Structure: **100 direct and short case scenarios** + **50 moderate-to-long integrated case scenarios**. Correct answers are randomized. Key mechanism terms are shown in **bold colored text**.

Scope: gallbladder stones and polyps, acute/chronic/acalculous cholecystitis, choledocholithiasis, cholangitis, sphincter disorders, choledochal cysts, gallbladder/biliary cancer, acute/chronic/autoimmune pancreatitis, pancreatic cysts, pancreatic ductal adenocarcinoma, pancreatic NETs, and complications.

Source use: questions are original and structured from the uploaded reference pool only; they are designed to test mechanism-based reasoning rather than recall.

A. Direct and short case scenarios - 100 questions

Q1. Cholesterol stone nucleation

A 42-year-old obese woman has recurrent post-prandial right upper quadrant pain. Ultrasound shows multiple mobile gallstones. A research fellow asks which molecular event best initiates most stones in this setting.

A. Bacterial beta-glucuronidase deconjugation of bilirubin inside infected bile ducts
B. MEN1-driven enterochromaffin-like cell proliferation with gastrin excess
C. Autoimmune IgG4 plasma-cell infiltration of the cystic duct wall
D. **Cholesterol supersaturation** of gallbladder bile with crystal nucleation in mucin gel and impaired gallbladder emptying
E. Hemolysis-induced polymerization of unconjugated bilirubin in sterile gallbladder bile

Answer: D - **Cholesterol supersaturation** of gallbladder bile with crystal nucleation in mucin gel and impaired gallbladder emptying

Mechanism pearl: Most Western gallstones are **cholesterol stones**: supersaturated bile + mucin nucleation + hypomotility.

Q2. Gallbladder hypomotility

A fasting parenteral-nutrition patient develops biliary sludge. The examiner asks why prolonged fasting promotes sludge formation despite no hemolysis or infection.

A. Postprandial sphincter relaxation becomes excessive and washes crystals away
B. Pancreatic trypsin directly precipitates calcium bilirubinate in the gallbladder
C. IgG4-related inflammation obstructs the common bile duct in all fasting patients
D. Reduced meal-induced **CCK-mediated gallbladder contraction** produces stasis and concentrates lithogenic bile
E. Somatostatin deficiency increases gallbladder emptying and bile dilution

Answer: D - Reduced meal-induced **CCK-mediated gallbladder contraction** produces stasis and concentrates lithogenic bile

Mechanism pearl: Absent enteral stimulation reduces **cholecystokinin** release; gallbladder stasis favors sludge and stones.

Q3. Black pigment stones

A 30-year-old woman with hereditary spherocytosis has recurrent biliary colic. Stones are small, hard, and radiopaque. Which mechanism best explains stone formation?

A. ABCG5/8 hypersecretion causes pure cholesterol monohydrate crystals
B. Chronic hemolysis increases bilirubin turnover, favoring sterile **calcium bilirubinate** precipitation
C. Biliary infection generates beta-glucuronidase in the common bile duct
D. Pancreaticobiliary malunion refluxes trypsin into the gallbladder as the dominant event
E. Somatostatin analogues induce gallbladder cancer through TP53 mutation

Answer: B - Chronic hemolysis increases bilirubin turnover, favoring sterile **calcium bilirubinate** precipitation

Mechanism pearl: Black pigment stones occur with hemolysis/cirrhosis; **brown pigment stones** occur with infection and stasis.

Q4. Brown pigment stones

A 67-year-old man with recurrent pyogenic cholangitis has soft brown common bile duct stones. What biochemical process best explains them?

A. HFE mutation increases biliary iron and causes cholesterol nucleation
B. Bacterial **beta-glucuronidase** deconjugates bilirubin in stagnant infected bile, producing calcium bilirubinate stones

C. MLH1 promoter methylation creates mucin-rich stones
D. Trypsinogen autoactivation produces black sterile pigment stones
E. CYP7A1 overactivity converts cholesterol into insoluble stones

Answer: B - Bacterial **beta-glucuronidase** deconjugates bilirubin in stagnant infected bile, producing calcium bilirubinate stones

Mechanism pearl: Brown stones are ductal infection/stasis stones; think bacterial enzymes and deconjugated bilirubin.

Q5. Biliary colic

A patient has episodic right upper quadrant pain 45 minutes after fatty meals. He is afebrile, leukocytes are normal, and pain resolves spontaneously. What is the mechanism of the pain?

A. Persistent bacterial infection of bile with systemic endotoxemia
B. Transient cystic duct obstruction with gallbladder contraction against an obstructed outlet
C. Full-thickness transmural necrosis of the gallbladder wall
D. Pancreatic duct disruption causing enzyme-rich ascites
E. IL-6 trans-signaling causing acinar neutrophil infiltration

Answer: B - Transient cystic duct obstruction with gallbladder contraction against an obstructed outlet

Mechanism pearl: Biliary colic is intermittent obstruction; fever, leukocytosis, and persistent pain suggest cholecystitis.

Q6. Acute cholecystitis

A 52-year-old woman has persistent RUQ pain, fever, leukocytosis, gallstones, wall thickening, pericholecystic fluid, and a sonographic Murphy sign. What mechanism best distinguishes this from biliary colic?

A. Persistent cystic duct obstruction triggers gallbladder distension, ischemia, mucosal injury, and secondary inflammation
B. Somatostatin receptor expression concentrates Ga-68 DOTATATE
C. Bacterial beta-glucuronidase deconjugates bilirubin in the common bile duct
D. Transient ampullary obstruction activates trypsinogen in pancreatic acini
E. GNAS mutation drives intraductal papillary mucin secretion

Answer: A - Persistent cystic duct obstruction triggers gallbladder distension, ischemia, mucosal injury, and secondary inflammation

Mechanism pearl: Acute cholecystitis requires sustained obstruction and inflammation, not just transient pain.

Q7. Acalculous cholecystitis

An intubated septic patient in ICU develops fever, leukocytosis, and a distended thick-walled gallbladder without stones. Which mechanism best explains the condition?

A. MEN1 mutation drives cystic duct gastrinoma
B. GNAS mutation produces mucinous pancreatic duct dilation
C. Cholesterol supersaturation from obesity is mandatory
D. Gallbladder ischemia and stasis in critical illness produce **acalculous cholecystitis**
E. Hemolysis produces black pigment stones in the gallbladder neck

Answer: D - Gallbladder ischemia and stasis in critical illness produce **acalculous cholecystitis**

Mechanism pearl: In ICU patients, **acalculous cholecystitis** is ischemic/stasis-driven and can progress rapidly.

Q8. Emphysematous cholecystitis

A diabetic man has RUQ pain and fever. CT shows gas in the gallbladder wall. Which mechanism is most likely?

A. Autoimmune granulocytic epithelial lesions of the gallbladder
B. VHL-driven serous cystadenoma compressing the cystic duct
C. S1P receptor modulation trapping lymphocytes in lymph nodes
D. Ischemic gallbladder injury with infection by gas-forming organisms such as Clostridium or enteric gram-negative bacteria
E. Sterile cholesterol crystal nucleation without inflammation

Answer: D - Ischemic gallbladder injury with infection by gas-forming organisms such as Clostridium or enteric gram-negative bacteria

Mechanism pearl: Gas in the wall in a diabetic patient suggests emphysematous cholecystitis: ischemia + gas-forming infection.

Q9. Hydrops/mucocele

A patient has a chronically obstructed cystic duct and a distended noninfected gallbladder filled with clear mucus. Which mechanism best explains the finding?

A. IgG4-positive plasma-cell pancreatitis with storiform fibrosis
B. Ongoing mucosal secretion into a gallbladder whose cystic duct remains obstructed, producing **hydrops**
C. Acinar trypsinogen activation with capillary leak
D. Main duct IPMN causing mucin extrusion from the papilla

E. Infected bile reflux into the bloodstream through high-pressure bile ducts

Answer: B - Ongoing mucosal secretion into a gallbladder whose cystic duct remains obstructed, producing **hydrops**

Mechanism pearl: Gallbladder **hydrops** is a mucocele from chronic cystic duct obstruction without acute infection.

Q10. Gallbladder polyp risk

A 63-year-old patient with PSC has an 11-mm sessile gallbladder polyp. Which mechanism-based reasoning supports cholecystectomy rather than ultrasound observation?

A. UDCA dissolves adenomatous polyps by reducing CEA production
B. Gallbladder polyps are diagnosed by acoustic shadowing and mobility
C. PSC protects against gallbladder dysplasia by increasing bile acid flow
D. Size, sessile morphology, age, and **PSC** increase probability of neoplastic epithelium rather than benign cholesterol polyp
E. All polyps below 20 mm are inflammatory and cannot be malignant

Answer: D - Size, sessile morphology, age, and **PSC** increase probability of neoplastic epithelium rather than benign cholesterol polyp

Mechanism pearl: Risk features for gallbladder polyp malignancy include **>=10 mm**, sessile morphology, age, and **PSC**.

Q11. Cholesterol polyp

A 38-year-old woman has multiple tiny non-shadowing gallbladder wall lesions that do not move. She has no PSC and no symptoms. What is the most plausible biology?

A. Direct KRAS-driven invasive gallbladder adenocarcinoma
B. IgG4-related lymphoplasmacytic cholecystitis in every case
C. Brown pigment stone adherent to the wall due to beta-glucuronidase
D. Pancreaticobiliary malunion causing bile duct dysplasia
E. Benign cholesterol-laden macrophage deposits in the gallbladder mucosa rather than true adenomatous neoplasia

Answer: E - Benign cholesterol-laden macrophage deposits in the gallbladder mucosa rather than true adenomatous neoplasia

Mechanism pearl: Small multiple gallbladder polyps are commonly **cholesterol polyps**, not true adenomas.

Q12. Porcelain gallbladder

A woman with long-standing gallstones has mural gallbladder calcification. Which mechanism explains why cancer risk is considered?

A. Bacterial toxin B glucosylates Rho proteins in the gallbladder wall
B. Cystic fibrosis transmembrane conductance regulator mutations directly methylate TP53
C. Chronic calculous inflammation can drive dysplasia-carcinoma progression in the gallbladder epithelium
D. Acute trypsinogen activation in acinar cells transforms cholangiocytes
E. Somatostatin receptor overexpression induces cholesterol stones

Answer: C - Chronic calculous inflammation can drive dysplasia-carcinoma progression in the gallbladder epithelium

Mechanism pearl: Gallbladder carcinoma is linked to chronic inflammation from stones, porcelain gallbladder, and anomalous pancreaticobiliary reflux.

Q13. Mirizzi syndrome

A patient with jaundice has a large stone impacted in the gallbladder neck and extrinsic compression of the common hepatic duct. Which mechanism explains the cholestasis?

A. VIP secretion causing achlorhydria and watery diarrhea
B. Inflammatory compression or erosion from an impacted cystic duct/Hartmann pouch stone causing **Mirizzi syndrome**
C. Main pancreatic duct mucin overproduction from IPMN
D. Primary ampullary sphincter spasm with normal bile duct anatomy
E. Infected necrosis causing pancreatic duct leak

Answer: B - Inflammatory compression or erosion from an impacted cystic duct/Hartmann pouch stone causing **Mirizzi syndrome**

Mechanism pearl: Mirizzi syndrome is mechanical inflammatory compression of the common hepatic duct by an impacted gallbladder-neck/cystic-duct stone.

Q14. Gallstone ileus

An 82-year-old woman has bowel obstruction, pneumobilia, and an ectopic calcified stone. What mechanism produced the obstruction?

A. Bacterial beta-glucuronidase causing purely intramural colonic stones
B. Sphincter of Oddi hypertension causing closed-loop small bowel obstruction
C. Cancer embolization through the portal vein into ileum
D. Chronic cholecystitis eroded into bowel, forming a **cholecystoenteric fistula** that allowed stone migration
E. Transient ampullary obstruction causing pancreatic edema

Answer: D - Chronic cholecystitis eroded into bowel, forming a **cholecystoenteric fistula** that allowed stone migration

Mechanism pearl: Gallstone ileus = **Rigler triad** logic: pneumobilia + obstruction + ectopic gallstone due to fistula.

Q15. Choledocholithiasis testing

A patient has gallstones, biliary pain, mildly abnormal liver tests, and no cholangitis. Ultrasound does not show a CBD stone. Which strategy best reflects mechanism-based risk stratification?

A. Avoid imaging because CBD stones cannot pass spontaneously
B. Treat with pancreatic enzymes because the primary problem is exocrine insufficiency
C. Proceed to ERCP in all patients because diagnostic ERCP has no pancreatitis risk
D. Use **EUS or MRCP** to detect occult duct stones before therapeutic ERCP when probability is intermediate
E. Use serum lipase alone to exclude choledocholithiasis

Answer: D - Use **EUS or MRCP** to detect occult duct stones before therapeutic ERCP when probability is intermediate

Mechanism pearl: Intermediate-risk CBD stones are evaluated with **EUS/MRCP**; ERCP is mainly therapeutic due to adverse event risk.

Q16. Ascending cholangitis

A 70-year-old woman with a CBD stone develops fever, jaundice, confusion, and hypotension. Why is urgent biliary drainage essential?

A. Cholangitis is primarily sterile immune-complex vasculitis
B. Bile duct drainage reverses KRAS mutations in cholangiocytes
C. The dominant problem is pancreatic exocrine insufficiency
D. Antibiotics cannot work unless gastric pH is above 6
E. Obstruction raises biliary pressure, allowing infected bile and endotoxin to reflux into systemic circulation

Answer: E - Obstruction raises biliary pressure, allowing infected bile and endotoxin to reflux into systemic circulation

Mechanism pearl: Cholangitis is infection plus obstruction; source control requires decompression.

Q17. Cholangitis antibiotic pharmacology

A patient with septic cholangitis is given broad-spectrum antibiotics and undergoes ERCP. Which pharmacologic principle is most important?

A. Antibiotics reduce bacteremia, but **source control** by biliary decompression corrects the high-pressure infected compartment
B. Antibiotics dissolve cholesterol stones by reducing bile saturation
C. ERCP works by suppressing TNF-alpha rather than drainage
D. Steroids are first-line because cholangitis is IgG4-mediated
E. Ursodeoxycholic acid rapidly sterilizes infected bile

Answer: A - Antibiotics reduce bacteremia, but **source control** by biliary decompression corrects the high-pressure infected compartment

Mechanism pearl: Sepsis in cholangitis cannot be treated by drugs alone when obstruction persists.

Q18. ERCP pancreatitis

A young woman develops pancreatitis after difficult cannulation for suspected CBD stone. What mechanism most directly initiates post-ERCP pancreatitis?

