

Acute and Chronic Pancreatitis

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Learning Objectives

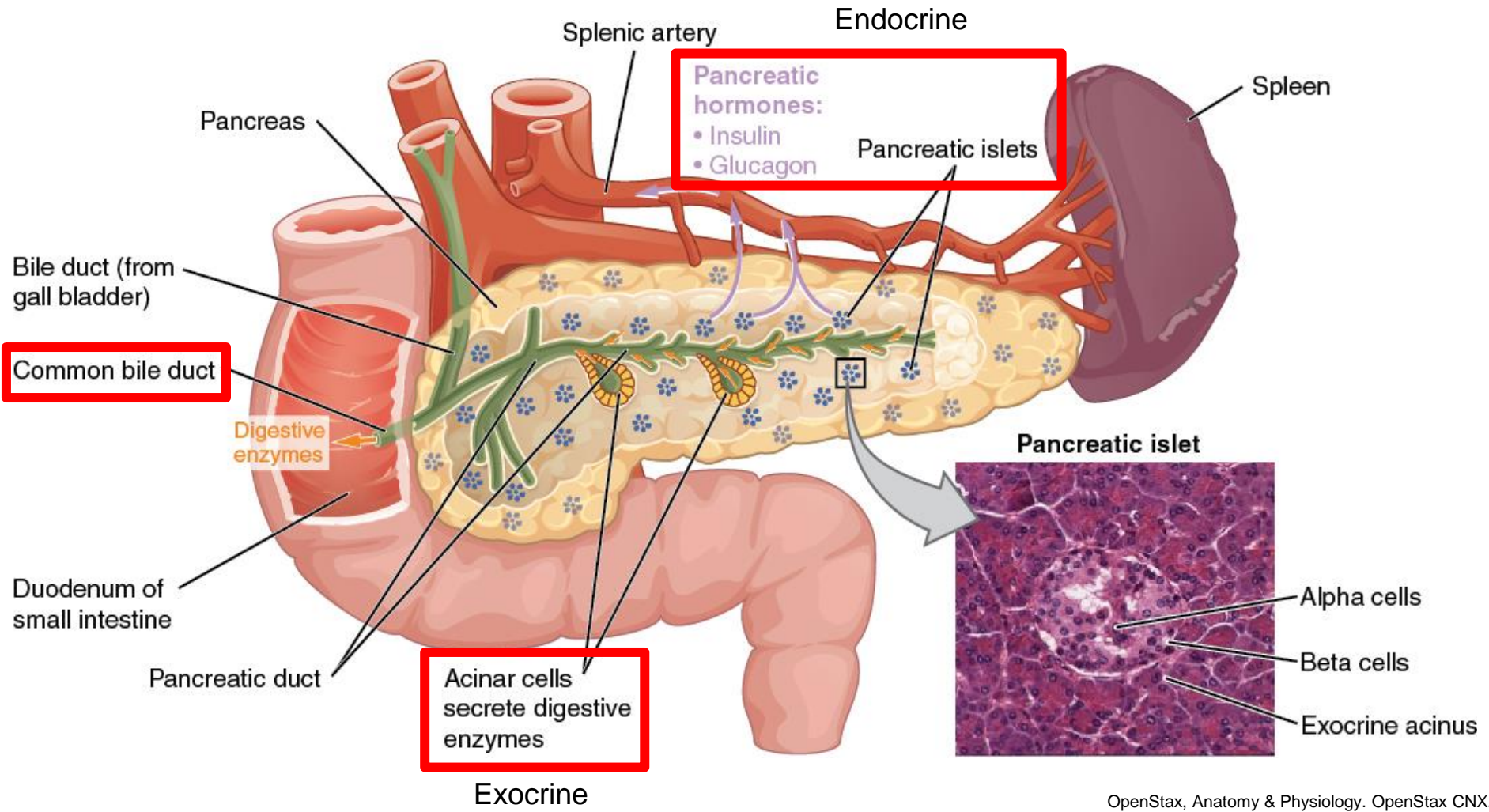
1. Describe basic anatomy and physiology of the pancreas.
2. Recognize clinical features of acute and chronic pancreatitis.
3. Identify risk factors and etiologies of acute and chronic pancreatitis.
4. Interpret test results in the work-up of acute and chronic pancreatitis.

Outline

- Anatomy and physiology
- Acute Pancreatitis
 - Pathophysiology
 - Clinical Features
 - Diagnosis and Laboratory Testing
 - Prognosis and Management
 - Example Case
- Chronic Pancreatitis
 - Pathophysiology
 - Clinical Features
 - Diagnosis and Laboratory Testing
 - Prognosis and Management
- Case Report
- Summary

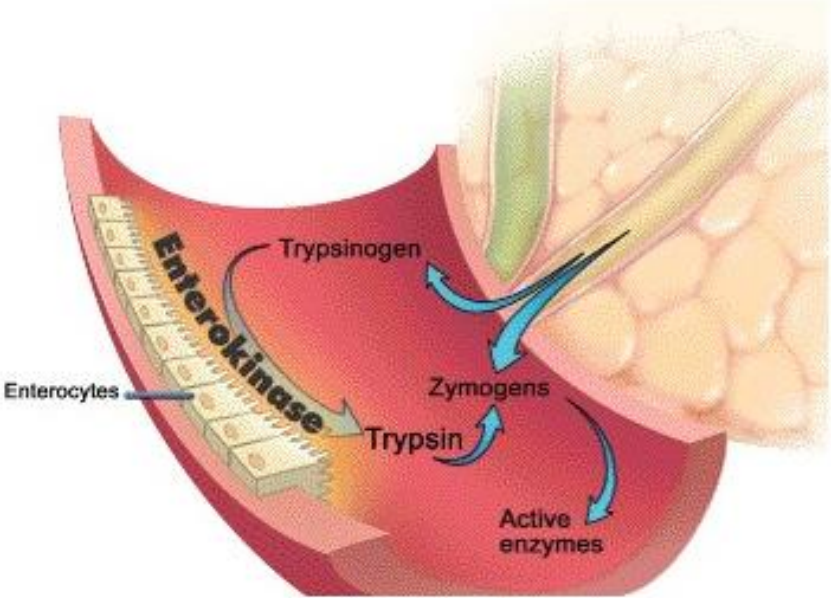
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- **Anatomy and physiology**
- Acute Pancreatitis
- Chronic Pancreatitis
- Case Report
- Summary

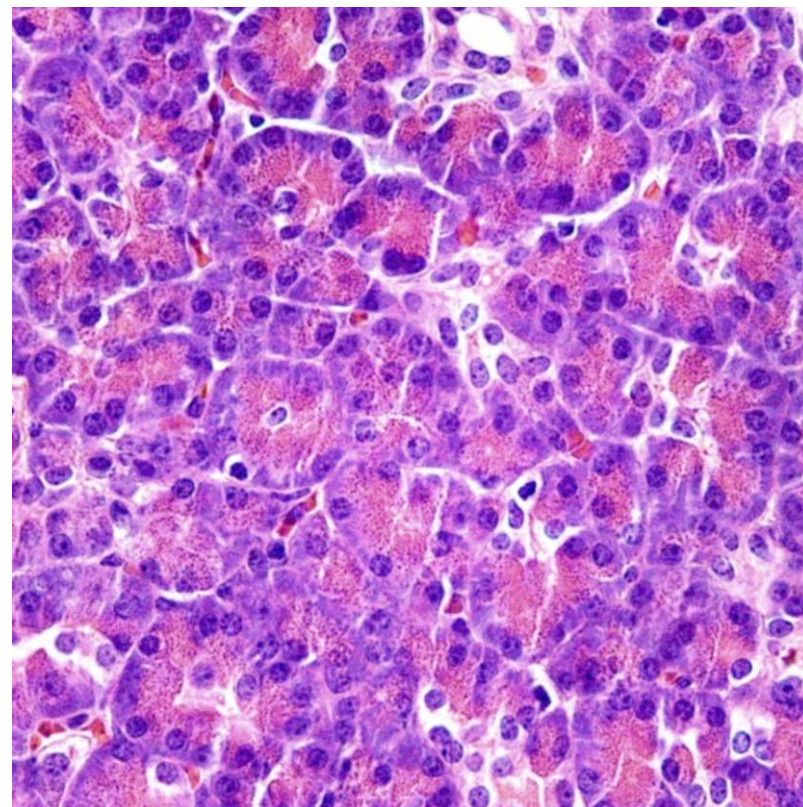
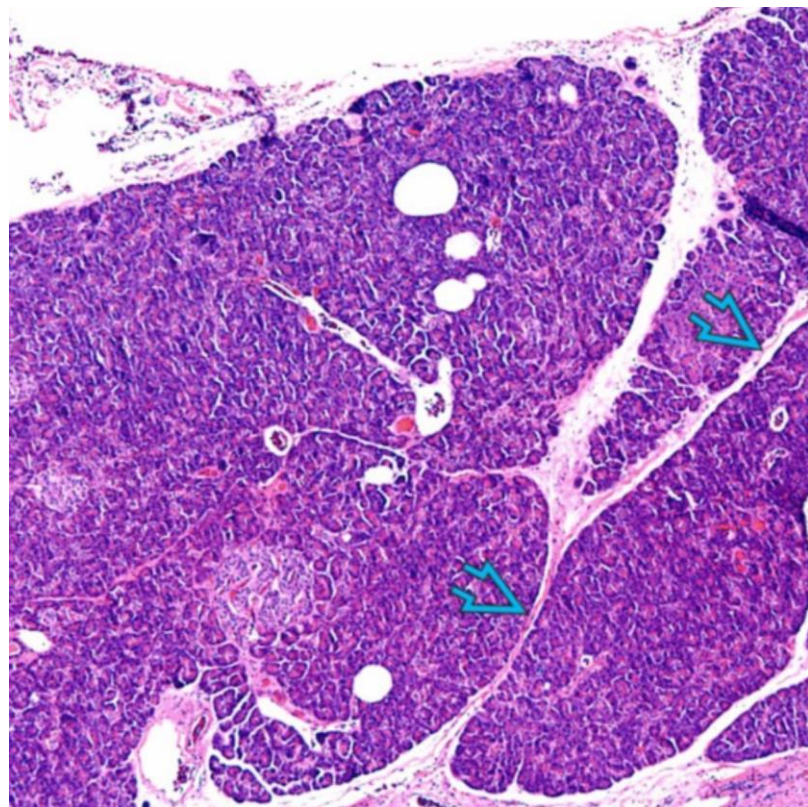


