Faculty/Presenter Disclosure

- **Faculty:** Dr Quais Mujawar
- Pediatric Gastroenterologist | HSC Winnipeg
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- **Relationships with commercial interests:**
  - **Grants/Research Support: CHRIM**
  - **Speakers Bureau/Honoraria:** None
  - **Consulting Fees:** Alexion Pharma Inc , Wilsons Disease Honorary Board
  - **Other:** Employee of Childrens Hospital ,WRHA Winnipeg , Asst Prof, Univ of Manitoba

Disclosure of Commercial Support

- **This program has NOT received financial support**
- **This program has NOT received in-kind support**
- **<u>Potential for conflict(s) of interest</u>:**
  - NONE FOR THIS PARTICULAR PRESENTATION BUT DR Mujawar is on Advosry Board for Alexion Pharma .

This slide is to be presented by the moderator/chair at the opening of the event, disclosing any commercial support, etc. for the event.

Mitigating Potential Bias

- This presentation is on pancreatitis and I shall not be discussing Wilsons Disease or its treatment options .

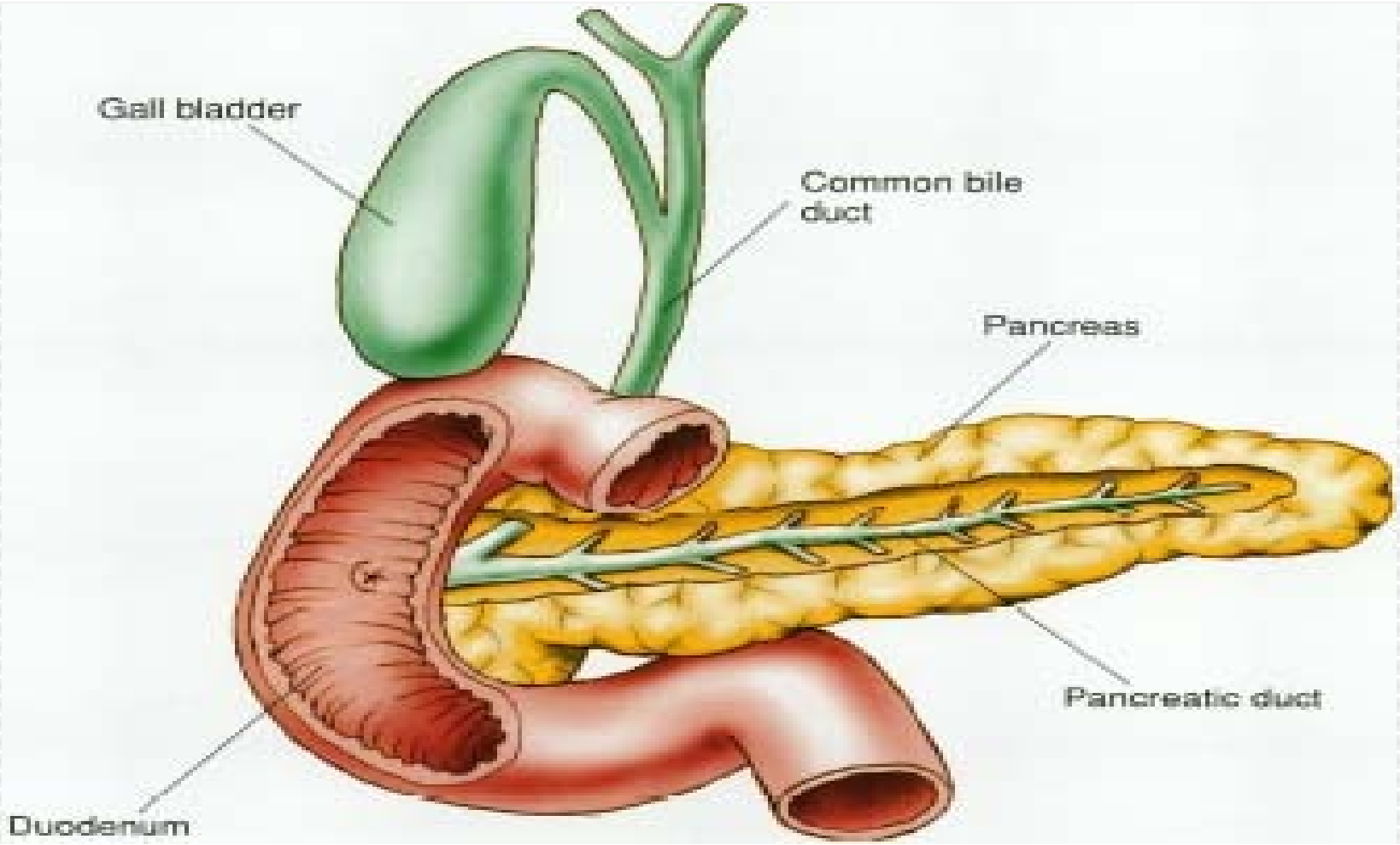
PANCREATITIS IN CHILDREN

Dr Quais Mujawar

Pediatric Gastroenterologist

Winnipeg Children's Hospital

Anatomy


Gall bladder
Common bile duct
Pancreas
Pancreatic duct
Duodenum

Objectives

- 1. Know how to diagnose acute pancreatitis.