A. Somatostatin receptor blockade causes neuroendocrine tumor secretion
B. Papillary trauma, hydrostatic injury, and contrast/thermal irritation trigger acinar injury and **trypsinogen activation**
C. APC mutation transforms pancreatic duct cells within hours
D. Gastrin hypersecretion inactivates pancreatic bicarbonate
E. Bacterial beta-glucuronidase precipitates calcium bilirubinate in pancreatic ducts

Answer: B - Papillary trauma, hydrostatic injury, and contrast/thermal irritation trigger acinar injury and **trypsinogen activation**

Mechanism pearl: Post-ERCP pancreatitis is procedure-induced acinar/ductal injury converging on early enzyme activation and inflammation.

Q19. Post-ERCP pancreatitis prevention

A high-risk patient undergoes ERCP. Rectal indomethacin is given. Which mechanism best explains its prophylactic rationale?

A. Irreversible inhibition of trypsin enzymatic activity in acinar granules
B. Blockade of somatostatin receptors on pancreatic NETs
C. Direct chelation of pancreatic duct calcium by NSAIDs
D. Suppression of bile cholesterol saturation through FXR agonism
E. COX inhibition reduces prostaglandin-mediated inflammatory amplification after papillary/acinar injury

Answer: E - COX inhibition reduces prostaglandin-mediated inflammatory amplification after papillary/acinar injury

Mechanism pearl: Rectal NSAIDs reduce post-ERCP pancreatitis risk through anti-inflammatory effects; pancreatic stenting reduces ductal obstruction in selected high-risk cases.

Q20. Sphincter of Oddi dysfunction

A post-cholecystectomy woman has biliary-type pain with episodic liver enzyme elevation and a dilated bile duct but no stone. What mechanism is most plausible?

A. Von Hippel-Lindau mutation producing serous microcysts
B. Gallbladder hypomotility due to low CCK despite prior cholecystectomy
C. Hemolysis causing black pigment stones in the gallbladder lumen
D. MCN with ovarian stroma arising in the pancreatic tail
E. Functional or structural sphincter outflow obstruction causing episodic biliary hypertension

Answer: E - Functional or structural sphincter outflow obstruction causing episodic biliary hypertension

Mechanism pearl: SOD is an outflow disorder; objective enzyme/ductal abnormalities are more persuasive than pain alone.

Q21. Choledochal cyst malignancy

A 24-year-old woman has fusiform extrahepatic bile duct dilatation and recurrent cholangitis. Why is excision recommended?

A. Somatostatin analogues reverse congenital duct dilation
B. UDCA reliably eliminates dysplastic epithelium
C. Chronic stasis and pancreaticobiliary reflux drive biliary epithelial inflammation, dysplasia, and **cholangiocarcinoma** risk
D. The cyst produces insulin and causes hypoglycemia
E. The cyst protects the bile duct from bacterial colonization

Answer: C - Chronic stasis and pancreaticobiliary reflux drive biliary epithelial inflammation, dysplasia, and **cholangiocarcinoma** risk

Mechanism pearl: Choledochal cysts are premalignant because of **stasis** and **pancreaticobiliary reflux**.

Q22. Pancreaticobiliary malunion

A child with recurrent pancreatitis has a long common channel outside the duodenal wall. Which mechanism explains both pancreatitis and biliary cancer risk?

A. Octreotide causes ductal dysplasia by somatostatin receptor activation
B. Loss of sphincteric separation permits reciprocal reflux of pancreatic juice into bile ducts and bile into pancreatic duct
C. Gastrinoma causes reflux of acid into the common bile duct
D. SPINK1 mutation directly dilates the extrahepatic bile duct
E. Excess CCK causes gallbladder contraction without duct communication

Answer: B - Loss of sphincteric separation permits reciprocal reflux of pancreatic juice into bile ducts and bile into pancreatic duct

Mechanism pearl: Pancreaticobiliary malunion creates abnormal reflux; choledochal cysts are commonly associated.

Q23. Gallbladder cancer biology

A patient from a region with high gallstone prevalence has a gallbladder mass invading the liver. Which long-term mechanism best explains most sporadic gallbladder carcinogenesis?

A. Chronic epithelial injury from stones and inflammation promotes metaplasia-dysplasia-carcinoma progression
B. Loss of CFTR alone produces gallbladder adenocarcinoma
C. All cases arise from MEN1-related neuroendocrine dysplasia
D. An acute cystic duct obstruction transforms epithelium immediately
E. Trypsinogen activation in acinar cells is the required first step

Answer: A - Chronic epithelial injury from stones and inflammation promotes metaplasia-dysplasia-carcinoma progression

Mechanism pearl: Gallbladder cancer is often inflammation-driven; stones are a risk marker and chronic irritant.

Q24. Acute pancreatitis diagnosis

A man has epigastric pain radiating to the back and vomiting. Lipase is 4 times the upper limit. CT is normal early. Which diagnostic logic is most appropriate?

A. CT necrosis is mandatory before diagnosis
B. Amylase must exceed lipase in biliary pancreatitis
C. Pain alone is sufficient even with normal enzymes and imaging
D. Acute pancreatitis can be diagnosed by 2 of 3 criteria: typical pain, enzymes >=3x, or imaging changes
E. CRP elevation at admission is required for diagnosis

Answer: D - Acute pancreatitis can be diagnosed by 2 of 3 criteria: typical pain, enzymes >=3x, or imaging changes

Mechanism pearl: Diagnosis requires **2 of 3**; early CT may be normal and is not always needed.

Q25. Biliary pancreatitis ALT

A 55-year-old woman has acute pancreatitis. Admission ALT is more than three times the upper limit of normal. What does this suggest mechanistically?

A. Transient or persistent ampullary obstruction by a migrating stone causing biliary pancreatitis
B. Autoimmune pancreatitis is confirmed by hepatocellular enzyme rise
C. Hypertriglyceridemia is excluded by ALT elevation
D. Pancreatic cancer is ruled out because ALT is high
E. Alcohol-induced CFTR inhibition is proven by ALT elevation

Answer: A - Transient or persistent ampullary obstruction by a migrating stone causing biliary pancreatitis

Mechanism pearl: In acute pancreatitis, marked early **ALT elevation** strongly suggests biliary etiology.

Q26. Gallstone size and pancreatitis

A patient has recurrent biliary pancreatitis with many small gallstones. Why are small stones particularly dangerous for pancreatitis?

A. Small stones express somatostatin receptors and block pancreatic secretion
B. Small stones cause hemolysis and black pigment stone formation
C. Small stones activate PRSS1 inside acinar cells without duct migration
D. Large stones dissolve faster and release toxic cholesterol monomers
E. Small stones can migrate through the cystic duct into the distal CBD/ampulla and transiently obstruct the papilla

Answer: E - Small stones can migrate through the cystic duct into the distal CBD/ampulla and transiently obstruct the papilla

Mechanism pearl: Small migrating stones and microlithiasis are classic triggers of **biliary pancreatitis**.

Q27. Acinar trypsinogen activation

A research case of acute pancreatitis shows early intracellular colocalization of lysosomal enzymes and zymogen granules. Which event is central?

A. Bacterial beta-glucuronidase activation of bilirubin
B. Cathepsin B-mediated premature **trypsinogen activation** within acinar cells
C. Somatostatin receptor internalization in islet cells
D. IgM rheumatoid factor binding anti-HCV IgG
E. MLH1 methylation causing microsatellite instability

Answer: B - Cathepsin B-mediated premature **trypsinogen activation** within acinar cells

Mechanism pearl: Acute pancreatitis converges on premature intrapancreatic enzyme activation, especially **trypsin**.

Q28. Calcium and pancreatitis

A patient with primary hyperparathyroidism develops pancreatitis. Which intracellular mechanism links hypercalcemia to acinar injury?

A. Calcium directly methylates KRAS in pancreatic duct cells
B. Sustained acinar **calcium signaling** favors premature zymogen activation and impaired cellular homeostasis
C. Calcium activates MLH1 repair and causes necrosis
D. Calcium suppresses all trypsin activity and causes duct obstruction
E. Calcium binds CEA in cyst fluid and creates mucin

Answer: B - Sustained acinar **calcium signaling** favors premature zymogen activation and impaired cellular homeostasis

Mechanism pearl: Pathologic acinar **Ca2+** signals promote zymogen activation and pancreatitis.

Q29. Alcohol pancreatitis mechanism

A chronic alcohol user develops recurrent acute pancreatitis. Genetic testing is negative. Which mechanism is most coherent?

A. Alcohol sensitizes acinar cells to injury and impairs ductal bicarbonate-rich secretion, partly through **CFTR** dysfunction
B. Alcohol methylates MLH1 in every pancreatic duct cell
C. Alcohol causes gallbladder contraction through CCK agonism
D. Alcohol directly forms black pigment stones by hemolysis
E. Alcohol blocks somatostatin receptors on NETs

Answer: A - Alcohol sensitizes acinar cells to injury and impairs ductal bicarbonate-rich secretion, partly through **CFTR** dysfunction

Mechanism pearl: Alcohol affects acinar and ductal biology, including secretion, calcium handling, and inflammatory susceptibility.

Q30. PRSS1 hereditary pancreatitis

A teenager has recurrent pancreatitis and a family history across generations. PRSS1 gain-of-function mutation is found. Which mechanism explains disease?

A. Bacterial toxins deconjugate bilirubin in pancreatic ducts
B. Loss of mismatch repair causes pancreatic acinar apoptosis
C. Reduced CCK secretion causes gallbladder hypomotility
D. Enhanced cationic trypsinogen activation or impaired inactivation increases intrapancreatic trypsin activity
E. IgG4-positive plasma cells obliterate pancreatic veins

Answer: D - Enhanced cationic trypsinogen activation or impaired inactivation increases intrapancreatic trypsin activity

Mechanism pearl: PRSS1 hereditary pancreatitis increases trypsin activity and raises pancreatic cancer risk over time.

Q31. SPINK1 modifier

A patient with recurrent idiopathic pancreatitis has a SPINK1 variant. Which role best explains susceptibility?

A. Activation of FXR increases ductal bicarbonate
B. Increased bile cholesterol secretion creates pigment stones
C. Reduced intrapancreatic trypsin inhibition lowers the threshold for enzyme-mediated injury
D. Loss of DPC4 creates invasive cancer immediately
E. Increased somatostatin receptor density causes hypoglycemia

Answer: C - Reduced intrapancreatic trypsin inhibition lowers the threshold for enzyme-mediated injury

Mechanism pearl: SPINK1 encodes a pancreatic trypsin inhibitor; variants act as susceptibility/modifier factors.

Q32. CFTR pancreatitis

A man with recurrent pancreatitis has a CFTR mutation but no classic cystic fibrosis lung disease. Which pancreatic mechanism is most relevant?

A. Excess insulin secretion from beta cells causes acinar necrosis
B. GNAS mutation creates a serous cystadenoma
C. Defective ductal chloride/bicarbonate transport makes secretions viscous and protein-rich, predisposing to ductal obstruction
D. IgG4-related storiform fibrosis is mandatory
E. Gallbladder bile becomes sterile and supersaturated with bilirubin

Answer: C - Defective ductal chloride/bicarbonate transport makes secretions viscous and protein-rich, predisposing to ductal obstruction

Mechanism pearl: CFTR variants impair ductal flushing and bicarbonate secretion, predisposing to recurrent pancreatitis.

Q33. Hypertriglyceridemic pancreatitis

A diabetic patient has pancreatitis with triglycerides 2400 mg/dL and lipemic serum. Which mechanism best explains pancreatic injury?

A. Pancreatic lipase hydrolyzes excess triglycerides into toxic free fatty acids causing microvascular and acinar injury
B. Triglycerides directly increase gallbladder CCK receptors
C. Triglycerides activate IL-4 receptor alpha on acinar cells
D. Triglycerides create IgG4-positive obliterative phlebitis
E. Triglycerides mechanically obstruct the ampulla as stones

Answer: A - Pancreatic lipase hydrolyzes excess triglycerides into toxic free fatty acids causing microvascular and acinar injury

Mechanism pearl: Severe hypertriglyceridemia injures via **free fatty acids** and microcirculatory toxicity.

Q34. Severity biomarkers AP

A patient with acute pancreatitis has rising IL-6 and later CRP. Which pathway links these markers to severe disease biology?

A. IL-6/gp130 signaling activates JAK-STAT and acute-phase responses, reflecting systemic inflammatory amplification
B. Somatostatin receptor density drives capillary leak
C. CA19-9 directly activates neutrophils through KRAS
D. Bacterial beta-glucuronidase triggers STAT3 in acinar cells only
E. CEA secretion from mucinous cysts predicts early organ failure

Answer: A - IL-6/gp130 signaling activates JAK-STAT and acute-phase responses, reflecting systemic inflammatory amplification

Mechanism pearl: IL-6 and **CRP** are severity-linked biomarkers because they reflect systemic inflammation.

Q35. NF-kB and acinar inflammation

An experimental model shows acinar NF-kB activation before extensive necrosis. What does this imply?

A. NF-kB activation proves pancreatic adenocarcinoma
B. NF-kB suppresses all chemokines and prevents neutrophil recruitment
C. NF-kB is activated only by somatostatin analogues
D. NF-kB activity excludes trypsinogen activation
E. Acinar cells participate in inflammatory cytokine generation, not merely passive victims of enzyme digestion

Answer: E - Acinar cells participate in inflammatory cytokine generation, not merely passive victims of enzyme digestion

Mechanism pearl: Acute pancreatitis is enzyme injury plus **immune signaling** from acinar, endothelial, and immune cells.

Q36. Atlanta classification

A pancreatitis patient has transient renal failure for 24 hours and a peripancreatic fluid collection. What category best reflects the revised Atlanta logic?

A. Mild acute pancreatitis because the kidney recovered
B. Autoimmune pancreatitis because renal dysfunction occurred
C. Chronic pancreatitis because a collection is present
D. Severe acute pancreatitis because any collection defines severe disease
E. Moderately severe acute pancreatitis because organ failure is transient and local complication is present

Answer: E - Moderately severe acute pancreatitis because organ failure is transient and local complication is present

Mechanism pearl: Revised Atlanta: severe = **persistent organ failure >48 h**; local complications alone can be moderately severe.

Q37. Necrotizing pancreatitis

CT shows nonenhancing pancreatic tissue and peripancreatic necrosis in acute pancreatitis. Why is this not a simple pseudocyst?

A. All fluid collections after pancreatitis are true pseudocysts
B. A pseudocyst is defined by internal solid necrotic material
C. Necrotizing pancreatitis contains nonviable solid debris and may mature into **walled-off necrosis**
D. Necrosis requires IgG4 positivity
E. A serous cystadenoma appears only after acute pancreatitis

Answer: C - Necrotizing pancreatitis contains nonviable solid debris and may mature into **walled-off necrosis**

Mechanism pearl: Distinguish **pseudocyst** (fluid) from **WON** (necrotic debris) after necrotizing pancreatitis.

