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Prader-Willi Syndrome Association | USA • www.pwsausa.org • (941) 312-0400

Comprehensive Review of Digestive Issues in Prader-Willi Syndrome

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Disclosures:

Research Support:
Co-investigator:
Harmony
Radius

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FPWR
NIH/NIMH

Off-label Use Of Medications

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Outline of Presentation

- Prevalence of gastrointestinal (GI) symptoms in Prader-Willi Syndrome
- Review of published clinical data, management approaches (evidenced-based and experiential in Prader-Willi syndrome)
  - Feeding/swallowing oral health
  - Gastric emptying/gastric dilation
  - Diarrhea
  - Constipation/rectal picking

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How Common Are GI-related Symptoms?

- Early feeding difficulties very common among infants with PWS
  - Major criteria for clinical diagnosis of PWS (Holm, et al., Pediatrics 1993)
- Frequent reports of reflux symptoms, and inability to vomit
  - Early deaths from aspiration (Reflux related?)
  - Significant morbidity from high pain threshold and vomiting threshold well documented

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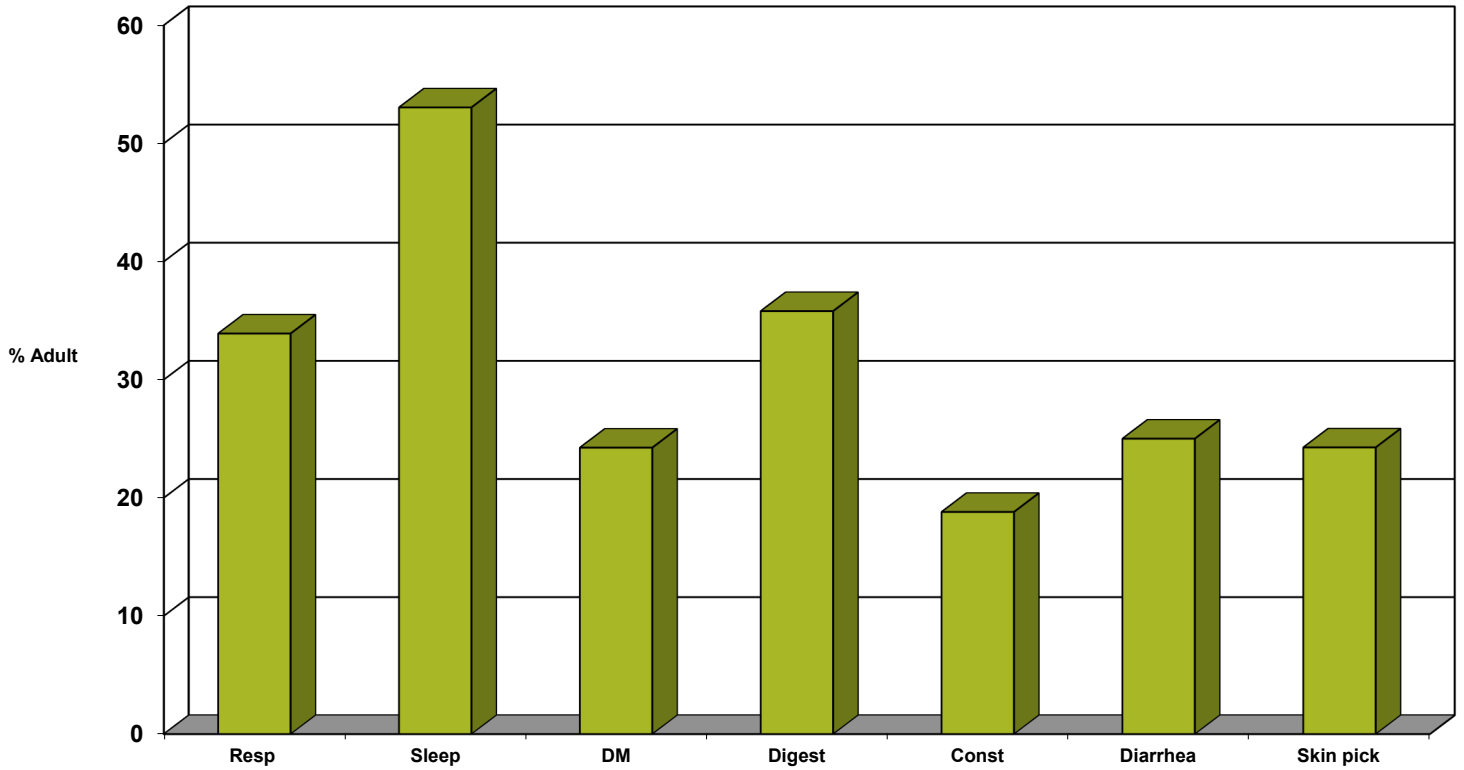
Symptom Prevalence Among Adults With Prader-Willi Syndrome



Combined data from JV Butler et al (2002), S Cassidy et al. (1995), and B. Whitman