Digestive Enzymes

Proenzyme	Active Form
	Lipase
	Amylase
Trypsinogen	Trypsin
Proelastase	Elastase



Normal Histology

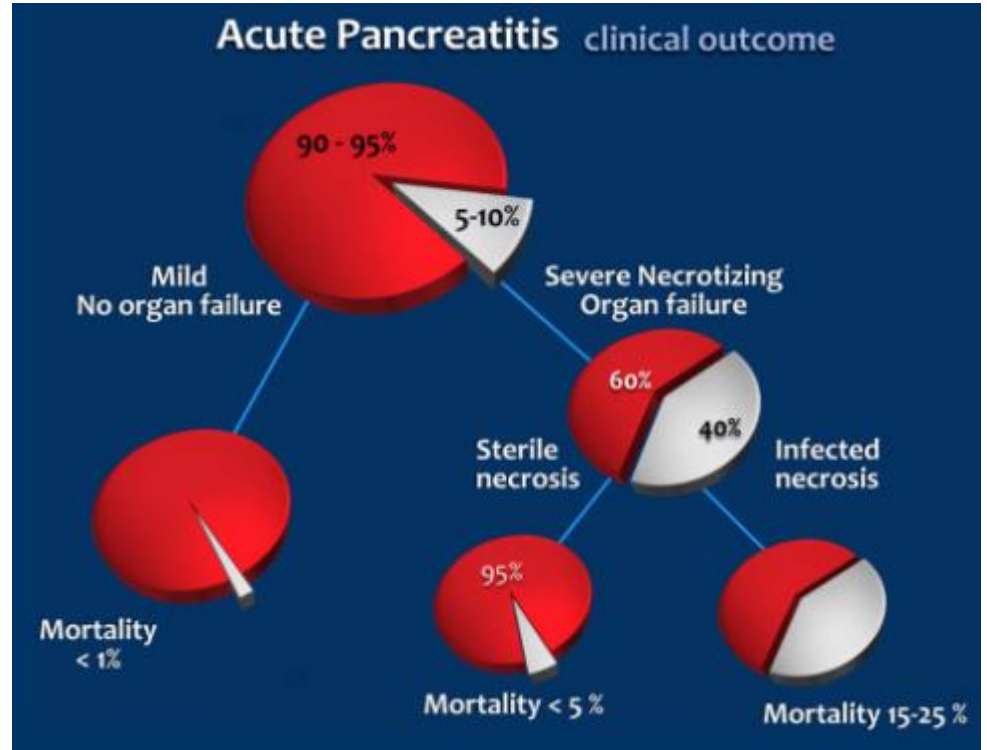


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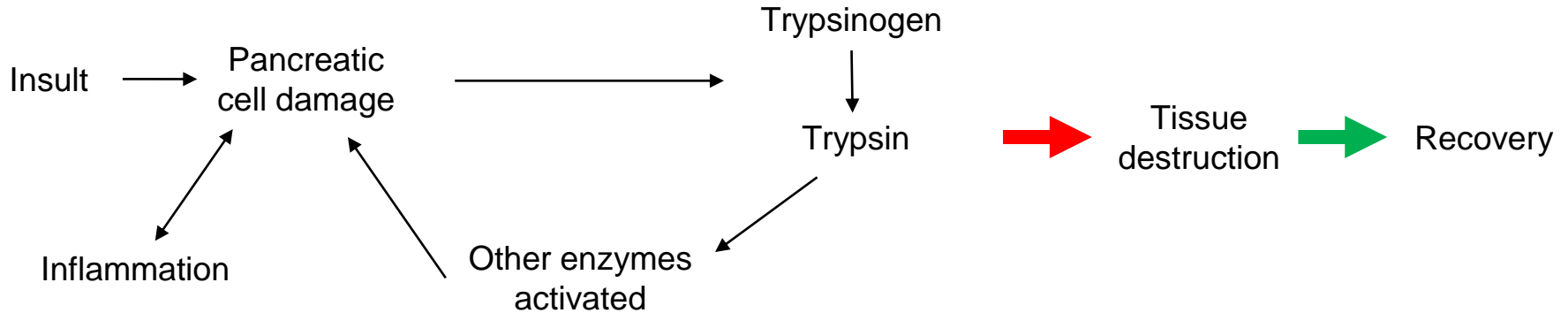
Acute Pancreatitis

- Reversible inflammatory process of the pancreas
- Often mild, but severe disease can have a mortality rate of up to 30%
- Common cause of hospitalization



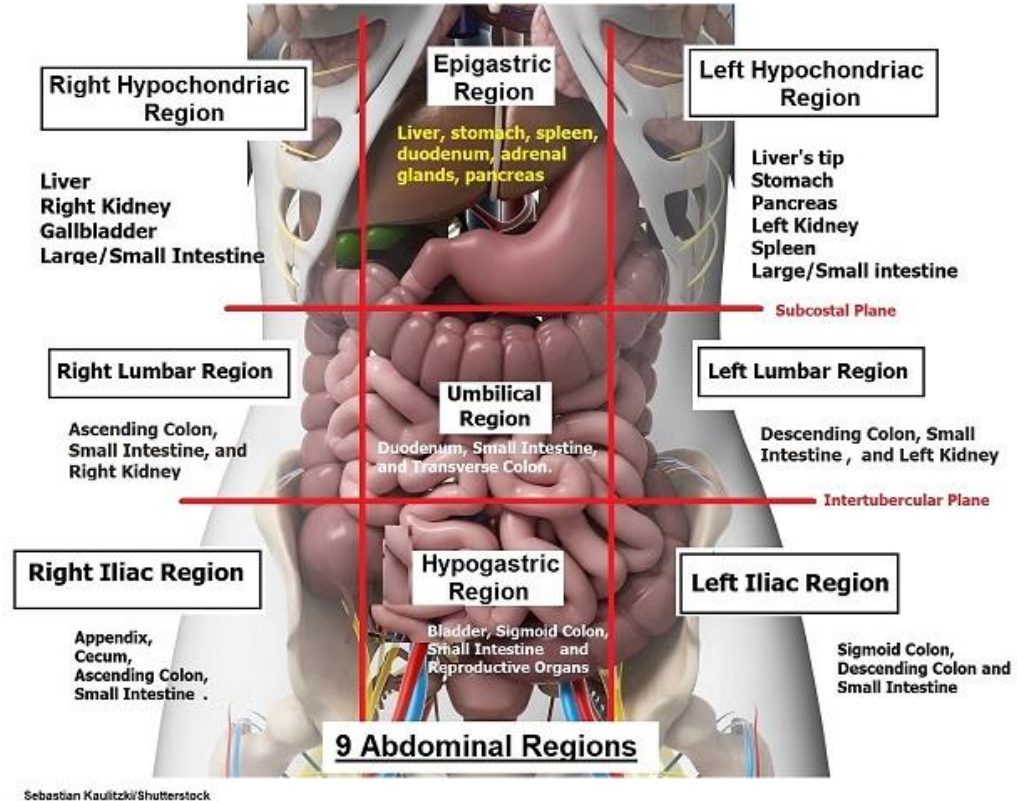
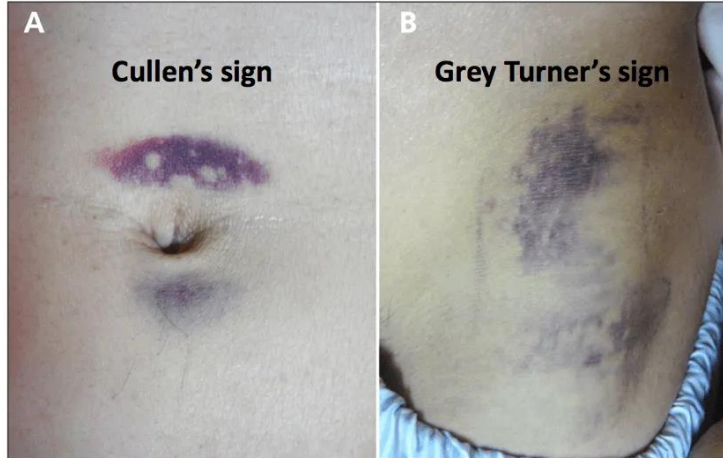
Pathophysiology