Q38. Pseudocyst

A patient has a persistent homogeneous fluid collection with mature wall 6 weeks after interstitial pancreatitis and no internal solid debris. What is the most accurate diagnosis?

A. Serous cystadenoma because the wall has matured
B. Main-duct IPMN because it developed after 4 weeks
C. Walled-off necrosis because all mature collections contain necrosis
D. Mucinous cystic neoplasm because all cysts after pancreatitis are premalignant
E. Pancreatic **pseudocyst** formed from enzyme-rich fluid after interstitial pancreatitis

Answer: E - Pancreatic **pseudocyst** formed from enzyme-rich fluid after interstitial pancreatitis

Mechanism pearl: A true **pseudocyst** is mature, fluid-filled, and lacks necrotic debris.

Q39. Infected necrosis

A patient with necrotizing pancreatitis deteriorates after 2 weeks with fever, sepsis, and gas in the necrotic collection. What mechanism-based intervention is most rational?

A. Immediate open necrosectomy in the first 48 hours for all necrosis
B. Octreotide to sterilize necrosis through SSTR2
C. High-dose steroids because necrosis is autoimmune
D. Antibiotics that penetrate necrosis plus step-up drainage/debridement when infected necrosis is suspected or confirmed
E. UDCA to dissolve necrotic debris

Answer: D - Antibiotics that penetrate necrosis plus step-up drainage/debridement when infected necrosis is suspected or confirmed

Mechanism pearl: Infected necrosis needs antimicrobial therapy and **source control**, often delayed/step-up when feasible.

Q40. No prophylactic antibiotics AP

A patient with sterile necrotizing pancreatitis is clinically stable. The intern asks for prophylactic broad-spectrum antibiotics. Which reasoning is best?

A. Steroids are safer than antibiotics for necrosis
B. Antibiotics dissolve walled-off necrosis
C. Sterile necrosis alone does not justify routine prophylactic antibiotics; treatment targets proven/suspected infection
D. Antibiotics prevent trypsinogen activation in all patients
E. All pancreatic necrosis is infected by definition

Answer: C - Sterile necrosis alone does not justify routine prophylactic antibiotics; treatment targets proven/suspected infection

Mechanism pearl: Avoid routine prophylactic antibiotics for sterile necrosis; use antibiotics for **infected necrosis** or extrapancreatic infection.

Q41. Enteral nutrition AP

A patient with severe pancreatitis cannot eat. The ICU team debates TPN versus enteral tube feeding. Which mechanism favors enteral nutrition when feasible?

A. Enteral feeding directly inhibits PRSS1 transcription
B. TPN suppresses IL-6 more effectively than gut feeding
C. TPN increases pancreatic duct bicarbonate and prevents necrosis
D. Maintaining gut barrier function reduces bacterial translocation and infectious complications
E. Enteral feeding dissolves gallstones through bile acid binding

Answer: D - Maintaining gut barrier function reduces bacterial translocation and infectious complications

Mechanism pearl: Early **enteral nutrition** supports mucosal barrier integrity in severe pancreatitis.

Q42. Fluid resuscitation AP

A patient presents early with acute pancreatitis, tachycardia, hemoconcentration, and rising creatinine. What mechanism explains early aggressive but monitored fluids?

A. Acinar necrosis is prevented by fasting alone
B. Fluid therapy inhibits KRAS signaling in duct cells
C. Pancreatitis causes hypervolemia through aldosterone excess
D. Inflammatory vascular leak causes intravascular depletion and pancreatic microcirculatory compromise
E. CBD stones are dissolved by lactated Ringer solution

Answer: D - Inflammatory vascular leak causes intravascular depletion and pancreatic microcirculatory compromise

Mechanism pearl: Early organ failure is linked to **capillary leak** and hypovolemia; resuscitation should be goal-directed.

Q43. ERCP in biliary pancreatitis

A woman with gallstone pancreatitis has improving pain and no jaundice or cholangitis. MRCP shows no retained CBD stone. Why is urgent ERCP not indicated?

A. ERCP is contraindicated in all gallstone pancreatitis
B. ERCP diagnoses hypertriglyceridemia better than serum testing
C. ERCP prevents gallbladder stones from forming after discharge
D. Urgent ERCP treats pancreatic necrosis directly
E. Most biliary pancreatitis follows transient obstruction; ERCP benefits mainly persistent obstruction or cholangitis

Answer: E - Most biliary pancreatitis follows transient obstruction; ERCP benefits mainly persistent obstruction or cholangitis

Mechanism pearl: Urgent ERCP is for **cholangitis** or persistent biliary obstruction, not every biliary pancreatitis.

Q44. Cholecystectomy after biliary AP

A patient recovers from mild gallstone pancreatitis. Why is same-admission cholecystectomy generally recommended when fit?

A. Cholecystectomy reverses pancreatic fibrosis
B. Removing the gallbladder prevents recurrent migration of stones or microlithiasis into the ampulla
C. Cholecystectomy eliminates IPMN malignant risk
D. Cholecystectomy treats hypertriglyceridemia directly
E. Cholecystectomy inhibits IL-6 trans-signaling

Answer: B - Removing the gallbladder prevents recurrent migration of stones or microlithiasis into the ampulla

Mechanism pearl: After mild biliary pancreatitis, definitive gallbladder therapy prevents recurrence.

Q45. Abdominal compartment syndrome AP

A patient with severe pancreatitis develops tense abdomen, oliguria, high airway pressures, and shock after large-volume resuscitation. Which mechanism is most relevant?

A. Bile acid malabsorption increases intraperitoneal pressure
B. Pancreatic NET secretion causes mesenteric desmoplasia
C. Gallbladder empyema directly compresses the left renal vein
D. Intra-abdominal hypertension reduces renal perfusion and venous return, worsening organ failure
E. IgG4 pancreatitis causes immediate abdominal wall fibrosis

Answer: D - Intra-abdominal hypertension reduces renal perfusion and venous return, worsening organ failure

Mechanism pearl: Severe pancreatitis can cause **abdominal compartment syndrome** through edema, ileus, and fluid accumulation.

Q46. Splenic vein thrombosis

A man with chronic pancreatitis develops isolated gastric varices with normal liver tests and patent portal vein. Which mechanism best explains this?

A. Cirrhotic sinusoidal fibrosis increases portal pressure globally
B. Pancreatic duct stenting increases hepatic vein pressure
C. VIPoma causes gastric varices by chloride secretion
D. Local pancreatic inflammation causes **splenic vein thrombosis**, producing left-sided portal hypertension
E. Acalculous cholecystitis obstructs the splenic artery

Answer: D - Local pancreatic inflammation causes **splenic vein thrombosis**, producing left-sided portal hypertension

Mechanism pearl: Pancreatitis-related splenic vein thrombosis causes isolated gastric varices without cirrhosis.

Q47. Chronic pancreatitis fibrosis

A long-term alcoholic patient has calcific chronic pancreatitis. Which cellular mechanism drives progressive fibrosis?

A. Serous cystadenoma glycogen accumulation
B. Loss of MLH1 mismatch repair in acinar cells
C. Sphincter of Oddi basal pressure below zero
D. Activation of pancreatic stellate cells with extracellular matrix deposition in response to injury and cytokines
E. IgM rheumatoid factor immune-complex deposition

Answer: D - Activation of pancreatic stellate cells with extracellular matrix deposition in response to injury and cytokines

Mechanism pearl: Pancreatic stellate cells are central to **fibrosis** in chronic pancreatitis.

Q48. Chronic pancreatitis pain

A patient with calcific chronic pancreatitis has persistent pain despite enzyme therapy and duct decompression. Which mechanism can explain refractory pain?

A. Pain is due only to bile acid diarrhea
B. Pseudocyst fluid always causes neuropathic pain
C. Neural inflammation and central sensitization can maintain pain beyond ductal hypertension
D. Pain requires high CA19-9
E. Pain proves active acute pancreatitis in every case

Answer: C - Neural inflammation and central sensitization can maintain pain beyond ductal hypertension

Mechanism pearl: Chronic pancreatitis pain is ductal, inflammatory, and **neuropathic**.

Q49. Pancreatic enzyme replacement

A patient with chronic pancreatitis has steatorrhea and weight loss. Which mechanism best explains benefit from pancreatic enzyme replacement?

A. Enzymes dissolve calcium stones in the pancreatic duct
B. Enzymes suppress IL-6 trans-signaling in acinar cells
C. Enzymes inhibit somatostatin receptors on NETs
D. Enzymes reverse endocrine beta-cell loss
E. Exogenous lipase improves intraluminal triglyceride digestion when pancreatic secretion is insufficient

Answer: E - Exogenous lipase improves intraluminal triglyceride digestion when pancreatic secretion is insufficient

Mechanism pearl: Steatorrhea usually appears after marked loss of exocrine output; **lipase replacement** is key.

Q50. PERT and acid suppression

A patient on pancreatic enzymes still has steatorrhea. Non-enteric-coated enzyme therapy is being used. Why may acid suppression improve response?

A. Gastric acid can inactivate lipase; raising duodenal pH improves enzyme activity and delivery
B. PPIs lower cyst fluid CEA
C. Acid suppression blocks CCK and increases gallbladder contraction
D. PPIs regenerate acinar tissue through EGFR
E. H2 blockers activate PRSS1

Answer: A - Gastric acid can inactivate lipase; raising duodenal pH improves enzyme activity and delivery

Mechanism pearl: Pancreatic **lipase is acid-labile**; pH matters for enzyme efficacy.

Q51. Pancreatic diabetes

A man with advanced chronic pancreatitis develops brittle diabetes with recurrent hypoglycemia. Which mechanism distinguishes type 3c diabetes?

A. MEN1-related insulinoma causing fasting hypoglycemia
B. SGLT2 activation causing glycosuria
C. Loss of both insulin-producing beta cells and glucagon-producing alpha cells impairs counterregulation
D. Pure insulin resistance from visceral obesity
E. Autoimmune beta-cell destruction with preserved glucagon

Answer: C - Loss of both insulin-producing beta cells and glucagon-producing alpha cells impairs counterregulation

Mechanism pearl: Pancreatogenic diabetes includes loss of **insulin and glucagon**, making hypoglycemia risk important.

Q52. Chronic pancreatitis duct stones

A patient with painful obstructive chronic pancreatitis has a dilated main pancreatic duct and obstructing stone in the head. Which mechanism supports endoscopic or surgical duct decompression?

A. Duct dilation proves pancreatic cancer is unresectable
B. Duct stones secrete VIP and cause watery diarrhea
C. Duct decompression reverses IgG4-positive fibrosis in all cases
D. Duct stones cause isolated gallbladder cholesterol supersaturation
E. Ductal hypertension upstream of obstruction contributes to pain and recurrent injury

Answer: E - Ductal hypertension upstream of obstruction contributes to pain and recurrent injury

Mechanism pearl: Obstructive chronic pancreatitis pain may improve when **ductal hypertension** is relieved.

Q53. Pancreatic duct leak

A patient develops high-amylase ascites after pancreatitis. Which mechanism best explains the ascites?

A. CA19-9 secretion increases vascular permeability
B. Disruption of the pancreatic duct allows enzyme-rich pancreatic fluid to leak into the peritoneal cavity
C. VIPoma causes ascites by chloride secretion
D. Gallbladder cholesterol stones leak bile directly through the pancreas
E. Portal hypertension from cirrhosis causes low-amylase transudate

Answer: B - Disruption of the pancreatic duct allows enzyme-rich pancreatic fluid to leak into the peritoneal cavity

Mechanism pearl: High-amylase ascites suggests **pancreatic duct leak/disruption**.

Q54. Disconnected duct syndrome

After necrotizing pancreatitis, a patient has recurrent fluid collections despite drainage. Imaging shows viable distal pancreas disconnected from the duodenum. What mechanism explains recurrence?

A. IgG4 disease obstructs the minor papilla only
B. NET hormones cause mucinous cyst recurrence
C. Serous cystadenoma secretes amylase-rich fluid
D. Continuing secretion from isolated upstream pancreas drains into collections rather than into the ductal system
E. The gallbladder continues to produce cholesterol crystals

Answer: D - Continuing secretion from isolated upstream pancreas drains into collections rather than into the ductal system

Mechanism pearl: Disconnected pancreatic duct syndrome causes recurrent collections after necrosis disrupts duct continuity.

Q55. Autoimmune pancreatitis type 1

A 64-year-old man has painless jaundice, diffuse pancreatic enlargement, elevated IgG4, and steroid responsiveness. Which pathobiology is most likely?

A. Acinar cathepsin B-mediated acute enzyme activation
B. KRAS-driven pancreatic intraepithelial neoplasia
C. Mucinous cystic neoplasm with ovarian-type stroma
D. IgG4-related lymphoplasmacytic sclerosing pancreatitis with storiform fibrosis and obliterative phlebitis
E. MEN1-associated islet-cell hyperplasia

Answer: D - IgG4-related lymphoplasmacytic sclerosing pancreatitis with storiform fibrosis and obliterative phlebitis

Mechanism pearl: Type 1 **autoimmune pancreatitis** is part of systemic **IgG4-related disease**.

Q56. Autoimmune pancreatitis type 2

A 32-year-old woman with ulcerative colitis develops pancreatitis. Histology shows granulocytic epithelial lesions and IgG4 is normal. Which diagnosis fits?

A. Type 2 autoimmune pancreatitis, often IBD-associated and not part of systemic IgG4 disease
B. Type 1 IgG4-related pancreatitis with multiorgan disease
C. Main duct IPMN with GNAS mutation
D. Alcoholic calcific chronic pancreatitis
E. VIPoma with WDHA syndrome

Answer: A - Type 2 autoimmune pancreatitis, often IBD-associated and not part of systemic IgG4 disease

Mechanism pearl: Type 2 AIP is **duct-centric**, may associate with IBD, and lacks classic IgG4 systemic features.

Q57. Steroids in AIP

A patient with suspected autoimmune pancreatitis has pancreatic head enlargement and obstructive jaundice. Why must cancer exclusion be careful before steroid trial?

A. Steroids prevent biliary drainage in cholangitis
B. Steroids directly mutate KRAS in all pancreatic cancers
C. Steroids can shrink inflammatory AIP but may delay diagnosis of pancreatic ductal adenocarcinoma that mimics it
D. Steroids always cure pancreatic adenocarcinoma
E. Steroids dissolve gallstones and mask choledocholithiasis

Answer: C - Steroids can shrink inflammatory AIP but may delay diagnosis of pancreatic ductal adenocarcinoma that mimics it

Mechanism pearl: AIP is steroid-responsive, but **pancreatic cancer mimicry** makes tissue/imaging context crucial.

Q58. Rituximab IgG4 disease

A patient with relapsing IgG4-related pancreatitis and cholangitis cannot taper steroids. Rituximab is considered. Which mechanism supports it?