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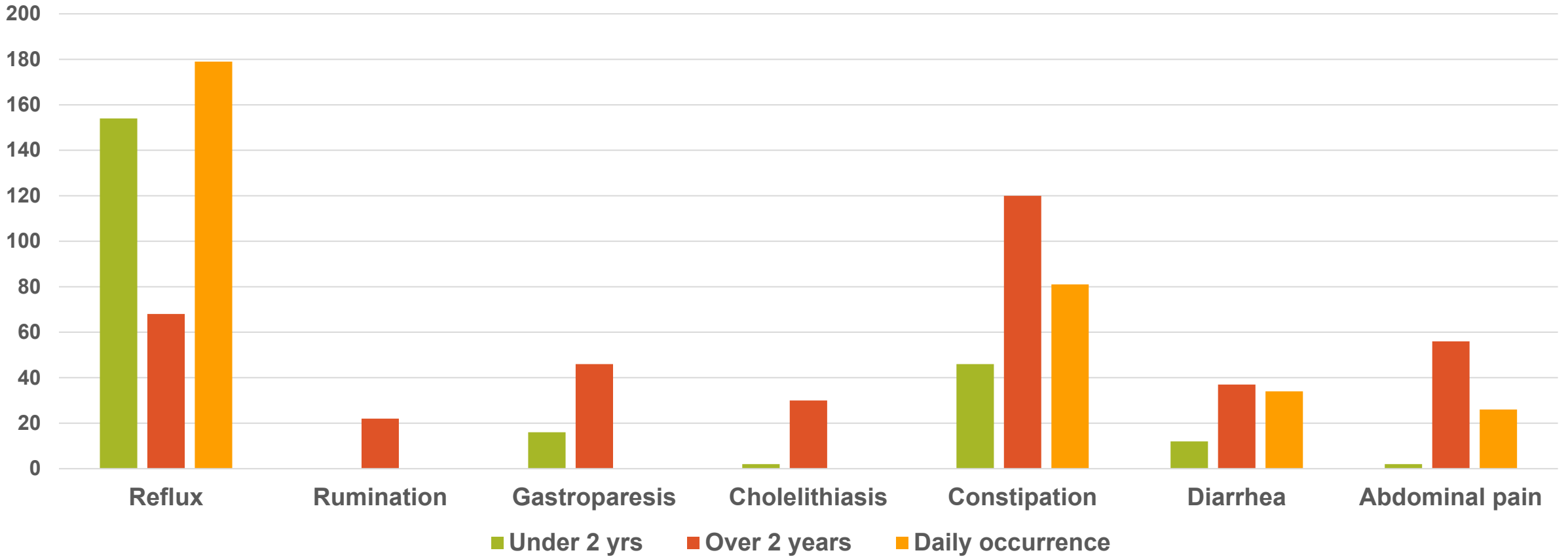
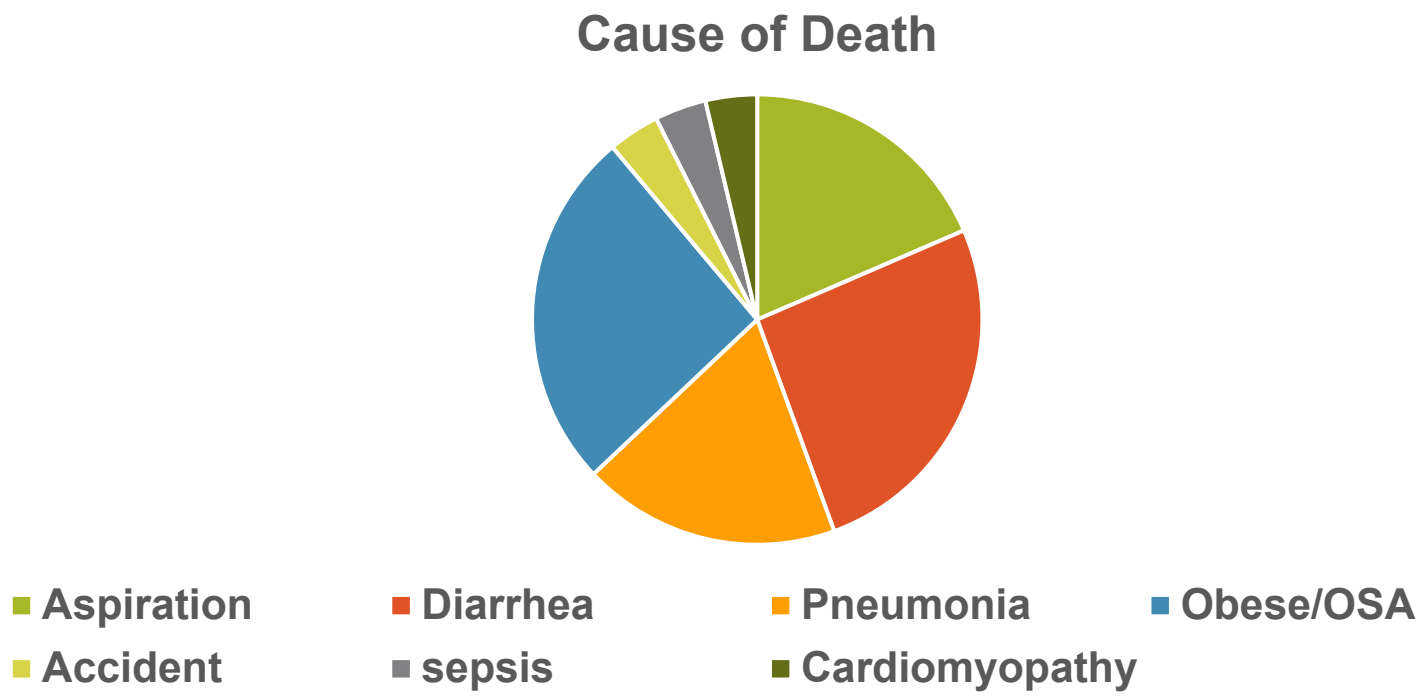
FPWR Registry 2019 : Frequency of Gastrointestinal Symptoms



Mortality in Children ≤ 5 years with Prader-Willi Syndrome: International Data



Pooled published data from Europe, Australia, Japan, US

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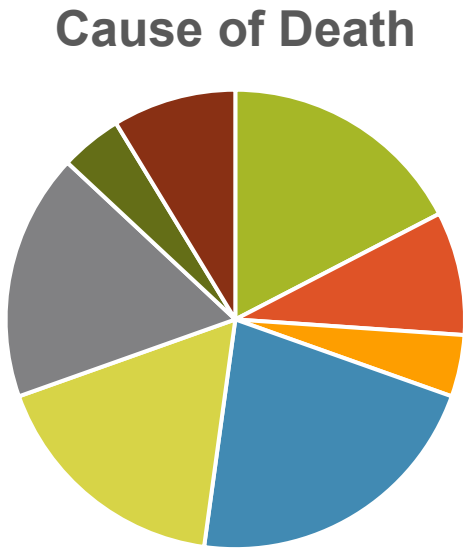
Mortality in Adults with Prader-Willi Syndrome: International Data



