Gastrointestinal Concerns in Rett Syndrome: What Do We Know in 2016?

Kathleen J. Motil, M.D., Ph.D.
USDA Children’s Nutrition Research Center
Baylor College of Medicine
Houston, TX 77030
Disclosures

- I am a Section Editor for Up-To-Date, Inc., an electronic textbook of medicine.
- I do not have any relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this presentation.
- I do not intend to discuss an unapproved or investigative use of a commercial product or device in my presentation.
From the variety of functional disturbances of the gastrointestinal tract, those of the motoric activity are especially important: cardiospasmus, pylorospasmus, nabelkoliken

“Neuropathie” corresponds to the syndrome of “sympathetic (autonomic) hypertonia”

Treatment always symptomatic; bucospan used for maximal spasmolytic effect without untoward side effects
“My daughter eats all of the time, but she doesn’t gain weight.”

“My daughter screams constantly. I know something is wrong.”

“My daughter’s stomach is full of air. It must hurt.”

“My daughter won’t go to the bathroom unless I give her something. I don’t want her to become addicted.”
Objectives

- Recognize problems potentially related to GI dysmotility in Rett syndrome
- Recognize “trigger” signs to call your physician
- Understand the rationale for selected GI tests
- Understand approaches to treat GI dysmotility in Rett syndrome
GI Problems in Rett Syndrome

- Feeding difficulty 81%
  - Chewing dysfunction 56%
  - Swallowing dysfunction 43%
- Gastrointestinal dysmotility 92%
  - Gastroesophageal reflux 38%
  - Delayed gastric emptying 14%
  - Biliary tract disease 3%
  - Gas bloating ?
- Constipation 80%

Enteric Nervous System

- MeCP2 found throughout GI tract
- MeCP2 found specifically in enteric nervous tissue
- MeCP2 found throughout development of GI tract
- GI dysmotility in Rett syndrome mediated directly through ENS dysfunction because of abnormal MECP2 (protein)

Wahba G, Neurogastroenterol Motil, 2015
Chewing/Swallowing Dysfunction

- **Definition - Chewing difficulty**
  - Poor mastication
  - Poor tongue lateralization
  - Poor food propulsion

- **Definition - Swallowing difficulty**
  - Pooling of liquids and solids in valleculae and pyriform sinuses
  - Laryngeal penetration of liquids
  - Tracheal aspiration of liquids
Why Treat Chew/Swallow Difficulty?

- Control symptoms
  - Hunger, feeding fatigue
- Prevent complications
  - Malnutrition, aspiration pneumonia
Parental Triggers

- Prolonged feeding >30 min/meal
- Coughing, choking, gagging with liquids and soft foods
- Feeding refusal
- Weight loss, poor weight gain due to inadequate dietary intake to meet growth needs
  - Worse during adolescence
  - Decreased body fat
  - Not related to repetitive movements
  - No malabsorption
Diagnostic Tests

- OT/Speech feeding assessment
- Swallowing function study
  - Speech pathologist
  - Thin, thick liquids; soft, pureed foods; cookie
- BMI “gold standard” for assessing nutritional status
  - Proportion of weight to height
  - Normal: 25-50th %ile (young), 10-25th %ile (older)
  - Trigger: <5th %ile
Treatment Approach (Chew/Swallow)

- Limited strategies
- OT/Speech therapy for oral skills
- No evidence of benefit with use of stimulators
Treatment Approach (Feeding Refusal)

- **Alternative feeding methods**
  - Oral formula supplements
  - Enteral feeding tubes or buttons
    - Nasogastric (short term)
    - Gastrostomy, gastrojejunostomy

- **Indications for alternative feeding methods**
  - BMI <5th %ile, progressive decline > 6 mo
  - Chewing/swallowing dysfunction
    - Aspiration pneumonia
  - Parental request
    - Feeding refusal, medication/fluid administration
Gastroesophageal Reflux

- Definition - involuntary passage of stomach contents backwards into esophagus and mouth
  - Acid, digestive enzymes, bile
- Caused by poor motility of esophagus, LES, stomach
  - Dietary, genetic, structural, hormonal, infectious, neurological, environmental factors
Why Treat GER?

- Control symptoms
  - Feels uncomfortable, tastes bad, interferes with eating and breathing
- Prevent complications
  - Esophagitis, ulcers, stricture, aspiration pneumonia, Barrett’s esophagus
Parental Triggers

- Irritability
- Screaming
- Nighttime awakening
- Vomiting
- Regurgitation
- Wet, dry burps
- Feeding refusal
- Wheezing
- Aspiration
Diagnostic Tests

- Medical history
- UGI series
- Impedance-pH probe monitoring
- Upper endoscopy/biopsy
- Gastric emptying scan
Treatment Approach

- **Diet**
  - Monitor spicy food, caffeine, chocolate, citrus consumption

- **Position**
  - Upright 30 minutes after eating
  - Elevate head of bed 45°

- **Medications**
  - Antacids (magnesium)
  - H₂-receptor blockers (ranitidine, famotidine)
  - Proton pump inhibitors (omeprazole, lansoprazole, esomeprazole)
  - Prokinetics (bethanechol, erythromycin)