A. FXR agonism reverses storiform fibrosis
B. COX inhibition prevents all IgG4 relapses
C. CD20-positive B-cell depletion reduces plasmablast-driven IgG4-related immune activity
D. SSTR2 blockade reduces pancreatic fibrosis
E. JAK2 activation reduces plasma cells

Answer: C - CD20-positive B-cell depletion reduces plasmablast-driven IgG4-related immune activity

Mechanism pearl: Relapsing **IgG4-related disease** can respond to B-cell depletion with rituximab.

Q59. Pancreatic cyst fluid CEA

A 68-year-old woman has an incidental pancreatic cyst. EUS cyst fluid shows high CEA and mucin. Which interpretation is best?

A. High CEA is typical of pseudocyst after pancreatitis
B. High CEA excludes IPMN
C. High CEA measures pancreatic exocrine insufficiency
D. High cyst-fluid CEA supports a **mucinous cyst** but does not alone prove invasive cancer
E. High CEA proves serous cystadenoma

Answer: D - High cyst-fluid CEA supports a **mucinous cyst** but does not alone prove invasive cancer

Mechanism pearl: Cyst-fluid **CEA** helps identify mucinous lineage; it is not a reliable cancer-stage marker alone.

Q60. Pseudocyst cyst fluid

A patient with prior pancreatitis has a pancreatic cyst. Fluid amylase is very high and CEA is low. What mechanism is most likely?

A. Nonfunctional pancreatic NET with cystic degeneration
B. Serous microcystic neoplasm with VHL pathway loss
C. Ovarian-type stromal mucinous neoplasm
D. Main-duct IPMN with high-risk dysplasia
E. Communication with pancreatic ductal fluid after pancreatitis, consistent with **pseudocyst**

Answer: E - Communication with pancreatic ductal fluid after pancreatitis, consistent with **pseudocyst**

Mechanism pearl: Pseudocysts often have **high amylase** and low CEA, reflecting pancreatic juice rather than mucinous neoplasia.

Q61. IPMN genetics

A main-duct pancreatic cystic lesion produces mucin and has a patulous papilla. Sequencing shows KRAS and GNAS mutations. Which diagnosis is most coherent?

A. Pancreatic pseudocyst from duct disruption
B. Solid pseudopapillary neoplasm with beta-catenin activation
C. IgG4-related pancreatitis with obliterative phlebitis

D. Serous cystadenoma with glycogen-rich epithelium
E. **Intraductal papillary mucinous neoplasm** with mucin-producing ductal epithelium

Answer: E - **Intraductal papillary mucinous neoplasm** with mucin-producing ductal epithelium

Mechanism pearl: IPMN is a mucin-producing ductal neoplasm; **GNAS** is a useful molecular clue.

Q62. Main duct IPMN risk

A patient has main pancreatic duct dilation to 12 mm and mural nodule within an IPMN. Why is surgery favored if fit?

A. Surgery is avoided because IPMN never progresses
B. Mural nodules are diagnostic of pseudocyst debris only
C. Octreotide eliminates mural nodules by SSTR2 activation
D. Main duct involvement and enhancing mural nodule indicate high probability of high-grade dysplasia or invasive carcinoma
E. Main duct dilation proves benign serous cystadenoma

Answer: D - Main duct involvement and enhancing mural nodule indicate high probability of high-grade dysplasia or invasive carcinoma

Mechanism pearl: Main duct IPMN and **mural nodules** are high-risk features.

Q63. Branch duct IPMN surveillance

A 72-year-old man has a 1.4-cm branch-duct IPMN without nodules, symptoms, or main duct dilation. Which reasoning supports surveillance rather than immediate surgery?

A. KRAS mutation excludes mucinous lineage
B. CEA-negative fluid proves no malignant potential
C. Small branch-duct IPMNs without high-risk features have lower malignant potential than main-duct disease
D. All branch-duct IPMNs are benign and need no follow-up
E. Branch duct location makes EUS impossible

Answer: C - Small branch-duct IPMNs without high-risk features have lower malignant potential than main-duct disease

Mechanism pearl: Risk stratification in IPMN depends on duct type, size, nodules, duct dilation, cytology, and symptoms.

Q64. Mucinous cystic neoplasm

A 48-year-old woman has a pancreatic tail cyst that does not communicate with the duct. Pathology shows mucinous epithelium and ovarian-type stroma. What is the diagnosis?

A. Pseudocyst because ovarian stroma follows pancreatitis
B. Serous cystadenoma because tail location is diagnostic
C. **Mucinous cystic neoplasm** with premalignant potential
D. Type 2 autoimmune pancreatitis
E. Branch-duct IPMN because all mucinous cysts communicate with ducts

Answer: C - **Mucinous cystic neoplasm** with premalignant potential

Mechanism pearl: MCN occurs mostly in women, often body/tail, with **ovarian-type stroma** and no duct communication.

Q65. Serous cystadenoma

A 69-year-old woman has a microcystic honeycomb pancreatic lesion with central scar. Fluid CEA is low. Which molecular association is most characteristic?

A. Serous cystadenoma with glycogen-rich epithelium, sometimes associated with **VHL** pathway disease
B. High-amylase pseudocyst from duct leak
C. MEN1 gastrinoma arising in duodenum
D. GNAS-mutant main duct IPMN
E. Ovarian-stroma mucinous cystic neoplasm

Answer: A - Serous cystadenoma with glycogen-rich epithelium, sometimes associated with **VHL** pathway disease

Mechanism pearl: **Serous cystadenoma** is usually benign, microcystic, low CEA, and can be VHL-associated.

Q66. Solid pseudopapillary neoplasm

A 24-year-old woman has a large encapsulated pancreatic mass with solid and cystic components. Which mechanism is most typical?

A. GNAS mutation causing ductal mucin secretion
B. Beta-catenin pathway activation in **solid pseudopapillary neoplasm** with low-grade malignant potential
C. PRSS1 mutation causing calcific pancreatitis only
D. IgG4 plasma-cell pancreatitis
E. VHL loss causing glycogen-rich serous cystadenoma

Answer: B - Beta-catenin pathway activation in **solid pseudopapillary neoplasm** with low-grade malignant potential

Mechanism pearl: Young woman + solid-cystic pancreatic mass = **solid pseudopapillary neoplasm**.

Q67. Pancreatic adenocarcinoma genetics

A pancreatic ductal adenocarcinoma shows KRAS mutation, CDKN2A loss, TP53 mutation, and SMAD4 loss. What concept does this illustrate?

A. VHL-associated benign microcystic neoplasm
B. Stepwise accumulation of driver alterations from PanIN to invasive ductal adenocarcinoma
C. MEN1-related well-differentiated endocrine tumor biology
D. IgG4-mediated reversible fibroinflammation
E. Acute inflammatory cytokine activation without clonal evolution

Answer: B - Stepwise accumulation of driver alterations from PanIN to invasive ductal adenocarcinoma

Mechanism pearl: PDAC progression involves **KRAS**, **CDKN2A**, **TP53**, and **SMAD4/DPC4** alterations.

Q68. CA19-9 limitation

A patient with pancreatic cancer has normal CA19-9 despite metastatic disease. Which mechanism explains a false-negative result?

A. Jaundice always lowers CA19-9 to zero
B. Lewis antigen-negative individuals cannot synthesize CA19-9 normally
C. CA19-9 is produced only by neuroendocrine tumors
D. CA19-9 is absent whenever KRAS is mutated
E. CA19-9 is a trypsin activation peptide

Answer: B - Lewis antigen-negative individuals cannot synthesize CA19-9 normally

Mechanism pearl: CA19-9 is useful but imperfect: Lewis-negative status can cause false-negatives; cholestasis can cause false-positives.

Q69. Pancreatic cancer desmoplasia

A biopsy of pancreatic adenocarcinoma shows dense stromal reaction. Which translational concept best explains drug resistance?

A. Bile acid sequestration blocks chemotherapy absorption
B. Somatostatin receptors mediate all resistance
C. The tumor lacks KRAS mutation in all cases
D. High vascularity rapidly delivers chemotherapy to every cell
E. Desmoplastic stroma and activated fibroblast/stellate-cell signaling create hypovascular barriers and immunosuppressive microenvironment

Answer: E - Desmoplastic stroma and activated fibroblast/stellate-cell signaling create hypovascular barriers and immunosuppressive microenvironment

Mechanism pearl: PDAC is not just malignant epithelium; **stroma** shapes hypoxia, drug delivery, and immune evasion.

Q70. Pancreatic cancer resectability

A patient has pancreatic head cancer. CT shows encasement of the superior mesenteric artery. Why is surgery not upfront curative?

A. Arterial encasement indicates locally advanced biology/anatomy with inability to obtain safe oncologic resection
B. EUS biopsy always converts unresectable tumors to resectable
C. CA19-9 alone defines surgical resectability
D. Any venous contact is unresectable by definition
E. SMA encasement proves autoimmune pancreatitis

Answer: A - Arterial encasement indicates locally advanced biology/anatomy with inability to obtain safe oncologic resection

Mechanism pearl: Pancreatic cancer management depends on **vascular involvement** and metastatic status, not size alone.

Q71. Pancreatic cancer painless jaundice

A 66-year-old man has painless jaundice, weight loss, Courvoisier sign, and double-duct dilation. What mechanism explains the biochemical pattern?

A. Chronic pancreatitis always presents with painless jaundice and no pain
B. Pancreatic head tumor obstructs distal bile duct, producing cholestasis and upstream duct dilation
C. Serous cystadenoma secretes bilirubin
D. Insulinoma causes obstructive jaundice through hypoglycemia
E. Tail tumor causes splenic infarction and isolated unconjugated bilirubin

Answer: B - Pancreatic head tumor obstructs distal bile duct, producing cholestasis and upstream duct dilation

Mechanism pearl: Double-duct sign with painless jaundice suggests pancreatic head/periampullary malignancy.

Q72. NET somatostatin receptor imaging

A patient has a well-differentiated pancreatic neuroendocrine tumor. Ga-68 DOTATATE PET is positive. What is being exploited?

A. CFTR-mediated bicarbonate secretion
B. CEA secretion from mucinous cysts
C. IgG4 plasmablast expansion
D. KRAS-mutant ductal adenocarcinoma glucose metabolism
E. Overexpression of **somatostatin receptors**, especially SSTR2, on well-differentiated NET cells

Answer: E - Overexpression of **somatostatin receptors**, especially SSTR2, on well-differentiated NET cells

Mechanism pearl: Well-differentiated NETs often express **SSTR**, enabling functional imaging and somatostatin-analogue therapy.

Q73. Octreotide in NET

A patient with metastatic functional pancreatic NET has hormone-mediated diarrhea and flushing. Octreotide improves symptoms. Which mechanism explains benefit?

A. EGFR blockade dissolves gallstones
B. Trypsin inhibition prevents ductal cancer secretion
C. COX inhibition prevents post-ERCP pancreatitis
D. Somatostatin receptor agonism suppresses hormone secretion from neuroendocrine cells
E. KRAS inhibition reverses PanIN lesions

Answer: D - Somatostatin receptor agonism suppresses hormone secretion from neuroendocrine cells

Mechanism pearl: Somatostatin analogues treat secretory symptoms and may slow growth in SSTR-positive NETs.

Q74. Gastrinoma

A man has refractory ulcers, diarrhea, fasting gastrin >1000 pg/mL, and gastric pH 1.5. Why does diarrhea occur?

A. Gastrin causes IgG4-related pancreatic fibrosis
B. Gastrin blocks bile acid synthesis through FXR
C. Gastrin precipitates cholesterol stones in gallbladder bile
D. Gastric acid hypersecretion inactivates pancreatic enzymes and injures small-bowel mucosa
E. Gastrin directly opens CFTR in colonocytes

Answer: D - Gastric acid hypersecretion inactivates pancreatic enzymes and injures small-bowel mucosa

Mechanism pearl: Zollinger-Ellison diarrhea is acid-mediated maldigestion and mucosal injury.

Q75. Insulinoma

A patient has fasting confusion with glucose 39 mg/dL, high insulin, high C-peptide, and negative sulfonylurea screen. Which mechanism best explains the syndrome?

A. Somatostatin secretion inhibits gallbladder contraction
B. VIP secretion opens intestinal chloride channels
C. Gastrin secretion causes acid hypersecretion
D. Autonomous beta-cell insulin secretion suppresses hepatic glucose output and lipolysis during fasting
E. Glucagon secretion causes necrolytic migratory erythema

Answer: D - Autonomous beta-cell insulin secretion suppresses hepatic glucose output and lipolysis during fasting

Mechanism pearl: Insulinoma produces endogenous hyperinsulinemic hypoglycemia: high insulin and **C-peptide**.

Q76. VIPoma

A patient has massive watery diarrhea, hypokalemia, and achlorhydria. Pancreatic tail mass is found. Which mechanism explains the diarrhea?

A. Gastrin blocks pancreatic lipase and acidifies the jejunum
B. Glucagon causes bile duct obstruction
C. VIP activates intestinal adenylate cyclase/cAMP signaling, increasing chloride and water secretion
D. Insulin suppresses hepatic glucose output
E. Somatostatin activates CCK release

Answer: C - VIP activates intestinal adenylate cyclase/cAMP signaling, increasing chloride and water secretion

Mechanism pearl: VIPoma = **WDHA**; cAMP-mediated secretion drives watery diarrhea and hypokalemia.

Q77. Glucagonoma

A diabetic patient has weight loss, glossitis, venous thrombosis, and necrolytic migratory erythema. What mechanism best explains the syndrome?

A. Excess VIP causes achlorhydria only
B. Excess glucagon produces catabolism, hyperglycemia, amino acid depletion, and characteristic rash
C. Excess gastrin causes diarrhea by acid overload
D. Excess somatostatin causes gallbladder contraction
E. Excess insulin causes fasting hypoglycemia and diaphoresis

Answer: B - Excess glucagon produces catabolism, hyperglycemia, amino acid depletion, and characteristic rash

Mechanism pearl: Glucagonoma is catabolic: diabetes, rash, weight loss, thrombosis.

Q78. Somatostatinoma

A pancreatic head NET secretes somatostatin. Which combination reflects hormone physiology?

A. Watery diarrhea from cAMP activation
B. Necrolytic rash from amino acid depletion
C. Diabetes, gallstones, steatorrhea, and hypochlorhydria due to broad inhibitory effects
D. Hypoglycemia, diarrhea, and high gastric acid
E. Refractory peptic ulcers from gastrin excess

Answer: C - Diabetes, gallstones, steatorrhea, and hypochlorhydria due to broad inhibitory effects

Mechanism pearl: Somatostatin inhibits insulin, CCK/gallbladder contraction, pancreatic secretion, and gastric acid.

