Pancreatitis in Childhood: An Update

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I have nothing to disclose that would create a conflict of interest.
Definitions

• **Acute pancreatitis** is a reversible, inflammatory disease of the pancreas
  – Subpopulation have recurrent episodes

• **Chronic pancreatitis** is a destructive, inflammatory condition that irreversibly damages the pancreas.

Thus, **acute pancreatitis** is an event whereas **chronic pancreatitis** is a process.
The Incidence of Acute Pancreatitis has Increased in Childhood

- First reported by Lopez in a single institution study
- Subsequently confirmed in reports from other centers in the USA and Australia
Incidence of Childhood Pancreatitis

CHP 1991-2004

NUMBER OF PATIENTS

YEAR

0 50 100 150

1991 1993 1995 1997 1999 2001 2003

All Cases New Cases
Incidence Estimates at CHP
First Known AP Admission

YEAR

NUMBER/100,000
0 2 4 6 8 10 12 14

CATCHMENT POPULATION

Catchment Incidence

Red: Catchment  Black: Incidence
Is Incidence Really Increasing?

Not in Western PA. It’s Increased Awareness!
Etiology of Acute Pancreatitis

CHP and Literature

![Bar chart showing the comparison between CHP and literature for different etiologies of acute pancreatitis.](chart.png)
Variation with Age
CHW 1996-2001

Number of Patients vs. Age (years)

Age (years):
- <1
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18

Number of Patients:
- 1
- 3
- 6
- 9
- 12
- 15
- 18
- 21
- 24
- 27
- 30
- 33
- 36
- 39
- 42
- 45
- 48
- 51
- 54

The number of patients varies significantly with age, with the highest number of patients in the age group 5 years.
Pancreatitis is a Clinical Diagnosis

• Need 2 out 3
  – Compatible history and symptoms
  – Amylase or lipase >3 x URL
  – Radiographic evidence
Clinical Presentation Varies by Age

<table>
<thead>
<tr>
<th>Children</th>
<th>Infants and Toddlers</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vomiting</td>
<td>• Vomiting 52%</td>
</tr>
<tr>
<td>• Abdominal pain 70%</td>
<td>• Fever 43%</td>
</tr>
<tr>
<td>• Back pain 8%</td>
<td>• Irritability 43%</td>
</tr>
<tr>
<td></td>
<td>• Abdominal Pain 33%</td>
</tr>
<tr>
<td></td>
<td>• Distended Abdomen 16%</td>
</tr>
</tbody>
</table>
Amylase and Lipase?
Should you do both?

• Majority of studies conclude that amylase improves the specificity of lipase

• Results in 369 pediatric patients
  – 93 had abnormal lipase alone
  – 19 had abnormal amylase alone
  – 257 had both
Radiographic Studies

- Ultrasound
- CT scan
- Magnetic resonance cholangiopancreatography (MRCP)
- Endoscopic retrograde cholangiopancreatography (ERCP)
Treatment of Acute Pancreatitis

- IV hydration at presentation
- Pain control
- Monitor for complications
- Nutrition support
Pancreatic Rest as Therapy

Dogma

Rest the inflamed pancreas.
Is Pancreatic Rest Important?

Fasting versus Oral Feeding

- Sixty patients with mild pancreatitis randomized to immediate oral feeding or fasting

- Two groups did not differ by clinical criteria at admission

- No differences in amylase, CRP, abdominal pain or number of GI symptoms during study
  - Oral feeding was safe and well-tolerated

- The length of hospital stay was shorter in the oral feeding group.
  - Oral feeding may be beneficial

Is Pancreatic Rest Important?

**Enteral Versus Parenteral Nutrition**

- Eight separate, randomized studies reached similar conclusions
  - Enteral nutrition is associated with
    - Reduced mortality
    - Fewer episodes of multiple organ failure
    - Fewer infections
    - Fewer surgical interventions
    - Lower cost

- Resting the pancreas with parenteral nutrition did not improve outcomes
Is Pancreatic Rest Important?