- **Surgery (fundoplication)**
Biliary Tract Disease

- Definition
  - Cholecystitis (inflammation)
  - Cholelithiasis (gallstones)
  - Biliary dyskinesia (dysmotility)
- Avoid complications including hepatitis and pancreatitis
- Frequency similar to unaffected children
  - Found primarily in older females
- Usual symptom abdominal pain
- Diagnostic tests AUS, HIDA scan
- Treatment surgery
Gas Bloating

- Definition - gastrointestinal gas trapping, abdominal distention, worse as day progresses, tympanic drum sound
- Caused by air swallowing from teeth grinding, breath holding, hyperventilation
- Caused by malabsorption (lactose intolerance, celiac disease), infection (giardiasis), small bowel bacterial overgrowth, constipation
Why Treat Gas Bloating?

- **Control symptoms**
  - Discomfort, abdominal pain, burping, flatulence
  - Gas derived from N\textsubscript{2} in air or CH\textsubscript{4}, CO\textsubscript{2}, and H\textsubscript{2} from bacterial digestion of↑ CHO beverages, sorbitol (artificial sweetener; pears, prunes), or legumes (stachyose, raffinose)

- **Prevent complications**
  - Pneumoperitoneum (rare)
Parental Triggers

- Poor appetite
- Hyperventilation
- Air swallowing
- Eructation (burping)
- Abdominal distention
- Irritability
- Abdominal pain
- Flatulence (gas)
- Diarrhea
Diagnostic Tests

- Medical history, exam
- Lab tests
  - Blood (celiac panel)
  - Stool (giardia, H pylori)
- Upper endoscopy/biopsy
- Hydrogen Breath Tests
  - Lactulose
  - Lactose
- Abdominal x-ray
Treatment Approach

- **Diet**
  - Reduce CHO or sorbitol consumption
  - Modify dairy (lactose) with lactase enzyme product
  - Initiate gluten-free diet if positive for celiac disease
- **Medications**
  - Anti-gas (simethicone)
  - Antibiotics (metronidazole)
  - Laxatives (polyethylene glycol, milk of magnesia, senna)
Constipation

- **Definition** - difficulty with defecation, causes distress, duration > 2 weeks
  - Bowel movements fewer than two times per week
  - Stools hard, small pebble or large ball size
- **Causes** - functional, structural (anal stenosis), neuromuscular (Hirschsprung disease, muscular dystrophy), endocrine (hypothyroidism), drug-induced (codeine, phenytoin)
Why Treat Constipation?

- Control symptoms
  - Abdominal, rectal or anal pain, poor appetite, diarrhea (overflow incontinence), bleeding
- Prevent complications
  - Fissure, impaction, encopresis, volvulus (obstruction)
Parental Triggers

- Frequency of bowel movements fewer than two times per week
- Change in consistency of stools (hard, watery)
- Blood on stool
- Abdominal distention, discomfort, pain
- Flatulence
- Urinary tract infection
- Feeding refusal, vomiting
Diagnostic Tests

- Medical history
- Abdominal, rectal exam
- Abdominal x-ray
- Sitz marker study
- Barium enema
- Rectal manometry
- Rectal biopsy
- Colonoscopy
Treatment Approach

- **Diet**
  - Fiber (fruits, vegetables, cereals)
  - Sorbitol (prunes, pears)
  - Probiotics

- **Medications (“softeners, pushers”)**
  - Laxatives (polyethylene glycol, lactulose, mineral oil, milk of magnesia, sennosides)
  - Chloride channel (lubiprostone, age $\geq 18$ y)
  - Suppositories (glycerin, bisacodyl)
  - Enema, cecal button (disimpact rectum)
  - Beware of herbals

- **Physical activity**
  - Walking, standing, physical therapy
Gastrointestinal Crises

- Severely ill, abdominal pain, abdominal distention, vomiting
- Surgical problems (stomach, intestines)
  - Volvulus (twisting)
  - Intussusception (sliding)
  - Perforation (hole)
- Cause of abdominal crises unknown
  - Air swallowing alone does not result in intestinal perforation
  - Chronic constipation, megacolon may increase risk for obstruction
- Volvulus, intussusception not unique to Rett Syndrome
GI problems (chewing/swallowing difficulties, feeding refusal, gastroesophageal reflux, delayed gastric emptying, gas bloating, constipation) commonly found in RTT.

- GI problems caused by dysmotility of GI tract, presumably due to abnormalities in enteric nervous system.
- Any symptom that causes parental concern should be evaluated by a physician.
- Treatment strategies should be discussed with a physician to improve symptoms, avoid complications, improve quality of life.

Any symptom that causes parental concern should be evaluated by a physician.

Treatment strategies should be discussed with a physician to improve symptoms, avoid complications, improve quality of life.