Q79. MEN1 and pancreatic NET

A 36-year-old man has hyperparathyroidism, pituitary adenoma, and multiple duodenopancreatic NETs. Which tumor suppressor mechanism is most relevant?

A. PRSS1 gain-of-function in acinar trypsinogen
B. GNAS activation in pancreatic ductal mucinous epithelium
C. IgG4 class-switching in plasma cells
D. VHL loss in serous cystadenoma only
E. Germline **MEN1** loss with second-hit inactivation of menin-dependent transcriptional regulation

Answer: E - Germline **MEN1** loss with second-hit inactivation of menin-dependent transcriptional regulation

Mechanism pearl: MEN1 causes multiple endocrine tumors; pancreatic/duodenal gastrinomas are often multifocal.

Q80. Everolimus in NET

A metastatic pancreatic NET progresses despite somatostatin analogue. Everolimus is considered. What pathway does it target?

A. Gastric H+/K+ ATPase in gastrinoma
B. CFTR chloride conductance in duct cells
C. COX-mediated prostaglandin synthesis in post-ERCP pancreatitis
D. Bacterial beta-glucuronidase in brown pigment stones
E. mTOR signaling involved in cellular growth and proliferation

Answer: E - mTOR signaling involved in cellular growth and proliferation

Mechanism pearl: Everolimus is a targeted **mTOR inhibitor** used in selected advanced NETs.

Q81. Sunitinib in pancreatic NET

A patient with progressive metastatic pancreatic NET is started on sunitinib. Which mechanism best explains its antitumor effect?

A. Multikinase inhibition including VEGF/PDGF receptor pathways, reducing angiogenic growth signaling
B. Dissolution of cholesterol crystals in bile
C. Inhibition of trypsinogen activation in acinar cells
D. Activation of somatostatin receptors on NETs
E. Direct neutralization of gastrin in the stomach

Answer: A - Multikinase inhibition including VEGF/PDGF receptor pathways, reducing angiogenic growth signaling

Mechanism pearl: Pancreatic NETs are vascular tumors; antiangiogenic kinase inhibition can slow progression.

Q82. PRRT

A well-differentiated metastatic pancreatic NET has high DOTATATE uptake. Peptide receptor radionuclide therapy is discussed. What is the mechanistic requirement?

A. High CA19-9 secretion by ductal adenocarcinoma
B. Absent MEN1 mutation

C. Persistent CBD stone obstruction
D. High cyst-fluid CEA from a mucinous cyst
E. Sufficient somatostatin receptor expression to deliver targeted radiation via radiolabeled somatostatin analogue

Answer: E - Sufficient somatostatin receptor expression to deliver targeted radiation via radiolabeled somatostatin analogue

Mechanism pearl: PRRT uses receptor-targeted radioligand delivery in SSTR-positive NETs.

Q83. Acute pancreatitis cytokines

A severe pancreatitis patient has pulmonary edema without primary cardiac disease. Which mechanism links pancreatic inflammation to lung injury?

A. Gallstones migrate through the diaphragm
B. Somatostatin receptor activation opens pulmonary chloride channels
C. Mucinous cysts embolize into pulmonary arteries
D. Gastrin hypersecretion causes alveolar acid injury
E. Systemic cytokine/complement/kinin activation increases endothelial permeability and capillary leak

Answer: E - Systemic cytokine/complement/kinin activation increases endothelial permeability and capillary leak

Mechanism pearl: Severe AP causes distant organ injury via **systemic inflammatory response** and endothelial leak.

Q84. Pancreatic cancer new diabetes

A 70-year-old man with weight loss develops new diabetes and vague epigastric pain. CT shows pancreatic body mass. Which mechanism best explains diabetes as a cancer clue?

A. Pancreatic cancer can induce paraneoplastic insulin resistance and beta-cell dysfunction before overt cachexia
B. Gallstones cause diabetes by cystic duct obstruction
C. Somatostatinoma is the commonest pancreatic cancer
D. CA19-9 directly destroys beta cells in every patient
E. All new diabetes after age 70 is autoimmune type 1 diabetes

Answer: A - Pancreatic cancer can induce paraneoplastic insulin resistance and beta-cell dysfunction before overt cachexia

Mechanism pearl: New-onset diabetes in older adults with weight loss can be a clue to **pancreatic cancer**.

Q85. Groove pancreatitis

A middle-aged alcoholic man has duodenal wall thickening and inflammatory change in the pancreaticoduodenal groove, mimicking cancer. Which mechanism is most plausible?

A. Serous cystadenoma with central scar
B. Gallbladder empyema eroding into the duodenum
C. Focal chronic inflammation/fibrosis around the minor papilla and pancreaticoduodenal groove
D. Main duct IPMN with diffuse mucin in the pancreatic duct
E. MEN1-driven endocrine tumor of the uncinate

Answer: C - Focal chronic inflammation/fibrosis around the minor papilla and pancreaticoduodenal groove

Mechanism pearl: Groove pancreatitis is a focal chronic pancreatitis pattern that can mimic malignancy.

Q86. Pancreas divisum

A patient with recurrent pancreatitis has dorsal duct drainage through the minor papilla. Why might this contribute to pancreatitis in selected patients?

A. It is identical to pancreaticobiliary malunion
B. It proves autoimmune pancreatitis type 2
C. It causes universal gallbladder stone formation
D. Relative minor papilla outflow limitation can increase dorsal ductal pressure in susceptible individuals
E. It prevents trypsinogen activation by separating ducts

Answer: D - Relative minor papilla outflow limitation can increase dorsal ductal pressure in susceptible individuals

Mechanism pearl: Pancreas divisum is common; causality is strongest when there is objective dorsal duct obstruction/recurrent pancreatitis.

Q87. Annular pancreas

A young adult has duodenal obstruction from pancreatic tissue encircling the second part of the duodenum. What is the developmental mechanism?

A. GNAS mutation causes mucinous ductal dilation
B. IgG4-related fibroinflammation produces ovarian-type stroma

C. Cystic duct impaction compresses the common hepatic duct
D. Abnormal migration/fusion of pancreatic buds creates a ring of pancreatic tissue around the duodenum
E. VHL loss causes diffuse endocrine tumors

Answer: D - Abnormal migration/fusion of pancreatic buds creates a ring of pancreatic tissue around the duodenum

Mechanism pearl: Annular pancreas is a congenital pancreatic rotation/fusion anomaly causing duodenal obstruction or pancreatitis.

Q88. Biliary stricture in chronic pancreatitis

A chronic pancreatitis patient has cholestatic jaundice from distal CBD narrowing within an inflamed pancreatic head. What mechanism explains the stricture?

A. Insulinoma causes bile duct smooth-muscle spasm
B. Fibrosis and inflammatory mass effect compress or narrow the intrapancreatic bile duct
C. Gallbladder cholesterol saturation directly occludes intrahepatic ducts
D. VIP secretion paralyzes the sphincter of Oddi
E. Serous cystadenoma always invades the CBD

Answer: B - Fibrosis and inflammatory mass effect compress or narrow the intrapancreatic bile duct

Mechanism pearl: Chronic pancreatitis can cause benign distal **biliary stricture** and secondary cholangitis/cirrhosis if persistent.

Q89. Pancreatic cancer vs chronic pancreatitis

A patient with chronic pancreatitis develops progressive jaundice and weight loss. Which mechanism-based concern justifies EUS-guided tissue diagnosis?

A. CA19-9 is always normal in cancer if pancreatitis exists
B. Chronic pancreatitis completely protects from cancer
C. Inflammatory masses and ductal adenocarcinoma can both produce focal pancreatic enlargement and duct obstruction
D. Weight loss proves exocrine insufficiency only
E. EUS cannot sample pancreatic lesions

Answer: C - Inflammatory masses and ductal adenocarcinoma can both produce focal pancreatic enlargement and duct obstruction

Mechanism pearl: Chronic pancreatitis increases cancer risk and can mask cancer radiologically.

Q90. Necrotizing AP timing

A patient with necrotizing pancreatitis is stable at day 5. The surgeon wants early debridement. What principle is best?

A. Delay intervention when possible until necrosis becomes encapsulated, unless urgent indications arise
B. Waiting converts necrosis into pancreatic cancer
C. All necrosis must be removed before day 3
D. Steroids mature necrosis faster than time
E. Necrosis is always sterile and never needs drainage

Answer: A - Delay intervention when possible until necrosis becomes encapsulated, unless urgent indications arise

Mechanism pearl: Delayed step-up intervention allows **walled-off necrosis** to mature and reduces morbidity.

Q91. Cholecystitis HIDA

A patient has suspected acute cholecystitis but ultrasound is equivocal. HIDA scan shows nonvisualization of the gallbladder. What mechanism explains the result?

A. Cystic duct obstruction prevents radiotracer entry into the gallbladder
B. Gallbladder cancer increases tracer washout
C. CBD obstruction prevents hepatic uptake in all cases
D. Pancreatic exocrine insufficiency prevents tracer secretion
E. Sphincter of Oddi relaxation blocks tracer entry

Answer: A - Cystic duct obstruction prevents radiotracer entry into the gallbladder

Mechanism pearl: HIDA nonvisualization reflects **cystic duct obstruction** in acute cholecystitis.

Q92. Charcot vs Reynolds

A patient with CBD stone has fever, jaundice, RUQ pain, hypotension, and confusion. Which pathophysiologic transition has occurred?

A. Biliary colic has become functional dyspepsia
B. Local biliary infection has progressed to systemic sepsis due to obstructed high-pressure infected bile
C. Pseudocyst has transformed into IPMN
D. Gallbladder polyp has secreted VIP
E. Chronic pancreatitis has reversed to acute interstitial pancreatitis

Answer: B - Local biliary infection has progressed to systemic sepsis due to obstructed high-pressure infected bile

Mechanism pearl: Reynolds pentad = cholangitis plus shock/altered mental status: systemic sepsis from obstructed infection.

Q93. Biliary pancreatitis microlithiasis

A patient has recurrent idiopathic pancreatitis. EUS shows gallbladder sludge/microlithiasis. Which mechanism explains recurrent attacks?

A. Sludge is always benign and unrelated to pancreatitis
B. Microliths transiently obstruct the papilla and trigger pancreatic duct hypertension/enzyme activation
C. Microlithiasis blocks insulin release and causes acinar injury
D. Sludge secretes IL-23 and causes autoimmune pancreatitis
E. Microliths create MEN1 mutations in islet cells

Answer: B - Microliths transiently obstruct the papilla and trigger pancreatic duct hypertension/enzyme activation

Mechanism pearl: Gallbladder **microlithiasis** is a common occult cause of recurrent pancreatitis.

Q94. Acute pancreatitis analgesia

A pancreatitis patient requires opioids. A trainee refuses morphine because of sphincter of Oddi spasm. What is the best mechanism-based response?

A. Analgesia increases trypsinogen activation directly
B. Octreotide is the first-line analgesic by SSTR2 activation
C. Pain control should be avoided to monitor necrosis
D. NSAIDs cure all pancreatitis by COX inhibition
E. Adequate analgesia is essential; clinically meaningful outcome differences between opioids are not driven by sphincter effects alone

Answer: E - Adequate analgesia is essential; clinically meaningful outcome differences between opioids are not driven by sphincter effects alone

Mechanism pearl: Exam trap: do not undertreat pancreatitis pain because of overemphasized opioid-sphincter concerns.

Q95. Cholesterol stone dissolution

A patient asks about ursodeoxycholic acid for gallstones. Which stone biology is required for medical dissolution to be plausible?

A. Small radiolucent cholesterol stones in a functioning gallbladder with patent cystic duct
B. Large calcified pigment stones with chronic infection
C. Porcelain gallbladder with dysplasia risk
D. Gallbladder carcinoma replacing the lumen
E. Brown CBD stones with acute cholangitis

Answer: A - Small radiolucent cholesterol stones in a functioning gallbladder with patent cystic duct

Mechanism pearl: UDCA dissolution works only for selected **cholesterol stones**; it is slow and recurrence can occur.

Q96. Ursodeoxycholic acid mechanism

A patient with small cholesterol stones receives ursodeoxycholic acid. What is the pharmacologic principle?

A. It suppresses gastrin secretion in Zollinger-Ellison syndrome
B. It activates PRSS1 in acinar cells
C. It blocks SSTR2 on pancreatic NETs
D. Hydrophilic bile acid therapy reduces cholesterol saturation of bile and promotes gradual cholesterol stone dissolution
E. It inhibits bacterial beta-glucuronidase in cholangitis

Answer: D - Hydrophilic bile acid therapy reduces cholesterol saturation of bile and promotes gradual cholesterol stone dissolution

Mechanism pearl: UDCA changes bile composition; it does not treat infected obstruction or pigment stones.

Q97. Gallbladder empyema

A patient with acute cholecystitis develops high fever, sepsis, and a gallbladder filled with pus. What mechanism best explains progression?

A. IPMN mucin travels into the gallbladder
B. Persistent obstruction permits bacterial overgrowth in an inflamed, poorly drained gallbladder
C. IgG4 disease transforms bile into pus
D. Sterile cholesterol crystals always remain noninfected
E. Glucagonoma causes purulent bile through hyperglycemia alone

Answer: B - Persistent obstruction permits bacterial overgrowth in an inflamed, poorly drained gallbladder

Mechanism pearl: Empyema = infected obstructed gallbladder; urgent source control matters.

Q98. Gallbladder perforation

An elderly diabetic patient with delayed acute cholecystitis develops localized abscess. Which mechanism explains perforation risk?

A. CA19-9 secretion perforates the gallbladder
B. CCK excess thins the wall without obstruction
C. Bile acid diarrhea causes transmural necrosis
D. Somatostatinoma contracts the gallbladder continuously
E. Distension compromises mural blood flow, causing ischemic necrosis and wall breakdown

Answer: E - Distension compromises mural blood flow, causing ischemic necrosis and wall breakdown

Mechanism pearl: Persistent obstruction can progress from inflammation to **ischemia**, gangrene, and perforation.

Q99. Biliary dyskinesia

A patient has biliary-type pain, no stones, and low gallbladder ejection fraction after CCK stimulation. Which mechanism is being tested?

A. KRAS mutation burden in gallbladder epithelium
B. Bacterial infection of bile through beta-glucuronidase
C. Somatostatin receptor density of NETs
D. Main pancreatic duct communication with cyst fluid
E. Gallbladder contractile response to CCK as a marker of functional gallbladder emptying

Answer: E - Gallbladder contractile response to CCK as a marker of functional gallbladder emptying

Mechanism pearl: Functional gallbladder disorder is a motility diagnosis; CCK-stimulated emptying is part of physiologic assessment.

Q100. SOD and ERCP risk

A patient with suspected functional biliary sphincter pain and no objective obstruction requests ERCP. Why is ERCP discouraged?