- Caused by auto digestion
- Pancreatic cell damage occurs leading to activation of trypsinogen
 - Other digestive enzymes are activated
 - Macrophages and neutrophils are recruited resulting in inflammation
- Cell damage is potentiated and the tissue is destroyed



Clinical Presentation

- Epigastric abdominal pain
- Nausea
- Vomiting
- Grey Turner sign
- Cullen sign



Differential Diagnosis

GI:

- Inflammation/Infection
- Obstruction
- Ulcers
- Cancer

Endocrine:

- Diabetic ketoacidosis

Cardiovascular:

- Heart attack

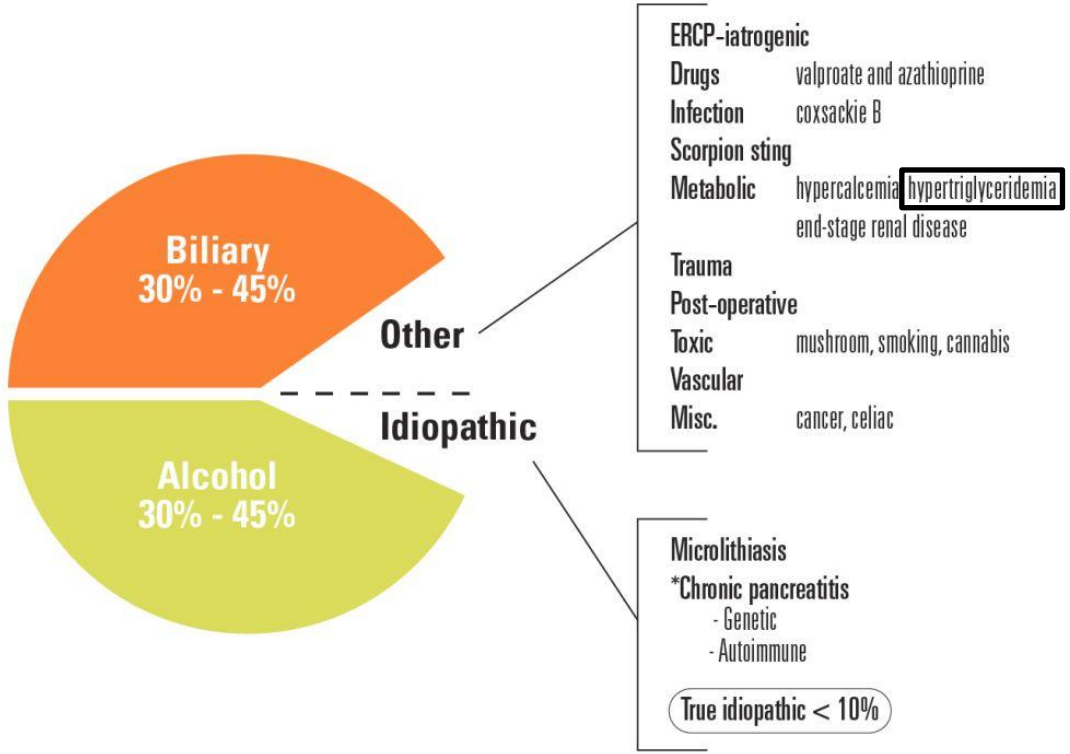
Genitourinary:

- Kidney stones

Gynecologic:

- Ectopic pregnancy

Etiologies



Diagnosis

The diagnosis requires two of the following three criteria:

Epigastric abdominal pain

Elevated lipase or amylase, > 3x the upper limit of normal

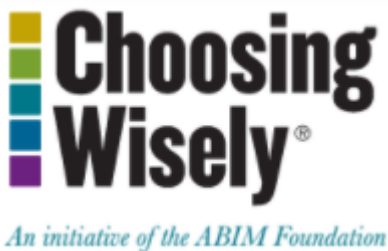
Imaging findings of pancreatic inflammation

Laboratory Testing

- Lipase/amylase testing is one of the three diagnostic criteria
- Other tests are used to monitor overall patient condition and guide management
- Some tests can be used for prognosis

Lipase

- Digests triglycerides and fatty acids
- Secreted mainly by the pancreas
- The best test for acute pancreatitis; sensitivity and specificity 80-100%
- Increases in 4-8 hours and peaks at 24 hours with concentrations remaining elevated for 7-14 days
- Increase in lipase is not proportional to severity



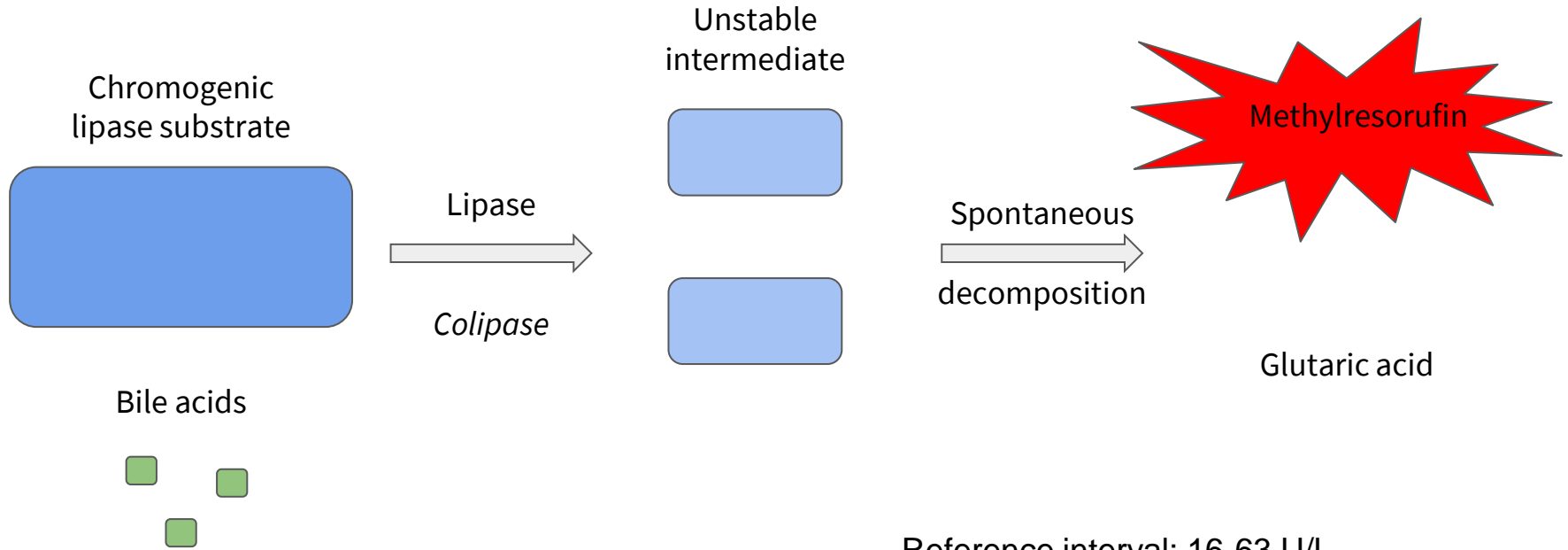
American Society for Clinical Pathology

[View all recommendations from this society](#)

September 14, 2016

Do not test for amylase in cases of suspected acute pancreatitis. Instead, test for lipase.