- 2. Differentiate b/w acute and chronic pancreatitis.
- 3. List common causes for acute, recurrent, and chronic pancreatitis.
- 4. Explain the utility of clinical symptoms, biochemical testing, and radiographic imaging in diagnosing acute and chronic pancreatitis.
- 5. Understand the management of acute pancreatitis and chronic pancreatitis

What is Pancreatitis

- It is a primary necro-inflammatory process derived from auto-necrosis of pancreatic tissue due to abnormal activation of proteolytic and lipolytic enzymes within the pancreatic parenchyma

Categories of Pancreatitis

- 1. Acute pancreatitis, with histological resolution after full clinical recovery
- 2. Acute recurrent pancreatitis (ARP)
- 3. Chronic Pancreatitis, leading to irreversible inflammatory fibrosis.

Types

Acute	Chronic
• Reversible	• Irreversible
• More Prevalent	• Less Prevalent
• No Definitive Changes	• Definitive Changes in Pancreas on Imaging

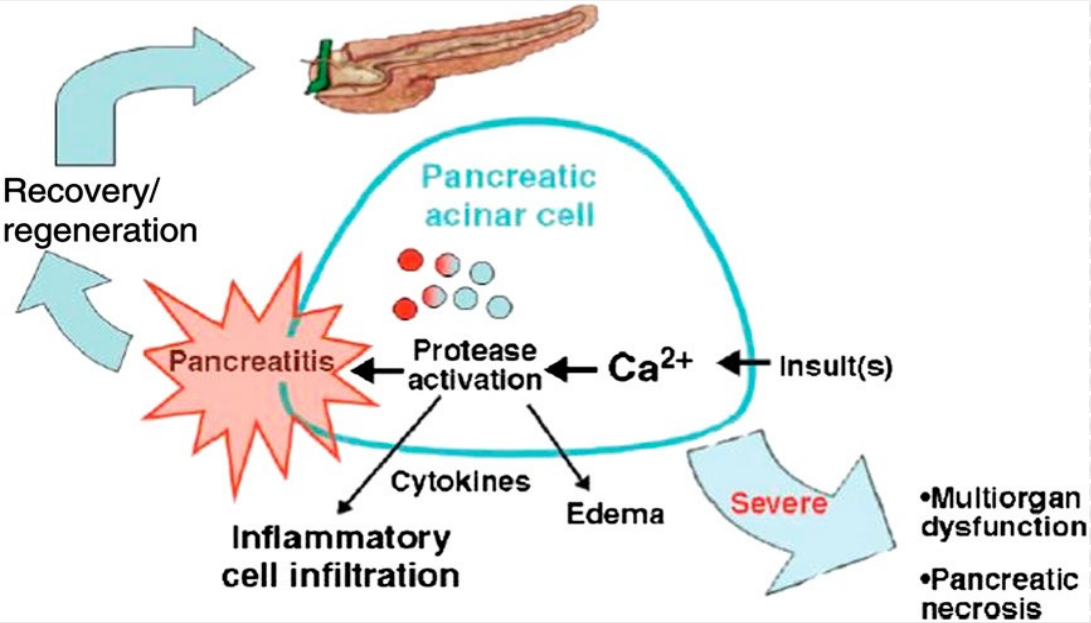
Acute Pancreatitis in Pediatrics

Epidemiology

- Recent studies from the United States, Mexico, and Australia have reported an increasing incidence over the past 2 decades
- Estimates suggest 3.6 to 13.2 cases per 100,000 individuals per year,
- Approaches the incidence of disease in adults.
- ? ?Increased physician awareness / Increased testing of amylase and lipase.