A. Pancreatic stenting causes gallbladder cancer
B. Sphincter pain is always malignant obstruction
C. Low likelihood of sphincter hypertension plus high risk of post-ERCP pancreatitis makes invasive therapy unfavorable
D. MRCP causes more pancreatitis than ERCP
E. ERCP cannot reach the papilla after cholecystectomy

Answer: C - Low likelihood of sphincter hypertension plus high risk of post-ERCP pancreatitis makes invasive therapy unfavorable

Mechanism pearl: Pain-only SOD/functional biliary pain is a high-risk ERCP trap.

B. Moderate-to-long integrated case scenarios - 50 questions

Q101. Integrated gallstone pancreatitis with cholangitis

A 59-year-old woman presents with severe epigastric pain radiating to the back after several weeks of biliary colic. Lipase is 2400 U/L, ALT is 420 U/L, bilirubin is 5.8 mg/dL, temperature is 39 C, and she becomes hypotensive. Ultrasound shows gallstones and a dilated CBD. The fellow asks why ERCP is urgent in this case, although many biliary pancreatitis cases do not need immediate ERCP.

A. This scenario combines pancreatitis with **persistent biliary obstruction and cholangitis**, so high-pressure infected bile requires decompression
B. ERCP is being used to diagnose hypertriglyceridemia
C. ERCP is needed because ALT elevation proves pancreatic cancer
D. ERCP is urgent in every gallstone pancreatitis because all stones remain impacted
E. ERCP directly prevents acinar trypsinogen activation even after stone passage

Answer: A - This scenario combines pancreatitis with **persistent biliary obstruction and cholangitis**, so high-pressure infected bile requires decompression

Mechanism pearl: Urgent ERCP is not for all biliary pancreatitis; it is for **cholangitis** or persistent obstruction.

Q102. Acute pancreatitis severity and biomarkers

A 48-year-old obese man presents 10 hours after onset of pancreatitis. Initial CT shows interstitial edema only. Over 24 hours he develops tachycardia, hemoconcentration, hypoxemia, and rising creatinine. IL-6 is high and CRP rises later. The consultant asks what these markers are actually reflecting.

A. CA19-9-driven cancer secretion from pancreatic ducts
B. Somatostatin receptor overexpression in pancreatic islets
C. Cyst-fluid CEA release from an occult mucinous cyst
D. Bacterial infection of necrosis, which is universal in the first 24 hours

E. Early systemic inflammatory amplification through **IL-6/gp130-JAK-STAT** and acute-phase signaling, not merely local pancreatic swelling

Answer: E - Early systemic inflammatory amplification through **IL-6/gp130-JAK-STAT** and acute-phase signaling, not merely local pancreatic swelling

Mechanism pearl: Severe AP is defined by organ failure biology; **IL-6** rises early and **CRP** peaks later as an acute-phase readout.

Q103. Necrotizing pancreatitis collection timing

A patient with severe alcohol-related pancreatitis has CT evidence of peripancreatic necrosis at day 6. He is febrile but blood cultures are negative and there is no gas in the collection. By week 5, he has persistent sepsis and imaging shows a mature encapsulated collection with solid debris. The team debates drainage.

A. All necrotic collections are sterile and should never be drained
B. A mature collection with solid debris is a serous cystadenoma
C. The day-6 collection was a pseudocyst and should have been drained immediately
D. Antibiotics alone dissolve necrotic debris once a wall forms
E. The mature collection is **walled-off necrosis**, and intervention is best delayed until encapsulation unless clinical deterioration mandates earlier source control

Answer: E - The mature collection is **walled-off necrosis**, and intervention is best delayed until encapsulation unless clinical deterioration mandates earlier source control

Mechanism pearl: Necrosis evolves: acute necrotic collection -> **WON** after about 4 weeks; debris distinguishes it from pseudocyst.

Q104. Recurrent idiopathic pancreatitis

A 37-year-old man has three episodes of acute pancreatitis. He does not drink, triglycerides and calcium are normal, and MRCP is unrevealing. EUS shows gallbladder microlithiasis. The attending asks why this finding changes management.

A. Microlithiasis indicates pancreatic NET with hormone secretion
B. Microlithiasis can transiently obstruct the papilla, so cholecystectomy or bile-directed therapy may prevent recurrent pancreatic injury
C. Microlithiasis proves autoimmune pancreatitis type 1
D. Microlithiasis is unrelated to pancreatitis unless CBD dilation is permanent
E. Microlithiasis should be treated with pancreatic enzyme replacement only

Answer: B - Microlithiasis can transiently obstruct the papilla, so cholecystectomy or bile-directed therapy may prevent recurrent pancreatic injury

Mechanism pearl: Occult **microlithiasis** is an important cause of recurrent pancreatitis in patients with an intact gallbladder.

Q105. Hereditary pancreatitis mechanism

A 16-year-old boy has recurrent pancreatitis beginning at age 8. His father had chronic pancreatitis and pancreatic cancer. Genetic testing shows a PRSS1 mutation. The examiner asks what unifying mechanism explains recurrent inflammation and later cancer risk.

A. PRSS1 methylates SMAD4 and causes cancer without inflammation
B. PRSS1 causes cholesterol supersaturation and gallbladder hypomotility
C. PRSS1 blocks somatostatin receptors and drives NETs
D. PRSS1 causes IgG4-related plasma-cell disease
E. Gain of trypsin activity produces repeated acinar injury, chronic inflammation, fibrosis, and injury-regeneration cancer risk

Answer: E - Gain of trypsin activity produces repeated acinar injury, chronic inflammation, fibrosis, and injury-regeneration cancer risk

Mechanism pearl: PRSS1 hereditary pancreatitis is a trypsin-pathway disease with cumulative injury and increased PDAC risk.

Q106. CFTR and alcohol interaction

A 34-year-old man with recurrent pancreatitis drinks moderately and has a CFTR variant. Secretin MRCP suggests reduced bicarbonate-rich ductal secretion. The examiner asks why this genotype can cause pancreatitis without classic pulmonary cystic fibrosis.

A. CFTR variants activate MEN1 transcription in endocrine cells
B. Partial CFTR dysfunction impairs ductal chloride/bicarbonate secretion, reducing washout and promoting protein-rich obstructive secretions
C. CFTR variants cause brown pigment stones through bacterial beta-glucuronidase
D. CFTR variants directly raise serum CA19-9 by Lewis antigen synthesis
E. CFTR variants produce IgG4-positive storiform fibrosis

Answer: B - Partial CFTR dysfunction impairs ductal chloride/bicarbonate secretion, reducing washout and promoting protein-rich obstructive secretions

Mechanism pearl: Pancreatic ductal **CFTR** function is essential for alkaline fluid secretion; partial defects can present as recurrent pancreatitis.

Q107. Hypertriglyceridemia pancreatitis

A 45-year-old man with uncontrolled diabetes presents with pancreatitis. Triglycerides are 3200 mg/dL, sodium is falsely low, and serum is milky. He has no gallstones. The faculty asks what injures the pancreas.

A. Local hydrolysis of excess triglycerides generates toxic **free fatty acids**, causing microvascular plugging, ischemia, and acinar injury
B. Triglycerides directly mutate KRAS and SMAD4 within hours
C. Triglycerides activate IgG4 class switching in plasma cells
D. Triglycerides crystallize in the ampulla like gallstones
E. Triglycerides bind somatostatin receptors and trigger hormone release

Answer: A - Local hydrolysis of excess triglycerides generates toxic **free fatty acids**, causing microvascular plugging, ischemia, and acinar injury

Mechanism pearl: Hypertriglyceridemic AP is a **free-fatty-acid** and microcirculatory toxicity disease.

Q108. AIP cancer mimic

A 66-year-old man develops painless jaundice and pancreatic head enlargement. IgG4 is mildly elevated. CT shows delayed enhancement, but weight loss and CA19-9 are also present. A junior wants to give steroids immediately. What is the most defensible mechanism-based concern?

A. AIP never causes obstructive jaundice
B. Steroids convert ductal adenocarcinoma into AIP
C. CA19-9 is never elevated in benign obstruction
D. Any IgG4 elevation excludes cancer
E. Autoimmune pancreatitis may respond dramatically to steroids, but pancreatic adenocarcinoma can mimic it and steroid trial can delay cancer diagnosis

Answer: E - Autoimmune pancreatitis may respond dramatically to steroids, but pancreatic adenocarcinoma can mimic it and steroid trial can delay cancer diagnosis

Mechanism pearl: AIP is a treatable mimic, but **cancer exclusion** is critical before relying on steroid response.

Q109. Type 1 AIP systemic disease

A 61-year-old man has pancreatic enlargement, sclerosing cholangitis, retroperitoneal fibrosis, salivary swelling, elevated IgG4, and steroid response. Biopsy shows lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis. Which mechanism best integrates the findings?

A. Type 2 AIP limited to granulocytic epithelial lesions and UC
B. Main duct IPMN with GNAS mutation and mucin extrusion
C. Metastatic pancreatic NET expressing somatostatin receptor
D. PRSS1 hereditary pancreatitis with acinar trypsin excess
E. Systemic **IgG4-related disease** with B-cell/plasmablast-rich fibroinflammatory injury across organs

Answer: E - Systemic **IgG4-related disease** with B-cell/plasmablast-rich fibroinflammatory injury across organs

Mechanism pearl: Type 1 AIP is the pancreatic manifestation of systemic **IgG4-RD**.

Q110. AIP relapse therapy

A patient with IgG4-related autoimmune pancreatitis relapses twice during steroid taper and develops steroid toxicity. Imaging excludes cancer. The team considers rituximab. Which rationale is strongest?

A. Rituximab repairs CFTR ductal bicarbonate transport
B. B-cell depletion targets the plasmablast/autoimmune driver of relapsing **IgG4-related disease**
C. Rituximab dissolves biliary stones by altering bile acids
D. Rituximab blocks SSTR2 on pancreatic NETs
E. Rituximab inhibits acinar trypsinogen activation directly

Answer: B - B-cell depletion targets the plasmablast/autoimmune driver of relapsing **IgG4-related disease**

Mechanism pearl: Relapsing IgG4-RD is often B-cell/plasmablast-driven; **rituximab** is mechanistically rational.

Q111. Chronic pancreatitis obstructive phenotype

A 52-year-old man with chronic calcific pancreatitis has disabling post-prandial pain, a 9-mm main pancreatic duct, and an obstructing stone in the pancreatic head. There is no mass. Why might ductal decompression improve symptoms?

A. Ductal decompression prevents gallbladder cholesterol supersaturation
B. Ductal decompression reverses diabetes by regenerating beta cells

C. Ductal decompression treats pancreatic cancer micrometastases
D. Ductal decompression suppresses all neuropathic pain centrally
E. Obstructing stones and strictures create ductal hypertension that contributes to pain and recurrent injury

Answer: E - Obstructing stones and strictures create ductal hypertension that contributes to pain and recurrent injury

Mechanism pearl: Pain in chronic pancreatitis can be obstructive and neuropathic; large duct disease may respond to decompression.

Q112. Small duct chronic pancreatitis pain

A 49-year-old woman with chronic pancreatitis has severe pain, normal-caliber pancreatic duct, and no dominant stone. EUS suggests parenchymal fibrosis. Why is simple duct drainage less attractive?

A. Pain may be driven by inflammatory-neural remodeling and small-duct fibrosis rather than a decompressive target
B. Normal duct caliber excludes chronic pancreatitis
C. Small duct disease proves serous cystadenoma
D. Duct drainage is always curative regardless of duct size
E. Pain is due to bile acid diarrhea unless the duct is dilated

Answer: A - Pain may be driven by inflammatory-neural remodeling and small-duct fibrosis rather than a decompressive target

Mechanism pearl: Duct anatomy guides intervention; no dominant obstruction means pain may be **neuropathic/fibrotic**.

Q113. Exocrine insufficiency and diabetes

A patient with long-standing chronic pancreatitis has steatorrhea, fat-soluble vitamin deficiency, and brittle diabetes with hypoglycemia. The examiner asks why his diabetes behaves differently from usual type 2 diabetes.

A. Bile acid malabsorption causes beta-cell hyperplasia
B. Destruction of pancreatic parenchyma causes both exocrine enzyme deficiency and endocrine loss of insulin plus glucagon counterregulation
C. SSTR2 expression suppresses glucagon only after meals
D. Gallbladder stones destroy pancreatic alpha cells directly
E. UDCA induces glucagon deficiency

Answer: B - Destruction of pancreatic parenchyma causes both exocrine enzyme deficiency and endocrine loss of insulin plus glucagon counterregulation

Mechanism pearl: Type 3c diabetes combines **exocrine failure** and endocrine islet loss, including impaired glucagon response.

Q114. Pancreatic ascites duct leak

A man with chronic pancreatitis develops tense ascites. SAAG is low, ascitic protein is high, and ascitic amylase is markedly elevated. CT shows a disrupted pancreatic duct. What is the mechanism?

A. VIPoma causes ascites through intestinal chloride secretion
B. Gallbladder perforation causes high-amylase ascites
C. Portal hypertension from cirrhosis is the dominant mechanism
D. Pancreatic duct disruption leaks enzyme-rich pancreatic juice into the peritoneal cavity
E. Hypoalbuminemia from exocrine insufficiency alone causes amylase-rich ascites

Answer: D - Pancreatic duct disruption leaks enzyme-rich pancreatic juice into the peritoneal cavity

Mechanism pearl: High-amylase, high-protein ascites in pancreatitis = **pancreatic duct leak** until proven otherwise.

Q115. Disconnected pancreatic duct

A patient survives necrotizing pancreatitis involving the pancreatic neck. Months later he has recurrent large collections after apparently successful cystgastrostomy. MRCP shows viable pancreatic tail separated from the duodenal ductal drainage. Why do collections recur?

A. CA19-9 secretion from cancer draws fluid into the cyst
B. The gallbladder keeps forming microliths after cholecystectomy
C. The disconnected upstream pancreas continues exocrine secretion into a blind segment, refilling collections
D. The collection is a mucinous cystic neoplasm with ovarian stroma
E. SSTR2-positive NET secretion increases amylase in the collection

Answer: C - The disconnected upstream pancreas continues exocrine secretion into a blind segment, refilling collections

Mechanism pearl: Disconnected duct syndrome should be suspected when collections recur after necrotizing pancreatitis.

Q116. Pseudocyst vs cystic neoplasm

A 62-year-old woman with no pancreatitis history has a 5-cm pancreatic body cyst. Fluid CEA is high, amylase is low, and MRI shows no duct communication. The first report calls it a pseudocyst. Which reasoning is best?

A. Mucinous cysts cannot occur in the pancreatic body

B. High CEA and low amylase are classic pseudocyst markers
C. All pancreatic cysts in adults are pseudocysts
D. Absence of pancreatitis plus high CEA and low amylase favors **mucinous cystic neoplasm** over pseudocyst
E. No duct communication proves branch-duct IPMN

Answer: D - Absence of pancreatitis plus high CEA and low amylase favors **mucinous cystic neoplasm** over pseudocyst

Mechanism pearl: Pseudocyst diagnosis requires clinical context; **cyst fluid chemistry** and morphology prevent misclassification.