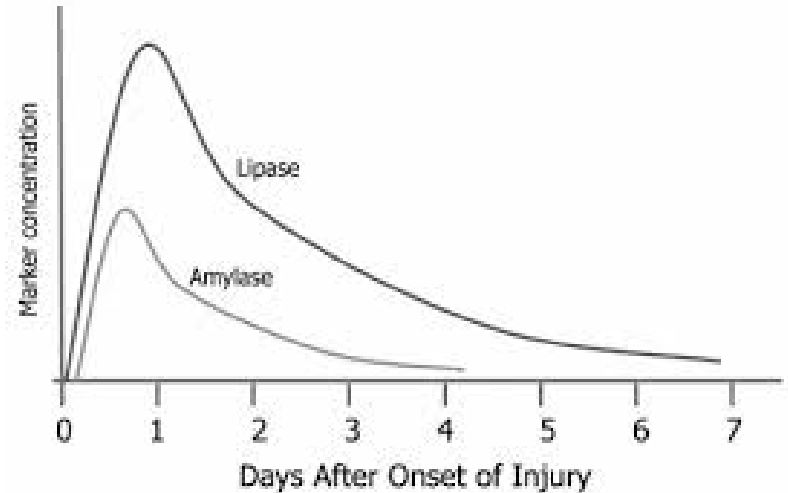
Lipase Method



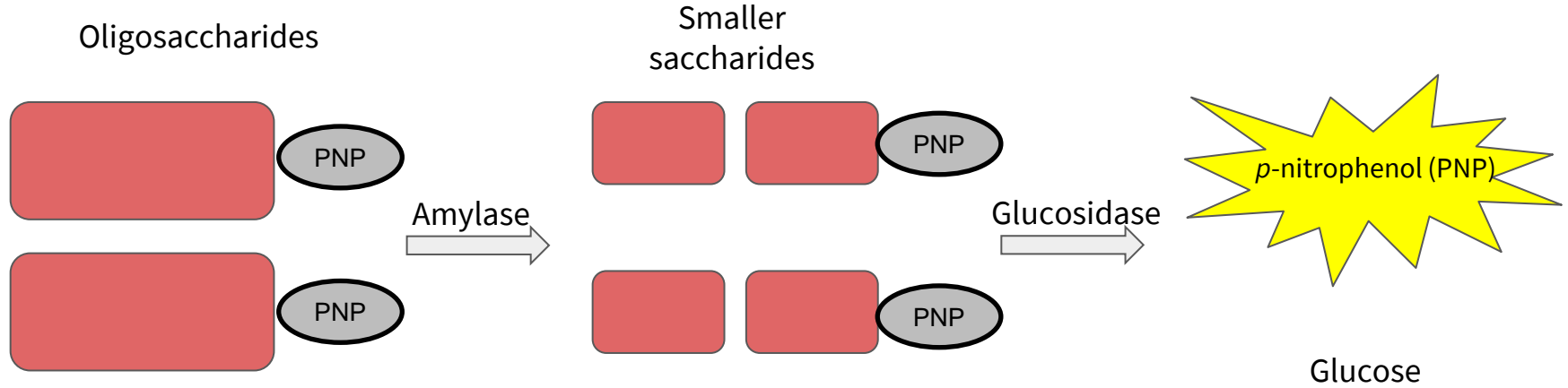
Reference interval: 16-63 U/L

Amylase

- Digests starches and glycogen
- Secreted by salivary glands, pancreas, and other organs
- Traditionally used with lipase in testing for acute pancreatitis, but is not a recommended test due to lack of specificity (20-60%)
- Rises rapidly within 5-8 hours of onset of symptoms in acute pancreatitis and stays elevated for 3-4 days



Amylase Method



Reference interval: 30-110 U/L

Pancreatic Amylase

- Represents 40-50% of amylase in serum by 5 years old
- Same method with the addition of antibodies against human salivary amylase to only measure the pancreatic isoform
- Increases the specificity of the test for pancreatitis to >90%
 - Elevation in P-AMY also seen in biliary tract diseases, other GI diseases
- Remains elevated in acute pancreatitis for longer than total amylase
- Lipase is still recommended per Choosing Wisely

Initial Work-up of Suspected Acute Pancreatitis

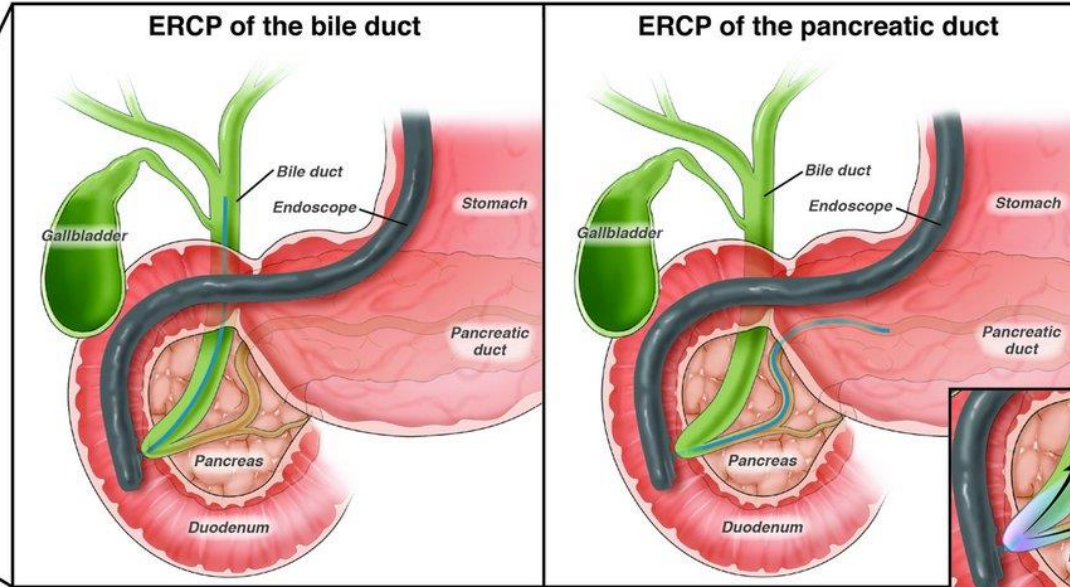
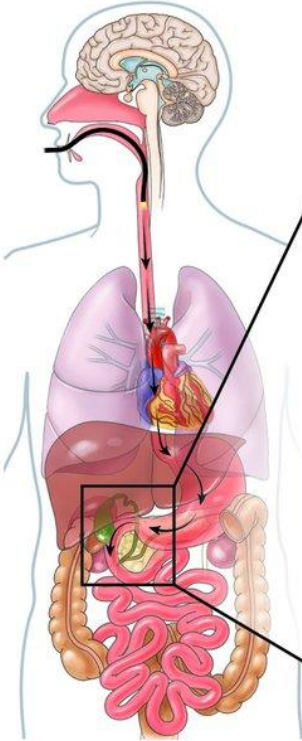
- Complete blood count (CBC)
- Basic metabolic panel (BMP)
- Liver function tests (LFTs)
- Triglycerides
- Lactate dehydrogenase (LDH)
- Lipase



Imaging

Patient undergoing ERCP

- Ult
- Cc
- Mæ
- Mæ
- En



Dye injected into the bile duct (1) or pancreatic duct (2)

Prognosis

- The mortality rate in patients with severe pancreatitis is 30%
- These patients need to be identified to be more closely monitored
- Risk stratification tools exist but aren't standardized
- Relevant tests include BUN, LDH, CRP, procalcitonin, trypsin, IL-6

Prognosis

Systemic Inflammatory Response Syndrome (SIRS) Criteria:

- Temperature $<36^{\circ}\text{C}$ or $>38^{\circ}\text{C}$
- Heart rate $<90/\text{min}$
- Respiratory rate $>20/\text{min}$ or $\text{PCO}_2 <32\text{ mmHg}$
- WBC $>12,000$, $<4,000$, or $>10\%$ immature/band forms

Management

- Most cases can be managed medically
- Pain control and fluid balance are the main aspects of management
- Surgery may be necessary in severe cases

Case 1: Patient Presentation

A 45 year old female presented to the emergency department with pain in her mid-upper abdomen for two hours. It felt worse after eating lunch and radiates to her back. She has felt nauseous and vomited just prior to coming to the ED.

