Clinical Chemistry
Trainee Council

PEARLS OF
LABORATORY MEDICINE

Hereditary Pancreatitis

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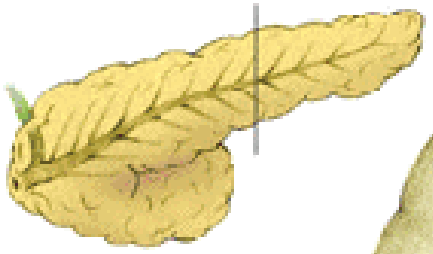
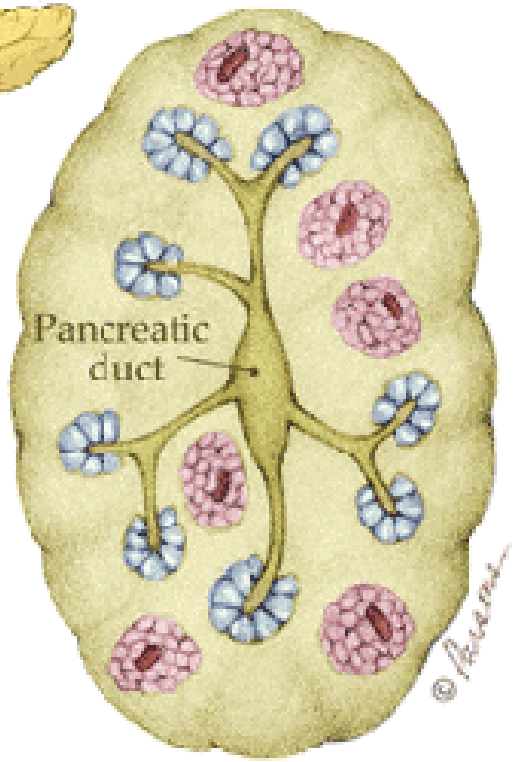
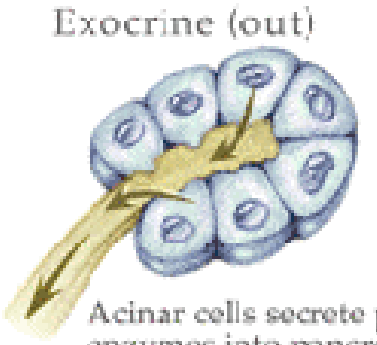
Pancreatic Function



Cross-section of the pancreas





Acinar cells secrete pancreatic enzymes into pancreatic duct

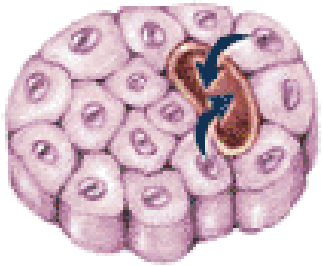
<u>DIGESTIVE ENZYMES</u>

Proteases

(Trypsin, Chymotrypsin)

Lipase

Amylase



Islets of Langerhan cells secrete hormones into blood vessels

<u>HORMONES</u>

Insulin

Glucagon

Types of Pancreatitis

- Acute
  - An inflammatory response to pancreatic injury
  - Is usually non-progressive and mostly painful
  - Serum amylase and lipase concentrations are elevated
  - Involves a large portion of the pancreas and a predominantly neutrophilic inflammatory response

Types of Pancreatitis

- Chronic
  - Progressive inflammatory and fibrotic changes in the pancreas resulting in permanent structural damage
  - Leads to impairment of exocrine and endocrine function
  - May be asymptomatic over long periods of time, present with a fibrotic mass, or have pancreatic insufficiency without pain