Obese/pneumonia
Accident
Unknown
Obese/OSA
Stroke/PE
Heart
Aspiration
GI

Pooled published data from Europe, Australia, Japan, US

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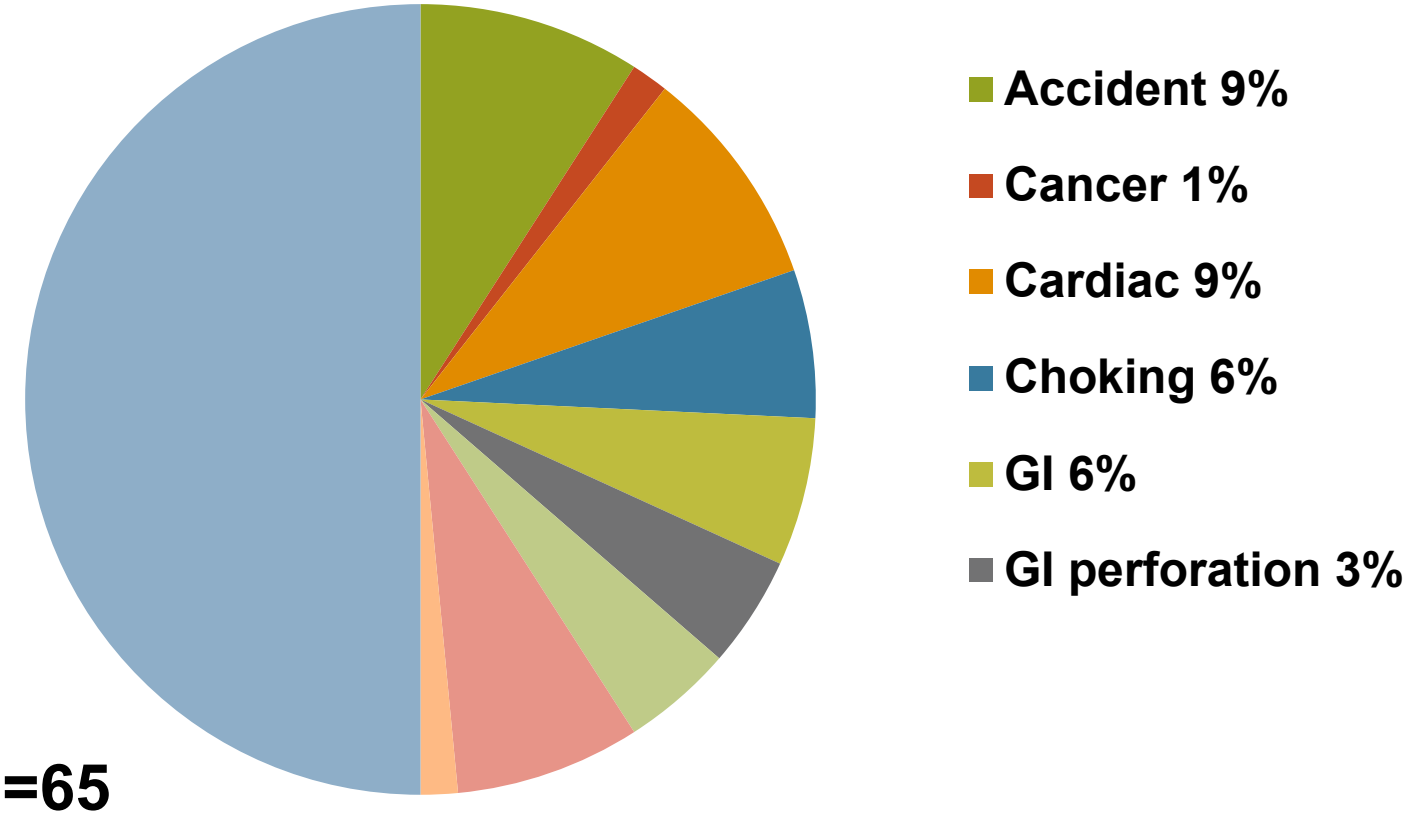
Pediatric Deaths: PWSA USA Data



N=65

Courtesy of Jim and Carolyn Loker and PWSA | USA

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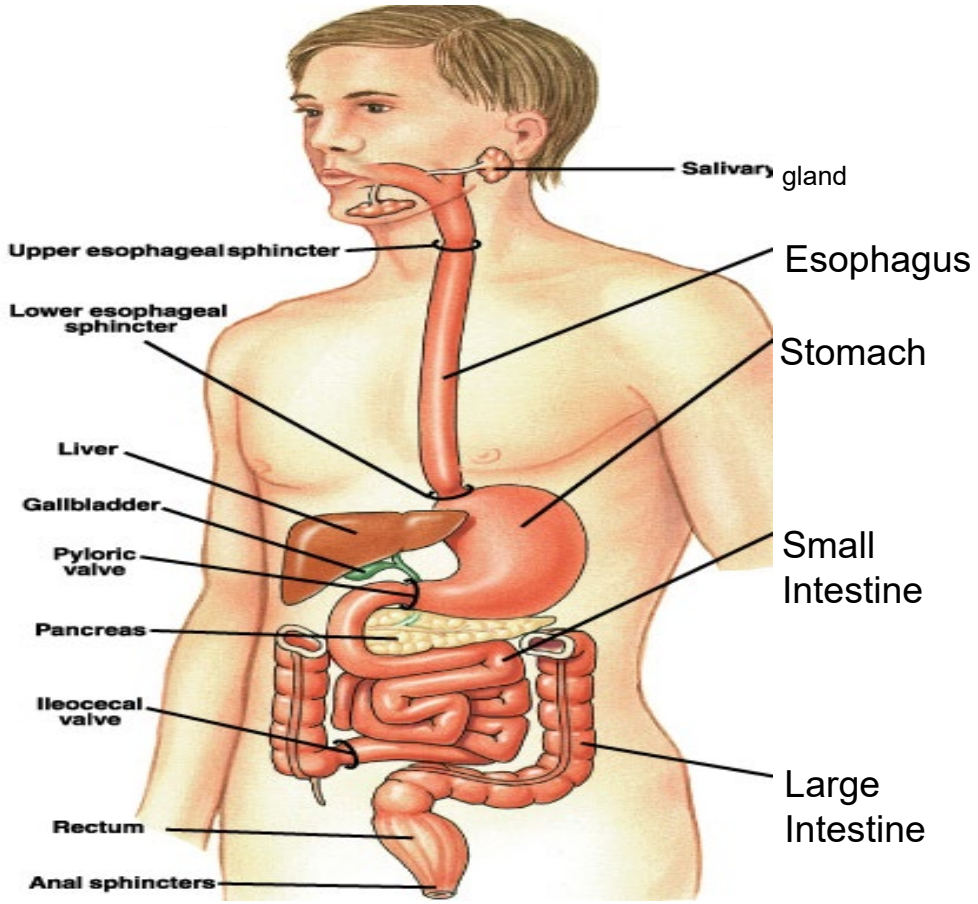
Overview of GI Anatomy