Past medical history: obesity

Social history: no alcohol, smoking, or drugs

Family history: cardiovascular disease

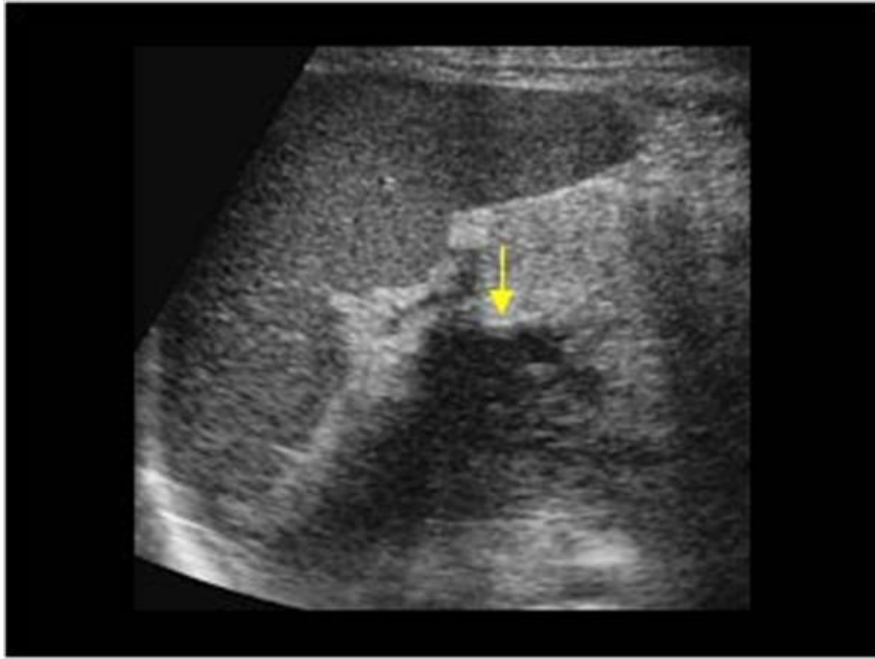
HR: 88, BP: 132/112, Temp: 98.8° F, Resp: 16, Oxygen: 98%

Case 1: Labs

- Complete blood count
- Basic metabolic panel
- Liver function studies
- Triglycerides
- Lactate dehydrogenase
- Lipase
- Troponin

Lipase	653 U/L (Ref Interval: 16-63)
AST	60 U/L (Ref Interval: 9-40)
ALT	54 U/L (Ref Interval: 5-40)
Alkaline Phosphatase	331 U/L (Ref Interval: 38-126)

Case 1: Ultrasound



Case 1: Diagnosis/Outcome

Acute pancreatitis, likely etiology: gallstone

Fluids as needed to balance fluid levels and electrolytes

Pain management

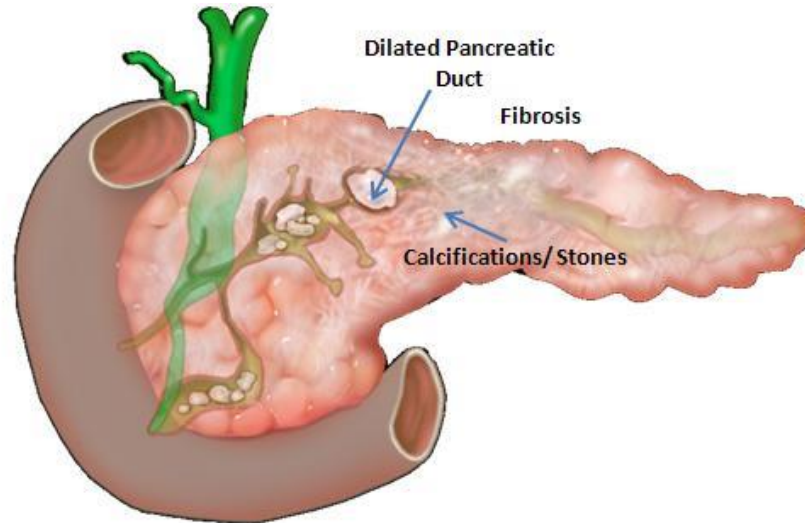
Meet with surgery to discuss possible cholecystectomy

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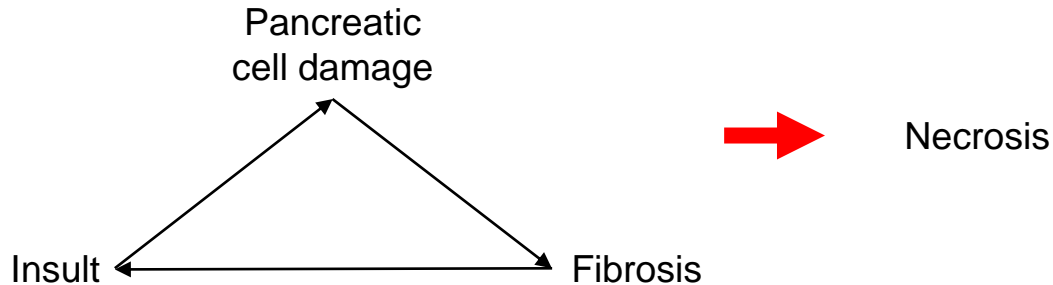
Chronic Pancreatitis

- Progressive inflammation of the pancreas leading to irreversible damage
- Can result in exocrine and endocrine insufficiency
- Increased risk of pancreatic cancer over time



Pathophysiology

- Not agreed upon or well understood
- Necrosis-Fibrosis theory: chronic fibrotic changes occur after recurrent acute insults to the pancreas
 - Probably more complex than this and multifactorial
- Degree of fibrosis doesn't seem to correlate with degree of dysfunction



Pancreatic Insufficiency

- Can't be demonstrated until at least 50% of acinar cells are destroyed, clinical signs at 90%
- Islet cells remain viable for longer than acinar cells
- Exocrine insufficiency leads to malnutrition due to protein and fat malabsorption
 - About two-thirds of patients have fat soluble vitamin deficiencies
 - 65% of patients get osteopenia or osteoporosis
- Endocrine insufficiency can lead to type 3c diabetes
 - 5-10% of patients develop this

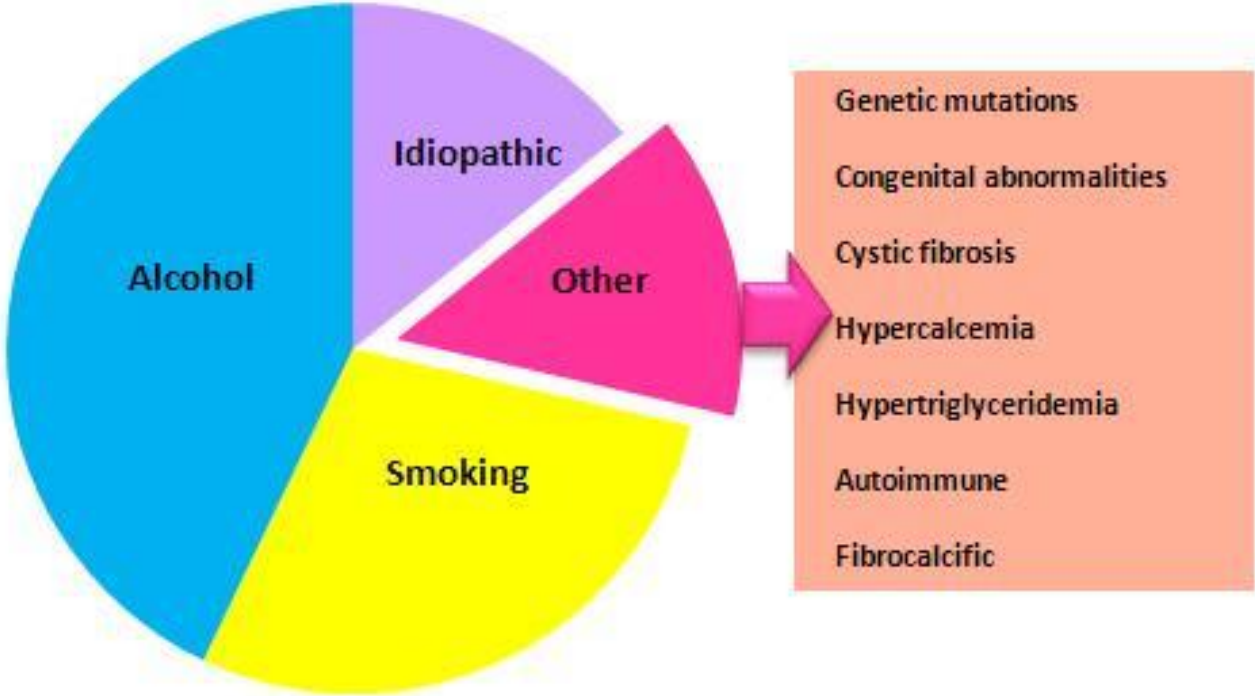
Clinical Presentation

- Recurrent episodes of epigastric pain that spreads to the back
- Constant abdominal pain
- Steatorrhea
- Diabetes
- Weight loss