Jejunal Feeds Decrease Pancreatic Secretion

Fig. 9: Relationship between Pancreatic Trypsin Secretory Response and Distance of Feeding down the Jejunum

Regression Plot

Y = 355.934 - 3.111 * X; R^2 = .309

Kaushik et al Pancreas 2005

- Trypsin
- Amylase
- Lipase

Duodenal
Mid-Jejunal
Randomized Trial of NG versus NJ

- NG 27 patients; NJ 22 patients
  - Location of NJ not given: “proximal jejunum”
- Low fat “semi-elemental” formula
- Severe pancreatitis by Glasgow and APACHE II scores
- No difference
  - Length of hospital stay
  - Length of stay in ICU
  - Mortality
  - Pain score or analgesia use
Other Trials of NG versus NJ

• Kumar et. al., J Clin Gastroenterol, 2006
• Piciucchi et. al., World J Gastroenterol, 2010
  – Both found no difference in outcomes
• Chang et. al. Crit. Care, 2013
  – Metanalysis
  – No difference in outcomes

• Issues
  – Small numbers
  – Patient selection varies
  – Placement of tubes is not always documented

• Currently, a randomized, multi-center, NIH-funded study of NG versus NJ in patients with severe acute pancreatitis is in progress.
When to Feed?

• Standard practice has been to wait 2-3 days with mild pancreatitis. Longer with severe pancreatitis

• Recent study compared patients
  – who were fed when they said they were ready
  – who were fed when the serum lipase was below 2x URL.
Optimal timing of Oral Refeeding

• Randomized 143 patients with mild pancreatitis to lipase directed or patient directed feeding

• Time from admission to feeding
  – Patient selected: 2 days (1-3 days)
  – Lipase selected: 3 days (2-4 days)

• Findings
  – No difference in postprandial pain
  – No difference in LOS
  – Time to reach full calories was not different

Tiech et. al. Pancreas 2010
How to Start Feeding?

Dogma

Start with clear liquids.
Patients With Mild Pancreatitis Can Be Fed Solid Diet

  - Prospective, randomized trial of clear liquids versus a low-fat solid diet as the initial meal in mild acute pancreatitis.
  - Randomized 65 to clears and 55 to solids

- **Moraes et. al., J Clin Gastroenterol, 2010**
  - Prospective, randomized trial of clear liquids versus soft diet versus full solid diet
  - Randomized 70 patients to each meal

- **In both studies**
  - Medical team determined when to start feeds
  - Standard meals provided
  - Decisions about advancing diet and discharge made by medical team
Findings

• No difference in pain relapse among the groups

• LOS the same in the first study, shorter for group receiving full solid diet in the second study

• Patients in the solid group consumed more calories and dietary fat

• Readmission rates similar for all groups
What to feed?

Dogma

Low-fat diet is preferred.
Fat or Lean?

• No direct data

• Two arguments for low fat
  1. Fatty acid-stimulated CCK release increases pancreatic inflammation
  2. High concentrations of serum lipids may cause pancreatic damage
Serum Lipids

- Elevated serum triglycerides associate with pancreatitis
  - Levels above 1000 mg/dl
    - Local hydrolysis of triglycerides in the pancreas may cause local toxicity to capillary membranes
    - High fatty acids may increase incidence of micro-thrombi leading to additional ischemic injury
  - No evidence that post-prandial rise of TG exacerbates pancreatitis
  - Intralipid infusion does not exacerbate pancreatitis
CCK Argument

Premise

- CCK stimulates pancreatic secretions

Premise

- Pancreatic stimulation exacerbates pancreatitis

Premise

- Dietary fat increases CCK secretion

Conclusion

- Patients with pancreatitis should be fed a low fat diet.
Is Fat the Only Worry?