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Common Oral Issues

- Oromotor weakness
  - Hypotonia
  - Palatal abnormalities
- Dental abnormalities
  - Micrognathia (Small jaw)
  - Microdontia (small teeth), delayed eruption and hypoplastic (weak) enamel, dental crowding and erosions from rumination
- Salivary abnormalities (xerostomia-thick saliva)
  - Salivary flow is only 20-50% of normals *(PS Hart, Ann NY Acad Sci 1998 and Saeves et al Arch Oral Biol 2012)*

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Phases of Swallowing

- Oral Preparatory
- Oral
- Pharyngeal
- Esophageal

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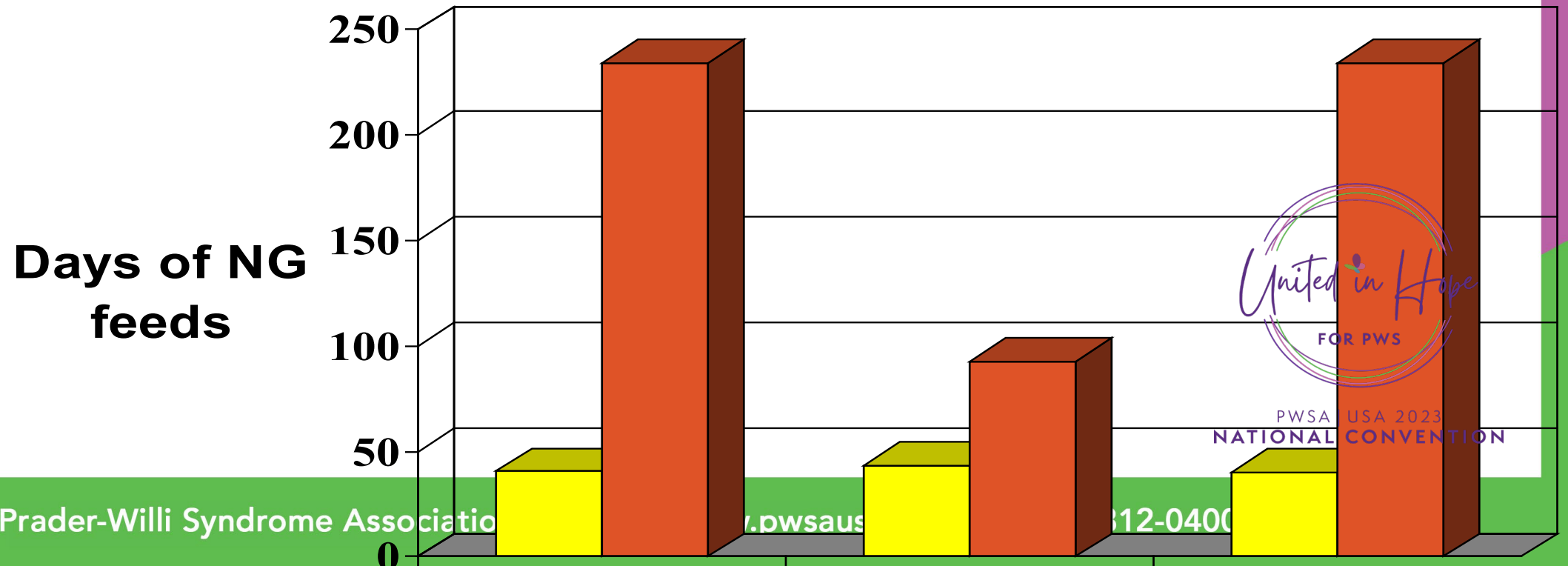
Feeding and Swallowing interventions : Nutritional Intervention and Oromotor Therapy on NG Feeds in TCH Infants



Choking/Prader-Willi Syndrome

- Review of data provided by families and collected through the PWSA bereavement program
  - 39% of families reported history of choking among the 52 families who completed questionnaires
  - Choking listed as cause of death in 12/152 patients (7.9%)
  - Average age 24 years (3-52 years)
  - 92% of patients were male

Stevenson, Scheimann et al.,AJMG 2008

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Choking/Prader-Willi Syndrome

- Factors predisposing to choking
  - Hyperphagia/Foraging
    - 25% of patients were food-stealing
  - Thick saliva
  - Weakness of pharyngeal muscles
  - Gastritis/Gastroesophageal Reflux
    - Gastritis noted in 38% at autopsy (3/8)

Stevenson, Scheimann et al.,AJMG 2008

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Swallowing Issues Among Adults and Children with Prader-Willi Syndrome