Differential Diagnosis

- Focal chronic pancreatitis
- Autoimmune pancreatitis
- Pancreatic adenocarcinoma

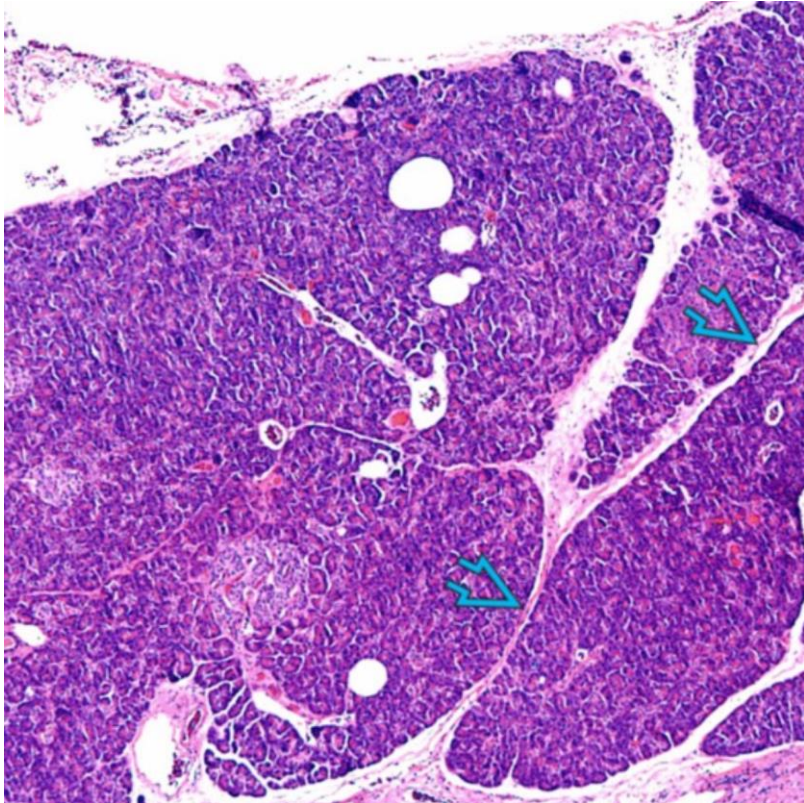
Risk Factors



Diagnosis

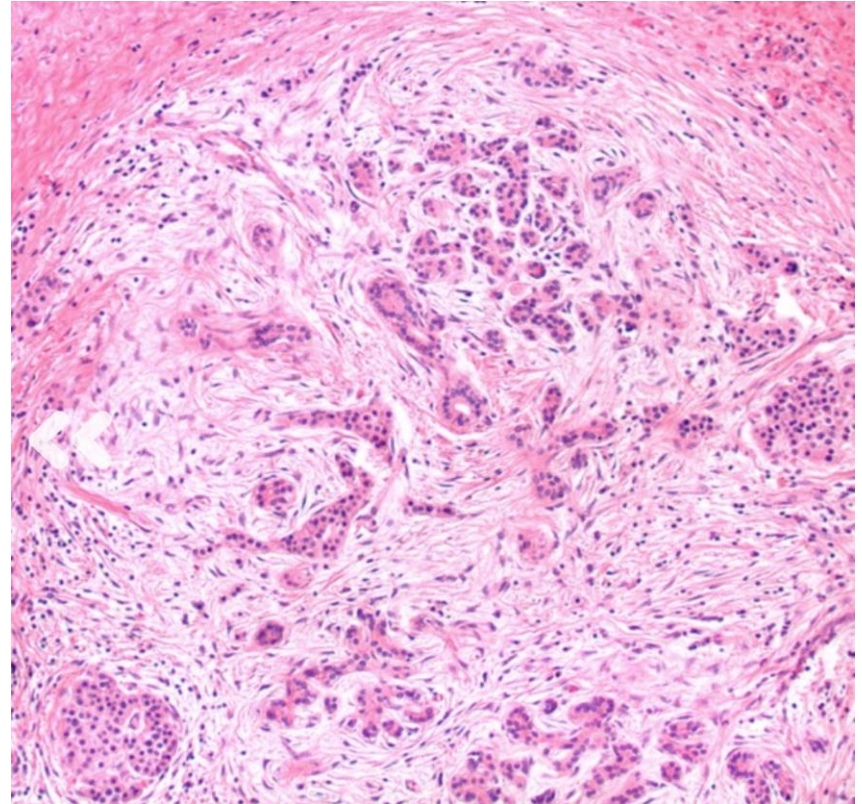
- Establishing a diagnosis can be challenging, especially early
- Histology is the “gold standard”, but biopsies are not routinely done
- Requires combination of clinical history, imaging, and lab testing

Normal Histology



Lamps, LW. Pancreas. Image: Lobular pancreas. ExpertPath.

Chronic Pancreatitis Histology



Yerian, L. Chronic Pancreatitis. Image: Fibrosis and chronic inflammation. ExpertPath.

Laboratory Testing

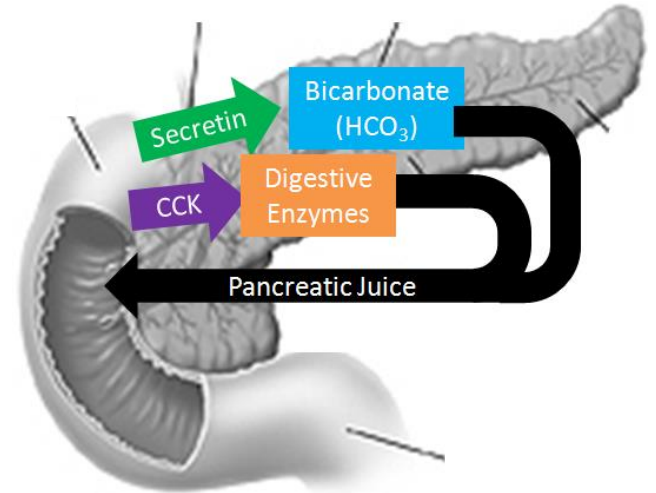
- Lab tests have limited sensitivity early in disease
- Tests need to be used in combination with imaging, and clinical features to make a diagnosis
- Some tests also help with risk assessment and guiding management
- Direct (invasive) and indirect (non-invasive) tests are available

Direct (Invasive) Testing

- Recommended testing for chronic pancreatitis by American Pancreatic Association
- Uses hormones to stimulate the pancreas
- Duodenal contents are aspirated to measure amylase, lipase, trypsin, and bicarbonate
- Tests not widely available, not validated for specimen type
- Requires a tube in the GI tract

Secretin-Cholecystokinin (CCK) Test

- Patient fasts overnight
- Tube is placed in the duodenum
- Secretin is given and duodenal fluid is collected at 15 min intervals for an hour
 - Stimulates secretion of pancreatic juices and bicarbonate
- CCK is then given which stimulates the secretion of pancreatic enzymes and fluid is collected