Morinville VD, Barmada MM, Lowe ME. Increasing incidence of acute pancreatitis at an American pediatric tertiary care center: is greater awareness among physicians responsible? Pancreas. 2010;39 (1):5–8

Pathophysiology



Trypsinogen

↓

Trypsin

↓

Intracellular activation of proenzymes

↓

Autodigestion

Multiple causes of acute pancreatitis can lead to abnormal intra-acinii calcium signaling. This signaling leads to intra-acinar zymogen activation and resulting pancreatic injury and cytokine response, as well as potential SIRS

Bai HX, Lowe ME, Husain SZ. What have we learned about acute pancreatitis in children? J Pediatr Gastroenterol Nutr. 2011; 52(3):262–270

Pancreatitis in Children

Common

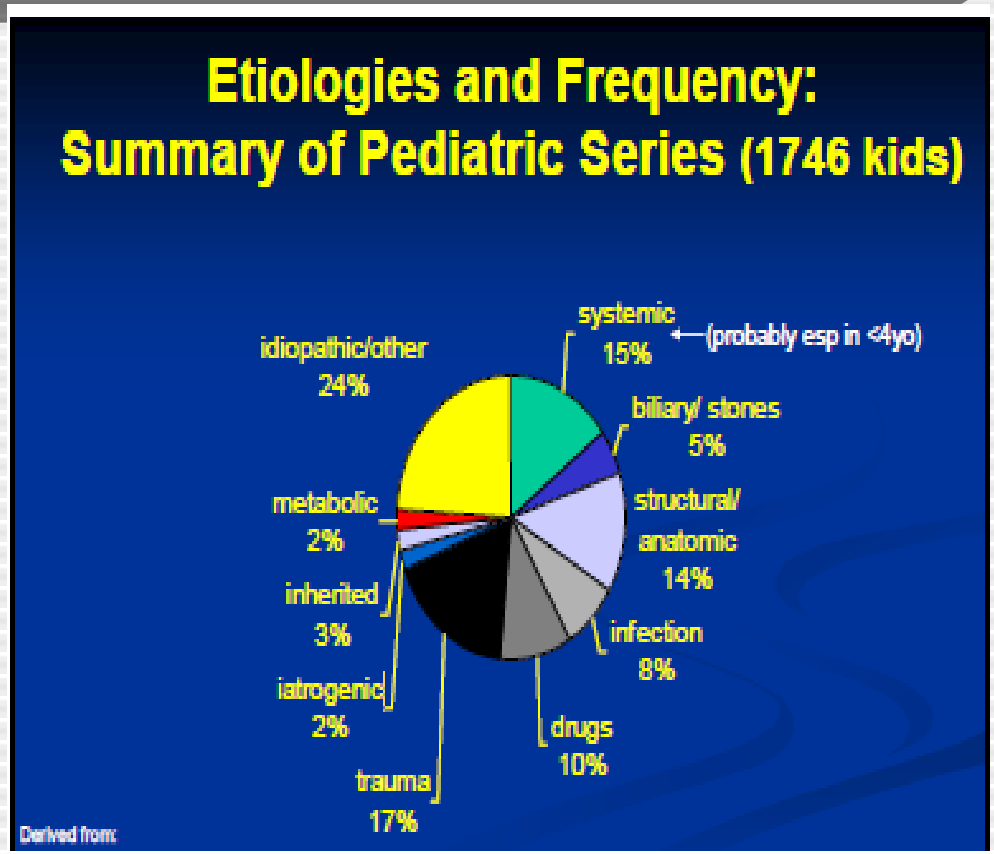
- Biliary Causes
- Medications
- Idiopathic
- Systemic
- Trauma

Less common

- Infection
- Metabolic diseases
- Genetic/hereditary disorders

Rare

- Autoimmune pancreatitis
- Anatomic pancreaticobiliary abnormalities



Biliary Causes

- Major etiology
- Biliary causes in 33% of causes
- (Gallstones, microlithiasis, structural, pancreas divisum, and Sphincter of Oddi dysfunction)
- Gallstone pancreatitis or other biliary disease should be suspected if the patient has elevations in transaminase levels and/or hyperbilirubinemia.

