Gastroesophageal Reflux - A Brief but Probing Inquiry

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Pathologic Gastroesophageal Reflux

- **quantitative definition**
  » 2 standard deviations beyond the mean (i.e. 2.5% of the population)

- **qualitative definition**
  » unusual or excessive symptoms related to esophageal acid exposure
Symptoms Attributed to GE Reflux in Infants

- regurgitation/vomiting
- feeding problems (including dysphagia)
- heartburn, chest pain, abdominal pain
- irritability, sleep disturbance
- frequent arching
- respiratory difficulties
- growth failure
- dystonic posturing (Sandifer syndrome)
Frequency of Symptoms with 511 Acid Reflux Events

- 33% no symptoms
- 67% any symptom

adapted from Jadcherla et al, Am J Gastro 2008;103:720
Temporal Association Between Symptoms and Reflux Episodes

adapted from Funderburk et al, J Ped Gastro Nutr 2016;62:556
The overwhelming majority of acidic and non-acidic reflux events are asymptomatic. The only symptom regularly associated with acidic and non-acidic reflux events is regurgitation. Fussiness, irritability, arching and feeding refusal do not clearly correspond with reflux events.
Omeprazole in Infant GER

adapted from Moore et al, J Peds 143:219, 2003
Efficacy of 4 weeks of Lansoprazole in Infants with Symptoms of GE Reflux

adapted from Orenstein et al, J Pediatr 2009;154:514
Acid Inhibition for GER in Infants

- Does not decrease the frequency or volume of vomiting/regurgitation
- Does not appear to decrease other symptoms often attributed to GE reflux
  » irritability
  » feeding refusal
  » arching
  » coughing
  » hoarseness
Do No Harm: is there a downside to acid inhibition?

- reduction of gastric acid secretion:
  - reduces the inoculum size of Salmonella sp, Listeria monocytogenes and Vibrio cholera necessary to induce disease
  - is associated with an increased risk of community acquired C. difficile disease, community acquired pneumonia and vitamin B12 deficiency in adults

Dial et al. JAMA 2005;294;2989
Laheij et al. JAMA 2004;292:1955
Valuck et al. J Clin Epidemiol 2004;57:422
Yang et al. JAMA 2006;296:2947
Do No Harm: is there a downside to acid inhibition?

- reduction of gastric acid secretion:
  - is associated with an increased incidence of community acquired pneumonia and gastroenteritis in infants and young children

Canani et al. Pediatrics 2006;117:e817
Orenstein et al, J Pediatr 2009;154:514
Do No Harm: is there a downside to acid inhibition?

- reduction of gastric acid secretion:
  - is associated with significant changes in the intestinal microbiota
    - decreased microbial diversity
    - lower abundance of gut commensals
    - increased abundance of oral commensals

Imhann et al. Gut 2016;65:740
Jackson et al. Gut 2016;65:749
Do No Harm: is there a downside to acid inhibition?

- Low microbial diversity early in life has been associated with an increased incidence of:
  - “milk protein allergy”
  - infantile colic
  - eczema
  - asthma
  - type 1 diabetes

Laursen et al. Front Micro 2017;8:356
Do No Harm: is there a downside to acid inhibition?

- Acid inhibition during pregnancy and during the first six months of life is associated with an increased incidence of allergic diseases during childhood
  
  Mitre et al. JAMA Pediatr 2018;172:e180315

- PPI usage during the first six months of life is associated with an increased incidence of bone fracture in childhood
  
  Malchodi et al. Pediatr 2019;144:e182625
Cessation of PPI therapy can precipitate symptoms of GER!

- 120 healthy adults without symptoms of GER were randomized to receive PPI or placebo for eight weeks.
  - In the 3 weeks after stopping therapy, 54% of those randomized to receive PPI had acid related symptoms as compared to 15% of those receiving placebo (p < 0.001)

Reimer et al, Gastro 2009;137:80
My Conclusions

- Gastroesophageal reflux is common in young children.
- Most children outgrow their reflux by the time they are a year of age.
- Serious complications of GE reflux are extremely rare.
- The role of GE reflux in the etiology of irritability, feeding refusal, arching, apnea, asthma and upper airway symptoms is unclear at best.
Most of the time, the best way to diagnose reflux is with a careful history and examination.

- None of the findings of commonly employed tests correlate with the severity of symptoms or predict outcome.

- An UGI is useful to define anatomy:
  - can exclude esophageal stricture, gastric outlet obstruction, malrotation, or pyloric stenosis.

- A pH/impedence study may be useful to associate unusual symptoms with reflux episodes:
  - Consider simultaneous sleep and/or video monitoring.
My Conclusions

- In children, only a few therapies for GE reflux have been proven clinically effective:
  - thickened feedings decrease vomiting and crying and prolong sleep
    - there are no clear contraindications to feeding infants solid foods at any age
My Conclusions

- Therapies that make sense but have not been proven to be *clinically* effective include:
  - avoiding "bad" positions that increase intra-abdominal pressure
  - avoiding juices, hyperosmolar fluids, and hypercaloric feedings as they empty out of the stomach slowly
My Conclusions

- Therapies that make sense but have not been proven to be *clinically* effective include:
  - assure the child isn’t constipated
    - constipation slows gastric emptying and can exacerbate or even precipitate the symptoms of GER
A Couple Final Caveats

- In neurologically normal infants
  - surgical treatment of gastroesophageal reflux is rarely warranted
  - isolated gastroesophageal reflux rarely causes growth failure
    - be sure the family is providing adequate calories
    - think about cystic fibrosis or other forms of malabsorption
    - hypertrophic pyloric stenosis develops over time
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