- Study (2014) funded by PWSAUSA by Gross, Gisser and Cherpes
  - Findings published in Dysphagia 10/2015
- Swallow studies in adults with PWS seen in Pittsburgh
- VFSS Swallow Studies using thin liquids and barium cookies in 30 adults with PWS
  - Significant, sometime substantial pharyngeal residue was present in 97% of subjects
  - Moderate to severe esophageal stasis was detected in 100% of participants
  - None could feel pharyngeal residue or esophageal stasis, regardless of the quantity

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Choking/Prader-Willi Syndrome

- Current Interventions
  - Heimlich maneuver training
  - Diet interventions
    - Supervised meals
    - Holiday monitoring
    - Meal pacing/Chewing prompts
    - Fluid intake with self regulation (straw)
  - Treatment of Gastritis/Gastroesophageal Reflux

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Choking/Prader-Willi Syndrome

- Potential Interventions- III
  - Treatment of gastritis/reflux
    - Conservative measures
      - Watch meal volume
      - Elevate head of bed
      - Minimize caffeine
      - Decreased fat

- Potential Interventions-III
  - Treatment of gastritis/reflux
    - Antacids
      - Tums/Calcium
    - Acid suppression
      - H_2 Receptor
      - Proton pump inhibitor

? Screen for Helicobacter pylori in stool

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Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on the surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. Entirely Liquid

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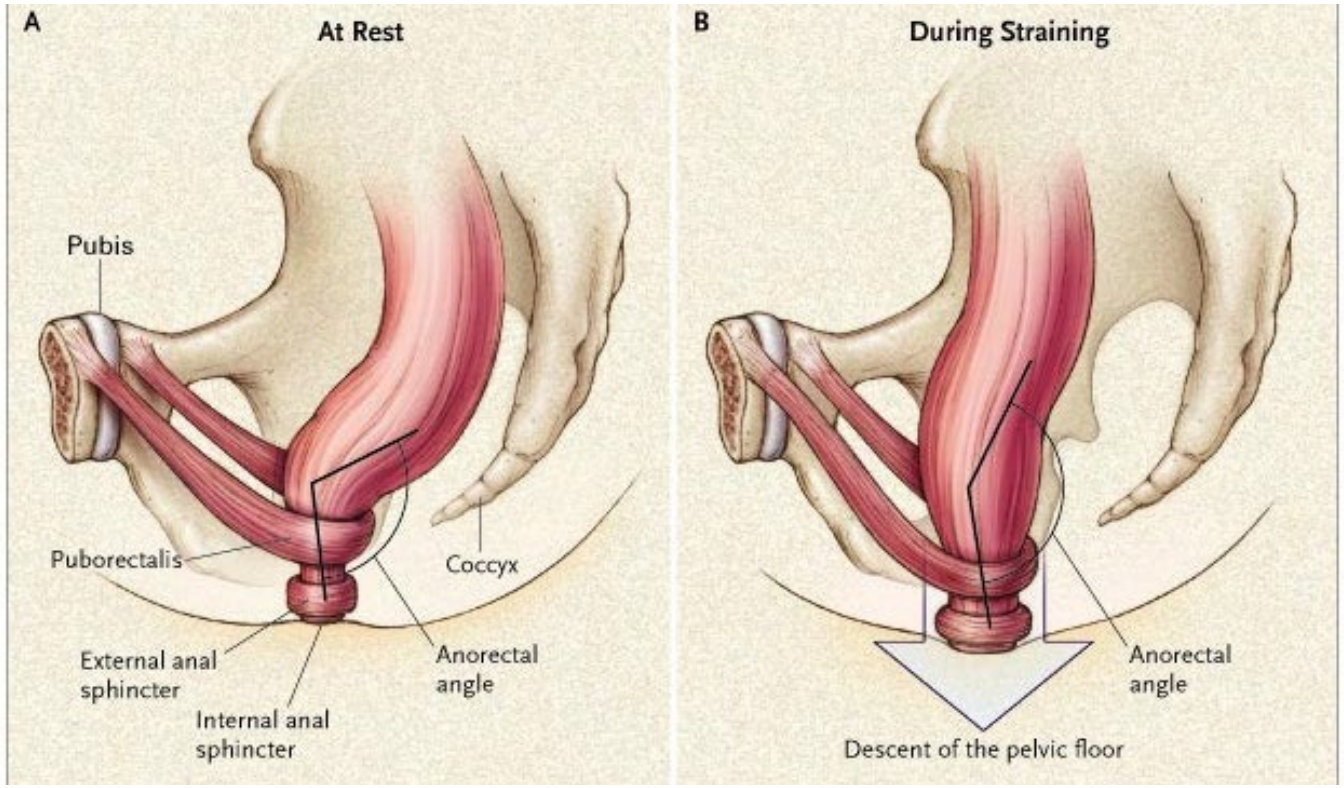
Anorectal Motility - Defecation



NASPGHAN motility teaching slide set

Image from http://msk-anatomy.com/

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Frequency of Constipation in Prader-Willi Syndrome

- 21 patients with PWS (median age 32 with median BMI 23.6) at Aarhus Center
  - Constipation history, rectal exam, rectal diameter by ultrasound, transit time
- 30 healthy volunteers (median age 26 and BMI 23.1) controls
- Symptoms
  - Infrequent stools (<3/week) 47%
  - Straining 37%
  - Hard Stools 32%
- No difference in rectal diameter or transit time between PWS and controls
- 29.3% of PWS adults through questionnaire study

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Kuhlmann et al, BMC Gastroenterology 2014; Equit Neurourology Urodynamics 2013

Constipating Conditions

- **Dysfunctional state**
  - Developmental (ADD, Cognitive)
  - Situational (Toilet/parent)
  - Psychogenic (Depression)
  - Constitutional (Genetic)
  - Reduced volume;drying
- **Metabolic/Endocrine**
  - Hypothyroid
  - Hypercalcemia
  - Lead
  - Diabetes mellitus
  - Hypopituitarism
- **Altered Anatomy**
  - Structural problem
    - (Position, Narrowing)
  - Acquired bowel stricture
  - Malrotation
  - Pelvic Mass
  - Aganglionosis (Hirschsprung's)
  - Abnormal abdominal muscles (prune belly)
  - Abnormal nerves (Spina Bifida)
  - Hypotonia (CP/Myopathy)
  - Connective Tissue Disorder (Scleroderma, Lupus)

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Treatment strategies for the preschool child

- For short duration stool withholding:
  - 1-2 initial cleansing enemas
  - Increase dietary fiber and softening agents
    - Milk of magnesia
    - Miralax
  - Goal is rectal emptying to allow gradual decrease in vault size with return of sensitivity

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Toilet seating- Not this

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Toilet seating- but this!