Park A, Latif SU, Shah AU, et al. Changing referral trends of acute pancreatitis in children: a 12-year single-center analysis. J Pediatr Gastroenterol Nutr 2009;49:316–22.

Medications

- Medications (26%)
- (Valproic acid, prednisone, mesalamine, trimethoprim/sulfamethoxazole, 6-MP/Azathioprine, L-asparaginase, furosemide, Tacrolimus, and antiretrovirals)

Park A, Latif SU, Shah AU, et al. Changing referral trends of acute pancreatitis in children: a 12-year single-center analysis. J Pediatr Gastroenterol Nutr 2009;49:316–22.

Idiopathic

- Still significant subfraction (20%) despite significant advances in diagnostics and imaging
- ? Incomplete investigation

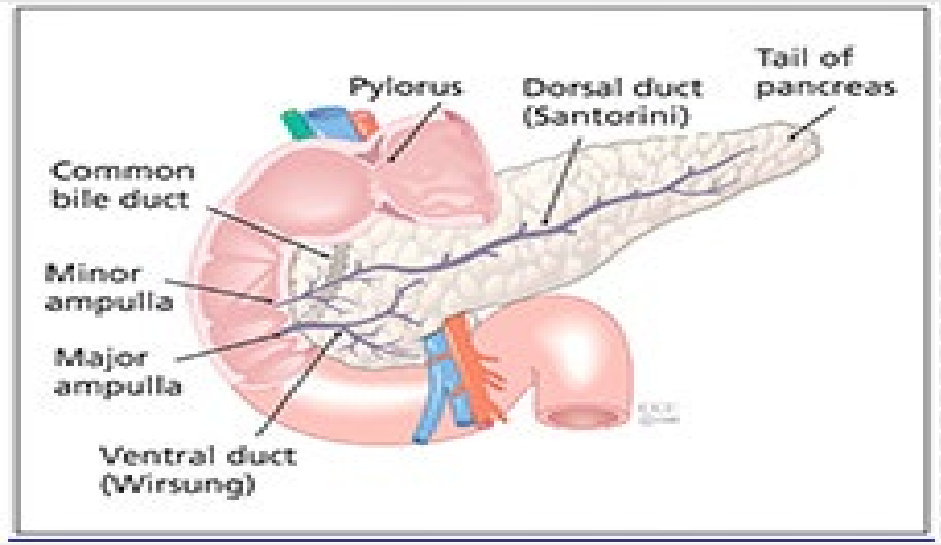
Lautz TB, Chin AC, Radhakrishnan J. Acute pancreatitis in children: spectrum of disease and predictors of severity. J Pediatr Surg. 2011;46(6):1144–1149

Other Causes

- Trauma in 9%,
- Viral infection in 8%,
- Metabolic conditions in 5% (DKA, Trigs(**>10mmol/L)** , IEMS, and hypercalcemia)
- ERCP 4%
- CF in 2%,
- Alcohol in 1%
- Genetic/Hereditary
- Autoimmune pancreatitis

Pancreatic Divisum

- Failure of the ventral and dorsal pancreatic ducts to merge, termed pancreas divisum
- Affects 5% to 10% of the population
- With other genetic factors,can predispose to pancreatitis
- Rx – Endotherapy



Diagnosis

- Mild/ Severe
- 2/3 Criteria

  - Abdominal pain s/o or compatible with acute pancreatitis (80-95%)

  - Amylase/Lipase >3X ULN (look for other causes ?)

  -Imaging findings compatible with diagnosis

Morinville VD, Husain SZ, Bai H, et al. Definitions of pediatric pancreatitis and survey of present clinical practices. J Pediatr GastroenterolNutr 2012;55:261–5.

Imaging

- USG (Stones ,can be obscured by bowel gas)
- CE CT (Useful to see pancreatic necrosis)
- MRCP (++cholelithiais,anatomic+ducts)
- EUS (++cholelithiais,Anatomic+ducts)

Question ??

- Are all Lipase/ Amylase elevations Pancreatitis ??