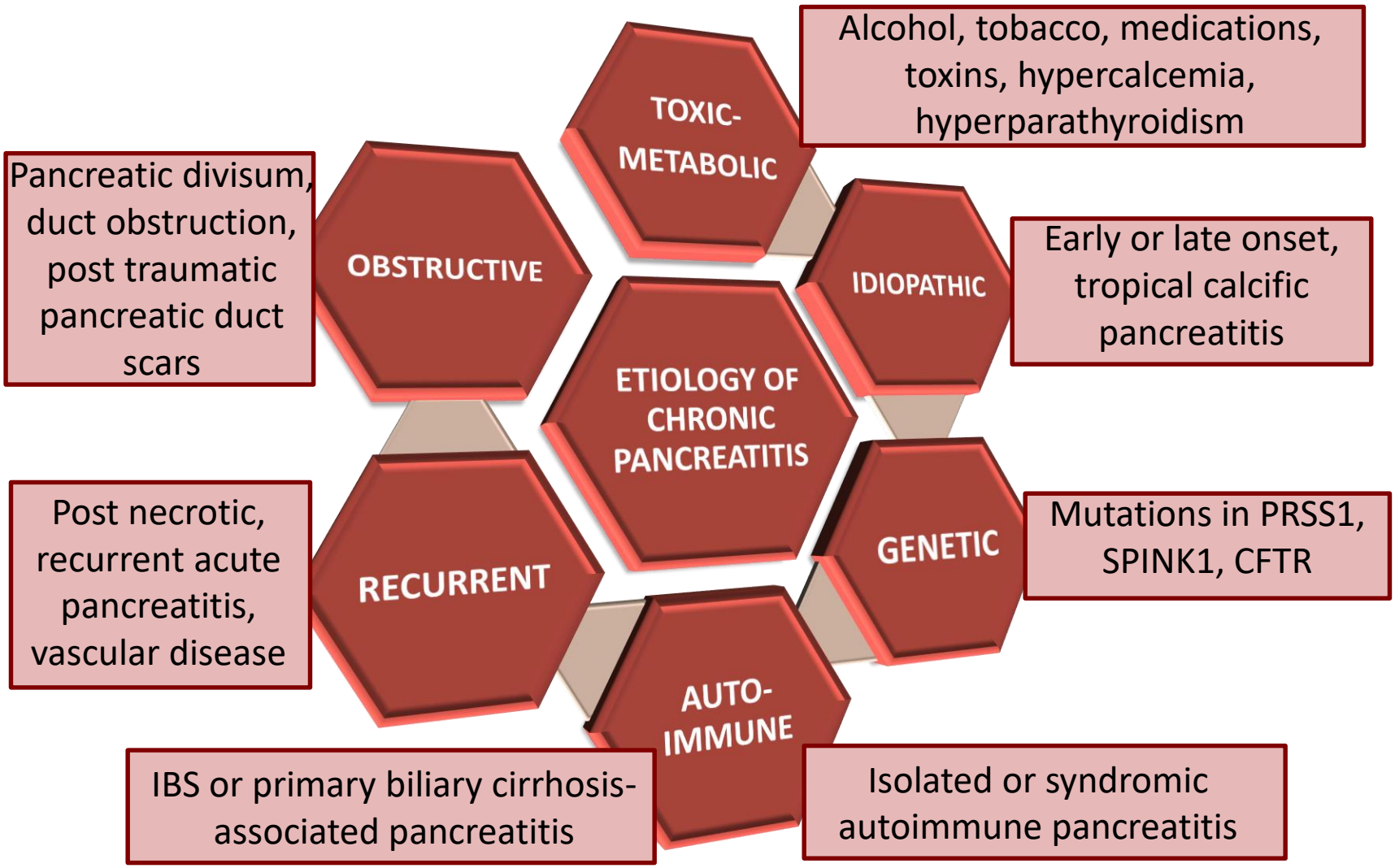
Chronic Pancreatitis - Demographics

- Incidence
  - Because of its varied presentation and clinical similarity to acute pancreatitis, the true global prevalence is unknown
  - In Europe (EUROPAC Study) the prevalence has been evaluated to be 1 in 300-800,000
  - Estimated 12 cases per 100,000 women and 45 cases per 100,000 men
  - The average age at diagnosis is 35 to 55 years

Chronic Pancreatitis - Demographics

- Etiology
  - Chronic alcohol use accounts for 70%
  - Idiopathic factors – 20%
  - Genetic Factors – 1-2%
  - Autoimmune pancreatitis – 5-6%
  - The TIGAR-O (Toxic-metabolic, Idiopathic, Genetic, Autoimmune, Recurrent and severe acute pancreatitis, Obstructive) classification system is based on risk factors for chronic pancreatitis

TIGAR-O Classification



Hereditary Chronic Pancreatitis

- HP or HCP [OMIM #167800]
  - Autosomal dominant or recessive pattern of inheritance
  - High penetrance
  - Causes chronic pancreatitis in both children and adults
  - Patients with HCP are at a higher risk for pancreatic cancer
  - Great example of locus heterogeneity