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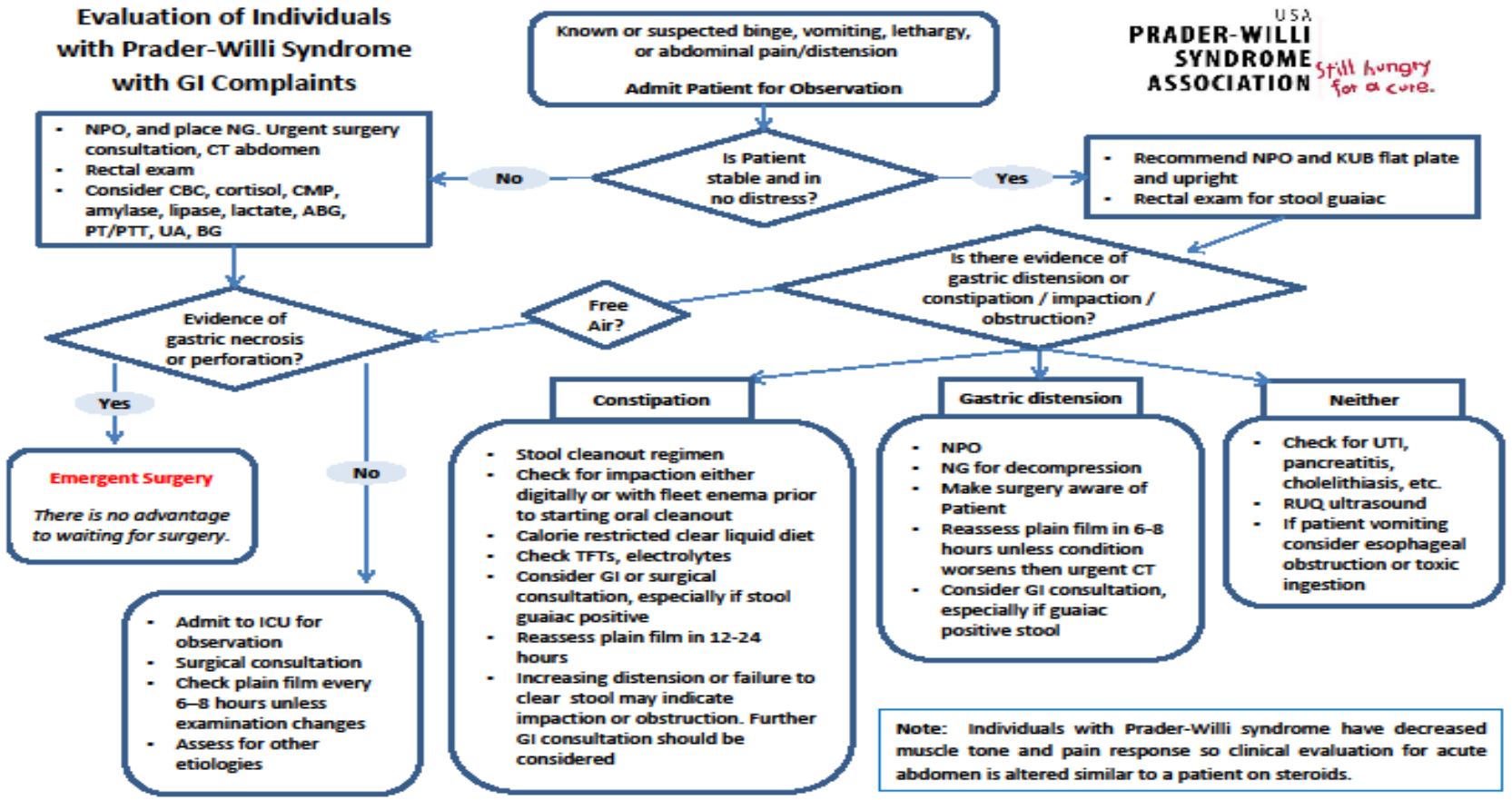
PWS GI Algorithm (Loker, Scheimann)



https://www.uptodate.com/contents/clinical-features-diagnosis-and-treatment-of-prader-willi-syndrome?csi=912ad77f-01f8-42ed-b533-8e2561b4b83f&source=contentShare

Management strategies for the school age child

- **Catharsis:**
  - Laxative- bisacodyl (5-10 mg) for 3-5 days or polyethylene glycol solution (Miralax/GoLytely)
  - Magnesium citrate

- **Maintenance**
  - Milk of Magnesia or Miralax
  - Toilet 5-10 minutes after meals with appropriate posture
  - Fiber rich diet plus water

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Interventions for Constipation