Table 2. Pediatric Conditions Associated With Elevation of Amylase or Lipase Levels

Condition	Amylase	Lipase
Abdominal	• Acute pancreatitis • Biliary tract disease • Intestinal obstruction/ischemia • Mesenteric infarction • Peptic ulcer • Appendicitis • Ruptured ectopic pregnancy • Ovarian neoplasm	• Nonpancreatic abdominal pain • Acute cholecystitis • Esophagitis • Intestinal obstruction/ischemia • Peptic ulcer
Salivary gland	• Trauma • Infection (ie, mumps) • Sialolithiasis • Irradiation	
Thoracic	• Pneumonia • Pulmonary embolism • Myocardial infarction • Cardiopulmonary bypass	
Infectious	• Viral gastroenteritis • Pelvic inflammatory disease	• Human immunodeficiency virus infection
Metabolic	• Diabetic ketoacidosis • Pheochromocytoma	• Diabetic ketoacidosis • Hypertriglyceridemia
Neoplastic	• Ovarian, lung, esophageal, or thymic tumors	
Drugs	• Opiates	
Trauma	• Cerebral trauma • Burns	
Renal	• Renal insufficiency • Renal transplantation	• Renal insufficiency
Inflammatory	• Macroamylasemia • Celiac disease	• Macrolipasemia • Celiac disease
Miscellaneous	• Cystic fibrosis • Acute liver failure • Viral gastroenteritis • Pregnancy • Eating disorders: anorexia, bulimia	

Management

- Identify treatable causes of acute pancreatitis
- Pancreatic rest (No enteral feeding)
- Antiemetics
- Analgesia (can use Opiods)
- Fluid support
- Monitoring for complications.

Pancreatic Rest

- *Early institution of nutrition*. Mild acute pancreatitis, oral feedings within 24 to 48 hours after admission
- ?? Liquid diet –not indicated
- ?? Low fat diet → controversial
- 10% pain –wait 24 hrs→restart feeds

Pancreatic Rest

- Don’t stop feeds if increase in enzymes
- Enteral feeding is preferred over TPN
- NJ vs G tube , Type of formula →instituitonal preference
- TPN only if ileus ,pancreatic fistulae and abd compartment syndrome

Fluids

- Keep Well Hydrated
- 1.5 times maintenance
- Limited adult data suggest that aggressive hydration in the first 24 hours decreases the risk of multiorgan system failure.

Nasr JY, Papachristou GI. Early fluid resuscitation in acute pancreatitis: a lot more than just fluids. Clin Gastroenterol Hepatol. 2011;9(8):633–634

Complications

- Ileus
- Pancreatic edema
- Pancreatic necrosis
- Pancreatic abscess
- Fat necrosis pancreatic hemorrhage
- ***Pancreatic pseudocyst***
- Pancreatic duct rupture
- Pancreatic duct stricture
- Thrombosis of adjacent blood vessels

Complications

- Shock
- Sepsis
- Hypermetabolic state
- Hypocalcemia
- Hyperglycemia
- Vascular leak syndrome
- Multiorgan system failure
- Disseminated intravascular coagulation
- Pleural effusions
- Acute renal failure
- Splenic artery pseudoaneurysm

Complications

- Pseudocysts → typically resolve over 8-12 weeks ,but may require surgical/IR drainage if duct block, bores into vessels, chances of rupture
- Pancreatic Insufficency → if severe pancreatitis and s/o pancreatic necrosis
- Don't forget Endocrine function of Pancreas

Outcome

- No mortality unless underlying chronic systemic disorders present
- Does not correlate to initial levels of Enzymes

Acute Recurrent Pancreatitis

Acute Recurrent Pancreatitis

- *> 2 episodes / year or >3/year in lifetime in a patient without Chronic Pancreatitis*
- *About 10-35% will have recurrence*
- *Pathophysiolology same ??? Genetic Predisposition*
- *Can progress to Chronic Pancreatitis*

Etiology ARP/CP

- Biliary calculi
- Congenital (Choledochal cyst,APB J, Panc Divisum, Annular Pancreas)
- Genetic (SPINK,CFTR,PRSS-1)
- Duodenal inflammation (Celiac , Crohns , Infections)
- Medications
- Sphincter of Oddi dysfunction
- Metabolic (Calcium, Hypertriglyceridemia)
- Intestinal duplication cyst
- Autoimmune (Pancreatic,Systemic)
- Idiopathic

ARP Management

- Diagnostic criteria & Rx for ARP episode similar to Acute Pancreatitis
- Screen for hereditary conditions (Genetics)
- Ultrasound if not prev for dupl cysts
- MRCP
- ERCP in select kids
- Screen for Crohns & Systemic Infl disease
- Sweat Test
- Autoimmune Pancreatitis (IgG4)