Q117. Main duct IPMN case

A 71-year-old man has weight loss, recurrent pancreatitis, mucin extrusion from the papilla, main pancreatic duct dilation to 13 mm, and an enhancing mural nodule. Cytology is suspicious. What mechanism drives symptoms and cancer risk?

A. IgG4 pancreatitis causes mucin extrusion from the papilla
B. Mucin-producing intraductal neoplastic epithelium obstructs ducts and carries high-grade dysplasia/invasive cancer risk
C. MEN1 gastrinoma dilates the pancreatic duct through acid
D. A sterile post-pancreatitis fluid collection has matured into a pseudocyst
E. VHL-related serous cystadenoma secretes watery fluid without malignant risk

Answer: B - Mucin-producing intraductal neoplastic epithelium obstructs ducts and carries high-grade dysplasia/invasive cancer risk

Mechanism pearl: Main-duct IPMN with **mural nodule** is high risk; mucin can cause pancreatitis.

Q118. Branch duct IPMN low risk

A 78-year-old man with major cardiac disease has a 12-mm branch-duct IPMN found incidentally. There is no mural nodule, no duct dilation, no symptoms, and no concerning cytology. Why is surveillance favored over resection?

A. Cardiac disease increases malignant transformation
B. High CEA alone mandates surgery in every patient
C. All pancreatic cysts require Whipple procedure
D. Branch-duct IPMN never progresses and should be ignored
E. Small branch-duct IPMN without high-risk stigmata has relatively low malignant risk, while operative risk is high

Answer: E - Small branch-duct IPMN without high-risk stigmata has relatively low malignant risk, while operative risk is high

Mechanism pearl: Management integrates cyst biology with **patient fitness** and high-risk features.

Q119. Mucinous cystic neoplasm case

A 45-year-old woman has a solitary pancreatic tail cyst. There is no duct communication. Resection shows mucinous epithelium over ovarian-type stroma. What is the key biologic implication?

A. This is an **MCN**, a premalignant mucinous cystic neoplasm typically in women and body/tail
B. This is type 1 AIP because women can have pancreatic cysts
C. This is a functional NET because tail lesions secrete insulin
D. This is a serous cystadenoma because ovarian stroma is benign glycogen-rich tissue
E. This is a pseudocyst because all tail cysts are post-pancreatitis

Answer: A - This is an **MCN**, a premalignant mucinous cystic neoplasm typically in women and body/tail

Mechanism pearl: Ovarian-type stroma is the defining clue of MCN.

Q120. Serous cystadenoma VHL

A 58-year-old woman with von Hippel-Lindau disease has multiple pancreatic microcystic lesions with central scars and low cyst-fluid CEA. She is asymptomatic. Which mechanism best explains conservative management?

A. VHL cysts are always main-duct IPMN with high invasive risk
B. Central scar is diagnostic of pancreatic adenocarcinoma
C. Serous cystadenomas are usually benign glycogen-rich epithelial neoplasms despite VHL association
D. Low CEA proves pseudocyst from duct leak
E. All cysts in VHL are insulinomas

Answer: C - Serous cystadenomas are usually benign glycogen-rich epithelial neoplasms despite VHL association

Mechanism pearl: Serous cystadenoma is typically benign; symptoms, uncertainty, or size may drive intervention.

Q121. Cyst molecular testing

A pancreatic cyst has equivocal imaging. Fluid shows KRAS mutation and high CEA; later testing detects GNAS. The examiner asks what these molecular data add.

A. They prove invasive cancer regardless of imaging
B. They support mucinous ductal neoplasia, especially **IPMN**, but must be integrated with imaging and cytology

C. They are markers of infected necrosis
D. They confirm autoimmune pancreatitis
E. They diagnose serous cystadenoma and exclude mucin

Answer: B - They support mucinous ductal neoplasia, especially **IPMN**, but must be integrated with imaging and cytology

Mechanism pearl: Molecular cyst markers help classify cyst lineage and risk; they do not replace clinical judgment.

Q122. Pancreatic cancer stromal biology

A patient has locally advanced pancreatic ductal adenocarcinoma. Biopsy shows sparse malignant glands embedded in dense desmoplastic stroma. The fellow asks why tumor shrinkage is often limited despite chemotherapy.

A. PDAC lacks stromal interaction and is purely epithelial
B. Stroma means the tumor is a neuroendocrine tumor
C. Dense stroma increases chemotherapy delivery uniformly
D. Activated stromal and stellate-cell networks create hypovascular, immunosuppressive, high-pressure microenvironment impairing drug delivery
E. Desmoplasia proves benign chronic pancreatitis only

Answer: D - Activated stromal and stellate-cell networks create hypovascular, immunosuppressive, high-pressure microenvironment impairing drug delivery

Mechanism pearl: PDAC treatment failure is partly a **tumor microenvironment** problem.

Q123. PDAC resectability and vascular anatomy

A 64-year-old man has pancreatic head adenocarcinoma. CT shows no metastasis but greater than 180-degree encasement of the SMA. CA19-9 is high. Why is immediate Whipple not appropriate?

A. A pancreatic head location is never resectable
B. EUS biopsy always cures borderline disease
C. CA19-9 alone makes all tumors unresectable
D. SMA encasement indicates locally advanced arterial involvement with inability to achieve safe margin-negative resection upfront
E. Any jaundice means metastatic disease

Answer: D - SMA encasement indicates locally advanced arterial involvement with inability to achieve safe margin-negative resection upfront

Mechanism pearl: Resectability in PDAC is determined mainly by **metastasis and vascular involvement**.

Q124. CA19-9 in cholestasis

A jaundiced patient with distal CBD obstruction has CA19-9 of 950 U/mL. After ERCP stenting and treatment of cholangitis it falls to 80 U/mL. How should the first value be interpreted?

A. The initial value proves metastatic pancreatic cancer
B. Falling CA19-9 confirms neuroendocrine tumor
C. CA19-9 values are unaffected by Lewis antigen status
D. Cholestasis/cholangitis can cause false CA19-9 elevation; reassessment after drainage improves specificity
E. CA19-9 cannot be secreted in benign biliary obstruction

Answer: D - Cholestasis/cholangitis can cause false CA19-9 elevation; reassessment after drainage improves specificity

Mechanism pearl: Interpret **CA19-9** in context: cholestasis can falsely elevate it; Lewis-negative patients can be falsely low.

Q125. New-onset diabetes PDAC

A 72-year-old lean man develops new diabetes, early satiety, mild epigastric pain, and 8-kg weight loss. CT later shows pancreatic body cancer. The examiner asks why diabetes can precede diagnosis.

A. Pancreatic cancer secretes insulin in most cases
B. Diabetes excludes pancreatic cancer because cancer causes hypoglycemia
C. PDAC can induce systemic insulin resistance and beta-cell dysfunction as a paraneoplastic metabolic effect
D. All diabetes in older adults is caused by chronic pancreatitis
E. Gallstones are the usual direct cause of new diabetes

Answer: C - PDAC can induce systemic insulin resistance and beta-cell dysfunction as a paraneoplastic metabolic effect

Mechanism pearl: New diabetes with weight loss in older patients may be a metabolic clue to **PDAC**.

Q126. Cancer-associated thrombosis

A man with metastatic pancreatic adenocarcinoma develops recurrent migratory thrombophlebitis despite no central venous catheter. Which mechanism explains this paraneoplastic sign?

A. Bile duct obstruction prevents anticoagulant absorption only
B. Pancreatic enzymes digest clotting factors and cause thrombosis
C. Tumor mucins, tissue factor, cytokines, and platelet/endothelial activation create cancer-associated hypercoagulability
D. Gallbladder stones trigger venous thrombosis by CCK release
E. Somatostatin receptors activate factor X directly

Answer: C - Tumor mucins, tissue factor, cytokines, and platelet/endothelial activation create cancer-associated hypercoagulability

Mechanism pearl: PDAC is highly thrombogenic; **Trousseau syndrome** reflects tumor-coagulation biology.

Q127. PDAC versus AIP with biliary stricture

A 68-year-old man has pancreatic head enlargement, distal biliary stricture, and painless jaundice. IgG4 is elevated twofold. EUS-FNB shows malignant glands with desmoplastic stroma. Which mechanism now dominates management?

A. Ductal adenocarcinoma is excluded by biliary stricture
B. Desmoplasia is unique to autoimmune pancreatitis
C. Steroids should be used first because all jaundiced masses are AIP
D. Mild IgG4 elevation proves type 1 AIP despite malignant histology
E. KRAS-driven ductal adenocarcinoma with stromal invasion, not steroid-responsive IgG4 fibroinflammation

Answer: E - KRAS-driven ductal adenocarcinoma with stromal invasion, not steroid-responsive IgG4 fibroinflammation

Mechanism pearl: IgG4 elevation can mislead; tissue evidence of **PDAC** overrides a steroid-trial reflex.

Q128. Gastrinoma MEN1 case

A 39-year-old man has recurrent jejunal ulcers, diarrhea, nephrolithiasis, hypercalcemia, and high fasting gastrin with gastric pH 1.2. Imaging suggests multiple duodenal lesions. What mechanism connects the findings?

A. Somatostatinoma stimulates CCK and acid secretion
B. MEN1-associated gastrinomas cause acid hypersecretion, while hyperparathyroidism increases gastrin/acid burden and ulcer risk
C. VIPoma causes acid hypersecretion and calcium stones
D. Insulinoma causes ulcers through hypoglycemia
E. Serous cystadenoma secretes gastrin from glycogen-rich cells

Answer: B - MEN1-associated gastrinomas cause acid hypersecretion, while hyperparathyroidism increases gastrin/acid burden and ulcer risk

Mechanism pearl: MEN1 gastrinomas are often multiple/duodenal; treat acid, localize disease, and address hyperparathyroidism.

Q129. VIPoma case

A 51-year-old woman has 6 L/day watery diarrhea that persists during fasting, potassium 2.4 mmol/L, achlorhydria, and a pancreatic tail mass. Colonoscopy is normal. Which signaling pathway is responsible?

A. Gastrin receptor activation increases acid-mediated maldigestion
B. Insulin receptor activation suppresses hepatic glucose output
C. Glucagon receptor blockade produces necrolytic rash
D. Somatostatin receptor activation contracts the gallbladder
E. VIP receptor activation increases adenylate cyclase and **cAMP-mediated chloride/water secretion**

Answer: E - VIP receptor activation increases adenylate cyclase and **cAMP-mediated chloride/water secretion**

Mechanism pearl: Secretory diarrhea that persists fasting + hypokalemia = **VIPoma/WDHA** physiology.

Q130. Insulinoma case

A 44-year-old woman has morning confusion relieved by juice. During supervised fast, glucose is 38 mg/dL, insulin and C-peptide are high, beta-hydroxybutyrate is suppressed, and sulfonylurea is negative. What mechanism best explains her neuroglycopenia?

A. Glucagonoma causes amino acid depletion and fasting hypoglycemia
B. VIP-mediated chloride secretion produces hypoglycemia
C. Somatostatinoma increases insulin release after meals
D. Gastrinoma inactivates pancreatic enzymes and lowers glucose
E. Autonomous endogenous insulin secretion suppresses hepatic glucose production and ketogenesis during fasting

Answer: E - Autonomous endogenous insulin secretion suppresses hepatic glucose production and ketogenesis during fasting

Mechanism pearl: Insulinoma is endogenous hyperinsulinism: high **insulin/C-peptide** and low ketones during hypoglycemia.

Q131. Glucagonoma case

A 58-year-old woman has diabetes, weight loss, stomatitis, anemia, DVT, and a migratory erythematous rash with blistering at the groin and legs. CT shows a pancreatic tail mass with liver lesions. What mechanism integrates the syndrome?

A. Excess insulin causes catabolism and rash
B. Excess glucagon causes catabolism, hyperglycemia, amino acid deficiency, thrombosis tendency, and necrolytic migratory erythema
C. Excess gastrin causes rash through acid injury
D. Excess VIP causes rash through cAMP in keratinocytes
E. Excess somatostatin causes hyperaminoacidemia and rash

Answer: B - Excess glucagon causes catabolism, hyperglycemia, amino acid deficiency, thrombosis tendency, and necrolytic migratory erythema

Mechanism pearl: Glucagonoma is a catabolic NET syndrome with **necrolytic migratory erythema**.

Q132. SSTR-positive NET treatment sequencing

A patient with metastatic well-differentiated pancreatic NET has low-volume liver metastases, positive DOTATATE scan, and hormone-mediated diarrhea. Symptoms improve on octreotide but tumor later progresses. Which mechanism supports PRRT consideration?

A. Persistent somatostatin receptor expression allows targeted delivery of radionuclide therapy to NET cells
B. KRAS mutation is required for PRRT uptake
C. PRRT targets gallbladder CCK receptors
D. Rising CA19-9 proves PRRT sensitivity
E. Low Ki-67 excludes receptor-targeted therapy

Answer: A - Persistent somatostatin receptor expression allows targeted delivery of radionuclide therapy to NET cells

Mechanism pearl: SSTR expression enables imaging, symptom control, and **receptor-targeted radionuclide therapy**.

Q133. PNET grade and differentiation

A pancreatic neuroendocrine neoplasm has liver metastases. Pathology shows well-differentiated morphology and Ki-67 8%. Another tumor has poorly differentiated small-cell morphology and Ki-67 80%. Why are they treated differently?

A. Differentiation and proliferative index reflect distinct biology: well-differentiated NET versus aggressive neuroendocrine carcinoma
B. Ki-67 measures cyst mucin content rather than proliferation
C. SSTR imaging is always positive in poorly differentiated carcinoma
D. All pancreatic neuroendocrine neoplasms are identical if metastatic
E. Functional hormone status alone determines all treatment

Answer: A - Differentiation and proliferative index reflect distinct biology: well-differentiated NET versus aggressive neuroendocrine carcinoma

Mechanism pearl: NET management depends on **grade and differentiation**, not just site or hormone secretion.

Q134. Cholangitis source control

A frail 83-year-old with known CBD stones presents with fever, jaundice, RUQ pain, confusion, lactate elevation, and acute kidney injury. Antibiotics are started. Ultrasound shows CBD dilation. What is the mechanistic reason antibiotics alone may fail?

A. Biliary bacteria are resistant to all antibiotics unless gallbladder is removed
B. Cholangitis is sterile until ERCP introduces bacteria
C. Obstructed infected bile remains a high-pressure septic focus until decompressed by ERCP or drainage
D. Kidney injury proves pancreatitis rather than cholangitis
E. Antibiotics increase bile pressure by closing the sphincter of Oddi

Answer: C - Obstructed infected bile remains a high-pressure septic focus until decompressed by ERCP or drainage

Mechanism pearl: In cholangitis, **decompression is source control**.