Flaxseed
-Adjunct
-EFA

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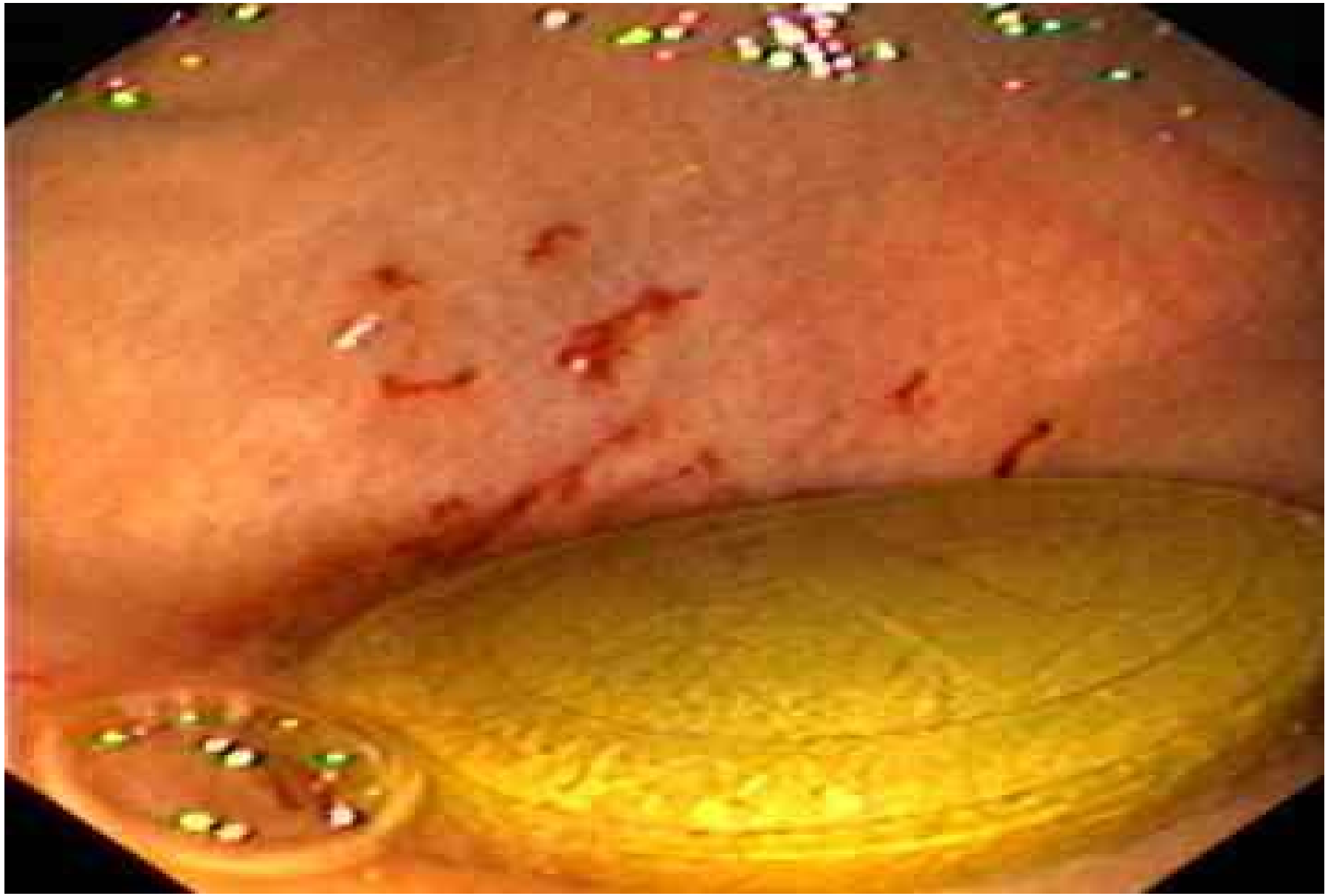

Coin lodged within the body of the stomach: from the Gastrolab Image Gallery

Treatment for Rectal Ulcer

- Relieve constipation and avoid straining during defecation
  - Consider stool softeners - titrate to keep stools soft
  - Decrease symptoms of pruritus ani from fecal bile acids
- Behavioral modification to decrease digging behavior
  - Supervised timed bathroom privileges
  - Reversed clothing to decrease anal access
  - Biofeedback/physical therapy to address toileting posture

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PWSA | USA Constipation Alert

- **Medical Alert on Constipation In Individuals with Prader-Willi Syndrome**
  - James Loker MD/CAB PWSAUSA
  - “Failure of standard methods to clear stool in a timely manner in the setting of pain, distension, decreased appetite warrants surgical or GI consultation.”

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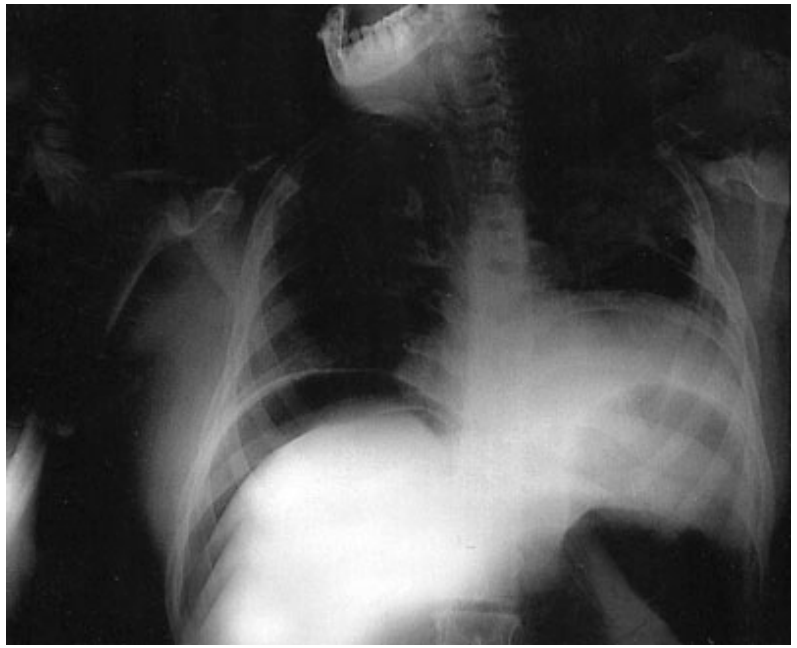
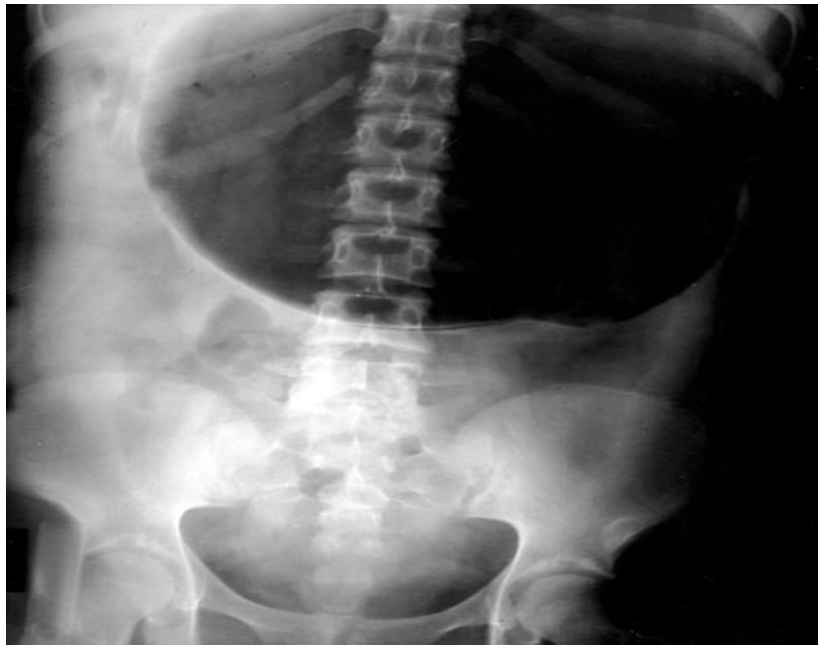
Gastric Dilation