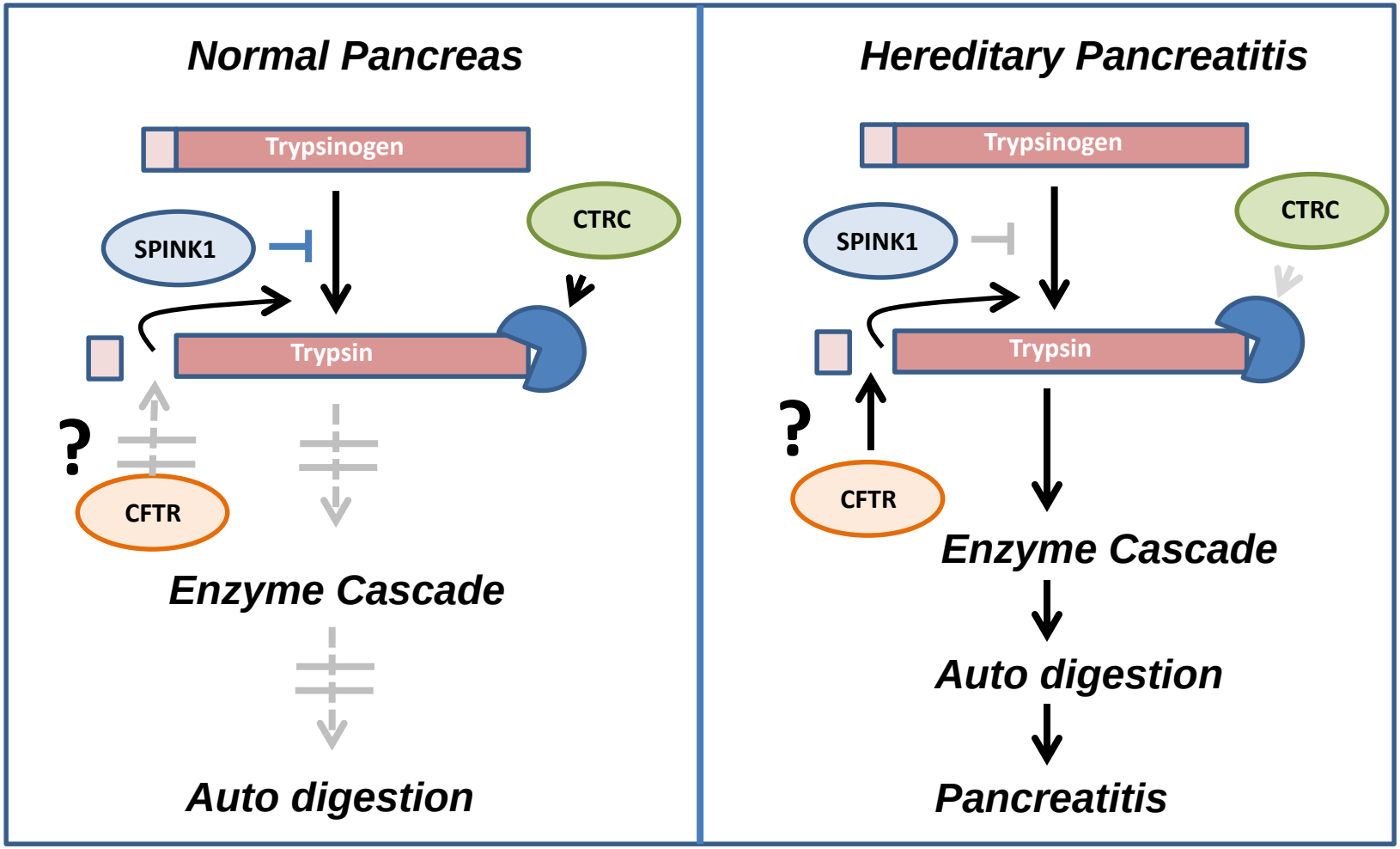
HP – Clinical Considerations

- Primary manifestations are:
  - abdominal pain
  - maldigestion due to pancreatic exocrine dysfunction, and
  - diabetes mellitus due to islet cell damage
- Median ages of first symptoms and diagnosis is about 10yrs and 19yrs, respectively
- HP is associated with a markedly increased risk for pancreatic cancer

Genes involved in HP

- Mutations in 4 genes are known to be involved
  - Cationic trypsinogen gene (*PRSS1*)
    - Located on 7q34, accounts for 52-81% of cases
  - Serine protease inhibitor Kazal type 1/Pancreatic secretory trypsin inhibitor (*SPINK1/PSTI*)
    - Located on 5q32, accounts for 50% of cases
  - Cystic fibrosis transmembrane conductance regulator (*CFTR*)
    - Located on 7q31; accounts for 20-55% of cases
  - Chymotrypsin C (*CTRC*)
    - Located on 1p36 ; acts as a modifier gene

Model of Inherited Pancreatitis



Modified from Rosendahl J, Bödeker H, Mössner J, Teich N. Hereditary chronic pancreatitis. Orphanet Journal of Rare Diseases 2007;2:1 (BioMed Central Open Access).

Testing for HP

- Indications for testing for PRSS1 or SPINK1 mutations in asymptomatic patients should be one of the following:
  - Recurrent unexplained attacks of acute pancreatitis and a positive family history
  - Unexplained chronic pancreatitis and a positive family history
  - Unexplained chronic pancreatitis without a positive family history
  - Unexplained pancreatitis episode in children

Differential diagnosis for HP

- CYSTIC FIBROSIS
  - ~70-80% of CF patients have pancreatic insufficiency
- ANATOMIC ANOMALIES, metabolic disorders, trauma and inflammatory bowel disease (IBS)
- Other rare differential diagnoses include:
  - hyperlipidaemia type I
  - familiar (hypocalciuric) hypercalcaemia (FBH)
  - hereditary hyperparathyroidism and
  - autoimmune pancreatitis (adult-hood)

Treatment and Management of HP

- Primarily management of symptoms
  - Pain control (analgesics)
  - Pancreatic enzyme supplement to suppress pancreatic exocrine secretion.
  - Cessation of alcohol intake and smoking.
  - Eat small meals that are low in fat.
  - Surgery may be indicated for patients who fail first line of therapy (as mentioned above) or if there is a suspicion of pancreatic cancer.

References

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Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

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