Q135. Brown stones recurrent cholangitis

A patient with biliary-enteric anastomosis has recurrent cholangitis and brown CBD stones. Cultures grow enteric organisms. What mechanism best explains recurrent stone formation?

A. Biliary stasis and colonization permit bacterial beta-glucuronidase activity, deconjugating bilirubin and forming calcium bilirubinate stones
B. GNAS mutation in bile duct epithelium secretes stone mucin
C. Anastomoses cause pure cholesterol supersaturation without infection
D. Gallbladder CCK hyporesponsiveness after anastomosis causes duct stones
E. Hemolysis is required for all brown stones

Answer: A - Biliary stasis and colonization permit bacterial beta-glucuronidase activity, deconjugating bilirubin and forming calcium bilirubinate stones

Mechanism pearl: Brown pigment stones are infection/stasis stones, especially in ducts or altered biliary anatomy.

Q136. Mirizzi with fistula

A 71-year-old woman has jaundice, cholangitis, and imaging showing a large impacted stone in Hartmann pouch compressing the common hepatic duct. ERCP suggests a cholecystocholedochal fistula. Why is this more than simple choledocholithiasis?

A. Bile duct cancer is excluded by gallstones
B. The cystic duct is irrelevant once jaundice occurs
C. A main-duct IPMN is obstructing the CBD with mucin
D. The stone formed inside the pancreatic duct and migrated upward
E. The impacted gallbladder-neck/cystic-duct stone causes extrinsic compression and inflammatory erosion into the bile duct

Answer: E - The impacted gallbladder-neck/cystic-duct stone causes extrinsic compression and inflammatory erosion into the bile duct

Mechanism pearl: Advanced **Mirizzi syndrome** can erode into the bile duct and complicate surgery.

Q137. Gallbladder polyp PSC

A 57-year-old man with PSC has no biliary pain. Surveillance ultrasound shows a solitary 9-mm sessile gallbladder polyp that was 5 mm one year ago. The trainee suggests routine 5-year follow-up because it is under 1 cm. What is the best reasoning?

A. Only mobile shadowing lesions are polyps
B. PSC makes gallbladder polyps less likely malignant
C. Growth suggests cholesterol polyp regression
D. PSC, sessile morphology, and interval growth increase neoplastic concern even near the 10-mm threshold
E. Polyp risk is determined only by symptoms

Answer: D - PSC, sessile morphology, and interval growth increase neoplastic concern even near the 10-mm threshold

Mechanism pearl: Gallbladder polyp management integrates **size, growth, morphology, age, and PSC**.

Q138. Gallbladder cancer chronic inflammation

A 69-year-old woman with decades of gallstones develops a mass replacing the gallbladder and invading segment IVb/V. Histology shows adenocarcinoma. What long-term sequence is most plausible?

A. Sphincter of Oddi dysfunction is the usual precursor lesion
B. Gallstones cause cancer by secreting insulin-like hormones
C. Every cholesterol stone contains invasive epithelial cells
D. Chronic stone-associated mucosal injury drives metaplasia, dysplasia, and invasive gallbladder adenocarcinoma
E. Acute biliary colic directly causes carcinoma within days

Answer: D - Chronic stone-associated mucosal injury drives metaplasia, dysplasia, and invasive gallbladder adenocarcinoma

Mechanism pearl: Gallbladder cancer is an inflammation-associated carcinoma; late presentation is common.

Q139. Choledochal cyst adult

A 31-year-old woman has recurrent cholangitis, pancreatitis, and fusiform extrahepatic bile duct dilatation. MRCP suggests anomalous pancreaticobiliary junction. Why is definitive excision recommended even after symptom control?

A. Antibiotics permanently reverse ductal dysplasia
B. Congenital duct dilation plus pancreaticobiliary reflux creates persistent epithelial injury and lifetime cholangiocarcinoma risk
C. Somatostatin analogues prevent cholangiocyte mutation
D. Biliary sphincterotomy removes the entire malignant risk
E. UDCA dissolves the congenital cyst wall

Answer: B - Congenital duct dilation plus pancreaticobiliary reflux creates persistent epithelial injury and lifetime cholangiocarcinoma risk

Mechanism pearl: Choledochal cyst management targets **premalignant anatomy**, not just acute cholangitis.

Q140. PBM mechanism

A 12-year-old has recurrent pancreatitis and biliary dilation. ERCP shows a long common pancreaticobiliary channel outside the duodenal wall. Bile amylase is markedly elevated. What is the core mechanism?

A. The sphincter cannot separately regulate bile and pancreatic ducts, allowing pancreatic juice reflux into biliary tree and bile reflux into pancreas
B. The pancreas contains ovarian-type stroma
C. The minor papilla drains the entire ventral pancreas
D. NET hormone secretion dilates bile ducts
E. The cystic duct is obstructed by a cholesterol stone

Answer: A - The sphincter cannot separately regulate bile and pancreatic ducts, allowing pancreatic juice reflux into biliary tree and bile reflux into pancreas

Mechanism pearl: A long common channel outside sphincter control explains **PBM**, biliary cancer risk, and pancreatitis.

Q141. Functional gallbladder disorder

A 35-year-old woman has classic biliary pain, normal liver tests, no stones, and low ejection fraction on CCK-stimulated cholescintigraphy. Symptoms are not daily and are not relieved by bowel movements. What mechanism is being invoked?

A. Disordered gallbladder motility causing painful contraction/emptying failure despite absence of stones
B. Acinar trypsinogen activation causing pancreatic necrosis
C. Ductal mucin neoplasm causing main pancreatic duct dilation
D. Microscopic infected bile duct stones causing cholangitis
E. Bile acid diarrhea causing visceral pain

Answer: A - Disordered gallbladder motility causing painful contraction/emptying failure despite absence of stones

Mechanism pearl: Biliary pain without stones may be a motility disorder, but careful symptom selection is essential.

Q142. SOD pain-only trap

A 44-year-old woman after cholecystectomy has daily epigastric pain, normal liver enzymes, normal CBD, normal lipase, and normal MRCP. She requests ERCP because a friend improved after sphincterotomy. What is the best mechanism-based answer?

A. Without objective obstruction, pain likely reflects functional pain processing; ERCP risk exceeds expected benefit
B. ERCP is risk-free if the duct is normal
C. Sphincterotomy treats visceral hypersensitivity by cutting sensory nerves
D. All post-cholecystectomy pain is sphincter stenosis
E. Normal liver tests prove pancreaticobiliary malunion

Answer: A - Without objective obstruction, pain likely reflects functional pain processing; ERCP risk exceeds expected benefit

Mechanism pearl: Pain-only suspected SOD is a classic advanced-exam trap: avoid high-risk ERCP without objective evidence.

Q143. Acute cholecystitis high-risk patient

An 86-year-old septic patient with severe cardiopulmonary disease has acute calculous cholecystitis. Surgery is unsafe. The team discusses percutaneous cholecystostomy. What mechanism does this address?

A. It treats CBD obstruction better than ERCP
B. Drainage decompresses an infected obstructed gallbladder when definitive cholecystectomy is unsafe
C. It dissolves cholesterol stones by changing bile composition
D. It prevents pancreatic cancer progression
E. It blocks CCK receptors and stops pain centrally

Answer: B - Drainage decompresses an infected obstructed gallbladder when definitive cholecystectomy is unsafe

Mechanism pearl: In high-risk cholecystitis, gallbladder drainage provides **source control**.

Q144. Acalculous cholecystitis ICU

A ventilated trauma patient on vasopressors develops fever and cholestatic enzymes. Ultrasound shows distended gallbladder, sludge, wall thickening, and pericholecystic fluid without stones. What is the pathogenesis?

A. Occult gallstones are required for all acute cholecystitis
B. Low triglycerides trigger gallbladder wall gas
C. IgG4-related disease is the usual ICU cause
D. MEN1 causes gallbladder ischemia
E. Critical illness causes gallbladder stasis and ischemia, leading to necroinflammatory acalculous cholecystitis

Answer: E - Critical illness causes gallbladder stasis and ischemia, leading to necroinflammatory acalculous cholecystitis

Mechanism pearl: Acalculous cholecystitis is an ICU ischemia/stasis disease with high perforation risk.

Q145. Sump syndrome

A patient with prior side-to-side choledochoduodenostomy has recurrent cholangitis and debris in the distal CBD remnant. What mechanism explains symptoms?

A. Main duct IPMN obstructs the papilla with mucin
B. The gallbladder continues to contract against an obstructed cystic duct
C. Hypertriglyceridemia generates free fatty acids
D. Poorly drained distal bile duct segment acts as a reservoir for debris and bacterial overgrowth
E. A pancreatic NET secretes gastrin into the duct

Answer: D - Poorly drained distal bile duct segment acts as a reservoir for debris and bacterial overgrowth

Mechanism pearl: Altered biliary anatomy can produce stasis-related cholangitis and stones.

Q146. Pancreaticobiliary cancer molecular profiling

A patient with metastatic cholangiocarcinoma has progression after gemcitabine-based therapy. Molecular profiling shows IDH1 mutation. The fellow asks why the test was ordered at all.

A. IDH1 mutation proves the tumor is gallbladder polyp rather than cancer
B. Biliary cancers may harbor actionable alterations, making molecular profiling relevant for targeted therapy selection
C. All IDH1-mutant tumors respond to pancreatic enzymes
D. Molecular profiling replaces drainage for cholangitis
E. IDH1 mutation diagnoses autoimmune pancreatitis

Answer: B - Biliary cancers may harbor actionable alterations, making molecular profiling relevant for targeted therapy selection

Mechanism pearl: Advanced biliary cancers increasingly require **molecular profiling** for precision therapy.

Q147. Post-ERCP pancreatitis high-risk anatomy

A 29-year-old woman with suspected sphincter dysfunction undergoes prolonged ERCP with repeated pancreatic duct cannulation. She develops pain and lipase elevation the next day. Which prevention bundle was most mechanistically relevant?

A. UDCA prevents papillary edema
B. Octreotide is universally superior to NSAIDs
C. Prophylactic antibiotics alone prevent acinar inflammation
D. Immediate cholecystectomy prevents post-ERCP pancreatitis
E. Rectal NSAID to blunt inflammation plus pancreatic duct stent/hydration in selected high-risk duct-injury situations

Answer: E - Rectal NSAID to blunt inflammation plus pancreatic duct stent/hydration in selected high-risk duct-injury situations

Mechanism pearl: Post-ERCP pancreatitis prevention targets **papillary edema, ductal obstruction, and inflammatory amplification**.

Q148. Chronic pancreatitis and biliary stricture

A 56-year-old man with calcific chronic pancreatitis develops pruritus, jaundice, and cholangitis. Imaging shows distal CBD stricture through the pancreatic head but no mass. What mechanism and complication should be considered?

A. Gallbladder polyps produce diffuse intrahepatic cholestasis
B. Insulinoma obstructs the bile duct through beta-cell hypertrophy
C. VIPoma commonly causes CBD strictures
D. Exocrine insufficiency causes conjugated hyperbilirubinemia directly
E. Fibrotic inflammatory narrowing of the intrapancreatic CBD can cause obstructive cholestasis, cholangitis, and secondary biliary fibrosis

Answer: E - Fibrotic inflammatory narrowing of the intrapancreatic CBD can cause obstructive cholestasis, cholangitis, and secondary biliary fibrosis

Mechanism pearl: Chronic pancreatitis can cause benign distal biliary strictures that may need endoscopic or surgical therapy.

Q149. Hemosuccus pancreaticus

A patient with chronic pancreatitis and a pseudocyst develops intermittent melena and epigastric pain. Endoscopy is initially negative, but blood is later seen from the ampulla. Which mechanism explains bleeding?

A. VIPoma causes colonic bleeding by cAMP activation
B. Bile acid diarrhea causes ampullary hemorrhage
C. Pseudoaneurysm erodes into the pancreatic duct, causing **hemosuccus pancreaticus**
D. Gallbladder cholesterol stones bleed through the cystic duct
E. AIP causes diffuse mucosal oozing from IgG4 cells

Answer: C - Pseudoaneurysm erodes into the pancreatic duct, causing **hemosuccus pancreaticus**

Mechanism pearl: Intermittent bleeding from the ampulla in pancreatitis suggests pseudoaneurysm into the duct.

Q150. Pancreatic pseudocyst drainage indication

A 49-year-old man has a 7-cm pancreatic pseudocyst 8 weeks after pancreatitis. He has early satiety, vomiting from gastric compression, and persistent pain. There is a mature wall and no solid debris. Why is endoscopic drainage reasonable?

A. Immature collections drain more safely before wall formation
B. All pseudocysts require drainage regardless of symptoms
C. Solid debris makes simple pseudocyst drainage ideal
D. Drainage is done to prevent gallstone recurrence
E. The pseudocyst is mature and symptomatic, with mass effect amenable to internal drainage

Answer: E - The pseudocyst is mature and symptomatic, with mass effect amenable to internal drainage

Mechanism pearl: Drain mature pseudocysts when **symptomatic, infected, bleeding, obstructing, or enlarging**.

Compact Answer Key

1. D	2. D	3. B	4. B	5. B	6. A	7. D	8. D	9. B	10. D
11. E	12. C	13. B	14. D	15. D	16. E	17. A	18. B	19. E	20. E
21. C	22. B	23. A	24. D	25. A	26. E	27. B	28. B	29. A	30. D
31. C	32. C	33. A	34. A	35. E	36. E	37. C	38. E	39. D	40. C
41. D	42. D	43. E	44. B	45. D	46. D	47. D	48. C	49. E	50. A
51. C	52. E	53. B	54. D	55. D	56. A	57. C	58. C	59. D	60. E
61. E	62. D	63. C	64. C	65. A	66. B	67. B	68. B	69. E	70. A
71. B	72. E	73. D	74. D	75. D	76. C	77. B	78. C	79. E	80. E
81. A	82. E	83. E	84. A	85. C	86. D	87. D	88. B	89. C	90. A
91. A	92. B	93. B	94. E	95. A	96. D	97. B	98. E	99. E	100. C
101. A	102. E	103. E	104. B	105. E	106. B	107. A	108. E	109. E	110. B
111. E	112. A	113. B	114. D	115. C	116. D	117. B	118. E	119. A	120. C
121. B	122. D	123. D	124. D	125. C	126. C	127. E	128. B	129. E	130. E
131. B	132. A	133. A	134. C	135. A	136. E	137. D	138. D	139. B	140. A
141. A	142. A	143. B	144. E	145. D	146. B	147. E	148. E	149. C	150. E

Note: The answer key is intentionally compact. Full explanations are provided under each question in the main text.