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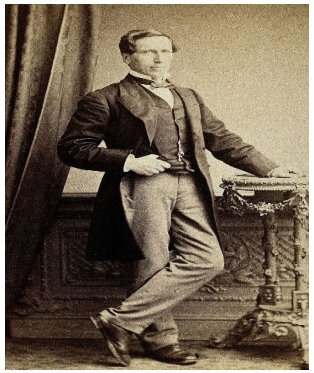
Gastric Dilation/Necrosis

- Severe acute gastric dilatation described by Simone-Emmanuel Duplay in 1883
- In dogs related to stretching then twisting of stomach along axis
- 1859 - Brinton suggested atony - inhibition of gastric motor nerves allowing progressive gastric distension
- Some models suggest feedback problem with solitary nucleus

Duplay,
wikipedia



William Brinton,
welcome images

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Gastric Dilation/Necrosis

- **Reported in anorexia and bulimia patients**
  - Undernourished patients complain of abdominal pain after meals
  - Attributed to significant binge eating
  - Possible role of bacteria producing gas and wall injury
  - Gastric wall becomes thin; vascular compromise
  - In some cases accompanied by pancreatitis
    - Pancreatitis resulted from severe dilatation

- **17 yo with Rett Syndrome presented with history of abdominal distension, vomiting and constipation and breathholding-hypotensive/cyanotic at presentation**
  - AXR with free Air with bloody ng lavage
  - Necrotic stomach at laparotomy with full thickness gastric necrosis
  - Etiology attributed to gastric atony and distension from air swallowing

Kim et al. Intl Med 2011; Abdu et al; Arch Surg 1987; Patocskai EJ et al, Eur J Surg 2002 ; Baldassarre et al Brain Dev 2006

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Gastric Dilation/Necrosis

- In dogs related to stretching then twisting of stomach along axis
- Previously reported in anorexia and bulimia patients
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Gastric Dilation/Necrosis

- Difficult to diagnosis
- High index of suspicion
- Clinical features include change in diet before development of abdominal distension and vomiting
- Abdominal films show large dilated stomach
- Treatment is gastric decompression and supportive care with careful monitoring for possible rupture

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Acute Gastric Dilatation with Gastric Necrosis in PWS

- Series of 6 women with vomiting and gastroenteritis developed rapidly progressive gastric dilatation followed by necrosis*
  - 2 Pediatric cases had spontaneous resolution
  - 1 patient died of sepsis
  - 3 patients had massive dilatation requiring gastrectomy in 2
- Another series of laparoscopic gastric banding reported one death in a patient with Prader-Willi Syndrome 45 days post procedure⁺

RH Wharton et al., Am J Med Genet 1997, 73: 437-41

⁺E Chelala et al., Surg Endo 1997, 268-71

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Gastric Rupture/Necrosis: Recent Data

- 4 patients out of 152 died from gastric rupture/necrosis; 3 additional suspected
  - Teen (BMI 22) binge eating on holiday followed by abdominal pain and vomiting
  - 2 Young adults (not obese) with abdominal pain and vomiting
  - Middle-aged obese adults with history of ulcer and gastritis
  - Child with abdominal pain and hematemesis

Stevenson D, Scheimann A, et al., JPGN

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Recent Case Report: Management of Recurrent Acute Gastric Dilatation in and Adult with PWS

- 36 yo male with PWS, BMI 30, controlled dietary intake in group home
- ER presentation with abdominal pain and vomiting after binge eat- CT with dilated stomach and free air- diagnostic laparoscopy negative. Treated with abx and ng tube HD 9

- 7 months later- abd pain, vomiting, resp distress after binge eating with acute gastric dilation and aspiration pneumonia- significant NG output. Had cardiac arrest and PE but survived
  - Subsequent EGD with residual food in stomach regurgitating to esophagus despite trials of neostigmine and metoclopramide
  - Had PEG placed with jtube extension to allow gastric venting and jejunal feedings (patient refused NG tube)

Mohammed AM and Dennis RJ. J Surg Case Rep 2016

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Diet Strategies for Gastroparesis

- Small frequent meals
- Watch fiber intake
- Prioritize protein in the diet
- Increase fluid in foods
- Chew foods well since stomach may not grind effectively
- Remain upright and move to help move food along

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Final Thoughts

Homaru "Omar" Cantu (1976-2015)

"The world is full of challenges, but with those come opportunity, and I am an opportunist.."

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Acknowledgements

- Collaborators
- Mentors
- Texas PWS Clinic Staff
- PWSAUSA, FPWR
- IPWSO
- Families of Children with PWS

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