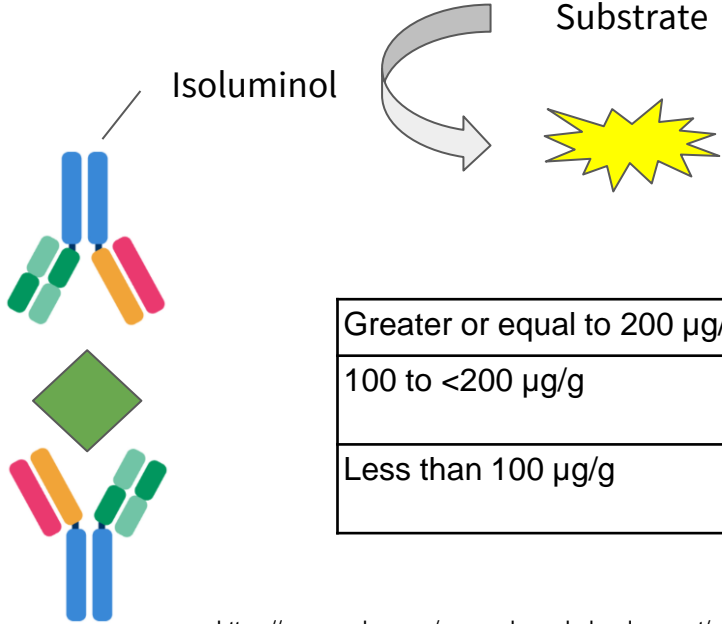
Indirect (Non-invasive) Testing

- Preferred to invasive testing in majority of situations
- Measure pancreatic enzymes in the blood or stool to get indirect measure of production
 - Fecal pancreatic elastase, serum trypsin

Pancreatic Elastase

- Quantitative determination of pancreatic elastase in stool is the primary test for chronic pancreatitis
- Elastase is excreted by the pancreas and goes through the rest of the GI tract without being degraded or inactivated
- Stool can't be watery or the enzyme could be diluted out making the result falsely low
- Treatment with pancreatic enzyme supplements does not interfere with assays that are human-specific

Pancreatic Elastase Method

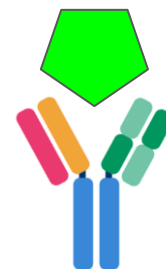
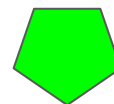
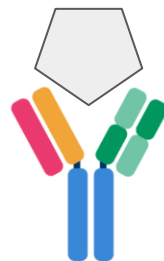
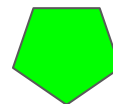
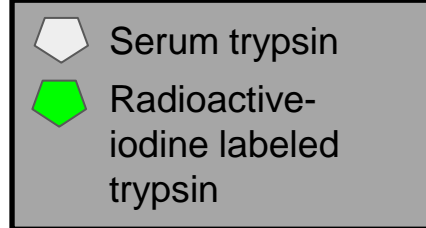


Greater or equal to 200 $\mu\text{g/g}$	Normal
100 to <200 $\mu\text{g/g}$	Moderate to mild exocrine pancreatic insufficiency
Less than 100 $\mu\text{g/g}$	Severe exocrine pancreatic insufficiency

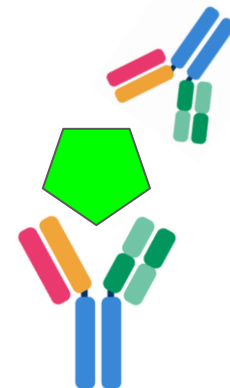
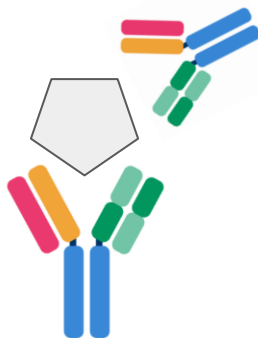
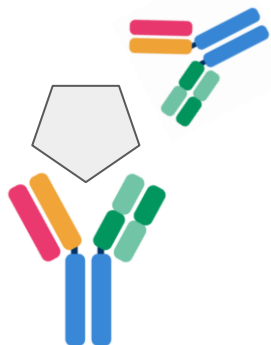
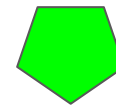
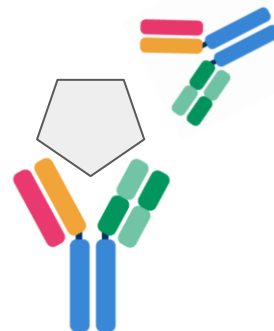
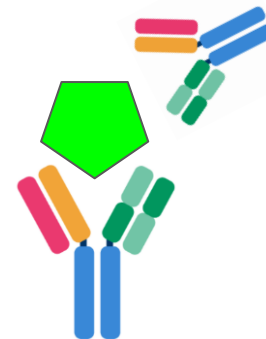
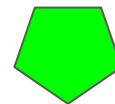
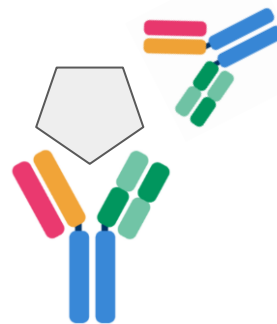
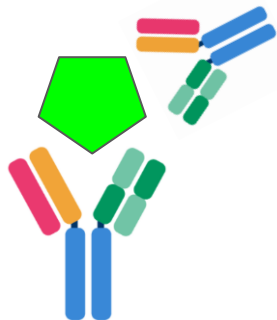
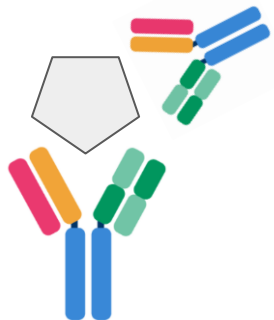
Trypsin

- Duodenal fluid/pancreatic juice
 - Can be measured spectrophotometrically with enzymatic assay
- Serum
 - Measured immunologically because in serum it is inactive
 - Low in 50% of chronic pancreatitis cases
 - High in 20% of chronic pancreatitis cases, likely in acute phase of disease
 - Steatorrhea is associated with low trypsin