Etiology

- Biliary calculi
- Congenital pancreaticobiliary abnormalities
- Genetic
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- Intestinal duplication cyst
- Autoimmune(IgG4 levels)
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Chronic Pancreatitis

Chronic Pancreatitis

- CP is defined as a process leading to irreversible destruction of the pancreatic parenchyma and ducts and loss of exocrine function.
- Many have underlying ARP
- ARP progresses to → CP (try to halt progression)

Pathophysiology/Diagnosis

- Long standing Inflammation
- Acute Pancreatitis → Chronic in susceptible individuals
- Clinical Diagnosis → Episodic Pain / malabsorption / Diabetes develops late
- Imaging Tests → CT,MRCP ,ERCP & EUS
- Pancreatic Function Tests

Clinical Features

- Recurrent Episodes of Pancreatitis
- Mild to intense abdominal pain, usually epigastric.
- Malabsorption , weight loss
- Steatorhhea ,
- Rarely Jaundice due to ductal obstruction
- Diabetes almost never in Pediatrics

Imaging

- CT, MRCP, ERCP, and EUS ?? All helpful

- **MRCP preferred**
- **ERCP** → better for ductal anatomy
- **CT** → calcifications,gland atrophy but not helpful in subtle changes

Pancreatic Function Tests

- Duodenal intubation with secretin cholecystokinin stimulation→ Gold Std
- Not easily available
- Fecal Elastase (useful even in PERT therapy)
- Poor sensitivity in mild to mod PI
- Less sensitive in diarrhea (false +ve)

Management

- Stage and Etiology (AP, ARP , CP)
- Pain Management (NSAIDS, Opiods , PERT ,Antioxidants)

- Endoscopic Stent /Sphincterectomy
- Surgical Resection
- Total pancreatectomy with islet cell autotransplant (Genetic Causes)
- Pancreatic enzyme replacement therapy

Complications

- Pain of CP does not “burn out.”
- Diabetes may take 2 or 3 decades to become clinically significant
- Pancreatic cancer is a long-term risk for all pediatric patients who have CP (0.5%) (4th decade)

Autoimmune Pancreatitis

Autoimmune Pancreatitis

- Sx: AP; obstructive jaundice
- Imaging: diffuse enlargement; diffuse irreg narrow PD ,sausage shaped pancreas
- Labs: ↑ IgG4; autoAbs
- +/- assoc with autoimmune disorders: PSC; Sjogren's; thyroid
- Path: lymphoplasmocytic infiltrate + pericanalicular fibrosis

Autoimmune Pancreatitis

- **Published pediatric cases AIP:**
- -Not ANY totally fulfill ADULT criteria
- -None ↑ IgG4; no autoimmunity
- -but all responded to **prednisone**
- ?A *somewhat different entity than Adult AIP?*
- -Refaat 2009. 11yo M; MR and laparotomy
- -Gargouri 2009. 10yo M. MRI not dx; ERCP dx
- -Blejter 2008. 16yo M. US/ MRCP/ laparoscopy

Summary

- Prevalence of acute pancreatitis is increasing
- An elevated amylase or lipase level in the absence of clinical symptoms or radiologic findings is not diagnostic of pancreatitis.
- Successful early feeding possible in treating acute pancreatitis .
- Low-fat diet or bypass of the ampulla of Vater is not necessary in mild cases .
- Chronic pancreatitis is a specific diagnosis characterized by irreversible pancreatic changes and can be diagnosed only via radiologic and biochemical evidence, in addition to clinical features

References

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- Sugumar A, Chari ST. Autoimmune pancreatitis. J Gastroenterol Hepatol. 2011;26(9):1368–1373
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Take Home

- **First episode?**
  - Review History, Meds, Family!
  - Discontinue any meds you can that could be culprit
  - Basic metabolic workup including triglycerides, calcium
  - Imaging: U/S, +/- CT (severe!); (MRI/ MRCP)
  - Keep in mind Biliary Causes – may need an intervention
- **Recurrent? (*or severe, prolonged, "idiopathic" 1st episode)**
  - Consider genetic workup (esp. CFTR/ sweat)
  - Consider more complete imaging

QUESTIONS ??

Thank You