CCK Stimulation

Meal Composition

Gallbladder Contraction (%)
Low Fat Diet

• The use of a low fat diet is based on “expert” opinion
  – If you say it often and loudly, it becomes true

• Does not make physiological sense

• Has not been directly tested
  – The little available data suggests it does not alter the course of pancreatitis
Summary of Care in Acute Pancreatitis

- Fluid Resuscitation
- Pain control
- Nutrition
  - Start within 24-48 hours
    - No clinical parameters predict who will have increased pain
  - Oral feeding with solid diet in mild pancreatitis
  - Tube feeding with severe pancreatitis
    - NG versus NJ is still unclear
    - Parenteral nutrition already started?
  - Diet in severe pancreatitis
    - Moderate fat
Acute Recurrent and Chronic Pancreatitis

Trigger for Acute Pancreatitis

Normal Pancreas

• Chronic pain
• Pancreatic Insufficiency
• Diabetes

Chronic Pancreatitis
• Very little information in the literature
  – Few studies
  – Small sample sizes

• **INSPPIRE** (International **Study Group of Pediatric Pancreatitis: In search for a cu**RE)** was created with the following objectives:
  – To better understand the epidemiology, etiologies, pathogenesis, natural history and outcome of pediatric pancreatitis.
  – To create a network of pediatric centers to engage in prospective studies and analyses of children with these disorders.
INSPPIRE Centers

• USA
  – Univ of Iowa (CC)
  – Univ of Pittsburgh
  – UT Southwestern
  – Baylor Texas Children’s
  – Nationwide Children’s
  – Medical College of Wisconsin
  – Univ of Minnesota
  – UCSF
  – University of Utah
  – Seattle Children’s

• Canada
  – Toronto Hospital for Sick Children
  – Montreal Children’s

• Israel
  – Hadassah Medical Organization, Jerusalem

• Australia
  – UNSW, Sydney
• September 2012-February 2014.

• 233 patients <19 y/o enrolled
  – 57% with ARP and 43% with CP
  – Data collected: demographics, past medical history, family and social history, medications, hospitalizations, risk factors, diagnostic work-up, treatments and outcome information.
Demographics

ARP and CP (233 Pt)

Age: 12.1 ± 4.6

Gender

Female: 44%
Male: 56%

CP (76 PT)

Age: Mean=13.0; Median=10.5; IQR=17.0

Gender

Female: 43%
Male: 57%
Demographics

ARP and CP (233 Pt)

CP (76 Pt)
Etiology of ARP and CP

ARP and CP (233 Pt)

- Genetic: 41%
- Obstructive: 28%
- Toxic/metabolic: 16%
- Autoimmune: 13%
- Unknown: 2%

CP (76 Pt)

- Genetic: 54%
- Obstructive: 26%
- Toxic/metabolic: 8%
- Autoimmune: 9%
- Unknown: 3%
Genetics of ARP and CP

ARP and CP (115 Pt)
- PRSS1: 42%
- CFTR: 29%
- SPINK1: 25%
- CTRC: 4%

CP (51 Pt)
- PRSS1: 55%
- CFTR: 23%
- SPINK1: 18%
- CTRC: 4%
Obstructive Etiologies

ARP and CP (80 Pt)
- Pancreas Divisum: 49%
- Gallstones: 21%
- SOD: 6%
- Pancreatic duct malunion: 6%
- Other: 18%

CP (76 Pt)
- Pancreas Divisum: 56%
- Gallstones: 22%
- SOD: 4%
- Pancreatic duct malunion: 7%
- Other: 11%
Toxic/metabolic Etiologies

**ARP and CP (37 Pt)**
- Alcohol: 14%
- Cigarette Smoke: 16%
- Hyperlipidemia: 11%
- Medications: 8%
- Metabolic Disease: 16%
- Other: 35%

**CP (8 Pt)**
- Alcohol: 20%
- Cigarette Smoke: 7%
- Hyperlipidemia: 7%
- Medications: 53%
- Metabolic Disease: 7%
- Other: 7%
Disease Burden

- Median of 5 pancreatitis episodes per patient
- Median of 6 hospitalizations lifelong
- Pancreatitis interferes with enjoyment of life very much in 30%
- Patients miss an average of 5.4 school days a month
- 63% of patients with CP have surgery
Conclusion

• Children have ARP and CP
• Unlike in adults, genetic and obstructive etiologies are the predominant causes of ARP and CP in children.
• ARP and CP significantly impact the lives of affected children.
• Novel approaches to treating ARP and CP are needed.
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