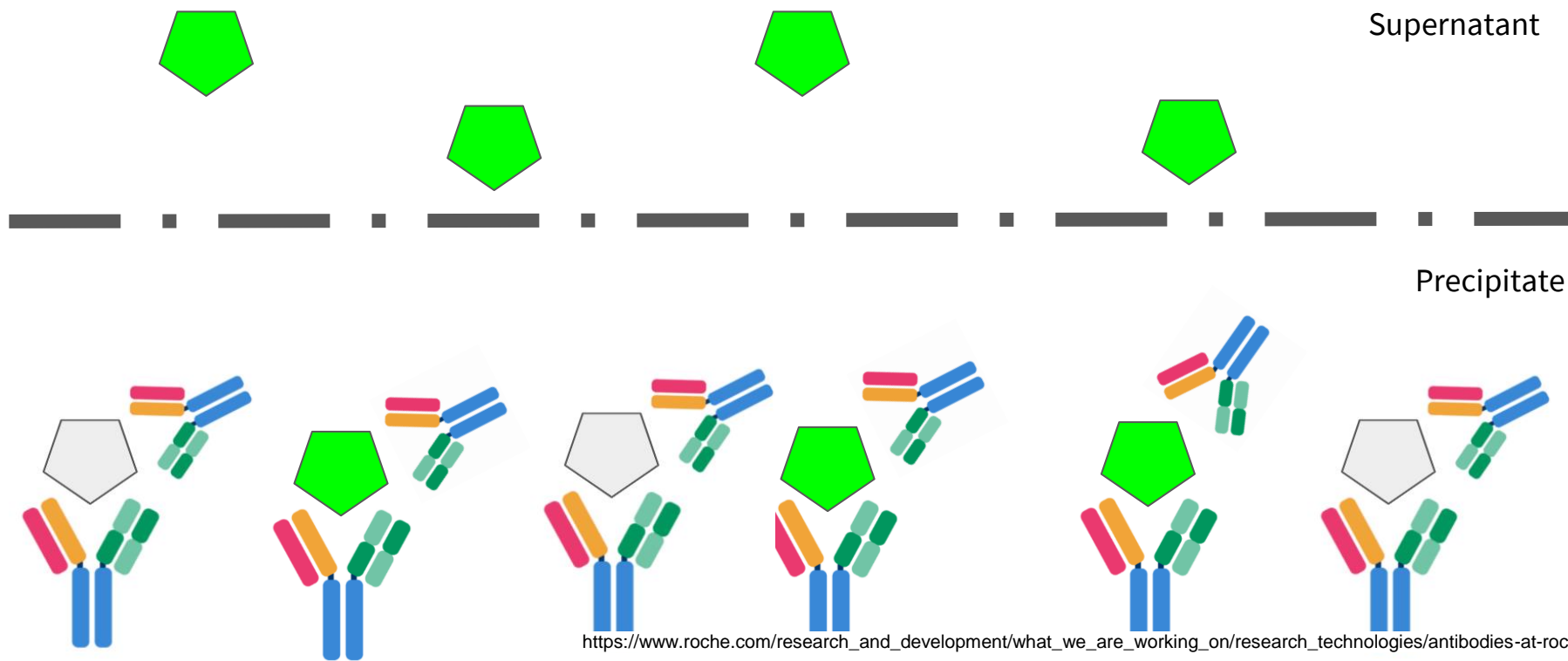
Trypsin Method, serum



Trypsin Method, serum

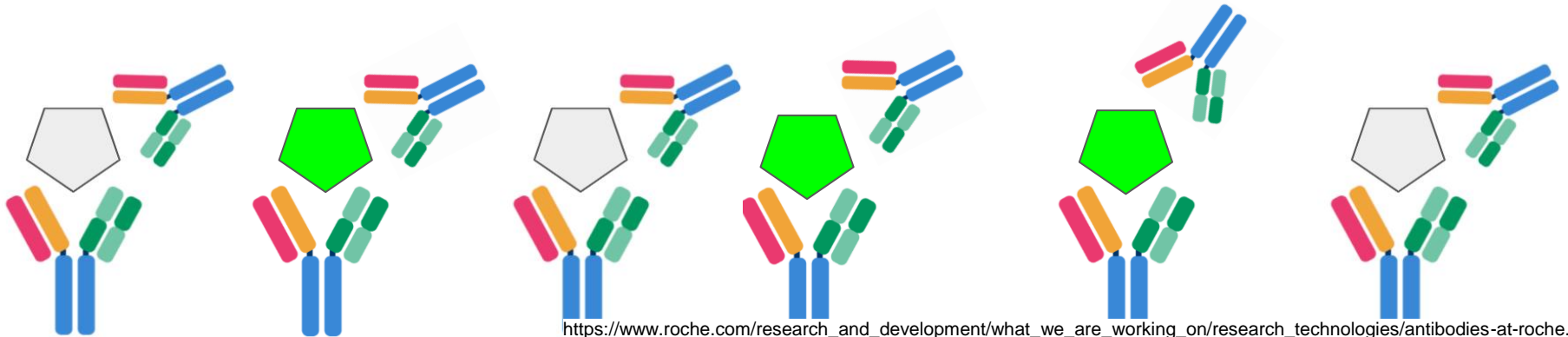
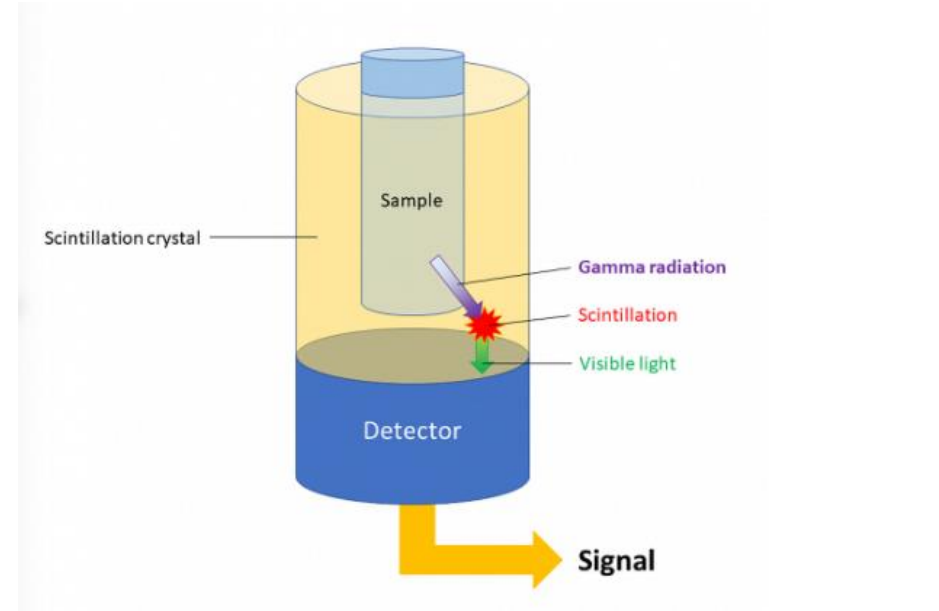


Trypsin Method, serum



Trypsin Method, serum

Reference interval: 180.5-885.3 ng/mL

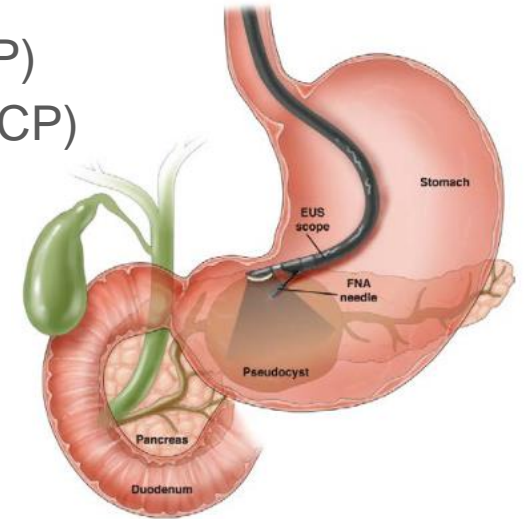


Imaging

- Computed tomography (CT)- best initial test
- Endoscopic Ultrasound (EUS)
- Magnetic resonance imaging (MRI)
- Magnetic resonance cholangiopancreatography (MRCP)
- Endoscopic retrograde cholangiopancreatography (ERCP)



https://en.wikipedia.org/wiki/CT_scan



<https://gastro.org/practice-guidance/gi-patient-center/topic/endoscopic-ultrasound-eus/?hilitte=%27endoscopic%27%2C%27ultrasound%27>

Management

- Pancreatic enzyme replacement therapy (PERT)
- Supplements and/or feeding tube if necessary
- Encourage abstinence from alcohol and smoking
- Pain management
- Imaging to surveil for pancreatic cancer (especially hereditary pancreatitis patients)
- Surgery if there is an obstructive process, intractable pain, enlargement of pancreatic head, suspicion for malignancy

Monitoring

- Fat soluble vitamins (A, E, D, K)
- Hemoglobin A1C
- 72 hour fecal fat
- Bone density (imaging)

Outline

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Case 2: Patient Presentation

A 35 year old obese Hispanic female presented with fever, dry cough, dyspnea, nausea, vomiting, and diarrhea for 8 days. She also had severe stabbing epigastric pain radiating to her back for 2 days.

Past medical history: obesity, anxiety

Social history: no alcohol, smoking, or drugs

HR: 110, Temp: 101.9° F, Oxygen: 85%

Case 2: Labs

Upper limits of normal:
Amylase- 103 U/L
Lipase- 82 U/L

Laboratory results on admission

White-cell count (per mm ³)	4800
Differential count (per mm ³)	
Total neutrophils	3768
Total lymphocytes	725
Total monocytes	298
Platelet count (per mm ³)	220,000
Hemoglobin (g/liter)	133
Albumin (g/liter)	36
Alanine aminotransferase (U/liter)	83
Aspartate aminotransferase (U/liter)	69
Total Bilirubin (mg/dl)	0.5
Direct Bilirubin (mg/dl)	0.23

Alkaline Phosphatase (U/liter)	78
Lactate dehydrogenase (U/liter)	415
Blood Urea Nitrogen (mg/dl)	6
Creatinine (μmol/liter)	80
Creatine kinase (U/liter)	430
Amylase (U/liter)	325
Lipase (U/liter)	627
Triglyceride (mg/dl)	136
Procalcitonin (ng/ml)	26.54
C-reactive protein (mg/liter)	19.50

Case 2: Imaging

Chest and abdomen CT:

- Multifocal bilateral ground-glass opacities in the lungs
- Normal gallbladder and bile duct
- Unremarkable pancreas

Case 2: Diagnosis/Outcome

Severe acute pancreatitis with acute respiratory distress syndrome

Admitted to ICU

Treated with fluids, pain management, empiric antibiotics for possible bacterial pneumonia

Developed acute hypoxic respiratory failure but eventually the respiratory failure and gastrointestinal symptoms resolved

Additional testing: COVID-19 positive

Case 2: Discussion

- Viral pancreatitis has been described to be due to mumps, measles, coxsackievirus, EBV, and hepatitis A
- Pancreatic injury has been reported in 17% of COVID-19 patients
- There are reports of other coronaviruses causing acute pancreatitis in ferrets and pigeons
- COVID-19 is thought to enter cells via the ACE-2 receptor and this is expressed in pancreatic islets
- Acute pancreatitis could be caused by direct viral cytopathic effect or secondary to the robust immune response induced by the virus

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Learning Objectives

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3. Identify risk factors and etiologies of acute and chronic pancreatitis.
4. Interpret test results in the work-up of acute and chronic pancreatitis.

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DiaSorin LIAISON Elastase-1 Package Insert

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